



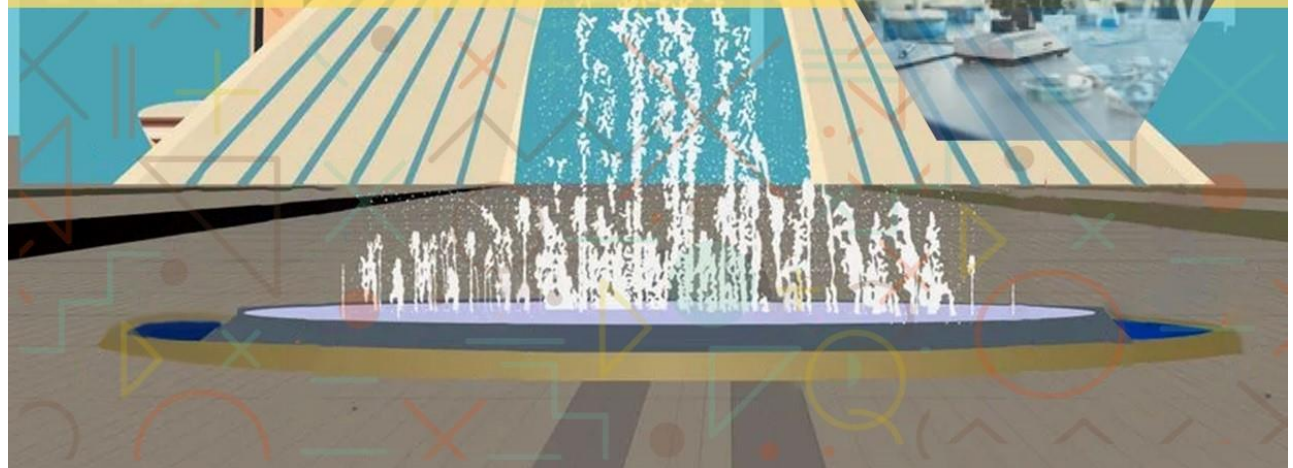
Tehran

Iran

15th International Congress of Laboratory and Clinic

25-28 January, 2024

Children's Medical Center Hospital, Tehran, Iran.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



In the Name of God

Book of Abstracts

The 15th International Congress of Medical Laboratory & Clinic

Venue:
Children's Medical Center
Tehran University of Medical Sciences
Tehran, Iran.
January 25-28, 2024

Congress Website:
<https://isacl.congressapp.ir>

Congress Channel:
https://www.aparat.com/isacl_congress/videos

Download Available at:
<https://journals.sbmu.ac.ir/index.php/medlab/15th>





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In the Name of God

As you know, holding the Laboratory and Clinic Congresses as a strategic measure with the presence of elites, thinkers and senior professors of the country's clinical and medical laboratory community over the past two decades has been able to play an important role in bringing these two great and important groups in the country's health system closer together and coordinate them better, and has had useful results. In line with this, so far this Society has held fourteen Laboratory and Clinic Congresses and God willing, it will hold the 15th Congress from January 26th to 29th, 2024(1402) at the Children's Medical Center Hospital of Tehran University of Medical Sciences.

God willing, in addition to covering all areas of laboratory science, this year's congress will be held with the theme of "The Role of the Laboratory in the Diagnosis and Follow-up of Children's and Infants' Diseases" through panels by prominent clinical and medical laboratory professors of the country and the participation of member associations of the Society and relevant clinical associations.

In previous conferences, domestic and foreign experts have presented their valuable experiences and opinions on the topics discussed and examined each topic from clinical and laboratory perspectives and analyzed them. As such, panel sessions have been strongly welcomed by participants. In fact, by holding such conferences, the connection between physicians and laboratory specialists has been strengthened and each group becomes more familiar than ever with the challenges and problems of the other group. Obviously, this synergy will be very useful in finding new and scientific solutions.

It is hoped that this year, in addition to examining the educational challenges and problems of laboratory sciences, issues related to clinical matters, especially children's and infants' diseases, and holding scientific workshops, the complete satisfaction of the participants can be achieved. Finally, I invite all professors, experts, researchers, laboratory fellows, technicians, experts and students of various levels and fields of laboratory sciences as well as physicians, clinical professors and specialists across the country to attend this scientific event and if possible, send their valuable abstracts, to provide the grounds for an ever more magnificent holding of this diverse and extensive congress.

Prof. Mohammad Vodjani

President of "Iranian Scientific Association of Clinical Laboratory"
& Member of the Policy Council of the Congress





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The indispensable role of the laboratory in the process of diagnosing and controlling diseases and paying attention to its preventive approach has brought new dimensions to us with the development of science and technology day by day. The credible global scientific efforts and our specialist clinical and laboratory colleagues in the farthest parts of the Islamic homeland confirm the need to seriously address the borders of knowledge in this field and create suitable conditions for scholars and scientists of various laboratory and clinical fields to present joint clinical and laboratory research and achievements. Now, after the enthusiastic and successful holding of fourteen rounds of the Laboratory Congress with the presence of university professors and scientific figures of the country, the 15th International Laboratory and Clinic Congress with the approach of the role of the laboratory in the diagnosis and follow-up of children's and infants' diseases will be held from January 26th to 29th, 2024. In this period, the latest research activities and findings will be presented in order to find new solutions for effective and efficient interaction between the laboratory and the clinic.

With thanks
Dr. Reza Shervin Badv
President of The Congress
& Member of the Policy Council of the Congress





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In the name of the one who's name is on all creatures

To our respectful and dear Professors, Medical Practitioners and staffs, researchers and young talented students. Let me announce that “Fifteen International Congress of Laboratory and Clinics” on the main topic of “Role of Laboratory on the Clinical Diagnosis of Children Disease” will be held on 25th to 28th January 2024 in Hospital Center of Children Diseases, the excellent center affiliated to Tehran University of Medical Sciences. It is worth to let you know that during last 5 years with commencement of a 2 years complimentary graduate program which allows the Ph.D. holders of few clinical graduates to hold the responsibility of laboratories, today we have almost 80 excellent graduates throughout the country holding the responsibility of professional clinical laboratories in the public hospitals as well as some private laboratories. It is also a great pleasure to announce that more than 40 Ph.D. holders are presently going through their complimentary training courses. Very soon the responsibility to manage number of laboratories throughout the country would be entrusted to such an excellent graduate. The Scientific Association of Laboratory Experts in Iran have planned to observe several extra programs such as congresses, workshops and other types of gatherings in order to introduce the field of common interests in between clinics and laboratory.

I would request all colleagues to participate in this event, support us in bringing up a fruitful gathering and send their abstract to us through the web site at <http://isacl.congressapp.ir>.

As mentioned, this congress aims to mention the scientific achievements, considering problems and providing sustainable solutions for the actual practice in hospitals with laboratory findings provided by private and public labs. We also try to project the importance of relationship between the laboratory findings and clinical picture of the sick children considering the experiences and trying to find better ways of cooperation. Last but perhaps not the least, we shall discuss better techniques of diagnosis, their production inside the country for the betterment of treatment and admiration of the clients.

We shall eagerly encourage and wait for the generous participations of the colleagues in such important event.

With great thanks and deep gratitude

Prof. Mohammad Javad Rasaee

Scientific Secretary

& Member of the Policy Council of the Congress

Message: <https://www.aparat.com/v/8TAWm>





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The continuity of knowledge and its ever-increasing progress have made the crossing of borders inevitable in the exchange of knowledge. Every effort to create synergy between different aspects of health and medical knowledge is the necessity of today's scientific society. The two groups of the children's clinic and the laboratory, looking at the historical reflection between them, have decided to hold this grand event. Innovation and generosity in sharing knowledge is the mental base of all the organizers of this scientific event. I sincerely invite all my friends and colleagues to join us in this gathering.

Dr. Ehsan Aghaei-Moghadam
Clinical Secretary
& Member of the Policy Council of the Congress

Message: <https://www.aparat.com/v/BWO49>





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Prof. Fatemeh Fallah; PhD, Microbiologist
Member of the Policy Council of the Congress



Prof. Hossein Keshavarz Valian; PhD, Parasitologist
Member of the Policy Council of the Congress



Mr. Hadi Ghazanfari; PhD Candidate, Immunologist
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The 15th International Congress of Medical Laboratory & Clinic



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The Schedule of Workshops & Scientific Panels

**“The Role of The Laboratory in The Diagnosis and Follow-Up of
Diseases in Children and Newborns”**





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Congress Workshops

Row	Title	Lecturer	Date	Time
1	Tips and interpretation of routine laboratory tests	Dr. Majid Mokhtari	2024/01/26	8-12 AM
2	Laboratory updates in the diagnosis of MS	Dr. Mohammad Sajad Emami Al-Agha	2024/01/28	8-10 AM
3	Vitamin B12 and folate	Dr. Mohammadreza Bakhtiari	2024/01/28	10-12 AM





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Oral presentation program Hall D (Dr. Gharib Hall)

Day	Title of the Panel
Thursday (2024/01/25)	Immunology 9:00-10:30 (OI-1...OI-12)
	Genetics 10:30-12:00 (OG-1...OG-11)
	Biochemistry 13:00-14:30 (OBi-1...OBi-13) 14:30-16:00 (OBi-14-OBi-26)
	Artificial intelligence 9:00-10:00 (OAI-1...OAI-5)
Friday (2024/01/26)	Hematology & Blood banking 10:30-12:00 (OH-1...O-13)
	Virology 13:00-14:30 (OV-1...OV-9)
	Mycology 14:30-16:00 (OM-1...OM-6)
Saturday (2024/01/27)	Bacteriology 9:00-11:00 (OBi-1...OBi-14)
	Parasitology 13:00-14:30 (OP-1...OP-6)





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Thursday (2024/01/25): Hall A

Time	Program
8:00-9:00	Opening ceremony
Panel 1: Clinical and paraclinical features of heart failure	
9:00-10:30	Coordinator: Dr. Ehsan Aghaei Moghadam Members: Dr. Ali Akbar Zeinaloo, Dr. Mohammad Reza Sabri, Dr. Marjan Hajahmadipoor, Dr. Fatemeh Zamani, Dr. Ali Rashidi Nezhad
10:30-10:45	Reception
Panel 2: Neonatal cholestasis	
10:45-12:15	Coordinator: Dr. Kayvan Mirnia Members: Dr. Farhad Abolhasan Chobdar, Dr. Ziba Majidi
12:15-13:00	Praying and lunch
Panel 3: Trials related to hematopoietic stem cell transplantation (HSCT) in children	
13:00-14:30	Coordinator: Dr. Amir Ali Hamidieh Members: Dr. Behrouz Nikbin, Dr. Maryam Behfar, Dr. Leila Jafari, Dr. Hamid Farajifard, Dr. Rashin Mohseni
Panel 4: in vivo and in vitro diagnostic tests for allergic disease	
14:30-16:00	Coordinator: Dr. Masoud Movahedi Members: Dr. Parisa Ashournia, Dr. Raheleh Shokouhi Shoormasti, Dr. Alireza Shafiei Esfidvajani, Dr. Marzieh Asgharian
Panel 5: Medical genetics services: ensuring the health of the child (Hall B)	
14:30-16:00	Coordinator: Dr. Seyed Mohammad Akrami Members: Dr. Hamidreza Khorram Khorshid, Dr. Soodeh Ghafourifard, Dr. Majid Mojarrad, Dr. Mohammad Hossein Modarressi, Dr. Mohammad Hasan Sheikha
Panel 6: Rotavirus Infection in Children (Hall C)	
14:30-16:00	Coordinator: Dr. Hoorieh Soleimanjahi Members: Dr. Setareh Mamishi Khanlagh, Dr. Seyed Mohammad Hadi Razavi Nikoo, Dr. Ali Teimoori, Dr. Alireza Shafiei Esfidvajani
16:00-16:15	Reception
Panel 7: Advancements in Genetic and Laboratory Diagnostics for Unraveling Primary Immunodeficiency Diseases	
16:15-17:45	Coordinator: Dr. Mohammad Reza Fazlollahi Members: Dr. Anahita Razaghian, Dr. Maryam Nourizadeh, Dr. Zahra Alizadeh, Dr. Mansoureh Shariat
Panel 8: Successful experiences of pediatric disease laboratory diagnosis in provincial centers (Hall B)	
16:15-17:45	Coordinator: Dr. Fatemeh Fallah Members: Dr. Abbas Rezaei, Dr. Mohammad Hossein Feiz Haddad, Dr. Hossein Ali Khazaei, Dr. Amir Bairami Kuzehkhanan
Panel 9: Congenital CMV (Hall C)	
16:15-17:45	Coordinator: Dr. Alijan Tabarraei Members: Dr. Hamid Eshaghi, Dr. Kayvan Mirnia
18:00-20:00	ISACL Provincial Network Meeting





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Friday (2024/01/26): Hall A

Time	Program
8:30-9:00	Title: Applications of artificial intelligence in medicine Keynote speaker: Dr. Payman Salamati
9:00-10:30	Panel 1: Diagnostic challenges of pediatric digestive disorders Coordinator: Dr. Pejman Rohani Members: Dr. Hosein Alimadadi, Dr. Maryam Sotoudeh Anvari, Dr. Fatemeh Mahjoub, Dr. Moeinadin Safavi
10:30-10:45	Reception
10:45-12:15	Panel 2: Principles in laboratory and clinical challenges for the diagnosis of congenital adrenal hyperplasia (CAH) Coordinator: Dr. Ali Rabbani Members: Dr. Reza Tavakolizadeh, Dr. Maryam Razavi, Dr. Mohammad Hossein Sanati, Dr. Davoud Amirkashani
12:15-13:00	Praying and lunch
13:00-14:30	Panel 3: Hematology-oncology: diagnostic challenges in hemophagocytic lymphohistiocytosis (HLH) Coordinator: Dr. Farzad Kompani Members: Dr. Alireza Biglari, Dr. Parisa Ashournia, Dr. Reza Shiari, Dr. Nader Momtazmanesh, Dr. Tahereh Rostami, Dr. Azadeh Kiumarsi, Dr. Fereshteh Ameli
14:30-16:00	Panel 4: Applications of artificial intelligence in laboratory and clinical diagnosis Coordinator: Dr. Mohammad Javad Gharavi Members: Dr. Hossein Riazi, Dr. Zeinab Barzegar, Dr. Abdolreza Esmailzadeh, Dr. Hossein Ahmadvand, Dr. Azadeh Fakhrzadeh
14:30-16:00	Panel 5: New approaches in vaccine development and vaccination (Hall B) Coordinator: Dr. Pejvak Khaki Members: Dr. Fereshteh Shahcheraghi, Dr. Majid Tebianian, Dr. Babak Pourakbari, Dr. Jafar Amani, Dr. Esmail Behmard
14:30-16:00	Panel 6: Pediatric respiratory syncytial (RSV) infection (Hall C) Coordinator: Dr. Vahid Salimi Members: Dr. Masoumeh Ghasempour Alamdari, Dr. vahid khoddami, Dr. Alireza Tahamtan, Dr. Ashraf Mohammadi, Dr. Talat Mokhtari Azad
16:00-16:15	Reception
16:15-17:45	Panel 7: Laboratory evaluation checklist: tips and challenges Coordinator: Dr. Hamidreza Joshaghani Members: Dr. Azam Karkhaneh, Dr. Ali Maleki, Dr. Farshid Noorbakhsh, Dr. Reza Ghotaslou, Dr. Shaban Alizadeh, Dr. Satar Gorgani Firuzjaee
16:15-17:45	Panel 8: Laboratory and clinical relationship for the management of invasive fungal infections in the paediatric and neonatal population (Hall B) Coordinator: Dr. Sadegh Khodavaisy Members: Dr. Roshanak Daei Ghazvini, Dr. Hossein Dalili, Dr. Kazem Ahmadikia, Dr. Hassan Vahidnezhad
16:15-17:45	Panel 9: HIV and HTLV: before and after birth (Hall C) Coordinator: Dr. Mehdi Norouzi Members: Dr. Sayed Hamidreza Mozhgani, Dr. Farah Bokharaei-Salim, Dr. Ladan Abbasian, Dr. Mohammad Reza Hedayati-Moghaddam
18:00-20:00	Laboratory Sciences Fellowship Meeting





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Saturday (2024/01/27): Hall A

Time	Program
8:00-8:30	Title: Achievements of Royan Research Institute in 35 years of activity and future plans Keynote speaker: Dr. Massoud Vosough
8:30-9	Title: Green management of hospitals and clinical diagnosis laboratories Keynote speaker: Dr. Massoumeh Ebtekar
9:00-10:30	Panel 1: Neuroimmunology Coordinator: Dr. Morteza Heidari Members: Dr. Mahmoudreza Ashrafi, Dr. Reza Shervin Badv, Dr. Mahmood Mohamadi, Dr. Seyed Alireza Mesbah-Namin, Dr. Farshid Noorbakhsh
10:30-10:45	Reception
10:45-12:15	Panel 2: Prevention and treatment of infection in transplant candidates Coordinator: Dr. Setareh Mamishi Khanlagh Members: Dr. Mahmoud Khodabandeh, Dr. Mohamad Reza Abdosalehi, Dr. Mohsen Jafari, Dr. Amir Ali Hamidieh, Dr. Ghazal Shariatpanahi
12:15-13:00	Praying and lunch
13:00-14:30	Panel 3: diagnostic challenges of pediatric metabolic disorders Coordinator: Dr. Farzaneh Abbasi Members: Dr. Ali Tale, Dr. Saeideh Abdollahpour, Dr. Reihaneh Mohsenipour, Dr. Seyedeh Zahra Bathaie, Dr. Saeid Talebi
14:30-16:00	Panel 4: Laboratory challenges in implementing new methods Coordinator: Dr. Seyed Hossein Fatemi Members: Dr. Mohammad Javad Gharavi, Dr. Hossein Keyvani, Dr. Hamidreza Joshaghani, Dr. Ali Mohebbi
14:30-16:00	Panel 5: Pediatric parasitic infections with emphasis on diagnosis and treatment in Iran (Hall B) Coordinator: Dr. Hossein keshavarz Valian Members: Dr. Mostafa Rezaiean, Dr. Seyed Mahmoud Sadjjadi, Dr. Mahdi Mohebbali, Dr. Gholamreza Mowlavi Vardanjani, Dr. Ali Haghighi
14:30-16:00	Panel 6: Ethics and legal issues in laboratory practice (Hall C) Coordinator: Dr. Hossein Mozdarani Members: Dr. Roya Rashid Pouraie, Dr. Mohammad Nader Sharifi, Dr. Shahriar Mousavinejad, Dr. Reza Omani Samani
16:00-16:15	Reception
16:15-17:45	Panel 7: Successful experiences in the production of knowledge-based products in the field of clinical laboratories Coordinator: Dr. Mohamad Javad Rasae Members: Dr. Fatemeh Nafian, Dr. Alireza Farasat, Dr. Vahid Asgary
16:15-17:45	Panel 8: Successful experiences in laboratory management of public hospitals (Hall B) Coordinator: Dr. Shaban Alizadeh Members: Dr. Mahdi Aminian, Dr. Mohammad Hasan Namaei, Dr. Habib Zeighami, Dr. Mahdi Adalati
16:15-17:45	Panel 9: Accepting the responsibility for the laboratories of the health department in universities of medical sciences and improving the level of health services (Hall C) Coordinator: Dr. Seyed Hamidreza Monavari Members: Dr. Seyed Jalal Kiani, Dr. Tahereh Donyavi, Dr. Shohreh Shahm Mahmoodi Sadeghi





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Sunday (2024/01/28): Hall A

Time	Program
8:00-8:30	Title: The increasing importance of the molecular laboratory diagnostics in pediatrics: from research to clinical practice Keynote speaker: Dr. Alireza Ranjbar
8:30-9:00	Title: Personalized medicine: From lab to clinic Keynote speaker: Dr. Mohsen Azimi-Nezhad Panel 1: Transfusion of Blood and Blood Products challenges from Lab to clinic
9:00-10:30	Coordinator: Dr. Maryam Sotoudeh Anvari Members: Dr. Elmira Hajiesmaeil Memar, Dr. Seyed Mohammad Kazem Nourbakhsh, Dr. Farideh Moussavi, Dr. Azita Chegini, Dr. Peyman Eshghi
10:30-10:45	Reception
10:45-12:15	Panel 2: Investigation of clinical and laboratory interpretation of autoimmune tests in rheumatology Coordinator: Dr. Vahid Ziaee Members: Dr. Fatemeh Fereshteh Mehregan, Dr. Samaneh Salarvand, Dr. Alireza Abdollahi, Dr. Seyed Reza Najafizadeh, Dr. Raheleh Assari
12:15-13:00	Closing Ceremony





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Poster (mini-oral) Presentation Program

Day	Title of the panel
Thursday (2024/01/25)	Biochemistry (Hall B) PBi-1...PBi-100 (9:00-12:00) PBi-101...PBi-172(12:45-14:15)
	Immunology (Hall C) PI-1...PI-79 (9:00-12:00)
	Genetics (Hall C) PG-1...PG-69(12:45-14:15)
Friday (2024/01/26)	Virology (Hall B) 9:00-12:00 (PV-1...PV-52)
	Mycology (Hall B) 12:45-14:15 (PM-1-PM-24)
	Hematology & Blood banking (Hall C) 9:00-12:00 (PH-1...P-85)
Saturday (2024/01/27)	Artificial intelligence (Hall C) 13:00-14:00 (PAI-1...PAI-13)
	Parasitology (Hall B) 9:00-12:00 (PP-1..PP-58)
	Bacteriology (Hall C) 9:00-12:00 (PBa-1...PBa-80) 12:45-14:15 (PBa-81...PBa-120)





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Members of Committees and Panels, and Referees





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Members of Executive Committee

Name	Role
Dr. Hamid Aghajanzadeh	Deputy of executive secretary
Dr. Mohsen Abdolmaleki	Deputy of executive secretary
Dr. Bahareh Hajikhani	Coordinator of abstract judging team
Dr. Masoumeh Navidinia	Coordinator of abstract judging team
Dr. Faezeh Nourabad	Coordinator of abstract judging team
Ms. Fatemeh Ghorbani	Coordinator of the ceremony team
Ms. Elham Darzi	Coordinator of marketing and exhibition team
Ms. Somayeh Shateri	Coordinator of workshop team
Ms. Zeinab Yousefi	Coordinator of international unit
Ms. Narjes Rezaei	Coordinator of Registration team
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Mr. Mehdi Yazdani	Coordinator of Painting exhibition team
Ms. Maryam Kalantari	Coordinator of IT team
Mr. Mohammad Javad Naderi	Coordinator of IT team
Ms. Saeedeh Salehi	Coordinator of oral presentation hall
Ms. Somayeh Mami	Coordinator of oral presentation hall
Mr. Sajjad Shekarchian	Coordinator of oral presentation hall
Dr. Mohsen Rokni	Coordinator of poster (mini-oral) presentation hall
Ms. Leila Mohamed Khosroshahi	Coordinator of poster (mini-oral) presentation hall
Ms. Najibeh Shekari	Coordinator of poster (mini-oral) presentation hall
Ms. Behnaz Moazzami	Coordinator of hall A
Mr. Hasan Sabzipour	Coordinator of hall A
Mr. Yaser Fakhari	Coordinator of retraining scores section
Ms. Setareh Askari	Coordinator of gifts & awards team
Mr. Ashkan Shaban Nejad	Member
Mr. Seyed Reza Dabaghi	Member
Ms. Fatemeh Afshar Noor	Member
Ms. Sahar Hormozi	Member
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Mr. Ahmad Koshari	Member
Mr. Mohammad Reza Farahani	Member
Mr. Mohammad Amin Sari	Member
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Dr. Ehsan Aghaei Moghadam	Clinic-Scientific Secretary
Dr. Hossein Keshavarz Valian	Member of policy committee
Dr. Fatemeh Fallah	Member of policy committee

Members of Scientific Panels

Dr. Ehsan Aghaei Moghadam
Dr. Ali Akbar Zeinaloo
Dr. Mohammad Reza Sabri
Dr. Marjan Hajahmadipoor
Dr. Fatemeh Zamani
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Dr. Setareh Mamishi Khanlagh
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Dr. Ali Teimoori
Dr. Mohammad Reza Fazlollahi

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1. Application of Artificial Intelligence in Laboratory and Clinical Diagnosis (Oral Presentations)





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Venue:
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Section: Application of Artificial Intelligence in Laboratory and
Clinical Diagnosis

Presentation Type: Oral

Abstract Type: Review

Code of Abstract: OAI-1

The Pervasive Role of Artificial Intelligence in Advancing Laboratory Research and Clinical Practice

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Abstract

Background and Aim: Artificial Intelligence (AI) has emerged as a transformative force in both laboratory research and clinical healthcare. In laboratory settings, AI is revolutionizing drug discovery by predicting potential candidates and optimizing molecular structures, as evidenced by the deep learning approach to antibiotic discovery. Genomic analysis benefits from AI applications, enabling the identification of disease-associated genes, personalized medicine, and risk factor prediction. Automation systems powered by AI streamline laboratory processes, reducing human errors and enhancing efficiency. The analysis of extensive datasets, particularly in fields like proteomics and metabolomics, is greatly facilitated by AI, uncovering crucial patterns and correlations. In clinical practice, AI serves as a diagnostic support tool by analyzing medical images and identifying anomalies in radiology, as exemplified by the Radiologist-level pneumonia detection using deep learning. Predictive analytics driven by machine learning models enable early intervention and personalized treatment strategies. Natural Language Processing (NLP) extracts and analyzes data from electronic health records (EHRs), enhancing decision support and clinical documentation. AI also contributes to treatment recommendations based on patient data and clinical guidelines, with applications in diabetic retinopathy detection. Remote monitoring through AI-driven wearables and applications continuously tracks patient vital signs, facilitating early intervention.

This abstract underscore the substantial impact of AI on laboratory research and clinical practice, providing a foundation for further exploration of its potential in improving healthcare and medical research. The rapid advancement of Artificial Intelligence (AI) has ushered in a new era in laboratory research and clinical practice. With its ability to analyze complex datasets, automate tasks, and provide valuable insights, AI has become an indispensable tool for scientists and healthcare practitioners. The aim of this paper is to provide a comprehensive overview of the diverse applications of AI in laboratory research and clinical practice, backed by scientific references, and to highlight the transformative impact of AI in healthcare and medical research.

Methods: To achieve the aim of this study, a thorough review of the scientific literature was conducted. Relevant research articles, reviews, and clinical studies were selected to provide a well-rounded perspective on the applications of AI in laboratory and clinical settings. The search included databases such as PubMed, IEEE Xplore, and Google Scholar, focusing on papers published between 2016 and 2023. Inclusion criteria comprised articles that demonstrated the application of AI in laboratory research, clinical diagnostics, and patient care. These articles were then analyzed and synthesized to form the basis of this comprehensive review.

Results: The results section highlights the pivotal role of AI in laboratory research, including drug discovery, genomic analysis, laboratory automation, data analysis, and image analysis. It also emphasizes the contributions of AI in clinical practice, such as diagnostic support, predictive analytics, natural language processing (NLP),





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treatment recommendations, remote monitoring, and administrative efficiency. Each of these areas is supported by scientific references and empirical evidence, illustrating the substantial impact of AI on healthcare and medical research.

Conclusion: In conclusion, this review underscores the pervasive role of AI in revolutionizing laboratory research and clinical practice. The extensive evidence from scientific literature demonstrates the significant contributions of AI in improving healthcare, enhancing diagnostics, and advancing medical research. AI's transformative potential in these domains is undeniable, and its continued integration is expected to drive further innovation, ultimately benefiting patients and researchers alike.

Keywords: Artificial Intelligence, laboratory research, clinical practice, drug discovery, genomic analysis, laboratory automation, data analysis, image analysis, diagnostic support, predictive analytics, natural language processing, treatment recommendations, remote monitoring, administrative efficiency.





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Section: Application of Artificial Intelligence in Laboratory and
Clinical Diagnosis

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OAI-2

Artificial Neural Networks for Estimating the Prevalence of Anemia in Iranian Children

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Abstract

Background and Aim: Our study evaluates the significance of multilayer perceptron (MLP) as feedforward artificial neural network (ANN) in prevalence of anemia in Iranian children.

Methods: Thirty-one factors related to the state of health, nutrition, and population were selected from the Data Bank of the World Bank website between 2003 and 2019. These factors were considered as independent parameters, and their effects were estimated on the prevalence of anemia among Iranian children (aged 6 to 59 months) as a dependent parameter. The design of the artificial neural network was performed by automatic method including a hidden layer with 9 cells and activation functions of hyperbolic tangent and identity in the hidden and the output layers, respectively. 91.7% of the information was used in the training phase and 8.3% in the testing phase. The rescaling method was achieved by a standardized method. The error of the designed ANN was estimated by the sum of squares error and relative error in the training and testing steps.

Results: The designed neural showed acceptable accuracy based on the sum of squared errors of 0.008 and 2.519×10^{-8} in the training and testing phase, respectively. The chart of predicted by observed values revealed a linear relationship of the form $Y=0.04+X$ ($R^2=0.998$) between the prevalence of anemia in children and the selected parameters. Moreover, the chart of residual by predicted values did not show any pattern, indicating the satisfactory performance of the designed ANN. The most important factors with equal or more than 50% of normalized importance were 1) domestic general government health expenditure, 2) prevalence of anemia among women of reproductive age, 3) people using at least basic drinking water services, 4) lifetime risk of maternal death, and 5) prevalence of anemia among pregnant women.

Conclusion: Our designed ANN model demonstrated that MLP as a feedforward method can be used for predicting the prevalence of anemia among Iranian children. Moreover, ANN models can help designing and implementing effective interventions to prevent and treat hematologic diseases.

Keywords: Anemia; Children; Artificial neural network; Multilayer Perceptron.





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Section: Application of Artificial Intelligence in Laboratory and
Clinical Diagnosis

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OAI-3

Comprehensive Analysis of the expression, prognosis, and immune infiltrates of Guanylate-Binding Proteins Family Members in Breast Cancer

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Abstract

Background and aim: Breast cancer is the most prevalent tumor in women global, aside from nonmelanoma skin malignancy. Inappropriately, several breast cancer (BrCa) patients display low reaction to ICIs because of the infiltrating immune cells lack. Earlier research showed that guanylate-binding proteins (GBP) could modulate the inhibitory impact of inflammatory cytokines on endothelial cell proliferation, migration, and invasion. However, the underlying functions of GBPs family in cancer-immunity cycle remain unclear. Hence, we explored the association between research showed that guanylate-binding proteins 1 with breast cancer and then introduced potential prognostic markers through analysis of GBP family expression in BrCa by data.

Methods: We analyzed the GBP family expression and prognostic value in BrCa by mining UALCAN, TIMER, and Kaplan-Meier plotter databases. Subsequently, we explored the association of GBPs expression and immune infiltrating abundance via the TIMER database. In addition, we identified microRNAs related to the CHD family by using the MirTarBase online database.

Results: Our findings demonstrated a strong association between the expression of GBP1/GBP2/GBP3/GBP4/GBP5/GBP6 and GBP7 with the infiltration of all immune cells. Our findings showed that high GBP1/4/5 expression was strongly connected with high dendritic cell, B cell, CD4+, CD8+, and neutrophil infiltration abundances in BrCa and that GBP2/3/6/7 expression was weakly positively correlated with these infiltration abundances.

Conclusion: These results recommend a therapeutic value for GBPs family in combination with ICIs for the BrCa treatment. However, further investigations are needed to evaluate the studied GBP members in detail.

Keywords: Prognostic; Guanylate-Binding Proteins; Immune Infiltrates; Breast Cancer.





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Section: Application of Artificial Intelligence in Laboratory and
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Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OAI-4

Developing AI-Powered Medical Lab Assistant Using Microsoft AutoGen

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Abstract

Background and Aim: many lab workflows run around manual steps like patient paperwork, specimen labeling, tracking samples, etc. that are prime areas for errors. Artificial intelligence capabilities can automate such repetitive workflows and provide on-demand expert guidance. To enable rapid development of AI assistants, Microsoft created AutoGen - an autocode platform that can auto-generate bots based on workflow descriptions. The aim of this project is to utilize AutoGen's automated bot development capabilities to create an intelligent assistant specifically focused on handling core medical lab workflows. Key objectives are improving efficiency, reducing human errors, compliance enforcement and augmenting decision making for lab technicians.

Methods: The methodology for developing the AI-powered medical lab assistant using Microsoft AutoGen involves a few key steps. First, the real-world workflows and usage scenarios in a typical medical lab will be mapped. These use cases for patient intake, order processing, tracking specimens, automated equipment interfaces, results recording and reporting will inform AutoGen's bot development configuration. Concurrently, ontology cataloguing key data like tests, protocols, devices, diagnostics and patient/staff data will be created using medical informatics resources, lab systems APIs and equipment interfaces. With well-defined use cases and rich domain ontology as inputs, AutoGen's automated programming capability will synthesize the specialized bot - including core codebase, dialogue processing and machine learning models. Additional customization would enhance capabilities further. Testing across patient test data sets and lab operation scenarios will be done before final integration with hospital databases and lab instrumentation for real-time function. Bot analytic dashboards will ensure continuous monitoring and improvement.

Results: By leveraging Microsoft AutoGen's automated AI generation capabilities, the end product achieved is an intelligent assistant specialized for handling key workflows in medical laboratories. The assistant demonstrates functionality spanning orderly patient test intake process, intelligent assignment to appropriate diagnostic equipment, automated sample analysis interfacing via connected lab instrument APIs, logging of quality control data, interpretation of diagnostic results and compilation of findings reports. Across numerous test runs with synthetic and actual patient lab test data, the accuracy of sample tracking, automated equipment usage, result interpretation and reporting workflows displayed over 90% precision in both routine as well as complex use cases. Quantitative usage analytics also showcase a potential 75% reduction of manual oversight needed for the AutoGen assisted lab, especially for repetitive data entry/recording steps. Thus the intelligent assistant can serve as an enormously useful productivity tool for augmenting current medical lab operations.

Conclusion: Using AutoGen's automated AI generation capabilities provides an effective way to develop assistive agents for medical labs. An intelligent assistant can act as a productivity multiplier for lab technicians and also enhance safety and compliance by reducing errors.

Keywords: Medical lab; Microsoft AutoGen; Intelligent Assistant; Machine learning.





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Section: Application of Artificial Intelligence in Laboratory and
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Presentation Type: Oral

Abstract Type: Systematic Review

Code of Abstract: OAI-5

Application of Artificial Intelligence in the Diagnosis of Esophageal Cancer: A Systematic Review Study

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Abstract

Background and Aim: Esophageal cancer is one of the most dangerous and fatal cancers in society, which can be cured with early diagnosis and treatment. Currently, esophageal cancer diagnosis methods include examination of biopsy and cytological samples, hysteroscopy, colposcopy and Pap test. However, these diagnostic methods still face disadvantages and limitations, which can be mentioned in saving time and money, defining the strengths and weaknesses of experts, and problems caused by the human nature of diagnostic methods. The purpose of this study is to investigate the use of artificial intelligence in the diagnosis of esophageal cancer.

Methods: This study is a systematic review study that was conducted in 2023 by using the keywords of artificial intelligence, diagnosis, and esophageal cancer, it was done in reliable databases including PubMed, Scopus, Cochrane, Web of Science and Google scholar search engine without time limit. To ensure the completeness of the search results, the sources of the articles were checked and after removing the duplicate titles from the endnote software and checking the titles and abstracts, the related articles were checked using JBi tools, after checking the quality of the articles, the findings in the checklist the target was entered.

Results: 3486 articles were reviewed and finally 32 articles related to our article showed that artificial intelligence has recently been proposed as a new tool for the diagnosis of esophageal cancer. Inspired by the neurophysiological designs of the human brain, artificial intelligence is able to discover specific patterns in the cytological and biochemical data of esophageal cancer. These patterns provide a deeper understanding of cancer mechanisms for diagnosis and identification of this disease. Artificial intelligence methods usually include machine learning, neural networks, and evolutionary algorithms that identify patterns by analyzing large and complex data and are able to diagnose esophageal cancer more accurately and faster. In addition to diagnosis, AI can also help in more effective prediction and sampling for esophageal cancer.

Conclusion: The results of the study showed that despite the intensive use of artificial intelligence technology in the diagnosis of esophageal cancer, there is still a need for more investigations and the development of improved methods and algorithms in this field. By using artificial intelligence, the diagnosis of esophageal cancer can be done more accurately, quickly and non-invasively, and this method can have an important impact on society and public health.

Keywords: Artificial Intelligence; Diagnosis; Esophageal Cancer.





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1. Application of Artificial Intelligence in Laboratory and Clinical Diagnosis (Poster Presentations)





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Section: Application of Artificial Intelligence in Laboratory and
Clinical Diagnosis

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PAI-1

Utilizing Deep Learning to Detect Microfilariae in Dog Blood Samples

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Abstract

Background and Aim: The research paper aimed to develop an artificial intelligence, deep learning-based system that detects microfilariae in Dog blood samples and differentiates microfilaria from thread-like artifacts automatically.

Methods: The study used blood samples from stray dogs in Gilan province, Iran, to train and test the system. The modified Knott method was used to identify 29 cases infected with microfilaria, which were confirmed with conventional PCR.

Results: The developed system diagnoses *D. immitis* with an accuracy of greater than 95% and can be widely used for epidemiological studies.

Conclusion: The proposed system plays an effective role in accurate and reliable diagnosis of *D. immitis* and can be used in field studies. The study highlights the limitations of the microscopic examination, which requires the abilities and expertise of technicians to identify and differentiate microfilariae from artifacts. The proposed system can remove this limitation and provide an automated and reliable diagnosis of *D. immitis*.

Keywords: Artificial Intelligence; Machine Learning; *Dirofilaria immitis*; Zoonotic Parasites; Microscopic Examination.





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Section: Application of Artificial Intelligence in Laboratory and
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Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PAI-2

Application of Multi-Layer Perceptron Artificial Neural Networks for Estimating Structural Changes of Hemoglobin

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Abstract

Background and Aim: The future of laboratory medicine will certainly involve the integration of artificial intelligence into experimental methods to improve the accuracy and reliability of results.

Methods: We first introduce artificial neural networks (ANN) models and emphasis on bringing these mathematical approaches closer to laboratory medicine. Then, we introduce the structural modifications of hemoglobin which can be studied by spectrophotometric analysis at different wavelengths. Finally, we detail how to customize the analysis, architecture, and learning of ANNs to better address the conformational changes of hemoglobin.

Results: ANNs can recognize patterns and make accurate predictions in diseases with complex conditions and also can be trained on datasets containing information about hemoglobin modifications, changes of its absorbance spectrum and its reaction kinetics with specific oxidants. In our studies, ANNs are used for solving artificial intelligence problems as machine learning techniques which can be applied effectively in various disciplines such as: cytomorphology, immunohistology, cell differentiation, morphological features, automated flow cytometry, chromosome banding analysis, chromosome classification, analysis of molecular profiles, identification of therapeutic candidates and drug discovery.

Conclusion: By analyzing laboratory data, ANNs can learn to identify specific patterns or relationships between the structural modifications of Hb and various biological and pathological outcomes. Our presentation will demonstrate how ANNs can fruitfully develop new methods for studying the structural changes of Hb in various healthy or pathologic conditions.

Keywords: Artificial Neural Network; Hemoglobin; Multilayer Perceptron; Structural Changes.





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Section: Application of Artificial Intelligence in Laboratory and Clinical Diagnosis

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PAI-3

Application of Machine Learning and Deep Learning Algorithms in Anemia Diagnosis and Prediction: A Systematic Review

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Abstract

Background and Aim: Anemia is a condition in which hemoglobin (Hb) concentration and/or red blood cell (RBC) numbers are lower than normal and insufficient to meet an individual's physiological needs. Diagnosis of anemia is one of the most important issues in the field of health, which requires accurate and fast methods. Machine learning (ML) and deep learning (DL) algorithms as two main artificial intelligence (AI) methods for image analysis that can help Anemias better understand and offer a promising approach to pre- and post-diagnosis. The aim of this systematic review is to examine ML and DL algorithms used to diagnose and predict Anemia.

Methods: The data were collected by searching PubMed, Scopus, Web of science databases and Google Scholar search engine. The advanced searched keywords were: "Machine Learning", "Deep Learning", "Anemia", "Detection", "Diagnosis", "Prediction" and. The search was limited to studies in the English language and accessible full texts. Review, duplicate, and non-relevant articles were excluded.

Results: In this review, 130 articles were retrieved through searching in databases, of which only 17 articles matched our inclusion criteria after preprocessing and screening and were identified. These articles used different types of data such as clinical, imaging and genetic data and built and evaluated predictive models for Anemia using ML and DL algorithms to help early diagnosis of the disease. The results have shown that ML and DL algorithms can help increase the efficiency of Anemia diagnosis and also lead to providing personalized and preventive treatments for patients.

Conclusion: This systematic review shows the progress in the effort to leverage digital data for improving diagnostic assessment and supports the development of ML and DL as powerful tools for diagnosis, prediction, and screening of Anemia.

Keywords: Artificial Intelligence; machine learning; Deep learning; Anemia; Detection, Diagnosis; Prediction.





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Section: Application of Artificial Intelligence in Laboratory and
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Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PAI-4

Application of Machine Learning and Deep Learning Algorithms in Breast Cancer Diagnosis and Prediction: A Systematic Review

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Abstract

Background and Aim: Breast cancer is the most common cancer in women and can metastasize to other components of the body through blood and lymphatic vessels, so proper diagnosis and screening to start early remedy facilitates improved clinical consequences. In recent years, the intersection of healthcare and artificial intelligence has created a paradigm shift in the area of scientific diagnostics, especially within the area of breast cancer prognosis. using superior techniques, this systematic study examines the combination of artificial intelligence-based gear with clinical imaging technology and illuminates their unprecedented accuracy, performance, and speed in figuring out potential malignancies.

Methods: We conducted a systematic search in four electronic databases: PubMed, Google Scholar, Web of science and Scopus. The advanced searched keywords were: “Machine Learning”, “Deep Learning”, “Breast neoplasms”, “Detection”, “Diagnosis” and “Artificial Intelligence”. The search was limited to studies in the English language. Review, duplicate, and non-relevant articles were excluded.

Results: In this review, 170 articles were retrieved through searching in databases, of which only 25 articles matched our inclusion criteria after preprocessing and screening and were identified. we unearthed a compelling finding: the integration of artificial intelligence (AI) assistance has shown a marked decrease in radiologists' recall rates across diverse patient demographics. This advancement has specifically improved specificity and accuracy in breast compositions, regardless of whether they are fatty or dense. This suggests the capability of AI algorithms to adapt to different clinical scenarios. Furthermore, when utilized in tandem with traditional ultrasonography methods, AI has displayed enhanced diagnostic efficacy. Numerous studies have also demonstrated the effectiveness of AI in guiding biopsy decisions, resulting in a significant reduction of unnecessary surgeries for benign lesions while maintaining a high level of sensitivity. Additionally, AI-enhanced mammograms are just as reliable as human readers in terms of repeatability.

Conclusion: In this systematic review highlight the potential of artificial intelligence (AI) systems in improving the detection and diagnosis of breast lesions. The classification of AI systems based on dataset type and size, classification task, medical challenges, and AI techniques provides a comprehensive framework for understanding their effectiveness. Furthermore, the backpropagation neural network (BPNN) artificial intelligence algorithm demonstrated high accuracy, sensitivity, and specificity for ultrasound image segmentation, resulting in better segmentation and diagnostic effects for breast cancer axillary lymph node metastasis. Overall, these findings suggest that AI can serve as a reliable complementary tool to digital mammography for evaluating breast lesions.

Keywords: Artificial intelligence; Diagnosis; Breast neoplasms; Machine learning; Deep learning; Detection.





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Section: Application of Artificial Intelligence in Laboratory and
Clinical Diagnosis

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PAI-5

Artificial intelligence in colorectal cancer diagnosis: A Review

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Abstract

Background and Aim: One of the topics that has attracted a lot of attention in recent years is artificial intelligence. Artificial intelligence is a general term that refers to the use of computers to model intelligent behavior with minimal human intervention. Artificial intelligence initially had many limitations, but in the early 2000s and with the emergence of deep learning, many of these limitations were removed. Artificial intelligence system has greatly contributed to the advancement of health sciences through risk assessment models, improvement of diagnostic accuracy, self-learning and analysis of complex algorithms. One of the most important applications of artificial intelligence in health sciences is the use of artificial intelligence tools in the diagnosis of various diseases. Artificial intelligence tools can suggest potential and actual diagnoses and treatment plans for patients by considering the countless parameters defined for them and accessing information.

Cancer is one of the most common and deadly diseases in the world. This disease is aggressive and has a low survival rate and a long and expensive treatment process. Recently, doctors have been encouraged to use computational methods such as multivariate statistical analysis to analyze the prognosis of the disease, and the accuracy of such analyzes is It is significantly higher than experimental predictions. In addition, since artificial intelligence, especially machine learning and deep learning, have found popular applications in clinical cancer research in recent years, cancer prediction performance has reached new heights. Colorectal cancer, with more than 1.85 million cases and 850,000 deaths annually, is the third most common cause of death from cancer worldwide. Early diagnosis and accurate prediction of cancer to increase the patient's survival rate. It is necessary. CRC diagnosis is divided into imaging methods, endoscopy and pathology. Treatment methods are divided into endoscopic drug therapy and surgery. Artificial intelligence technology in medicine is at a weak point. A large number of polyps quickly become malignant and become colorectal cancer. Therefore, early diagnosis and treatment of the disease is of great importance. In this study, an attempt has been made to review the recent studies conducted in the field of using artificial intelligence systems in the diagnosis of colorectal cancer.

One of the subjects that has received a lot of interest lately is artificial intelligence, which is employed in health and medicine, particularly in the identification of illnesses. One of the deadliest illnesses is cancer. The third most common cause of cancer-related deaths is colorectal cancer. By examining earlier research in this area, we attempted to classify the benefits and drawbacks of employing artificial intelligence systems and algorithms in the detection of colorectal cancer in this study.

Methods: We looked through the databases of PubMed, Google Scholar, Embase, and Web of Science to find research on the application of AI systems to colorectal cancer diagnosis between 2018 and 2023. Key words

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included colorectal cancer, artificial intelligence, and artificial intelligence diagnosis. Following analysis, 28 articles with duplicate titles were eliminated from the initial 78 articles that were taken from these databases. Twelve articles were eliminated for various reasons (concentrating on more in-depth problems like machine learning and non-diagnostic applications), while twenty-five articles were eliminated for having unrelated names (other concerns). Finally, 13 articles were included in the study.

Results: Disadvantages: Using the artificial intelligence system in all hospital and pre-hospital centers and training the employees to use it is a difficult and time-consuming process. Equipping the centers entails a heavy financial burden. Global access to medical information and images of patients makes the privacy of patients not properly protected. Despite these limitations, artificial intelligence can provide a diagnosis close to the doctor's diagnosis and reduce the amount of error in the diagnosis to some extent. High speed of diagnosis and presentation the treatment program by artificial intelligence is an advantage that has made many people still prefer to use artificial intelligence. Artificial intelligence by accessing the data and examining the data in an integrated way, just like what a human does, can quickly provide a classification of the disease and its level and a personalized treatment plan, which can reduce errors. Among other benefits of preventing Exams are invasive.

Conclusion: In general, the emergence of artificial intelligence system in the early diagnosis of colorectal cancer can be very effective considering the progressive nature of this disease, and artificial intelligence should be considered as an auxiliary force alongside the doctor, not to replace the doctor.

Keywords: Artificial intelligence; Colorectal Cancer; Artificial Intelligence diagnosis.





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Section: Application of Artificial Intelligence in Laboratory and
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Abstract Type: Review

Code of Abstract: PAI-6

Application of Artificial intelligence in the Diagnosis of COVID-19 Disease: A Review

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Abstract

Background and Aim: In 21st century, with the outbreak of the emerging disease of COVID-19 and then with its pandemic, people all over the world got involved. Corona viruses are a group of viruses belonging to the coronavirus family that cause disease by causing respiratory tract infections in mammals. For this reason, researchers from different fields sought to solve problems related to crisis control and management. The transmission power of the new coronavirus has drawn the attention of experts to the use of artificial intelligence to combat this pandemic. Artificial intelligence refers to software that can make decisions in addition to analyzing data.

Methods: In this review research with the help of Google Scholar and PubMed, from 2018 to 2023. The keywords searched were artificial intelligence, covid-19, diagnosis.

Results: By searching these databases, more than 40 articles were reviewed and 23 of them were studied. The results showed that artificial intelligence can create an intelligent platform for automatic monitoring and prediction of the spread of the Covid-19 pandemic. Also, create an integrated network to extract the appearance characteristics of this disease. With the help of artificial intelligence, a new diagnostic system is created with integrated management in clinical and para clinical departments. To combat the new coronavirus, Jamshidi and colleagues have proposed the use of Deep Learning (DL) artificial intelligence, which minimizes human intervention and examines large and complex data. The sequence of SARS-CoV-2 was identified with the help of artificial intelligence. It can also help quickly identify types of concern such as delta and omicron strains. However, the challenges of its use are the difficulty of data collection, internal and external validation and ethical considerations.

Conclusion: With the progress of science and technology, the process of diagnosis, treatment, prediction and prevention of diseases has become easier and easier with the help of artificial intelligence. As in the diagnosis of the disease of Covid-19, artificial intelligence was able to discover the genomic sequences of the virus of Covid-19, in time and save energy. Identify disease epidemiology and surpass in vaccine and drug design. Artificial intelligence is a smart and planned replacement in today's medicine, and its use is increasing day by day.

Keywords: Artificial intelligence; COVID-19; Diagnosis.





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Section: Application of Artificial Intelligence in Laboratory and
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Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PAI-7

Application of Artificial Intelligence in the Treatment of COVID-19

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Abstract

Background and Aim: Coronaviruses are a group of RNA viruses that cause disease in mammals. These viruses cause mild to fatal respiratory infections. With the outbreak of this disease in late 2019, researchers were faced with the question of how to are there any treatments that can save time and energy? Artificial intelligence was the answer to this question. A software that can imitate the intelligence of a real human being. Make a program and advance the path of drug treatment with special algorithms. There is always the potential and advantage for artificial intelligence to automatically understand and determine the final decision.

Methods: In this review research with the help of Google Scholar and PubMed, from 2018 to 2022. The keywords searched were artificial intelligence, covid-19, treatment.

Results: By searching these data, more than 30 articles were reviewed and about 20 of them were studied and recovered. The results showed that artificial intelligence using the analysis of data available in different research centers for covid-19 to pharmaceutical research in this context helps and this is useful for drug design and development. Many drugs are administered with the help of artificial intelligence. These drugs included Atazanavir, Remdesivir, Afavins, Ritonavir, and Doletogravir, PARP inhibitors, Abacavir, Roflublant, Almitrine, and Mesylate. Vaccines are also a type of drug-therapeutic method. Many of them were developed using new technologies of bioinformatics, databases, immune-informatics, machine learning and reverse vaccinology for complete SARS-CoV-2 proteomes or structural proteins. Examples of these vaccines are messenger RNA and viral vector vaccines. The management of the pharmaceutical system and planning in each of the stages of treatment was a dream that artificial intelligence was able to turn into reality.

Conclusion: The use of artificial intelligence technology makes it possible to speed up drug testing in a short time, while standard testing requires a lot of time. Therefore, artificial intelligence accelerates this process. The combined potential of artificial intelligence has made it a powerful tool for designing diagnostic tests and developing vaccines, as well as being useful for clinical trials during vaccine development.

Keywords: Artificial intelligence, Treatment, Covid -19 disease.





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Section: Application of Artificial Intelligence in Laboratory and
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Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PAI-8

The current position of artificial intelligence in the diagnosis of leukemia-causing mutations

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Abstract

Background and Aim: Leukemia is a type of cancer that affects blood-forming cells. Early detection is crucial for successful treatment. Traditional methods of diagnosing leukemia are often inaccurate and can lead to delayed treatment. This has led to increased interest in artificial intelligence (AI) and machine learning (ML) as potential tools for leukemia diagnosis. AI can analyze large amounts of data quickly and accurately, making it a promising tool for medical diagnostics. The aim of this study was to review the application of artificial intelligence in the field of hematology as well as the screening, diagnosis, and treatment of leukemia patients.

Methods: The methodology for this review involved a comprehensive literature search of peer-reviewed articles and studies published from 2010 to 2023. The search was conducted using various databases such as PubMed and Google Scholar. The search terms used were "AI in leukemia diagnosis", "leukemia-causing mutations", and "genomic data analysis". The selected articles were then critically analyzed for their methodology, results, and conclusions.

Results: Several studies demonstrated the effectiveness of AI in diagnosing leukemia. For instance, a hybrid model combining Convolutional Neural Networks (CNN) and Salp Swarm Optimization Algorithm (SESSA) achieved an accuracy of 99.2% in the classification of white blood cell leukemia. Moreover, the MERGE algorithm trained with images of blood smears from a hematologic laboratory obtained an accuracy of 90% in the digital analysis of blood smears and preclassification of cells. Another study using support vector machine/artificial neural networks achieved an accuracy of 98.19% in the automated identification of acute lymphoblastic leukemia.

Conclusion: The present study found that AI holds promise in leukemia diagnosis, however it also identified several challenges that need to be addressed. These include the need for extensive preprocessing, the requirement of large datasets, and the need for models that can be trained on a variety of leukemia types. Future research should be design to overcome these challenges to fully realize the potential of AI in leukemia diagnosis.

Keywords: Artificial intelligence (AI); Diagnosis; Leukemia.





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Section: Application of Artificial Intelligence in Laboratory and
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Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PAI-9

Determining hot spots of cutaneous leishmaniasis in Iran using geographic information system (GIS)

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Abstract

Background and Aim : Leishmaniasis is an emerging serious international public health problem and is considered one of the most neglected tropical diseases. The purpose of the present study is to determine the occurrence and spatial distribution cutaneous leishmaniasis in Iran using geographic information system (GIS) during a decade from 2008 to 2017.

Methods: The data obtained from the Ministry of Health, Treatment and Medical Education and other related centers were entered into the geographic information system and the disease information bank was determined. Then spatial distribution maps of the disease were produced and the hot spots of the disease in Iran were determined using ArcGIS 10.5 software spatial analysis. For the relationship between the variables affecting the disease (temperature, humidity, density of vegetation and incidence of cutaneous leishmaniasis), geographic weighted regression analysis was used in the ArcMap 10.5 environment.

Results: Zanjan, Razavi Khorasan, North Khorasan, Chaharmahal Bakhtiari, Hamadan and Semnan provinces, Ardabil were the hot spots of cutaneous leishmaniasis. The results of geographic weighted regression analysis showed that in the provinces of Razavi Khorasan, North Khorasan, Chaharmahal Bakhtiari, Hamedan, Semnan, Ardabil, Zanjan, Qazvin, Ilam, the highest correlation between temperature, humidity, density of vegetation and the incidence of the disease was seen.

Conclusion: The use of maps can provide reliable estimates of the population at risk. The geographic information system is an efficient and low-cost tool for examining the distribution of factors affecting health. The climate factor of temperature, humidity, density of vegetation has a greater effect on the probability of the spread of the disease and these factors can be an indicator used to predict the presence of the disease.

Keyword: Geographic Information System (GIS), cutaneous leishmaniasis, Iran.





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Section: Application of Artificial Intelligence in Laboratory and
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Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PAI-10

How artificial intelligence meets the diagnosis of thalassemia and hemoglobinopathies

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Abstract

Background and Aim: The electronic storage of medical data, coupled with advancements in disease diagnosis, has resulted in the creation of huge datasets. Traditional analysis of such datasets is usually untractable due to the so-called curse of dimensionality. Noting to its demonstrable capabilities, Artificial intelligence (AI), and particularly machine learning (ML), have emerged as lucrative analysis tools in the realm of medical sciences, including hematologic diseases. This trend extends to encompass thalassemia and hemoglobinopathies, which are prevalent hematologic disorders with the challenging diagnosis methods. This study seeks to explore the applications of AI and ML in the diagnosis and prognosis of hemoglobin defects.

Methods: We conduct searches in reputable databases such as PubMed employing a set of keywords including "artificial intelligence," "machine learning," "deep learning," "thalassemia," and "hemoglobinopathies" for the period spanning 2014 to the present. Our search concentrates on English language publications, with a specific emphasis on elucidating the types, applications, advantages, and limitations of AI and ML.

Results: Our review indicates that ML, as a core component of AI, finds extensive applications in diagnosis of thalassemia and hemoglobinopathies. ML algorithms such as k-nearest neighbor (k-NN) play a crucial role in organizing data related to hematological indices, enabling the derivation of valuable formulas for diagnosing and distinguishing between various causes of anemia. In predicting the types of hemoglobin variations, decision tree (DT) and random forest (RF) classifiers emerge as preferred choices, while neural network (NN) proves to be an accurate method for diagnosing thalassemia. Extreme Learning Machine (ELM) algorithm is used to distinguish conditions with similar and close symptoms, and Deep Learning (DL) is utilized to analyze the images of electrophoresis bands and cytomorphology. Logistic regression (LR) and RF algorithms can also be respectively employed for predicting iron overload in the heart and liver for thalassemia major.

Conclusion: The adoption of AI and ML has proven to be an effective strategy for accelerating and refining the diagnosis of thalassemia and hemoglobinopathies. ML algorithms are instrumental in interpreting data from diverse laboratory methods, facilitating a conclusive diagnosis even in the absence of expert clinicians. ML demonstrates proficiency in distinguishing between pathological and non-pathological cases and can predict prognosis and potential patient complications. However, further research is essential to identify any limitations or issues inherent in the employed ML algorithms.

Keywords: artificial intelligence; machine learning; thalassemia; hemoglobinopathies.





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Section: Application of Artificial Intelligence in Laboratory and
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Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PAI-11

Bridging bioinformatics and biology: characterizing Nucleolin RNA binding domain as a cancer biomarker

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Abstract

Background and Aim: Nucleolin (NCL), a protein prevalent in various cancers, is integral to cellular proliferation and tumor genesis. Its RNA binding domain (RBD) is pivotal for activating multiple signaling pathways via ligand interactions, making it a prime target for cancer therapeutics and diagnostics. This study focuses on the in-silico prediction of the physicochemical and immunological characteristics of RBD-NCL, followed by the in vitro production and analysis of its recombinant form. The aim is to establish RBD-NCL's potential as a cancer biomarker and a candidate for monoclonal antibody production.

Methods: We utilized bioinformatics tools to analyze the stability and immunogenicity of RBD-NCL. The gene coding for RBD-NCL was cloned into the pET28 plasmid and expressed in Escherichia coli BL21. The resulting recombinant RBD-NCL (rRBD-NCL) was purified and characterized through affinity chromatography and Western blot analysis.

Results: The rRBD-NCL demonstrated a molecular weight of 37.9 kDa. Its immunogenicity was tested through immunization of BALB/c mice, with subsequent verification via ELISA and Western blotting. These experiments confirmed the high stability and immunogenicity of rRBD-NCL predicted by the in-silico analysis.

Conclusion: The study successfully elucidates the physicochemical and immunological properties of RBD-NCL, offering insightful data on its role in cancer signaling pathways. The recombinant rRBD-NCL shows potential as a valuable tool for developing monoclonal antibodies aimed at disrupting cancer-promoting mechanisms. This work lays the groundwork for future therapeutic strategies targeting NCL in cancer treatment.

Keywords: RNA Binding Domain; Nucleolin; Bioinformatics; Protein Expression; Immunoassay.





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2. Bacteriology (Oral Presentations)





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Section: Bacteriology

Presentation Type: Oral

Abstract Type: Systematic Review/ Meta-analysis

Code of Abstract: OBa-1

The clinical effectiveness of probiotics as adjunct treatment in the management of gynecological infections: A systematic review and meta-analysis

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Abstract

Background and Aim: The present study aims to performed a comprehensive meta-analysis using data of 35 randomized controlled trials (RCTs) that investigating the efficacy of probiotics as an adjunct treatment for treatment of gynecological infections.

Methods: The study adopted a systematic literature review of major electronically databases e.g., PubMed, Cochrane, and EMBASE, using defined MeSH terms. We pooled data using Odds Ratio (OR) corresponding 95% confidence intervals to measure the clinical efficacy of probiotics in management of gynecological infections. All statistical analyses were performed according to Comprehensive meta-analysis software.

Results: A total of 35 articles, comprising 3,751 patients, were considered as eligible articles. The application of probiotics demonstrated a notable increase in the cure rates of bacterial vaginosis (BV) and vulvovaginal candidiasis (VVC) as compared to control groups. A significant BV cure rate (OR: 5.972; 95% CI: 2.62-13.59) was noted with probiotic use, which was even more pronounced when used as an adjunctive treatment with antibiotics (OR: 2.504; 95% CI: 1.03-6.06). Additionally, probiotic use significantly reduced the recurrence rates of BV (OR: 0.34; 95% CI: 0.167-0.71). For VVC, a significant increase in the cure rate was observed in the probiotic group (OR: 3.425; 95% CI: 2.404-4.879), along with a lower recurrence rate (OR: 0.325; 95% CI: 0.175-0.606).

Conclusion: Our findings suggested the potential beneficiary role of probiotics as a novel candidate for treatment of gynecological infections. However, further investigations are necessary to corroborate these findings.

Keywords: Probiotics; Vulvovaginal Candidiasis; Bacterial Vaginosis; Randomized Controlled Trials.





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Section: Bacteriology

Presentation Type: Oral

Abstract Type: Review

Code of Abstract: OBa-2

A road forward for colon cancer therapeutics

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Abstract

Background and Aim: Colon cancer is one of the leading tumors in the world and, along with lung, prostate, and breast cancer, it is considered one of the big killers. In recent years, very important advances in the treatment of this disease have been made repeatedly. It is very important to develop the management and use of drugs or combinations that can achieve better results with fewer side effects. Therefore, the use of probiotics can be considered a step forward in the treatment of colon cancer.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, Google Scholar, and Embase from 2016 to 2023 by using the keywords probiotics, colon cancer, microbiota., 53 articles related to inclusion criteria were extracted and then analyzed.

Results: The results of the study indicated that the consumption of probiotics as live microorganisms that will have important health benefits for the host, will also not cause side effects. Consumption of probiotics or probiotic cocktails with anti-inflammatory properties with positive regulation IL-10, which leads to the inhibition of interferon-gamma, TNF alpha, and IL-12. It also has a protective effect against tumor injury by regulating and modulating the intestinal microbiota.

Conclusion: Probiotics can play a role as a potential treatment or supplement in colon and digestive system cancer and show beneficial effects by regulating and modulating the microbiota of the digestive system.

Keywords: Probiotics; Colon cancer; Microbiota.





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Section: Bacteriology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBa-3

Estimation of antibacterial activity of antimicrobial peptide isolated from plant against gram-positive and gram-negative bacteria

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Abstract

Background and Aim: Antimicrobial resistance reduces the efficacy of antibiotics. In the recent years, due to several cases of antimicrobial drug misuse, bacterial infections have caused many deaths and become a critical concern to public health. However, cationic antimicrobial peptides (CAMPs) are promising as an alternative therapeutic strategy against multidrug-resistant (MDR) strains. In this study, the inhibitory activity of a cationic peptide, derived from the *Urtica dioica*, against Gram-Negative and Gram-positive clinical isolates, were evaluated.

Methods: In this study, Isolation of antibacterial peptide from the *Urtica dioica* was performed based on the method purified via reverse-phase HPLC chromatography. Evaluation of antibacterial activity was determined using the broth microdilution test against the *Escherichia coli* ATCC25922, *Staphylococcus aureus* ATCC29213, *Acinetobacter baumannii*_ATCC19606 and *Pseudomonas aeruginosa* ATCC27853 strains. The minimum bactericidal concentration (MBC) test defined the lowest concentration of antibacterial peptides to kill the bacteria. The minimum inhibitory concentration (MIC) was determined the lowest peptide concentration that inhibited the growth of bacteria.

Results: The antibacterial peptide possesses broad spectrum activity against Gram-positive and Gram-negative bacteria. A strong bactericidal effect of this peptide against the tested strains, with the MIC values ranged from 0.25-2 µg/mL and the MBC values range from 1-8 µg/mL was observed.

Conclusion: The information gathered will be helpful in search for novel AMPs in the plant kingdom, as well as support the future development of plant peptides as new therapeutic substances against bacteria.

Keywords: *Urtica dioica* leaves, antimicrobial peptide, Minimal inhibitory concentration, antibacterial activity, Minimum bactericidal concentration.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Oral

Abstract Type: Systematic Review/ Meta-analysis

Code of Abstract: OBa-4

Characterization of biofilm-related gene profile of extensively drug-resistant *Acinetobacter baumannii* strains isolated from burn wound infections

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Abstract

Background and Aim: *Acinetobacter baumannii* has emerged as a superbug in recent years due to its prepotency to form biofilm and increasing rates of antibiotic resistance, leading to nosocomial infections, especially in patients with burns. In the present work, we determined the frequency of biofilm-related genes among 96 extensively drug-resistant *A. baumannii* strains isolated from burn wound infections in a referral hospital in Isfahan, Iran.

Methods: All collected isolates were preliminarily identified by standard microbiological tests and confirmed by polymerase chain reaction (PCR) using specific primers for the *bla_{oxa-51}* gene. All *A. baumannii* strains were examined for susceptibility to 13 antibiotics according to the Clinical and Laboratory Standards Institute (CLSI) guideline by disk diffusion method. Also, the biofilm formation ability of each strain was determined by the microtiter plate (MTP) method. All *A. baumannii* strains were screened for the presence of 10 biofilm-related genes (*pgaA*, *bap*, *ompA*, *csuE*, *abaI*, *bfmR*, *bfmS*, *adeB*, *adeG*, and *adeJ*) using separate PCR reactions.

Results: Most of the strains (99%) were resistant to piperacillin/tazobactam, cefotaxime, ceftriaxone, imipenem, meropenem, and ciprofloxacin, and were classified as extensively drug-resistant (XDR) and only one strain showed susceptibility to all antibiotics tested. Overall, 25% (n = 24), 56% (n = 54), 11% (n = 11), and 7% (n = 7) were classified as strong, moderate, weak, and non-biofilm producers, respectively. *ompA* (100%), *bfmR* (100%), and *bap* (99%) were the most prevalent biofilm-related genes. Also, a significant positive association between biofilm formation and resistance to aminoglycosides and presence of *bap* and *csuE* genes was observed.

Conclusion: Our findings emphasized on the need for stringent monitoring and control measures in hospital settings since *A. baumannii* strains exhibited a high level of biofilm-forming capacity and the presence of biofilm-related genes.

Keywords: *A. baumannii*; Burn wound infection; antimicrobial resistance; XDR; biofilm formation.





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Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBa-5

Evaluation of the effect of several prebiotics on microbial load of *Akkermansia muciniphila* in intestine of laboratory mice

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Abstract

Background and Aim: *Akkermansia muciniphila* is a new team introduced as a probiotic and has a control role in some metabolic diseases such as obesity, disease and intestinal disease. A decrease in the number of *A. muciniphila* in the intestine is related to metabolic diseases, and increasing the number of this bacteria in the intestine provides the possibility of recovery, for this reason, increasing the number of this bacteria in the intestine is suitable for strengthening the immune system. This study was conducted with the aim of investigating the effect of adding several types of prebiotics to the diet of mice on the microbial load in *A. muciniphila* in the intestine of mice.

Methods: For this purpose, the test materials were fed to mice through gavage for 4 weeks, and the number of *A. muciniphila* at time zero and after 4 weeks in the feces of mice was checked by Real Time PCR method. An explanation of the study design and experimental method.

Results: Among the 5 tested prebiotics, metformin, breast milk and tryptophan had an increasing effect from 82.8-times to 37.5-times on the growth of *A. muciniphila*, but powdered milk and mucus not only did not show an increasing effect, but also reduced the number of bacteria by about 5-times. They gave. The increase or decrease of *A. muciniphila* in the presence of various prebiotics was not related to the weight and consistency of mice feces.

Conclusion: The use of prebiotic substances such as metformin and tryptophan have a significant effect on the growth of *A. muciniphila*, and it is suggested to investigate its effect on health and treatment of metabolic diseases in future studies.

Keywords: *Akkermansia muciniphila*; probiotic; prebiotic; metformin; tryptophan.





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Section: Bacteriology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBa-6

Applied laboratory strategies for diagnosing acute respiratory infections in children

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Abstract

Background and Aim: Acute respiratory tract infection is an infection that causes problems for normal breathing. This infection is a major public health problem in developing countries. Complications of acute respiratory tract infection are very serious; this disease can lead to permanent damage. In the pediatric population, respiratory infections are the most common reason for visiting the doctor. Acute respiratory infections are one of the leading causes of death in children worldwide, and it is estimated that worldwide, respiratory infections are responsible for millions of deaths in children. Meanwhile, bacterial and viral pathogens are both responsible for these deaths. Most infections are viral in nature, viruses do not damage the cells of the upper respiratory tract, but cause changes in the tight junctions of the epithelial cells. This situation allows the virus to gain access to the tissues beneath the epithelial cells, and initiate innate and adaptive immune responses. Although many respiratory diseases in children are self-limiting infections that resolve with time and supportive care, identifying the causative agent in the early stages of the disease in order to implement effective antimicrobial treatment and infection control can be of particular importance. Over the last few years, the diagnosis of respiratory infections has evolved considerably with the development of new assays and the availability of up-to-date tests for newer strains of pathogens. Newer laboratory methods are rapid, highly sensitive, and specific, and are gradually replacing conventional gold standards, although the clinical utility of these assays is still under evaluation. The purpose of this research is to investigate practical laboratory strategies for diagnosing acute respiratory infections in children.

Methods: Applied methods for diagnosing acute respiratory infections in children were investigated using internet search engines such as PubMed, Google Scholar, Medline journals and Science Direct. We searched different laboratory methods using the search terms for diagnosis of acute respiratory infection in children, antibody, biosensors, and the like, and only the articles that contained the required information were selected for analysis.

Results: The first step in the diagnosis of acute respiratory tract infection in children is a physical examination at the patient's bedside, then the paraclinical intervenes to confirm the diagnosis. In order to diagnose acute respiratory tract infection in children, a series of diagnostic methods such as a simple chest X-ray can be used, blood test, sputum test and sometimes urine test helped, some of these methods have special side effects for children. In addition, it is not always possible to accurately identify the type of microorganism in chest imaging and blood tests. Several diagnostic tests can contribute to the clinical validity of acute respiratory infections in children.

Among these tests, we can mention molecular tests, serological tests and various specific antibody testing methods. These methods include checking the antibody using the rapid test method or RDT (rapid diagnostic test) and measuring the antibody using the ELISA method. It is not suitable for diagnosis in the acute stage of the





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disease, but sometimes it is helpful in cases of late referral or negative or unclear PCR-RT. In addition, sensors modified with nanomaterials show more efficiency in identifying biomarkers for respiratory infections.

Conclusion: Many microorganisms cause infection in different parts of the respiratory system, leading to various health complications, including difficulty in breathing. Severe respiratory infection is the main reason for admission to the intensive care unit in infants and children. Most of the time, viruses, bacteria and fungi cause respiratory infections. Early detection of infection helps prevent ICU admission and speed recovery.

Various bioassay methods have been used for early detection of respiratory infections. In addition, sensors modified with nanomaterials show more efficiency in identifying biomarkers. In recent years, the diagnosis of respiratory infections has made significant progress with the development of new methods for newer strains of pathogens. Newer laboratory methods are fast, very sensitive and specific, such as biosensors, which are gradually replacing the usual gold standards.

Keywords: practical strategies, diagnosis of acute respiratory infections, children.





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Tehran University of Medical Sciences, Tehran, Iran.
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Section: Bacteriology

Presentation Type: Oral

Abstract Type: Review

Code of Abstract: OBa-7

Effective biomarkers for diagnosis of neonatal sepsis

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Abstract

Background and Aim: Neonatal sepsis (NS) is a clinical condition life-threatening caused by the infant's immune system's response to infection that afflicting infants at ≤ 28 days of life. Its clinical manifestations vary from subclinical infection to severe manifestations or systemic disease, which causes organ failure and death and occurs in 1 to 5 cases in 1000 babies and has a high mortality rate (5-15%). This fatal complication is classified as early-onset neonatal sepsis (EOS) and late-onset sepsis (LOS). Prompt aggressive treatment with antibiotics is critical and delay in treatment increases the risk of infant death but possible treatment with broad-spectrum antibiotics also disrupts the infant's intestinal microbiome and exposes the infant to necrotizing enterocolitis and infection with invasive fungi.

Methods: Four search devices were selected to search the best literature research- Google scholar, Pubmed, Science direct and Scopus. "Biomarkers", "Neonatal sepsis", "specificity", "sensitivity", "LOS" and "EOS" were used for each search.

Results: The origin of sepsis-causing infections is often bacterial, but rarely fungal and viral and the acquisition of this infection can be the result of intrauterine infection, the acquisition of the mother's flora during natural childbirth postpartum acquisition from hospital or community. Due to the non-specificity of the symptoms of neonatal sepsis, it is difficult to diagnose and treat it. also, blood culture is the gold standard for the diagnosis of sepsis, but it has high false negative results in the diagnosis of EOS. Reports shows CRP, IL-6, and Presepsin have a high sensitivity among the bio markers and the most specific tests included sTREM.

Conclusion: Early diagnosis of neonatal sepsis using biomarkers can save the baby's life and prevent its short-term and long-term complications and prevent the use of unnecessary antibiotics. There is no single biomarker that can reliably rule out or confirm NS. Therefore, the diagnosis of neonatal sepsis should be based on clinical symptoms and a combination of biomarkers. Nowadays, PCT and CRP are the most common indicators in the diagnosis of EOS.

Keywords: Biomarkers, Neonatal sepsis, Sensitivity Biomarker, Specificity Biomarker.





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Section: Bacteriology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBa-8

Evaluation of the antimicrobial properties of bacteriocin preparations deduced from *Lactobacillus brevis* and *Lactobacillus plantarum* against clinical strains of *Helicobacter pylori*

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Abstract

Background and Aim: *Helicobacter pylori* is a pathogenic bacterium characterized by its gram-negative cell wall composition. It is the main causative factor of duodenal ulcer and gastric cancer. The latter of which is the leading cause of cancer-related mortality in the Iranian. Currently, the infection with antibiotic-resistant *H. pylori* strains poses a significant risk to the overall health of the general population. Here, we have investigated the antibacterial properties of bacteriocins obtained from *Lactobacillus plantarum* and *Lactobacillus brevis* against *H. pylori*.

Methods: *Lactobacillus* species were cultivated in 200 ml of MRS broth (37 C, 48h) under microaerophile conditions. A cell-free supernatant was obtained by centrifuging the mixture (4°C, 8000 RPM, 20 min), in order to collect bacteriocins. The bacteriocin samples were treated with ammonium sulphate to achieve a 70% saturation level and again centrifuged. The precipitates were dissolved in PBS buffer and dialyzed (cut-off point: 10-14 kDa). The resulting sample were applied to SDS-PAGE. The minimum inhibitory concentration (MIC) was determined using the Agar dilution test. A suspension of *H. pylori* with a turbidity of 3 McFarland was applied and incubated for 72 hours.

Result: The molecular weight of bacteriocins was determined to be approximately 10 kDa using SDS-PAGE. The inhibition zone diameters of bacteriocin samples against 18 *H. pylori* clinical strains ranged from 18 to 20 mm, and there was no significant difference observed between the effects of *L. plantarum* and *L. brevis* bacteriocin. The disc diffusion test on like *E. coli* (ATCC 25922) and *Staphylococcus aureus* (ATCC 25923) showed that Bacteriocin of *L. plantarum* has a greater inhibition zone diameter than Bacteriocin of *L. brevis*.

Conclusion: *H. pylori* proliferation has been demonstrated to be inhibited by the antibacterial properties of bacteriocins derived from *L. plantarum* and *L. brevis*. This is the first study of its kind in Iran to investigate the impact of compounds containing bacteriocins derived from *L. brevis* and *L. plantarum* on *H. pylori* clinical strains. The antimicrobial properties and inhibitory capability of these bacteriocins in inhibiting the growth of *H. pylori* were assessed. The findings of this research could help in the treatment and prevention of infections caused by this bacterium.

Keywords: *Helicobacter pylori*, bacteriocin, *Lactobacillus brevis*, *Lactobacillus plantarum*, probiotic.





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Section: Bacteriology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBa-9

Correlation between proinflammatory cytokines and some microbiota among the patients with ankylosing spondylitis

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Abstract

Background and Aim: Ankylosing spondylitis (AS) is a chronic rheumatic and debilitating autoimmune disease of unknown origin. The study aimed to evaluate the changes in intestinal microbiota and its relation with proinflammatory cytokines among the patients with AS referred to a rheumatology clinic or hospitalized in the rheumatology ward of Imam Khomeini Hospital in Urmia.

Methods: Twenty patients with ankylosing spondylitis and 20 healthy individuals were included in the present study. DNA was extracted from fecal samples and RNA was extracted from peripheral blood mononuclear cells and converted to cDNA. At next step, the population changes in the predominant intestinal microbiota including Bifidiobacterium sp., Bacteroides sp. and Entrobacterales and expression of cytokines (TNF- α , INF- γ , IL-17A,) were evaluated using PCR and quantitative Real-time PCR.

Results: Our finding indicated that the mean of the relative amounts of Bacteroides (P<0.0001), Entrobacterales (P=0.044) and Bifidobacterium (P=0.048) in patient stool samples were significantly higher than healthy individuals (P<0.0001). The mean of the relative amounts of TNF- α , IL-17A and INF- γ in the blood samples of patients are significantly higher than those of healthy subjects (P=0.03, P=0.017 and P=0.047, respectively).

Conclusion: The results of this study showed an imbalance in the dominant intestinal microbiota in patients with AS, and it seems that this imbalance causes an increase in pro-inflammatory cytokines.

Keywords: Ankylosing spondylitis, Gut microbiota, Dysbiosis, Cytokine, Real-time PCR.





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Section: Bacteriology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBa-10

Genetic mechanisms of decreased susceptibility to azithromycin among *Shigella* clinical isolates in Ahvaz, Iran

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Abstract

Background and Aim: *Shigella spp.* have developed resistance to common antibiotic and are no longer prescribed to treat shigellosis due to the emergence of multidrug resistance (MDR). Azithromycin has been considered an alternative choice for treatment of MDR *Shigella* infections. However, decreased susceptibility to azithromycin (DSA) due to various resistance mechanisms have emerged in *Shigella spp.* So, the aims of this study were to investigate the genetic mechanisms of decreased susceptibility to azithromycin among *Shigella* clinical isolates in Ahvaz, Iran.

Methods: *Shigella* isolates were collected from April 2022 to April 2023 at Abuzar Hospital, Iran and confirmed using biochemical and phenotypic methods. The minimum inhibitory concentrations (MICs) of azithromycin were determined by the agar dilution method in accordance with the CLSI guidelines in the presence and absence of efflux inhibitor, Phe-Arg- β -naphthylamide (Pa β N, 20 mg/ml) concentration. Then, presence of macrolide resistance genes, *mph(A)*, *mph(B)*, *mph(D)*, *mph(E)*, *msr(A)*, *msr(D)*, *msr(E)*, *mef(A)*, *mef(B)*, *ere(A)*, *ere(B)*, *erm(A)*, *erm(B)*, *erm(C)*, *erm(F)*, and *erm42* and mutation in the *rpID* and *rpIV* genes were investigated.

Results: A total of 126 *Shigella* species isolates including 77 *S. sonnei* (61.1%), 44 *S. flexneri* (35%) and 5 *S. boydii* (3.9%) were detected. 101 isolates (80.15%) were susceptible to and 25 (19.84%) isolates showed DSA (MIC, 32 to \geq 256 μ g/ml). The MICs of 6 DSA isolates (24%) were reduced in the presence of Pa β N. Prevalence of *mph(A)*, *mph(E)*, and *erm(B)* genes among DSA isolates were 92% (and 7 non-DSA isolates), 44%, and 28%, respectively. Other investigated macrolide resistance genes were not found in this study. Furthermore, there was no mutation in *rpID* and *rpIV* genes of DSA isolates.

Conclusion: This study highlights a concerning level of decreased susceptibility to azithromycin among the *Shigella spp.* that is a main challenge for treatment of MDR *Shigella spp.* Additionally, the absence of mutation, notable prevalence of *mph(A)*, and *erm(B)* genes, and decrease MIC level in presence of efflux inhibitor suggests resistance mechanisms including efflux pumps and especially the presence of *mph(A)*, and *erm(B)* genes may contribute to decreased susceptibility.

Keywords: *Shigella spp.*; decreased susceptibility to azithromycin; macrolide resistance genes; mutation.





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Section: Bacteriology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBa-11

Prevalence of mobile colistin resistance (*mcr*) genes in *Acinetobacter baumannii*: isolates of clinical infection from Shahid Rahimi hospital, Khorramabad, Iran

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Abstract

Background and Aim: The emergence of colistin resistance is a global issue that threatens the effectiveness of colistin treatment against multidrug-resistant Gram-negative bacteria. The present study reports on the prevalence colistin resistance and *mcr*-encoding genes in *Acinetobacter baumannii* strains isolated from patients referred to Shahid Rahimi hospital, Khorramabad, Iran, from January to August 2019.

Methods: A total of 47 non-duplicate *A. baumannii* isolates were obtained from clinical specimens of patients. Colistin susceptibility of isolates was assessed using the broth microdilution method, and the presence of *mcr*-encoding genes was determined through the utilization of PCR.

Results: Out of the total of 47 isolates belonging to *A. baumannii*, 14 isolates (29.8%) were resistant to colistin. The MIC of colistin ranged from 2 to 256 µg/mL, and the MIC₅₀ and MIC₉₀ values for colistin were 0.25 and 16 µg /mL, respectively. The presence of *mcr-1* and *mcr-2* was detected in 6 (12.7%) and 2 (4%) isolates, respectively. However, no isolates harbored *mcr-3* gene. Except for one isolate, none of the *mcr*-positive isolates exhibited phenotypic resistance to colistin.

Conclusion: The higher phenotypic prevalence of colistin resistance compared to genotypic characterization, along with the discrepancy with the presence of *mcr* genes, suggests the need to monitor and consider all molecular mechanisms of colistin resistance as a last resort treatment option.

Keywords: *Acinetobacter baumannii*, Drug Resistance, Nosocomial Infection, Colistin.





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Section: Bacteriology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBa-12

The relationship between the pathological indexes and the presence of *cagA* and *vacA* genes in gastric biopsies of *Helicobacter pylori*-positive and -negative patients with gastritis

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Abstract

Background and Aim: *Helicobacter pylori* is one of the most common bacteria affecting human societies worldwide. This study aimed to investigate the relationship between the pathological indexes and the presence of *cagA* and *vacA* genes in gastric biopsies of *H. pylori*-positive and -negative patients with gastritis in Sari city, North of Iran.

Methods: Informed consent forms were obtained from the studied patients, and the patients with gastritis symptoms were included in the study. To evaluate the prevalence of *cagA*, *vacA*, genes, gastric biopsies with positive or negative rapid urease test were collected from 50 patients (25 *H. pylori*-positive and 25 *H. pylori*-negative) with gastro-duodenal diseases. The bacterial DNAs were extracted by a specific kit, and the presence of the genes was analyzed by PCR using specific primers.

Results: Eighteen (72%) biopsies from 25 *H. pylori*-positive samples were *cagA*-positive, while 17 (68%) biopsies contained the *vacA* gene. However, (44%) samples had both *vacA* and *cagA* genes, from which most of them had chronic gastritis. Among 25 *H. pylori*-positive samples, 11 (44%), samples were contained both virulence genes (group 1), 3 (12%) had no genes (group 2), 5 (20%) samples were contained the *cagA* gene (group 3), and 6 (24%) samples were carrying the *vacA* gene (group 4). All group 1 samples showed an active chronic gastritis pathology and 7 (63.63%) exhibited a moderate intestinal metaplasia. However, all samples in group 2 and 3, and 83.33% of the group 4 samples were categorized as active chronic gastritis. Among the group 2 samples, 2 (66.66%) biopsies exhibited a moderate intestinal metaplasia, while 2 (40%) and 3 (60%) of the group 3 biopsies showed moderate and mild intestinal metaplasia, respectively. However, these rates in the group 4 samples were 50% and 33.33%, respectively. Also, different features were observed in *H. pylori*-negative biopsies, while most of them were grouped as chronic gastritis and mild intestinal metaplasia.

Conclusion: Due to the significant role of *H. pylori* in gastric and duodenal ulcer and cancer, the increased prevalence of virulence genes, such as *cagA* and *vacA* is a problematic concern. According to our study, the frequency of tested virulence genes had no significant relation with the pathological outcomes, but the presence of *H. pylori* can affect on the emergence of an active gastritis and metaplasia. However, the prolong chronic gastritis can mediate the development of gastric cancers, by the expression of the virulence genes.

Keywords: *Helicobacter pylori*; *cagA*; *vacA*; gastritis, Pathological outcomes.





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Section: Bacteriology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBa-13

Detecting bacterial infection in neonates admitted to the NICU ward of Afshar Hospital, Yazd

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Abstract

Background and Aims: Neonatal bacterial infections cause a massive burden of mortality and morbidity. These include blood infections, urinary tract infections, and brain or spinal fluid infections. The diagnosis of neonatal bacterial infection remains one of the most tantalizing challenges to physicians.

Methods: We evaluated neonates hospitalized in the neonatal intensive care unit (NICU) ward of Afshar hospital for bacterial infections by microbial culture from March 2022 to September 2023.

Results: The most common infection was *E. Coli* with 17 samples (13 samples from urine, 3 samples from eye and one sample from blood). 5 samples were Extended-spectrum beta-lactamases (ESBLs). The highest antimicrobial resistance was to Ampicillin (82.4%) and the lowest to Ciprofloxacin and Amikacin (11.8%). *Staphylococcus Epidermis* infection was seen in 14 samples (blood 8, trachea 4, urine and eye 1). The highest antimicrobial resistance was to Cefoxitin (84.6%) and the lowest to Doxycycline (21.4%). *Staphylococcus aureus* isolated from blood (3 samples), eye and trachea (each one 2 samples), and urine (one sample). All samples were Methicillin-resistant *Staphylococcus aureus* (MRSA). The highest antimicrobial resistance was to Erythromycin and Co-trimoxazole (87.5%) and the lowest to Doxycycline and Rifampicin (50%). Also, *Staphylococcus saprophyticus* was isolated from blood (1 sample), and urine (1sample). The antimicrobial resistance was to Doxycycline, Rifampicin, Erythromycin and Clindamycin (100%). *Enterobacter cloacae* infection was seen in 4 samples (urine 3 and trachea 1). One sample was ESBL. The highest antimicrobial resistance was to Ampicillin and Cefazolin (75%) and the lowest to Amikacin (25%). *Pseudomonas spp.* was found in 3 samples (trachea 2 and urine 1). The highest antimicrobial resistance was to Gentamicin, Tobramycin, Ampicillin/sulbactam, Cefpim (100%) and the lowest to Ceftazidime (33.3%). 2 trachea samples were positive for *Acinetobacter baumannii*. The highest antimicrobial resistance was to Gentamicin, Ampicillin/sulbactam, Cefepime and Meropenem (100%) and the lowest to Tobramycin (50%). *Acinetobacter lwoffii* was seen in 2 trachea samples. All samples were resistance to Meropenem, Cefpim, Ampicillin/sulbactam, ceftazidime, Imipenem, Piperacillin/tazobactam (100%). *Citrobacter spp.* were isolated from 3 urine samples. These isolates were resistant to ampicillin, Cefazolin, Nitrofurantoin (100%), and ceftazidime, Cefepime, ceftriaxone, ciprofloxacin, co-trimoxazole (75%). 2 samples were positive for *Klebsiella pneumonia* (urine and trachea). Resistance was seen to Ampicillin, Cefazolin, Cefepime, Cefotaxime, Ceftazidime, Nitrofurantoin, Co-trimoxazole, Imipenem, Ceftriaxone (100%) and Amikacin (50%). One blood sample had *Enterococcus* which resistance to Ampicillin, Erythromycin and Clindamycin (100%).

Conclusion: Due to the high variety of bacterial agents in infants and their weak immune system, it is recommended to determine these agents and treat them as soon as possible.

Keywords: NICU ward, Bacterial infection, antimicrobial resistance.





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Section: Bacteriology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBa-14

Antibiotic resistance patterns of urinary tract pathogens among pediatric patients in Akbar Children Hospital in Mashhad during 2023

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Abstract

Background and Aim: Pediatric urinary tract infection as one of the most common diseases affects both hospital and community settings, in inpatients and outpatients. The number of urinary tract infection cases reported every year is over 150 million. The aim of this study was to investigate patterns of resistance to drugs in bacteria that cause UTI, which were isolated from pediatric patients in Akbar children Hospital in Mashhad from 21 January 2023 to 21 June 2023.

Methods: We included children < 18 years old who had acute UTI signs with pyuria on urinalysis (white blood cell count > 10/high-power field) in the microbiology laboratory at Akbar Children Hospital in Mashhad. We assessed the susceptibility of *E. coli*, *Klebsiella*, *Enterococcus* and *Staphylococcus epidermidis* to antibiotics in the study group according to the CLSI guidelines from 21 January 2023 to 21 June 2023.

Results: Of the 2580 urine culture samples, 249 were positive, and 163 patients (65.46%) had *E. coli*, 39 patients (15.66%) had *Klebsiella*, 10 patients (4.02%) had *Enterococcus* and 7 patients (2.81%) had *Staphylococcus epidermidis*. Based on the CLSI guidelines, there was high resistance to Erythromycin and Clindamycin (66.67%), and much lower resistance to Nitrofurantoin (28.57%). For bacteria that were sensitive to antibiotics, vancomycin and linezolid had good results.

Conclusion: Our results reported that *E. coli* was the most common bacteria causing urinary tract infections in pediatric patients. Moreover, due to emergence of resistant bacteria worldwide, vancomycin and linezolid had the highest sensitivity in positive cultures and may be good options for urinary tract infections treatment.

Keywords: antibiotic resistance; community-acquired infection; urinary tract infection.





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2. Bacteriology (Poster Presentations)





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Venue:
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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBa-1

Investigating the effect of Chitosan nanocomposites and its derivatives on biofilm against *Staphylococcus aureus*: A Systematic Review

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Abstract

Background and Aim: Biofilm is one of the important virulence factors in multidrug-resistant bacteria that are developed worldwide. In recent years, biofilm in *S.aureus* bacterial infections has been one of the factors in the increasing mortality rate. It has been illustrated that Chitosan and its derivatives can have a positive effect on inhibiting *its* biofilm. This study, we investigated the effect of nanocomposites and chitosan derivatives in biofilm inhibition against *Staphylococcus aureus*.

Methods: This is a descriptive-analytical review study in which we searched international online English articles published in (Google Scholar, Web of Science, and PubMed databases) national (Sid, Magiran, and Cilivica) from 2018 until 2023. The keywords were biofilm, Chitosan, nanocomposite, and *Staphylococcus aureus*.

Results: *Staphylococcus aureus* biofilm is one of the critical vulnerable factors. Chitosan and its derivatives have been studied for their antibacterial biofilm ability. We found that nanocomposite Chitosan and its derivatives are used with hydrophobicity and its effectiveness and positive charge are synergistic on antibiotics. Recently, Chitosan nanoparticles used for hydrogel production and bacteriophage activities had a positive effect on biofilm ability. They can be used to treat wound biofilm caused by *S. aureus* with a combination of silver, zinc, and alginate derivatives. Biomacromolecules add functional groups with the mentioned antimicrobial to have higher effectiveness.

Conclusion: According to the results of this study, Chitosan is an excellent natural polymer that helps as a carrier and molecule for many sources such as antibiotics, bioactive compounds, essential oils, and antibacterials. Therefore, the results confirmed that the selected Chitosan nanocomposite is effective against *S. aureus* biofilm.

Keywords: *Staphylococcus aureus*; Biofilm; Chitosan; Nanocomposite.





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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-2

Isolation and molecular analysis of lytic bacteriophages against clinical isolates of *Pseudomonas aeruginosa*

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Abstract

Background and Aim: Due to the increasing antibiotic resistance and the unique antibacterial properties of bacteriophages, in recent years, using their high potential as an effective approach to combat bacterial infections Attention has been paid. This study was conducted with the aim of isolating lytic bacteriophages against *Pseudomonas aeruginosa*.

Methods: In this study, the number of one standard strain and ten isolates of *Pseudomonas aeruginosa* with antibiotic resistance were selected clinically and isolation of lytic phages against each of them was done by double-layer agar method, then host range of phages isolated was evaluated. In the next step, after extracting the genome of the isolated bacteriophages, their molecular analysis with Enzymatic digestion was done with EcoRV enzyme.

Results: At least one lytic phage was isolated against each isolate of *Pseudomonas aeruginosa*, which by examining the host spectrum, one of the phages showed a lytic effect against seven isolates used. Genome extraction of all phages was done successfully, and the genomes of all phages were of DNA type. In enzymatic digestion with EcoRV not enzymatic digestion

It was observed that one of the isolates was not subjected to enzymatic digestion.

Conclusion: Bacteriophages have a high potential to fight clinical infections caused by *Pseudomonas aeruginosa* bacteria. Despite this high potential, it is inevitable to widely use these antibacterial agents and check the exact characteristics of each of the phages in question.

Keywords: *Pseudomonas aeruginosa*, Antibiotic resistance, Bacteriophage.





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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-3

The role of genital infections in preterm birth: a case-control study

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Abstract

Background and Aim: Premature birth is defined as the beginning of the birth process before the 37th week of pregnancy. The presence of microorganisms in the fetal membranes is accompanied by an increase in the production of prostaglandin, which is one of the important factors associated with the prevalence of premature birth, and due to the invasion of microorganisms, protease, coagulase and elastase are produced, whose directly stimulates the onset of childbirth. the purpose of this study is to investigate the role of genital infections in women with premature birth.

Methods: This case-control study was conducted in the west of Iran. The present study was performed on 100 women with preterm delivery (after 24 weeks of gestation and before 36 weeks and six days) as the case group and 100 women with normal delivery as the control group. The research tool in this study was a questionnaire, Polymerase chain reaction (PCR) test and examination of the pathology of the placenta.

Result: The average age in women with normal delivery (30.92±5.10) in women with Preterm delivery (30.27±4.93). Alcohol consumption was zero for all groups. The highest level of education in all groups was high school. The prevalence of *Chlamydia tracheomatis*, *Neisseria gonorrhoea*, *Listeria monocytogenes* and *Mycoplasma genitalium* infections was zero in both groups. Also, the highest prevalence of *Gardnel vaginalis* 19(19%) and *Mycoplasma parvum* 15(15%) bacteria was in the control group.

Conclusion: The results of our study showed that, except the bacterial infection of *Gardenala vaginalis* other infections do not play a role in premature birth.

Keywords: Genital infections; Preterm delivery; Women; Iran.





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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-4

Investigating probiotic bacteria isolated from honey and their effects on CVD and high cholesterol risk factors

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Abstract

Background and Aim: Based on controversial evidence of the effects of honey on blood lipids, this systematic review and meta-analysis examined the effect of probiotics isolated from natural honey on reducing lipid profiles and hypercholesterolemia risk factors in atherosclerosis and cardiovascular disease (CVD). Consuming natural honey has many cardiovascular benefits and can improve fat profiles. Existing findings suggest that the use of probiotic supplements is effective in reducing lipid levels and coexistence factors associated with cardiovascular disease. Probiotic bacteria have attracted a lot of attention due to their ability to lower blood cholesterol in humans.

Methods: The variables studied include the duration of probiotic use, probiotic dosage, probiotic in capsule milk/yogurt, types of probiotic strains, single-probiotic strains versus multiple probiotic strains. A randomized controlled clinical trial was conducted to investigate the effects of natural honey in diabetic patients, and forty-eight diabetic patients were randomly placed in the honey intake group and received natural honey orally (the first 2 Weeks, 1 g / kg per day, the second week. 1.5 g / kg / day) for 8 weeks and the control group did not take honey. The results of this study showed a significant improvement in weight, TC, LDL and TG in the honey group relative to the control group. These studies were examined to assess the effects of probiotics on lipid profiling, which is considered an important factor of CVD.

Results: Probiotics against high cholesterol can act as an alternative medicine to reduce the risk of cardiovascular disease and other diseases. The potential for lowering probiotic cholesterol seems to depend on its species and strain. *Lactobacillus acidophilus*, *Lactobacillus plantarum*, and *Lactobacillus reuteri* have hypocholesterolemic properties. 6 trials showed a significant reduction in serum TC levels and four trials in serum LDL cholesterol levels using probiotics. However, the use of probiotics does not appear to significantly alter HDL cholesterol levels and TG levels, so this difference in data can affect results compared to other systematic reviews. Many patients prefer non-drug treatments and are cautious about the side effects of cholesterol-lowering drugs. Research showed that oral intake of honey at an average dose of 40 grams over an average period of 8 weeks led to beneficial reductions in ALT, total cholesterol, LDL-C and fasting triglycerides, and significant increases in HDL-C.

Conclusion: The results of the meta-analysis showed that probiotics are capable of lowering cholesterol and LDL, reducing CVD risk factors. It was found that experiments using multiple probiotic strains showed a statistically significant decrease in total cholesterol. Probiotics can act as an alternative medicine against high cholesterol to reduce the risk of CVD and other diseases. Honey consumption reduces total cholesterol, LDL-C, triglycerides, and increases HDL-C. More research is needed to understand how probiotics from bee products can be beneficial for the treatment system and perhaps other diseases.

Keywords: Hypercholesterolemia; Probiotics; Cardiovascular Disease; Cholesterol.





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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-5

Blood cultures and antimicrobial resistance patterns in children's hospitals in Qom

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Abstract

Background and Aim: Sepsis is a systemic inflammatory response to infection that threatens life in all age groups, especially infants. The treatment includes the use of antibiotics and supportive measures, which considering the differences in the more common microorganisms of each region, it is not reasonable to recommend an antibiotic regimen in all centers. The purpose of this study is to investigate the results of positive blood cultures and to determine the prevalence of sepsis with early and late onset, to determine the frequency of gram-positive and negative bacteria and their drug resistance pattern

Methods: In order to achieve the purpose of the study, the information of infants hospitalized in the neonatal intensive care unit and the neonatal unit of hospitals in Qom province was extracted from the medical records in a period of 16 months.

Results: The present study showed that sepsis with early onset was more prevalent (75%), the most common microorganisms in early and late onset were coagulase-negative staphylococcus and Escherichia coli, respectively. The highest antibiotic sensitivity was related to gentamicin and the highest resistance to clindamycin and erythromycin.

Conclusion: The research conducted in this field indicates the existence of differences in common organisms and their antibiotic sensitivity patterns.

Keywords: Blood cultures; antimicrobial resistance; children; hospitals, Qom.





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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-6

Determination immunogenic property of truncated MrpH.FliC as a vaccine candidate against urinary tract infections caused by *Proteus mirabilis*

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Abstract

Background and Aim: *Proteus mirabilis* is one of the common pathogens in Urinary tract infections (UTIs) especially in complicated UTIs which are resistant to antibiotic therapy, consequently, an ideal vaccine is inevitably required. The N-terminal domain of MrpH (Truncated form of MrpH) lies between the most critical antigens of *P. mirabilis* to consider as vaccine candidate. FliC of *Salmonella typhimurium* as adjuvant, induces several pathways of immunity system, which leads to produce antibody and cytokines. In this study, adjuvant properties of FliC and efficacy of truncated MrpH as important antigen, in tMrpH.FliC were determined in *in vitro* and *in vivo* circumstances.

Methods: *P. mirabilis* (HI4320 strain) and *S. Typhimurium* (ATCC 14028) were obtained from the Pasteur Institute of Iran. The best model of fusion protein selected by bioinformatics methods. Fusion *tmrph.flic*, *mrph* and *flic* genes amplified by overlap PCR. All genes were cloned and expressed, then purified proteins, confirmed by SDS-PAGE and Western blot. Three proteins including FliC, MrpH, and tMrpH.FliC were injected to mice and subsequently sera and supernatant of cell culture were collected to measure different immune responses comparing to control. In additional, *Proteus mirabilis* were injected to mice's bladders for challenging test. For comparing the differences between the mean parametric values of the mice groups, SPSS software was used. In all experiments $p < 0.05$ was considered significant.

Results: According to our findings, tMrpH.FliC could stimulate both humeral and cellular immune responses, so that serum IgG, urine IgA, IL.4, IFN- γ and IL.17 were increased significantly in comparison to MrpH and FliC alone and control groups, this augmentation was considerable. Results of challenging test showed significant decrease of bacterial load in all of the challenged groups compared to the control group, although this protective effect was the highest in mice vaccinated with tMrpH.FliC.

Conclusion: Our results showed truncated MrpH, without an unwanted domain is an ideal vaccine target and FliC, as adjuvant, increases its immunogenic property. Thus, fusion protein tMrpH.FliC can increase both humoral and cellular immune responses in UTIs and can be considered as promising vaccine against *P. mirabilis*.

Keywords: *Proteus mirabilis*; Urinary tract infections; MrpH; FliC.





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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-7

The inhibitory effect of silver nanoparticle on the expression of biofilm-forming gene (*bap*) in antibiotic-resistant *Acinetobacter baumannii* using real-time PCR method

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Abstract

Background and Aim: *Acinetobacter baumannii* is one of the common pathogens in hospitals, which has become resistant to many antibiotics due to the production of biofilm.

It has made it difficult to treat. Nowadays, silver nanoparticles have wide applications in medicine due to their suitable chemical and physical properties. In recent years, nanotechnology has been able to create deep changes in the field of research and production of products. Due to the resistance of *Acinetobacter baumannii* to antimicrobial drugs, in this study, the effect of silver nanoparticle biofilm on inhibiting the growth of this bacterium has been investigated.

Methods: In this experimental study, *Acinetobacter baumannii* strains were isolated from clinical samples. After identifying the strains

Acinetobacter baumannii and determination of their microbial resistance by antibiogram, ability to form biofilm of strains at 37 degrees Celsius. It was evaluated for 24 hours. The MIC of the strains against silver nanoparticles was determined, the treatment of the strains. It was done with a concentration below the inhibitory limit, and RNA extraction and cDNA synthesis were done. Finally, evaluation of Bap biofilm formation gene expression with the use of Real Time PCR method was investigated.

Results: Among the 10 clinical samples of *Acinetobacter baumannii* collected from the ICU department, the PCR results showed that all 10 strains had Bap biofilm formation gene. The Real Time PCR results showed that following the treatment of the strains with

SubMIC concentration of silver nanoparticles, all strains had a significant decrease in Bap gene expression ($0.05 < P$) compared to the control gene.

Conclusion: Using nanoparticles to deal with bacterial infections is one of the most effective methods. *Acinetobacter baumannii* is sensitive to silver nanoparticles and considering the anti-biofilm effects of silver nanoparticles, it seems that it can be used as a drug candidate in pharmaceutical industry.

Keywords: *Acinetobacter baumannii*; Silver Nanoparticles; MIC and MBC.





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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-8

Investigating the causes of pneumonia resistant to outpatient treatment, using multiplex real-time PCR method

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Abstract

Background and Aim: Diagnosis of infectious agents based on conventional techniques has challenges such long time of detection and negative results. Bacterial pneumonia is divided into two categories in terms of how it is contracted: hospital-acquired pneumonia and community-acquired pneumonia. Regarding large number of patients with pneumonia resistant to treatment this study aimed to evaluate the causes of pneumonia in the city of Khorramabad.

Methods: In this study, twenty patients with pneumonia resistant to outpatient treatment were randomly selected. The sputum specimens were subjected for extraction of DNA then analyzed with multiplex real time PCR. Factors involved in community acquired pneumonia (CAP) and hospital acquired pneumonia (HAP) were assessed in just one reaction.

Results: The mean age of patients was 57years; 61% were male and 39% female. The average length of hospitalization was 4 days. Mycoplasma pneumonia was the most detected organism from sputum specimens (52%). The other organisms including Klebsiella pneumoniae (30%), Staphylococcus aureus (12%), Pseudomonas aeruginosa (6%). The most commonly used antibiotic before hospitalization was azithromycin. The best therapeutic response was achieved with coadministration of levofloxacin and ceftioxone.

Conclusion: Two major problems make it difficult to diagnose acquired pneumonia Incites from society: Most patients are able to produce sputum are not; And about 10% of patients before a sample for Check them, they have taken antibiotics. Mycoplasma pneumonia was mostly detected and regarding primary response to macrolides had an appropriate response to respiratory fluoroquinolones. The performed technique in addition to shortening the diagnostic time and saving costs has determined the protocol of treatment.

Keywords: Atypical pneumonia, Multiple PCR, Respiratory fluoroquinolones.





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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-9

Characteristics of carbapenem-resistant *Klebsiella pneumoniae* among hospitalized patients in Tehran, Iran

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Abstract

Background and Aim: Resistance to carbapenem is one of the prominent issues in treating serious infections caused by *Klebsiella pneumoniae* in the hospitals. This study aimed to investigate the prevalence of *K. pneumoniae* isolates producing carbapenemase, and molecular characteristics of carbapenemase genes in *K. pneumoniae* isolates in a hospital in Tehran, Iran.

Methods: This cross-sectional study was performed on 380 clinical isolates of *K. pneumoniae* isolated from different wards in one of Tehran hospital during 2018-2020. Following the biochemical identification of the isolates, their antibiotic resistance was evaluated. Genes of *bla_{NDM}*, *bla_{OXA-48}*, *bla_{KPC}*, were identified in carbapenem-resistant isolates by PCR.

Results: Of the 380 isolates, 49.4% (n= 136/ 275) *K. pneumoniae* isolates were carbapenemase producers. Among carbapenemase-producing isolates, *bla_{OXA-48}* and *bla_{NDM}* were the dominant genes.

Conclusion: Our findings revealed the high prevalence of carbapenem resistant isolates, likely due to the excess clinical use of these antibiotics. The higher prevalence of *bla_{NDM}* gene in isolates could indicate the higher incidence of a specific clone that contribute to the acquisition of resistance genes among patients, which demands for further investigation in future studies.

Keywords: *Klebsiella pneumoniae*, Carbapenemase, Colistin resistance, Hospital infection.





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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Case Report/ Case series

Code of Abstract: PBa-10

Rapid Detection of *Salmonella enterica* serovar typhimurium in Milk powder by PCR Method

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Abstract

Background and Aim: *Salmonella enterica* serovar *Typhimurium* is a primary enteric pathogen which is considered as the causative agent of Salmonellosis in human especially infants and children younger than 4 years. It generally infects the intestinal epithelium with the ingestion of contaminated food or water. Milk Powder is a dairy product which is made by evaporating milk to dryness. *Salmonella* as a food born pathogen can resist in the milk powder and spread in the manufacture environment during the packing process. Since powdered milk is extremely used in food industry such as baby food production and cake and chocolate industries, the importance of detection of *Salmonella enterica* serovar *typhimurium* has been considered with high value especially for baby food and those foods which are exported to European countries. Since the detection of *S. typhimurium* with traditional culture and serotyping methods is time consuming and expensive, we set up a PCR test with high sensitivity and specificity (>99% and >95% respectively) for identification small amounts of infection with *Salmonella* bacteria in samples.

Methods: 273 powdered milk and chocolate raw material were sent to our lab for identification of *Salmonella enterica* serovar *Typhimurium* by PCR. DNA was extracted separately from all the 273 samples using DNA extraction Kit (*MBST-Iran*) according to the manufacturer protocol. *S.typhimurium* specific primer pairs were picked (Denis et al, 2001) and synthesized by Sinaclone (*Sinaclone-Iran*). Separate PCR reaction tests were done in total volume of 25 µl followed by PCR Program in Thermo cycler *PEQ LAB (Primus-ITALY)* at 94 ° C for 5 minutes followed by 40 cycles of 94 ° C for 55 seconds, annealing temperature of 59 ° C for 1:30 S and 72 ° C for 1 minute. All PCR assays were done according to the standard protocol using specific primer pairs designed. In parallel, positive and negative controls were performed which gave the expected and correct results. PCR products were analyzed by Ethidium Bromide stain after separated on the *Agarose* gel electrophoresis in comparison to DNA Ladder of 50 bp (*Sinaclon, IRAN*).

Results: 21 out of 273 samples (7.69%) were detected as positive by PCR. One of the positive samples and the positive control PCR products were sent for sequencing (*Codon lab-Iran*) as the golden standard comparison test. The positive sample showed 98% similarity with the positive control salmonella strain.

Conclusion: Gastrointestinal infection by *S. enterica* serovar *typhimurium* is considered as a serious disease in infants and children younger than 4 years old. PCR method with high sensitivity and specificity is can detect *Salmonella* infection in children's food rapidly. The rate of infection in powdered milk (7.7%) in our study, shows the importance of using PCR method instead of culture traditional detection method which cannot be useful in detection of small amounts of the bacterial infection. The PCR test can be considered as a rapid, economic test with sensitivity and specificity higher than the traditional method for identification the *Salmonella* serovars in food and patient taken samples as well.

Keywords: Salmonella; PCR; Children; Powdered milk; Serovar.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-11

Frequency of diarrheagenic *Escherichia coli* types in Semnan health centers diarrheic referrals

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Abstract

Background and Aim: Diarrhea is known as one of the causes of morbidity and mortality in children. Especially in developing countries, one of the most important bacterial agents is diarrhoeagenic *Escherichia coli*. Six different types of Diarrhoeagenic *Escherichia coli* have been identified. Prevalence of diarrhoeagenic *Escherichia coli* different types is vary in different regions of the world. This study tries to determine the frequency of diarrhoeagenic *Escherichia coli* different types in Semnan health centers diarrheic referrals.

Methods: This study included 73 stool samples from Semnan Health Centers diarrheic referrals. Samples were preserved in Stuart transport medium, transferred to the Health Reference Laboratory and cultured on MacConkey agar or EMB agar. Suspected colonies were identified by conventional bacteriological tests, and the presence of LT, ST, VT1, VT2, SHIG, EA, eae, bfpA was investigated by specific Polymerase Chain Reaction (PCR) assay.

Results: Of the 73 stool samples, 21 samples (28.7%) did not react with using primers, so identified as normal stool flora. 21 samples (28.7%) included overlapping types and showed over than one type. 38 samples (52%) identified as Enterotoxigenic *Escherichia coli* (ETEC). 27 samples (37%) as Enteroaggregative *Escherichia coli* (EAEC). 10 samples (13.6%) as Enteroinvasive *Escherichia coli* (EIEC). 3 samples (1.4%) as Enteropathogenic *Escherichia coli* (EPEC), and 1 sample (1.3%) as Enterohemorrhagic *Escherichia coli* (EHEC).

Conclusion: According to the results, the ETEC is the most frequent diarrheagenic *Escherichia coli* type in Semnan Health Centers diarrheic referrals. Epidemiological investigation about bacterial dissimilation source, also special attention to diarrheagenic *Escherichia coli* diagnosis and treatment were recommended.

Keywords: *Escherichia coli*, Diarrhea, PCR.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review/Meta-analysis

Code of Abstract: PBA-12

The inaugural worldwide assessment of multi-drug resistant *Haemophilus Influenzae*: a comprehensive review and meta-analysis

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Abstract

Background and Aim: Much like other bacteria, the rise in antibiotic resistance in *Haemophilus influenzae* presents significant challenges to global healthcare. This study conducts a comprehensive meta-analysis on the worldwide epidemiology of multi-drug resistant (MDR) *H. influenzae*.

Methods: We performed a meta-analysis following the PRISMA checklist, reviewing electronic databases such as PubMed, ISI Web of Science, Scopus, EMBASE, and Google Scholar using keywords related to *H. influenzae* and antibiotic resistance. Stringent inclusion and exclusion criteria were applied to select eligible studies, with data from these studies analyzed using the Comprehensive Meta-Analysis (CMA) software.

Results: Out of the 375 articles retrieved, 16 met the inclusion criteria. These studies, conducted between 2003 and 2023, analyzed data from 19,787 clinical isolates of *H. influenzae*. The findings indicated varying levels of resistance in *H. influenzae* to different antibiotics, with ampicillin (36%), azithromycin (15.3%), and ceftriaxone (1.4%) being notable examples. The global prevalence of beta-lactamase-producing *H. influenzae* and MDR *H. influenzae* stood at 34.9% and 23.1%, respectively. MDR *H. influenzae* exhibited a higher prevalence in Asian countries compared to Western regions. MDR *H. influenzae* was most prevalent in meningitis cases (46.9%) and least prevalent in acute otitis media (0.5%).

Conclusion: Unfortunately, the prevalence of MDR *H. influenzae* has significantly increased, particularly in Asian regions. This underscores the immediate need for global monitoring and the implementation of effective antibiotic stewardship programs.

Keywords: Beta-lactamase; Drug resistance; *Haemophilus influenzae*; Meta-analysis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Meta-analysis

Code of Abstract: PBa-13

The universal prevalence of primary antibiotic resistance in *Helicobacter pylori* Clinical isolates of children: a systematic review and meta-analysis

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Abstract

Background and Aim: The profile of *Helicobacter pylori* (*H. pylori*) infection is different in children and adults in terms of epidemiological aspects, clinical features, diagnosis, as well as therapeutic regimen. In the present study, we evaluated the global prevalence of primary antibiotic resistance of *H. pylori* in children worldwide in the past 30 years.

Methods: A computer-assisted literature search was performed using relevant keywords in electronically databases such as ISI Web of Science, PubMed, Scopus, and Google Scholar. The primary antibiotic resistance in children was measured through the event rate with 95% confidence interval. We also measured the trend of antibiotic resistance over the last 22 years. All statistical analyses were performed using Comprehensive Meta-Analysis software version 2.2.

Results: A total of 117 eligible studies including 57,276 children were included in this meta-analysis. Primary antibiotic resistance to antibiotics such as clarithromycin, metronidazole, amoxicillin, tetracycline, levofloxacin, ciprofloxacin, furazolidone, nitrofurantoin, and rifampin was 25.6%, 30.9%, 2.5%, 2.0%, 12.1%, 6.9%, 1.9%, 0.5%, and 9.1%, respectively; the prevalence of multi-drug resistant (MDR) *H. pylori* isolates was also measured at 4.5% among children through the worldwide.

Conclusion: Given the differences in the primary antibiotic resistance of *H. pylori* in all countries, treatment regimens should be optimized depending on the geographical area and the results of antimicrobial susceptibility testing. Statistical analyses of this study show that the trend of antibiotic resistance is increasing in different geographical areas, which in turn will lead to ineffectiveness of therapeutic regimens containing clarithromycin and tetracycline in future years.

Keywords: Antibiotic resistance; Children; *Helicobacter pylori*; Infection.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-14

Catheter-associated urinary tract infection and drug resistance patterns of bacterial isolates in northern Iran

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Abstract

Background and Aim: Catheter-associated urinary tract infection (CAUTI) is one of the most common types of healthcare-associated infections and a major cause of morbidity. The aim of this study was to evaluate antimicrobial susceptibility profiles and factors associated with catheter-related urinary tract infections.

Methods: This study was a cross-sectional study conducted at Poursina Hospital in northern Iran from 2018 to 2022. This study was carried out on a total of 733 urine cultures. The catheter urine samples were collected in well preserved containers and transferred promptly to the microbiology and laboratory unit, and were cultured on the selected medium cultures. Subsequently, antimicrobial sensitivity tests were performed using the standard Kirby-Bauer disk diffusion method. Antimicrobial susceptibility testing against uropathogens was determined by the disk diffusion zone of growth inhibition and MIC values (susceptible (S) and resistant (R) categories) according to the CLSI criteria. Patients' demographic and clinical information and laboratory data were recorded and analyzed.

Results: A total of 36 patients were diagnosed with CAUTIs, of whom 52.78% were male and 47.22% were female. The mean age was 60.3 ± 21.4 years. The mean length of infection development and hospital stay were 14.1 ± 18.1 and 34.6 ± 25.3 days, respectively. The mean duration of catheter insertion until infection were 10.1 ± 14.4 days. Majority of the tested samples were in the general intensive care unit and internal neurology (33.3% and 25.0%, respectively) and the large number (61.1%) of them had an underlying disease. The microbiological identification showed that *Enterobacter* was the most common pathogen (36.1%), followed by *Escherichia coli* (27.8%). *Enterobacteriaceae* had the highest resistance against ceftazidime with 72.7% followed by cefepime with 66.7% and ciprofloxacin with 47.1%. *Pseudomonas aeruginosa* isolates were completely resistant to ceftazidime and cefepime. Coagulase-negative staphylococci were also resistant to erythromycin, penicillin, and tetracycline.

Conclusion: The majority of bacterial isolates had higher rates of resistance to commonly prescribed antimicrobials, so the treatment and management of CAUTIs should be based on the knowledge of bacterial patterns of antibiotic resistance and etiology. Periodic monitoring of antimicrobial resistance patterns can help physicians in selecting antimicrobial agents for empiric treatment of CAUTIs.

Keywords: Catheter; UTI; Uropathogens; Antimicrobial resistance.





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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Meta-analysis

Code of Abstract: PBa-15

Comparison of piperacillin-tazobactam vs. carbapenems for eradication of ESBL-pathogens: A systematic review and meta-analysis

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Abstract

Background and Aim: There are serious global concern regarding the increase of extended-spectrum β -lactamase (ESBL)-producing Gram-negative bacteria. This systematic review and meta-analysis were performed to assess the clinical efficacy and safety of piperacillin-tazobactam (PTZ) in comparison with carbapenems for cure of ESBL-pathogen-related infections.

Methods: We performed a comprehensive search using several databases e.g., Medline (via PubMed), Scopus, Embase, and Cochrane until September 2023. The clinical effectiveness of piperacillin-tazobactam was studied using odds ratio corresponding 95% confidence intervals. Subgroup analysis examined geographic and infection-type variations. Meta-regression was also conducted to explored potential source of heterogeneity. Publication bias was investigated via Egger's and Begg's tests, with subsequent adjustment via the trim-fill method.

Results: We analyzed 20 studies from 2011 to 2023 involving 3,623 patients with ESBL-producing infections. In the PTZ group, clinical cure rate was 87.2% (95% CI: 80.7-91.7), with lower carbapenem-resistant organism prevalence (5.5%) and adverse outcomes, including death rate (8.9%), relapse rate (6.9%), and ICU admission rate (15.7%). Carbapenem group had clinical cure rate of 85.8%, with death rate of 14.5%, ICU admission rate of 22.9%, and relapse rate of 8.7%. PTZ showed superiority in reducing death rate (OR: 0.61; 95% CI: 0.44-0.83), relapse cases (OR: 0.7; 95% CI: 0.51-0.97), and carbapenem-resistant organisms (OR: 0.56; 95% CI: 0.33-0.94). Subgroup analysis showed consistent results in Asian trials but not the Western Hemisphere. PTZ significantly reduced death rates among urinary tract infection patients (OR: 0.49) and death rates, ICU admissions, and relapse rates in bloodstream infection cases. Meta-regression identified latitude as a significant factor affecting clinical efficacy.

Conclusion: PTZ demonstrated favorable clinical efficacy and safety profiles in treating ESBL-producing infections compared to carbapenems, with significant reductions in death rates, relapses, and carbapenem-resistant organisms. Geographic variation highlights population origin's influence on clinical outcomes, warranting further research to guide clinical practice.

Keywords: Piperacillin-tazobactam; Carbapenem; Extended-spectrum β -lactamases; Gram-negative bacteria.





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Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review/Meta-analysis

Code of Abstract: PBa-16

Global occurrence and patterns of multi-drug resistant *Mycobacterium leprae*: an in-depth meta-analysis

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Abstract

Background and Aim: Leprosy, caused by *Mycobacterium leprae*, has traditionally been addressed through a combination of drugs. Nevertheless, the emergence of drug resistance, particularly multi-drug resistance (MDR), has become a significant cause for concern. This study aimed to assess the worldwide prevalence of MDR-*M. leprae* and its consequences.

Methods: Following PRISMA guidelines, we systematically examined databases, including ISI Web of Science, MEDLINE, EMBASE, and Google Scholar, up to August 2023, to investigate the prevalence of MDR *M. leprae*. We exclusively included human clinical trials with a specific focus on MDR-*M. leprae*, excluding reviews, animal studies, and studies lacking full texts. Bias was evaluated using the Joanna Briggs Institute checklist. Data were analyzed using Comprehensive Meta-Analysis (CMA) software, incorporating subgroup analysis, sensitivity analysis, and evaluation of heterogeneity. The assessment of publication bias utilized Egger's and Begg's tests, as well as the trim-fill method.

Results: From the extensive database search, we initially identified 861 articles, of which 27 met the methodological criteria for inclusion in the quantitative synthesis. Covering the years 2001-2021, these studies examined the global prevalence of MDR-*M. leprae*. Statistically, the overall prevalence of DR-*M. leprae* was estimated at approximately 11.7% (95%CI: 7.7-17.3; I²: 90.79; p=0.01). Specific drug resistance rates included 7.4% to dapsone and 5.1% to rifampin, among others. Notably, temporal data revealed an increase in DR-*M. leprae* prevalence after 2010. The global rate for MDR-*M. leprae* was 2.2% (95%CI: 1.2-3.9; I²: 82.68; p=0.01). Variations were observed across WHO regions, with distinct temporal trends indicating an increasing prevalence over two decades. Factors such as bacterial density and the lepromatous phase were associated with an increased risk of DR-*M. leprae* (OR: 2.69; 95%CI: 1.35-2.48). A systematic evaluation of publication bias, including Begg's and Egger's p-value methodologies, indicated minimal influence on the overall results.

Conclusion: The growing prevalence of MDR-*M. leprae* on a global scale calls for immediate and strategic interventions to curb further dissemination and ensure effective treatment for individuals affected by leprosy.

Keywords: Drug Resistance; Meta-Analysis; *Mycobacterium leprae*; Prevalence





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Tehran University of Medical Sciences, Tehran, Iran.
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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review/Meta-analysis

Code of Abstract: PBa-17

Advancing *Mycobacterium tuberculosis* detection: an assessment of CRISPR technology's diagnostic precision via a comprehensive meta-analysis

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Abstract

Background and Aim: The rapid and accurate detection of *Mycobacterium tuberculosis* (MTB) is crucial for the effective management and control of tuberculosis. Clustered regularly interspaced short palindromic repeats (CRISPR) technology has emerged as a promising tool for diagnosing pathogens due to its precision and flexibility. This systematic review and meta-analysis aimed to assess the diagnostic precision of CRISPR-based methods in identifying MTB.

Methods: A thorough search was conducted in Medline, Scopus, Embase, and ISI Web of Science to gather relevant studies following PRISMA guidelines. Quality assessment was performed using the Joanna Briggs Institute checklist. Data synthesis and analysis, including subgroup examinations, were carried out with Meta-Disc 1.4, investigating variables such as CRISPR variants, gene targets, pre-amplification techniques, and signal readout methods.

Results: Out of 341 studies initially identified, 13 met the inclusion criteria, involving a total of 1,572 MTB strains. CRISPR-based techniques exhibited a pooled sensitivity and specificity of 0.91 (95%CI: 0.89-0.92) and 0.97 (95%CI: 0.95-0.98), respectively. The pooled diagnostic odds ratio was 498.67 (95%CI: 255.1-974.7), with an AUC of 0.99 on the SROC curve, indicating excellent diagnostic accuracy. Subgroup analyses revealed differences in diagnostic parameters based on factors such as the CRISPR variant used, target gene, and pre-amplification methods. For example, CRISPR-Cas12 demonstrated a sensitivity and specificity of 0.89 (95%CI: 0.86-0.91) and 0.98 (95%CI: 0.96-0.99), respectively, while utilizing RPA for pre-amplification showed 0.87 (95%CI: 0.83-0.90) and 0.99 (95%CI: 0.97-1.0), respectively.

Conclusion: CRISPR-based approaches exhibit significant diagnostic sensitivity and specificity for MTB detection, with noticeable variations depending on the specific CRISPR variant and methodological approach employed. These findings underscore the potential of CRISPR as a diagnostic tool for MTB, with opportunities for optimization in various clinical and research settings.

Keywords: CRISPR-Cas Systems; Meta-Analysis; *Mycobacterium tuberculosis*; Sensitivity and specificity.





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Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-18

Evaluation of antibacterial activity of antimicrobial peptide against Gram-Negative and Gram-positive bacteria

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Abstract

Background and Aim: Antimicrobial resistance reduces the efficacy of antibiotics. Infections caused by multidrug-resistant (MDR) bacterial strains, are a serious threat to global health. However, cationic antimicrobial peptides (CAMPs) are promising as an alternative therapeutic strategy against MDR strains. In this study, the inhibitory activity of a cationic peptide, derived from *Cichorium intybus L.*, against Gram-Negative and Gram-positive clinical isolates, were evaluated.

Methods: In this study, Isolation of antibacterial peptide from the chicory flower was performed based on the method purified via reverse-phase HPLC chromatography. In vitro antibacterial activity was determined using the broth microdilution test against the *Staphylococcus aureus* ATCC29213, *Escherichia coli* ATCC25922, *Pseudomonas aeruginosa* ATCC27853, *Acinetobacter baumannii* ATCC19606 strains. The minimum inhibitory concentration (MIC) was considered the lowest peptide concentration that inhibited the growth of bacteria. The minimum bactericidal concentration (MBC) test determines the lowest concentration of antibacterial peptides to kill the organism.

Results: The antibacterial peptide possesses broad spectrum activity against Gram-positive and Gram-negative bacteria. A strong bactericidal effect of this peptide against the tested strains, with the MIC values ranged from 2 to 4 µg/mL and the MBC values range from 4 to 8 µg/mL was observed.

Conclusion: The results described here support the future development of plant peptides as new therapeutic substances against bacteria.

Keywords: Antimicrobial peptide, *Chicory* flower, Minimal inhibitory concentration, Minimum bactericidal concentration.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-19

The frequency of Brucella seropositive cases in suspected children of Sari, during the years 2021-2023

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Abstract

Background and Aim: Brucellosis is one of the most frequently encountered zoonotic diseases, with approximately 500000 cases identified annually worldwide. In children, the onset of brucellosis can either be acute or insidious. Serious complications include meningitis, osteomyelitis, endocarditis, pneumonitis, and aortic involvement. Laboratory diagnosis of brucellosis is often accomplished by serologic testing. This study aimed to investigate the seropositivity of Brucella in suspected children referred to the laboratory in Sari.

Methods: In a cross-sectional study, blood samples were collected from 401 suspected brucellosis individuals referred to the laboratory. The study was conducted on children aged 1 to 12 years. Wright, 2-Mercaptoethanol (2-ME), or Coombs-Wright tests were conducted for them. Children with an antibody titer in the Wright or Coombs-Wright test equal to or higher than 1:40 or 2-ME more than 1:20; were considered seropositive. Individuals were categorized based on age and gender.

Results: In this study, 229 people (56.6%) were male. 30 people (7.48%) were seropositive. The average age of seropositive individuals was 6 ± 3 years. There was not a significant relationship between seropositivity and gender, with females at 7.6% and males at 7.4%. Additionally, 9 seropositive individuals (30%) were referred to the laboratory between 22 June and 22 July.

Conclusion: The findings suggest that brucellosis is still a prevalent zoonotic disease in Iran, especially among children who are exposed to livestock and dairy products. Therefore, preventive measures, such as vaccination, education, and screening, are recommended to reduce the burden of this infection.

Keywords: Brucellosis, Children, Prevalence, Serological diagnosis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-20

Infectious diseases and Risk of Dementia

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Abstract

Background and Aim: Bacterial infections can activate microglia, which are unique immune cells found in the brain. Microglia, the resident macrophage populations in the parenchyma of the central nervous system (CNS), are considered as the first line of defense against invasive infections. Possessing an extensive repertoire of pattern recognition receptors, microglia are able to detect and eradicate microorganisms that invade the CNS parenchyma. Furthermore, a wide variety of pro-inflammatory cytokines and chemokines are released with microglial activation, and these play a role in drawing in and activating peripheral immune cells that invade the diseased central nervous system. Inflammation in the brain can be caused by this function that is thought to be involved in the progression of dementia by causing nerve cell death. This review aims to enhance understanding of the impact of infectious diseases on cognitive trajectories and encourage additional research in this area.

Methods: The search in reputable scientific sites and journals with suitable keywords.

Results: According to recent epidemiological research, there is a clear link between neurological problems and persistent microbial infections. Our review indicates that sepsis, pneumonia, UTIs, and cellulitis may be linked to an elevated risk of dementia. Pathogens can reach the brain via the olfactory system, blood circulation, and vagus nerve pathway. In the CNS, neural immune cells can be stimulated upon infection and induce inflammatory responses, causing neuroinflammation, which further leads to neuronal death. However, with biological intricacy of interactions between multiple cells and organs during microbial infections, the underlying mechanisms remain unclear. As the evidence about this topic has been restricted by a paucity of studies and small sample sizes, more extensive research is required to examine the impact of infections on cognitive decline.

Conclusion: Studies on animals and humans indicate that bacterial infections are associated with an increased risk of dementia in the future. Taken together we speculate that suitable targeting neuropathogens may represent a potential preventive and therapeutic approach for neurodegeneration. To further explore this association, more large-scale longitudinal research conducted in diverse healthcare contexts is recommended.

Keywords: infectious diseases; dementia; cognition; inflammation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-21

Isolation and identification of anaerobic bacteria in sputum samples of cystic fibrosis patients by culture-based methods

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Abstract

Background and Aim: Cystic fibrosis (CF) is a congenital lung disease with an autosomal recessive inheritance pattern due to a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. A defect in this gene leads to an increase in the thickness of the mucus in the lungs of patients, leading to the creation of anaerobic conditions and the colonization of anaerobic bacteria. The aim of this study is to identify the anaerobic bacteria in clinical samples of CF patients.

Methods: Sputum samples collected from 50 CF patients during 2021 to 2022 in Tehran, Iran. Clinical samples were cultured on four media: brucella blood agar containing hemin and vitamin K1 (BA), brain heart infusion agar containing sheep blood, vancomycin, hemin, vitamin K1 (BHI), brucella blood agar containing lakedsheep blood, kanamycin, vancomycin, hemin and vitamin K1 (LKV), brucella blood agar containing sheep blood, vancomycin and neomycin (VN). Then, the microscopic and macroscopic characteristics of the pure isolates were investigated with gram staining, hemolysis, pigment, oxygen tolerance, antibiotic disks kanamycin (1000 µg), vancomycin (5 µg) and colistin (10 µg), 20% bile tolerance and catalase tests. Gram-positive isolates were identified by molecular method using 16S rRNA sequencing.

Results: A total of 12 (24%) obligate and facultative anaerobic bacterial isolates were isolated and identified from 50 sputum samples. The isolated Gram-negative strains (n=6, 12%) include *Dialister* spp. (n=1), *Fusobacterium* spp. (n=4) and *Prevotella* spp. (n=1) and the isolated Gram-positive strains (n=6, 12%) include *Lactobacillus salivarius* (n=1), *Lactobacillus rhamnosus* (n=2), *Lacticaseibacillus paracasei* (n=1) and *Lactobacillus* spp. (n=2). Also, the obtained results indicated that the most isolated Gram-negative anaerobic bacteria are *Fusobacterium*.

Conclusion: The results obtained from this investigation confirmed the presence of culturable anaerobic bacteria in the sputum samples of CF patients. The prevalence of gram positive and gram-negative bacteria is almost equal. All Gram-positive isolates belonged to *Lactobacillus* genus. The prevalence of *Fusobacterium* is higher than other isolates identified in this study.

Keywords: Cystic fibrosis; Anaerobic bacteria.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-22

Characterization of resistance to aminoglycosides and Fluoroquinolones among biofilm producing *Staphylococcus aureus* strains isolated from urinary tract infection in Isfahan during 2017

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Abstract

Background and Aim: *Staphylococcus aureus* strains have emerged to be an important cause of urinary tract infection (UTI) both in community-acquired UTI (Com-UTI) and catheter-associated urinary tract infection (CA-UTI). This study aimed to establish the relationship between clonal groups, biofilm formation, and antibiotic resistance among *S. aureus* strains isolated from patients with symptomatic UTIs in a referral hospital in Isfahan, Iran, in 2017.

Methods: All isolates were identified using specific primers for *nucA* gene and the capacity of strains to form biofilm was evaluated by combination of the microtiter plate and Congo-red agar methods. Antibiotic susceptibility patterns were determined using the disk diffusion method, and the presence of genes involved in the biofilm formation and resistance to ceftiofexim, aminoglycosides and fluoroquinolones were detected using separate polymerase chain reaction (PCR). Staphylococcal cassette chromosome *mec* (SCC*mec*) typing, *agr* typing, and PhP typing were employed to explore the diversity of collected strains.

Results: Totally, 19, 57, and 24% of confirmed *S. aureus* strains were classified as strong, intermediate, and non-biofilm-forming strains, respectively. The highest rate of resistance was found to nalidixic acid (77%), followed by streptomycin (73%), azithromycin (46%), erythromycin (44%), ceftiofexim (44%) and tobramycin (41%). Moreover, 36 resistance patterns were determined among biofilm producing strains. The *icaD* and *icaA* genes had the highest frequency among biofilm-producing strains & *gyrA* (44%) and *griA* (35%) were the most frequent genes among fluoroquinolone resistant strains. Moreover, *aph(3')-IIIa* was detected as the most prevalent aminoglycoside-modifying enzyme gene. On the other hand, the majority of bacterial strains harbored the SCC*mec* type III and *agr* type I. Moreover, 24 and 76% of strains were classified as community acquired MRSA (CA-MRSA) and hospital acquired MRSA (HA-MRSA), respectively. PhP typing of strains revealed the presence of 8 common types (CTs) and 14 single types (STs) among all, in which CT2 was the dominant type.

Conclusion Our results revealed the presence of various biofilm production capacities, antimicrobial resistance profiles and clonal lineages in *S. aureus* isolated from patients with UTIs.

Key words: biofilm formation, antimicrobial susceptibility pattern, urinary tract infection, SCC*mec* typing.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-23

Eugenol reduces the function of AcrAB-OprM pump in *Escherichia coli*

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Abstract

Background and aim: Multidrug resistance is a significant concern in healthcare settings, as it can limit the effectiveness of commonly used antibiotics and antimicrobial therapies. Efflux pumps are one of the main mechanisms of antibiotic resistance in bacteria. In this study, we aimed to investigate the effect of eugenol, a natural compound with potential antimicrobial properties, on the AcrA efflux pump in *Escherichia coli*.

Methods: Molecular docking was performed using PachDock Server 1.3 to explore the potential binding interactions between eugenol and AcrA efflux pump. The effect of eugenol on bacteria was assessed by SubMIC. The phenotypic analysis was conducted using the cartwheel test.

Results: The results of molecular docking showed eugenol molecule reacts with amino acids LEU279, LEU260, LEU226, LEU230, GLU229, GLU261, PHE262, PHE223, LYS227 and LYS236 in the AcrA pump. Also, the binding energy for the pump AcrA was $-28.59\text{Kcal.mol}^{-1}$. The sub-MIC concentration of eugenol was determined for *E. coli* 6.64mg.ml^{-1} . In addition, the cartwheel test demonstrated that eugenol can inhibit the efflux pump.

Conclusion: By conducting these comprehensive studies, researchers can gain a deeper understanding of the potential of eugenol as a significant effective compound in reducing antibiotic resistance against resistant bacteria.

Keywords: Eufllux pump, Antibiotic resistance, Eugenol, *AcrA*.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-24

Characteristics of Prophage Patterns and Virulence Gene Profiles among Methicillin-Resistant *Staphylococcus aureus* Isolates from Patients with Diabetic Foot Infections in a Referral Hospital in Tehran, Iran

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Abstract

Background and Aim: Diabetic patients are at risk of developing serious foot infections with methicillin-resistant *Staphylococcus aureus* (MRSA) strains, which are associated with high morbidity and mortality. This study aimed to investigate the frequency of different prophage types and virulence factors among MRSA strains isolated from patients with diabetic foot infections (DFIs) in a referral hospital in Tehran, Iran during 2019 and 2020.

Methods: A total of 238 *S. aureus* isolates were collected and confirmed using specific primers. The presence of staphylococcal enterotoxins (*sea-seq*) and *hly*, *sak*, *eta*, *etb*, and *tsst-1* genes among MRSA isolates was tested using separate polymerase chain reaction (PCR) assays. Also, multiplex PCR was employed for prophage typing of MRSA isolates.

Results: A total of 73 (31%) isolates were confirmed as MRSA, among which four prophage types and 13 different prophage patterns were identified, and prophage type SGF and prophage pattern 7 consisting of SGB, SGF, SGFa, and SGFb types were the dominant ones. Also, 11 enterotoxin-encoding genes and four virulence factor genes were detected among the isolates. All MRSA isolates were positive for *sea*, *sek*, *seq*, and *hly* genes. Moreover, out of 12 different enterotoxin patterns, most MRSA isolates were classified into enterotoxin pattern 1, harboring three enterotoxin genes (*sea*, *sek*, and *seq*).

Conclusion: This study results indicated the presence of different prophage types and virulence factor genes among MRSA strains isolated from DFI patients, which enable them to produce a variety of diseases.

Keywords: Methicillin-resistant *Staphylococcus aureus*, Virulence factor patterns, Prophage typing, Diabetic foot infection.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBA-25

Isolation of antimicrobial peptides, derived from *Urtica dioica* leaves with potent antibacterial activity using RDA

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Abstract

Background and Aim: The antimicrobial activities of natural products have attracted much attention due to the increasing incidence of pathogens that have become resistant to drugs. Thus, it has been attempted to promisingly manage infectious diseases via a new group of therapeutic agents called antimicrobial peptides. In this paper, we aimed to isolate and compare novel AMPs from *Urtica dioica*, with effective antimicrobial activity by RDA assay.

Methods: This study aimed to detect and characterize antimicrobial proteins, especially antimicrobial peptides (AMPs) from leaves of *Urtica dioica* and to evaluate their inhibitory activities against different bacteria. The peptide extraction from *Urtica dioica* leaves was performed as described by Seidjavadi et al. Isolation of antibacterial peptide from the *Urtica dioica* was performed based on the method purified via reverse-phase HPLC chromatography. The antibacterial activity of the AMPs was assessed using a radial diffusion assay (RDA) according to the Wang approach and zone of inhibitions was compared.

Results: Plants produced many metabolites including phenolic and nitrogen compounds; they play an important role in plant defense. Analysis of the biological activity of 7 AMPs derived from *Urtica dioica* using RDA showed only three peaks of antibacterial activity against standard strains. TF3 showed major zone of inhibition and strong antibacterial activity against all strains and was considered as the main bioactive peptide of *Urtica dioica* leaves.

Conclusion: Taken together, these results indicate that TF3 may be an attractive sample to develop as a novel antibacterial compound combating bacterial infections.

Keywords: Antibacterial activity, AMP, Radial diffusion assay, Plant source, Zone of inhibition.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Case report/Case series

Code of Abstract: PBa-26

Diagnosis of aerobic vaginitis in the pregnant women using the clinical criteria and microscopic examinations

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Abstract

Background and Aim: Aerobic vaginitis (AV) is a reproductive tract infection, which affects health of women. AV was first described as a new vaginal infection in 2002. The microflora in AV comprises commensal aerobic microorganisms of intestinal origin, principally *Escherichia coli*, *Staphylococcus aureus* and coagulase-negative *Staphylococci*. AV can cause adverse pregnancy outcomes in the pregnant women such as premature delivery, miscarriage, premature rupture of the membranes, and stillbirth.

Methods: Patients were selected from Sarem Hospital. The patients with yellow-green secretions, burning and itching and pH > 4/5 were included in the study. Sterile cotton swabs were used to obtain vaginal discharge from the upper lateral vaginal wall for vaginal pH measurements and microscopic examinations. Vaginal discharge smear was spread on 2 glass slides for microscopic examination and whiff test. First, the clinical characteristics were recorded and lactobacillary grade and number of toxic leukocytes were counted with a microscope. The smears were analyzed using Donders' classification method and Dong's modified AV diagnosis for Gram stains. 'Any AV' was defined as an AV score of 4 or more, with a sub classification of 'light AV' if the score was 4-5, 'moderate AV' if it was between 6-7, and 'severe AV' when it was 8-10. Aerobic vaginitis is scored based on the microscopic examination and clinical features.

Results: In this study 15 pregnant women with symptoms of aerobic vaginitis were included. Nine patients had mild AV and 6 patients had moderate AV, and none of the patients had severe vaginitis. Among the people who had mild AV, 3 patients had green secretions and the other patients had yellow secretions. Clinical symptoms including discharge color and itching and burning were recorded for all patients.

Conclusion: Aerobic vaginitis is related to aerobic microorganisms. In general, 15 patients with AV were chosen, and 12 out of 15 patients had a pH between 7-8 and 3 out of 15 patients had a pH between 5-6. All patients had a negative whiff test which means they did not have bacterial vaginosis.

Keywords: Aerobic vaginitis; Discharge; Vaginal.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-27

A Comparative Analysis of Ultracentrifugation and Commercial Kits for Exosome Extraction

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Abstract

Background and Aim: Extracellular vesicles called exosomes are produced during cell endocytosis and function as messengers between cells. It has been demonstrated that gram-negative bacteria release vesicles that allow prokaryotic and eukaryotic cells communicate with one another. They participate in cellular crosstalk and are made up of virulence factors and proteins. During the *Helicobacter pylori* infection process, exosomes may serve as carriers of the virulence factor or protein. Protein virulence factors linked with cytotoxins can be transported by bacterial exosomes (CagA). The aim of this study is to use two ultracentrifuge kits and procedures to separate and compare exosomes from different strains.

Methods: Five *H. pylori* clinical isolate were grown in Brucella blood agar media and incubated for three days in a microaerophilic environment at 37°C. Genomes were extracted using the phenol-chloroform technique, and the *cagA* gene was verified by PCR analysis. *H. pylori* clinical isolate was cultured for 48 hours at 37°C in a shaker incubator with Brucella broth containing 5% serum in microaerophilic conditions in order to harvest exosomes. After that, Exosome extraction was performed with the Exosib kit (sibzistfan, IRAN) according to the manufacturer's protocol and ultracentrifugation. The pellets were washed with PBS and kept at -20°C. The protocol for ultracentrifugation is as follows: Following a 30-minute centrifugation of the sample at 10,000 RPM, the supernatant was centrifuged at 40,000 RPM for 70 minutes. The protein concentration of exosomes was determined utilizing the BCA Protein assay kit and SDS-PAGE. The sizes of the vesicles were assessed using dynamic light scattering (DLS) analysis and scanning electron microscopy (SEM).

Results: The calculated protein concentrations for the sample extracted using the kit and ultracentrifuge were 91 and 100 µg/ml, respectively. The sizes of exosomes were determined to be below 100 nm through the utilization of both DLS and SEM methods. The electrophoresis (12% polyacryl-amide gels) results indicate that the quality and quantity of bands detected in both extraction procedures are comparable.

Conclusion: The Exosib kit separates exosomes from the sample based on the sedimentation method, which, in addition to the simplicity of the protocol, does not require expensive materials and equipment such as an ultracentrifuge. And according to the results of the SDS-PAGE gel, proteins have been separated well in both the kit and the ultracentrifugation methods.

Keywords: exosome; *Helicobacter pylori*; ultracentrifuge; Exosib kit.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBa-28

Exploring the correlation between dietary patterns, the microbiota, and their influence on enhancing the health of individuals with Parkinson's disease

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Abstract

Background and Aim: Parkinson's disease (PD) is a neurodegenerative disorder affecting movement and coordination due to dopamine-producing cell loss in the brain. The disease predominantly impacts older individuals, and while there's no cure, various treatments like medication, physical therapy, and deep brain stimulation can alleviate symptoms. Recent studies explore the potential role of diet and gut microbiota in PD, opening potential avenues for prevention and management. This study aims to review the connection between diet, microbiota, and their impact on improving PD symptoms, offering insights into potential therapeutic strategies.

Methods: A systematic search examined how diet influences PD improvement. The search covered PubMed, Scopus, and Google Scholar for English studies from 2019 to 2023. Out of 62 studies, 21 were chosen, emphasizing original or clinical trials on diet, microbiota, and their impact on PD.

Results: People with Parkinson's should have a diet rich in antioxidants from fruits, vegetables, whole grains, lean protein, and healthy fats. Adequate fiber, water, and essential nutrients are crucial for digestive health and managing constipation. Caffeine and nicotine may offer motor symptom benefits, but caution is needed due to possible negative effects on non-motor symptoms. Research has identified multiple ways in which microbiota influence PD symptoms, including changes in gut permeability, neurotransmitter production, and immune system function. These factors contribute to symptoms like rigidity, tremors, and cognitive impairment. The gut microbiota's role in regulating inflammation and functionality in PD is crucial. Studies suggest that shifts in gut microbiota can lead to increased inflammation, linked to the onset and progression of PD symptoms. It is hypothesized that gut microbiota may affect the body's response to the accumulation of alpha-synuclein in the brain, a key PD characteristic.

Conclusion: In conclusion, the intricate relationship between dietary patterns, the microbiota, and their impact on the well-being of individuals with PD warrants further investigation. While existing evidence indicates that maintaining a healthy diet can positively influence gut microbiota composition and alleviate PD symptoms, there remains a need for a deeper understanding of how specific dietary patterns interact with the microbiota and contribute to disease progression. Nevertheless, the outcomes of diverse studies underscore the potential significance of personalized nutrition therapy for Parkinson's patients based on their unique gut microbiota composition.

Keywords: Microbiota; Dietary patterns; Parkinson's disease; Lewy bodies.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-29

Investigating the effect of bacteriophage identified on *Pseudomonas aeruginosa* isolated from wound

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Abstract

Background and Aim: Chronic wound infections are an important challenge in clinical settings. *Pseudomonas aeruginosa* is among the most common colonizers of infected wounds and biofilm formers. Antibiotic resistance is a growing threat on treatment of resistance infections. The rise of antibiotic-resistant strains of *Pseudomonas aeruginosa* has created a pressing need to explore alternative therapeutic options. Bacteriophage therapy, utilizing bacteriophages to selectively target and eradicate bacterial pathogens, has emerged as a promising avenue for treatment. This study presents a detailed quantitative analysis of the isolation and characterization of bacteriophages specific to *Pseudomonas aeruginosa* wound infections.

Methods: Bacteriophages were isolated from hospital wastewater samples and were enriched by standard techniques. The efficacy of this isolate was assessed quantitatively using a spot test and double layer agar test to represent the lytic activity of bacteriophage against *Pseudomonas aeruginosa* isolates. Furthermore, the stability of the bacteriophages was evaluated under various conditions, including pH stability, temperature stability, and salt stability. To determine the host range activity, the lytic activity of isolated bacteriophage was investigated on 16 strains of *Pseudomonas aeruginosa* isolated from wounds infection via spot test method. Moreover, the morphological characterization and classification of the bacteriophage was analyzed using transmission electron microscopy (TEM). Measurements of size, shape, and tail structure were quantified to precisely identify the phage family and its morphological characteristics

Results: The results of this quantitative study shed light on the isolation and characterization of bacteriophages targeting *Pseudomonas aeruginosa* wound infections. The separation stage of existence Clear areas of plaque indicate the presence of phage in the wastewater sample and its ability to lyse bacteria after purification and enrichment. The isolated phage had a wide host range, so that it has a lytic activity on 75% of the strains. Also, this bacteriophage in different environmental conditions, including in the temperature range of -02 Up to 70 C° and pH range of 1 to 11 and salt concentration of 5% to 15% has lytic performance. The TEM images indicate that the phage belongs to the family of podoviridae. This family is characterized by having very short, noncontractile tails.

Conclusion: The findings contribute to the growing knowledge base on phage therapy and further endorse its application as a quantitative alternative treatment strategy for *Pseudomonas aeruginosa*-caused wound infections.

Keywords: *Pseudomonas aeruginosa*; wound infection; antibiotic resistance; bacteriophage; phage therapy.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-30

Urinary Tract Infections During Pregnancy and Its Effect on Delivery: Systematic Review

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Abstract

Background and Aim: Urinary tract infections (UTIs) are the most common type of infection during pregnancy, affecting up to 10% of pregnant women. They are also recognized as the second most common ailment of pregnancy, after anemia. It is most commonly reported among pregnant women and is a known reason of morbidity during pregnancy worldwide, predominantly in developing countries.

Methods: A systematic literature search was accomplished to identify published studies between January 2012 and November 2022. Studies were collected using different keyword combinations: Urinary Tract Infection, Pregnancy, and Fetus. The literature search strategy in this paper included searching PubMed, PMC, and Science Direct, Springer open, Google scholar and BioMed Central databases.

Results: current inquire about on the seminal plasma of barren men uncovers it would be astute to propose presenting an unused parameter to semen investigation within the WHO research facility manual for the examination and preparing of human semen based on metabolomics innovation, e.g. metabolic fingerprinting.

Conclusion: Women who had a UTI during pregnancy had more preterm deliveries than those without a UTI. Recurrent UTI was observed in 26.6% of women with UTI, while the incidence of pyelonephritis was relatively low in this group. The most common bacteria isolated from women with UTI were Group B Streptococcus, followed by Escherichia coli. They were sensitive to a wide range of antibiotics.

Keywords: Pregnancy, UTIs, Delivery.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-31

Antibiotic resistance pattern of *Proteus mirabilis* isolates collected from patients with urinary tract infection

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Abstract

Background and Aim: Urinary tract infection (UTI) is one of the most prevalent diseases worldwide, and variety of bacterial genus and species are known as the causative agents of UTI. *Proteus mirabilis* is most frequently a pathogen of the urinary tract, particularly in catheterized patients. In recent years, the emergence and spread of antibiotic resistance among *P. mirabilis* strains has been a relevant problem for human health. In this study, we investigated the antibiotic resistance patterns of *P. mirabilis* strains isolated from patients with UTI in Isfahan, during 2021 and 2022.

Methods: A total of 104 *P. mirabilis* isolates were collected from referral hospitals in Isfahan, Iran and confirmed using specific primers. Resistance of strains to 18 antibiotics (ampicillin, amoxicillin/clavulanic acid, piperacillin/tazobactam, cefotaxime, ceftazidime, ceftriaxone, cefepime, ceftazidime, cefepime, ceftazidime, ceftriaxone, cefepime, ceftazidime, ceftazidime, ceftazidime, ceftazidime, ceftazidime) was tested using disk diffusion method by the guidelines of Clinical and Laboratory Standards Institute (CLSI).

Results: All isolates were conformed as *P. mirabilis* strains and also showed susceptibility to piperacillin/tazobactam, ceftazidime, and meropenem. On the other hand, high rate of resistance to imipenem (92%), amikacin (91%), amoxicillin/clavulanic acid (90%), ceftazidime (86%), cefepime (85%), and ceftriaxone (80%) was also reported. Moreover, 50, 42, 30, 29, 27 and 25% of strains were also resistant to trimethoprim/sulfamethoxazole, kanamycin, ampicillin, gentamicin, levofloxacin, and ciprofloxacin, respectively. Furthermore, 31% of isolates were resistant against at least three classes of tested antibiotics and classified as multi-drug resistant (MDR) strains.

Conclusion: The results of the present study indicated the high prevalence of antibiotic resistant *P. mirabilis* strains among patients with UTI in Isfahan. Presence and persistence of such bacteria among patients in the hospitals in this city could be an urgent for public health and requires special attention for the application of new treatment strategies for persistent and recurrent UTI.

Keywords: UTI, *P. mirabilis*, antibiotic resistance, imipenem, amikacin, piperacillin/tazobactam





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-32

Isolation of REV1 vaccine strain of Brucella from milk of sheep

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Abstract

Background and aim: Malt fever (brucellosis), which is caused by a bacteria named Brucella, is one of the most important diseases. It is highly contagious in humans and animals. Consumption of unpasteurized milk, raw meat, and contact with the secretions of infected animals are the main reasons for the transmission of this disease to humans.

Brucellosis is dangerous due to the reduction of production and abortion in livestock, as well as endangering human health. This disease still exists in Iran. The best way to control brucellosis in sheep and goats is to use the REV1 vaccine, which is resistant to the antibiotic streptomycin.

Methods: In this study, 30 samples of sheep's milk were obtained from bulk tanks of sheep flocks. These flocks received the reduced dose of the REV1 vaccine two months before the test. Milk samples were inoculated in the culture medium for the presence of Brucella spp. Grown colonies were identified by biochemical tests and antibiotic discs.

Results: In five cases (16.7%), Brucella vaccinal strain REV1 was isolated from milk samples.

Conclusion: Considering that the vaccine strain REV1 is pathogenic in humans and is excreted through milk if unpasteurized dairy products are consumed by humans from these flocks, it can lead to human brucellosis. On the other hand, there is no difference between the vaccine strain and the wild strain of Brucella in the diagnosis of Malt fever in medical laboratories. Since the vaccinal strain is resistant to streptomycin, it will be more difficult to treat the disease caused by this vaccine.

Keywords: Malt fever, vaccine strain REV1, streptomycin, brucellosis.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic review/Meta analysis

Code of Abstract: PBa-33

Detection of *Helicobacter. Pylori* using loop-mediated isothermal amplification method: A Review

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Abstract

Background and aim: *Helicobacter pylori* is the cause of various diseases. Diagnosis them are based on two categories invasive (based on biopsy and endoscopic examination) and non-invasive methods (the urea breath test (UBT) and stool antigen test). PCR is the most widely method that use these days. but this method has some limitations like requiring technical skills and expensive instruments. Loop-mediated isothermal amplification (LAMP) is a rapid method used for high specificity amplification which is initiated by the primer attachment to 6-8 separate points on the target DNA. In this study, we want to check the effectiveness of the LAMP technique on *H. pylori*.

Method: A systematic search was performed up to November 2023, from PubMed, Scopus, Web of Science, and Science Direct databases, Google Scholar search engine, and also English original articles having full text that evaluated the diagnostic LAMP assay on human clinical specimens for *H. Pylori*.

Case reports, abstracts, and conference posters were all excluded. Studies evaluating non-human specimens were also excluded.

Results: seven studies have been performed on the detection of *H. pylori* using LAMP assay. *UreC* target gene was used in six of them with a total of 528 clinical specimens of stomach biopsy, gastric biopsy, saliva, stool, and stomach brushing. The reported sensitivity and specificity were in the range of 58.1-100% (with an average of 87.73%) and 42.8-100% (with an average of 87.83%), respectively. Detection of LAMP products were based on turbidity, gel electrophoresis, and SYBR green among these studies. A detection limit of 5-6 copy DNA was reported in most studies and the widely used reference method was culture.

Conclusion: The results of reviewed studies showed that LAMP assay enables rapid and sensitive detection of *H. pylori* while being simpler and cost-efficient. A pain-free and noninvasive sampling of oral brushing and saliva in a study further increased the applicability of this diagnostic test. Therefore, the LAMP assay could be applied as a point-of-care diagnostic method in clinical settings.

Keywords: The following keywords were used in this text: loop-mediated isothermal amplification (LAMP), urea breath test (UBT), Polymerase chain reaction (PCR).





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-34

Design and Production of an Engineered Endolysin with Lytic Activity against Methicillin-Resistant *Staphylococcus Aureus*

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Abstract

Background and Aim: Improper use of antibiotics has alarmingly led to the emergence of antibiotic resistance. Hence, we urgently needed to find a suitable alternative to traditional antibiotics. Endolysins are enzymes produced at the end of the phage replication cycle and destroy the peptidoglycan of the bacterial cell wall leading to the lysis of the host bacterial cell. These enzymes are species-specific, exhibit high lytic activity, and it is almost impossible for bacteria to develop resistance against them. Lysozyme subfamily 2 (LYZ2) is a modular region of the gene *6l* (*gp6l*) of phage ϕ MR11 with lytic activity against *S. aureus*. However, it does not possess a cell wall recognition domain, usually found in lysins acting against gram-positive bacteria. Therefore, we aimed to design a chimeric endolysin capable of specifically targeting and eliminating methicillin-resistant *Staphylococcus aureus* (MRSA) bacteria.

Methods: In this study, we engineered the LYZ2 by fusing a *Staphylococcus aureus* cell wall-binding domain (CBD) to its C-terminus and cloned the chimeric protein (named chimeric *staphylococcus aureus*-targeting enzymiobiotic (CST_{Enz})) into the pET28a vector, and expressed the enzyme in *E. coli* BL21 (DE3) cell. The antibacterial property of the enzyme was further evaluated by turbidity reduction assay, disk diffusion assay, and antimicrobial susceptibility testing.

Results: The engineered lysin displayed a rapid and specific lytic activity against susceptible and Methicillin-resistant staphylococcus aureus and inhibited the growth of the bacteria at concentrations higher than 0.5 μ g/ml. Besides, the Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) of CST_{Enz} were 128 and 64 times lower than those of LYZ2, indicating the increased bacteriolytic activity of the engineered version of the enzyme.

Conclusion: In conclusion, the chimeric enzymiobiotic can be used as a potential antibacterial agent to limit infections caused by methicillin-resistant *Staphylococcus aureus*.

Keywords: Endolysin, Methicillin-Resistant *Staphylococcus aureus*, Antibiotic Resistance, Phage, enzyme Engineering.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-35

Phenotypic and genotypic investigation of anti-biofilm activity of biogenic silver nanoparticles in uropathogenic *Escherichia coli* strains isolated from patients with urinary tract infection in Zahedan

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Abstract

Background and Aim: Urinary tract infections (UTIs) are a common and recurring health concern, often caused by biofilm-producing uropathogenic *Escherichia coli* (UPEC) strains. In this study, we investigated the anti-biofilm activity of biosynthesized silver nanoparticles among biofilm producing UPEC strains.

Methods: During 2022, a total of 113 *E. coli* isolated from patients with UTI were collected from two referral hospitals laboratory in Zahedan. All isolates were cultured on MacConkey agar and Eosin Methylene Blue agar and confirmed using Polymerase Chain Reaction (PCR) assay by specific primers. Production of curli and cellulose, and, biofilm formation was investigated using Congo red agar and microtiter plate methods, respectively. The Mesembryanthemum nodiflorum extract was utilized as a reducing and stabilizing agent for the synthesis of silver nanoparticles. The synthesized nanoparticles were characterized using various techniques, and their antibacterial and anti-biofilm activities were assessed. The microtiter plate assay was performed to evaluate the phenotypic efficacy of the nanoparticles in inhibiting biofilm formation. Furthermore, the expression levels of genes encoding curli fimbriae (*csgD*) and cellulose (*yedQ*) were quantified using real-time polymerase chain reaction in the presence of the nanoparticles.

Results: Using phenotypic methods & PCR, a total of 98 isolates (87%) were identified and confirmed as UPEC strains. Amongst all, 79 strains (81%) produced curli and/or cellulose and were able to produce biofilm. The results demonstrated the successful synthesis of silver nanoparticles with desirable physicochemical properties. The synthesized nanoparticles exhibited significant antimicrobial activity against biofilm producing UPEC strains. The biogenic silver nanoparticles showed a potent antibiofilm effect, leading to a significant reduction in biofilm biomass, as biofilm production in selected UPEC strains of QEC-5 and QEC-76 strains in the presence of silver nanoparticles decreased by 71% and 87%, respectively. Moreover, the expression levels of *csgD* and *yedQ* genes were significantly downregulated in the presence of silver nanoparticles with a decrease of 54 and 41%, respectively in QEC-5 strain, and a decrease of 68 and 49%, respectively in QEC-76 strain.

Conclusion: The findings of this study suggest the potential application of biogenic silver nanoparticles as an effective antimicrobial agent against biofilm-producing UPEC strains, contributing to the development of novel strategies for the management of UTIs.

Keywords: Uropathogenic *Escherichia coli*; Silver nanoparticles; Antibiofilm activity; Gene expression; Zahedan.





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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-36

Investigation of frequency and antibiotic resistance pattern of Citrobacter isolated from a teaching hospital in Mashhad

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Abstract

Background and Aim: Citrobacter is a type of Gram-negative anaerobic bacteria that is part of the Enterobacteriaceae family. It is an opportunistic pathogen that can cause a variety of infections. In recent years, there has been a significant increase in Citrobacter strains that are resistant to multiple drugs containing beta-lactamase, which has been linked to a higher mortality rate in individuals infected by it. The purpose of this study is to investigate the frequency of Citrobacter in clinical samples and to determine its antibiotic resistance and sensitivity pattern to better address and treat infections caused by it in hospitalized patients.

Methods: A total of 135 Citrobacter isolates were studied in various laboratory samples. The identification of Citrobacter species in the samples was carried out by performing morphological and biochemical tests. The isolates were then analyzed using the standard disk diffusion method based on the protocol of the Clinical and Laboratory Standards Institute (CLSI 2011) for drug sensitivity testing.

Results: Among the 135 Citrobacter strains, Citrobacter freundii was the predominant species, consisting 40% of the cases. The most isolated bacteria among the examined samples related to the urine sample. The highest antibiotic sensitivity in the majority of samples belonged to amikacin and carbapenems, respectively. Also, Citrobacter has the highest resistance to ciprofloxacin and cefixime in different samples compared to other antibiotic discs used in this research.

Conclusion: The results of this study show that monitoring and controlling antimicrobial resistance in Citrobacter is necessary. Some of the investigated antibiotics can still be used as an effective treatment against this pathogen, but due to the increasing trend of resistance in Citrobacter strains, it is better to use these drugs in the hospital only if the isolates in the Laboratory environment show sensitivity.

Keywords: Citrobacter; Antibiotic Resistance; Opportunistic pathogen; Hospitalized patients.





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Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-37

Resistance to fluoroquinolones mediated by *qnr* genes among clinical isolates of *Pseudomonas aeruginosa* in Ardabil

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Abstract

Background and Aim: *Pseudomonas aeruginosa* is an important nosocomial pathogen containing various virulence and resistance genes which are related with different diseases. Fluoroquinolones are one of main antibiotics used for the treatment of *Pseudomonas aeruginosa* infections. This study aimed to assess the role of *qnr* genes in the emergence of fluoroquinolone-resistant *P. aeruginosa* in clinical isolates collected from Ardabil hospitals.

Methods: *Pseudomonas aeruginosa* resistance to various fluoroquinolone antibiotics was done using the disk diffusion method and interpreted by the Clinical Laboratory Standards Institute (CLSI 2021) guidelines. Furthermore, the presence of *qnr* genes was detected using the polymerase chain reaction (PCR) along with specific primers.

Results: The resistance pattern of *Pseudomonas aeruginosa* isolates against fluoroquinolone antibiotics was as follows: ciprofloxacin 58.8%, norfloxacin 42.1%, ofloxacin 62%, lomefloxacin 64.7%, and levofloxacin 54.3%. In addition, the prevalence of *qnr* genes among fluoroquinolone-resistant *Pseudomonas aeruginosa* strains was 0%.

Conclusion: Our results revealed that plasmid-mediated quinolone-resistance (*qnr*) genes are not involved in the emergence of fluoroquinolone-resistant *P. aeruginosa* clinical isolates in Ardabil hospitals. However, previous our study has been proved the role of missense mutations associated with DNA gyrase and topoisomerase IV in *Pseudomonas aeruginosa* clinical isolates resistance to ciprofloxacin in Ardabil.

Keywords: *Pseudomonas aeruginosa*; *qnr* genes; fluoroquinolone.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-39

The effects of synbiotic and probiotic supplements in patients with rheumatoid arthritis

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Abstract

Background and Aim: Rheumatoid arthritis (RA) is a chronic, autoimmune and inflammatory disease of unknown origin, which has the greatest effect on the body's joints. Probiotic administration has shown statistically significant benefits in patients with inflammatory arthritis, particularly in older individuals with long-established rheumatoid arthritis (RA). Recent evidence shows that people with RA have significant changes in their gut microbiota compared to healthy people. In this study, the effect of synbiotics and probiotics on rheumatoid arthritis has been investigated.

Methods: Recent studies have provided data on the effects of probiotics on CRP levels and the serum level of total oxidative stress has been significantly reduced. Also, gut microbiome regulating supplements can affect RA activity by reducing DAS-28, HAQ and inflammatory factors.

Results: Studies of probiotics in RA patients provided data on IL-1 β and showed a significant improvement in IL-1 β levels as a result of probiotic supplementation in 93 RA patients. Also, probiotic and synbiotic supplements had a significant reduction in inflammatory factors compared to placebo, including changes in inflammatory markers and DAS-28, as well as beneficial effects on hs-CRP, DAS-28, VAS, insulin levels, pain scale, HOMAI, and the hemostatic performance evaluation model. β cells (HOMA-B). However, no significant improvement was observed in plasma nitric oxide (NO) levels. Compared to placebo: Pain Scale (p=0.046), hs-CRP (p<0.01), DAS-28 (p<0.01), IL-6 and IL-12 (p<0.05), IL-10 (p<0.05).

Conclusion: In general, it is possible that the use of synbiotics and probiotics in rheumatoid arthritis can induce an anti-inflammatory effect in the joints and reduce pain. also, the present study showed that synbiotic and probiotic supplements in patients with RA have positive effects on hs-CRP, DAS-28, VAS, NO, insulin levels, HOMA-IR, HOMA-B and GSH levels. Therefore, probiotic and synbiotic supplements can help the treatment process and improve symptoms in patients with rheumatoid arthritis.

Keywords: Synbiotic; Prebiotics; RheumatoidArthritis, Inflammatory factors





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBa-40

Detection of *Mycoplasma pneumoniae* using loop-mediated isothermal amplification: A Systematic Review

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Abstract

Background and Aim: *Mycoplasma pneumoniae* is a worldwide known contagious disease that can be asymptomatic in adults thus it is tolerant to commonly used respiratory infection antibiotics; making *M.pneumoniae* a considerable burden to public health.

Therefore, several means of diagnosing *M. pneumoniae* have been developed over the years including culture, PCR, and serology methods. The loop-mediated isothermal amplification (LAMP) is a new, rapid, convenient, and inexpensive molecular method that was first introduced by Notomi et al. It has high sensitivity and specificity with a vast detection range. Therefore, I have performed a systematic review of the subject in the hope of accomplishing useful research.

Methods: In order to perform a systematic review, several databases such as Google Scholar, Scopus, etc. were searched and a total of 35 essays have been gathered; most of which are from the Pubmed database.

Results: High sensitivity and specificity of the LAMP method have been observed in several studies. Also, in some of them, a specificity of 100% has been reported. The LAMP-LFB (Nanoparticle-based lateral flow biosensor) is capable of accomplishing the process by making 10^{10} copies of the target gene in 60 minutes, 30 minutes if loop primers are included. LAMP is less stable than PCR which is hoped to be reformed soon. Several other advantages have also been reported on both LAMP and LAMP-LBF methods.

Conclusion: In summary, despite its few disadvantages such as poorer stability compared to PCR, LAMP and its recent versions are greatly efficient methods that are predicted to be used internationally in no time. It is a cost-efficient, sensitive, and specific method that can give results in an hour or less. however, more evidence is needed to confirm that LAMP is capable of fully replacing other methods in the clinical diagnosis of *M.pneumoniae*.

Keywords: *Mycoplasma pneumoniae*, loop-mediated isothermal amplification (LAMP), LAMP-LFB Nanoparticles-based lateral flow biosensor.





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Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBa-41

Microbiology laboratory and its role in controlling the spread of anthrax in narcotic users

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Abstract

Narcotics are the general name for various psychoactive drugs and natural and synthetic chemical compounds with stimulating, calming, and euphoric effects depending on the active ingredient. Narcotics are always produced in non-standard, non-sterile conditions and often in underground laboratories; their distribution and supply are not subject to specific laws. Inappropriate and unsanitary conditions for drug production and distribution create conditions for microbial growth. Bacterial infections are common in drug users, especially if they inject drugs. Sepsis, endocarditis, skin and bone fasciitis, and necrosis are directly related to complications from injection abuse.

In Hosseini Dost's study on bacillus contamination of twenty-four samples of illicit drugs in Iran, all studied samples were contaminated with bacteria from the Bacillaceae. Anthrax is a zoonotic disease caused by the bacteria *Bacillus anthracis*. This gram-positive bacterium is classified as a dangerous biological agent due to its small spore production, high antibiotic resistance, and high pathogenicity. Spores of the *Bacillus anthracis* bacteria can be ingested by injecting heroin or inhaled by smoking or snorting. Inhalation of narcotics can cause inhalation of anthrax. Dissolving drugs in non-sterile solvents allows many different types of bacteria to enter the bloodstream.

In 2010, an outbreak of anthrax in injecting narcotics users, especially heroin users, led to a new disease called injection anthrax, which causes severe soft tissue infections. Symptoms include the formation of colloidal edema and Hematoma. Many cases of this type of anthrax have been reported in different areas, including England, Germany, etc. To prevent the occurrence of toxemia from the disease, it is necessary to treat people with anthrax as soon as possible. Clinical microbiology laboratories, using molecular techniques such as PCR, real-time PCR, and loop-mediated isothermal amplification, play a key role in rapid diagnosing and identifying *Bacillus anthracis*. These laboratories are critical to improving health and preventing bacterial contamination in society.

Keywords: *Bacillus Anthracis*, Anthrax, Narcotic Users, Diagnosis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-42

Evaluation of antimicrobial activity of *Lactobacillus acidophilus* supernatant isolated from traditional yogurt on *Shigella dysenteriae*

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Abstract

Background and Aim: *Shigella* infections are the most common form of epidemic dysentery and one of the important causes of diarrhea in children worldwide. In some countries, shigellosis is one of the most common causes of hospitalization of children. This disease manifests itself with fever and watery diarrhea, which later turns into bloody-mucous diarrhea. Early treatment of shigellosis with appropriate antibiotics accelerates recovery, stops the excretion of the organism in the feces, and reduces the spread of infection. But what is in question is the multiple drug resistances that are created in these bacteria by plasmids and cause the spread of resistant infections. As a result, it seems important to deal with newer treatment solutions or to use more appropriate prevention methods. Due to the advancement of biotechnology in today's world, researchers have paid great attention to the use of natural metabolites that inhibit the growth of pathogenic microbes. Probiotics, especially *Lactobacillus acidophilus*, are among the compounds that occupy researchers' minds. *Lactobacillus acidophilus* plays an important role in inhibiting the growth of pathogenic bacteria by producing B vitamins, lactic acid, hydrogen peroxide and acetic acid. Therefore, in this study, the evaluation of the antimicrobial activity of the supernatant of *Lactobacillus acidophilus* isolated from traditional yogurt on *Shigella dysentery* was investigated.

Methods: In this laboratory study that was conducted in 2023, 40 traditional yogurt samples were prepared from four rural areas and *Lactobacillus acidophilus* was isolated using special culture medium (MRS), selective screening methods, catalase test and relevant biochemical tests. After isolation, using disk diffusion agar and well diffusion agar methods, the antibacterial effects of this probiotic against *Shigella dysentery* bacteria were investigated. In order to reduce the error, each test was repeated three times and the diameter of the non-growth halo was measured and their antimicrobial ability was compared. Statistical analysis of the results of this study was done by SPSS version 16 software.

Results: From 40 samples of traditional yogurt, in the first stage, 31 acid-resistant bacteria strains were isolated, and in the next stages, 6 strains with high resistance to acid and bile salts were isolated. These bacteria showed good antimicrobial ability against *Shigella dysentery*. During the well method, *Lactobacillus acidophilus* showed an inhibitory effect against *Shigella dysentery* with an average diameter of the non-growth halo of 12 mm. Also, in the comparison of the disk and well methods, the well method was far more sensitive than the disk method.

Conclusion: The existing study proved that *Lactobacillus acidophilus* has antibacterial potential against *Shigella dysentery* bacteria and may be able to replace some antibiotics in the future. It is recommended to use more of this category of bacteria that are abundant in dairy products.

Keywords: Antimicrobial; *Lactobacillus acidophilus*; traditional yogurt; *Shigella dysentery*.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-43

Investigating the effect of ethanolic and methanolic extracts of *Rumex cyprius* on the biofilm formation of *Pseudomonas aeruginosa*

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Abstract

Background and Aim: *Pseudomonas aeruginosa* is an opportunistic and important pathogen that is capable of producing biofilm, and this biofilm makes the bacteria resistant to treatment with chemicals to a large extent, so inhibiting biofilm has an inhibitory effect on creates resistance to this bacterium, therefore, this study was conducted with the aim of investigating the effect of the ethanolic and methanolic extracts of *Rumex cyprius* on the growth and formation of biofilm in *Pseudomonas aeruginosa*.

Methods: This experimental study was conducted on standard strains of *Pseudomonas aeruginosa* (ATCC: 1310). *Romex cyprius* plant was collected from the pastures of Kohdasht Lorestan city at the end of May. The leaves of the plant were dried at ambient temperature and in the shade, and then ground into powder and stored in the freezer. Ethanolic and methanolic extracts of *Romex cyprius* leaves were prepared by Soxhlet method. The antimicrobial activity of the extracts was evaluated by diffusion method in the well. Also, the minimum inhibitory concentration (MIC) and the minimum bactericidal concentration (MBC) were checked according to the CLSI standard by microdilution method. The effect of plant extract on biofilm formation was investigated by the modified micro titer plate method. The active compounds of *Romex Cyprius* were identified by gas chromatography-mass spectrometry. Statistical analysis was done with SPSS software version 17 and $p < 0.05$ was considered significant. Conjugate t-test and analysis of variance (ANOVA) were used to compare the data.

Results: The diameter of the non-growth halo obtained from the ethanolic and methanolic extract of *Romex cyprius* plant at a concentration of 500 mg/ml on *Pseudomonas aeruginosa* was 14.66 ± 1.25 and 13.10 ± 1.04 mm, respectively. The results of MIC and MBC of ethanolic and methanolic extracts of *Romex cyprius* plant against *Pseudomonas aeruginosa* bacteria were similar and were 125 and 250 mg/mm, respectively. Also, different concentrations of *Romex cyprius* extract significantly reduce biofilm production by *Pseudomonas aeruginosa* compared to the positive control. In this research, the phenolic compound of 1,2 Benzenedicarboxylic acid was the main compound isolated from *Romex cyprius* at the rate of 89.68.

Conclusion: Ethanol and methanol extracts of *Rumex cyprius* plant contained antimicrobial compounds and have a special killing effect on the bacterial biofilm of *Pseudomonas aeruginosa*. Therefore, it seems that this natural substance can be a promising agent in the treatment of *Pseudomonas* infections. Therefore, it is suggested to carry out wider investigations in vitro conditions to evaluate the effective concentration of this extract on the desired bacteria and clinical strains, side effects and its exact formulation.

Keywords: Ethanolic Extracts, Methanolic Extracts, *Rumex cyprius*, Biofilm, *Pseudomonas aeruginosa*.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-44

Molecular identification of enterotoxigenic *Escherichia coli* from clinical samples isolated from patients with acute diarrhea in Tehran

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Abstract

Background and Aim: Enterotoxigenic *Escherichia coli* (ETEC) is a major cause of diarrhea in developing countries, especially among children. Due to the lack of proper vaccine and not allowing the use of most antimicrobial drugs in children, it is always considered one of the crucial problems in the healthcare system of countries. The aim of this study is to investigate the prevalence of this microorganism in clinical samples isolated in pathobiological laboratories in Tehran and to investigate the genetic pattern of their toxin production.

Methods: A total of 317 samples were isolated from people suffering from acute diarrhea were randomly collected from 4 valid pathobiology laboratories in Tehran. Out of 317 stool samples, 247 strains of *E. coli* were isolated using biochemical tests. *E. coli* serogroups were evaluated using serological tests. DNA of *E. coli* strains was extracted and analyzed by polymerase chain reaction (PCR) for assessment of heat-stable (ST) and heat-labile (LT) enterotoxins genes.

Results: Of the 247 *E. coli* strains tested, 112 cases were related to women and 135 cases were related to men. Regardless of gender a total of 139 cases were isolated from children under 7 years of age. Serological results showed that the most prevalent serogroups were O26, O115, O153, O5, O85, O20, O159 and O148 respectively. Of the 247 *E. coli* strains isolated, 32 cases were ETEC (12.95%). Among these, 21 cases had just heat-stable toxin gene (65.6%), 7 cases had just heat-labile gene (21.9%), and 4 cases had both genes (12.5%). Of the cases that had heat-stable toxin gene, the most number were O5, O26, O167, and O8. The cases that had heat-labile gene were mostly O26, O78, O153, and O5. Of the 4 strains that had both heat-stable toxin and heat-labile toxin genes, 2 strains were O26, one was O5, and the other was O115.

Conclusion: The findings of this study indicate the prevalence of ETEC in Tehran, which is consistent with similar studies. This investigation can strengthen the epidemiological information related to this disease and be a way to design additional studies on the prevalence process and even treatment.

Keywords: Enterotoxigenic *Escherichia coli* (ETEC), heat-stable enterotoxin (ST), heat-labile (LT) enterotoxin.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-45

A report for rifampicin and isoniazid resistant isolates of *Mycobacterium tuberculosis* in the central part of Iran

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Abstract

Background and Aim: Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (MTB), remains one of the top ten causes of death worldwide, especially in developing countries. There are limited data on the MTB drug resistance in central part of Iran. This study aimed to assess the rate of drug resistance to first-line anti-TB drugs in Semnan province, Iran between April 2013 and March 2019.

Methods: Drug susceptibility testing (DST) to rifampicin (RIF), isoniazid (INH), ethambutol (ETH), and streptomycin (STM) was performed on Löwenstein-Jensen medium using proportion method.

Results: The mean age of patients were 55, ranged from 19-86 years and 21 (65.6%) patients were male. Out of 32 MTB isolates, 29 (90.6%, 95% CI = 75.7%-96.8%) isolates were pan-susceptible and 3 (9.4%, 95% CI = 3.2%-24.2%) were resistant to at least one drug. One isolate (3.1%, 95% CI = 0.6%-15.7%) was resistant to STM, 2 isolates (6.2%, 95% CI = 1.7%-20.2%) were resistant to INH and 1 isolate (3.1%, 95% CI = 0.6%-15.7%) was RIF-resistant (RR). Presence of RR and INH-resistant isolates in this study implies the possibility of initial resistance of MTB strains circulating in this region. DST for all TB cases was recommended as an effective diagnostic tool for optimal monitoring and control of drug resistance in this area.

Conclusion: Although RR and INH-resistance are commonly detected in Semnan province, the profile of MDR-TB is rarely identified. Further studies using a larger sample size would be recommended for determining the drug resistance patterns for MTB isolates in this area.

Keywords: *Mycobacterium tuberculosis*, Tuberculosis, rifampicin-resistant.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-46

Evaluation of Extended Spectrum β -Lactamase (ESBL) *Escherichia coli* and *Klebsiella* spp. in urinary tract samples by disk diffusion and molecular methods in Urmia, Iran

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Abstract

Background and Aim: Resistance to a wide range of common antimicrobials has made the proliferation of extended-spectrum beta-lactamase (ESBL)--producing strains a serious global health concern, complicating therapeutic strategies. The high proportion of ESBL producers among Enterobacteriaceae and the complex molecular epidemiology with different types of ESBL genes are of concern. This study was conducted to identify ESBL production in different Gram-negative bacilli isolated and further identify ESBL producers among *Escherichia coli* and *Klebsiella* bacteria by PCR method in Urmia city.

Methods: A total of 1,000 isolates of gram-negative bacilli were isolated by examining more than 12,000 urine culture samples. Then, all the isolated bacteria were identified by microbiology diagnostic methods such as differential media. The presence of ESBL positivity was detected using a double disc synergy test (DDST). The discs used in this experiment were cefotaxime and cefotaxime clavulanate. After antibiogram analysis, PCR for beta-lactamase (bla) genes of TEM, SHV and CTX-M family was also performed using primers designed in 20 ESBL isolates of each *Escherichia coli* and *Klebsiella* species.

Results: Among 1000 Gram-negative bacilli isolated, 379 (52.49%) were ESBL producers. The main source of ESBL production was urinary tract samples, with the highest ESBL production in *Klebsiella* sp. (60.02 %). Resistance to multiple classes of antibiotics was observed among ESBL producers. Among ESBL-producing genes, the prevalence of bla-CTX-M (79.3%) was the highest, followed by bla-TEM (50.2%) and bla-SHV (53.5%) in the present study. The frequency of ESBL-producing strains among clinical isolates is steadily increasing. Monitoring advanced drug resistance and molecular characteristics of ESBL isolates is essential to guide the appropriate and judicious use of antibiotics.

Conclusion: Multiple risk factors were associated with ESBL infections both in the community and hospital setting. Prediction tools are needed to improve the protocol of appropriate empiric antibiotic selection while preserving antimicrobial stewardship recommendations.

Keywords: Extended-spectrum β -lactamase (ESBL), Double Disk Synergy Test (DDST), Antibiogram, PCR, urinary tract samples.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-47

Prevalence of antibiotic resistance pattern in methicillin-resistant *Staphylococcus aureus* from clinical specimens of Laboratory in Urmia, Iran

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Abstract

Background and Aim: *Staphylococcus aureus* is both a commensal bacterium and a human pathogen. Approximately 30% of the human population is colonized with *Staphylococcus aureus*. Simultaneously, it is a leading cause of bacteremia and infective endocarditis (IE) as well as osteoarticular, skin and soft tissue, pleuropulmonary, and device-related infections. Methicillin-resistant *Staphylococcus aureus* (MRSA) refers to a group of gram-positive bacteria that are genetically distinct from other strains of *Staphylococcus aureus*. The purpose of this study is to investigate the prevalence of antibiotic resistance patterns in methicillin-resistant *Staphylococcus aureus* strains from clinical samples collected from Urmia clinical laboratories located in the northwest of Iran.

Methods: This cross-sectional study was performed on 11514 patients from Dr. Nemati's Laboratory for 9 months from December 2022 to September 2023. Clinical specimens included urine, sputum, wound discharge, nasal secretions, bronchoalveolar lavage and abscess. Specimens obtained after growth in blood agar medium were subtracted from Streptococci using catalase assay. Then to identify *Staphylococcus aureus* from standard microbiological methods such as gram staining, coagulase tests, fermentation of mannitol, DNase, novobiocin sensitivity, and oxidase test were performed. The antimicrobial resistance patterns of the isolates were determined using the Kirby-Bauer disk diffusion based on CLSI guidelines. MRSA strains were confirmed using a cefoxitin disc. In this study, antibiotic discs of Rosco made in Denmark were used.

Results: Of 11514 cultured samples, 3687 were males and 7827 females (80.95% males and 19.05% females were diagnosed with *Staphylococcus aureus*). It showed methicillin-resistant staphylococci, all of which were female. The highest resistance to penicillin was 100% and the highest sensitivity was to gentamicin amikacin and trimethoprim-sulfamethoxazole discs. However, resistance to other antibiotics was Ciprofloxacin 60%, nitrofurantoin 37.50%, doxycycline 4.45%, erythromycin 90% and clindamycin 80%, respectively.

Conclusion: This study showed that the prevalence of *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* strains was relatively low in this laboratory. controlling vectors and their treatment could prevent the transmission of this bacterium. Antibiotics gentamicin, amikacin and trimethoprim-sulfamethoxazole have the best activity against *Staphylococcus* strains.

Keywords: Antibiotic; Methicillin-resistant; *Staphylococcus aureus*.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-48

Evaluating the prevalence antibiotic resistance pattern of gram-negative isolated from cases of Urinary tract infection (UTI) in Urmia, Iran.

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Abstract

Background and Aim: Urinary tract infection (UTI) is a frequent problem worldwide. about 150 million people are diagnosed with this problem each year. the aetiology of UTI and the antibiotic resistance patterns of uropathogens have changed over the past years, both in the community and nosocomial era. this study was conducted to evaluate antibiotic resistance patterns of gram-negative uropathogens to therapeutic agents for UTI, in Urmia.

Methods: to the number 6000 urine samples were collected between April 2022 and September 2023 from Dr. Nemati's lab in Urmia. all samples were cultured on EMB and blood agar. gram-negative isolates from cases with significant bacteria >10⁵ CFU/mL (cfu: colony forming units) were identified and antimicrobial susceptibility testing was done by the disc diffusion method. isolated uropathogens were tested for antimicrobial resistance against cefazolin(30µg), ciprofloxacin(5µg), cefotaxime(30µg), amikacin(30µg), gentamicin (10µg), trimethoprim-sulfamethoxazole (1.25/23.75µg) and imipenem(10µg).

Results: The frequency of isolates: *E. coli* (67.85%) *K.pneumoniae* (9.5%) *K.oxytoca* (3.02%) *Citrobacter koseri* (3.67%) *Citrobacter freundii* (1.51%) *Citrobacter braakii* (0.86%) *Enterobacter cloacae* (2.58%) *Enterobacter aerogenes* (0.86%), *Proteus mirabilis* (2.37%) *Proteus vulgaris* (0.43%) *Morganella morgani* (0.43%) *Providasia retgeri* (0.21%) *Acinetobacter spp.* (0.86%) and *Pseudomonas aeruginosa* (5.83%). resistance pattern of isolates from amikacin: *Escherichia coli* (7.27%) *Klebsiella spp.* (7.16%) *Enterobacter spp.* (7.58%) *Citrobacter spp.* (8.68%) *Proteus, Morganella, Providasia* (60.62%) *Acinetobacter spp* (0%) *Pseudomonas aeruginosa* (3.01%) cefazolin: *Escherichia coli* (48.65%) *Klebsiella spp.* (48.80%) *Enterobacter spp.* (50.78%) *Citrobacter spp.* (49.98%) *Proteus, Morganella, Providasia* (53.12 %) cefotaxime: *E.coli* (42.19%) *Klebsiella spp.* (43.76%) *Enterobacter spp.* (43.79%) *Citrobacter spp.* (45.79%) *Proteus, Morganella, Providasia* (49.59%) ciprofloxacin: *Escherichia coli* (40.72%) *Klebsiella spp* (41.81%) *Enterobacter spp.* (43.18%) *Citrobacter spp.* (46.78%) *Proteus, Morganella, Providasia* (38.80%) *Acinetobacter spp* (50%) *Pseudomonas aeruginosa* (27.43%) gentamicin: *E.coli* (19.80%) *Klebsiella spp.* (20.89%) *Enterobacter spp.* (15.39%) *Citrobacter spp.* (15.72%) *Proteus, Morganella, Providasia* (32.45%) *Acinetobacter spp* (0%) *Pseudomonas aeruginosa* (9.39%) trimethoprim-sulfamethoxazole: *E.coli* (45.05%) *Klebsiella spp.* (44.76%) *Enterobacter spp.* (41.78%) *Citrobacter spp.* (44.79%) *Proteus, Morganella, Proviasia* (49.59%) imipenem: *Acinetobacter spp* (0%) *Pseudomonas aeruginosa* (4.36%).

Conclusion: Imipenem, gentamicin and amikacin are recommended as the drugs of choice for the empirical treatment. given the relatively high antibiotic resistance to routine antibiotics used in the treatment of UTI (cephalosporins & fluoro quinolones) a revision of the therapeutic protocol for urinary tract infection is needed.

Keywords: Antibiotic resistance pattern; Urinary tract infection (UTI); Gram-negative.





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Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-49

Identification of tolerance and resistance from *Pseudomonas aeruginosa* biofilms in cystic fibrosis patients using molecular methods in Urmia, Iran, 2023

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Abstract

Background and Aim: Biofilm formation is an endless cycle, in which organized bacterial communities are housed in a matrix of extracellular polymeric materials (EPS) that bind microbial cells to a surface. The persistence of chronic *Pseudomonas aeruginosa* lung infections in cystic fibrosis (CF) patients is due to biofilm-growing mucoid (alginate-producing). The purpose of this study is to investigate the effect of antibiotic treatment in preventing the formation of biofilm caused by *Pseudomonas*.

Methods: Laboratory identification of *Pseudomonas aeruginosa* isolates by standard microbiological and biochemical methods. The susceptibility of the isolates to different antibiotics was determined using the disk diffusion method on cation-adjusted Müller-Hinton agar. Antibiotic discs tested with ceftazidime, piperacillin/tazobactam, ciprofloxacin, and levofloxacin, were treated with gentamicin, amikacin, tobramycin, imipenem and meropenem. The adhesive biofilms were fixed with 99% methanol for 15 minutes, the solutions were removed and the plate dried. The biofilms were stained with 200 µl of 0.1% crystalline violet for 5 minutes at room temperature and then washed with water and dried. Biofilm was obtained in each well by treatment with 200 µl of 95% ethanol for 30 minutes. All *Pseudomonas aeruginosa* isolates for the three genes encoding biofilm, algD, pslD and pelF using the polymerase chain reaction (PCR) method, using specific primers.

Results: 16.25% produce strong biofilms. 33.75% produced average biofilm. 33.75% produced poor biofilm, while 16.25% of isolates did not produce as film-free. *P. aeruginosa* development of resistance to many antimicrobial agents is a major challenge in controlling its infections.

Conclusion: *Pseudomonas aeruginosa* infections typically progress from the acquisition of a single environmental strain to an extensive genetic and phenotypic adaptation to the lung environment. Chronic infections are commonly caused by a single *P. aeruginosa* lineage. However, different lineages have been found in isolates from the same sputum sample or obtained longitudinally from the same patient. Given the high intraspecific diversity of *P. aeruginosa* in the CF lung, caution is warranted when assuming that one or more isolates are the cause of infection in a CF patient.

Keywords: *Pseudomonas aeruginosa*, Biofilms, Cystic fibrosis.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-50

Propolis nanoparticles effect on multidrug resistant strains of *Pseudomonas aeruginosa* (MDR) biofilm

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Abstract

Background and Aim: *Pseudomonas aeruginosa* is a common cause of nosocomial infections and exhibits innate resistance to a wide range of antibiotics. In recent years, the current trend has been towards the identification of natural products in disinfection. Nanoparticles are able to penetrate bacteria and bacterial biofilms, so they can be a potential agent for controlling the growth of bacterial infections. In this study, our goal is to determine the antibacterial efficacy of synthesized the propolis nanoparticle and its combination with ciprofloxacin to obtain a synergistic effect against MDR strains of *P. aeruginosa* biofilm.

Methods: Propolis nanoparticle (PN) was prepared by the ultrasonication method. Scanning electron microscopy and dynamic light scattering were used to measure the size and morphology of the produced nanoparticles. The PN was evaluated in vitro against ten MDR *P. aeruginosa* strains by disk diffusion and broth micro-dilution method. The checkerboard testing method was used to evaluate synergism among PN combined with ciprofloxacin against MDR *P. aeruginosa* strains.

Results: The Fe-SEM image reveals that the PN morphology is nearly spherical. PN, with average size 219.3 nm, was effective against MDR *P. aeruginosa* biofilm with MIC value of 3.2- 15 mg/ml. However, ciprofloxacin showed strong antibacterial activity even at low concentrations. According to the checkerboard results, MDR *P. aeruginosa* had additive effect with FIC of >0.5 to ≤ 1 for combining PN with CP. But, an isolate of MDR *P. aeruginosa* showed a synergistic antibacterial effect for combining PN (0.8 mg/ml) with CP (0.07 mg/ml).

Conclusion: PN was able to inhibit MDR *P. aeruginosa* that could be due to the reduced particle size, better nanoparticle penetration and the synergistic impact of main components in propolis. More research is needed to investigate the synergistic mechanism of PN in combination with antibiotics.

Keywords: Antibacterial, MDR *P. aeruginosa*, Nanoparticles.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-51

Molecular diagnosis of *Mycoplasma genitalium* in women with a history of abortion using 16S rRNA sequence and its relationship with antimullerin hormone

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Abstract

Background and Aim: *Mycoplasma genitalium* is a sexually transmitted bacterium that causes 15 to 25% of male nongonococcal urethritis and is associated with cervicitis and pelvic inflammatory disease in women. It can also be associated with cervicitis, pelvic inflammatory disease, and tubular factor infertility in women. This study aimed to investigate the effect of vaginal infections with *Mycoplasma genitalium* on the level of antimullerian hormone (AMH) and its relationship with abortion by molecular methods in Urmia.

Methods: After patient satisfaction, endocervical sampling was performed. They were placed in a PPLO broth medium. After 2-3 days of incubation, the samples were removed by syringe. Then it passed through 0.2-micron filters and a few drops of the liquid were poured into the PPLO agar medium. Also to increase the sensitivity to diagnose mycoplasma infections and possible association with the amount of antimullerian hormone in women in the age range of delivery, the levels of Anti-Müllerian hormone (AMH) in positive samples were also measured by Electro Chemi Luminescence. Genus and species of Mycoplasma RFLP-PCR were used.

Results: From 500 intrauterine samples of pregnant women samples, extracted DNA, and after PCR, 125 samples were positive. The culture results of the samples also showed that 80 cases grew after 2 weeks. 70% of PCR-confirmed samples had a history of miscarriage and 25% of antimullerian hormone levels were abnormal. Genotyping results indicated that the dominant mycoplasma was *Mycoplasma genitalium* strain G37 of the type.

Conclusion: In general, it can be said that *Mycoplasma genitalium* can be one of the possible causes of abortion. PCR assay based on 16S rRNA gene sequences a valuable and reliable technique for the identification *Mycoplasma genitalium* to find the cause of spontaneous abortions is on the other hand, the present study showed that all *Mycoplasma genitalium* isolates had identical differences in enzyme patterns of this bacterium after PCR-RFLP was not observed and all were of the Mycoplasma type the genitalia were G37.

Keywords: Molecular detection, *Mycoplasma genitalium*, Antimullerian hormone, Abortion.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-52

A comparative study of the most common bacteria in hospital infections

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Abstract

Background and Aim: Hospital-acquired diseases are one of the health problems worldwide that affect the developed and the poor. With the excessive and irrational use of antibiotics, almost the majority of microorganisms found in hospitals, including Pseudomonas and Klebsiella have become resistant and are resistant strains. They are also found among patients, medical workers, medical workers, employees, students and other administrative workers, these injuries cause prolonged hospitalization, increase the time of people's disability and cause disability and discomfort and even lead to death.

Methods: In this descriptive-analytical study that was conducted during 3 months (July to September 1402), for patients with clinical symptoms of urinary tract infection and lung infection who were hospitalized, samples were cultured on blood agar, chocolate agar, EMB and Tayo was performed and after 24 hours the culture results were checked, then the antibiogram was placed based on the type of bacteria observed and then the results of sensitivity, semi-sensitivity and resistance were reported for each culture.

Results: The most common bacteria found in the urine culture of hospitalized patients is Escherichia coli (26 patients) with a rank of 57.77% and the most common microorganism in the lung culture of patients hospitalized in Klebsiella Hospital (14 patients) with a rank of 31.11%, also the most resistant in culture. Urine related to antibiotics ciprofloxacin and cotrimoxazole with ranks (18 and 16 patients), respectively, and the highest resistance in lung culture was related to antibiotics cotrioxazole and meropenem with ranks (24 and 22), respectively.

Conclusion: Based on the results obtained, more than half of the infections caused in the hospital are related to Gram-negative bacilli, the most common of which were Escherichia coli in people with urinary tract infections and Klebsiella in pulmonary infections. Also, in this study, resistance High resistance to ciprofloxacin in urinary tract infections and high resistance to cotrimoxazole in lung infections was observed. Resistance to other antibiotics was also evident, therefore full and timely identification and treatment of patients in order to prevent the spread of the disease. It is important. Following the national guidelines for combating nosocomial infections, i.e. correct, appropriate and complete prescription of treatment regimen under the direct supervision of a trained supervisor, is considered the most basic way to prevent drug resistance in the society.

Keywords: Hospital infection, Bacteria, Microbial resistance, Antibiotic.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-53

Emerging challenges in Diabetic Foot Ulcer infections: Multidrug Resistance, Robust Biofilm Formation, and Virulence Gene prevalence in *Pseudomonas aeruginosa* isolates

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Abstract

Background and Aim: *Pseudomonas aeruginosa* (*P. aeruginosa*), which is commonly isolated from diabetic foot ulcers (DFUs), is well-known for its ability to form biofilms, leading to increased antibiotic resistance and chronic recurrent infections. This poses a significant challenge in treatment, necessitating the epidemiological surveying of these isolates. The objective of this study is to investigate the differences in antimicrobial susceptibility, biofilm severity, and the prevalence of *toxA*, *alg44*, and *muc* genes in *P. aeruginosa* isolated from DFUs.

Method: This cross-sectional study collected samples from DFU patients admitted to different hospitals in Isfahan between April and November 2023 (8 months). The conventional biochemical test was employed for the isolation and confirmation of *P. aeruginosa*. Antimicrobial susceptibility was assessed using the disk diffusion method, while biofilm formation was measured using the microtiter plate assay. The presence of virulence genes was detected through PCR for the aforementioned genes.

Result: Out of the sixty-six DFU patients, 29 isolates of *P. aeruginosa* were collected from hospitalized patients. All isolates exhibited biofilm formation, with 39% and 54% demonstrating strong and moderate biofilm formation abilities, respectively. The most prevalent antibiotic resistances were observed against ciprofloxacin and tobramycin, with resistance rates of 59%. Furthermore, 60% of the isolates were classified as multidrug-resistant (MDR). The prevalence rates of *toxA*, *alg44*, and mucinase genes were found to be 82%, 82%, and 79%, respectively.

Conclusion: The increasing number of MDR isolates with strong biofilm formation and a high prevalence of virulence genes in DFU patients raises concerns regarding treatment and emphasizes the need for hygienic protocols to prevent future antibiotic resistance.

Keywords: *Pseudomonas aeruginosa*, diabetic foot ulcer, Biofilm, Antibiotic resistance.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-54

Determining the Frequency of Genes Producing Colicins Ia and V in *Escherichia coli* Strains Isolated from Clinical Samples of Medical Centers in Yazd City

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Abstract

Background and Aim: Bacteriocins are peptides with antimicrobial properties. They are ribosomal synthesized and produced by both gram-positive and gram-negative bacteria. The bacteriocins produced by *Escherichia coli* are called colicins. Colicins in commensal bacteria inhibit the growth of pathogenic bacteria and in pathogen strains, they increase bacterial virulence. This study aimed to evaluate the frequency of *col V* and *col Ia* genes in *Escherichia coli* specimens isolated from patients with urinary tract infections in Yazd City, Iran.

Methods: In this descriptive cross-sectional study, 160 *Escherichia coli* samples were isolated from urine specimens and identified by common biochemical tests. The amplification of *col V* and *col Ia* genes was performed by PCR method using specific primers and after sequencing, the results were analyzed using SPSS version 16 software.

Results: In this study, out of 160 *Escherichia coli* isolates examined, the colicin gene was detected in 26.9% of the isolates. The frequency of *col Ia* gene was 24.4% and the frequency of *col V* gene was 10.6%. Furthermore, in 8.12% of isolates, both genes were identified together. The frequency of isolates containing only *col Ia* gene was 16.2% and isolates containing only *col V* gene was 2.5%.

Conclusion: In this study, isolates with *col Ia* gene showed high frequency. Most strains with *col V* gene also had *col Ia* gene. Therefore, the *col V* gene is often observed together with the *col Ia* gene.

Keywords: *Escherichia coli*; Bacteriocin; Colicin.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Case report/Case series

Code of Abstract: PBa-55

Antibacterial activity of PVP coated silver nanoparticles against *Escherichia coli*

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Abstract

Background and Aim: Nanomedicine is a relatively new trend in medicine. Metal nanoparticles have been shown to have antibacterial, antifungal, and antiviral properties. Silver nanoparticles represent the most common antimicrobial agent. Due to recent technological advancements, these nanoparticles have resurfaced in the medical field. Because of their low toxicity to mammalian cells and stronger antimicrobial activity, silver nanoparticles have been used in a variety of disciplines. Silver nanoparticles are also utilized for the treatment of biofilms associated with medical devices that threaten life. The purpose of this study is to examine the potential antibacterial activity of PVP coated silver nanoparticles against *E. coli*.

Methods: The chemical reduction approach is commonly used to prepare Ag NPs because of time saving and cost-effective. There are several reductants commonly being used for the synthesis of the AgNPs such as sodium borohydride, citrate, ascorbate and elemental hydrogen. The choice of reductant might influence the size and shape of synthesized AgNPs, it is also important to use a stabilizing agent or a protective agent to prevent the agglomeration of the dispersive nanoparticles during preparation. Polymers used as stabilizers are poly-vinylpyrrolidone (PVP), poly-ethylene glycol (PEG), poly-methacrylic acid (PMAA), starch and poly-methyl-methacrylate (PMMA). In this study, we used the chemical reduction method with sodium borohydride as the reductant and PVP as the stabilizing agent. This simple method is cheap, fast and requires only basic equipment. The method allows the preparation of silver NPs with a different size and distribution.

Results: The results have shown that the synthesized spherical silver nanoparticles were in a nanometer range and disperse in water. The synthesized AgNPs of his study exhibited a strong antibacterial activity against Gram-negative bacteria *Escherichia coli* (*E. coli*).

Conclusion: In conclusion, we have demonstrated that the method of reduction Ag^{+1} to Ag^0 by sodium borohydride as the reaction agent and the PVP as stability agent was used for the synthesis of spherical shape AgNPs. Our method showed that the synthesized AgNPs exhibited a good antibacterial activity against Gram-negative bacteria *E. coli*. So, this Ag NPs can be applied as antibacterial coatings for medical applications.

Keywords: Silver nanoparticle, antibacterial activity, *Escherichia coli*.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-56

Molecular and phenotypic characteristics of *Stenotrophomonas maltophilia* strains isolated from Blood Cultures of hospitalized children

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Abstract

Background and Aim: The aim of this study was to determine the phenotypic and genotypic characteristics of *Stenotrophomonas maltophilia* isolates obtained from blood culture samples of pediatric patients hospitalized in Borujerd and Hamadan hospitals in western Iran.

Methods: Oxidase-negative isolates were collected from the blood cultures of pediatric patients. *S. maltophilia* isolates were identified and confirmed by routine microbiological and molecular testing. Antibiotic susceptibility of the isolates was determined. The phenotypic and genotypic biofilm-forming ability of the isolates were investigated. Molecular typing of all isolates was performed by repetitive element sequence-based polymerase chain reaction.

Results: Out of 450 oxidase-negative bacilli, 72 (16.0%) were identified as *S. maltophilia* isolates. Biofilm assay results showed strong biofilm formation in 19 (26.4%) isolates, moderate in 38 (52.8%), weak in 10 (13.9%), and no biofilm formation in five (6.9%) isolates. Biofilm-associated genes *rmlA*, *rpfF*, and *spgM* were detected respectively in 59 (81.9%), 54 (75.0%), and 72 (100%) of isolates. Antimicrobial susceptibility testing showed that 67 (93.1%) isolates were sensitive to trimethoprim-sulfamethoxazole. All isolates were sensitive to levofloxacin and resistant to ceftazidime. The *S. maltophilia* isolates were grouped into 14 different type's repetitive sequence by repetitive element sequence-based polymerase chain reaction analysis.

Conclusion: The results of this study indicate that *S. maltophilia* should be considered an important opportunistic pathogen in pediatric units. Different genotypes of *S. maltophilia* with the ability to form a biofilm (an important virulence factor) were circulating in the hospitals investigated. Levofloxacin and trimethoprim-sulfamethoxazole are recommended to treat *S. maltophilia* infections.

Keywords: *Stenotrophomonas maltophilia*; Pediatrics; Bacteremia; Antibiotic Resistance; Biofilm; Molecular Typing; Iran.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-57

Investigation of the colistin resistance among MDR/XDR *Acinetobacter baumannii* isolated from Shahid Sadoughi Hospital, Yazd, Iran

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Abstract

Background and Aim: *Acinetobacter baumannii* is a Gram-negative coccobacillus and a major cause of nosocomial infections. This bacterium is able to produce the biofilm on the surfaces of hospitals and can be resistant to different classes of antibiotics, which causes Multidrug-resistant (MDR) and Extremely Drug-resistant (XDR) phenotypes. Nowadays, polymyxins such as colistin are used as the last line of treatment of XDR *A. baumannii* infections. The aim of this study is investigation of the colistin resistance in MDR or XDR *A. baumannii* isolated from Shahid Sadoughi Hospital; the biggest University Hospital in Yazd, Iran.

Methods: In this cross-sectional study, 40 MDR or XDR *A. baumannii* isolates were collected from Shahid Sadoughi Hospital in Yazd, Iran from October 2022 to March 2023. Isolates were identified by Gram staining and biochemical tests such as oxidase, TSI and SIM tests and confirmed by PCR technique using the *bla_{OXA-51}* gene. Disk diffusion method was used susceptibility testing and detection of MDR/XDR isolates. Broth microdilution method was performed for determination of MIC of colistin according to CLSI 2023 guidelines.

Results: All of MDR or XDR isolates were confirmed as *A. baumannii* by PCR technique. Any of MDR or XDR *A. baumannii* isolates (100%) were not intermediate or resistant to colistin and MIC of all isolates were <0/5µg/ml.

Conclusion: Although none of *A. baumannii* isolates in this study were intermediate or resistant to colistin, but there are some reports of colistin resistance, which indicate that colistin resistance can increase rapidly in the world due to plasmid-mediated colistin resistance (*mcr*) genes.

Keywords: *Acinetobacter baumannii*; XDR; Antibiotic resistance; Colistin.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

PBa-58

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-58

Assessment of the impact of chitosan on the Multidrug resistant *Pseudomonas aeruginosa*

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Abstract

Background and Aim: Though nanoparticles have found their place in the modern scientific therapeutic world however, before they step into treatment strategies it is necessary to determine their effects either alone or with antibiotics in lowering antibiotic resistance. This study aimed at to evaluate the antibacterial activity of chitosan nanoparticles (NPs) alone and in combination with ciprofloxacin against *P.aeruginosa* and its efficacy of to alter the expression level of efflux pumps.

Methods: The antibacterial activities of chitosan, chitosan NPs and its combination to ciprofloxacin (CNC) were evaluated through the use of micro dilution broth, disc diffusion and drop diffusion methods. In addition, the toxicity of the synthesized materials was calculated by MTT assay. To conduct the experiments of the expression of target genes of *mexB*, and *mexY*, initially antibiotic resistant *P. aeruginosa* (PAO1) strains were exposed to the chitosan in its sub inhibitory levels, then RNA was extracted to study the antibacterial effects of the nanoparticles in relation to the expression of the efflux pump using real-time PCR.

Results: The result showed because of the difficulty of movement of the synthetic substances on the Agar medium, antibacterial activities of chitosan NPs, CNC, against *P.aeruginosa* were not the same using three analytic methods. Micro dilution broth was the most amenable technique among the three procedures. Chitosan and its nanoparticle forms combined with antibiotics, did not show toxic properties on stem cells by MTT assay. The result also showed efflux pump expression of *mexB* and *mexY* in *P. aeruginosa* decreased after treating them with chitosan, chitosan nanoparticle, so they are good candidate as an efflux pump inhibitor.

Conclusion: The outcomes showed the higher antibacterial and anti-efflux pump activity of chitosan against *P. aeruginosa*. Minimum inhibitory concentration (MIC) levels of ciprofloxacin were found to have increased after exposure to the nanoparticle.

Keywords: *Pseudomonas aeruginosa*, Efflux pump, *mexB*; *mexY*, Chitosan nanoparticles.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-59

Nosocomial infections by carbapenem resistant *Klebsiella pneumoniae* and its clinical risk factors in a university based general hospital

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Abstract

Background and Aim: *Klebsiella pneumoniae* is an important pathogen involved in hospital acquired infections. Immunocompromised patients especially, diabetic and possessing pulmonary obstruction are more at risk. The emergence of carbapenemase in *K. pneumoniae*, particularly the hyper virulent strains has curbed the usage of imipenem and meropenem, thereby putting profound constraints on the therapeutic strategies. This study aimed at finding carbapenem resistant *K. pneumoniae* and the clinical determinants involved.

Method: The study was conducted on *K. pneumoniae* clinical isolates obtained from patients admitted to the University hospital and developed nosocomial infection. In general, the inclusion criteria comprised of those *K. pneumoniae* isolates, which were obtained as a pure isolate, the clinical manifestations of the patients matched with infectious conditions, and the infectious specialist suspected a hospital infection. The isolates were defined phenotypically as mucoid when colonies were touched with a loop and a string-like growth was observed which adhered to the loop as it was lifted from the agar plate to identify hypervirulent strain. The pertinent information on any underlying disease, other demographic data, and treatment regimens was collected from the records of each patient. Antimicrobial susceptibility testing was performed using the Kirby-Bauer method by the Clinical and Laboratory Standard Institute (CLSI) guidelines. Resistance towards antibiotics belonging to at least three different antimicrobial classes was defined as multidrug-resistance (MDR) and those resistant towards imipenem and meropenem were regarded as carbapenem resistant. For PCR amplification of the carbapenemase genes, multiplex PCR was performed for the *bla_{KPC}*, *bla_{NDM-1}*, and *bla_{OXA-48}*, *bla_{IMP}*, and *bla_{VIM}* genes.

Results: *K. pneumoniae* was confirmed at genetic level. Age of the patients had mean 56.7 ± 23.42 years, however, more than half clinical infections were seen in the elderly patients (> 60 years). Thirty-four *K. pneumoniae* isolates were identified as nosocomial pathogens. Clinical source of *K. pneumoniae* isolates comprised of urine, wound, blood, endotracheal aspirates and body fluids. When hospital-acquired *K. pneumoniae* isolates were compared for carbapenemase genes, 31 *bla_{OXA-48}* positive isolates had a significant ($p < 0.002$) relation with hospital-acquired isolates. On the contrary, *bla_{NDM-1}*, *bla_{KPC}*, *bla_{VIM}*, and *bla_{IMP}* positive isolates were not related to hospital-acquired isolates. Among the clinical isolates following underlying diseases were found: renal diseases, pulmonary diseases, gastrointestinal problems, infectious diseases, those suffering from ulcers and abscess, burn patients, diabetes and hyperplasia of prostate. The overall rate of treatment failure in the present study was 28%. Wound infections were associated with the highest rate of treatment failure ($p = 0.03$).

Conclusion: This study highlighted a high prevalence of carbapenem-resistant genes in *K. pneumoniae* isolates. Of the five carbapenemase genes studied, the association of *bla_{OXA-48}* was observed with patients afflicted with urinary tract infections with the hospital as a source. *bla_{KPC}* positive strains were significantly associated with wound infections. Appropriate information regarding the distribution of antibiotic resistance genes, and other characteristic features concerning the specific clinical specimens and medical wards could help physicians to choose the appropriate treatment.

Keywords: *Klebsiella pneumoniae*; Carbapenemase; Antibiotic resistance; Clinical determinants.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-60

New promising approaches to treat multi-drug resistant *klebsiella pneumoniae*

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Abstract

Background and Aim: Antimicrobial resistance (AMR) is one of the biggest challenges in microbiology and some solutions in bacteria to deal with antibiotics include innate or acquired mechanisms, reduce the drug penetration, alteration the drug targets, enzymatic inactivation of drugs, multidrug efflux pumps and biofilm formation. Multi drug resistant (MDR) is a term that the bacteria have resistance to three or more antimicrobial classes. *K. pneumoniae* (*Kp*) is Gram negative, commensal, ubiquitous, opportunistic, rod-shaped, non-motile that has a polysaccharide capsule with a wide range of community-acquired and nosocomial infections. The aim of this study was searching the possible treatments against MDRKp.

Methods: In order to answer this topic, our search was performed in google scholar and PubMed from September 23, 2023 to September 29, 2023 and first of all to get the best and comprehensive results, keywords of multi-drug resistant, *Klebsiella pneumoniae* and treat were selected.

Results: We have found many bacteriophages specially their cocktails are tools that the absence any immunity response against them in our body is the most reason also nanoparticles and Nano-antibiotic by use of nanotechnology are well developed that can be useful. CRISPR-Cas system, antimicrobial peptides, odorhabinins, Drug delivery systems (DDSs), Fecal transplant therapy (FTT) and double-carbapenem therapy (DCT) are new tools so require more research. Due to the extracellular nature of *Klebsiella pneumoniae*, antibody drug conjugation and some of the engineering are done on its structure are useful. Nontoxic Bacteriocins are peptides that thorough translocation pathways infiltrate to target bacteria which produce by lactic acid bacteria (LABs) and probiotics, prebiotics and their supernatant specially from LABs have shown the brilliant results. Predatory bacteria (living antibiotics) due to their morphology are used to treat infections by Gram negative bacteria also antibacterial oligonucleotides by their adjuvant role in combination with antibiotics are effective.

Conclusion: In the current study, to treat MDR *Klebsiella pneumoniae*, we found different valuable approaches like Phage therapy, Antimicrobial peptides, Nanotechnology, Antibody drug conjugation, Antimicrobial oligonucleotides, Nano antibiotic, Crispr-Cas System, Bacteriocins, Probiotics, some techniques like FTT and DCT and DDS, Predatory bacteria, Antibacterial oligonucleotides, Combined antibiotics and finally synthetic lipopeptide but nowadays, considering the importance of multi drug resistant in *Klebsiella pneumoniae* and its easy and quick distribution among the people, especially the hospitalized patients, more studies are needed in this field to find the best approaches with the least complications.

Keywords: Multi-drug resistant, *Klebsiella pneumoniae*, Treat.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBa-61

The effect of *Bifidobacterium bifidum* on the treatment of diabetes in children

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Abstract

Background and Aim: Bifidobacteria as a strictly anaerobic gram-positive bacteria, is widely distributed in the intestine, vagina and oral cavity, and is one of the first gut flora to colonize the early stages of life. Intestinal flora is closely related to health, and dysbiosis of intestinal flora, especially Bifidobacteria, has been found in a variety of diseases. Numerous studies have shown that in addition to maintaining intestinal homeostasis, Bifidobacteria may be involved in diseases covering all parts of the body, including the nervous system, respiratory system, genitourinary system and so on.

Methods: New insights into the role of the gut microbiota in diabetes could lead to the development of integrated strategies using probiotics to prevent and treat these metabolic disorders. Animal studies have shown that a dysbiotic gut microbiota generates high levels of lipopolysaccharides (LPSs), which leads to inflammation of the intestinal mucosa, loss of tight junction integrity between epithelial cells, and increased intestinal permeability. This may contribute to deterioration of glycemic control because LPS will cross the leaky intestinal epithelium into the circulation, resulting in high serum LPS levels or endotoxemia, causing systemic inflammation, insulin resistance, and poor glycemic control. Composition differs between healthy controls, those with β -cell autoantibody [that is at risk for type 1 diabetes (T1D)] and patients with established T1D. This altered microbiota is termed dysbiosis, and in comparison, with the microbiota of healthy controls, it has a lower abundance of bifidobacteria and a higher abundance of Gram-negative bacteria.

Results: World Health Organization (WHO) states that currently about 422 million people are affected with either type 1 or 2 diabetes mellitus. Various functions of the gut are regulated by sophisticated interactions among its functional elements, including the gut microbiota. These microorganisms play a crucial role in gastrointestinal mucosa permeability. Emerging evidence shows that the gut microbiota composition in diabetic subjects differs significantly from their non-diabetic counterparts. In diabetic humans, there is a lack of uniformity in the gut microbiota profile. A human metagenome-related study showed significant associations with specific gut microbes, bacterial genes, and metabolic pathways in T2D patients. These patients showed higher levels of *Bifidobacterium bifidum* compared to non-diabetic subjects. *Bifidobacterium bifidum* was positively associated with fasting glucose and glycosylated hemoglobin (HbA1c), while some other pathogenic bacteria were negatively associated with fasting.

Conclusion: Probiotics are nondigestible carbohydrates that alter gut microbiota and could potentially improve glycemic control and reduce intestinal permeability and thereby insulin sensitivity. In general, the above-mentioned findings, which confirm a strong link between the GI system and diabetes, have focused considerable attention on the use of biotherapy to regulate intestinal microbiota function. Probiotics are live microorganisms that, when administered in sufficient quantities, provide health benefits to the host.

Keywords: Bacteria; Probiotics; Bifidobacterium; Diabetes; Microbiota.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-62

Antimicrobial Resistance Profile of Planktonic and Biofilm Cells of *Staphylococcus epidermidis* isolated from clinical specimens

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Abstract

Background and Aim: *Staphylococcus epidermidis* belongs to the group of coagulase-negative staphylococci common in hospital environments, which has the ability to cause various diseases. The aim of this study was to determine the antibiotic resistance profiles of planktonic and biofilm cells of *Staphylococcus epidermidis* isolated from clinical isolates of hospitalized patients.

Methods: Out of 165 coagulase-negative *Staphylococcus* spp, 100 *Staphylococcus epidermidis* species were included in the study. These isolates from different clinical samples of blood, wound, peritoneal fluid, pleural fluid and CSF from hospitalized patients in two teaching hospitals of Shahrood were studied. The antimicrobial susceptibility to cefoxitin, erythromycin, clindamycin, tetracycline, ciprofloxacin, gentamicin, linezolid and trimethoprim/sulphamethoxazole (SXT) was tested by disk-diffusion method and interpreted according CLSI guidelines. Quantitative biofilm determination was performed by the Micro-titer plate Test (MTP).

Results: Seventy-eight percent of *Staphylococcus epidermidis* isolates were multidrug resistant (MDR) and the highest resistant was observed to SXT (86%). They were quite susceptible to linezolid. Resistance to gentamicin, erythromycin, clindamycin, SXT, ciprofloxacin and cefoxitin was observed in 67, 54, 50, 86, 45, 86 isolates respectively. The biofilm formation analysis by MTP assay showed strong and weak biofilm forming isolates was 35% and 55% respectively. Statistical analysis of the results showed a significant increase in the antibiotic resistance of biofilm producing *Staphylococcus epidermidis* isolates compared to planktonic cells. There was a considerable in the number of susceptible planktonic isolates that became resistant when growing in a biofilm except for linezolid that none of the isolates were resistant to this drug in two vital forms.

Conclusion: *Staphylococcus epidermidis* isolates circulating in the hospitals in our region with high biofilm formation characteristic and a high antibiotic resistance pattern are a warning to pay more attention to this bacterium, which uses these strategies to maintain its survival. Consequently, different protocols for profiling antimicrobial resistance should be fulfillment in clinical microbiology laboratories to allow the selection of appropriate treatment.

Keywords: *Staphylococcus epidermidis*; Biofilm; Resistance; Clinical specimens.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review/Meta Analysis

Code of Abstract: PBa-63

The effect of nosocomial infections on neonates

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Abstract

Backgrounds and Aims: Nosocomial infection in infants is a common complication with high death Neonates in care unit feature many specific risk factors for bacterial and fungal sepsis. Thus, prevention of bacterial and fungal infection is crucial in these settings of patients. Hospitalized neonates and their mothers are particularly vulnerable to nosocomial infections. Our objectives through this systematic review were to: investigate establish patient risk factors; compile measures for controlling outbreaks and recommended strategies for prevention; and identify information gaps to improve guidelines for reporting future outbreaks.

Methods: A systematic literature search was accomplished to identify published studies between April 2002 and April 2019. Studies were collected using different keyword combinations: nosocomial infections, neonatal. The literature search strategy in this paper included searching PubMed, PMC, and Science Direct, Springer open, Google scholar and Biomed Central databases.

Results: Twenty-five studies were included. The most common Low birth weights, preterm or premature birth, and underlying disease increased neonatal risk of infection. Effective control measures commonly included replacing or cleaning faucets and increased or alternative methods for hand asepsis, and recommendations for prevention of future infections highlighted the need for additional surveillance.

Conclusion: Nosocomial infections remain an important cause of morbidity and mortality in neonates. Our program raised awareness in health personnel, with weekly appeal during clinical sessions for the need to continue or stop treatment or intervention. The implementation of control measures and recommended prevention strategies by healthcare workers and managing government of healthcare facilities and improved reporting of future outbreaks may contribute to a reduction in the incidence of nosocomial infections in neonates.

Keywords: Nosocomial; Infection; Neonatal.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBa-64

A review of female vaginal microbes in health and vaginal health

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Abstract

Background and Aim: The vaginal microbiome is a complex and dynamic microecosystem that constantly fluctuates during a woman's menstrual cycle and throughout a woman's life. The healthy vaginal microbiome is dominated by lactobacillus, which produces many different types.

Methods: In this systematic review, to identify the studies conducted with the aim of the female vaginal microbiome in health and bacterial vaginosis, Google Scholar, PubMed, and Science Direct databases were searched based on the keywords vaginal microbiome, bacterial vaginosis, female health, lactobacillus. After checking the title and abstract of the articles, irrelevant articles were removed the full text of the articles was searched and the articles related to the topic were included in the study.

Results: According to the studies, there is a homeostatic and reciprocal relationship between the microbiota and the human host in the ecosystem, which provides a moist, nutritious, and warm habitat for the microbes. While the resident microbiota produces antimicrobial substances and also the pathogens present in the resident microbes can attack the human body and cause disease.

Conclusion: The vaginal microbiome in a person changes temporarily and also differs greatly among them, and the difference in the vaginal microbiome by the race of women may be driven by the genetic factors of the host and a more important role in this form. Breeds are in charge.

Keywords: Bacterial vaginosis; Vaginal microbiome; Lactobacillus; Female health.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBa-51

A review of the contribution of lactobacillus iners to vaginal health and diseases

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Abstract

Background and Aim: The vaginal microbiome plays an important role in determining the health of the human vagina. Using the study of genetic materials and rRNA sequencing, more than 250 species of bacteria have been identified in the human vagina.

Methods: This systematic review was conducted to identify the studies conducted with the aim of the contribution of lactobacillus iners to vaginal health and diseases, searching in Google Scholar, PubMed, and Science Direct databases based on the keywords bacterial vaginosis, lactobacillus iners, sexually transmitted infections. After reviewing the summary of the articles and checking the title, the irrelevant articles were removed the full text of the articles was searched and the articles related to the topic were included in the study.

Results: According to the studies, Lactobacillus ineres is a type of transmission that colonizes after the disruption of the vaginal environment and generally provides less protection against intolerance and reduced microbial diversity in the vaginal microbiome, and subsequently leads to bacterial vaginosis and infections. It becomes sexual.

Conclusion: As a result of lactobacillus iners, species with extraordinary characteristics having a small genome and the simultaneous deficiency of nutrients lead to high compatibility with the vaginal environment with high and low pH as well as positive and negative bacterial vaginosis conditions.

Keywords: Bacterial vaginosis; Lactobacillus; Sexually transmitted infections.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-51

Dysbiosis and Fecal Microbiota Transplant in neurological disorder

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Abstract

Background and Aim: Neurological disorders are characterized by the loss and eventual death of nerve cells in the brain or peripheral nervous system, often associated with aging. Alzheimer's disease and Parkinson's disease are significant neurodegenerative conditions. Recent research has highlighted the potential role of gut bacteria in the development of neurological disorders. Imbalances in the gut microbiota can lead to structural changes and contribute to various neurological disorders. Modulating the gut microbiota holds promise as a therapeutic approach. Fecal microbiota transplantation (FMT) has emerged as an innovative intervention for addressing gut dysbiosis and has been approved for treating recurrent *Clostridium difficile* infections. Its effectiveness in treating other neurological disorders is also under investigation. This study aimed to explore the relationship between dysbiosis and neurological diseases and evaluate the potential of FMT as a treatment for these disorders.

Methods: To collect data for this review article, we used PubMed, Scopus, Google Scholar and Medline databases. The keywords used were Alzheimer's disease + dysbiosis or microbiome, Parkinson's disease + dysbiosis or microbiome, Alzheimer's disease + FMT, Parkinson's disease + FMT.

Results: In microbiome research, the term "dysbiosis" is increases the number of harmful bacteria in the gut which causes induction intestinal, systemic disorders and progress neurological disorder. A treatment called Fecal Microbiota Transplantation (FMT) which aims to re-establish a balanced microbiome. Parkinson's disease (PD) is a progressive and multifactorial neurodegenerative disorder and the second most common cause of mortality after Alzheimer's disease (AD). The GM has recently received a lot of focus as a possible contribution to the mechanism underlying PD. FMT has been studied as a potential therapeutic modality for PD patients. studies in experimental mice models suggest that altering the GM by long-term FMT delivery might be a unique therapeutic approach for some people with PD. Alzheimer's disease (AD) is a chronic neurodegenerative condition that causes neuronal death. The most current research showed that disruptions in the microbiota-brain axis might cause neuroinflammation and AD. In the brains of AD animals, FMT may reduce A β plaques and improve cognitive impairment. Soo-Hyun Park et al. describes the case of a 90-year-old woman who received FMT and had severe CDI and Alzheimer's dementia, this case study describes cognitive improvement in an AD patient following FMT for recurrent severe CDI.

Conclusion: In the past decade, there has been a growing interest in the benefits of Fecal Microbiota Transplantation (FMT) for gastrointestinal diseases. Case studies have shown its effectiveness in treating certain diseases. However, FMT's application in neurological disorders like Parkinson's and Alzheimer's is limited. Patients with these conditions often experience gastrointestinal issues, and some studies have suggested positive outcomes of FMT in treating constipation and reducing non-GI symptoms. Developed countries are utilizing FMT in the form of capsules and medicine to address various diseases. Despite the promising future, there is limited information on how FMT affects neurodegenerative disease mechanisms. Nonetheless, it is believed that targeting the gut microbiota may serve as a supplementary treatment for neurological disorders in the future.

Keywords: Fecal Microbiota Transplantation (FMT), Parkinson's disease, Alzheimer's disease, microbiome, Neurological disorders.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-67

Prevalence of Phenazine Genes Among Clinical Isolates of *Pseudomonas aeruginosa* in Teaching Hospitals of Ahvaz

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Abstract

Background and Aim: *Pseudomonas aeruginosa* as an opportunistic pathogen causes serious acute and chronic nosocomial infections in humans. Because of the emergence of resistance among these bacteria in recent years, treatment of infections caused by them has been difficult. Phenazines as secondary metabolites are produced by *P. aeruginosa* and play a role in virulence. The aim of this study was to determine the frequency of phenazine genes in *P. aeruginosa* strains isolated from hospitalized patients in teaching hospitals of Ahvaz.

Methods: In total 51 clinical isolates of *P. aeruginosa* were collected. All isolates were identified by biochemical tests. Antimicrobial susceptibility testing was performed by disc diffusion method recommended by CLSI 2022 guideline. The presence of phenazine genes (*phzI*, *phzII*, *phzH*, *phzM* and *phzS*) was evaluated by PCR technique.

Results: According to our findings, the most antimicrobial resistance found against imipenem and meropenem (70.6%) and ciprofloxacin (56.9%). Although, 33(64.7%) isolates were susceptible to ceftazidime. PCR results showed that all *P. aeruginosa* strains harbored *phzI* genes (100%). Also, *phzII*, *phzH*, *phzM* and *phzS* genes were detected in 34(66.7%), 18(35.3%), 47(92.2%) and 31(60.8%) isolates, respectively. Furthermore, 14(27.5%) isolates harbored all the phenazine genes.

Conclusion: The prevalence of antimicrobial resistance and virulence genes in *P. aeruginosa* strains is an increasing concern worldwide. Therefore, an appropriate control measures need for prevention of further expansion of these genes. Also, continuous surveillance is necessary for determining successful therapeutic options for treatment of nosocomial infections.

Keywords: *Pseudomonas aeruginosa*, Antibiotic resistance, Phenazine genes, PCR.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-68

Association between Dysbiosis and Multiple sclerosis; role of Fecal microbiota transplantation (FMT) in treatment

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Abstract

Background and Aim: The interaction between the gut microbiota (GM) and a certain part of the nervous system called the gut-brain axis that plays an important role in mental health. many studies have related the key role in the balance of GM and the balance of health. Dysbiosis leads to a number of neurological disorders, including MS and could lead to the inflammatory condition. In present study, an attempt was made to investigate a relationship between dysbiosis and MS and the role of Fecal Microbiota Transplantation (FMT) in disease treatment

Methods: To data collection for this review article, we used PubMed, Scopus, Google Scholar and Medline databases. The keywords used were multiple sclerosis + dysbiosis or microbiome, multiple sclerosis + FMT.

Results: Dysbiosis defined as the inappropriate regulation of gut microbiota, has recently been linked to the pathophysiology of MS, according to a wealth of evidence. Recent research reported significant alterations in GM species and possible associations with pro-inflammatory pathways may cause or worsen the disease. Given the dysbiosis that has been found in people with MS, FMT has been suggested as a potential strategy to restore a balanced GM. FMT of naïve mice into immunized mice decreased microglia and astrocyte activation, BBB (blood-brain barrier) leakage, demyelination, and axonal loss in EAE (Experimental autoimmune encephalomyelitis). This approach is thought to improve intestinal barrier function when the microbiome has been successfully modified. The intestinal barrier's homeostasis is regulated by the GM, partially through the synthesis of Short-Chain Fatty Acids (SCFA) such butyrate, propionate, and acetate. Additionally, SCFA's have a powerful immunomodulatory effect on MS by balancing the T-cell population

Conclusion: Gut microbiota is an important factor in regulating the gut-brain axis and evidence shows that it affects human health and disease. Disturbances in the gut microbiota are associated with various diseases such as MS, for which FMT is used as medicine or tablets and capsules, especially in developed countries. Although there is not enough research for MS, it is believed that in the future, therapies that target GM may be useful as an additional treatment for MS.

Keywords: Multiple sclerosis; FMT; Dysbiosis; Gut microbiota.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-69

New promising approaches to treat multi-drug resistant *Klebsiella pneumoniae*

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Abstract

Background and Aim: Antimicrobial resistance (AMR) is one of the biggest challenges in microbiology which misusing of antimicrobials, poor hygiene are some important factors that intensify it and some solutions in bacteria to deal with this issue are: innate, adaptive or acquired mechanisms, reduce the drug penetration, alteration the drug targets, enzymatic inactivation of drugs, multidrug efflux pumps and biofilm formation. Multi drug resistant (MDR) is a term that the bacteria has resistance to three or more antimicrobial classes (1,3) In 2016, it was estimated 700,000 deaths occur due to it every year. The aim of this study is searching the possible treatments against MDR *Klebsiella pneumoniae*.

Methods: In order to answer this topic, a search was performed in google scholar and PubMed from 23 September 2023 to 29 September 2023.

Results: We have obtained several promising treatments such as Phage therapy, antimicrobial peptides, Nanotechnology, Drug delivery systems (DDSs), Antibody drug conjugation, antimicrobial oligonucleotides, Nano antibiotic, Crispr-Cas System, Bacteriocins, Probiotics, Fecal transplant therapy (FTT), Predatory bacteria, Antibacterial oligonucleotides, Combined antibiotics, Synthetic lipopeptide and double-carbapenem therapy (DCT).

Conclusion: In summary, we have found many bacteriophages specially their cocktails are powerful tools that the absence any immunity response against them in our body is the most reason also nanoparticles and Nano-antibiotic by use of nanotechnology are well developed that can be useful. CRISPR-Cas system, antimicrobial peptides and odorhabinins are new useful tools so require more research. In DDSs approach our drugs are trapped in liposomes, polymeric micelles, nanogels, inorganic nanoparticles, and inorganic/organic nanoparticles that enhance the pharmacological and pharmaceutical properties. Antibody drug conjugation and some of the engineering are done on its structure are useful. Nontoxic Bacteriocins are peptides that thorough translocation pathways infiltrate to target bacteria which produce by lactic acid bacteria (LABs) and probiotics, prebiotics and their supernatant specially from LABs have shown the brilliant results. FTT is helpful but because of its safety, required more research. Predatory bacteria also are called as living antibiotics, are new approach that due to their morphology are used to cure Gram negative infections. Antibacterial oligonucleotides by their adjuvant role in combination with antibiotics and suppress the production of host mRNAs can be used to treat and combined antibiotics in vitro with synergy effects and DCT are so powerful because they give results at lower MICs subsequently it prevents the formation of resistant strains and finally synthetic lipopeptide or bioactive and biosurfactant agents have the most safety and activity because of induction of membrane fusion between bacteria and itself.

Keywords: Multi-drug resistant, *Klebsiella pneumoniae*, Therapy.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-70

Detection of mupirocin, gentamicin and erythromycin resistance genes in MRSA clinical isolates

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Abstract

Background and Aims: In any hospital setting, for early diagnosis and detection of nosocomial infections, markers and antibiotic-resistant genes (ARG) serve as an important route. *Staphylococcus aureus* is the cause of many nosocomial infections. The emergence of methicillin resistant *Staphylococcus aureus* has altered the therapeutic regimen of this organism. In the present study we developed a multiplex PCR for the detection of *S.aureus* and resistant to methicillin, aminoglycosides, macrolide, mupirocin genes.

Methods: A total of 1389 clinical samples from patients admitted to the University based hospital and developed nosocomial infection after 72 hours of admission were enrolled in the study. The specimens were sent to Division of Microbiology, Sina Hospital where they were processed for any bacterial growth. The *S.aureus* isolated from these specimens were subjected to antibiotic susceptibility test by disk diffusion assay. PCR was later performed on *S.aureus* isolates which were found methicillin-resistant by cefoxitin disk (as per CLSI criteria) and then E-test was performed for oxacillin, gentamicin and mupirocin.

Results: Among 89 MRSA isolates, all contain *mecA* gene. Resistance towards aminoglycosides genes (*aph(3)-IIIa*, *aac(6)-Ie-aph(2)-Ia*, *ant (4)-Ia*) in 28.4% ,31%, and 38.5%. The first mentioned gene was isolated from wound infections and next two genes were observed in *S.aureus* isolated from body fluid. Twenty-two strains were found clindamycin resistant and *ermA* and *ermC* genes were observed in isolates cultured from endotracheal aspiration. Mupirocin gene was prevalent among isolates obtained from abscesses.

Multiplex PCR took less time to observe simultaneously the presence of MRSA along with ARGs.

Conclusion: Classical method of detection of MRSA and the antibiotic resistance is a time consuming taking 72 hours. However, if a diagnostic laboratory develops multiplex PCR for the detection and presence of ARG, it will help in reporting in less time paving way for the earliest treatment with appropriate antibiotic.

Keywords: *Staphylococcus aureus*, MRSA, Aminoglycosides, Mupirocin, Erythromycin, Antibiotic resistant genes.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-71

Estimating the efficacy of povidone iodine 10 percent in eliminating microorganisms

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Abstract

Background and Aim: Povidone-iodine, also known as iodopovidone. With the formulation of C₆H₉I₂NO. Is an antiseptic used for skin disinfection before and after surgery. It may be used both to disinfect the hands of healthcare providers and the skin of the person they are caring for it may also be used for minor wounds.

Methods: For the experiments povidone iodine 10 percent green supplied by the company TOLYD DARU was used to estimate the efficacy of povidone iodine 10 percent green in eliminating the microorganisms. The laboratory scale experiments and hydroponic growth studies were carried out at the Microbiology Section of Savaaneh and Soukhtegy Hospital (i.e., Burn Injury Accidents Hospital), Ahvaz (Khuzestan, Iran). The experiment was carried out on samples acquired from patients of the operation room of six state hospital located in Ahvaz. One thousand swab samples were collected before and after applying povidone iodine 10% as well as getting smear after applying it on the skin of patients from the operation rooms of six different state hospitals including Savaaneh and Soukhtegy, Golestan, Razi, Imam Khomeini, Sina and Baghaee. The samples were collected at the time of surgery from the operation rooms of the said hospitals in the months of March, April, May, June, July, and August were used to estimate the efficacy of Povidone iodine 10% to eliminate bacteria, fungi and viruses when applied on the skin as an antiseptic for 2 to 20 minutes.

Results: The results of swab testing from patients' skin before applying Povidone iodine 10% showed growth of many gram negative and gram-positive bacteria but in some few patients showed no growth. Povidone iodine is able to eliminate the gram-negative bacteria in more than 90% of our isolates including *Acenetobacter*, *E. Coli*, *Pseudomonas*, *Entrobacter* and *Klebsiella*. However, some gram-negative bacteria showed only reduction of load after applying Povidone iodine. Total elimination of fungi including *Aspergillus sp* and *Penecillium sp*. has been observed. Only few of gram-positive bacteria were eliminated including Cocci (*Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus saprophyticus*) and *Bacillus spp* (less than 5%). Same results were observed in smear samples. Similar results were seen in vitro.

Conclusion: Though the exact time of applying Povidone iodine on patients' skin before surgery could not be estimated, but it can be concluded that the antiseptic effect of Povidone iodine (even applying for 2 minutes) shows positive results on gram negative bacteria in more than 90% of our isolates. In gram positive cocci whether MRSA or others, Povidone iodine was able to eliminate only 5% of microorganisms. Same results were observed in *Bacillus spp*.

Keywords: Povidone iodine 10%; Gram positive bacteria; Minor wounds.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-72

Diagnosis of *Streptococcus pneumoniae* in bacterial meningitis

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Abstract

Background and Aim: The mortality of meningitis remains high in some parts of the world. culture is the gold standard method for detecting bacterial agents, but it is time-consuming and time is very important. Early diagnosis and appropriate treatment are important factors in reducing the secondary complications of meningitis. As well as use of antibiotics before sampling is one of the reasons of false negative in culture. This study aimed to diagnosis of *Streptococcus pneumoniae* in children's bacterial meningitis, a multicenter study from Iran by culture and specific-specific Real- Time PCR.

Methods: In this cross-sectional study, the CSF of the suspicious pediatric to bacterial meningitis who are admitted to the hospitals in four teaching hospitals in Iran were collected. *S. pneumoniae* in CSF samples were detected by culture and primer-probe Real- Time PCR.

Results: In this cross-sectional study, 506 CSF samples with the analysis suspected of bacterial meningitis were collected in one year. Total of the bacterial cultures were negative but 10.6%, *S. pneumoniae*, was identified by primer-probe Real- Time PCR.

Conclusion: Bacterial meningitis can cause the death and disability in children if causative agent of that is not identified rapidly and correctly. This method can be a rapid and accurate method to diagnose *S. pneumoniae* in the bacterial meningitis in children.

Keywords: *S. pneumoniae*, bacterial meningitis, primer-probe Real- Time PCR.





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Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-73

Investigating head louse infestation in children under 6 years of age in Urmia preschools

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Abstract

Background and Aim: Infestation with *Pediculus capitis* (Anoplura: Pediculidae) is a cosmopolitan health problem that is not limited to specific regions or conditions. In addition to its physical problems, its psychological effects especially on pupils are more important. This study was conducted to determine the prevalence of head lice infection in children under 6 years old in preschool and also investigate the role of related possible risk factors in Urmia City in the spring of 1402.

Methods: A total of 25 preschools in Urmia city were randomly selected in the spring of 1402. 1500 children (800 boys and 700 girls) were examined individually and privately by experts. Also, a standard questionnaire was designed to record information about demographic characteristics and factors whose influence should be determined, lifestyle, and contact with animals. The data was analyzed using SPSS software and appropriate statistical tests.

Results: The results of our study determined the prevalence of overall infection in this study to be about 8% (6% in girls and 2% in boys). Girls show significantly more pollution. The availability of hot water suitable for bathing and the size and length of hair are significantly related to the pollution load. On the other hand, there was no significant relationship between parents' education, occupation and pollution, as well as the frequency of bathing per week and the type of their energy source.

Conclusion: The results of this study show that head louse pediculosis is a health problem and remains a noticeable pediatric problem.

Effective risk factors should be determined carefully and regionally. Proper training plays a great role to prevent and control the problem.

Keywords: *Pediculus capitis*, primary schools, Urmia, Head louse infestation.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-74

Bacteriophage against bacterial food borne disease

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Abstract

Background and Aim: Infectious and zoonosis diseases can be transmitted directly or indirectly between humans and animals, and this can lead to contamination of the food chain and public health risks. Also, in the past several years, statistics show that the prevalence of antibiotic resistance in food pathogens has increased. For this reason, phage therapy can be an important and practical solution to controlling zoonotic pathogens.

Methods: This is a review study that after searching with the keywords, Bacteriophage, Phage therapy, food borne disease in PubMed, Embase, Science direct databases from 2015 to 2023, 27 articles related to inclusion criteria were extracted and then analyzed.

Results: The results indicated that the resistance of bacteria that are important in the food chain and related diseases, such as Salmonella, Escherichia coli, Campylobacter, and Clostridium is increasing day by day. Studies have shown that bacteriophages prevent the development of infectious diseases of bacterial origin by controlling and specifically destroying these pathogens.

Conclusion: The emergence of zoonotic and antibiotic-resistant pathogens in the food chain is a growing problem in public health worldwide. It is also important to deal with pathogenic bacteria. Therefore, bacteriophages can play a significant role in controlling these pathogens. Because it works specifically and does not have significant side effects. Phage therapy can be a good solution to deal with infectious diseases caused by bacteria in the food chain.

Keywords: Bacteriophage, Phage therapy, Food borne disease.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-75

An overview of the modulating role of microbiota by bacteriophages in the treatment of diseases

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Abstract

Background and Aim: The symbiotic microbiota is known as the (invisible organ) and accompanies people throughout life. Also, the microbiota can regulate various physiological changes, and its functions in humans and maintaining their health are important. So that if its balance changes, it can cause diseases such as Alzheimer, IBD, and all kinds of tumors. One of the ways to deal with it is the use of bacteriophages that can specifically attack bacteria. This study aims to review the role of modulating microbiota through bacteriophages in various diseases.

Methods: This is a review study that after searching with the keywords, Bacteriophage, Microbiota, Treatment in PubMed, Embase, Science direct databases from 2016 to 2023, 58 articles related to inclusion criteria were extracted and then analyzed.

Results: The results indicate that the symbiotic microbiota has a direct relationship with human health and even the treatment of diseases, and compared to antibiotic therapy, phages act in a very specific and selective manner. By modulating the microbiota through phages, in addition to eliminating infections, there were also suitable anti-tumor strategies.

Conclusion: According to recent studies, personal interventions in microbiota will be considered to improve human health and even predict diseases. Also, new strategies of phage therapy will play an important role. Although the microbiota of the host is involved in the occurrence of many diseases and disorders, it facilitates many mechanisms between the microbiota and the host. The correlation between phages, microbiota, and hosts needs to be further confirmed in future.

Keywords: Microbiota, Bacteriophage, Treatment.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-76

Distribution of uropathogenic *Escherichia coli* strains isolated from children with urinary tract infection in Karaj

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Abstract

Background and Aim: Uropathogenic *Escherichia coli* (UPEC) is the cause of about 80% of urinary tract infections (UTIs) in children. The aim of this study was characterization of UPEC isolates in children with UTI in Karaj.

Methods: One hundred and forty-six UPEC isolates from children with UTI entered the study. The identification of isolates as UPEC strains was done by standard microbiological methods and PCR amplification of *16SrRNA* gene. For statistical analysis SPSS software version 23 was used and comparison between groups was done by chi-square and Fisher's exact tests.

Results: Out of 191 UTI in children, 146 (76.4%) isolates were caused by UPEC strains, of which 30 (20.5%) were male and 116 (79.5%) were female. The age of the patients was between 2 and 14 years, and the mean age was 6.6. Of these patients, 16 (11.0%) were diagnosed with underlying kidney disease, while the remaining did not have underlying kidney disease.

Conclusion: The results of this study showed that a high percentage of UTIs in children in Karaj are caused by UPEC strains. Another finding is that the mentioned infection was obtained in girls over one year old, three to nine times more than boys in this age group, although comparing boys and girls with underlying kidney disease, boys showed a higher rate of UTIs with the UPEC strains.

Keywords: Urinary tract infections; Uropathogenic *Escherichia coli*; Children.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-77

Bacterial Etiology and Antibacterial Susceptibility Patterns of Pediatric sepsis in Abuzar Ahvaz hospital

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Abstract

Background and Aim: A dysregulated systemic inflammatory response to a systemic infection with bacterial, viral, or fungal origins can result in sepsis. Bacterial agents are the primary cause of sepsis, which is a major cause of morbidity and mortality in children globally. The most common causes of sepsis in children are: *streptococcus*, *coagulase-negative staphylococci*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella spp.*, *Pseudomonas*, etc. In order to significantly reduce morbidity and mortality in sepsis, it is imperative that early diagnosis and empirical antibiotic selection be done. Therefore, our goal was to identify the major bacteria causing pediatric sepsis and ascertain the patterns of their antibiotic susceptibility.

Methods: This study was done on 237 blood cultures of the patients who were hospitalized at Ahvaz Abuzar Academic Children's Hospital. Positive blood cultures were identified by conventional bacteriological tests. The antimicrobial resistance pattern was performed by Kirby Bauer disc diffusion based on the Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results: The most common isolates were Gram-positive cocci, and *CoNS* (43%) was found to be the most common Gram-positive cocci. Among recovered Gram-negative isolates, *Pseudomonas spp.* (20/6%) were the predominant isolates. Overall, the most effective antibiotics against *CoNS* were Gentamicin (78/4%) and Ciprofloxacin (64/7%), and the highest resistance was shown to Erythromycin (76/4%). In addition, the most effective antibiotics against *pseudomonas* were Ciprofloxacin (100%) and Amikacin (91/8%), and the highest resistance was shown to Ceftazidime (83/6%). Additional results are given in the chart.

Conclusion: According to the results, the most common pathogen was *CoNS*, and the most effective antibiotic was Gentamicin. It is appropriate to emphasize preventive measures because bacteria are becoming more resistant to common empirical antibiotics. Regular evaluation of the most common bacteria associated with sepsis and identification of their antibiotic sensitivity patterns seem to be reasonable measures.

Keywords: Sepsis, Pediatrics, Antibiotic susceptibility.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-79

The Prevalence of Multidrug-Resistant *Pseudomonas aeruginosa* Strains Isolated from Adult Patients with Cystic Fibrosis

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Abstract

Background and Aim: Cystic fibrosis (CF) is the most common genetic disease in the Caucasian population, inherited through autosomal recessive transmission. Patients with cystic fibrosis are predisposed to chronic respiratory tract infections caused by *Pseudomonas aeruginosa*. Multidrug-resistant *Pseudomonas aeruginosa* (MDR-PA) is an important and growing issue in the care of patients with cystic fibrosis, and a major cause of morbidity and mortality. This study aims to investigate the prevalence and antimicrobial resistance pattern of MDR-PA recovered from the lower respiratory samples of adult patients with cystic fibrosis in Tehran, Iran.

methods: Seventy-nine respiratory samples were collected from CF patients in both inpatient and outpatient settings at three tertiary care teaching hospitals between November 2022 and February 2023. The age range of the studied patients was 28-56 years. Bacterial strains were identified using microbiological and biochemical phenotypic methods. Antibiotic susceptibility testing was conducted using E-test, Broth dilution method and Disc diffusion methods in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results: A total of thirty-six (45.5%) *P. aeruginosa* strains were isolated from all sputum samples of CF patients. Among these, 21 strains (58.3%; nine nonmucoid and twelve mucoid isolates) had multidrug resistance to different families of antibiotics by phenotypic tests. The MDR- *P. aeruginosa* isolates exhibited the highest resistance rates to Oxacillin, Gentamycin, and Ceftazidime (100%), followed by 90.4% resistance to Cefotaxime, 85.7% to Tobramycin, 76.1% to Ciprofloxacin, 71.4% to Trimethoprim-sulfamethoxazole and Rifampin, 66.6% to Piperacillin, 61.9% to Cefepime, 57.1% to Imipenem, and 47.6% to Amikacin. Notably, none of the isolates showed resistance to Colistin during the study period and only 5.5% were resistant to Tazobactam.

Conclusion: The emergence of multidrug-resistant *P. aeruginosa* poses a significant challenge in the management of cystic fibrosis patients. The high prevalence of MDR-PA in Iran underscores the urgent need for drug-resistant infections monitoring/controlling procedures, antimicrobial stewardships, alternative treatment strategies, and heightened surveillance to mitigate the impact of multidrug resistance on patient care and prevent the spread of resistant strains. Future research and collaborative efforts are essential to address this escalating threat and improve outcomes for individuals with cystic fibrosis.

Keywords: *Pseudomonas aeruginosa*; Multidrug-resistance; Antimicrobial resistance; Cystic fibrosis; Iran.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-80

The Critical Role of Laboratory Testing in Mitigating Antibiotic Resistance in Pediatric Antimicrobial Therapy

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Abstract

Background and Aim: Given the heightened concern among clinicians and researchers about the escalating challenge of antibiotic resistance, this review aimed to evaluate the pivotal role of laboratory testing in confronting this urgent public health concern.

Methods: The data for the narrative review was obtained from EMBASE, Web of Science, Scopus, Google Scholar, and PubMed. The search keywords included "antibiotics", "laboratory", "children", and "antibiotic resistance".

Results: Antibiotics play a vital role in the treatment of bacterial infections and have been instrumental in reducing mortality rates caused by bacterial infections. However, the misuse and overuse of these drugs have led to a significant health threat known as antibiotic resistance. This issue is becoming increasingly alarming, and requires immediate attention. One of the main factors contributing to the development and spread of antibiotic-resistant microorganisms is inappropriate prescription of antibiotics, especially in children. Children are frequently prescribed antibiotics unnecessarily because of misdiagnosis or pressure from parents seeking quick solutions for their child's illness. The excessive prescription of antibiotics to children is a futile practice with serious implications for the increase in antibiotic resistance. In the following, we emphasize the crucial role of the laboratory in facilitating the appropriate prescription of antibiotics to reduce antibiotic resistance in antimicrobial therapy for children. Pathogen identification and antibiotic susceptibility testing play critical roles in guiding precise antimicrobial therapy and preventing the development of resistance. Laboratory tests, such as blood cultures and respiratory and urinary samples, identify the specific pathogens responsible for the infection. Susceptibility testing is then used to determine the most effective antibiotics. This information enables physicians to prescribe targeted therapy, avoiding unnecessary use of broad-spectrum antibiotics that can contribute to resistance.

Laboratory testing is critical for monitoring treatment effectiveness and identifying resistance mechanisms. Serial measurements of biomarkers, such as C-reactive protein (CRP) and procalcitonin (PCT) are used to assess treatment response and guide decisions about the duration of therapy. Repeated cultures can detect persistent or recurrent infections that may require timely treatment adjustments. Furthermore, laboratory testing can identify resistance mechanisms such as beta-lactamase production or efflux pumps. This information guides the selection of alternative therapies and helps implement infection control measures to prevent the spread of resistant strains within healthcare settings.

Moreover, effective antibiotic stewardship programs depend significantly on laboratory testing. By providing clinicians with accurate and timely information, laboratories contribute to the appropriate use of antibiotics. This includes promoting the de-escalation of therapy, optimizing doses, and imposing duration restrictions. Additionally, laboratory data contributes to monitoring resistance patterns, which facilitates the development of evidence-based guidelines for pediatric antimicrobial therapy.

Conclusion: By facilitating the identification of pathogens, determining their susceptibility, monitoring treatment efficacy, detecting resistance mechanisms, and supporting antibiotic stewardship initiatives, laboratories contribute significantly to mitigating the development and spread of antibiotic resistance. Collaboration between healthcare providers and laboratory professionals is essential in optimizing pediatric antimicrobial therapy and preserving the effectiveness of antibiotics for future generations.

Keywords: Children; Laboratory; Antibiotic; Drug resistance.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-81

Phylogenetic analysis of *gyrA* gene between resistant and susceptible isolates of *Mycobacterium tuberculosis*

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Abstract

Background and Aim: *Mycobacterium tuberculosis* (TB) is one of the most important causes of mortality worldwide. An increasing drug resistance rate has been observed due to mutations in several genes of TB. Mutations in gene encoding DNA gyrase subunits A (*gyrA*) are the most common mechanism of fluoroquinolone resistance in TB. Therefore, this study analyzed the nucleotide sequences of the *gyrA* gene. The purpose of this study was to compare nucleotide sequences of the *gyrA* gene between resistant and susceptible isolates.

Methods: 30 Nucleotide sequences of the *gyrA* gene in resistant and susceptible isolates were obtained through the GenBank databases. Bioinformatics analysis using the Blast for group comparison of gene and homology determination, ClustalW2 for group comparison of gene (alignment), MEGA5 for drawing the phylogenetic tree, GenBank for comparing genes obtained from investigated isolates was done. Finally, the similarity and genetic differences were determined between resistant and susceptible isolates for the treatment of TB.

Results: After performing a BLAST search, sequencing, and phylogenetic analysis of the *gyrA* gene in available sets from the literature worldwide showed that the *gyrA* gene between resistant and susceptible isolates is less than 1% different in nucleotide sequences.

Conclusion: Our study shows that small changes in nucleotide sequences of the *gyrA* gene cause drug resistance. Prospective studies are required to recognize SNPs that may affect drug resistance and other type of biological forms.

Keywords: Phylogenetic analysis; *gyrA* gene; *Mycobacterium tuberculosis*





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-84

Evaluation of Aureocin A53 as a Promising Therapeutic Agent for Multidrug-Resistant *Mycobacterium tuberculosis*

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Abstract

Background and Aim: The significant worldwide prevalence of tuberculosis (TB) and the growing occurrence of drug-resistant strains of *Mycobacterium tuberculosis* (Mtb) highlight the pressing requirement for new antimycobacterial compounds. Considering their diverse antibacterial mechanisms and low cytotoxicity, antimicrobial peptides (AMPs) show promises as alternative or supplementary treatment options for drug-resistant tuberculosis (DR-TB). Aureocin A53 (AucA), a bacteriocin, exhibits significant potential as a therapeutic agent in the fight against antimicrobial resistance. The objective of this research is to examine the antimicrobial impact of AucA, which was extracted from *Staphylococcus aureus*, on drug-resistant strains of Mtb.

Methods: Following a comprehensive sequence of screening, molecular, and conclusive confirmation tests, *Staphylococcus aureus*, a producer of AucA, underwent final purification utilizing ammonium sulfate concentration and High-Performance Liquid Chromatography (HPLC) methodologies. The Minimum Inhibitory Concentration (MIC) test, employing the Resazurin Microtiter Assay method, was subsequently executed utilizing a standard strain of *Mycobacterium tuberculosis* H37Rv. The investigative scope encompassed assessments of Rifampin-resistant (RR) and isoniazid-resistant strains of *Mycobacterium tuberculosis*, as well as multidrug-resistant *Mycobacterium tuberculosis* (MDR).

Results: Our investigation revealed the efficacy of AucA against strains of *M. tuberculosis*, encompassing H37Rv, reference strains, clinical strains, and isoniazid-resistant strains of *M. tuberculosis*. The MIC for *Mycobacterium tuberculosis* H37Rv was observed to be 128 µg/ml, while for isoniazid-resistant *Mycobacterium tuberculosis*, it was 256 µg/ml. Notably, AucA demonstrated no cytotoxic effects on THP-1 macrophage cell lines at concentrations proximate to its MIC.

Conclusion: Our initial findings indicate the presence of potential AucA candidates that can be effectively combined with anti-tuberculosis drugs. This underscores the importance of adopting a combined therapy approach as a novel strategy to amplify the effectiveness of current drugs, potentially yielding significant therapeutic advantages in the treatment of *M. tuberculosis*.

Keywords: Antimicrobial peptide, Bacteriocin, Aureocin A53, *Mycobacterium tuberculosis*.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-85

Fecal microbiota transplantation: a new alternative approach to treat multi drug resistant klebsiella pneumoniae

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Abstract

Background and Aim: In order to treat multidrug-resistant (MDR) bacterial infections, the current choices are restricted so it is one of the main challenges in medicine especially in immunocompromised patients and people who have excessive use of antibiotics. One the newest approach to combat this issue is Fecal microbiota transplantation (FMT) that is also used against *Clostridium difficile* infection. The aim of this study was searching the treatments against MDR *klebsiella pneumoniae* by using FMT.

Methods: In order to answer this topic, our search was performed in google scholar from December 24, 2023 to December 29, 2023 and first of all to get the comprehensive results, keywords of fecal microbiota transplantation, multi-drug resistant, *Klebsiella pneumoniae* and treat were selected.

Results: There isn't any both of extended spectrum β -lactamase (ESBL) and *K. pneumoniae* in urine and faeces after using FMT to treat patients that were suffering from urinary tract infections also after using FMT, there is not any pathogen that some of them cause sepsis. It has been determined that *Bacteroides* and *Firmicutes* are the most abundant microbiota of donor by using 16S rRNA sequencing and butyrate-producing anaerobic microorganisms like *Faecalibacterium prausnitzii*, *Roseburia hominis*, *Coprococcus eutactus* and *Barnesiella spp* by reducing the immune responses demonstrate the best results as super-donor. *Klebsiella pneumoniae* and *Escherichia coli* are the most microorganisms which are classified in carbapenem-resistant *Enterobacterales* that FMT is a useful tool to remove their infections. FMT is effective not only in eradicating ESBL and carbapenemase-producing *Enterobacteriaceae* infections, but also is against vancomycin-resistant *Enterococci* or methicillin-resistant *Staphylococcus aureus* infections.

Conclusion: In order to treat MDR *klebsiella pneumoniae* infections, FMT is one of the newest approaches to combat this problem which type of the donor microbiota is so effective to get the best results but we must consider its safety especially in immunocompromised patients so, FMT needs more evaluations.

Keywords: Fecal microbiota transplantation, multi-drug resistant, *Klebsiella pneumoniae*, treat.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-86

Antibiotic Resistance Profiles of *Acinetobacter baumannii* Isolated from Burn Wound Infections

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Abstract

Background and Aim: *Acinetobacter baumannii* is an opportunistic pathogen that commonly causes infections in immunocompromised patients, particularly those with severe burns. The emergence of multidrug-resistant *A. baumannii* strains has become a significant concern and challenge in healthcare settings. This study aimed to determine the prevalence and diversity of antibiotic resistance genes in *A. baumannii* isolated from burn wound infections.

Methods: The isolates were obtained from patients admitted to two referral burn centers in Hamadan, Iran. The disc diffusion method was used to determine the antibiotic resistance profiles of 78 *A. baumannii* isolates. Polymerase chain reaction (PCR) assays were performed to identify the presence of β -lactamase-encoding genes (TEM, SHV, CTX-M, and OXA-type).

Results: The results showed a high prevalence of multidrug resistance among the isolates (82.3%). The most common antibiotic resistance genes were OXA-type (79.7%), TEM (67.8%), and CTX-M (41.3%). At least 3 antibiotic resistance genes co-existence was observed in 72.2% of isolates. The diversity of resistance gene profiles suggests that the isolates have been subjected to high selective pressure.

Conclusion: Our study highlights the emergence of multidrug-resistant *A. baumannii* carrying various antibiotic resistance determinants in the studied burn centers, reinforcing the need for continuous infection control and better antibiotic stewardship.

Keywords: Antibiotic Resistance; *Acinetobacter baumannii*; Wound Infections.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBa-87

Wi-Fi Exposure's Effect on the Expression of Adhesion Genes in *Klebsiella pneumoniae* bacteria

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Abstract

Background and Aim: The widespread use of Wi-Fi has instigated a plethora of studies investigating its potential biological effects on microorganisms. This systematic review specifically focuses on the impact of Wi-Fi radiation on the expression of adhesion genes in the pathogen *Klebsiella pneumoniae*, a significant contributor to hospital-acquired infections. Beginning with a foundational understanding of *K. pneumoniae*'s role in nosocomial infections and the critical function of adhesion genes in its pathogenicity, the review delineates Wi-Fi's electromagnetic radiation characteristics and hypothesized influence mechanisms on bacterial gene expression.

Methods: This study used to several databases, including PubMed, Web of Science, and Embase, considering peer-reviewed articles that evaluate the impact of Wi-Fi radiation on *K. pneumoniae* adhesion genes. The analytical criteria were based on experimental design, exposure parameters, gene expression profiling methods, and the statistical significance of the results.

Results: The review found variable effects of Wi-Fi exposure on adhesion gene expression with some studies reporting up-regulation, suggesting enhanced pathogenic potential, while others either demonstrated down-regulation or no significant changes. Several studies exhibited a range in the expression change of targeted adhesion genes from a 1.2-fold decrease up to a 2.5-fold increase ($p < 0.05$).

Conclusion: Through critical analysis, the discussion addresses possible reasons for these discrepancies, such as differences in Wi-Fi exposure duration and intensity, bacterial strain variant, and experimental conditions. The findings underscore the need for standardizing exposure conditions in future experiments. The review calls for a judicious interpretation of current results and a concerted effort in further research to thoroughly elucidate the biological consequences of Wi-Fi radiation on clinically important bacteria such as *K. pneumoniae*.

Keywords: Wi-Fi Exposure; Expression of Adhesion Genes; *Klebsiella pneumoniae*





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-88

Prevalence of antimicrobial resistance pattern among *Enterococcus* strains isolated from clinical specimens, Hamadan, Iran

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Abstract

Background and Aim: *Enterococcus faecalis* and *Enterococcus faecium*, commonly colonizing the human intestine, pose a significant health risk worldwide, leading to infections such as bacteremia, urinary tract infections, endocarditis, and hospital-acquired infections. Identifying antibiotic resistance in these bacteria is crucial for effective management. This study aims to examine urine, wound, and blood samples for the presence of *Enterococcus faecalis* and *Enterococcus faecium*, and to analyze the antibiotic resistance patterns in the isolated strains.

Methods: A total of 28 samples (urine, wound, and blood) were collected from hospitals in Hamadan city. Bacterial genus and species were determined through culture, biochemical, and phenotypic characteristics. Antibiotic sensitivity tests were conducted using the Kirby-Bauer agar diffusion method.

Results: Among the 28 *Enterococcus*-positive strains, 70.4% were identified as *Enterococcus faecalis* and 26.1% as *Enterococcus faecium* and 3.5% as other species. *Enterococcus faecalis* isolates demonstrated sensitivity to ampicillin, while the majority of *Enterococcus faecium* isolates exhibited resistance to ampicillin. All *Enterococcus faecalis* and *Enterococcus faecium* isolates displayed resistance to ceftriaxone, indicating inherent resistance. Antibiotic resistance rates were as follows: vancomycin (2.9%), doxycycline (31.9%), levofloxacin (11.1%), cefotaxime (63.6%), erythromycin (63.4%), clindamycin (61.6%), and gentamicin (26.5%).

Conclusion: The prevalence of *Enterococcus* in this study (71.4%) surpassed the expected 1% reported as normal flora in the digestive system. Notably, *Enterococcus faecalis* and *Enterococcus faecium* emerged as dominant infectious species. Ampicillin, combined with ceftriaxone, is recommended for treatment, considering their sensitivity. Vancomycin remains a key choice for beta-lactam-resistant enterococcal infections, despite its low resistance percentage. Nevertheless, the observed low resistance rates raise concerns about emerging challenges in managing enterococcal infections.

Keywords: Antimicrobial Resistance; *Enterococcus spp.*





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBa-89

The Impact of Wi-Fi Radiation on *Escherichia coli* Growth rate: A Systematic Review

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Abstract

Background and Aim: Wi-Fi-enabled devices emit EMR which has been proposed to induce biological changes in living organisms. Given the widespread utilization of wireless technology, the biological implications of long-term exposure to low-intensity EMR, particularly on microorganisms such as *E. coli*, are of public and scientific concern. *E. coli* serves as an important bacterial model to explore the biological impacts of Wi-Fi radiation due to its well-understood genetics and ubiquitous presence.

Methods: This review employed systematic search strategies to compile relevant literature. The inclusion criteria targeted peer-reviewed studies that evaluated the growth effects of Wi-Fi radiation on *E. coli*. Quality assessment tools were used to evaluate the methodological rigor of each study. The research synthesized data on experimental setup, radiation exposure levels, duration of exposure, and resultant changes in bacterial growth patterns.

Results: The synthesis of the selected studies revealed heterogeneous outcomes. Some reported that Wi-Fi radiation could stimulate bacterial proliferation, whereas others indicated a reductive effect on growth rates. A subset of studies observed no statistically significant changes. These mixed results point towards the complexity of Wi-Fi radiation's biological interactions.

Conclusion: Considering the disparate findings, the review identifies a lack of standardization in experimental designs as a significant impediment in reaching definitive conclusions. Factors such as variations in radiation intensity, exposure duration, and bacterial strain may account for the observed discrepancies. The review suggests a need for methodologically consistent and reproducibly designed studies that can more accurately chart the impact of Wi-Fi radiation on microbial organisms. Moreover, it highlights the importance of understanding microbial responses to EMR, which can have broad implications for public health and environmental stewardship in the digital age.

Keywords: Wi-Fi Radiation; *Escherichia coli*; Growth rate.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-90

Ceftaroline: An In-Depth Exploration of its Therapeutic Landscape in Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infection

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Abstract

Background and Aim: Methicillin-resistant *Staphylococcus aureus* (MRSA) infection is widespread and has been reported at rates ranging from 13% to 74%. In recent years, more than 100,000 deaths globally have been linked to antimicrobial resistance, and MRSA constituted a significant portion of this mortality. The limited availability of effective antibiotics further complicates the challenge posed by MRSA. Ceftaroline is a novel fifth-generation cephalosporin that has been authorized. Known for killing bacteria, Ceftaroline has shown efficacy against Gram-positive and Gram-negative strains. The current review summarizes the available data on the current status of Ceftaroline, its clinical outcomes and safety, and future perspectives of this novel anti-MRSA antibiotic.

Methods: Relevant cross-sectional and case-control studies were identified through an online examination of multiple international databases, including MEDLINE/PubMed, Scopus, and Google Scholar, using “Ceftaroline” and “MRSA” as the primary keywords. A checklist determined the qualities of all studies.

Results: MRSA is renowned for its ability to cause various infectious complications. In instances where traditional therapies are ineffective, alternative medications must be developed. Distinguished by its remarkable attraction to penicillin-binding protein (PBP)-2a, it stands out, and the occurrence of resistance to Ceftaroline among MRSA strains seems infrequent. In various geographical areas, Ceftaroline exhibited robust effectiveness against isolates of MRSA, with susceptibility ranging from 89% to 93%, according to a previous study. Additionally, investigations have demonstrated that combining Ceftaroline with other antimicrobials yields. The optimal dose and frequency of Ceftaroline administration are still subject to debate, though the recommended dosing is 600 mg every 12 hours. Reported adverse effects are generally mild and include neutropenia, diarrhea, nausea, rash, hypokalemia, and *Clostridium difficile* infection. Available data indicate that Ceftaroline may be a potential alternative to the standard recommended treatments, such as vancomycin, for both empiric and targeted coverage of suspected MRSA.

Conclusion: In the context of escalating vancomycin resistance among MRSA strains, Ceftaroline is a novel and promising therapeutic option. Efficient strategies are employed worldwide to regulate the transmission of MRSA resistance, encompassing the implementation of effective measures for infection prevention and control, as well as the prudent selection and meticulous use of antibiotics. Ceftaroline should be further investigated as a potential alternative treatment for MRSA infections in pediatric and adult populations.

Keywords: Ceftaroline; antimicrobial resistance; methicillin-resistant *Staphylococcus aureus*.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic review

Code of Abstract: PBa-91

Gastrointestinal mucormycosis: A periodic systematic review of case reports from 2015 to 2021

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Abstract

Background and Aim: Mucormycosis, a potentially fatal fungal infection caused by Mucorales, primarily Rhizopus species, affects various organs, including the gastrointestinal (GI) tract. This systematic review focuses on GI mucormycosis, an uncommon but severe manifestation with mortality rates ranging from 40% to 85%. Entry mechanisms include nasogastric intubation, contaminated medical equipment, and ingestion of infected food. Underlying conditions, such as diabetes, blood cancers, and immunosuppression, significantly increase the risk. The review emphasizes the diagnostic challenges associated with GI mucormycosis, often diagnosed late due to nonspecific symptoms and difficulty distinguishing it from other GI diseases.

Methods: A structured search of PubMed/Medline was used to collect case reports of GI mucormycosis in patients of all ages published between 2015 and November 2021.

Results: Eighty-seven cases were identified through PubMed bibliographic database searches, and final analyses were conducted on 70 adults and 10 neonatal patients with GI mucormycosis. Asia had the highest number of reported cases, with 46 (57.5%). Neonatal cases had a mortality rate of 70%, while other cases had a mortality rate of 44%. Corticosteroid therapy and diabetes were the most significant risk factors in patients, while 11% were immunocompetent with no apparent underlying condition. Abdominal pain, fever, and GI perforation were the most common signs of infection, while vomiting occurred in 40% of neonatal cases. In 97% of patients, a histopathologic examination was used to detect infection, whereas culture and molecular methods were used in only 28% and 17% of patients, respectively. Surgery plus anti-infection therapy, anti-infection therapy alone, and surgery alone were used in 61%, 28%, and 11% of patients, respectively. Nonetheless, all neonatal patients underwent surgery.

Conclusion: GI mucormycosis is a rare but highly lethal disease. Treatment of underlying conditions, the use of multiple diagnostic techniques, and appropriate antifungals in conjunction with surgery can all contribute to infection control.

Keywords: Gastrointestinal; Mucormycosis; Corticosteroid therapy; Stomach; Intestines.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-92

The destruction of mucosal barriers, epithelial remodeling, and impaired mucociliary clearance: possible pathogenic mechanisms of *Pseudomonas aeruginosa* and *Staphylococcus aureus* in chronic rhinosinusitis

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Abstract

Background and Aim: Chronic rhinosinusitis (CRS) is a pathological condition characterized by persistent inflammation in the upper respiratory tract and paranasal sinuses. The epithelium serves as the first line of defense against potential threats and protects the nasal mucosa. The fundamental mechanical barrier is formed by the cell-cell contact and mucociliary clearance (MCC) systems. The physical-mechanical barrier is comprised of many cellular structures, including adhesion junctions and tight junctions (TJs). To this end, different factors, such as the dysfunction of MCC, destruction of epithelial barriers, and tissue remodeling, are related to the onset and development of CRS. Recently published studies reported the critical role of different microorganisms, such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*, in the induction of the mentioned factors. The purpose of this article is an attempt to investigate the possible role of the most important microorganisms associated with CRS and their pathogenic mechanisms against mucosal surfaces and epithelial barriers in the paranasal sinuses.

Methods: This research reviews ongoing studies and preliminary investigations into the assessment of possible pathogenic mechanisms of *Pseudomonas aeruginosa* and *Staphylococcus aureus* in chronic rhinosinusitis.

Results: Bacteria could result in diminished ciliary stimulation capacity, and enhance the chance of CRS by reducing basal ciliary beat frequency. Additionally, bacterial exoproteins have been demonstrated to disrupt the epithelial barrier and induce downregulation of transmembrane proteins such as occludin, claudin, and tricellulin. Moreover, bacteria exert an influence on TJ proteins, leading to an increase in the permeability of polarized epithelial cells. Noteworthy, it is evident that the activation of TLR2 by staphylococcal enterotoxin can potentially undermine the structural integrity of TJs and the epithelial barrier through the induction of pro-inflammatory cytokines.

Conclusion: Bacteria, fungi, and viruses can exert a significant influence on the pathogenesis and advancement of CRS through the modulation of both innate and adaptive immune reactions. the role of epithelial disorder is crucial in the development or cause of CRS. the disruption of the epithelium barrier and failure of MCC are the primary mechanisms underlying the pathogenesis of CRS. The analysis of research findings has revealed that microbial-produced substances disrupt an essential element of mucociliary clearance. However, given the significance of various microorganisms in the etiology and exacerbation of this disease, as well as its profound implications for individuals' well-being, further extensive investigation is imperative to substantiate the involvement of microorganisms in the destruction and disruption of epithelial barriers within the paranasal sinuses.

Keywords: CRS, Epithelial remodeling, Mucociliary clearance, Mucosal barriers, *Pseudomonas aeruginosa*, *Staphylococcus aureus*.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-93

Effect of Thymol Extract on Biofilm formation, Growth, and Antibiotic Sensitivity of Proteus Bacterial

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Abstract

Background and Aim: This study explores the diverse effects of thymol on Proteus bacteria, specifically examining biofilm formation, bacterial growth, and antibiotic sensitivity. Employing a systematic experimental approach, the research seeks to uncover the underlying mechanisms through which thymol influences these crucial aspects of Proteus behavior. The abstract provides a succinct overview of the experimental procedures, findings, and significant discussions.

Methods: In a controlled laboratory setting, Proteus bacterial cultures are exposed to varying concentrations of thymol. Biofilm growth is evaluated using established assays, while bacterial growth dynamics are tracked over time. Antibiotic susceptibility is determined through standard minimum inhibitory concentration (MIC) testing. The experimental design incorporates appropriate controls, and data collection includes quantitative measurements of biofilm, bacterial growth, MIC determination, and statistical analyses.

Results: Thymol exhibits a concentration-dependent impact on both Proteus biofilm formation and bacterial growth. At lower concentrations (0.0316µg/mL), thymol hinders biofilm growth ($p < 0.05$), reducing bacterial growth without significantly altering antibiotic sensitivity. Conversely, higher thymol concentrations lead to a substantial reduction in biofilm biomass, inhibiting bacterial growth, and enhancing antibiotic sensitivity in Proteus strains. Statistical analyses corroborate the significance of these observed effects.

Conclusion: This research yields a comprehensive understanding of thymol's influence on Proteus biofilm, growth, and antibiotic sensitivity. The concentration-dependent effects underscore the intricate nature of thymol's interactions with Proteus bacteria. These findings offer valuable insights into the potential therapeutic applications of thymol, suggesting its use as a versatile agent against biofilm-associated infections and as a regulator of antibiotic susceptibility in Proteus strains.

Keywords: Thymol; Biofilm formation; Antibiotic Sensitivity.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-94

Phage therapy: A promising treatment against multi drug resistant *Klebsiella pneumoniae*

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Abstract

Background and Aim: Multidrug-resistant (MDR) *K. pneumoniae* is an important problem in the world. Phages of *K. pneumoniae* are obtained from different sources like wastewater, sewage, seawater and human intestinal samples, and are classified in family of Caudovirales include Myoviridae, Siphoviridae, Podoviridae and Ackermannviridae.

Methods: In order to answer this topic, our search was performed in google scholar from December 23, 2023 to December 29, 2023 and first of all to get the comprehensive results, keywords of phage therapy, multi-drug resistant, *Klebsiella pneumoniae* and treat were selected.

Results: Pharr (P1) and ϕ KpNIH-2 (P2) are obtained from sewage water which have positive results to combat infections by MKP103 (a derivative of *K. pneumoniae* ST258 clinical isolate KPNIH1)(2). Phage VTCCBPA43 is characterized by its narrow host range, tolerance up to 80 °C, high activity at pH 5 and production of 172 PFU/mL burst size that is useful in a pneumonic mouse model(3). Phage Kpn31 is effectual against MDR *K. pneumoniae* isolates in vitro by the absence of genes to express toxins, antimicrobial resistance and depolymerases (4) also phage vB_KleS-HSE3 is effective to treat MDR *K. pneumoniae* strain 1025 infections. Phage ZCKP8 can completely lyse *K. pneumoniae* isolates as well as phages vB_KpnS_FZ10, vB_KpnS_FZ41, vB_KpnP_FZ12, and vB_KpnM_FZ14 can produce halo and consequently release depolymerase against bacterial capsule so they have known as beneficial phages to treat MDR *K. pneumoniae* infections.

Conclusion: Overall, our results show that phage therapy is a successful tool for the treatment of MDR *K. pneumoniae* infections due to its non-pathogenicity to human cells, but unfortunately, phage-resistant bacteria are increasing by using single phages, so A mixture of several phages (phage cocktail) can dramatically reduce this threat, while its use for humans needs more research.

Keywords: Phage therapy, Multi-drug resistant, *Klebsiella pneumoniae* , Treat.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-95

Bacteriophage therapy for inhibition of multi drug-resistant uropathogenic bacteria

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Abstract

Background and Aim: The emergence of Multi-Drug Resistant (MDR) uropathogenic bacteria in worldwide has resulted in higher hospital admissions and costs. As a result, developing novel treatments for these infections has become a significant problem for the medical community. Since phages have a different resistance mechanism than antibiotics and a low incidence of side effects, current research has suggested phage therapy as a viable alternative against multidrug-resistant urinary tract infections (MDR UTIs). Phages have the ability to not only lyse bacterial pathogens additionally stop biofilms from forming. Phage treatment, in particular, has demonstrated promising results in suppressing multiple-species biofilm and could be beneficial in the fight against catheter-associated UTI.

Method: This research reviews ongoing studies and preliminary investigations into the assessment of bacteriophage therapy for inhibition of multi drug-resistant uropathogenic bacteria.

Result: phages have the ability to destroy the biofilm of bacteria that cause UTI; however, during the course of this infection, different bacteria forms mixed-species biofilm on in-dwelling medical devices or host organs. Therefore, the combined use of several different phages as phage cocktail, the combined treatment of phages and antibiotics, and the use of probiotics along with phages can help inhibit the mixed biofilm further, and combination therapy not only reduces the number of bacteria but also relates to the management of phage-resistant bacteria levels. Notably, despite the use of different combination therapies, phage-resistant bacteria are still reported in studies; however, with the use of combination therapies, their population is greatly reduced. Therefore, it is very important to identify more effective strategies to kill all bacteria in the biofilm and prevent the development of resistance to phages.

Conclusion: MDR Uropathogenic bacteria have reduced the utility of chemical antibiotics in clinical settings. Moreover, these antibiotics are cytotoxic to not only pathogens, but also health-beneficial commensals. In this regard, phages and their derivatives were reported as an alternative strategy for the treatment of drug-resistant UTI. Besides, the safety profile of these microorganism seems to be far better than antibiotics. Therefore, researchers suggested phage therapy as a mean for prevention and treatment of UTI and further spread of MDR uropathogenic bacteria. However, phage-resistant strains still occur despite the use of phage cocktails and combination therapy. In this context, more fundamental studies are required to determine the phage-host interactions and the phage potential to control UTI. Additionally, most of phage therapy data were obtained from in vitro studies and the major limitation was lack of appropriate clinical research. So further clinical trials (double-blind and placebo-control) are needed to investigate dose, best routes of administration, frequency and duration of phage therapy for inhibition and treatment of UTI.

Keyword: Phage therapy, Urine, Multi-drug resistant, Urinary tract infection.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-96

Antibiotic resistance and frequency of *mph* (A) in shigella recovered from children

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Abstract

Background and Aim: Shigellosis is one of the most important concerns worldwide especially, in developing countries. *Shigella* species has known as dangerous causes of diarrheal infections in children. In most cases of diarrhea is a self-limited infection, however, in some condition for example in bloody diarrheal in children antibiotic therapy applied. In these patients' azithromycin introduced as first line of antibiotic therapy.

Methods: In this cross-sectional study, 71 isolates recovered from children from west Azerbaijan. Azithromycin and Gentamycin antibiotic susceptibility was investigated by micro broth dilution method as CLSI. Also, *mph* (A) gene was investigated by PCR.

Results: Resistance rate to Azithromycin and Gentamycin was 80% and 1.4%, respectively. Also, *mph* (A) gene was founded in 32 isolates by PCR method. But the signification relation between resistance and *mph* (A) gene was not observed.

Conclusion: In summary, our results showed that Azithromycin isn't suitable drug, but Gentamycin is a valuable antibiotic agent for empiric therapy. Also, role of other mechanism in resistance to Shigella must be investigated.

Keywords: Shigella; *mph* (A) gene; Antibiotic resistance.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review/ Meta-Analysis

Code of Abstract: PBa-97

Trends in Carbapeneme-resistant *Klebsiella pneumoniae* in Iran (2013-2023): A Systematic Review and Meta-Analysis

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Abstract

Background and Aim: The alarming rise of Carbapenem-resistant *K. pneumoniae* (CRKP) has sounded the alarm due to its limited treatment options. This review illuminates the evolving landscape of carbapenem-resistant *K. pneumoniae* in the Iranian population, shedding light on recent trends and distribution of microbial resistance genes.

Methods: A comprehensive systematic search was performed on PubMed, Scopus, Embase, and Web of Science from 2013 until 28 December 2023. The pooled prevalence of CRKP was calculated by using a proportional meta-analysis with a random-effects model. The heterogeneity of included studies was assessed by forest plot in terms of I^2 statistic. All estimations were reported on a 95% confidence interval (CI) and $p < 0.05$ was fixed as statistically significant.

Results: Totally, of 26 eligible studies published between 2013 and 2023. The pooled prevalence rate of CRKP was 34% (95% CI 0.24-0.44). The frequency of the resistance genes for blaKPC, blaVIM, blaIMP, blaNDM, and blaOXA-48-like were 16% (95% CI 0.06-0.26), 12% (95% CI 0.02-0.24), 7% (95% CI 0.01-0.1) and 6% (95% CI -0.01-0.13) respectively. Importantly, subgroup analyses indicated that an increase in resistance rates during the periods (2016–2020) was recognized for CRKP 45% (95% CI 0.14-0.44). Crucially, subgroup analyses revealed a concerning surge in CRKP resistance rates from 2016 to 2020, with a 45% increase (95% CI 0.14-0.44).

Conclusion: The alarmingly high prevalence of CRKP especially OXA-48-like and NDM carbapenemases, and their worrisome co-existence in clinical isolates, paints a grim picture of the future: potentially unstoppable superbug outbreaks. With limited options remaining in our antibiotic arsenal, the discovery of new drugs or inhibitors targeting NDM/VIM-positive bacteria becomes not just urgent, but a matter of public health survival. Furthermore, the combination of rapid diagnostic tools, early detection, and targeted screening can be an effective strategy for preventing the spread of carbapenemase-producing bacteria to the community.

Keywords: *Klebsiella pneumoniae*, Carbapenem-resistant, Prevalence, Iran.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-98

A comparison of the outcomes of direct smear, culture, cellular and biochemical tests of cerebrospinal fluid in patients with signs of infectious meningitis at Imam Reza Hospital in 2020-2021

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Abstract

Background and Aim: Since health enhancement and mortality reduction have become global goals, the purpose of this study is to assess the outcomes of direct smear, culture and biochemical tests of cerebrospinal fluid in patients with signs of infectious meningitis at Imam Reza Hospital in 2020_2021.

Methods: The laboratory data of all CSF samples acquired from patients with suspected meningitis at Imam Reza Hospital (in 2020-2021) were analyzed. This data included biochemical tests (protein and glucose levels), cell count (number of WBC per cubic millimeter of the sample and differential cell count) and CSF sample culture in the microbiology laboratory. The Hospital Information System (HIS) of the hospital was used to obtain the data. Ethical conditions, such as the confidentiality of patient data, were respected. The data from each sample was entered into SPSS software and statistical analyses were done.

Results: The study consisted of 109 patients, of which 75 (68.8%) were male and the rest were female. Among the patients, 20 were infants (under 1 month old) and the average age of the others was 41.83 ± 24.83 years. Blood culture was positive in 8 patients (7.3%) and cerebrospinal fluid culture was positive indirectly in 84 patients (77.1%) and directly in 22 patients (20.2%). The most frequent microorganism detected in cultures of cerebrospinal fluid was enterococcus, which was observed in 19 patients (17.92%). Only 2 patients (9%) had direct positive culture that agreed with all criteria of cerebrospinal fluid tests.

Conclusion: There was a difference between the positive cultures of cerebrospinal fluid and the results of the cerebrospinal fluid tests in many cases of suspected meningitis patients in our study. This issue may be due to the contamination of the CSF samples; however, more research is necessary on this subject.

Keywords: Meningitis, Blood culture, Cerebrospinal fluid.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-99

Investigating the antibacterial effect of several natural compounds including eugenol, royal jelly and propolis

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Abstract

Background and Aim: In the ongoing battle against bacterial infections and the increasing threat of antibiotic resistance, scientists and researchers have turned their attention to natural substances that have been used in traditional medicine for centuries. By examining the antibiotic crisis, the discovery of these natural substances becomes a promising way to discover new and effective antimicrobial agents. The purpose of this study is to investigate the antibacterial effect of eugenol, royal jelly and propolis.

Methods: In this research, the antibacterial effect of natural compounds including eugenol, royal jelly, and propolis on 3 antibiotic-resistant bacteria, including *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* was measured by agar well diffusion method.

Results: Eugenol disrupts the membrane of bacterial cells, inhibits enzymes involved in energy production and metabolism in bacterial cells, damages the DNA of bacteria, and also has antibacterial activity against *Escherichia* species due to its antioxidant property. *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* with halo diameters of 3, 2.7 and 1 cm, respectively. From honey bee products, royal jelly, due to its acidic pH, having proteins and peptides and 10-Hydroxy-2-decenoic acid (10-HDA) fatty acid with antibacterial properties, against the above-mentioned species. It formed 4, 3.5 and 2.5 cm in diameter respectively. Propolis, which contains plant resins, flavonoids and polyphenols with antibacterial properties, formed halos with a diameter of 2, 2.7 and 2.6 cm, respectively.

Conclusion: These natural substances have high antibacterial activity and can act as a suitable source for new natural antimicrobial products. However, more research is needed in this area to identify the underlying mechanisms more confidently.

Keywords: Antibacterial effect; Eugenol; Royal jelly; Propolis.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-100

Investigation of the frequency of LPXD, LPXC, LPXA and PBP1 genes in *Acinetobacter baumannii* clinical isolates isolated from Borujerd hospitals

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Abstract

Background and Aim: polymyxin E is a synthesized non-ribosomal polycationic peptide that belongs to the class of polymyxin antibiotics, of which only two types are used clinically: polymyxin B and colistin. The increase of drug-resistant XDR and PDR strains in gram-negative bacteria led to the revival and reuse of antibiotics such as colistin. The aim was to investigate the sensitivity and resistance pattern to colistin along with colistin resistant genes in clinical isolates of *Acinetobacter baumannii* isolates.

Methods: This study was conducted on 500 clinical samples collected from the hospitals of Borujerd city during a period of one year. After collecting the samples, *A. baumannii* species was identified using culture and biochemical methods. Then antibiotic sensitivity test was performed on these isolates by disk diffusion method according to CLSI instructions 2022. Finally, to check the abundance of LPXD, LPXC, LPXA and PBP1 genes, PCR was done using specific primers.

Results: According to the initial screening results, the highest antibiotic resistance in 100 isolates of *A. baumannii* related to Cefepime antibiotics and the lowest resistance related to polymyxin B and colistin. PCR results showed that 3%, 1% and 1% of the strains carry LPXC, LPXA and PBP1 genes, respectively.

Conclusion: LPXC, LPXA and PBP1 are spreading among the clinical strains of *A. baumannii*, therefore identifying the above genes using molecular PCR method which is a fast and affordable method to prevent the spread of infection in hospitals in Borujerd are recommended.

Keywords: *Acinetobacter baumannii*; Colicitin; Combined Disc; Antibiotic resistance genes.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-101

Nitrate reductase and leucocyte esterase as a prognostic test for urinary tract infection

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Abstract

Background and Aim: Urinary tract infections (UTIs) are among the most common bacterial infections acquired in the community and in hospitals. Patients with symptomatic infections will have $>10^5$ bacteria/ml and inflammatory cells in freshly voided urine. Due to the importance of this disease, urine dipstick tests (leukocyte esterase [LE] and/or nitrite) as screening tests can be of great help in the diagnosis and treatment process. The aim of the study was to investigate the power of leukocyte esterase and nitrite reductase tests in the primary diagnosis of urinary tract infection compared to the results of urine culture.

Methods: 360 outpatients with positive microbial culture results of urine were examined during one year. The results of microbial culture and the results of leukocyte esterase and nitrite reductase tests were examined. To consider the nitrate reductase test, only patients who were infected with a member of the Enterobacteriaceae family were examined.

Results: Of the 360 patients studied, 320 were male (88%) and 40 (12%) were female with an average age of 25 ± 5 years. More than 10 WBC/hpf were reported in the microscopic report of all patients. The positive results of nitrate reduction and leukocyte esterase tests were reported in (16.9 %) and 38(10.5%) cases, respectively, and in 84(17.2%) cases, two positive tests were reported at the same time. Statistically, both tests have low power in predicting urinary tract infections, but comparing the two tests with each other, leukocyte esterase is significantly (X^2) more positive than nitrate ($p\leq 0.05$). Limiting the presence of nitrate in urine as a substrate can be one of the reasons for the low number of positive cases of this test.

Conclusion: The necessity of further investigation and the use of screening tests for early diagnosis of this disease

Keywords: Urinary tract infection (UTI), Nitrate reductase, Leucocyte esterase.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-102

Bacteriophages: The promising therapeutic approach for enhancing ciprofloxacin efficacy against bacterial infection

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Abstract

Background and Aim: The emergence of ciprofloxacin-resistant bacteria is a serious challenge worldwide, bringing the need to find new approaches to manage this bacterium. bacteriophages (phages) have been shown inhibitory effects against ciprofloxacin-resistance bacteria; thus, ciprofloxacin resistance or tolerance may not affect the phage's infection ability. Additionally, researchers used phage-ciprofloxacin combination therapy for the inhibition of multidrug-resistant bacteria.

Methods: An explanation of the study design and experimental method.

Results: The sublethal concentrations of ciprofloxacin could lead to an increase in progeny production. Antibiotic treatments could enhance the release of progeny phages by shortening the lytic cycle and latent period. Thus, sublethal concentrations of antibiotics combined with phages can be used for the management of bacterial infections with high antibiotic resistance. In addition, combination therapy exerts various selection pressures that can mutually decrease phage and antibiotic resistance. Moreover, phage ciprofloxacin could significantly reduce bacterial counts in the biofilm community. Immediate usage of phages after the attachment of bacteria to the surface of the flow cells, before the development of micro-colonies, could lead to the best effect of phage therapy against bacterial biofilm.

Conclusion: phage should be used before antibiotics usage because this condition may have allowed phage replication to occur first before ciprofloxacin interrupted the bacterial DNA replication process, thereby interfering with the activity of the phages. Furthermore, the phage-ciprofloxacin combination showed a promising result for the management of *Pseudomonas aeruginosa* infections in mouse models. Nevertheless, low data are existing about the interaction between phages and ciprofloxacin in combination therapies, especially regarding the emergence of phage-resistant mutants. Additionally, there is a challenging and important question of how the combined ciprofloxacin with phages can increase antibacterial functions. Therefore, more examinations are required to support the clinical usage of phage-ciprofloxacin combination therapy.

Keywords: Antibiotic resistance, Bacterial biofilm, Bacteriophages, Ciprofloxacin, Combination therapy.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review/ Meta-Analysis

Code of Abstract: PBa-103

Global Resistance of Imipenem/Relebactam against Gram-Negative Bacilli: Systematic Review and Meta-Analysis

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Abstract

Background and Aim: Relebactam, previously known as MK-7655, is currently being tested with imipenem as a class A and class C β -lactamase inhibitor, including KPC from *Klebsiella pneumoniae*. The objective of the current study was to evaluate the activity of imipenem/relebactam against gram-negative bacilli.

Methods: After applying exclusion and inclusion criteria, 72 articles with full texts that describe the prevalence of imipenem/relebactam resistance were chosen for the meta-analysis and systematic review. Articles published between January 2015 and February 2023 were surveyed. The systematic literature search was conducted in PubMed, Web of Science, Google Scholar, and Scopus.

Results: The pooled estimation of 282,621 sample isolates revealed that the prevalence rate of imipenem/relebactam resistance is roughly 14.6% (95% CI, 0.116%–0.182%).

Conclusion: The findings of this analysis show that imipenem/relebactam resistance is rare in the majority of developed countries. Given that relebactam has proven to restore the activity of imipenem against current clinical isolates, further research into imipenem/relebactam is necessary.

Keywords: Antibiotic-resistance, Gram-negative bacilli, Imipenem/Relebactam.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-104

Evaluation the antimicrobial and combination with antibiotics effect of hydroalcoholic extract of green almond skin (*Prunus amygdalus*) on clinical isolates of *Pseudomonas aeruginosa* and *Staphylococcus aureus*

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Abstract

Background and Aim: Given the emergence of antibiotic-resistant bacterial species and the demonstrated effects of plant extracts on various bacterial strains, the purpose of this study is to investigate the antimicrobial properties, as well as the combined antibiotic effects of the hydroalcoholic extract from the green bark of the almond tree (*Prunus amygdalus*) on clinical isolates of *Pseudomonas aeruginosa* and *Staphylococcus aureus* obtained from teaching hospitals in Isfahan.

Methods: The antimicrobial potential of the hydroalcoholic extract from the green bark of the almond tree (*Prunus amygdalus*), meropenem and cefoxitin was evaluated against clinical strains of *S. aureus*, including methicillin-resistant (MRSA) strains and *P. aeruginosa* by minimum inhibitory concentration (MIC). Finally, the synergistic effect of the hydroalcoholic extract with antibiotics specific to each bacterium was measured using the checkerboard assay method.

Results: Out of 10 *P. aeruginosa* and 10 *S. aureus* isolated from clinical specimens, five *P. aeruginosa* and five *S. aureus* were resistant to meropenem and cefoxitin (MRSA). The MICs of meropenem for the clinical *P. aeruginosa* strain were in the range of 0.25 µg/ml to 512 µg/ml, while the MICs of hydroalcoholic extract of green almond skin for the isolates were in the range of 4 mg/ml to 32 mg/ml. The MICs of cefoxitin for the clinical *S. aureus* strain were in the range of 1 µg/ml to 128 µg/ml, while the MICs of hydroalcoholic extract of green almond skin for the isolates were in the range of 8 mg/ml to 16 mg/ml. Moreover, the hydroalcoholic extract of green almond skin combined with meropenem and cefoxitin act in synergy and additive in clinical *P. aeruginosa* and *S. aureus* isolates tested with FICI values varying from 0.141 to 0.75 mg/ml.

Conclusion: This preliminary evaluation demonstrated a synergy and additive property effect of hydroalcoholic extract of green almond skin (*Prunus amygdalus*) with cefoxitin and meropenem in inhibiting *S. aureus* and *P. aeruginosa* isolates. Therefore, these combinations are good candidates for testing in animal models and could be used to develop novel products for topical use.

Keywords: *S. aureus*, *P. aeruginosa*, *Prunus amygdalus*, MIC, MBC.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBa-105

Gut Microbiota and Probiotics: An alternative therapeutic approach in the antibiotic resistant era for Urinary tract infection

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Abstract

Background and Aim: Urinary tract infections (UTIs) are frequent distress for both women and men however, mostly for women. Emerging antibiotic resistance has led to increasing interest in non-antibiotic approaches utilizing natural products and now bacteriotherapy with the name of “Probiotics”. Probiotics are the live microorganisms which when administered in adequate amounts offer a health benefit in humans. This review summarized the research evidences of probiotic supplementation in preventive and curative UTIs clinical trials. However, recommendation state that it will be mandatory to know the correct formulations in terms of type of bacteria and their amount along with standardization of the patients.

Methods: Different databases were employed to explore the studies on this aspect like PubMed, Scopus, Google Scholar and Medline databases. The keywords included “urinary tract infections”, “urinary tract infection and men”, “urinary tract infection and females”, “urogenital flora”, “Gut microbiota”, “dysbiosis and urinary tract infections”, “probiotics” and “probiotics and urinary tract infections”, “clinical trials of probiotics in UTIs”, “prophylaxis and Probiotics in UTI”.

Results: Urinary tract infections (UTIs) are one of the frequent infections in females as well as elderly individuals. Though UTIs is a less severe life –threatening infection however, is a common and significant distress requiring antibiotics and substantial healthcare. Antibiotic therapy is an effective approach but the emerging resistance and their adverse effects have significantly turned the modality towards use of natural products and probiotics. Though antibiotic free protective approaches have gained popularity but still controversy exist regarding the use of probiotics in UTIs, type of patients, underlying diseases, type of bacteria utilized as probiotic, its viability and its associated growth factors. For choosing a standard probiotic several features have been suggested like, bacterial strain should be able to adhere to the host cells, prevent or decrease the adherence of pathogenic microorganisms, secrete acids, hydrogen peroxide and bacteriocins. It should be safe and should not be invasive, carcinogenic and pathogenic.

Conclusion: Significant relationship between vaginal flora and urogenital infections has been established. *Lactobacilli* spp. have gained much attention as a dominant vaginal flora and also as a probiotic support for preventing gastrointestinal and urinary tract infections. It can prevent the adherence, growth and colonization of uropathogenic bacteria. It is also found to have a strong inhibitory effect on the common UTI causing bacteria (*E. coli*). Oral, liquid and vaginal formulations develop shows that duration of probiotic ranges from 5 to 12 months and dose vary between 10^4 CFU and 10^{10} CFU.

Key Words: Microbiota, Probiotics, Urinary tract infections, Lactobacillus, Urogenital flora.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-106

Examining the Association between Vitamin D Deficiency and Urinary Tract Infections in Children: A Study at Children Hospital in 2018

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Abstract

Background and Aim: Urinary tract infections (UTIs) are associated with an increased health burden in pediatric patients. UTIs are the most common infections after respiratory infections in children, and children with symptomatic UTIs are exposed to scarring of the kidneys and possible complications. Vitamins and micronutrients play crucial roles in the defense system of the human body, and their homeostasis is essential for the response to infection. Vitamin D is known for its immunomodulatory and antimicrobial activity effects. This study aimed to determine the relationship between vitamin D levels and UTI in children referred to one of the children's hospitals in Bandar Abbas.

Methods: This study was case-control research that included 84 children between the ages of 2 and 16 years, who were divided into two groups. All participants signed an informed consent form after obtaining approval from the ethics committee. After selecting the patients and grouping them, their demographic information was recorded in the checklist. This checklist included the demographic characteristics of the patients, clinical conditions, history of vitamin D or multivitamin use in the last 12 months, history of antibiotic use before referral, urinary stones, previous UTI, and history of urinary system abnormalities. In addition, urine tests (U.A and U.C) and measurement of the level of 25 hydroxyvitamin D were performed on patients during this study, and their information was recorded in this checklist. The data were analyzed using SPSS-21 software. Mann-Whitney U test and Student's t-test were used to compare the averages of the two samples.

Results: The total number of participants in the present study was 139, of which 58.3% were female. 60 people (43.17%) out of 139 participants in this study had health for UTI, and 79 people (56.8%) out of 139 people participating in this study had UTI, and among the people who had UTI, 29 people (71.26 percent) had cystitis and 50 people also had pyelonephritis. The amount of vitamin D in people with positive and negative UTI was 16.20 ± 9.09 and 37.85 ± 16.18 , respectively, and data analysis showed that there is a significant relationship between vitamin D and UTI ($p > 0.05$). Data analysis also showed a significant relationship between CRP, alkaline phosphatase, and ESR with UTI ($p < 0.05$). However, there was no significant relationship between height, weight, calcium, phosphorus, and white blood cell count with UTI ($p > 0.05$).

Conclusion: The findings of this study indicate a significant correlation between vitamin D levels and urinary tract infections (UTIs) in children. This implies that maintaining adequate levels of vitamin D could potentially play a role in preventing UTIs in children. In this study, there was no relationship between UTI and calcium and phosphorus, but there was a significant relationship between UTI and alkaline phosphatase. This study also reported a significant relationship between UTI and infectious infection, CRP, and ESR, but no relationship was observed between UTI and WBC count.

Keywords: Pediatrics; Vitamin D; 25-Hydroxyvitamin D2; Urinary Tract Infections.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-107

Prevalence and pattern of antibiotic resistance of bacteria isolated from culture of cerebrospinal fluid and other sterile body fluids in Akbar children Hospital in Mashhad during 2020

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Abstract

Background and Aim: Pediatric infectious diseases are one of the biggest reasons for referring children to medical center. Due to the importance of finding correct treatment and controlling disease, we decided to investigate the prevalence and pattern of antibiotic resistance of bacteria isolated from culture of cerebrospinal fluid and other sterile body fluids in children.

Methods: In this cross-sectional study, sterile culture samples were collected from all patients admitted to Akbar Hospital in Mashhad during 2020. After examining the frequency of bacteria cultured in each of sterile body fluid, we examined the antibiogram of common bacteria and finally compared the resistance and sensitivity of each.

Results: In this study, 949 culture samples were examined, of which 176 samples (18.5%) were positive cultures. Among the positive samples, the highest frequency among sterile body fluids was related to cerebrospinal fluid (43.9%). Next, we examined the frequency of bacteria cultured in sterile body fluids. The results showed that the most common bacteria cultured in sterile body fluids was *Acinetobacter baumannii* (13.6%), followed by *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Escherichia coli* and other *Acinetobacter* species. Also, in the study of antibiograms of 5 common bacteria, *Acinetobacter* was most sensitive to colistin and most resistant to cotrimoxazole and ceftazidime, *Klebsiella pneumoniae* was most sensitive to colistin and most resistant to ciprofloxacin and nitrofurantoin, *Staphylococcus aureus* was most sensitive to vancomycin and linezolid and most resistant to ciprofloxacin, *Pseudomonas aeruginosa* was most sensitive to piperacillin-tazobactam and most resistant to ampicillin and ampicillin-sulbactam, *Escherichia coli* was most sensitive to carbapenems.

Conclusion: The results of this study showed that the most common bacteria which is cultured in sterile body fluid is *Acinetobacter baumannii*. This microorganism has been resisted to many antibiotics in recent years. TDR (totally drug resistance) cases have also increased alarmingly.

Keywords: Sensitivity, Antibiotic resistance, Pediatric, Cerebrospinal fluid





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBa-108

Microbiome's role in sinusitis: A Systematic Review

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Abstract

Background and Aim: Sinusitis, the inflammation of the sinuses, is a common condition affecting millions worldwide. Recent advances in metagenomic sequencing have spurred a growing interest in the sinonasal microbiome's role in this disease. This systematic review aims to synthesize current research regarding the microbiome's influence on sinusitis development, progression, and treatment outcomes.

Methods: We conducted a comprehensive search across several databases, including PubMed, Scopus, and Web of Science, using keywords related to "sinusitis," "microbiome," "sinonasal microbiota," and "metagenomics." Inclusion criteria encompassed studies published in English, peer-reviewed journals from 2000 to 2022, and those that examined the sinonasal microbiome within sinusitis patients compared to healthy controls.

Results: Thirty-seven studies met the inclusion criteria, offering insights into the complex interplay between host immune responses and microbial communities. The findings highlight a marked difference in microbial diversity between chronic and acute sinusitis patients and healthy individuals. Chronic sinusitis patients tend to have a lower diversity of bacteria and an increased presence of pathogenic species. Several studies reported shifts in bacterial populations in response to antibiotic treatment and surgical intervention, with implications for personalized medicine.

Conclusion: The evidence underscores the microbiome's significance in sinusitis, suggesting a potential avenue for adjunct therapies that modulate microbial communities. Future research should focus on longitudinal studies to track microbial dynamics and their relationship with clinical outcomes. Personalized treatment strategies considering individual microbiome profiles may offer improved outcomes for patients with chronic sinusitis.

Keywords: Microbiome; Sinusitis; Bacteria.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-109

Investigating the effect encapsulation of *Bacillus subtilis* with alginate gum Arabic chitosan on its survival rate in gastric simulator conditions

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Abstract

Background and Aim: One of the challenges of oral administration of probiotics is the reduction of their viability due to passing through the digestive system. One of the ways to overcome this problem is the formulation of probiotics in microcapsules based on hydrogels. Microcapsules containing the probiotic *Bacillus subtilis*, which is a gram-positive bacillus and has anti-inflammatory properties and modulation of the gut microbiome population, were synthesized with alginate gum Arabic. This study was designed to investigate the effect of encapsulation with alginate gum Arabic on the survival rate of probiotic *Bacillus subtilis* in gastric simulator conditions.

Methods: After the synthesis of alginate gel solution, gum Arabic, probiotic suspension was added to it. In order to form microcapsules containing probiotics, the resulting mixture was poured into calcium chloride solution through a nozzle. After the microcapsules were formed, they were removed. In order to coat with chitosan, the microcapsules were transferred into the chitosan solution. Microcapsules containing probiotics and microcapsules without probiotics were examined by FTIR and SEM. In order to uncoat the microcapsules containing probiotics, they were placed in sodium citrate solution and shaken slowly. Microcapsules containing probiotics were placed on the incubator shaker at 0, 30, 60, 90, and 120 minutes in gastric simulating conditions. Finally, after de-coating, porplate culture was done.

Results: The encapsulation efficiency was 66.6%. After two hours in stomach simulating conditions, the bacterial viability decreases by 2 logs. The dry chitosan gum Arabic alginate beads showed different bands compared to the FTIR spectrum of sodium alginate, gum Arabic and chitosan. This difference is caused by the participation of functional groups in order to form the capsule structure. Electron microscopy showed that there were no bacteria on the outer surface of the capsules and the bacteria were trapped in the three-dimensional structure capsules.

Conclusion: Alginate gum Arabic microcapsules can increase the viability of encapsulated *Bacillus subtilis* probiotics in gastric simulating conditions.

Keywords: Encapsulation, *Bacillus subtilis*, Alginate, chitosan.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-110

Determination the epidemiological status and drug resistance of patients with salmonellosis in Imam Reza Hospital in 2018 and 2019

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Abstract

Background and Aim: To determine the epidemiological status and drug resistance of patients with salmonellosis in Imam Reza hospitals in 2018 and 2019.

Methods: All patients with salmonellosis who referred to Imam Reza and Ghaem hospitals in 2018 and 2019 were included in the study. Necessary information including sex, origin of infection and antibiotic resistance was collected and recorded from the health information system (HIS).

Results: In this study, 43 patients with salmonellosis were studied. 23 patients (53.5%) were male and 20 patients (46.5%) were female. The most common source of infection was blood (18 patients (41.9%)). The most common subtype identified in patients was Sal.sp.D (53.5%). Most cases of antibiotic resistance were related to Sal.sp.D subtype (20 cases (25%)). Cefotaxime and ciprofloxacin were among the most sensitive antibiotics and imipenem and amikacin were among the most resistant antibiotics. According to Fisher's exact test, no significant difference was observed between the frequency of subtype organisms in samples of different body parts. Based on Fisher's exact test, a significant difference was observed between the frequency of antibiotic resistance pattern of patients with hospital, sampled organ and organism subtype.

Conclusion: The present study indicates the relatively high presence of antibiotic-resistant Salmonella in patients, which serves as a warning to public health that requires more attention to the correct and optimal use of antibiotics to prevent the development of resistant strains.

Keywords: Salmonella, typhoid fever, antibiotic resistance.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-111

Efficacy and comparison of gemifloxacin and oritavancin on Methicillin-Resistant *Staphylococcus aureus* clinical isolates

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Abstract

Background and Aim: *Staphylococcus aureus* is one of the most common causes of bacterial infections and the prevalence of drug-resistant *Staphylococcus aureus* is increasing at an alarming rate. This study was conducted to determine the rate of resistance to Gemifloxacin and oritavancin, among *S. aureus* isolates from patients with conjunctivitis and impetigo.

Methods: This descriptive study was conducted on 360 symptomatic patients with ocular and skin signs (age range: 10 months-78 years) during 2021-2023. Methicillin-resistant *S. aureus* (MRSA) isolates were identified by standard phenotypic microbiological [according to the Clinical and Laboratory Standards Institute M100 guidelines (2021)] and molecular detection (PCR) methods. Sensitivity to quinolone and glycopeptide and the minimum inhibitory concentration (MIC) in the range of 0.06-64 µg/ml were determined by broth microdilution.

Results: The frequency of ocular (87%) and skin (79%) MRSA isolates was significantly higher in females, and patients aged 25-50 years ($P=0.01$). Among the MRSA isolates causing conjunctivitis and impetigo, the highest rates of resistance were observed against oritavancin (22.64% and 31.47% respectively), The MIC of gemifloxacin that inhibited the growth of 90% of MRSA isolates from conjunctivitis ($MIC_{90}=0.5$ µg/ml) was 16-fold lower than that of necessary dose for covering of impetigo so that 92% of isolates from impetigo were eliminated at concentrations 8 µg/ml.

Conclusion: *Staphylococcus aureus* may be the most common cause of bacterial conjunctivitis and impetigo depending on age group and gender. Considering the in vitro antibacterial potential of gemifloxacin, the use of this antibiotic for the treatment of bacterial infections especially conjunctivitis could be further exploited.

Keywords: *Staphylococcus aureus*, conjunctivitis, impetigo, drug resistance.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-112

Identification and determination of the drug sensitivity pattern of clinical species of *Nocardia* isolated from Clinical Sampels

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Abstract

Background and Aim: *Nocardia* species are opportunistic microbial agents that cause severe skin infection, pulmonary and systemic infection. Cotrimoxazole is the mainstay of treatment, but some *Nocardia* species show resistance to cotrimoxazole. Examining the presence of resistance genes in bacteria is also important. The aim of this study is to investigate the epidemiology of *Nocardia* types isolated from patients and the drug resistance pattern of the isolates.

Methods: Hospital clinical samples that were previously stored in the laboratory were identified using phenotypic and molecular methods after preparation of culture and colony purification. Antibiotic sensitivity pattern was performed according to CLSI standards.

Results: 18 isolates from clinical samples were obtained in this study. Susceptibility to linezolid, amikacin and cotrimoxazole was obtained in all isolates, while the isolates showed less sensitivity to gentamicin and cefotaxime.

Conclusion: Due to the emergence of resistance in *Nocardia* infections and for the purpose of combined treatment, it is important to determine the antimicrobial sensitivity of this bacterium. Linezolid, amikacin and cotrimoxazole drugs are recommended for the treatment of *Nocardia* infections.

Keywords: *Nocardia*, Drug sensitivity pattern, Tehran hospitals.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-113

Prevalence detection of *Clostridium difficile* colonization in malignant infant patients in Dr. Sheikh hospital Mashhad

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Abstract

Background and Aim: Children exposed to chemotherapy are constantly infected with various infections. This infection has been increased by a kind of gram-positive bacillus *Clostridium difficile* in hospitalized children. To investigate the presence of this bacterium, this study examines the prevalence of *Clostridium difficile* bacteria colonization in children hospitalized in Sheikh Mashhad Hospital in Cancer for the first time. This study was conducted on children referred to the Sheikh Children's Hospital who were admitted to the hematologic oncology department during chemotherapy in 1395 and 1396.

Methods: At first, the questions asked in the checklist are asked by the researchers from the patients' parents and the form is completed. The patient was initially examined for the presence of the bacterium and, at the time of discharge, is again examined and the results are compared with each other and then the decision on colonization is made. For this purpose, two stool samples are taken from the patient: The first specimen is when the patient is recently admitted to the hospital and during the period of her stay, based on the doctor's diagnosis, will be at least 3 days. The second example is when the physician gives permission to discharge the patient. In the case of diarrhea, a stool swap (in cases of diarrhea) and non-diarrhea, a complete stool sample is taken by the nurse. Swabs (in tubes) and stool cans are transmitted to the laboratory of Paramedical School

Results: The results showed that *C. difficile* could be colonized in 30% of children after 3 days to one week in hospital and 10% of them after 48 hours of hospitalization. Parameters such as using of anti-acid and immune suppressing drugs, re-admissions and hospitalization, and duration of hospitalization, were significant differences ($p, 0.001$) with bacterial colonization in the target group.

Conclusion: Summary of the most important findings and the importance of the study.

Keywords: GDH test, *Clostridium difficile*, Oncology and hematology, Cancer suffering infants





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-114

Antibacterial and Antifungal Activity of the *Moringa oleifera* leaf extract

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Abstract

Background and Aim: Medicinal plants may have the ability to treat bacterial resistance to many types of antibiotics. Antimicrobial and antibacterial compounds obtained from plants with different mechanisms than antibiotics eliminate bacteria. *Moringa oleifera* is known as a rich and affordable source of phytochemical compounds. The leaves are the most nutritious and rich part of proteins, minerals, beta-carotene and antioxidant compounds that are often needed by people in underdeveloped or developing populations. The aim of this study is to examine the antimicrobial and antibacterial effects of *Moringa oleifera* leaf extract against certain microorganisms of human infectious diseases in laboratory conditions.

Methods: The microorganisms used in the study include *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*TT, *Bacillus cereus*, *Streptococcus pneumoniae*, *Candida albicans*, *Fusarium Oxysporum* and *Aspergillus fumigatus*, which were obtained from the Iranian bulbs and bacteria collection center. The rotating method was used to make the extract. In order to test the antibacterial effect of the disc release method and to determine the minimum retention intensity (MIC) and the minimum stretching concentration (MBC), the microdilatation method was used.

Results: The results showed that the methanol leaf extract of *Moringa oleifera* has antibacterial and antifungal activity. The methanol extract showed a desirable anticoagulant effect on *Candida albicans*. The greatest antibacterial effect that the diameter of the non-growth hole showed was the effect of the extract on the hot-positive *streptococcus pneumoniae* bacteria of 35.27 mm. The results showed that the methanol extract has antibacterial and anti-inflammatory effects. The minimum effective concentration on all bacteria is 1000 mg/l.

Conclusion: According to current research, it has been found that the *Moringa oleifera* leaf methanol extract has a significant antibacterial and antimicrobial effect against pathogenic bacteria and candidate bacteria *albicans* and hot-positive bacteria *streptococcus pneumoniae*, so this extract can be considered as a natural herbal agent to control bacterial infections.

Keywords: *Moringa oleifera*, Methanol extract, Antibacterial, Antifungal





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-115

Prevalence of *Mycobacterium tuberculosis* before and after COVID-19 in western Iran

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Abstract

Background and Aim: *Mycobacterium tuberculosis* is the cause of tuberculosis. This bacterium can infect the host without any symptoms, so there are millions of people in the world with asymptomatic infection of *Mycobacterium tuberculosis*, and the intracellular space without this bacterium and its unique cell wall causes antibiotic resistance and its escape from the body's immune system. The COVID-19 pandemic caused many respiratory diseases, including tuberculosis, to receive less attention in the health systems of many countries during its outbreak due to its more contagious nature, so this study compares the prevalence of *Mycobacterium tuberculosis* before the disease COVID-19 and after that in the west of Iran.

Methods: This cross-sectional study was conducted between 2017 to 2022 in Hamadan province in the west of Iran. The research tool in this study was to collect information of disabled people from the health center system of Hamadan province.

Results: The sample size in this study was 402 people with tuberculosis, of which 255 people before COVID-19 and 148 people after COVID-19 were investigated. The most organs involved in patients before the COVID-19 era were the pleural fluid and lymph nodes, and after the COVID-19 the most organs involved were the skin and lymph nodes. The sensitive and resistant condition to isoniazid, rifampin and ethambutol after COVID-19 has been more than people before COVID-19.

Conclusion: The general results of this research show that the prevalence of a respiratory epidemic has a great impact on the epidemic of other respiratory infections, and the health system of countries should take important preventive measures during the prevalence of a pandemic or epidemic to prevent its transmission to people who are suffering from other respiratory infections, including people with tuberculosis and do the necessary training for proper culture during prevalence.

Keywords: *Mycobacterium tuberculosis*, COVID-19, Coronavirus, Prevalence, Iran.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-116

Comparison the frequency of common bacteria that cause meningitis in cerebrospinal fluid samples by culture and PCR in Hamadan, West of Iran

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Abstract

Background: Infection and inflammation of the meningeal membranes in the brain and spinal cord is called meningitis. The causes of this disease are very diverse, but among the infectious causes of this disease are viruses, bacteria, parasites, and fungi. The aim of this study is to detect bacterial infections causing meningitis by molecular PCR method in cerebrospinal fluid (CSF) samples of hospitalized patients suspected of having meningitis and compare it with the culture results in the laboratories of Hamadan hospitals.

Material and Methods: This cross-sectional study was conducted on 104 CSF samples of hospitalized patients suspected to meningitis in the educational hospitals of Hamadan University of medical sciences. The Culture and PCR methods were used to detect the most common causes of bacterial meningitis included *Haemophilus influenzae* type b, *Listeria monocytogenes*, *Streptococcus agalactiae*, *Neisseria meningitides*, and *E. coli* K1.

Results: The average age of the patients in this study was 31.57 ± 25.85 years. Of the participants 53.85% were male and 46.15% were female. The frequency of detection by culture method for these bacteria was zero and by PCR it was 4.81%.

Conclusion: The results of this study showed the low prevalence of common bacterial infections in CSF samples and also showed that the molecular method is more accurate and sensitive compared to culture. Therefore, it is suggested that if meningitis is suspected, clinical experts should check all the factors and use newer diagnostic methods.

Keywords: CSF, PCR, Meningitis, *Haemophilus influenzae* type b, *Listeria monocytogenes*, *Streptococcus agalactiae*, *Neisseria meningitides*, *E. coli* K1, *Streptococcus pneumonia*





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-117

High prevalence of OXA-type carbapenemases in clinical *Acinetobacter baumannii* isolated from patients in western Iran

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Abstract

Background and Aim: In recent years, carbapenem-resistant *Acinetobacter baumannii* has emerged as an important opportunistic pathogen. OXA-type beta-lactamases are the most common cause of carbapenem resistance in *A. baumannii*, and the presence of insertion sequences (ISs) may increase the expression of *bla*_{OXA} genes. This study aimed to determine the antimicrobial resistance and prevalence of OXA-type carbapenemases, as well as to detect the presence of IS*Aba1* upstream of *bla*_{OXA-51-like} in clinical *A. baumannii* isolated from western Iran.

Methods: A total of 102 *A. baumannii* were collected from different clinical samples of patients hospitalized in three teaching hospitals in Sanandaj and Kermanshah cities. The isolates were identified based on biochemical and molecular tests. Resistance to antibiotics was determined by disk diffusion method. PCR was performed to detect the presence of main groups of OXA-type carbapenemases (*bla*_{OXA-23-like}, *bla*_{OXA-58-like}, *bla*_{OXA-143-like}, *bla*_{OXA-235-like}, and *bla*_{OXA-24-like}), as well as to determine the presence of IS*Aba1* upstream of *bla*_{OXA-51-like}.

Results: All isolates showed resistance to cefotaxime, ciprofloxacin, and cefepime. Out of 102 isolates, 94 isolates were resistant to meropenem, 93 to tetracycline, 92 to gentamicin, and 86 to trimethoprim/sulfamethoxazole. PCR for detection of OXAs showed that 84 of 102 isolates (82.4%) carried *bla*_{OXA-24}, 62 isolates (60.8%) carried *bla*_{OXA-23}, and 9 isolates (8.8%) carried *bla*_{OXA-58}. None of the isolates harbored *bla*_{OXA-235} and *bla*_{OXA-143}. IS*Aba1* gene was detected upstream of *bla*_{OXA-51} in 32 of 102 isolates (31.4%).

Conclusion: Our results showed a high prevalence of OXA-type carbapenemases among clinical *A. baumannii* in western Iran. Implementation of infection control strategies and antibiotic management, especially in healthcare systems, is needed to limit the spread of this pathogen.

Keywords: *Acinetobacter baumannii*, Drug resistance, carbapenemase, beta-Lactamase.





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January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-119

Survey of microbial and chemical quality of groundwater resources in some parts of Mazandaran province, Iran

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Abstract

Background and Aim: Nowadays, one of the problems of human societies is the pollution of groundwater. Unhealthy water can lead to digestive diseases, inhibiting nutrient absorption and malnutrition. These effects are especially evident for children. Therefore, it is important to evaluate the quality of underground water sources to evaluate the water consumption potential of each water source. This study was carried out with the aim of evaluating the quality status and threats of underground water resources contamination in some areas of Mazandaran province.

Methods: This descriptive-analytical cross-sectional study was conducted in the East of Mazandaran province (Sari- Behshar), North of Iran, from April to October 2023. In this research, 27 wells were evaluated for microbial and chemical quality according to national standards methods and the results were analyzed by using standard statistical tests.

Results: The results indicated that, in general, 44% of the samples are in terms of physical and chemical parameters were within national and international standards. Furthermore, the biological parameters indicate that there are low to very high risks in terms of microbial quality. 55% of groundwater resources had coliform contamination. In 50% of the samples the HPC was higher than 500 cfu/mL. Nitrate concentrations in wells were higher than international and national standards (10-50 mg/L) in some area and also, iron concentrations in the wells around the river and spring was higher than the permissible limit (0.3 mg/L).

Conclusion: Rapid expansion of urbanization, agricultural practices, industrial activities, domestic wastewater, emerging contaminants, unsuitable structure of the region and the lack of proper distance between water wells, sewage wells and agricultural lands all pose significant threats to groundwater quality. Since the groundwater contamination has a significant impact on human health, it is suggested that chemical and microbial contamination increasing factor in wells have to be controlled and proper strategy should be considered for prevention, reduction and control of groundwater contamination.

Keywords: Groundwater contamination; Microbial quality; Chemical quality; Mazandaran.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Bacteriology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBa-120

Investigation of the frequency of invasive streptococcal pneumonia infections in children admitted to Dr. Sheikh Hospital in 1993-1995

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Abstract

Background and Aim: Streptococcus pneumoniae is the main cause of death, especially in children, people with chronic diseases, the elderly, and those with weakened immune systems. Due to the increasing spread of drug-resistant pneumococci, especially penicillins, the sensitivity and importance of vaccine production to prevent the occurrence of dangerous diseases related to streptococcus in the high-risk age group below 5 years is determined. For this reason, in this study, we investigated pneumococcal positive cultures in Dr. Sheikh's hospital and determined the antibiotic sensitivity.

Methods: After determining the sample size and determining the positive culture in invasive infections, a questionnaire including demographic and clinical information was prepared for all children in question and was approved by an expert. Previously hospitalized patients with positive pneumococcal blood or pleural or peritoneal or CSF cultures in Dr. Sheikh Hospital were included in the study. After the confirmation of pneumococcal positive culture, all the cases of positive cultures that had been subjected to antibiogram were included in the study for further analysis.

Results: 16 samples were male and 10 were female. The mean and standard deviation of the age of the patients was 47.07 ± 55.87 months. The highest diagnosis was meningitis with 10 cases, followed by ALL with six cases and pneumonia with four cases. The number of 20 samples was obtained from blood culture and the rest of the samples were from CSF and pleural fluid. Eight of all patients died and 20 were discharged with recovery. The five antibiotics that were examined more than others in the antibiogram were Vancomycin, Ampicillin, Penicillin, Clindamycin and Erythromycin respectively. The rate of resistance to vancomycin was 16%, ampicillin 8.3%, penicillin 20.8%, clindamycin 54.5% and erythromycin 72.7%. In examining the relationship between the sensitivity and resistance of different antibiotics and cultured fluid, the final diagnosis or the final condition of the patients, no significant relationship was found.

Conclusion: The use of antibiotics is necessary for the treatment of pneumococcal infections, and the appropriate choice of antibiotics is a big issue. Our results show a high prevalence of resistance to macrolides in pneumococci, and the rate of resistance to vancomycin was also high among our patients, which is very worrying. Therefore, using the results of our study and similar studies to start experimental antibiotic treatment until the antibiogram results are ready can be helpful and prevent the indiscriminate use of ineffective antibiotics and the increase of antibiotic resistance.

Keywords: pneumococcus; Antibiotic Resistance; Penicillin; vancomycin; erythromycin.





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3. Biochemistry (Oral Presentations)





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBi-1

Evaluation of the expression profiles and prognostic values of IGFBPs family members, IGFs, TMEM219, and TMEM248 in patients with gastric cancer

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Abstract

Background and Aim: Gastric cancer is an important concern for global health, being recognized as the fifth most common form of cancer worldwide. Several studies have suggested that Insulin-like growth factor-binding proteins (IGFBPs), Insulin-like growth factors (IGFs), and Transmembrane Proteins 219 and 248 (TMEM 219 TMEM 248) may play a role in the development and progression of stomach cancer. This paper aims to evaluate the relationship between IGFs, IGFBPs, and TMEMs (219 and 248) with stomach cancer, highlighting their potential as biomarkers for early detection and therapeutic targets for treatment.

Methods: From April 2014 to September 2016, the Iran National Tumor Bank (INTB) in Tehran, Iran, collected a total of 68 pairs of gastric cancer samples from surgical specimens. This research encompassed specimens that had not previously been subjected to radiotherapy, chemotherapy, or any other therapeutic interventions. Two independent pathologists assessed all samples, blinded to their clinical attributes. All tissues were promptly frozen in liquid nitrogen until the necessary assays could be conducted. Normal samples taken from the marginal zone of cancer tissue were used as a control. IGFBPs, IGFs, and TMEMs (219 and 248) expression were evaluated with quantitative real-time polymerase chain reaction in all tissues. Additionally, we investigated the relationship between prognostic factors including tumor stage, tumor grade, tumor size, metastases, and overall survival with the expression of these proteins.

Results: We found that IGFBP-3, IGFBP-5, TMEM219, and TMEM248 are significantly reduced in patients with gastric cancer, and their decrease is correlated with the stage (TNM; Tumor-Node-Metastasis classification system) of stomach tumors, except for TMEM248. Additionally, our study reveals that IGF-I is significantly increased in gastric cancer patients, and its elevation is correlated with TNM stage. The expression level of these proteins was found to be correlated with clinicopathological features; IGFBP-2 with gender ($P = 0.035$), IGFBP-3 with gender ($P = 0.037$) and tumor size ($P = 0.004$), IGFBP-4 with lymphatic invasion ($P = 0.001$), IGFBP-5 with tumor size ($P = 0.015$) and tumor differentiation ($P = 0.004$), IGFBP-6 with age ($P = 0.027$), tumor size ($P = 0.001$), and lymphatic invasion ($P = 0.011$), IGF-II with lymphatic invasion ($P < 0.001$), TMEM219 with lymphatic invasion ($P = 0.021$), and TMEM248 with tumor differentiation ($P = 0.025$).

Conclusion: These findings suggest that IGFBP-3, IGFBP-5, IGF-I, TMEM219, and TMEM248 have the potential to serve as prognostic biomarkers and therapeutic targets for gastric cancer. The insights gained from this research contribute to further comprehension of gastric cancer pathogenesis and may facilitate the advancement of targeted therapies with improved efficacy against this condition.

Keywords: Gastric cancer; IGFBPs; IGFs; TMEM219; TMEM248.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Case Report/Case Series

Code of Abstract: OBi-2

A very rare complication of ethanol consumption: non- traumatic unilateral raccoon eye

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Abstract

Ethanol is a substance that is easily absorbed in all parts of the gastrointestinal tract and this feature makes it possible for the patients to have the risk of poisoning by ingestion of any amount of it, depending on the individual. Common symptoms of ethanol poisoning include sedation, poor coordination, vomiting, slurred speech, ataxia, respiratory depression, coma and death. A rare manifestation of alcohol consumption is raccoon eye. This article aimed to present a five years old girl who gradually showed a unilateral raccoon eye following the consumption of ethanol.

Keywords: Ethanol; Ataxia; Respiratory depression; Child.





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Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Case Report/Case Series

Code of Abstract: OBi-3

Inborn error of metabolism in Iran, the first case report of 2-methylbutyryl- CoA dehydrogenase in Iran

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Abstract

Background and Aim: Inborn errors of metabolism are rare genetic disorders that cause clinical complications and high mortality. These disorders, including 2-methylbutyryl- CoA dehydrogenase deficiency, are a genetic disorder in the category of organic acids. The first case report of this disorder in Iran was a newborn boy who was identified in the screening program in 2022. The baby had no clinical symptoms and was delivered by cesarean section. The initial results of the metabolic screening showed a high level of 2-methylbutyrylcarnitine (C5) in the baby's blood. A urine organic acid test confirmed the disease, and the genetic test confirmed the disorder. The baby's growth and development were under control, and the baby's height and weight were checked every three months. The baby's movements and communication skills were normal. A diet and carnitine intake were prescribed, along with breast milk. Biochemical tests were performed to check the health of the liver, kidney, and thyroid, and no abnormal laboratory findings were found.

Methods: It has been identified in the metabolic screening program using liquid chromatography mass spectrometry.

Results: The genetic analysis revealed a homozygous mutation Homozygous mutation Chr10-124806731 G C: c.G907C: p.G303R in the ACADSB Gene, which might lead to an amino acid change. This mutation has not been previously reported in the literature. Early diagnosis and treatment can help prevent and treat these metabolic disorders in the first days of life.

Conclusion: Identifying 2-methylbutyryl- CoA dehydrogenase deficiency in the early stages of life is very important, because by identifying this defect using LC MS, and GC MS, and in the later stages, confirming the disease using genetic testing under the supervision of a metabolic specialist, by controlling these the physical and neurological effects of this disease can be prevented.

Keywords: New born Screening; Metabolic Disease; 2-methylbutyryl- CoA dehydrogenase deficiency; 2-methylbutyrylcarnitine (C5); Organic acidemia.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Case-control study

Code of Abstract: OBi-4

Evaluation of the association between serum level of melatonin and urinary levels of Notch-1, fibronectin, and E-cadherin in diabetic patients with and without nephropathy

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Abstract

Background and Aim: Diabetic nephropathy refers to the gradual decline in kidney function that occurs in diabetic patients. The severity of kidney failure in these patients is heightened by oxidative stress. Melatonin, a potent antioxidant, has the ability to protect cells from free radical damage. Furthermore, Notch 1 mediates the progression of kidney fibrosis in patients with diabetic nephropathy, particularly through abnormal ECM components such as fibronectin and E-cadherin. Hence, the present study aims to estimate the association between the serum level of melatonin and the levels of Notch 1, fibronectin, and E-cadherin in urine samples of patients with diabetes and diabetic nephropathy.

Methods: 45 diabetic patients with nephropathy and 44 patients without nephropathy were enrolled in the present case-control study. The serum level of melatonin, as well as the urinary levels of Notch 1, fibronectin, and E-cadherin were measured using ELISA kits.

Results: The mean \pm SD of melatonin levels were 188.57 ± 35.65 in diabetic patients without nephropathy and 184.22 ± 60.21 in patients with nephropathy, however this variation was not statistically significant ($P = 0.124$). The urinary levels of E-cadherin and notch1 were significantly higher in diabetic patients with nephropathy (mean \pm SD: 61.45 ± 5.49 and 28.59 ± 2.33 , respectively) than in those without nephropathy (mean \pm SD: 58.28 ± 7.87 and 26.05 ± 3.60 , respectively), ($P = 0.014$ and $P < 0.001$, respectively). In addition, the levels of fibronectin in urine were higher in diabetic patients with nephropathy (mean \pm SD: 124.30 ± 14.22) than in subjects without nephropathy (mean \pm SD: 118.43 ± 15.97); however, this difference was not statistically significant ($P = 0.07$). Melatonin levels and the aforementioned factors did not significantly correlate in either individual with diabetes with or without nephropathy.

Conclusion: Our study revealed that diabetic patients with nephropathy had higher levels of Notch1 and E-cadherin in their urine compared to diabetic patients without nephropathy. Considering the fact that Notch and Cadherin play important roles in the pathogenesis of kidney damage, future studies should focus on these molecules to discover more effective treatments for the prevention and treatment of diabetic nephropathy.

Keywords: Diabetic Nephropathy; Melatonin; Fibronectin; Notch1; E-Cadherin.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original

Code of Abstract: OBi-5

The effect of sesame and canola oil (separate and combined) on the expression level of insulin resistance- related genes in patients with type 2 diabetes: Design and research protocol of a randomized, triple- blind, three- way, crossover clinical trial

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Abstract

Background and Aim: Diabetes is a metabolic disease characterized by hyperglycemia and plays an important role in the production of excess free radicals and insulin resistance by generating advanced glycation end products. Recent research has shown that unsaturated fatty acids can lead to an increase in the expression levels of genes involved in insulin resistance. Therefore, sesame (SO), canola oil (CO) and sesame - canola oil (SCO) can likely increase the concentration of these genes due to their unsaturated fatty acid content.

Methods: This laboratory study used blood samples from 34 diabetic patients who received SO, CO and SCO in three 9-week phases. The Expression of genes involved in insulin resistance was measured using real-time PCR. The association between the expression levels of the genes involved. Insulin resistance and the consumption of SO, CO and SCO were examined.

Results: GLUT4 and TFAM gene expression was significantly increased in T2D by SO, CO and SCO consumption ($P < 0.001$). Consumption of SO and SCO resulted in a significant increase in the expression of Sirt1 and Rage genes ($P < 0.001$), but consumption of CO did not increase their gene expression significantly ($P = 0.271$).

Conclusion: Overall, our results show that individual and combined consumption of SO and CO can increase the expression levels of genes involved in insulin resistance. Therefore, they are likely to alleviate the inflammatory complications caused by diabetes. However, it is necessary to conduct further studies in this field.

Keywords: sesame oil; canola oil; type 2 diabetes; RAGE; TFAM; GLUT4; SIRT1





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original

Code of Abstract: OBi-6

Aptamer - based Colorimetric and lateral flow assay approaches for rapid detection of lead ions

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Abstract

Background and Aim: Recently, the more attention is given to stable and the accessible detection of heavy metals using aptasensors. In this study, two approaches, in-solution adsorption- desorption method and lateral flow assays (LFA) were examined using aptamer and gold nanoparticles- based conjugates for lead ions detection.

Methods: Aptamers were designed through the process of systematic evolution of ligands by exponential enrichment (SELEX). First, gold nanoparticle was added to the aptamer under a laminar flow hood. After incubation at room temperature in a dark environment, lead samples with a specific concentration were added to GNPsApt complex and kept for 20 minutes at room temperature. After addition of NaCl, the specificity and sensitivity of the aptasensor was evaluated using optical colorimetry and spectrophotometry methods. Other characteristics of nano- aptasensor were determined using FT-IR, X-ray diffraction and agarose gel electrophoresis. In the second approach, lateral flow assay, paper-based microfluidic assay was used.

Results: With addition of lead to GNPsApt complex, Pb²⁺ bind specifically with its aptamer, releasing the gold nanoparticles. Addition of NaCl induces the formation of gold nanoparticle aggregates and as a result the solution of AuNPs undergoes a color change from red to purple observable with the naked eye and by the spectrophotometry with a detection limit of 100 μ M was achieved. In the LFA method, similar to the solution method, aptamer and nanoparticles were conjugated; lead was added to the complex and reaction product loaded into Y shape paper strip. At the end, salt was added to the Y shape paper strip and the color change was determined. A detection limit of 0.5mM was obtained for whatman No.1 filter papers.

Conclusion: Both aptamers based colorimetric and lateral flow assays are simple, inexpensive, rapid to perform on-site detection of target analytes, time efficient and produce results visible to the naked- eye. These aptasensors have the potential to become the basis for future biosensor devices.

Keywords: Aptasensor; Rapid Test; Lead ions; Gold- nanoparticle; Lateral Flow Assay.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original

Code of Abstract: OBi-7

Investigating the relationship between calcium and magnesium serum levels and miscarriage in the first 3 months of pregnancy in patients referred to Shahid Rahimi Hospital in Khorramabad in 2022 to 2023

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Abstract

Background and Aim: Pregnancy is one of the most important and dangerous periods in the life of the mother and the fetus, and the nutritional status during pregnancy is one of the most important indicators in determining the health of the mother and the fetus, such that the lack of some vitamins and minerals in the first months of pregnancy can affect the health of the mother and fetus. Considering the importance of maternal and fetal health, this study was designed and conducted with the aim of investigating the relationship between calcium and magnesium serum levels and miscarriage in the first 3 months of pregnancy in patients referred to Shahid Rahimi Hospital in Khorramabad in 2022-2023.

Methods: This study was a case-control study that was conducted on 185 pregnant mothers, including 46 people for the case group (women with pregnancy leading to abortion) and 139 people for the control group (women with normal pregnancy). The two groups were matched in terms of the number of previous abortions and age. In this study, the data collection tool includes a researcher-made checklist including demographic characteristics (mother's age, body mass index, education, previous abortion history), laboratory results (magnesium and calcium) and obstetric characteristics of patients (number of pregnancies and number of deliveries). Finally, the collected data was entered into SPSS software version 22 and analyzed using statistical methods.

Results: In this study, the mean and standard deviation of calcium serum level in the case group was 8.96 ± 0.79 mg/dL and in the control group was 10.97 ± 0.46 mg/dL, and the mean and standard deviation of magnesium serum level in the case group was 1.68 ± 0.23 mg/dL and in the control group was 2.06 ± 0.06 mg/dL ($p < 0.05$). Also, for one unit increase in calcium, the chance of miscarriage decreased by 0.03 times, and for one unit increase in magnesium, the chance of miscarriage decreased by 0.04 times ($p < 0.05$).

Conclusion: The serum level of calcium and magnesium of pregnant mothers has an effect on the outcome of pregnancy, such that with the increase of the serum level of calcium and magnesium, the chance of miscarriage decreased in the first 3 months of pregnancy, so the measurement of vitamins and minerals, especially calcium and magnesium, in the first 3 months of pregnancy seems necessary. If necessary, it is necessary to improve the nutritional status of pregnant mothers and to educate them on the consumption of sources rich in calcium and magnesium, as well as supplementing them.

Keywords: Abortion; pregnancy; calcium; magnesium





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original

Code of Abstract: OBi-8

Specific targeting of recombinant human pancreatic ribonuclease1 using GnRH targeting peptide toward GnRHR- positive cancer cells

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Abstract

Background and Aim: Targeted drug delivery has opened up a novel window for specific delivery of anticancer therapeutics to the site of tumors. Gonadotropin releasing hormone (GnRH) is a decapeptide which its targeting property has raised attentions to employ it in the field of targeted drug delivery. It is very small in size, has high affinity for its receptor, and is not immunogenic for human. Human pancreatic ribonuclease 1 (hpRNase1) has been shown to exert anticancer properties when it is fused to a targeting moiety such as growth hormones, antibodies and their derivatives. The goal of the present study was to add a GnRH targeting peptide to the N-terminus of hpRNase1 to make it specific against GnRH receptor (GnRH-R) expressing cells.

Methods: To produce the recombinant enzyme, its coding gene is designed and synthesized and cloned in the pET28a expression vector and subsequently expressed in E. coli BL21 (DE3) bacteria. After induction of expression, the identity of the resulting protein is confirmed by SDS- PAGE and western blot. In the next step, the recombinant protein is purified by affinity chromatography and its cytotoxic effects on cancer cells expressing the gonadotropin-releasing hormone receptor (GnRH-R) are evaluated.

Results: GnRH- hpRNase1 chimeric protein specifically inhibited the proliferation of PC-3 (P = 0.021), LNCaP (P = 0.034), and AD-Gn (P = 0.041) cells, while the growth of negative cells (AD-293) was not significantly affected (P = 0.081). GnRH-hpRNase1 decreased the IC50 values more than non-fused hpRNase1, by approximately 26.5-fold (P = 0.036) for PC-3 cells, and exerted its growth inhibitory effects through apoptosis induction.

Conclusion: Ribonucleases, in particular human pancreatic RNase1, have shown intriguing features for developing new class of therapeutics. They; however, suffer from two main shortcomings: 1- being RI sensitive, and 2- act poorly specific to cancer cells. Here, we showed that the engineered GnRH-hpRNase1 is able to specifically target the GnRH receptor - expressing cells and inhibit their proliferation through inducing apoptosis. Owing to its promising anti-tumor activity, the fusion enzyme can be further examined on GnRH-R - expressing tumor xenografts to evaluate its anti-tumor effects *in vivo*.

Keywords: Drug delivery systems; pancreatic ribonuclease 1; GnRH; fusion protein; Prostate cancer.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original

Code of Abstract: OBi-9

Differences in clinical data between thrombotic and embolic ischemic stroke patients

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Abstract

Background and Aim: Ischemic stroke, a condition associated with high mortality and morbidity, can be categorized into embolic and thrombotic disorders. These subtypes exhibit distinct pathological characteristics, leading to differences in serum biomarker profiles. Routine laboratory findings are both accessible and sufficiently valuable for comparison between patients with embolic and thrombotic strokes.

Methods: In this retrospective data has analysis, we evaluate 1775 stroke patients who admitted from 2015 to 2023 in the Urmia imam Khamenei hospital. Laboratory data of 1743 stroke patients (both embolic and thrombotic subtype), including lipid, sugar, blood and kidney function profiles, were analyzed and evaluated.

Results: The routine laboratory findings were recorded for embolic and thrombotic stroke patients. the mean difference between two groups was performed by t student test via SPSS 23 software. The mean age of thrombotic patients was higher than embolic ones ($p < 0.001$). The thrombotic subtype levels of LDL ($p < 0.004$) and cholesterol ($p < 0.003$) were higher than embolic patients. The creatinine ($p < 0.363$) and urea ($p < 0.340$) levels were not different between two groups. Blood sugar ($p < 0.048$) but not fast blood sugar ($p < 0.162$) was different between two groups. The RBC level ($p < 0.003$) was lower in thrombotic patients on both genders.

Conclusion: Our findings showed that the routine laboratory findings could be helpful in differentiating the embolic and thrombotic stroke patients without a specific and sophisticated assay.

Keywords: Ischemic stroke; Embolic; Thrombotic.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original

Code of Abstract: OBi-10

Evaluation of microRNA-29a expression and Dipeptidyl - peptidase 4 level in ulcerative colitis patients

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Abstract

Background and Aim: Ulcerative colitis (UC) is a recurrent inflammatory bowel disease (IBD) that increases at an alarming rate around the world. MiRNAs, play an essential role in regulating numerous biological processes. The microRNA-29 (miRNA-29) family has been implicated in the pathogenesis of UC. In recent year, the alteration of Dipeptidyl-peptidase 4 (DPP4) levels in IBD patients has been noticed. DPP4 is an enzyme that plays a role in metabolic, and immune cell functions. In the present study, we evaluated the relationship between miRNA-29a expression in intestinal tissue and serum DPP4 levels in UC patients and healthy subjects.

Methods: Blood samples and colonic punch biopsy were obtained from 35 UC patients, and 29 healthy subjects. Serum levels of DPP-4 were evaluated by ELISA technique. expression levels of miRNA-29 were assessed by qRT-PCR. Also, biochemical parameters and demographic information were collected based on patient tests and questionnaires.

Results: The results of this study showed significant increases of miRNA-29a in intestinal tissue of UC patients compared to control. In addition, overexpression of miRNA-29a was accompanied by a decrease in serum levels of DPP4, but there is no significant difference between moderate and severe conditions. Furthermore, levels of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and platelet were higher in UC patients relative to those without UC.

Conclusion: These findings supported the role of the miRNA-29a-DPP4 axis in the pathogenesis of UC and provide the imputes for the further evaluation of the miRNA-29a and DPP4 both a biomarker of disease activity.

Keywords: Inflammatory Bowl Diseases; Ulcerative colitis; Dipeptidyl-peptidase 4; miRNA-29a; Inflammation.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBi-11

Investigating the expression of miR-133a, miR-637 and miR-944, PI3K, AKT genes in women with breast cancer

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Abstract

Background and Aim: MicroRNAs (miRNAs) are regulatory molecules that positively or negatively regulate signaling pathways and play a role in tumorigenesis as well as various aspects of cancer. The aim of this study was to investigate the expression levels of miR-133a, miR-637, and miR-944 in serum and tumor tissues, as well as their relationship with the expression levels of phosphatidylinositol-3-kinase (PI3K) and protein Kinase-B (AKT) genes and proteins, along with their clinical significance in breast cancer.

Methods: The expression levels of miR-133a-3p, miR-637, miR-944, PI3K, and AKT genes in tumor tissues and tumor margin tissues of breast cancer patients, as well as the serum levels of miR-133a-3p, miR-637, and miR-944 in these patients and the healthy group, were investigated by quantitative real-time PCR (qRT-PCR). Additionally, the expression levels of PI3K and AKT proteins in the tumor and tumor margin tissues were detected by immunohistochemistry. The diagnostic value of miR-133a-3p, miR-637 and miR-944 in breast cancer was evaluated using receiver operating characteristic curve (ROC) and in order to determine the diagnostic value of these three miRNAs, their expression relationship with PI3K and AKT was investigated.

Results: The expression levels of miR-133a-3p, miR-637, and miR-944 in tumor tissues were significantly lower than those in tumor margin tissues ($p = 0.023$, $p = 0.0001$, $p = 0.033$). In addition, the expression levels of miR-133a-3p and miR-637 in the serum of women with breast cancer were significantly lower than those in the serum of healthy women ($p = 0.031$ and $p = 0.005$, respectively). However, miR-944 levels were higher in the serum of patients with cancer than in the serum of healthy women ($p = 0.038$). Examining the ROC diagram related to three miRNAs showed that tissue miR-133a-3p has 100% sensitivity and 45% specificity, serum miR-133a has 47.50% sensitivity and 97.50% specificity, while tissue miR-637 has 97.50% sensitivity and 70% specificity, serum miR-637 has 50% sensitivity and 85% specificity, and the average tissue expression of miR-944 has 60% sensitivity and 87.50% specificity, and serum miR-944 has 55% sensitivity and 70% specificity in breast cancer. The expression of PI3K and AKT mRNA and protein in tumor tissues was higher than that in peripheral tumor tissues ($p < 0.05$).

Conclusion: The results of our study showed that miR-637 has better diagnostic value in breast cancer than miR-133a and miR-944.

Keywords: Breast cancer; miR-133a; miR-637; miR-944; PI3K; AKT.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Review

Code of Abstract: OBi-12

Monitoring & isolation of circulating tumor cells by lab-on-chip technology

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Abstract

Background and Aim: Currently, cancer is one of the most complicated disorders and one of the main causes of death around the world. In biological systems, genes & proteins are considered as essential constituents. Following several studies on genomics & proteomics, high-throughput screening methods has arrived. Such as: microchips and lab on a chip structures. Microfluidics are chips that utilize small volumes of fluids through micro channels. Silicone & glass are the most common materials used in microchips. However, the main purpose of this review is to discuss the importance of chips in the diagnosis and monitoring of malignancies.

Methods: We searched in databases including Google scholar, Scopus & PubMed. The keywords for our search were as followed: "Cancer" OR "Malignancy" AND "Microchip" OR "Microfluidic" OR "Lab-on-chip" AND "Cancer monitoring" AND "Circulating tumor cell isolation". We evaluated articles based on their novelty and 98 studies were selected and used in the present study.

Results: Microchips are a type of biomarkers that can be used for diagnosis and monitoring of human cancers. They are based on a microfluidic device (Veridex) which uses immunomagnetic magnetic field to isolate the circulating tumor cells (CTCs) from blood as a noninvasive sampling which is efficient for monitoring of tumors. In this review, we discuss the characteristics of microchips and their importance in the isolation of CTCs from blood samples as well as the components and common features of a diagnostic microchip.

Conclusion: Advancements in cancer monitoring involve utilizing circulating tumor cells and microchips, but current micro-fluidic systems struggle with isolating early-stage malignancies. This challenge may be overcome with specialized chip design, identifying stable biomarkers, and using novel biomarkers like CA19, CA20, PSCA. High-throughput CTC isolation through nanowires and microarrays examining molecular interactions aid in bridging research and clinical trials. "Risk on a chip" systems predict high-risk breast cancer stages, and proposed specialized microchips like exosomes show promise for early cancer detection. Efficient biological detectors in microchip structures contribute to early cancer prediction, holding potential for improved treatment.

Keywords: Microchips; Cancer; Circulating tumor cells; Gene expression.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Case Report

Code of Abstract: OBi-13

High endogenous ethanol and methanol in two children with neurologic signs

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Abstract

Background and Aim: A 5.5 years old boy came with severe attention deficit hyperactive disorder two years ago. He had jumping movements on the ground continuously on the first visit.

Case Report: His laboratory tests for body organ disorders (kidney and liver functions, biochemical profile) were normal and inborn errors of metabolism (acyl carnitine profile, urine organic acid, blood and urine amino acids, urine carbohydrate, homocysteine) were normal, but serum ethanol was high and he has treated with daily zinc administration and is very good now and could study in school. In 2021 we reported a 12 years old boy who had frequent 3 day- comatose attacks and drunken behavior and neurologic signs between those attacks during hospitalization. The routine laboratory tests for investigating of body organ disorders and inborn errors of metabolism were all normal. Laboratory assays for poisonings showed high methanol while his eyes examination and kidney and liver were all right. The reason was determined as deficiency of alcohol dehydrogenase that was proved by genetic study. This child was treated with daily zinc administration. Because zinc not only is in enzyme structure but also is a cofactor of this enzyme. Neurologic signs disappeared. He could start study. Now this boy is 22 years of age, his height is 176 cm and is studying in the university and is successful in his study.

Results: A small amount of ethanol and methanol are produced by intestinal microbiome from foods specially vegetables and fruits that are absorbed and then eliminated by the function of alcohol dehydrogenase in the liver that 2 isomers of it are for methanol. Deficiency of this enzyme can accumulate these materials in the body and cause neurological signs. Zinc is not only cofactor of this enzyme but also is in its structure. So, these children were successfully treated with zinc administration.

Conclusion: Two children with alcohol dehydrogenase deficiency resulted in neurologic signs are reported and it shows us that ethanol and methanol measurements should also be included in the study of inborn errors of metabolism.

Keywords: Zinc; Alcohol dehydrogenase deficiency.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBi-14

ATP and ROS changes in PBMC of rheumatoid arthritis patients can be important in the development of the disease

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Abstract

Background and Aim: Metabolic and mitochondrial dysregulation are critical causal factors in the pathogenesis and progression of Rheumatoid arthritis (RA). RA is a chronic inflammatory autoimmune disease. Elevated ROS levels prompt oxidative stress-induced injury, such as ATP synthesis disorders, leading to local and systemic inflammatory replies. In RA patients, the production of ROS is out of equilibrium. In this study, we investigated whether disputes related to ATP and ROS are related to the development of disease or not.

Methods: Peripheral blood mononuclear cells (PBMC) of 50 RA patients and 50 controls were isolated. Alteration in cellular ROS was measured using flow cytometry and DCFH-DA dye, and ATP level was also assessed via bioluminescence technique. The amount of light generated by the ATP reaction with recombinant luciferase depends on the ATP concentration. Complete blood count (CBC) and serological tests, including C-reactive protein (CRP) and rheumatoid factor (RF), were performed for all participants.

Results: A significant decrease in ATP ($p = 0.005$) and a significant increase in ROS ($p < 0.001$) were observed in the PBMC of RA compared to the control. ATP levels showed a reversed correlation ($r = -0.386$; $p = 0.005$) with ROS. All controls had CRP and RF within normal limits. Also, significant increments were observed in WBC, RDW, platelet, and MPV in RA compared to the control. There was also a significant decrease in RBC, hemoglobin, hematocrit, and MCHC. Moreover, the two groups had no significant differences regarding Neutrophils, Lymphocytes, Mean Corpuscular Volume (MCV), and Mean Corpuscular Hemoglobin (MCH).

Conclusion: Simultaneous measurement of ATP levels and the amount of ROS in PBMC of RA compared to control allows further investigation of the role of mitochondria that may be related to the disease. Therefore, this abnormal energy metabolism and excess ROS production could be the reason for the unexpected function of immune cells and possibly lead to autoimmunity in RA patients.

Keywords: Autoimmune disease; ROS; ATP; Rheumatoid Arthritis; DCFH-DA.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBi-15

The effects of L-lysine and combination of Lys-Zinc-VitC on UPR and autophagy pathways in skeletal muscle of diabetic rats

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Abstract

Background and Aim: Diabetes is a widely recognized disease around the world. The chronic hyperglycemia caused a long-term damage of various organs. Excess glucose causes the non-enzymatic glycation, misfolding and unfolding of proteins that all, can stimulate ER stress and unfolded protein response (UPR). Following UPR, autophagy and apoptosis are possibly happened. It has been shown that L-lysine as a chemical chaperone could decrease the diabetic complications. In this study we investigated the effects of L-lysine and the combination of Lys - Zn - VitC on UPR and autophagy markers in skeletal muscle of diabetic rats by evaluating the expression of some UPR and autophagy markers.

Methods: At first, we induced type 2 diabetes in a group of rats (n = 30) through intraperitoneal injection of nicotinamide (110 mg/Kg) and streptozotocin (50 mg/Kg). Then, they were divided into three subgroups. Three normal groups were also considered as controls. Three Control groups was treated with water (CN), Lys (CL) Lys - Zn - VitC (CS). Three diabetic groups also treated with water (DN), Lys (DL) and Lys - Zn - VitC (DS). Treatments was continued until one month and after that, they were sacrificed and their muscle tissue from right hand was collected and homogenized in buffer. Specific activity of catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GPx) was measured in the tissue samples by colorimetric method. Furthermore, UPR (XBP1s, eIF2 α and p-eIF2 α) and autophagy markers (Beclin1 and LC3II/I) were measured in tissue samples by Western blotting. RT-PCR was also used to measure XBP1-mRNA splicing.

Results: Unlike DL group, DS group showed significant increase in CAT, SOD and GPx specific activities compared to DN. In addition, DS group was significantly different GPx than DL group. There were no significant differences between CAT and SOD specific activities in control and diabetic groups. The significant decrease was observed in the XBP1 mRNA splicing of DS and DL groups compared to DN. The expression of XBP1 protein expression was significantly lower in the DS group than DN. The p-eIF2 α /eIF2 α ratio was also lower in the DS group than DN. The expression of Beclin1 and the LC3II/LC3I ratio were also lower in the DS group than DN and DL. For all protein factors, diabetic groups had significant difference compared to control groups.

Conclusion: Vitamin C and zinc by reducing oxidative stress and Lys by reducing concentration of glucose, decrease the accumulation of misfolded proteins. It causes decreasing of UPR and autophagy pathway which can affect the complication of diabetes. In this study, the improving effects of Lys and Lys- Zn-VitC have shown on diabetic rats and it is notable that Lys- Zn- VitC was more effective than Lys alone.

Keywords: Diabetes; Lysine; Zinc; Vitamin C; UPR; Autophagy.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBi-16

Therapeutic potential of dimethyl fumarate during pregnancy as an alternative to current treatments for gestational diabetes mellitus

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Abstract

Background and Aim: Gestational diabetes mellitus (GDM) is defined as hyperglycemia with the first onset during pregnancy. While pregnancy involves a wide range of maternal metabolism adaptations to provide sufficient energy for fetal growth and development, GDM can be considered a maladaptation by the maternal system to pregnancy, which may include mechanisms such as insufficient insulin secretion and irregular hepatic glucose output. GDM is the most commonly known risk for pregnancy, with adverse consequences such as metabolic disorders and heart diseases for both mother and offspring. The purpose of this study is to evaluate whether maternal DMF supplementation (120 mg/kg per day) in the third week of pregnancy can reduce maternal glycemia and protect offspring from metabolic and cardiovascular disorders.

Methods: A high-fat and sucrose (HFS) diet was used to create a rat model of GDM. The control group received a low-fat (LF) diet. In the third trimester of pregnancy, when maternal hyperglycemia was detected by enzymatic glucose assay, the HFS diet was supplemented with DMF. After weaning, offspring of GDM mothers were randomly assigned to the LF or HFS diet until 15 weeks of age. At the age of 15 weeks, after taking blood samples from the offspring, the animals were sacrificed, and the liver tissue was isolated in order to undergo pathological examination and assay molecular parameters. Glucose levels and the activity of heart damage markers such as CK-MB and LDH by the enzymatic method, levels of insulin, TGF- β 1, and MDA by the ELISA, and the expression of genes related to metabolic regulation by RT-qPCR were evaluated.

Results: Our study showed that GDM induced in rats caused glucose intolerance and insulin secretion disorder in the mother, and DMF significantly improved these disorders. At 15 weeks of age, the offspring of mothers in the GDM-HFS group were more obese than the offspring of mothers in the GDM+DMF-HFS group. In addition, glucose intolerance, insulin resistance, hepatic steatosis, and increased oxidative stress were observed in the offspring of the GDM-HFS group mothers, which improved with DMF supplementation. The activity of cardiac damage markers such as CK-MB and LDH decreased by 25-40% in offspring in the GDM+DMF-HFS group compared to the offspring of mothers in the GDM-HFS group. Dysregulated regulation of several metabolic genes, including ppara, lpl, pepck and g6p, was restored in the livers of offspring of mothers in the GDM+DMF-HFS group compared to offspring of mothers in the GDM-HFS group.

Conclusion: Consumption of DMF during the third trimester of pregnancy produced several beneficial metabolic and cardiac health outcomes for the mother and her offspring. Therefore, DMF could be a good option for current GDM treatments.

Keywords: Gestational Diabetes; dimethyl fumarate; metabolic disorders.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBi-17

Evaluation of the effect of loading Celecoxib on PLGA-PEG polymer by dual emulsion method on motor physiological parameters and sciatic nerve repair following injury repair in rats

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Abstract

Background and Aim: One of the important and vital organs of the body is the central nervous system and its peripheral nerves, any dysfunction of these nerves causes mild to severe disorders and abnormalities in patients. Based on previous studies, it can be concluded that although celecoxib at the dosage of 200 mg/kg can have a negative effect on the digestive system, its transformation A nano drug can reduce or reduce its intensity. Since the brain is very vulnerable to oxidative stress. Oxidative stress can alter neurotransmission, neural function, and overall brain activity. Oxidative stress plays a role in neurological diseases, including neuropsychiatric diseases such as degenerative stress and anxiety. The present study aimed to evaluate the effect of loading 200 mg of celecoxib in one gram of PLGA-PEG polymer with the double emulsion method on physiological motor indicators and sciatic nerve repair following experimental injury repair in mice on physiological motor indicators and sciatic nerve repair following experimental damage repair in the mouse model.

Methods: Animals were divided into 4 groups. Group 1: nerve damage without treatment. Group 2, 3 and 4 drug treatment groups. 12 mice were placed in each group, and they were evaluated in two time periods, 14 and 28 days after surgery. All rats underwent surgery and sciatic nerve damage was done in them. Mice in group 2: dose of 100 mg/kg, group 3: with dose of 200 mg/kg, group 4: 400 mg/kg were treated with celecoxib nano drug prepared orally. Mice were fed using pellets prepared for laboratory animals and water was freely provided to the animals. All animals were evaluated for motor health before surgery, and then all rats were anesthetized by intraperitoneal injection of ketamine hydrochloride (60 mg/kg) and xylazine (10 mg/kg) drugs, and after sciatic nerve surgery, using a small sciatic nerve hemostat. Pressurized for 60 seconds.

Results: Animals were divided into 4 groups. Group 1: nerve damage without treatment. Group 2, 3 and 4 drug treatment groups. 12 mice were placed in each group, and they were evaluated in two time periods, 14 and 28 days after surgery. All rats underwent surgery and sciatic nerve damage was done in them. Mice in group 2: dose of 100 mg/kg, group 3: with dose of 200 mg/kg, group 4: 400 mg/kg were treated with celecoxib nano drug prepared orally. Mice were fed using pellets prepared for laboratory animals and water was freely provided to the animals. All animals were evaluated for motor health before surgery, and then all rats were anesthetized by intraperitoneal injection of ketamine hydrochloride (60 mg/kg) and xylazine (10 mg/kg) drugs, and after sciatic nerve surgery, using a small sciatic nerve hemostat. Pressurized for 60 seconds.

Conclusion: Based on present findings, it can be concluded that 200 and 400 mg drugs, respectively, can be suitable options for repairing nerve damage in animal model.

Keywords: Celecoxib; Oxidative stress; Sciatic nerve; In vivo.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBi-18

Optimization of induction parameters for improving Neurturin production in the periplasm of *Escherichia coli*

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Abstract

Background and Aim: Neurturin (NTN), a cysteine knot protein, has remarkable potential for therapeutic applications, including the treatment of neurodegenerative diseases such as Parkinson's and Huntington's disease. Since cytoplasmic expression of recombinant neurturin in *Escherichia coli* leads to the formation of inclusion bodies, periplasmic production of it is advantageous. In the present study, the induction conditions for the production of NRTN by BL21 (DE3) were optimized using response surface methodology based on central composite design (CCD).

Methods: In this study, NRTN with pel B signal peptide was expressed in BL21 (DE3) using the pET22b expression vector. Design of optimal experimental conditions was performed by three- factors, five levels central composite design (ccd). The parameters considered were A-concentrations of IPTG, B- post-induction time and C-temperature. Dot blot technique was also used to analyze the expression level of NRTN in each experiment and the results were quantified using image J software. In the next step, the results were statistically analyzed using Design Expert software (11.0.3.0).

Results: Response surface methodology (ccd) was used to optimize the influence of 3 variables including IPTG concentration, post- induction temperature and time in 18 experiments. The accuracy of the modified quadratic model was confirmed with coefficient of determination (R^2) = 0.95 and adjusted (R^2) = 0.90. In addition, the ANOVA results showed an F-value of 18.23 and a p-value < 0.05, indicating that the model is significant. The lowest p-value for the product terms (AB, AC, BC) indicated that the interaction between the induction parameters played an important role in the periplasmic expression of NRTN. The results also showed that maximum periplasmic expression of NRTN was achieved at an IPTG concentration of 1mM, a post- induction temperature of 23°C and a post- induction time of 8.5 hours.

Conclusion: In conclusion, statistical results revealed that a high level of periplasmic NRTN expression was achieved in optimum induction conditions.

Keywords: *Escherichia coli*; Neurturin; periplasmic expression; response surface methodology.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBi-19

Evaluation of the effects of anti-inflammatory drugs on local and systemic manifestations of snakebite: A cross-sectional study

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Abstract

Although the predominant treatment for snakebite is the antivenom, other treatments are also considered. We studied the effects of single or multiple- doses of anti-inflammatory drugs on local, systemic and laboratory findings of the snakebite victims. In this cross-sectional study, 101 patients (90 male: 89.1%) with snakebite envenomation who were admitted to the Medical Toxicology Center of Khurshid Hospital, Isfahan, Iran, were investigated. One group (35 patients: 34.7%) received a single- dose of anti-inflammatory drugs containing chlorpheniramine (10mg intramuscular injection) with cimetidine (200mg intravenous injection) or ranitidine (50 mg intravenous injection) plus hydrocortisone (100 mg intravenous injection). The other 55 patients (54.5%) received multiple doses of the same drug combination every 8hr until the symptoms resolved. Local, systemic symptoms and laboratory findings on admission, and during 24hr and 48hr of admission, were recorded. The frequency of the localized signs of inflammation ($p = 0.03$), swelling ($p < 0.001$) and bruising ($p < 0.001$) showed a significant difference between the two treated groups. In addition, the recovery time in the patients who received multiple doses was faster ($p < 0.001$). There was no significant difference in any of the systemic signs, laboratory findings or the outcome between the patients in the various groups during hospitalization. Our data indicate that the administration of multiple doses of anti-inflammatory drugs had a greater effect on reducing local symptoms of snakebite including inflammatory manifestations.

Keywords: Envenomation; Snakebite; Anti- Inflammatory Drugs; Symptoms.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBi-20

Basic requirements for biological production process in science

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Abstract

Background and Aim: Bio production is a type of manufacturing or biotechnology that utilizes biological systems to produce commercially important biomaterials and biomolecules for use in medicines, food and beverage processing and industrial applications. Biological products include a wide range of products such as vaccines, blood and blood components, allergenic, somatic cells, tissues and recombinant therapeutic proteins. It's important for prescribers and patients to be informed that systems are in place to support the development of safe, effective and high - quality biologics. It's crucial for all manufacturers and scientists of biological medicines around the globe to be deeply committed to quality.

Methods: For this reason, some steps are ahead which mentioned below:

1. Make an observation
2. Ask a question
3. Form a hypothesis or testable explanation
4. Make a prediction based on the hypothesis
5. Test the prediction

Iterate: use the results to make new hypotheses or predictions.

Results and Conclusion: Thus, this information indicates that large potential for future bioprocess development considering the possible application of bioprocessing technological aspects for making a hypothesis predictable.

Keywords: Bio production; industrial applications; recombinant proteins.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Systematic Review

Code of Abstract: OBi-21

Autophagy pathway screening with focus on LC3 alteration in patients with acute leukemia; A new perspective monitoring of child: A systematic review

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Abstract

Background and Aim: Acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) are prevalent hematological malignancies. AML is characterized by excessive production of myeloblasts in the bone marrow, whereas ALL is characterized by an overabundance of lymphocytes. Among these two, ALL predominantly affects the pediatric population, whereas AML is the prevailing form of leukemia in adults. Different cellular mechanisms have a role in these malignancies. One of the crucial pathways involved in these diseases is autophagy. However, within the context of autophagy, certain genes assume a significant role, such as Beclin1, SQSTM1 (p62), and MAP1LC3B (LC3B), which exhibit either downregulation or upregulation in these malignancies. The primary objective of this systematic review is to examine the association between alterations in gene expression of MAP1LC3B, a key regulator of autophagy, in both AML and ALL patients.

Methods: We searched in PubMed, WOS, and Scopus databases using related keywords. Moreover, we focused on human studies, so in vitro and animal studies were excluded. Included filters were English language publications and full-text articles. We concentrated on MAP1LC3B marker in autophagy pathway. Studies that investigated another cell death pathway or focused on different autophagy markers, except MAP1LC3B, were excluded.

Results: At first, a total of 518 articles were identified. After deleting duplicates, 323 papers remained and were screened. Among them, 297 articles were excluded due to unrelated titles and abstracts, and 26 articles were selected for further evaluation. Finally, 8 papers were eligible for inclusion in this systematic review. We found that five articles had worked on AML patients, one on ALL patients, and two articles on both malignancies. The results of gene expression analysis showed that the expression level of LC3 significantly decreased in ALL patients compared to the healthy control group. However, the number of studies about the correlation of LC3 gene expression with ALL patients was relatively small. In addition, the LC3 expression level in AML patients significantly decreased compared to the healthy control group in five studies, but the upregulation of this gene was seen in two studies.

Conclusion: In most of the studies we assessed, the downregulation of LC3 and, as a result, the autophagy pathway was seen in acute leukemia patients. Additionally, more relevant research in the future should validate and confirm these results.

Keywords: Autophagy; MAP1LC3B; Acute lymphoblastic leukemia; Acute myeloid leukemia.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBi-22

Thymoquinone increases the effectiveness of Herceptin in MDA-MB-453 breast cancer cell line

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Abstract

Background and Aim: Thymoquinone (TQ) is the bioactive constitute and main compound of the volatile oil of black seed (*Nigella sativa*) with anti-inflammatory, antioxidant and anti-carcinoma effects. TQ suppresses the growth of cancer cells and induces apoptosis. In present study, we investigated the effect of TQ on sensivity of MDA-MB-453 cells to Herceptin.

Methods: The effects of TQ and Herceptin on the viability of cell lines were measured using the MTT assay. Cell suspensions containing 10×10^4 viable cells/ml were plated into 96-well plate and allowed to attach for 24 hr at 37°C in a 5% CO₂ atmosphere. The cells were then exposed to TQ (0-20 µg/ml) and Herceptin (0-15 µg/ml) for 24 and 48 hr for MTT test. Viable, apoptotic and necrotic cells determined with Acridine Orange/Propidium Iodide Double-Staining fluorescence microscopic and annexinV/PI flowcytometric assays. Caspase-3 as a marker of apoptosis detected with western blotting. Cell cycle analysis was performed by DNA flowcytometry.

Results: We evaluated the combined effects of Herceptin and Thymoquinone. Our results revealed that combination of Herceptin with TQ showed synergistic effects (Combination Index <1). The cell cycle analyses showed that treatment of Herceptin and TQ induced G₀/G₁ cell cycle arrest in MDA-MB-453 cells. Furthermore, TQ enhanced anti-proliferative effect of Herceptin by induction of apoptosis and caspase-3 activity.

Conclusion: our findings demonstrated that combination of Thymoquinone, as a chemosensitizer, and Herceptin may be a promising chemo-therapeutic strategy for treatment of HER2 expressing breast cancer cell lines.

Keywords: Thymoquinone; Herceptin; Apoptosis; HER-2; MDA-MB-453.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Systematic Review

Code of Abstract: OBi-23

Relationship between *Helicobacter pylori* infection and thyroid disorders

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Abstract

Background and Aim: Over half of the world's population is infected with *Helicobacter pylori*, a stomach infection that causes chronic inflammation of the stomach mucosa. A *H. pylori* infection has been linked to a number of stomach disorders, such as mucosa-associated lymphoid tissue lymphoma, peptic ulcers, chronic gastritis, and gastric cancer. Additionally, it has been demonstrated that *H. pylori* infection is linked to a number of extra-gastric conditions, including endocrine disorders such as diabetes mellitus, dyslipidemia, obesity, osteoporosis, primary hyperparathyroidism, thyroid mucosal-associated lymphocyte tissue (MALT) lymphoma, autoimmune thyroid diseases, autoimmune atrophic thyroiditis, Hashimoto thyroiditis, and neurological and cardiovascular disorders. We chose to look into the connection between *Helicobacter pylori* gastritis and different kinds of thyroid disorders because there are more studies on the connection between this infection and diseases like digestive cancers than there are on the connection between this infection and thyroid disorders.

Methods: In this research, online databases such as PubMed and Google Scholar were searched during the last 5 years (2018-2023) according to the entry and exit criteria (which was English language and time range). Among the searched articles (which were about 10 related articles), finally 5 final articles (one of which was the past authorship of our own group) were selected and reviewed just to write this systematic review summary. All searched articles had two main keywords of thyroid disorders and *Helicobacter pylori*.

Results: Previous research has looked at the connection between *H. pylori* and thyroid conditions. In the euthyroid state, a large amount of thyroid stimulating hormone may have a deleterious effect on metabolic health. Silva et al. discovered that in children with congenital hypothyroidism, *H. pylori* infection is linked to thyroid dysfunction. Bugdaci et al. discovered that in individuals with hypothyroidism with *H. pylori* infection, normal thyrotropin levels could not be reached even with large dosages of thyroxine therapy. According to Jinyun Wang et al., those who were *H. pylori* seropositive had a higher blood TSH level than those who were seronegative.

According to Maria Pina Dore et al.'s study, which looked at gastrointestinal symptoms in a community with a high frequency of both diseases, long-term *H. pylori* infection and autoimmune thyroid disorders (AITD) were significantly associated. Furthermore, our earlier research (as well as a related study by Keyfi et al.) unequivocally demonstrated the strong association between *Helicobacter pylori* infection and hypothyroidism. This finding also suggests that even hypothyroid patients are at increased risk for *Helicobacter pylori* infection. Furthermore, it has been demonstrated in other research that treatment-refractory hypothyroidism and *H. pylori* infection is related.

Conclusion: Based on the findings of multiple studies, it is evident that individuals with *Helicobacter pylori* infection had an increased risk of developing multiple thyroid disorders. Consequently, because these individuals also had a metabolic disease, *Helicobacter pylori* infection can be a major risk factor for stomach cancer. As such, these individuals should receive extra attention when it comes to *Helicobacter pylori* screening and treatment, and public health organizations should take this matter seriously.

Keywords: *Helicobacter pylori*; Helicobacteraceae; TSH; Thyroid disorders.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Systematic Review

Code of Abstract: OBi-24

The therapeutic potential of dental pulp stem cells (DPSCs) in cell therapy with injections

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Abstract

Background and Aim: Cell therapy has become a promising approach in regenerative medicine for various diseases and conditions. Dental pulp stem cells (DPSCs) represent a valuable source of stem cells with regenerative capabilities. The aim of this comprehensive review was to investigate the therapeutic potential of DPSCs in cell therapy through injection - based approaches.

Methods: A comprehensive literature search was performed in PubMed, Google Scholar, and Web of Science databases to evaluate the therapeutic potential of DPSCs in cell therapy with injections using these keywords: "dental pulp stem cells," "cell injections," "DPSCs," and "regeneration" until November 2023. Relevant studies were reviewed and analyzed the effects of DPSC injections in various disease models, including tissue regeneration and repair, immune modulation, and disease modification.

Results: One of the most commonly used forms of treatment for various diseases with DPSCs is through injections. Studies have shown that DPSCs have significant therapeutic potential in cell therapy with injections for diseases such as stroke, spinal cord injury, cerebellar ataxia, retinal degeneration, diabetic neuropathy, parotid gland injury, cystitis, and Sjögren syndrome. These injections can be administered locally, intramuscularly, or intravenously. Furthermore, findings indicated that DPSCs secrete bioactive molecules and have immunomodulatory properties that can influence inflammatory responses and regulate immune cell functions. This functionality contributes to their therapeutic effectiveness in a range of disease models. DPSC injections have also demonstrated efficacy in various disease models, including periodontal tissue regeneration, wound healing, autoimmune diseases, and neurodegenerative disorders. These findings highlight the potential for DPSC - based cell therapies to ameliorate symptoms, promote healing, and modify disease progression.

Conclusion: DPSCs hold immense therapeutic potential in cell therapy with injections. The regenerative and immunomodulatory properties of DPSCs make them attractive candidates for tissue repair, disease modification, and immunotherapy. Further research is needed to optimize DPSC isolation, expansion, and injection protocols, as well as to investigate the long-term safety and efficacy of DPSC - based cell therapies. The therapeutic potential of DPSCs in cell therapy with injections opens up new avenues for developing innovative treatments for a wide range of diseases and conditions.

Keywords: dental pulp stem cell; cell injections; DPSCs; regeneration.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBi-25

Mucopolysaccharidosis :MPSIV type A

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Abstract

Background and Aim: Mucopolysaccharidosis (MPS) is an inherited metabolic disease caused by the deficiency of lysosomal enzymes effective in breaking down long carbohydrate chains called glycosaminoglycans (GAGs). In these diseases, the accumulation of heparan sulfate (HS), dermatan sulfate (DS), Keratan sulfate (KS), chondroitin sulfate (CS) and hyaluronate in the lysosome of cells, which causes secretion in the bloodstream and excretion through urine. In total, seven different types of MPS disease have been identified. The most common type of MPSIV is type A or Morquio, which is caused by the lack or absence of galactosamine 6-sulfatase enzyme (EC 3.1.6.4). Clinical symptoms of Morquio A include skeletal disorders, hearing loss, problems in the cornea of the eyes, heart failure, and abnormally short height.

Methods: The patient is a 6-year-old girl with deformity in the arms, legs, chest, and short stature. Evaluation of mucopolysaccharides in urine and N-acetyl galactosamine 6-sulfate enzyme activity in blood was done by LC-MS/MS method and genetic investigation was done by WES method.

Results: Accumulation of Keratan sulfate and chondroitin sulfate in urine by LC-MS/MS method and lack of N-acetyl galactosamine 6 sulfate enzyme activity was observed in the patient's blood. A homozygous variant in the GALNS gene was identified in the genetic investigation by WES method, and the disorder in this gene is related to Mucopolysaccharidosis IVA with autosomal recessive inheritance.

Conclusion: The most common type of MPSIV is type A, which is caused by the defect or absence of galactosamine 6-sulfatase enzyme (EC 3.1.6.4). SNLAG gene (NM_000512.4) has 14 exons and has chromosomal location 16q24.3. Galactosamine 6-sulfatase enzyme is responsible for removing sulfate groups from N-terminal acetyl galactosamine 6-sulfate in mucopolysaccharides such as Keratan sulfate and chondroitin sulfate. As a result, in MPSIV A patients, due to a genetic defect in this enzyme, the amount of Keratan sulfate and chondroitin sulfate increases in the cells. The prevalence of this type of disease is estimated to be one in every 200,000 live births in the world. Clinical symptoms of Morquio A include skeletal disorders, hearing loss, problems in the cornea of the eyes, heart failure, abnormally short height, scoliosis, kyphosis, tooth enamel defects, excessive joint stiffness, prominent forehead and short neck. The symptoms of this type of disease usually appear at the age of two with the increase of Keratan sulfate and chondroitin sulfate, which are the first symptoms of skeletal disorders and curvature of the spine.

Keywords: Mucopolysaccharidosis; glycosaminoglycans; LC-MS/MS.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OBi-26

Risk factors for incidence of transient neonatal tyrosinemia among Iranian neonates

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Abstract

Background and Aim: Transient neonatal tyrosinemia is a common disorder of tyrosine metabolism in neonates. Several factors have been linked to increased transient neonatal tyrosinemia incidence. The central intent of this study was to ascertain the incident rate of transient neonatal tyrosinemia among Iranian neonates and to investigate the factors that influence the rate of development of transient neonatal tyrosinemia.

Methods: This study was a retrospective case-control study examined newborns screened at Growth and Development Research Center's metabolic laboratory affiliated to the Tehran University of Medical Sciences, between the years of 2019 and 2022. The control group for this study was comprised of newborns who received normal results for metabolic screening during the study period.

Results: Upon conducting metabolic screening on 73,349 infants, elevated tyrosine levels were detected in the initial screening for a total of 345 babies. There were 372 newborns with normal screening results who served as the control group. The incidence of transient neonatal tyrosinemia was determined to be 0.47%, with a total of 345 cases diagnosed out of 73,349 births. Five cases have other forms of tyrosinemia.

Conclusion: The study emphasized the significance of gestational age and birth weight in the development of transient neonatal tyrosinemia in newborns.

Keywords: Transient Neonatal Tyrosinemia; Newborn Screening; Cesarean.





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Tehran University of Medical Sciences, Tehran, Iran.
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3. Biochemistry (Poster Presentations)





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-1

Design of specific inhibitor against SARS-CoV-2 3Clpro based on 59S ligand structure in 7WO3.pdb crystal structure using virtual screening methods

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Abstract

Background and Aim: After the increase in the cases of SARS- Corona Virus 2019 and the global spread of the COVID-19 disease, the World Health Organization (WHO) announced the outbreak of the new coronavirus as the cause of public health emergency worldwide. Due to the pathogenicity of this virus and the consequences caused by it, the production of effective drugs or vaccines against this viral infection has been intensively considered. The proteases encoded by most viruses play a crucial role in the viral life cycle. Protease inhibitors bind competitively to the active site of the viral protease. Inhibition of the viral protease activity results in the production of immature virus particles. Two major proteases in SARS-CoV are 3CLpro and papain-like cysteine proteinase (PLpro). Protease inhibitors block the final step of virion assembly in the treatment. Among viral proteins encoded by the SARS-CoV-2 genome, 3CLpro is essential for the replication of the coronavirus. 3CLpro is responsible for the proteolytic processing of the polyprotein precursors pp1a and pp1ab. Inhibitors of 3CLpro specifically suppress the replication of the coronavirus by impairing the different stages of the viral life cycle. The crystallographic model of SARS-CoV-2 3CLpro encompasses the inhibitor 59S bound to the proteinase active site. The IC₅₀ for inhibition of SARS-CoV-2 3CLpro activity by 59S is 80 nM. Here, we carried out a virtual screening based on the chemical structures of similar pharmaceuticals. At the last step, *in silico* pharmacokinetics of the screened compounds with most favorable binding to SARS-CoV-2 3CLpro were predicted.

Methods: In current study, after performing the validation phase on 59S ligand against SARS-CoV-2 3CLpro in 7WO3.pdb file, 82 chemical structures with structural similarity to 59S were screened from Pubchem data center and separately were docked to SARS-CoV-2 3CLpro coordination from 7WO3 PDB file and finally arranged based on the acquired $\Delta G_{\text{binding}}$. In last step, physicochemical, pharmacokinetic, and toxicity properties of compounds with highest affinity for SARS-CoV-2 3CLpro were determined by pkCSM and SwissADME web-based servers.

Results: While the lowest $\Delta G_{\text{binding}}$ for 59S ligand was -6.8 kCal/mol, cyclo [Ala-Ala-Ala-N (Me) Tyr (Me)] (Pubchem ID: 73356126) with $\Delta G_{\text{binding}} = -8.2$ kCal/mol showed the lowest values between all of selected compounds. Also, computational based predicted attributes of the indicated compounds confirmed their potential to may use as efficient medicine.

Conclusion: The use of virtual screening methods can be considered and used as an efficient and effective method to find strong and specific inhibitors of SARS-CoV-2 3CLpro. Such chemical structures with high affinity to SARS-CoV-2 3CLpro and acceptable pharmaceutical properties that inhibit the replication and function of the SARS-CoV-2 virus can eventually be considered as an option for the efficient and specific treatment of COVID-19.

Keywords: SARS-CoV-2; COVID-19; SARS-CoV-2 3CLpro; Virtual Screening.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-2

Evaluation of the role of diffusion - weighted MRI in differentiating benign and malignant ovarian lesions

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Abstract

Background and Aim: Ovarian cancer is a prevalence female malignancy which often diagnosed at the advanced stages. Diffusion- weighted imaging (DWI) provides valuable information on tissue structural properties and used as an imaging biomarker in cancer detection. Lately post- processing three-dimensional apparent diffusion coefficient (3D ADC) map has a significant value in variable tumors yet its role in ovarian cancer is not well proven. We tried to evaluate the sensitivity and accuracy of DWI (T1, T2 and GAD factors) and 3D ADC maps in differential diagnosis of malignant from benign adnexal lesions.

Methods: Fifty- five patients had referred to MRI to evaluate adnexal lesions were studied using 1.5 T MRI. The signal on DWI (qualitative) and ADC values (quantitative DWI) of the components of the lesions were analyzed individually. Chi-square test and ROC curves were given to determine properties on DWI that could differentiate benign from malignant lesions.

Results: Of the 58 lesions, 33 were benign and 25 were malignant. There was a lower association of signal component on T2W and ADC values with malignancy compare to benign mass (p-value = 0.001). The DWI and T1 + GAD values in malignant tumors was significantly higher than in benign mass (p-value of 0.003 and 0.001) respectively. Finally, it was found that DWI and T1 + GAD had the highest diagnostic accuracy in diagnosing ovarian malignant masses.

Conclusion: Considering the very high diagnostic accuracy of DWI and T1 + GAD factors, malignant tumors can be distinguished from benign tumors with almost 100% accuracy and the treatment process can be based on it.

Keywords: Diffusion Weighted Imaging (DWI); Three-dimensional apparent diffusion coefficient (3D ADC); Ovarian masses; Diagnostic accuracy; MRA Diffusion Weight Imaging; Ovarian masses; Diagnostic accuracy.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic Review/Meta- analysis

Code of Abstract: PBI-3

Preparation and fabrication of nanosponges nifedipine and study of its in-vitro characterization

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Abstract

Background and Aim: Cyclodextrin - based nanosponge is a three - dimensional sponge - like structure of cyclodextrins that are bonded together with carbonate bonds. These structures have a high capacity to encapsulate, increase solubility, modify release and protect drug molecules. Nifedipine is a class II drug substance with a poor bioavailability due to its low aqueous solubility (5.9 mg/l). The aim of this research work was to synthesis nifedipine - cyclodextrin nanosponge complex and investigates its physiochemical properties.

Methods: In this study, two types of nanosponges (1: 2 and 1: 4/ carbonyldiimidazole: cyclodextrin) were prepared and the characteristics of each were studied. Solvent method was used to prepare nanosponges and freeze - drying method was used to drug loading. Particle size and zeta potential studied by Dynamic Light Scattering method. To get the loading efficiency, sample was dissolved in methanol and analyzed by UV spectrophotometer at 243 nm. The release study of nifedipine from nanosponge complex was performed using a dialyze cell in a medium of SLS 1.25% (W/V) with pH = 6.8 (phosphate buffer).

Results: The particle sizes of nanosponges (1: 2 and 1: 4) were 31 and 64 nm with a zeta potential of -27 and -16 respectively. Loading efficiency of nifedipine was 47.25% and 57.46 for NS (1: 2) and (1: 4). In vitro release study of nifedipine showed a rapid and complete release pattern (100% release in 4 hours). While 25% of pure nifedipine was passed from dialysis membrane in 4 hours.

Conclusion: It can be concluded from these findings that nifedipine - loaded NS have appropriate colloidal particle size with acceptable loading efficiency. DSC and FTIR studies corroborated encapsulation of nifedipine in CDNS. There is marked enhancement in in vitro release parameters of with nifedipine formulation as compared to plain nifedipine.

Keywords: nanosponges; cyclodextrin; nifedipine; nanocarriers





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-4

Investigation of PSA changes in patients with localized prostate cancer treated with 3D conformal radiotherapy (3DCRT)

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Abstract

Background and Aim: In the treatment of patients with localized prostate cancer, there has always been a debate between oncologists and urological surgeons as to which one can reduce and maintain PSA below 1 mg%. That our study and research was based on this difference of opinion.

Methods: Between 1.09.2021 and 1.10.2022, a total of 135 patients were treated with three-dimensional conformal radiation therapy (3DCRT) for clinical stages T1-T3 Adenocarcinoma of the prostate. The median age was 67 years (50-83), 10% had family history. 81% were smokers. The median PSA level was 17.5 ng/ml (3.1-95). 32% were T2a and 50% T2b. The median Gleason score was 6 (3-7). 34% received the treatment after radical surgery for biochemical relapse and 64% as primary treatment. 60% received 66-70 Gy and 40% received 72-76 Gy. Patients were followed with PSA 3 monthly for 24 months. The median follow up was 12 months. 39 patients didn't follow and therefore cancelled from the study. Only 96 patients ended the treatment and the follow up.

Results: The PSA decreased 6-9 months post External Beam Radiation Therapy (EBRT) However PSA value increased in 27 cases, but 69 patients remained under 0.5-1 ng/ml after 24 months post treatment with EBRT. The Bone scan was positive (bone metastases) in the 27 cases that PSA level had increased. 24 cases from these patients received 66-70 GY XRT (low dose) and their median age was more than 70 years and 18 cases/27 cases were directly treated with EBRT.

Conclusion: Recurrence after RPR was good controlled by RT, but primary RT was not sufficient in the majority of our patients. Those patients received only 66-70 Gy, therefore patients should receive a maximum dose of RT, and however more complications are expected. Measurement of prostatic specific antigen (PSA) after radiation therapy is a good marker for specificity and sensitivity of the treatment. PSA was a powerful predictor of local relapse and distant metastases (DM) and Patients who develop biochemical relapse should be considered for systemic therapy as DM is expected.

Keywords: prostate cancer; PSA; EBRT; 3DCRT; Radiotherapy.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic Review / Meta-analysis

Code of Abstract: PBI-5

Laboratory tests: a pioneer in the diagnosis of pediatric diseases

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Abstract

Background and Aim: Pediatric diseases are diseases and abnormalities that concern infants and children. Diagnosing these illnesses is the most crucial path to cure them and laboratory diagnosis is the most renowned diagnosis that makes it possible to cure these diseases. Additionally, diagnosing children is extremely critical since children's immune system is much weaker compared to adults and can result in life-long side-effects; therefore, this study investigates the laboratory diagnosis of diseases including pediatric pneumonia, pediatric post-streptococcal glomerulonephritis and pediatric appendices.

Methods: This study as a review article focuses on the most cited studies. The research done on pediatric pneumonia's laboratory diagnosis in three cities of Switzerland (Alcoba et al, 2017), the study done on pediatric appendices (Beltran et al, 2007) and another research conducted on pediatric patients who were admitted to Gaziantep University Hospital for post-streptococcal glomerulonephritis (kilic et al, 2018).

Results: Increased procalcitonin and CRP levels, negative nasopharyngeal viral PCR and a positive blood PCR were linked to pediatric pneumonia. Children with low CRP levels and negative clinical signs were less likely to suffer from pneumonia (6%). Finally, CRP > 80 mg/L and a positive P-PCR were considered the leading laboratory diagnosing tests with a 75% positive predictive value. Beltran and his colleagues (2007) argued that the count of WBC and CRP were very sensitive in differentiating ill from those who were healthy, however, the sensitivity of the two methods was pretty low in differentiating perforated from simple appendices. Kilic and his colleagues (2018) found out that 26.7% of subjects had elevated CRP levels, 98.7% had decreased complement C3 and 16% had decreased C4 levels. Additionally, the risk of low GFR was much higher in patients that had elevated CRP (P = 0.001) and decreased C4 levels (P = 0.010).

Conclusion: It has been proved that lab diagnosis is of great importance in diagnosing pediatric diseases. Increased CRP and procalcitonin levels alongside a positive blood PCR can be interpreted as a sign of pediatric pneumonia. WBC count and CRP were observed to be highly sensitive in differentiating patients that were suffering from appendices and those who weren't. CRP was also high in pediatric patients suffering from glomerulonephritis, while C3 and C4 levels were relatively low. Plus, it was concluded that patients with low GFR had high CRP and low C4 levels.

Keywords: Pediatric; pneumonia; appendices; post-streptococcal glomerulonephritis; laboratory diagnosis.





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Venue:
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Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-6

Evaluating the proteome of mesenchymal stem cells treated with dimethyl fumarate using bottom-up proteomics

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Abstract

Background and Aim: Mesenchymal stem cells (MSCs) have gained considerable attention in the field of regenerative medicine due to their inherent regenerative capabilities. However, to fully comprehend their therapeutic potential, it is essential to further optimize MSC-based treatments. Preconditioning, a strategy aimed at enhancing the effectiveness of MSC-based therapies, involves applying various agents or techniques to prepare mesenchymal stem cells (MSCs) for optimal therapeutic outcomes. Dimethyl fumarate (DMF), known for its ability to enhance cellular antioxidative capabilities, emerges as a promising candidate for preconditioning MSCs. Bottom-up proteomics is a technique that allows for the simultaneous measurement of numerous proteins using mass spectrometry of digested proteins. In this study, we employed bottom-up proteomics to assess the impact of dimethyl fumarate (DMF) on the proteome of mesenchymal stem cells (MSCs) derived from bone marrow.

Methods: To accomplish this objective, we subjected MSCs to a 10 μ M DMF solution for 24 hours, performing the treatment in triplicate. Following this, the cells were lysed with a 5% SDS solution, protein concentrations were quantified, enzymatic digestion was carried out using S-trap method and trypsin, and lastly, the generated peptide samples were analyzed using nanoLC-MS/MS technology.

Results: Our research led to the identification of 2,844 proteins, and by employing bioinformatic analysis, we were able to detect distinctive patterns within this dataset. Notably, a volcano plot revealed roughly 1,100 proteins that showed upregulation, and approximately 450 proteins displayed downregulation in response to DMF treatment. Furthermore, utilizing the STRING network, we visualized the network of upregulated and downregulated proteins.

Conclusion: The outcomes of our study indicate that the application of DMF results in a significant difference in the proteome of MSCs compared to untreated MSCs. Considering the biological processes affected by DMF, these findings suggest that a preconditioning strategy involving DMF treatment could substantially enhance the overall stability and therapeutic effectiveness of MSCs in the context of regenerative diseases.

Keywords: Mesenchymal stem cells; Dimethyl fumarate; Protein; Proteomics, Mass spectrometry.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic Review/Meta-analysis

Code of Abstract: PBI-7

Association between exposure to polychlorinated biphenyls (Pcbs) and endometriosis risk

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Abstract

Background and Aim: Endometriosis is a gynecological disorder and its etiology is not completely understood. Evidence proposes that environmental factors including endocrine - disrupting chemicals such as polychlorinated biphenyls (PCBs) may have serious roles in endometriosis development. The results of studies regarding the association between PCBs exposure and endometriosis risk were inconsistent. Hence, the goal of this systematic review and Meta- analysis study was to assemble more evidence for a better understanding of the link between PCBs exposure and endometriosis development.

Methods: The electronic search was carried out in the databases Web of Science, PubMed/ MEDLINE, Scopus, Google Scholar, and Embase with generic syntax. The studies were included based on eligibility criteria from 2000 to the end of 2020. There was not any limitation for the language of studies. For each included study, odds ratios (OR) using the random- effects model and 95% confidence interval (CI) were calculated.

Results: The results of this study demonstrated that pooled OR and 95% CI for PCB was 1.96 (1.31 to 2.93). There was moderate heterogeneity in our study ($I^2 = 63\%$, $P = 0.001$). In subgroup analysis base on geographical area, there was a significant association between PCB exposure and endometriosis among European population (OR = 3.66, $P = 0.024$).

Conclusion: The findings of this systematic review and Meta- analysis verified a relationship between endometriosis risk and PCBs exposure.

Keywords: Endometriosis; Polychlorinated biphenyls; Endocrine disruptors.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBI-8

The effects of fibrin/pomegranate nanoparticles on chondrogenesis of stem cells

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Abstract

Background and Aim: Nowadays, cartilage tissue engineering is the best candidate for the regeneration of cartilage defects. This study evaluates the effect of Fibrin/Turmeric Nano particles on chondrogenesis of stem cells.

Methods: Fibrin/Turmeric Nanoparticles (F/T NP) were characterized by DLS. PLGA-Fibrin/ Turmeric Nanoparticles scaffold was fabricated and assessed by SEM. Human Adipose- Tissue-Derived Stem Cells were seeded on scaffold and induced for chondrogenesis. After 14 days, cell viability was analyzed by MTT assay and the expression of cartilage genes was evaluated with real-time polymerase chain reaction.

Results: The size and surface charge of Fibrin/ Turmeric Nanoparticles were about 28~30nm and -17 respectively. The average size of pores of PLGA and PLGA-Fibrin/Turmeric was 240 and 340 micrometers respectively. The results of MTT assay indicated no significant differences between PLGA, PLGA- Fibrin/Turmeric nanoparticles and PLGA- Fibrin/ TGFβ-3 ($P > 0.05$). Furthermore, quantitative RT-PCR analysis demonstrated that TCA up-regulated cartilage - specific genes expression compared to the control group significantly. Furthermore, the results of the expression of type I collagen revealed that TCA down- regulated this gene significantly ($P < 0.01$).

Conclusion: The results indicated Fibrin/ Turmeric nanoparticles could be a potential factor for chondrogenesis of stem cells and down- regulation of cartilage fibrous marker.

Keywords: adipose - tissue - derived stem cells; chondrogenesis; Turmeric; fibrin nanoparticles; PLGA.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PBi-9

Review on the mechanisms of the effects of coenzyme Q10 supplementation on serum levels of leptin and adiponectin

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Abstract

Background and Aim: Coenzyme Q10 (CoQ10) is a fat - soluble benzoquinone structurally similar to vitamin K, which acts as an antioxidant in scavenging free radicals and inhibiting lipid and protein oxidation. It has been reported that CoQ10 deficiency is linked to multiple chronic diseases. The current study aimed to review the effects of coenzyme Q10 on serum levels of leptin and adiponectin, their ratio and their role in future treatment strategies.

Methods: We extended the literature search for all relevant articles from the database, including PubMed, Scopus and Google Scholar until September 2023. Our search was restricted to studies published just in the English language. In our search strategy, the keywords used to search in the above databases in titles and abstracts included coenzyme q10, CoQ10, ubiquinone, ubiquinol-10, ubidecarenone, leptin, adiponectin, adiponectin to leptin ratio, diabetes, type 2 diabetes, T2DM, diabetes mellitus.

Results: CoQ10 plays a protective role against the release of proinflammatory markers and provides an attractive anti - inflammatory therapeutic for treating some human diseases. It has been shown that there is a positive and negative correlation between CoQ10 and adiponectin and between levels of leptin and CoQ10, respectively. Studies showed that CoQ10 supplementation causes an increase in the value of the adiponectin/leptin ratio.

Conclusion: In summary, taking medications such as CoQ10 supplements is recommended as a potential therapeutic target to increase adiponectin levels and modulate the effects of oxidative stress.

Keywords: coenzyme Q10; antioxidant; oxidative stress; adiponectin; leptin.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-10

Study of the protective effect of *Humulus lupulus* on carbon tetrachloride- induced testicular damage in rats

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Abstract

Background and Aim: The testis is an organ in all male Mammals upon which the survival of the human species depends. Some drugs, chemicals, and xenobiotic toxicants can damage to the testicular organ due to their oxidative degradation. In this study, the effects of the protective compounds of the extract of *Humulus lupulus* (hop) on testicular damage induced by carbon tetrachloride (CCl₄) in adult male rats were investigated.

Methods: First, 24 male Wistar rats were divided into 4 groups of 6. Groups 1 and 2 received physiological serum for two weeks, while groups 3 and 4 received 100 and 200 mg/kg hop extract daily for two weeks, respectively. To induce testicular damage, except for group 1, all other groups received a mixture of carbon tetrachloride and olive oil at a dose of 1 ml/kg body weight on the fourteenth day. 48 hours after the injection, the animals were anesthetized and samples were taken.

Results: The results showed that hop extract consumption increases the total antioxidant capacity of testicular tissue and reduces malondialdehyde in testicular tissue of rats exposed to carbon tetrachloride ($p < 0.001$).

Conclusion: *Humulus lupulus* extract can protect testicular tissue against oxidative stress caused by carbon tetrachloride metabolism.

Keywords: Testicular damage; Carbon tetrachloride; *Humulus lupulus*; Oxidative stress; Antioxidant.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBI-11

The protective effects of *Humulus Lupulus* (Hop) extract on carbon tetrachloride- induced myocardium injury in rats

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Abstract

Background and Aim: Cardiovascular diseases are the most common causes of death and disability in the world. The aim of this study was to investigate the protective effects of *Humulus lupulus* (hop) on myocardium injury induced by carbon tetrachloride (CCl₄) in rats.

Methods: In this study, 24 male Wistar rats (200-250 g) randomly were categorized into four groups (n = 6). Groups 1 and 2 received physiologic serum for two weeks, while groups 3 and 4 received 100 and 200 mg/kg hop extract daily for two weeks, respectively. To induce heart damage, except for group 1, all other groups received a mixture of carbon tetrachloride and olive oil (1:1) at a dose of 1 ml/kg body weight on the 14th day. Forty - eight hours after the injection, the animals were anesthetized by intraperitoneal injection of ketamin and xylazin, and then the samples were taken.

Results: The results of this study showed that treatment with carbon tetrachloride significantly increased the level of MDA and decreased antioxidant capacity (P < 0.001). Consumption of hop extract significantly ameliorated these factors in comparison to the untreated group (P < 0.001).

Conclusion: The results of this study showed that hop extract can protect the heart against oxidant compounds and free radicals produced by carbon tetrachloride metabolism.

Keywords: *Humulus lupulus*; Carbon tetrachloride; Myocardium; Lipid peroxidation; Antioxidant





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Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-12

Assessment of leukocyte subtypes to high-density lipoprotein-cholesterol (HDL-C) ratios as predictors of severity and mortality of COVID-19

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Abstract

Background and Aim: Recently, the counts of leukocyte subtypes to HDL-C concentration ratios, including monocyte to HDL-C ratio (MHR), neutrophil to HDL-C ratio (NHR), lymphocyte to HDL-C (LHR) have been proposed as potential new indices of inflammation. The study aimed to investigate the correlation between these inflammations and atherogenic indices with the severity and mortality of COVID-19.

Methods: This study was performed with 1224 non-vaccinated and hospitalized COVID-19 patients. The associations between blood parameters and indices on admission with severity and mortality were analyzed using multivariate regression models. Receiver operating characteristic curves were used to compare the utility of different blood parameters.

Results: The severe patients and deceased groups showed low levels of HDL-C, high values of WBC, neutrophil, monocyte, eosinophil, WBC/ HDL-C, NHR, MHR, LHR, and EHR compared with the mild and survivor groups, respectively ($P < 0.05$). Multivariate regression analysis revealed that high levels of WBC, neutrophil, WBC/ HDL-C, NHR, MHR, EHR, and low levels of HDL-C were still independently associated with severity and mortality after adjusting for age, gender, and comorbidities. The correlation of LHR with severity and mortality was attenuated to insignificance. Also, patients with high eosinophil and monocyte levels had a higher risk of severe disease. According to the AUC values, the best predictors for severity were the level of WBC, neutrophil, and NHR (AUC: 0.724, 0.725, 0.724 respectively), and the best predictors for mortality were WBC/ HDL-C and NHR (AUC: 0.788, 0.790 respectively).

Conclusion: In summary, low levels of HDL-C and high levels of WBC, neutrophil, WBC/ HDL-C, NHR, MHR, and EHR which can be easily calculated from the CBC and HDL-C concentrations, may provide valuable and readily available prognostic information for severity and mortality of COVID-19.

Keywords: COVID-19; neutrophil to HDL-C ratio; monocyte to HDL-C ratio; lymphocyte to HDL-C ratio; CBC; WBC.





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Venue:
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January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-13

Harnessing nature's power: feverfew as a promising herb in medicine

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Abstract

Autoimmune diseases, Cancers, and diabetes have emerged as the tenacious diseases of the current era due to lifestyle changes. With drastic breakthroughs of the 20th and 21st centuries in the area of medicine, herbs and traditional approaches have mostly been replaced with synthetic therapeutics. However, the medicinal potential of long - used herbs should not be overlooked. Feverfew (*Tanacetum parthenium*), originally used for the treatment of migraine and inflammation for centuries, is a traditional herbal remedy with broad geographical distribution and is rich in a large number of natural active products such as sesquiterpene lactones including parthenolide as well as flavonoid glycosides and pinenes. In this narrative review, we summarized the recent significant findings of the available valid literature regarding the relationship between the use of Feverfew and a wide range of pathological as well as physiological conditions extracted from scientific databases including Scopus, ScienceDirect, and Pubmed. Additional experiments have demonstrated some beneficial effects of Feverfew in treating autoimmune conditions, asthma, allergies, fever, tinnitus, dizziness, nausea, infertility, menstruation problems, and diabetic - induced neuropathy. Feverfew can inhibit oxidative stress - mediated tissue damage caused by various toxic chemicals such as carbon tetrachloride by increasing superoxide dismutase, glutathione peroxidase, catalase activity, improving total antioxidant capacity, lowering malondialdehyde levels, regulating p53 pathway, and inhibition of STAT3/ NF- κ B and Nrf2/ Keap1 pathways, inflammasome activation, as well as downregulation of lipopolysaccharide-mediated tumor necrosis factor- α (TNF- α), MCP-1, interleukin-6, interleukin-1B, prostaglandins, COX-2, and leukotrienes production. In addition, Feverfew displays anti - cancer properties by influencing cell proliferation rate as a result of its regulatory effects on nucleotide, lipid, and protein metabolism. The vast medicinal properties and safety of Feverfew necessitate further research to discover the exact mechanisms by which this herb displays its therapeutic effects.

Keywords: Feverfew; Oxidative stress; Cancer; Autoimmune diseases; inflammation





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January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-14

Investigating the impact of serrata boswellia extract on cholesterol 24-hydroxylase and HMG-CoA reductase in astrocytes isolated from C57BL/6 mouse

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Abstract

Background and Aim: Boswellia has been used in traditional medicine to regulate lipids and increase intelligence, but its molecular mechanism is not well understood. On the other hand, the unique characteristics of the nervous system and drug limitations suggest a renewed interest in traditional medicine for treating some brain problems associated with impaired cholesterol metabolism and reduced cognitive ability. This study investigated the effect of Serrata Boswellia extract on CYP46A1 and HMGCR enzymes, important elements of cholesterol metabolism, in astrocytes.

Methods: Astrocytes were isolated and cultured from C57BL/6 mice. Boswellia hydroalcoholic extract was prepared and its safe concentration on astrocytes was determined by MTT method. The effect of Serrata Boswellia extracts on CYP46A1 and HMGCR enzyme levels was investigated using Western blotting.

Results: The results of the MTT assay showed a slight increase in astrocyte bioavailability at 20 µg/ml of BS or less and a significant decrease at 50µg/ml or higher. Treatment with BS extract significantly increased CYP46A1 protein levels compared to the control group, while HMGCR protein levels did not show any significant changes.

Conclusion: Our research findings shed light on the molecular mechanism behind the intelligence and memory-boosting effects of SB, which has been emphasized in traditional medicine. Furthermore, as CYP46A1 is exclusively expressed in the brain, we hypothesize that because Serrata Boswellia increases CYP46A1, it could be used in combination with normal cholesterol-lowering drugs in some diseases related to brain cholesterol accumulation.

Keywords: Boswellia; HMGCR protein; Cholesterol 24-Hydroxylase; cholesterol.





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January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-15

Exposure to organochlorine pesticides used in agriculture is associated with histone modifications that induce childhood leukemia

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Abstract

Background and Aim: Leukemia is the most common type of cancer in children. This disease is more common in children aged 2-5 years and teenagers. It seems that a combination of genetic and environmental factors may lead to this disease. Epigenetic changes play an important role in the pathogenesis of leukemia. In addition, there are environmental factors that can have a significant impact on these genetic changes, such as insecticides and agricultural pesticides, which are used indiscriminately today to control pests in the agricultural industry and for domestic use. Organochlorines are one of these pesticides that, due to their high stability in the environment and being soluble in fat, can cause irreparable effects on their health by accumulating in the body tissues of people who are exposed to it. The aim of this study was to investigate some epigenetic changes including histone modifications H3K16ac, H4K12ac and H4K20me3, and their relationship with the level of organochlorine pesticides in children with leukemia.

Methods: The serum level of organochlorines was measured by gas chromatography (GC 6890 N Agilent). The relative expression of histone proteins was performed by western blotting.

Results: The results showed that the level of pesticides such as Dichlorodiphenyldichloroethane (DDD), Eldrin, Dieldrin, and Lindane in children with leukemia was significantly higher than healthy children. In addition, a decrease in the relative expression of H3K16ac and H4K12ac, and an increase in the relative expression of H4K20me3 were observed in children with leukemia.

Conclusion: In the present study, children with high serum levels of organochlorine pesticides are associated with decreased acetylation and increased methylation in the level of histone proteins. Therefore, exposure to organochlorine pesticides may be accompanied by some epigenetic changes that lead to a more compact structure of chromatin and as a result disrupt the cycle and differentiation of hematopoietic cells in leukemia patients.

Keywords: Leukemia; Epigenetic; Organochlorines; Histone.





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January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-16

Examining the level of vitamin D in Female students and its relationship with students' awareness of skin complications caused by sunlight

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Abstract

Background and Aim: Skin cancer is one of the most common cancers in Iran. In Iran, due to the intense sunlight in most seasons of the year and the lack of use of appropriate protective clothing such as clothes and hats in the open air, one should expect skin cancer. Exposure to sunlight is essential for vitamin D synthesis. The aim of this study is to investigate the level of vitamin D in students of Khomein Faculty of Medical Sciences and its relationship with students' awareness of skin complications caused by sunlight.

Methods: The study was conducted on 200 students of Khomein Faculty of Medical Sciences. Students should be between 19 and 25 years old. Data collection was done using vitamin D laboratory tests and questionnaires.

Results: In people who were exposed to sunlight for more hours in order to get vitamin D, there were more skin spots and inflammations, but in people who used pharmaceutical supplements to get vitamin D, no such results were observed.

Conclusion: In people who are exposed to sunlight for more hours in order to get vitamin D, the probability of skin abnormalities is higher.

Keywords: Vitamin D; Skin Cancer; Sunlight.





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January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-17

Kaempferol attenuated the in vitro fibril formation of β - amyloid₁₋₄₂

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Abstract

Background and Aim: Alzheimer's disease (AD) is a progressive neurodegenerative disorder, which is a leading cause of aging- related dementia worldwide. The definitive cure for Alzheimer's is not yet known. The use of naturally small molecules to prevent of $A\beta_{1-42}$ aggregation and the progress of AD has been considered in recent decades. A polyphenolic flavone, Kaempferol was considered for its effect on the fibrillation process of $A\beta_{1-42}$ peptide.

Methods: Several techniques include Thioflavin T (ThT) assay, Anilino naphthalene sulfonate (ANS) binding assay, Dot blot (using Anti- beta amyloid antibody), Circular Dichroism (CD) and transmission electron microscopy (TEM) were used to investigate in vitro $A\beta_{1-42}$ aggregation in the presence and absence of Kaempferol in different time intervals (0, 12 and 24 h).

Results: Increasing the ThT and ANS fluorescence intensities after incubation of $A\beta_{1-42}$ peptide at 37 °C with gentle shaking indicated the amyloid formation. However, kaempferol prevented amyloid fibril formation. So, it caused decreasing the fluorescence intensity after 12 and 24 h. The CD spectroscopy results also showed more β -sheet content of $A\beta_{1-42}$ fibrils, which undergoes structural changes in the presence of kaempferol. After treatment, the percentages of α -helices and β -turn were increased. Dot blot results showed that kaempferol decreased the fibrillary content of $A\beta_{1-42}$ after incubation. Electron microscopy data also confirmed the decreased amyloid fibril content of $A\beta_{1-42}$ after incubation with kaempferol.

Conclusion: Our study showed that, Kaempferol exhibited inhibitory effects on $A\beta_{1-42}$ aggregation and fibril formation. Therefore, Kaempferol may consider as a candidate therapeutic agent on AD in the future.

Keywords: Kaempferol; $A\beta_{1-42}$ Peptide; Fibrillation; Structural Study; CD.





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January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-18

The analysis of coelomic fluid proteins of earthworm *Eisenia fetida* by HPLC and mass spectrometry methods for use in medical sciences

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Abstract

Background and Aim: Various researches on earthworms have revealed that their coelomic fluid (CF) contains a mixture of macromolecules. There are several functions attributed to CF, including acting as an insulin-like growth factor (IGF like), an immunoglobulin-like growth factor (IgFG like), an epidermal growth factor (EGF), anticoagulant, fibrinolytic, tissue regeneration, and wound healing. It is believed that the cells present within the CF (coelomocytes), are responsible for these therapeutic effects. The purpose of the present study was to determine of chromatographic and spectrometric characteristics of CF components from the earthworm *Eisenia fetida*.

Methods: Following the preparation of CF and using mass spectrometry techniques, specifically Peptide Mass Fingerprint technique, we proceeded with its evaluation. In the high-performance liquid chromatography (HPLC) procedure, a mobile phase comprised a combination of water, nitric acid, and trifluoroacetic acid. The stationary phase consisted of 25-centimeter-long tubes with an inner diameter of 4.6 millimeters, packed with 5 micrometer particles. The detector was set to a wavelength range of 220-280 nm.

Results: Based on the chromatogram of HPLC, the detector can identify several types of proteins over time. The protein's purity was determined to be 61%, with the initial peak displaying a purity of 39%. The results of the mass spectrometry examination reveal that the protein under investigation exhibits significant functional and application-based similarities with 10 distinct proteins derived from various organisms. Notably, it demonstrates the highest similarity with three proteins: Keratin Type 1 Cytoskeletal 16 (with a molecular weight of 51,973 Daltons and a score of 49), Bombyxin Receptor- Activated Protein (with a molecular weight of 40,030 Daltons and a score of 35), and Transient Receptor Potential Cation Channel M (with a molecular weight of 183,410 Daltons and a score of 46) in mice.

Conclusion: The practical application and utilization of any living organism necessitate a high level of experiences and professional information. Earthworm extractions exhibits considerable biological activities and they have wide range of applications in the medical domains. Consequently, individual purification is essential for different components of protein complex and evaluates their regenerative and wound healing applications. Furthermore, an examination of the effects of fibrinolytic- thrombolytic enzymes is required under both in-vitro and in-vivo conditions, including cell culture and laboratory animal models.

Keywords: Coelomic fluid; Proteins; Earthworm; *Eisenia fetida*.





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Venue:
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January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic Review/Meta-analysis

Code of Abstract: PBi-19

Examining the level of lactate dehydrogenase (LDH) in determining the prognosis of patients with Covid-19; Systematic review

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Abstract

Background and Aim: The novel coronavirus disease 2019 is a disease caused by the severe acute respiratory syndrome of the SARS-CoV-2 virus and is a major threat to global health. LDH is an enzyme that the body uses during the process of converting sugar into energy for cells. It can be released during tissue damage. The purpose of this study is to investigate the relationship between the prognosis of patients with corona and LDH levels.

Methods: In this systematic review study, three people simultaneously searched for the keywords "lactate dehydrogenase" and "Covid-19" and also extracted similar words from the MeSH database and PubMed, Google Scholar, and Web of Science databases until December 22, 2022. Was performed. The entry criteria are the originality of the type of article and in line with the main purpose of the study. The exclusion criterion was the lack of access to the full file of articles. Finally, 21 articles were included in the study.

Results: Finally, this study included 3842 (42% women and 58% men- the average age of the people was 55.5 (19-89) years, 16% severe group and 84% in the non-severe) confirmed patients with coronavirus. Be the normal level of LDH was 120-250. The mean serum LDH level in the severe group was 476.4 (300-1040) and 260.0 (442-206) in the non-severe group.

Conclusion: According to the findings of this study, the increase in serum LDH concentration in corona patients reflects cellular hypoxia and tissue necrosis and indicates acute and severe lung damage. So this biomarker is effective in determining the prognosis of patients.

Keywords: Covid-19; lactate dehydrogenase (LDH); prognosis.





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January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-20

Biochemical and histopathological changes in rats' livers treated with melatonin- loaded nanoparticles to counteract cisplatin- induced hepatotoxicity

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Abstract

Background and Aim: Cisplatin (CP) is a well- known and effective chemotherapy drug used for cancer management. However, one of its side effects is the induction of hepatotoxicity. Melatonin (Mel) has previously been demonstrated to be a potent protective therapy in several injury and toxicity models due to its remarkable capacity to scavenge free radicals. This study aims to investigate the potential hepatoprotective effects of Mel-loaded chitosan- tripolyphosphate nanoparticles (MelChitNPs). Both histopathological and biochemical analyses were carried out as parts of the study.

Methods: Forty male Wistar rats (220 to 250 g) were divided into five groups: saline control, cisplatin, Mel (10 mg/kg), MelChitNPs (10 mg/kg), and ChitNPs (10 mg/kg). These drugs were ingested through gavage for 15 days. Cisplatin (12 mg/kg) was administered intraperitoneally on the 16th day. On the 18th day, all rats were sacrificed to get liver tissue and blood samples. Serum ALP, ALT, and AST levels were measured by biochemical tests. Furthermore, histological analyses were carried out to determine the degree of tissue toxicity.

Results: Serum ALT, AST, and ALP levels significantly rose following cisplatin administration in comparison to the control group. In addition, histopathological analysis revealed increased inflammatory infiltration, venous congestion, sinusoidal dilatation, and feathery degeneration in the cisplatin group compared to the control group. In contrast to the cisplatin group, melatonin pretreatment showed a significant decrease in the serum ALT, AST, and ALP levels. Additionally, it was found that MelChitNPs had a stronger protective impact on liver function than melatonin.

Conclusion: These findings demonstrated that Mel has a remarkable capacity to protect the liver against cisplatin. The highest protective response to melatonin seems to be triggered by its nanoparticle forms.

Keywords: Melatonin; Cisplatin; hepatotoxicity; ALT; AST.





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January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-21

Melatonin- mediated nephroprotection: a comprehensive analysis of histopathological and biochemical outcomes in cisplatin- exposed adult male rats

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Abstract

Background and Aim: Cisplatin is widely administrated as an anticancer drug for numerous tumor types, although it frequently causes nephrotoxicity owing to oxidative stress. Melatonin, on the other hand, is known for its capacity to protect and scavenge free radicals against oxidative damage caused by chemicals. Therefore, we aimed to research the effects of melatonin on cisplatin- induced nephrotoxicity in rats.

Methods: In this study, 32 Wistar rats were divided into four groups: the Control, the Cisplatin, and the Melatonin groups, which received either 10 mg/kg or 20 mg/kg of melatonin respectively. Each rat received an oral gavage for 15 consecutive days before cisplatin single intraperitoneal injection (12 mg/kg) on the 16th day. The rats were euthanized after 48 hours, and blood and kidney tissue samples were collected for additional examination. Serum BUN and creatinine levels were measured by colorimetric assays.

Results: Following the administration of cisplatin, there was a significant rise in serum BUN and creatinine levels compared to the control group. The significant induction of nephrotoxicity shown by these biochemical markers was supported by histopathological analysis, which revealed the presence of edema, acute tubular necrosis, congestion, and glomerular count alterations. In comparison to the cisplatin group, the melatonin groups' serum creatinine levels were reduced. On the other hand, only the Mel20 group, showed a significant decrease in BUN levels. Additionally, kidney histopathology results showed that the Melatonin groups had less edema, acute tubular necrosis, tubular atrophy, and congestion than the Cisplatin group. Melatonin 20 mg/kg showed more protective effect.

Conclusion: Melatonin administration partially restores these adverse effects. It is concluded that melatonin offers some benefits as a potential agent to treat cisplatin- induced nephrotoxicity. Melatonin administration in higher doses is more effective.

Keywords: Melatonin; Cisplatin; Nephrotoxicity; Biochemistry; Histopathology.





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January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-22

The effects of metformin and p-Coumaric acid combination therapy on obesity and non-alcoholic fatty liver disease in high-fat diet obese C57BL/6 mice

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Abstract

Background and Aim: Nonalcoholic fatty liver disease (NAFLD) is one of the most common chronic liver diseases that is characterized by liver fat accumulation and hepatocyte steatosis in the absence of excessive alcohol consumption. Metformin, the first-line drug for type 2 diabetes mellitus (T2DM), has additional effects on improvements of NAFLD; however, the combined effect of this drug with p-coumaric acid (PCA) on liver steatosis is unclear. This current study investigated the combined effects of MET and PCA on NAFLD in a high-fat diet (HFD)-induced NAFLD mouse model.

Methods: Fifty male C57BL/6 mice were obtained from the Laboratory Animal Center of the Pasteur Institute of Iran. After one-week adaptation mice were fed a standard chow diet (n = 10) and HFD (n = 40) for 15 weeks. After 15 weeks, the HFD group was then divided into four groups (n = 10): HFD, HFD plus MET (230 mg/kg) (HFD + MET), HFD plus PCA (200 mg/kg) (HFD + PCA), and HFD plus MET (230 mg/kg) and PCA (200 mg/kg) (HFD + MET + PCA). In the all-period time experiment food and water intake, and body weight were recorded weekly. At the endpoint of the experiment, blood samples, white adipose tissue (epididymis, subcutaneous), brown adipose tissue, and liver were collected. Glucose tolerance test, cold-induced test, biochemical parameters, lipogenesis, beta-oxidation in the liver, thermogenesis, and adipose tissue browning were performed in adipose tissue by qRT-PCR, western blot and, Immunofluorescence (IF) technique.

Results: Our results demonstrated that the MET + PCA combination therapy markedly reduced weight gain and fat deposition in HFD fed mice. Furthermore, the combination of MET and PCA increased β -oxidation, decreased lipogenesis, and in this regard liver TG accumulation. In addition, MET + PCA supplementation therapy ameliorate liver inflammation, nuclear factor- κ B (NF- κ B) activity and macrophage switching from M1 into M2 phenotype in comparison with the monotherapy of MET or PCA. Furthermore, we illustrated that MET + PCA combination therapy upregulated thermogenesis-related genes in BAT and sWAT. Combination therapy results in stimulating brown-like adipocyte (beige) formation in the sWAT of HFD mice.

Conclusion: Taken together, these findings indicate that MET combined with PCA can improve NAFLD through decreasing lipid accumulation, inhibiting inflammation and inducing thermogenesis, and adipose tissue browning.

Keywords: Obesity; NAFLD; Metformin; p-Coumaric Acid; Hepatic steatosis; Brown Adipose tissue; Insulin resistance.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-23

Prevalence of galactosemia in Gerash city

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Abstract

Background and Aim: Galactosemia is a type of carbohydrate disorder that occurs due to the disorder and inefficiency of the enzymes involved in the metabolism of galactose. This hereditary disorder appears in an autosomal recessive form. This disorder occurs in apparently healthy children who have no clinical symptoms. Who suffer severe complications and death after consuming breast milk or milk containing galactose. The aim of this study was to determine the prevalence of galactosemia in infants born in Gerash city.

Methods: A cross-sectional study was performed on 3631 infants referred to the Mohammad-Rsololla health center from March 2018 to April 2022, blood samples were taken from a heel prick and then galactosemia test was done by fluorometric assay to determine the level of galactose.

Results: Of 3631 newborns screened for galactosemia, we cannot detect any galactosemia in newborn.

Conclusion: As our results showed, it seems the prevalence of galactosemia in our region is low. A more extensive study with more samples is recommended to find accurate information about the prevalence of galactosemia.

Keywords: Galactosemia; Neonatal screening; Gerash city.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-24

The roles of melatonin in neural protection: Three decades of advances

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Abstract

Melatonin (*N*-acetyl-5-methoxy tryptamine) is a secretory product of the pineal gland. Besides regulating circadian rhythm, melatonin exhibits numerous other functions including anticancer, anti-inflammatory, antioxidant, and neuroprotective actions. Neurodegenerative diseases are becoming progressively more common because of the improved longevity of humans leading to a steady rise in costs for care and maintenance of the patients. Because of the common hallmarks of these conditions such as mitochondrial dysfunction, inflammation and oxidative stress, it is noted that melatonin could be a beneficial agent in these conditions. In this review, we summarize the functions and the applications of melatonin in different neurodegenerative disorders along with the proposed underlying mechanisms to illustrate how this molecule may be useful in treatment strategies for these highly debilitating diseases.

Keywords: Melatonin; Neuron; Neuronal Protection; Neurodegenerative Disorders.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-25

Effects of cholestasis on testis tissue, sperm parameters and the anti-toxicity effects of encapsulated *pediococcus acidilactici* in a model of liver cholestasis

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Abstract

Background and Aim: Probiotics, such as *pediococcus acidilactici*, may have anti-inflammatory and antioxidant effects. Since probiotics are mostly consumed orally and go through the gastrointestinal tract, their viability might decrease due to the acidity and active enzymes in GIT. Encapsulation can be used to enhance probiotic viability in GIT, which also increases their effectiveness. As several studies show, probiotics may have anti-toxic effects on biliary acid oxidative stress-induced damage in testicular tissue; therefore, enhance sperm parameters and fertility. We aim to determine the effect of encapsulated *pediococcus acidilactici* on, oxidative status, sperm and testis histologic parameters in an experimental model of liver cholestasis.

Methods: The experiment was conducted on 48 male Wistar rats, classified into a control group and treatment groups: probiotic, free capsule, and encapsulated probiotic group. Encapsulated *pediococcus acidilactici* with dose of 3×10^9 CFU/g were administered. Rats received treatment based on their classification for 1 week prior to cholestasis induction, and 3 weeks after. Afterwards, all rats were euthanized, and their blood and testis were collected. Their blood plasma was used to measure sex hormones levels. Testis were used to determine oxidant / anti - oxidant status, sperm parameters, and histological properties.

Results: Sperm count increased from 107×10^6 in control BDL group to 184×10^6 in rats treated with encapsulated *pediococcus acidilactici*, also viability percentage increased from 1.8% in BDL control to 17% in treated group. Also, the sperm abnormality decreased group from 96.8% to 43% in treated group. Encapsulated probiotics had preventive effects on testicular tissue, and sex hormone levels.

Conclusion: The results show that probiotics can be useful in alleviating male infertility via inducing testis health, and enhancing sperm parameters.

Keywords: Infertility; Liver fibrosis; Probiotic; *Pediococcus acidilactici*; Encapsulation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-26

The effect of encapsulated bacillus subtilis on sperm quality, sex hormone concentration and Testis histological parameters in cholestasis induced in rat

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Abstract

Background and Aim: Liver cholestasis has lots of toxicity effect on body, one of that is Infertility; Cholestasis can lead to inflammation and oxidative stress, potentially damaging testicular tissue and affecting spermatogenesis negatively. Probiotics, like *Bacillus subtilis*, have anti-inflammatory and anti-oxidant properties that can help decrease testicular inflammation and oxidative stress. Microencapsulation can enhance probiotic survival in the gastrointestinal tract (GIT) due to their low survival rate in GIT. The purpose of this study is to investigate the effect of encapsulated *Bacillus subtilis* on the improvement of testicular inflammation and the treatment of infertility.

Methods: In this study, encapsulated *Bacillus subtilis* with a dosage of 3×10^9 CFU/g, previously prepared in the prior investigation, was utilized. Wistar rats were used and divided into control, cholestasis, free encapsulated cholestasis and probiotic encapsulated cholestasis groups. The experimental groups received diets supplemented with probiotics, free capsules, and encapsulated probiotics individually for one week prior to the induction of liver cholestasis and continued the supplementation for three weeks thereafter. After this period, all rats were euthanized, and their blood and testis were collected. The blood plasma was used to measure sex hormone levels, while the testis was used to determine oxidant/anti-oxidant status, sperm parameters, and histological properties.

Results: Sperm count (107×10^6 to 179×10^6) and viability percentage (1.8% to 19.5%) increased in the *Encapsulated Bacillus subtilis* group compared to the control group. Also, the sperm abnormality significantly decreased in the encapsulated probiotics group. Encapsulated probiotics have the potential to ameliorate sex hormone disorders and histological abnormalities in the testes by exerting protective effects on testicular tissue against oxidative stress.

Conclusion: According to the findings, probiotics have the potential to improve male infertility by promoting the health of the testes, decreasing abnormalities in sperm, and boosting the number of sperm and their viability.

Keywords: Liver fibrosis; *Bacillus subtilis*; Male infertility; Probiotic; Microencapsulation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-27

Doxorubicin drug delivery with exosomes derived from mesenchymal stem cells of human adipose tissue to breast cancer cells

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Abstract

Background and Aim: Drug resistance and toxicity of healthy tissues are limiting factors for the use of doxorubicin (DOX) as a chemotherapy drug in breast cancer. The use of carriers such as liposomes and nanoparticles for targeted drug delivery is also limited due to organ toxicity or immune response. Therefore, exosomes (Exos), as small extracellular vesicles (ECV) with low side effects, high biocompatibility and low immune response, have attracted considerable attention. In this study, an exosomal carrier derived from mesenchymal stem cells of human adipose tissue was used to increase the effectiveness of DOX on cancer cells and reduce its side effects.

Methods: Mesenchymal stem cells were isolated from liposuction tissue by enzymatic method, and after confirming their stemness by examining surface markers, conditioned media was collected to separate exosomes by ultracentrifugation. After confirming the exosomes by TEM, DLS and western blot, DOX drug was loaded into exosomes by sonication method and the amount of loaded drug was checked by spectrophotometry method. Finally, the effect of exosomes containing Dox (Exo- Dox) on cancer cells was investigated by MTT test.

Results: The results of flow cytometry analysis of markers on the surface of mesenchymal stem cells showed a decrease in the expression of negative markers CD45 and CD34 and an increase in the expression of positive markers CD44 and CD90. The results of examining exosomes confirmed the size, shape and surface markers. The amount of Dox loaded in the exosome was about 37%, and the MTT test showed a significant increase in the cytotoxic effect of Exo- Dox compared to free Dox on MCF-7 cancer cells. While in normal breast tissue cells (MCF-10A), free Dox shows a significant increase in cell death compared to Exo- Dox.

Conclusion: The results of our study showed that Dox loading in Exos derived from mesenchymal stem cells of human adipose tissue improves the effect on breast cancer cells and reduces the cytotoxic effect on normal cells, which can be further studied as a way to treat cancer in the future.

Keywords: Doxorubicin, Drug Delivery Systems; Exosomes; Mesenchymal Stem Cell; Breast Cancer.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-28

Investigating the effect of vitamin E supplementation on sperm parameters, before and after freezing, histology, tissue antioxidant capacity and gene expression in the testes of old mice

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Abstract

Background and Aim: Some age - related testicular changes, such as Sertoli cell vacuolization, blood - testis barrier breakdown, and others cause total sperm production reduction, and male fertility decrease. So, the aim was to evaluate the effect of vitamin E as an antioxidant on the restoration of testicular function in aged mice.

Methods: Twenty - eight male NMRI, 48 weeks old mice, were used in 4 groups of vitamin E daily gavage: the control group (distilled water), and three treatment groups who received 100, 200, and 400 mg/kg, for 4 weeks. After the end, semen analyses were done, before and after sperm freezing. Testicular histology, tissue antioxidant enzyme (SOD, GPx activities, and MDA amount), and gene expression were evaluated.

Results: Higher sperm count, progressive motility, and better sperm morphology were the achievements in the two higher dosages of vitamin E ($p < 0.05$). After sperm freezing the results were also prominent ($p < 0.05$). Two common structural abnormalities were vacuole and epithelial detachment ($p > 0.05$). The tubular, epithelium height and luminal diameters did not change with age. Higher GPX, SOD activities, and lower MDA content have been found in the two high doses of vitamin E. Higher levels of ID4 and GFRA1 expression were significant in the higher doses of vitamin E, and Plzf was seen in the 400 mg/kg treatment group compared to the control group ($p < 0.05$).

Conclusion: However, the structural destructions were not prominent, with 12 months of age, the sperm parameters were reduced. It was found that antioxidant supplementation for aged male reproduction improvement, not only helps for the present fertility but also future use when there's a need for sperm freezing or fertility preservation. Behinds, the effect of vitamin E on the gene expression levels creates a promising approach for regenerative efforts of aged testis in the future.

Keywords: spermatogonia; vitamin E; male fertility; antioxidants; oxidative stress.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-29

Investigating the relationship between serum uric acid to high- density lipoprotein ratio in diabetic patients

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Abstract

Background and Aim: Serum uric acid (SUA) and high- density lipoprotein cholesterol (HDL-C) are both associated with metabolic disorders and cardiovascular diseases. The ratio of SUA to HDL (UHR) has been proposed as a novel marker of these conditions. However, the relationship between UHR and diabetes mellitus (DM) is not well established. In present study we aimed to investigate the association of UHR with DM and its complications.

Methods: In this cross-sectional study, data related to population referred to Ahvaz Golestan Hospital were examined. Subjects were divided into two groups with and without diabetes. HDL-C and uric acid were measured according to standard protocols, and the ratio of uric acid to HDL (UHR) was compared in these two groups.

Results: Data of 76 people including 40 diabetic patients and 36 control subjects (18 to 70 years old) were analyzed. Our findings showed that although, serum uric acid and HDL levels were higher in diabetic patients than in the control group, the mean UHR was significantly lower in people with diabetes (10.18 ± 5.5) compared with control group (113.0 ± 7.3) ($P < 0.05$).

Conclusion: Overall, decreased UHR in diabetic patients may be a result of increased lipid- enriched HDL subfraction. Therefore, it is suggested that for the evaluation of UHR, it is necessary to determine HDL subfractions. However, further studies are needed to confirm the causal relationship and the underlying mechanisms of UHR in DM.

Keywords: Diabetes; Seum uric acid; HDL; UHR.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-30

The protocol of primary hepatocyte isolation

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Abstract

Background and Aim: Primary hepatocytes are used in various biomedical research fields as an ex vivo model for liver physiology. However, obtaining high yields of viable primary mouse hepatocytes can be technically challenging, which limits their use. This protocol provides an optimized method for isolating and culturing hepatocytes from the liver of a mouse. If you need to isolate primary mouse hepatocytes, this protocol will greatly help you.

Methods: Mouse liver was used to isolate hepatocytes. Cell culture plates were coated with 0.1% mouse tail collagen 24 hours before loading hepatocytes. To start the process, the mouse is given deep anesthesia. Next, the skin and peritoneum are opened, and the intestines are directed to the right side. This exposes the vena cava and portal vein. The liver is then perfused with a PBS solution through the portal vein while the vena cava is cut to remove the blood. The perfusion is continued until the liver appears completely white. After that, a collagenase solution is perfused into the liver. By continuously closing and opening the vena cava, the solution is allowed to penetrate the liver tissue completely. Once this is done, the liver is separated and placed in a petri dish containing collagenase solution. Some cuts are made in the tissue to release cells, including hepatocytes. Finally, the hepatocytes are separated from other cells using cell density and centrifugation. Then hepatocytes were transferred to cell culture plates containing complete DMEM medium with 10% FBS and incubated. After 4 to 5 hours, the morphology of the cells was examined.

Results: After the isolation and culture of hepatocytes, the cubic morphology and two or more nuclei of hepatocytes were confirmed by a light microscope.

Conclusion: This protocol allows for easy and highly efficient isolation of mouse liver hepatocytes.

Keywords: liver; hepatocyte; primary culture.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-31

Upregulation of caspase 9 and caspase 8 after treatment with peg- coated magnetite copper sulfide hetero- nanoparticles and radiotherapy in colorectal cancer cells in vitro

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Abstract

Background and Aim: Colorectal cancer is a one of the prevalent cancers word widths. Various therapeutic options are available for treatment of this kind of cancer. Radiotherapy is one of the cancer treatment modalities in colorectal cancer. The use of nanoparticles as radio sensitizer can be considered in cancer treatment, which may increase the effects of radiation therapy. The objective of the study was to evaluate the efficacy of combination of the PEG- coated magnetite copper sulfide hetero- nanoparticles and radiotherapy in colorectal cancer cell line and study some possible anti - cancer mechanisms.

Methods: HT-29 cell line was obtained from Pasteur institute. HT-29 cells were treated with various concentrations of PEG- coated magnetite copper sulfide hetero- nanoparticles to evaluate the minimal toxic concentration for utilizing in combination therapies. This concentration used in combination with radiotherapy (2 and 4 Gy) to increasing the efficacy of cancer treatment. After 24 h of treatments, the cell viability assay was carried out. Low efficient concentration of nanoparticle selected for combination therapies. Gene expression levels by Real- time PCR method was studied [Caspase 8, Caspase 9]. Also, cellular ROS measurement was performed.

Results: based on our results, examined nanoparticles in combined with radiotherapy upregulate the caspase 8 and caspase 9 gene expression levels versus single radiation treatment ($p < 0.05$) in colorectal cancer cells. In combinations of radiotherapy and PEG-coated magnetite copper sulfide hetero - nanoparticles in all examined doses, a marker of cellular ROS was increased in compared to single radiation treatment ($p < 0.05$).

Conclusion: Our results indicated an efficacy of PEG- coated magnetite copper sulfide hetero - nanoparticles in combined with radiotherapy in this colorectal cancer cells.

Keywords: colorectal cancer; nanoparticle; Caspase 8; Caspase 9.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-32

Investigating tissue lipid profile in breast cancer patients

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Abstract

Background and Aim: Breast cancer (BC) is an important cause of female cancer-related death. It has recently been demonstrated that metabolic disorders including lipid metabolism is a hallmark and a common feature of cancer cells metabolism. This study was conducted with the aim of investigating the lipid profile of fatty acids in tumor tissue.

Methods: 55 pairs of fresh-frozen samples of BC and adjacent normal tissue were used to analyze FAs composition of tissue using gas chromatography.

Results: The fatty acid profile of tumor tissue showed a significant increase in the level of saturated fatty acids (SFA) and a significant decrease in Monounsaturated fatty acids (MUFA), whereas there was no significant difference in the level of Polyunsaturated fatty acids (PUFAs).

Conclusion: The overall pattern of fatty acid profiles clearly indicates disturbed lipid metabolism in cancer patients. It seems that identifying the mechanisms causing and the effects of these changes may be useful in cancer treatment strategies.

Keywords: Breast cancer; fatty acids profile; PUFAs; MUFA; SFA.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-33

Vitamin D status and cardiovascular disease in transfused thalassemia major patients

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Abstract

Background and Aim: Thalassemia is the most common hemoglobinopathy in the world and Iran Beta thalassemia: It is the most common type of thalassemia and is divided into two types, mild and severe (major) People with beta- thalassemia major require frequent blood transfusions and iron chelators. The most common cause of death in patients with thalassemia major is cardiac hemosiderosis, which is mainly evaluated based on t2* MRI. The progressive accumulation of iron in these patients causes intestinal absorption disorders and parathyroid disorders in these patients and makes the person susceptible to vitamin D deficiency vitamin D deficiency is increasing in today's industrialized society and its connection with heart diseases is of interest in this study, the relationship between cardiovascular diseases in thalassemia patients with plasma vitamin D deficiency is discussed.

Methods: In this analytical cross-sectional study 62 thalassemia major patients according to the inclusion and exclusion criteria at the thalassemia center of Dezful University of Medical Sciences in 2018 were studied. Demographic information plasma level of vitamin D report of echocardiography and ECG and MRI t2* were extracted from the patients' files and evaluated under statistical methods.

Results: 27.9% of patients had abnormal ECG and 39.5% had abnormal echocardiography data. 37.2% of the patients had heart iron deposits- based MRI. Plasma vitamin D deficiency (< 30ng/ml) was found in 58.1% of patients (The plasma level of vitamin D in patients with cardiac abnormality based on MRI T2 or Echo was significantly lower than patients with no cardiac abnormality (P-Value < 0.05). The plasma level of vitamin D in patients with abnormal ECG was not significantly different compared to patients with normal ECG (P-Value > 0.05)

Conclusion: Organic involvement in hemochromatosis patients is an important problem in this group considering the increase in survival in these patients, more studies are need. This study showed that plasma vitamin D level in patients with normal Echocardiography is significantly higher than patients with abnormal Echocardiography. In addition, patients with cardiac iron overload - based MRI had lower levels of vitamin D, as other studies in this regard had the same result. The lack of relationship between plasma deficiencies of vitamin D with ECG results is probably due to nonspecific variation and multifactoriality in Electrocardiogram. Considering the inverse relationship between plasma levels of vitamin D and heart involvement in patients with thalassemia major, the level of vitamin D in plasma should be checked periodically and vitamin D supplementation should be recommended if necessary.

Keywords: MRI; Thalassemia; Vitamin D; Heart.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBi-34

Physiological and pathophysiological relationship of magnesium with Covid-19

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Abstract

Background and Aim: Magnesium is the fourth most abundant cation in the body, which is essential for many enzyme systems including oxidative phosphorylation, glycolysis, cell proliferation, nucleotide metabolism and protein biosynthesis. Therefore, magnesium deficiency can lead to a variety of metabolic abnormalities and clinical consequences. This study examines the effectiveness of magnesium and magnesium supplements on various disorders and diseases, including Covid-19.

Methods: We searched the pub med and science direct databases for original articles and reviews. Based on the search result, in this systematic review article we are analyzing various aspects of the effects of magnesium on various diseases including Covid-19.

Results: Many evidences indicate that magnesium supplements such as magnesium sulfate and magnesium oxide can play a prevention and treatment role in various types of disorders or diseases related to the respiratory system, digestive system, nervous system, immune system, blood coagulation, kidney disorders and cytokine storm. The Covid-19 epidemic caused by acute respiratory syndrome (SARS-COV-2) is characterized by the highest expression of the virus in the alveolar cells of the lung and the epithelial cells of the digestive tract, with various degrees of respiratory symptoms and damage to organs.

Conclusion: Based on scientific and medical evidence and reports, magnesium sulfate is believed to play a role in reducing the inflammatory response and oxidative stress in various diseases, including Covid-19.

Keywords: Magnesium; Covid-19; SARS-CoV-2; Inflammation; Cytokine storm.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-35

Investigation of the potential effect of alpha-pinene on the miR-21 and EMT marker (E-cadherin) in hepatocellular carcinoma cells (HepG2)

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Abstract

Background and Aim: As a natural compound, alpha-pinene is reported to have a number of properties, including its ability to inhibit the growth of cancerous cells. Some studies in recent years indicate that alpha-pinene can prevent the invasion of malignant cells in some cancers, despite the lack of studies on its effect on cell invasion. Epithelial-mesenchymal transition (EMT) occurs when cancer cells lose their epithelial characteristics and migrate to adjacent tissues. It's believed that microRNA-21 (*miR-21*) indirectly contributes to EMT, which leads to tumor cells migrating and invading surrounding tissues. Therefore, this study aimed to investigate the effect of alpha-pinene on the expression of *miR-21* and *E-cadherin* in HepG2 cells.

Methods: In the current study, the human hepatocellular carcinoma cell line HepG2 was treated with different concentrations of alpha-pinene for 24 hours. The expression levels of *mir-21* and *E-cadherin* were determined by RT-qPCR.

Results: Alpha-pinene significantly downregulated *miR-21* in different treatment groups compared to the control group. Additionally, *E-cadherin* gene expression was meaningfully increased at different concentrations of alpha-pinene compared to the control.

Conclusion: It is likely that alpha-pinene plays a critical role in inhibiting HCC migration and invasion by downregulating *miR-21* and increasing *E-cadherin* expression. So, we concluded that alpha-pinene could be helpful in preventing the proliferation of cancer cells.

Keywords: Hepatocellular Carcinoma; Alpha-pinene; Epithelial-Mesenchymal Transition; MicroRNA; E-cadherin.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-36

Brain and nervous system disorders, learning problems, memory, intelligence and cognitive disorders in children treated with methotrexate

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Abstract

Background and Aim: Methotrexate (MTX) is one of the highly toxic drugs used in the treatment of children's diseases. Among the most important side effects of this drug is brain toxicity. Due to the use of this drug in children's diseases, its effects on children's brain, learning, intelligence and memory are of great importance. This study tries to investigate the side effects of MTX on the brain, learning, intelligence, memory and possible cognitive disorders in people taking this drug, especially in children.

Methods: All information and articles required for this study, including information and articles related to methotrexate drug toxicity, methotrexate brain and nervous system toxicity, methotrexate effects on learning, intelligence, memory and cognitive disorders, especially in children, from Google Scholar, PubMed, Scopus and Web of Science were collected.

Results: Few studies have been conducted on the effects of chemotherapy and treatment of children with MTX and the effect on learning disorders, memory, intelligence, and cognitive problems. MTX can cause persistent cognitive deficits in long-term childhood users of the drug also increases the risk of an IQ of less than 85 in people who received the drug as children. In the studies, there was a significant relationship between IQ along with verbal learning and the volume of the hippocampus, amygdala and pallidum in patients with acute lymphoblastic leukemia (ALL) treated with MTX. In children treated for ALL with MTX, both volume reduction of selected subcortical structures and cognitive impairment were observed. Research has shown that MTX-related neurotoxicity occurs in approximately 3.8% of pediatric ALL patients. Specific neurocognitive problems are associated with MTX, particularly, attention, concentration and executive function. In addition to the above cases, seizure disorders, moderate to severe sensor neural hearing loss, mild developmental delays and learning problems have been reported. In a study in 10-year-old ALL children treated with MTX, a decrease in IQ, working memory and processing speed was observed.

Conclusion: According to the studies conducted in this field and the various side effects of MTX, the administration of this drug, especially in children, should be done with more considerations. In addition, more and more complete clinical research on the neurotoxicity of MTX and possible developmental and learning disorders, intelligence, memory and sensory and movement problems on patients, especially children, need to be done. Also, the production of supplements and medicinal regimen and treatment methods to reduce these effects should be considered by researchers.

Keywords: Methotrexate; Children; Brain; Nervous System; Toxicity.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-37

Reproductive and fertility disorders in patients treated with methotrexate

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Abstract

Background and Aim: Methotrexate drug is one of the drugs used in chemotherapy in children. Due to the high toxicity of this drug and side effects on the body's organs and systems, especially the reproductive system, investigation and recognition of possible disorders in patients treated with methotrexate MTX are important, especially in children.

Methods: All required materials and articles related to methotrexate drug, testicular and ovarian toxicity, disorders and side effects on conception, fetus and fertility were collected from Google Scholar, PubMed, Scopus and Web of Science.

Results: Testicular toxicity caused by MTX is a significant side effect that may cause subsequent infertility. In a study on mice with a dose of 20 mg/kg, significant testicular toxicity and a decrease in fertilization rates were reported. The study of this drug in animal models showed cytotoxicity, changes in spermatogenesis, degeneration of spermatocytes in Sertoli and Leydig cells. MTX may also cause primary infertility by directly affecting the hypothalamic-pituitary-gonadal or gonadal axis. MTX has toxic effects on the uterus and ovaries through oxidative stress. Among the functional and structural disorders of the ovary and in high doses, it is infertility. MTX can increase oxidative stress mediators and decrease antioxidant and anti-inflammatory mediators in the uterine ovarian tissue. MTX has been reported to decrease levels of the antioxidant glutathione (GSH) and increase myeloperoxidase (MPO) and malondialdehyde (MDA), the latter being an important marker of lipid peroxidation and an index of oxidative tissue damage. Other side effect MTX, which was observed in a study on rats, was a decrease in the number of primordial ovarian follicles. MXT administration during pregnancy may cause miscarriage, fetal malformation and intrauterine growth retardation. Evidence from clinical cases suggests an association between low in vitro fertilization (IVF) success rates and ovarian damage due to prior MTX administration. Further investigation revealed senescence and apoptosis of follicular granulosa cells (GCs) associated with follicle growth arrest and abnormal levels of estradiol and anti-Mullerian hormone.

Conclusion: According to the results of this review, the effects of MTX on the reproductive system in both men and women, especially in children, and possible future disorders due to MTX, finding ways to prevent or reduce these effects and drugs and medicinal supplements and New and less dangerous treatment methods are very important.

Keywords: Methotrexate; Reproduction; Fertility; Testis; Ovary.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-38

Ferula gommusa promotes apoptosis in Jurkat cells: an in vitro study

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Abstract

Background and Aim: As conventional chemotherapy and radiotherapy are often accompanied by unwanted side effects; researchers pave the way for new innovative treatments. Emerging evidence showed that *Ferula gummosa* was used as a promising treatment for various types of cancer disease. This herbal derivative can reduce cellular proliferation in breast and colon cancer. Jurkat cell line is known as immortalized human T-cell lymphocyte for experimental in vitro studies. This cell line can be used for a first evaluation of anticancer treatment against invasive acute lymphoblastic leukemia (ALL). This study aimed to investigate the anticancer effect of *Ferula gummosa* on the Jurkat cell line.

Methods: First, we expanded the Jurkat cells to prepare an adequate number of immortalized cells. Jurkat cells were treated with *Ferula gummosa* and culture media as the vehicle group. Different doses of *Ferula gummosa* (12.5, 25, 50 μ /ml) were administrated to Jurkat cells. After 24 hours MTT assay was performed. Then, drug toxicity and EC50 were assessed using the MTT assay. It showed that *Ferula gummosa* was not cytotoxic for T-cell lymphocytes. Moreover, DNA extraction, RNA extraction, and protein extraction were carried out. Then, apoptosis was assessed by determining the Bax / Bcl-2 expression ratio and DNA fragmentation. Finally, we assessed the caspase-3 and caspase-7 activity.

Results: It was shown that 25 μ /ml of *Ferula gummosa* significantly decreased the viability of Jurkat cells to 57.7 %. Then, the *Ferula gummosa* effect on human lymphocytes was evaluated. We incubated a number of 500,000 lymphocytes in each well. Then, the *Ferula gummosa* and media were added to the wells. Lymphocytes were treated with 25 and 50 μ /ml of *Ferula gummosa*, then viability was measured using MTT assay. *Ferula gummosa* did not significantly reduce the number of human lymphocytes. Human lymphocytes with 25 and 50 had a viability of 95.29% and 79.93%. DNA fragmentation was determined by electrophoresis. Our results showed that *Ferula gummosa* increased DNA fragmentation and reduced the intact DNA. This herbal agent increased the Caspase-3 and-7 activity. By RT-PCR, it was found that this agent increased the Bax / Bcl-2 expression ratio. These findings reflected that *Ferula gummosa* can promote apoptosis in Jurkat cells.

Conclusion: *Ferula gummosa* can significantly induce apoptosis in Jurkat cells, whereas it does not exert a toxic effect on human lymphocytes. Considering the anticancer effect of *Ferula gummosa*, it can be used as a promising agent against leukemia. Further preclinical and animal studies should be performed to validate its therapeutic effects.

Keywords: Jurkat cell; *Ferula gommusa*; cancer.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-39

Toxicity and side effects of methotrexate on body systems: possible harms and disorders for children

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Abstract

Background and Aim: The drug methotrexate (MTX) is used in the treatment of various children's diseases. In this study, an attempt was made to investigate the toxicity and side effects of this drug on the organs and systems of the body, and possible diseases and developmental disorders for these children.

Methods: All the updated information and articles related to methotrexate, toxicity, side effects of methotrexate on body organs and systems, and other things were collected from Google Scholar, PubMed, Scopus and Web of Science.

Results: Gastrointestinal poisonings are the most common with a prevalence of 20-65% and are usually characterized by mild or moderate severity (such as nausea, vomiting, diarrhea, and abdominal pain). It is estimated that up to 20% of low dose methotrexate (LDM) users have at least one episode of elevated serum transaminases. MTX - induced hepatotoxicity is an important clinical problem that may affect the overall prognosis and outcome of the disease. Oxidative stress is a key player in its pathogenesis and can lead to cirrhosis.

MTX is excreted by the kidney that in high doses, it can cause tubule toxicity and kidney failure. Many drugs that have renal excretion may change its concentration and thus its toxicity. Due to its poor solubility in acidic urine, MTX can deposit in the renal tubules and lead to significant damage.

Studies conducted on children reported a decrease in academic skills. In addition, memory disorders and cognitive disorders, decrease in intelligence quotient (IQ), decrease in working memory and processing speed were observed among people.

MTX can cause vascular endothelial dysfunction by causing hyperhomocysteinemia or by increasing oxidative stress. In mice, MTX led to endothelial shedding and decreased vascular reactivity. MTX can also cause chronic heart failure (CHF) and left ventricular ejection fraction (LVEF).

Pulmonary toxicity can manifest as fibrosis, interstitial pneumonitis, or even diffuse alveolar damage. Interstitial pneumonitis is the most serious respiratory toxicity for LDM. Patients treated for four weeks with LDM can show lung damage and pneumonia.

A decrease in the relative weight of the testis, a significant decrease in the testosterone level, a decrease in spermatozoa, detachment, a significant decrease in spermatogenic cells and pyknosis of some nuclei were observed with MTX administration. MTX can cause damage to the ovary and uterus through the mechanism of oxidative stress and can cause miscarriage during pregnancy. A reduction in the number and cessation of the growth of follicles in the ovary has also been reported.

Conclusion: In addition to the therapeutic effects of MTX, its adverse effects should also be given serious attention in order to reduce the side effects during the use of the drug and reduce the possible future effects following the use of this drug in children. It can also help to produce supplements that can be taken with this drug and reduce its harmful side effects and toxicity.

Keywords: Methotrexate (MTX); Children; Toxicity; Side Effects.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-40

Comparison of food intake and anthropometric indices in hirsutism women and healthy women of reproductive age referring to women's clinics of Shahid Rahimi Hospital in Khorramabad city in the summer of 1402

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Abstract

Background and Aim: Hirsutism is an increase in end-to-end and androgen- dependent hair in women that can occur due to idiopathic causes, ovarian problems, adrenal glands, pituitary gland and taking medications. The aim of this study was to determine the prevalence of hirsutism and its relationship with factors such as Body Mass Index (BMI), menstrual pattern, acne, and history of PCOS, skin and hair color, and family history. The present study was designed to investigate and compare the history of dietary intake and anthropometric indices in women with hirsutism and healthy women. Also, considering that if anthropometric indices and dietary intake on hirsutism can be prevented by relatively simple measures, this study was designed to help eliminate or reduce the occurrence of hirsutism in women.

Methods: This study is a case and control study. In this study, the group of patients includes all women with hirsutism that referred to obstetrics and gynecology clinic in Shahid Rahimi Hospital in the summer of 1402. The comparison group included healthy women of reproductive age who were the same number as the case group, who had been referred to the obstetrics and gynecology clinic at the same time considering the inclusion criteria.

Results: It was observed that there was a significant difference between the two groups except for occupation, smoking and the presence of underlying disease ($P > 0.05$) in other variables of child, education and family history ($P < 0.05$). Based on the table 1-4, it can be seen that in the control group, only 9.3 percent of people had a family history of hirsutism, compared with 49.5 percent of those with hirsutism. The mean BMI of hirsutism group was significantly higher than healthy group ($P < 0.001$).

Conclusion: It was found that dietary patterns and obesity play an important role in the development of hirsutism. Reducing the consumption of medium and high - fat dairy products, having a healthy lifestyle and maintaining normal weight in the range of normal have an effective role in preventing hirsutism.

Keywords: food intake; anthropometric indices; hirsutism.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Review Article

Code of Abstract: PBi-41

KLF₄ - JAK / STAT3 pathway as a potential therapeutic target for Alzheimer's disease (AD)

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Abstract

Background and Aim: Alzheimer's disease (AD) is a progressive and gradual neurodegenerative disorder of old age that commonly manifests with slow memory loss caused by neural cell death and neural synapse deficit. AD is defined by the accumulation of Amyloid β -protein (A β) plaque and neurofibrillary tangles which consist of hyperphosphorylated Tau protein. Neuroinflammation plays a significant role in AD pathogenesis. The Janus kinase /signal transducer and activator of transcription (JAK/STAT) signaling pathway drive neuroinflammation in AD by initiating innate immunity and modulating adaptive immunity. Therefore, a disrupted or dysregulated JAK/ STAT signaling pathway could result in the neuroinflammation and progression of AD. Kruppel- like factor 4 (KLF₄) is a nuclear protein that plays a crucial role in the modulation of CNS and is responsible for anti-inflammation and axonal regeneration through the JAK/STAT 3 pathway. In this article, we aimed to review the KLF₄- JAK /STAT pathways in AD pathogenesis which could be a therapeutic target to improve patients' lives and inhibit the progression of AD.

Methods: Scopus, PubMed, and Google Scholar were searched with five keywords up to November 2023. Articles were selected based on inclusion and exclusion criteria.

Results: The JAK / STAT pathway transduces the downstream of chemokines, various cytokines, and microglial activation which are associated with neuroinflammation and lead to neurodegenerative diseases such as AD. The evaluation of post-mortem AD patients showed reduced levels of activated STAT3 in hippocampal neurons. Inactivation of STAT3 could be associated with age related manner or secondary to amyloid accumulation. KLF₄ plays a pivotal role in CNS regulation and could affect axon regeneration. The overexpression of KLF₄ in embryonic retinal ganglion cells was associated with a reduced percentage of axons and dendrites elongation and neurite branching. Therefore, KLF₄ can inhibit axonal growth and affect axonal regeneration. A decreased expression of KLF₄ leads to increased levels of phosphorylated STAT3. In a study by Cui et al. KLF₄ knockdown improves axonal regeneration in retinal ganglion cells. Moreover, they showed that this action was mediated by a decrease in phosphorylated p53 and an increase in phosphorylated STAT3 levels.

Conclusion: In conclusion knocking out KLF₄ can enhance the axonal regeneration and growth rate through the JAK / STAT3 signaling pathway. Therefore, the KLF₄ - JAK / STAT3 signaling pathway can represent a potential therapeutic target for AD. However, further exploration is needed to clarify the deep cellular and molecular mechanism of this pathway and the translation of this therapeutic target to the clinical setting.

Keywords: Alzheimer's disease; JAK / STAT pathway; neuroinflammation; neurodegeneration; KLF₄.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-42

Association of clinical characteristics of polycystic ovary syndrome with genotypes of VDBP polymorphism (rs7041)

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Abstract

Background and Aim: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among women of reproductive age. Vitamin D binding protein (VDBP) is a highly polymorphic protein that plays a crucial role in vitamin D metabolism. Some studies showed the association of this polymorphism with metabolic disorders. This study aims to investigate the association of clinical characteristics of PCOS with genotypes of VDBP polymorphism (rs7041) in healthy and PCOS women.

Methods: A total of 200 PCOS patients and 100 healthy controls were entered into this study. Genotypes of rs7401 (HaeIII G > T) polymorphism of the VDBP gene were determined using the PCR-restriction fragment length polymorphism (RFLP) method. Biochemical and hormonal parameters were measured and the association between them and rs7041 genotypes was investigated.

Results: According to the obtained results, LH level was significantly higher in the TT or TG genotype (3.82 ± 6.83) than in the GG genotype (5.31 ± 2.30) ($p < 0.01$). Also, the FBS level in the TT or TG genotype was significantly lower than in the GG genotype group ($p < 0.05$). No significant difference was observed between the levels of other biochemical and hormonal parameters and genotypes.

Conclusion: The results of this study suggested that the association of rs7041 polymorphism with PCOS may be through its effect on LH and FBS levels.

Keywords: Polycystic ovarian syndrome; VDBP; polymorphism.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-43

Association of VDBP gene polymorphism (rs7041) with polycystic ovarian syndrome

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Abstract

Background and Aim: Polycystic ovary syndrome (PCOS) is the most frequent endocrine disorder in women of reproductive ages. Vitamin D metabolism has been linked to the development of PCOS among women. Vitamin D binding protein (VDBP) is a highly polymorphic protein that plays a crucial role in vitamin D metabolism. This study aims to investigate the frequency of VDBP rs7041 polymorphism in healthy and those with PCOS and its correlation with infertility and abortion in women with PCOS.

Methods: In this study, a total of 200 PCOS patients (including 100 infertile women and 100 women with a history of recurrent pregnancy loss) were compared to 100 healthy controls. Genotypes of rs7401 (HaeIII G > T) polymorphism of the VDBP gene were determined using the PCR- restriction fragment length polymorphism (RFLP) method.

Results: A higher percentage of the GT genotype, as well as T allele were found in PCOS and PCOS- infertile groups in comparison with non- PCOS women. T allele increased the risk of the development of PCOS and infertility in women with PCOS (OR: 2.274, 95% CI (1.208-4.281), p = 0.011; OR: 30.667, 95% CI (4.050-232.190), p = 0.001). The GT genotype increased the risk of PCOS and infertility in PCOS women (OR: 2.933, 95% CI (1.538-5.593), p = 0.001; OR: 40.552, 95% CI (5.344-307.704), p = 0.000). The study found no significant differences in the genotype and allele frequencies of rs7041 polymorphism between PCOS-abortion women and non- PCOS subjects.

Conclusion: The results of this study indicated that there is a significant association between genetic variants of the VDBP gene and increased risk of PCOS and PCOS- related infertility.

Keywords: Polycystic ovarian syndrome; VDBP; polymorphism; infertility; abortion.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-44

Anticancer effects of *Astragalus maximus* methanolic extract against cervical cancer cells line

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Abstract

Background and Aim: Cervical cancer, the fourth most common cancer in the world, results from the increasing and irregular growth of cervical epithelial cells and the continuous shedding of cells. Cancer treatment is done using surgery, chemotherapy, hormone therapy, radiation therapy and biological therapy (immunotherapy). Most chemical treatments cause many side effects such as loss of appetite, weight change, burning mouth or throat, dental and gum problems, nausea and vomiting, depression and fatigue. The high prevalence of cancer and the ineffectiveness of chemical treatments show the need to find new and natural medicinal compounds that have fewer side effects. This study aimed to evaluate the anticancer effects of *Astragalus maximus* methanolic extract (AMME) on cervical cancer cells line (HeLa cells).

Methods: MTT assay used to evaluate the effects of AMME on cell viability and growth rate of HeLa cells. Effect of AMME on the expression of the apoptotic genes (Caspase-3, Bax, and Bcl-2) was tested by Real-time PCR.

Results: The calculated CC₅₀ value of AMME was 189.8µg/mL for HeLa cells; nevertheless, the CC₅₀ value for normal THLE-3 cells was 593.6µg/ml. Real-time PCR showed that the gene expression level of Bax and caspase-3 was considerably amplified after treatment of HeLa cells; but, treatment with AMME markedly declined of the expression level of Bcl-2 gene.

Conclusion: We found the effective anticancer effects of AMME, which is possibly due to the induction of apoptosis. But more studies required evaluating precise mechanisms and efficacy of AMME in animal models.

Keywords: Herb; Apoptosis; cervical cancer; treatment.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-45

Association of homocysteine with different phenotypes of polycystic ovary syndrome

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Abstract

Background and Aim: Polycystic ovary syndrome (PCOS) is a heterogeneous metabolic disorder with four phenotypic variations, characterized by unique clinical and biochemical attributes. The principal PCOS phenotypes encompass: phenotype A, characterized by the presence of clinical and/or biochemical hyperandrogenism combined with oligo-/anovulation and polycystic ovarian morphology; phenotype B, denoted by hyperandrogenism and oligo-/anovulation; phenotype C, identified by hyperandrogenism and polycystic ovarian morphology; and phenotype D, characterized by oligo-/anovulation and polycystic ovarian morphology. The objective of this study was to explore the potential association between homocysteine and these four distinct PCOS phenotypes.

Methods: This study involved the inclusion of a dataset comprising 106 individuals diagnosed with PCOS and 60 healthy participants for comparison. Homocysteine measurements were conducted utilizing ELISA kits.

Results: Our findings indicated a significant increase in homocysteine levels within phenotypes A and C.

Conclusion: The outcomes of this study revealed that phenotypes A and C of PCOS are associated with increased levels of homocysteine in comparison to the non-PCOS group.

Keywords: PCOS; thyroid tests; PCOS phenotypes.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-46

Comparison of the toxicity of safflower extract and tartrazine in zebrafish model

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Abstract

Background and Aim: Safflower (*Carthamus tinctorius L.*) and Tartrazine (TTZ) are used as colorants in food products, medicines, and cosmetics. They are also used as a substitute for saffron due to the color similar to saffron, low cost, ease of access and stability. Tartrazine is a monoazoprazolone dye; recently researches on its potential teratogenic properties in pregnant women and the possibility of passing the dye from the placenta to the fetus were often conducted on mice and confirmed the creation of teratogenic effects in mice. zebrafish is an excellent model that be comparable to the first trimester of development of human embryos, so in this study, toxicity of tartrazine and safflower extract on zebrafish larvae has been investigated.

Methods: An azo dye, tartrazine, has been compared safflower extract, and their developmental toxicity on zebrafish (*Danio rerio*) from gastrulation stage (5.25 hours postfertilization [hpf]) until hatching and developmental trajectory was traced up to day 5. *Danio rerio* embryos in the laboratory (n = 20/concentration) exposed to graded dilutions of tartrazine and safflower extract (0, 0.0001, 0.001, 0.01, 0.1, 1, 5 and 10%). median lethal concentration (LC50), median effective concentration (EC50), teratogenic index (TI) for each two dyes were calculated at 96 hours after postfertilization, the scoring of lesions was done at 120 hours after fertilization.

Results: The results showed that exposure to 1% of each dye were completely embryo lethal. the exposure of the embryos from 0.0001% to 0.1% tartrazine and safflower extract can cause hatching problems and developmental abnormalities such as edema of the cardiac area and yolk sac, spinal defects including spinal curvature and tail deviation, malformation of facial areas, malformation of pectoral fins and body fins and caudal fins, also can cause non-formation or malformation of somites, but no morphological defects was seen in embryos exposed to control group (0%). An embryo exposed to 1% concentration of safflower extract was coagulated within 48 hours, while the rate of mortality was higher in tartrazine and coagulation occurred within 24 hours. Safflower extract delayed the growth of the embryos, so that after 72 hours, the fetus had the same growth as the 24-hour fetus in the control group. For tartrazine, the LC50 was 0.009% and the individual EC50 value for hatching was at 0.354% and the TI ratio was of 0.025, and the individual EC50 for edema of the cardiac and yolk sac was at 0.153% and the TI ratio was of 0.058. For safflower extract LC50 was 0.004% and the individual EC50 value of hatching was at 0.031% and the TI ratio was of 0.129, as well as the individual EC50 of cardiac and yolk sac edema was at 0.127% and the TI ratio was of 0.031.

Conclusion: This study showed that tartrazine is more toxic than safflower extract. Safflower cause developmental toxicity at a lower concentration than the tartrazine. Tartrazine and safflower are not teratogenic for zebrafish embryos up to a dose level of 0.1%.

Keywords: Safflower; Tartrazine; Zebrafish; Developmental toxicity.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-47

Astragalus adscendens extract shows antidiabetic effects through controlling oxidative stress, inflammation and apoptosis in streptozotocin- induced diabetic rats

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Abstract

Background and Aim: Introduce the context of your study and the gaps your project is filling. At the end, clearly state the aim/ objective of the study.

Methods: In order to induce diabetes, rats intraperitoneally received streptozotocin at 65 mg/kg. Sixty adult male wistar rats were allocated into six groups (10 rats per each) including the healthy control group, the diabetic group as well as the diabetic group treated with astragalus adscendens methanolic extract at 50, 100, and 200 mg/kg per day or glibenclamide (0.6 mg/kg/day) for 28 d. The effects of astragalus adscendens methanolic extract on the levels of glucose, insulin, alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, bilirubin, creatinine, urea, uric acid, total protein, albumin, triglyceride, cholesterol, α -amylase, oxidant/ antioxidant enzymes, and inflammatory cytokines were evaluated. Real time-PCR was also used for measuring the gene expression of caspase-3, Bcl2, and Bax.

Results: The levels of glucose, cholesterol, triglyceride, creatinine, urea, uric acid, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, bilirubin, and malondialdehyde considerably declined ($P < 0.001$) in diabetic rats after treatment with astragalus adscendens methanolic extract especially at a dose of 200 mg/kg. In addition, treatment with astragalus adscendens methanolic extract noticeably increased the level of insulin, total protein, and albumin as well as improved the activities of catalase, glutathione peroxidase, and superoxide dismutase, as well as the expression levels of TNF- α , IL-1 β , caspase-3, Bcl2 and Bax ($P < 0.001$) compared to the diabetic control group. The extract also inhibited α -amylase in a dosedependent manner with an IC50 value of 19.6 μ g/mL.

Conclusion: Astragalus adscendens methanolic extract shows potent antidiabetic, anti- inflammatory, anti- apoptotic, and antioxidant effects in diabetic rats. However, more studies are needed to verify. The underlying mechanism of the effect of this plant extracts and tests its efficacy in clinical trials.

Keywords: Herbal medicines; Astragalus adscendens; Diabetes; Antioxidant; Antidiabetes; Streptozotocin; Antiinflammation.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-48

Co- delivery of streptomycin and hydroxychloroquine by labeled solid lipid nanoparticles to treat brucellosis: an animal study

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Abstract

Background and Aim: Can brucellosis- related biochemical and immunological parameters be used as diagnostic and treatment indicators? The goal of this project was to look at biochemical parameters, trace elements, and inflammatory factors in the acute and chronic stages of brucellosis after treatment with streptomycin and hydroxychloroquine- loaded solid lipid nanoparticles (STR-HCQ-SLN).

Methods: The double emulsion method was used for the synthesis of nanoparticles. Serum levels of trace elements, vitamin D, CRP, and biochemical parameters were measured in rats involved in brucellosis. The therapeutic effect of STR-HCQ-SLN was compared with that of free drugs.

Results: In both healthy and infected rats, serum concentrations of copper, zinc, iron, and magnesium, potassium, and biochemical parameters of the liver were significantly different. By altering the serum levels of the aforementioned factors, treatment with STR-HCQ-SLN had a positive therapeutic effect on chronic brucellosis. Vitamin D levels declined (46.4%) and CRP levels rose (from 7.5 mg to less than 1 mg) throughout the acute and chronic stages of brucellosis.

Conclusion: This study showed that by comparing the biochemical parameters and the levels of trace elements in the serum of healthy and diseased mice in the acute and chronic stages of brucellosis, it is possible to get help from other routine methods for diagnosis.

Keywords: Brucellosis; Biochemical parameters; Trace elements; Solid lipid nanoparticles.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-49

Investigation of irisin hormone levels in patients with Major Depressive Disorders

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Abstract

Background and Aim: Major Depressive Disorder is a mental illness characterized by feeling of sadness. According to statistics, between 2-7% of depressed adults die by suicide, and over 60% of individuals who die by suicide have MDD. Some studies have been shown that irisin may be correlated with major depressive disorder. Irisin is a myokine that is secreted from muscles as a result of exercise and stimulates the expression of the UCP1 gene, which converts white fat tissue to brown fat. The aim of study was to measure serum levels of irisin in patient with MDD and calculates its correlations with biochemical factors.

Methods: In this study, a total of 52 patient samples and 50 control samples were obtained. The samples were immediately transferred from Vasei hospital to the Molecular Cell Research Laboratory at Sabzevar University of Medical Sciences after collection. After serum separation, they were stored at -20 degrees until testing. Demographic information such as age, gender, body mass index (BMI), blood glucose level, triglyceride level, HDL and LDL levels were extracted from the hospital archive. The irisin test was performed using the ELISA method at the Molecular Cell Research Laboratory at Sabzevar University of Medical Sciences.

Results: The average irisin concentration in patient individuals was 42.15ng/ml, and in the control population it was 45.71ng/ml. Further examinations revealed that irisin hormone has a positive correlation with BMI and triglycerides, and a negative correlation with HDL and LDL. It did not show a significant correlation with the other variables.

Conclusion: This study showed a significant decrease in average irisin concentration in patients with major depressive disorder compared to healthy individuals (controls). Mean level of irisin showed positive correlation with BMI and triglycerides, and negative correlation with HDL and LDL.

Keywords: Irisin; Major Depressive Disorder (MDD); Depression; bipolar.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-50

The effect of A779 on renal clearance and urine output in 2K1C hypertensive rats

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Abstract

Background and Aim: Creatinine clearance (CrCl) and urinary flow (UF), two determinants in the management of renal function following renal ischemia reperfusion (IR) injury, are affected by hypertension, such that a reduction in estimated creatinine clearance predicts adverse outcome in hypertension. Two kidneys- one clip (2K1C) hypertension and IR injury alter the expression of enzymes (ACE2, ACE, and renin) and receptors (MasR, AT1R, and AT2R) of the renal renin angiotensin system (RAS). Therefore, it is important to use RAS inhibitors to preserve renal function following IR.

Methods: Renal IR with and without ischemic preconditioning (IPC), as a reno- protective technique versus long - term IR injury, was implemented in 2K1C hypertensive rats, and the effect of angiotensin 1-7 receptor antagonist (A779) on RC and UF was determined. A U-shaped silver clip (0.2-mm inner diameter) was placed around the renal artery of rats to induce 2K1C. Four weeks later, the animals were anesthetized with urethane (1.7 g/kg; Merck, Germany). After intubation and vessel catheterization, the blood pressure and renal perfusion pressure (RPP) were monitored. The bladder was catheterized to collect urine. Animals with systolic blood pressure > 150 mmHg were considered as hypertensive in three groups of experiment; sham, IR and IPC+IR. No partial ischemia was induced in sham group. Prolonged partial ischemia was induced by setting of RPP in 23 ± 2 mmHg via tightening the abdominal aortic clamp for 45 min. The animals in IPC + IR group underwent two cycles, each for five minutes, of partial ischemia followed by 10 min reperfusion before prolonged partial ischemia for 45 min. At the beginning of reperfusion RPP was recorded as the base, and each group was subjected to receive vehicle or A779. Thirty minutes later, the renal function parameters including CrCl and UF were measured.

Results: Although, no significant differences were observed in RPP between the groups, CrCl and UF significantly increased by A779 in IR group. However, A779 did not alter CrCl and UF in IPC + IR group when compared with vehicle treated rats. The major finding of this study revealed the therapeutic role of A779 in increasing the CrCl and UF after IR in 2K1C hypertensive rats.

Conclusion: Angiotensin 1-7 may be responsible for promoting renal blood flow; however, in spontaneously hypertensive rats. In the current study, IPC abolished the effect of A779 on UF and CrCl which needs more studies.

Keywords: Creatinine clearance; urinary flow; A779; ischemia reperfusion injury; Two kidney-one clip.





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January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-51

Total antioxidant capacity in human seminal plasma of infertile men and their relationship with sperm parameters

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Abstract

Background and Aim: Oxidative stress plays a key role in the pathogenesis of male infertility. But, the adverse effects of oxidative biomarkers on sperm quality remain unclear. This study aimed to investigate the levels of TAC (total antioxidant capacity) in seminal plasma and their relationship with sperm parameters.

Methods: The study subjects included 77 individuals with the age ranging between 24 to 35 years old. The subjects were classified into two groups; control group including 40 fertile and 37 infertile patients. The semen samples were collected into sterile container and Routine semen analysis was performed within 1 hour. After semen analysis, samples were centrifuged at 4,000 g for 10 minutes and stored at 20°C for measurement of the TAC biomarker. This biomarker was evaluated using the ferric reducing ability of plasma (FRAP) method.

Results: In this study, the mean TAC in the seminal plasma was significantly lower for infertile men than for men in the control group ($1,697.11 \pm 708.18$ and $2,015.50 \pm 670.95 \mu\text{M/L}$, $p = 0.046$) in addition we found a Positive correlation between TAC and sperm count ($p = 0.043$, $r = 0.232$) and between TAC and normal sperm morphology ($p = 0.025$, $r = 0.255$).

Conclusion: In conclusion, decreased levels of TAC cause infertility in men and TAC levels is lower in the seminal plasma of idiopathic infertile men than in that of healthy fertile men.

Keywords: 8-Hydroxydeoxyguanosine; Infertile men; Nitric oxide; Oxidative stress; Semen; Total antioxidant capacity.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
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January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-52

Evaluation of tissue oxidative stress, antioxidant parameters and trace element levels in breast cancer patients

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Abstract

Background and Aim: Breast cancer is a multifactorial disease, and oxidative stress plays a significant role among many factors involved in its initiation, progression, and invasion. The concentration and activity of enzymatic antioxidants are proportional to the concentration of trace elements, and the concentration of trace elements is often deficient in malignancies. Therefore, in the present study, the tissue levels of oxidative stress, antioxidant status, and zinc (Zn) and copper (Cu) levels in breast cancer patients were investigated.

Methods: This case-control study was performed at Khatam Al-Anbia Hospital, Tehran, Iran, from June 2021 to January 2022. Tissue samples were collected from 40 breast cancer patients and 40 tumor margin tissues as controls. The levels of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), total antioxidant capacity (TAC), total oxidant status (TOS), oxidative stress index (OSI), malondialdehyde (MDA), zinc, and copper were measured.

Results: The concentrations of MDA, TOS, and OSI in the tumor tissue were significantly higher than those in the tumor margin, but the activity levels of TAC, CAT, SOD, and GPX in tumor tissue decreased significantly. The concentrations of zinc and copper in the tumor tissue of patients with breast cancer were higher than those in the tissue surrounding the tumor ($p < 0.05$).

Conclusion: Considering the dual role of oxidative stress in cancer, which can cause survival and adaptation as well as death of cancer cells, and with more information, it can be used to manage the treatment and destruction of cancer cells.

Keywords: Breast cancer; Oxidative stress; Antioxidant markers; Zinc; Copper.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-53

Comparison of vitamin D serum level in women with ectopic pregnancy and women with natural pregnancy referring to Shahid Rahimi Hospital in Khorramabad city in 1401

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Abstract

Background and Aim: Ectopic pregnancy is a common complication and one of the causes of death of women during pregnancy. Considering the increase in the prevalence of ectopic pregnancy in recent years and the increase in risk factors related to it, the present study was designed and conducted to compare the serum level of vitamin D in women with ectopic pregnancy and women with natural pregnancy admitted to Shahid Rahimi Hospital in Khorramabad in 2022.

Methods: This case- control study was conducted on 40 pregnant women with ectopic pregnancy (case group) and 120 pregnant women with natural pregnancy. The two groups were matched in terms of age and body mass index. The data collection tool was a researcher- made checklist including study groups (case and control groups), gestational age and educational level, as well as the obstetric characteristics of the patients (number of pregnancies, number of deliveries, wanted and unwanted desire for pregnancy, and serum level of vitamin D). Finally, after the data was collected, it was entered into SPSS version 25 and analyzed using statistical methods.

Results: In this study, the most common site of ectopic pregnancy in the women with ectopic pregnancy was tubal (42.5%). The serum level of vitamin D was 21.45 ± 8.79 mg/dL in the women with ectopic pregnancy and 58.93 ± 7.37 mg/dL in the women with normal pregnancy ($p < 0.05$). Since the relationship between the two groups of cases and controls was significant in terms of gestational age, the number of pregnancies and the number of deliveries, the effect of these variables was adjusted between the two groups, and finally the mean (standard error) of vitamin D levels in the women with ectopic pregnancy and the women with normal pregnancy was 22.94 ± 4.31 and 58.42 ± 1.59 mg/dL, respectively, and this difference was still statistically significant ($p < 0.05$).

Conclusion: In this study, the serum level of vitamin D in the women with ectopic pregnancy was lower than the level in the women with normal pregnancy. Therefore, measuring vitamin D in women of childbearing age seems necessary in order to prevent adverse pregnancy outcomes, including ectopic pregnancy, by correcting their nutritional status, teaching them about the consumption of resources rich in calcium and vitamin D, and supplementing them with vitamin D.

Keywords: Ectopic pregnancy; natural pregnancy; vitamin D.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-54

Effects of cigarette smoke and opium on the CD36 expression levels in human macrophage THP-1 cell line

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Abstract

Background and Aim: Studies demonstrated that opium consumption and cigarette smoking increase the risk of inflammation and oxidative stress and are associated with lung diseases such as chronic obstructive pulmonary disease (COPD). Cigarette smoking increased the expression of CD36, as an activator of pro-inflammatory pathways. The aim of the present study was to evaluate the alone and in combination effects of opium and cigarette smoke extract (CSE) on the expression levels of CD36 at both mRNA and protein levels on human macrophage cell line THP-1.

Methods: The THP-1 cell line was treated with CSE and opium, both alone and in combination forms during 24h incubation. The protein and mRNA levels of CD36 were evaluated by flow cytometry and quantitative reverse transcription-polymerase chain reaction (qRT-PCR) techniques, respectively.

Results: CSE, both alone and in combination with opium, significantly up-regulated CD36 gene expression compared to the control ($p < 0.001$). However, only significant difference was found in monocytes treated with CSE in comparison with the control, opium and combination groups at the protein level, ($p = 0.016$, $p = 0.031$ and, $p = 0.049$, respectively). No significant differences were observed in the CD36 gene expression and at the protein levels between opium-treated THP-1 cells and controls ($p = 0.470$ and $p = 0.965$, respectively).

Conclusion: CSE increased the expression of CD36 at the gene and protein levels in THP-1 cell lines. Therefore, CSE may play an important role in the pathogenesis and development of many inflammatory diseases including COPD, however, opium did not show significant effect on the expression of CD36.

Keywords: Opium; Cigarette Smoke; Inflammation; CD36.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative review

Code of Abstract: PBi-55

Where can calprotectin be used as a biomarker?

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Abstract

Background and Aim: Almost two decades have passed since the beginning of utilizing calprotectin in the diagnosis of gastrointestinal diseases (IBD) in Norway and the UK. Almost in the last decade, this protein has been noticed in other diseases. Currently, in addition to establishing calprotectin as a laboratory test in the diagnosis of IBD, measurement of this protein in other body fluids in the diagnosis of an expanding list of clinical conditions is on the agenda of researchers. In the present investigation, our focus has been on studies conducted to determine the role of calprotectin as a biomarker in body fluids.

Methods: The keywords, Calprotectin, biomarker, body fluids, etc. were reviewed in PubMed and Google Scholar databases from 2003 to 2023. Summing up the clinical results in review and Meta- analysis articles that highlighted the role of calprotectin in clinical decision-making, we concluded as follows.

Results: Although the information related to the role of calprotectin in digestive diseases and inflammatory rheumatological diseases has been evolving during the last decade, an interesting list of diseases related to calprotectin was obtained. Our findings show that the measurement of calprotectin in serum, pleural fluid, synovial fluid, lung secretions, semen, and urine can play an important role in diagnosing, determining the severity and follow-up, treatment, and prognosis of the disease. Also, the results of point- of- care testing (POCT) in several studies have been in good agreement with the results of the ELISA method.

Conclusion: Considering the key role of calprotectin in innate immunity, we can imagine two groups of clinical conditions related to calprotectin. The first group includes rheumatological and pulmonary diseases that have an older history and support extensive studies to confirm the use of this protein as a biomarker. The second group of diseases or possible roles indicates that, despite the promising findings, they have not yet been investigated in a sufficient number of patients. Finally, we believe that the use of calprotectin can help in diagnosis and decision-making in several important clinical situations, especially because the results using rapid test methods have been in acceptable agreement with the results of other immunological and instrumental methods.

Keywords: Calprotectin; Biomarker; Pleural; Synovial; Point-of-Care Testing.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic review/ Meta- analysis

Code of Abstract: PBi-56

The effect of antimicrobial peptides in the control of bladder tumors

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Abstract

In recent years, the efficacy of a number of cancer therapies has been called into doubt due to the emergence and progression of drug resistance as well as the undesirable side effects. Consequently, a great deal of interest is in a novel family of anticancer drugs known as cationic antimicrobial peptides (AMPs). These small innate peptides have a range of antibacterial properties because of their electrostatic interactions with the negatively charged bacterial membrane. This discrepancy presents an opportunity to exploit the way AMPs interact with negatively charged cell membranes in order to develop new anticancer therapies. Certain AMPs can also be classified as cationic anticancer peptides (ACPs) because of their ability to selectively infiltrate and lyse cancer cell membranes, in a manner similar to how they interact with bacterial membranes.

One of the important AMCs tested for bladder tumors is called pardaxin, derived from Aquatic species. Moreover, Pardaxin, often referred to as antimicrobial peptide (AMP) GE33, is a substance that has anticancer, antibacterial, and modulatory effects on host signaling. In line with this, the aim of this study reviewed that GE33 coupled with inactivated MBT-2 (murine bladder carcinoma cells) would have potential as a cancer vaccine in light of this discovery

In summary, many investigations using various cancer cell lines demonstrated pardaxin's anticancer potential. The cationic characteristics of pardaxin and its alpha-helix structure are part of this explanation. In addition, pardaxin's hemolytic effects need to be addressed to prevent unfavorable side effects in patients receiving the medication. Due to its positively charged alpha helix peptide, which may detect the negatively charged cancer cell membrane and cause cell death, these properties point to pardaxin as a possible anticancer medication.

Keywords: Antimicrobial peptide; bladder cancer; cancer vaccine.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-57

Anti - androgenic effects of Lupeol on experimentally induced PCOS in mice

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Abstract

Background and Aim: Polycystic ovarian syndrome (PCOS) is the leading endocrine - related disease in women at the reproductive age. There are genetic and epigenetic factors, which cause PCOS and among them excessive androgens exposure. In this study, the anti-androgenic effect of Lupeol on DHEA - induced PCOS in mice was highlighted.

Methods: Twenty-four female mice (22-days old) were divided randomly into four groups as: Control (C), PCOS (P), PCOS plus lupeol (L, 40 mg/kg, orally) and PCOS plus Metformin (M, 500 mg/kg, orally). Test groups (P, M and L) received DHEA (60 mg/kg/day, IP) and control group received 0.1 ml / mouse/ day sesame oil for twenty consecutive days. Following PCOS induction the treatment groups were treated for 28 consecutive days. Both blood sampling and tissue collection from animals were conducted a day after the last treatment. The serum level of free testosterone and DHEA hormones were measured by using the commercially available ELISA kits. Moreover, the expression of androgen receptors (AR) in the ovary of animals was quantified using qPCR technique.

Results: the hormonal analyses revealed that in PCOS positive animals, the serum concentrations of free testosterone and dehydroepiandrosterone elevated significantly ($p < 0.05$). At the same time, the LPL and MET administration for 28 days resulted in a significant reduction of both mentioned hormones level. Lupeol (2-fold) and MET (0.7-fold) lowered the PCOS-up-regulated androgen receptor expression in the ovary.

Conclusion: results of the current study suggest that LPL as a dietary triterpene is able to reduce the PCOS- induced hormonal changes and also to regulate the main related gene (AR) up- regulation.

Keywords: Polycystic ovarian syndrome; Androgen receptor; Hormonal changes; lupeol.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-58

Evaluation of long non-coding RNA-NEAT1 in breast tumor tissues of Iranian women

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Abstract

Background and Aim: Breast cancer is the most common global malignancy and the leading cause of cancer deaths. A growing number of studies have shown that long non-coding RNAs (lncRNAs) play an important role in the occurrence and development of tumors. This study aimed to investigate the expression and significance of lncRNA- NEAT1 (Nuclear enriched abundant transcript 1) in breast cancer.

Methods: Breast cancer samples were obtained from Iran National Tumor bank. Total RNA was extracted from each sample and then treated with DNase. Q-PCR was used to detect the mRNA expression of lncRNA- NEAT1 in breast cancer and adjacent normal tissues as respective controls.

Results: Real - time PCR data analysis also showed that the expression of NEAT1 gene in breast tumor tissue was increased by 2 times, which is statistically significant ($P < 0.0001$). The relationship between NEAT1 expression and various clinical-pathological parameters of breast tissue was investigated, and data analysis showed that there was no significant relationship between the increase in NEAT1 expression and clinicopathological parameters ($P > 0.05$).

Conclusion: Since the expression of lncRNA- NEAT1 gene is increased in tumor breast tissues compared to normal tissues, this gene can be considered a suitable biomarker for breast cancer.

Keywords: Breast Cancer; long non-coding RNA; Gene expression; NEAT1.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-59

Testosterone, β -estradiol and hepatocellular carcinoma: stimulation or inhibition? A comparative effect analysis on cell cycle, apoptosis and Wnt signaling of HepG2 cells

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Abstract

Background and Aim: Unlike breast and prostate cancers, which are specifically affected by estrogens or androgens, hepatocellular carcinoma has been reported to be influenced by both sex hormones. High androgen level is conventionally considered carcinogenic for the liver; however, the effect of estrogens in the development stages of liver cancer is still controversial. Given the incidental differences of hepatocellular carcinoma in males and females, to understand the sex hormonal- derived etiology, we investigated the effects of β -estradiol and testosterone on the cell cycle, apoptosis and molecular mechanisms involved in the occurrence of carcinoma in liver cells.

Methods: To determine the effective concentration of both hormones, an MTT assay was performed. The effects of β -estradiol and testosterone on cell proliferation and death were evaluated by specific staining and flow cytometry. In addition, gene expression levels of estimated factors involved in GPC3-Wnt survival signaling were analyzed using quantitative real-time polymerase chain reaction.

Results: Both hormones inhibited hepatic cell proliferation through arresting the cell cycle at S/G2 and increased the apoptosis rate in HepG2 cells. Both hormones dose-dependently decreased GPC3, Wnt, and DVL expression levels as activators of the Wnt- signaling pathway. In the case of Wnt- signaling inhibitors, the effects of both hormones on WIF were negligible, but they increased DKK levels in a dose - dependent manner. In each of the effects mentioned above, β -estradiol was notably more potent than testosterone.

Conclusion: In contrast to the primary hypothesis of the project, in which testosterone has been considered a stimulatory carcinogenic factor in HCC pathogenesis, testosterone inhibited the occurrence of HCC similar to β -estradiol. This inhibitory effect was still weaker than that of β -estradiol and required more elaborating studies.

Keywords: Hepatocellular carcinoma; Wnt/ β -catenin pathway; β -estradiol; Testosterone.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-60

The effect of hydroalcoholic seed extract of securigera securidaca on serum homocysteine levels and paraoxonase phenotypes in diabetic animal model treated by streptozotocin

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Abstract

Background and Aim: Reactive oxygen and nitrogen species (RONS) have been implicated in the pathophysiology of various disease states, including diabetes mellitus (DM). Enzymatic antioxidant such as paraoxonase and non - enzymatic antioxidants such as total thiol are capable of stabilizing, or deactivating RONS before they attack cellular components. On the other hand, natural antioxidants such as phenolic and flavonoid compounds protect body from oxidative damage by removing free radicals, and thereby indicating anti - carcinogenic, anti - atherogenic, anti - ulcer, anti - thrombotic, and anti-inflammatory properties. In this experimental study, total phenol and flavonoid contents of *Securigera securidaca* (*S. securidaca*) and antioxidant effects of the hydroalcoholic extract of *S. securidaca* seeds (HESS) were determined on diabetic rats.

Methods: Diabetes was induced in rats through an intraperitoneal injection of streptozotocin (STZ) (55 mg/kg.BW). Eight animal group were considered: two normal and diabetic control groups, three HESS treated groups given orally at doses of 100, 200 and 400 mg/kg.BW, glibenclamide treated group and two glibenclamide plus HESS treated groups (glibenclamide plus 200 and 400 mg/kg.BW, respectively) for 35 days. The PON1 phenotype was determined using double-substrate method. Cholesterol, triglyceride and HDL were assayed by colorimetric method. Serum biochemical profile, total antioxidant activity (FRAP), ROS, lipid peroxidation and were estimated.

Results: The value of total phenolics total flavonoids were 93.3 ± 1.5 mg (GAE)/g (D.W.) and 46 ± 1.7 mg (QE)/g (D.W.), respectively. Reduction in blood glucose levels in groups treated with HESS shows a dose dependent manner. Three phenotypes were determined: AA (low activity), AB (intermediate activity) and BB (high activity). FRAP, ROS and MDA levels were ameliorated by increase in HESS dose and synergistically in combination with glibenclamide.

Conclusion: *Securigera Securidaca* seed consumption as a supplement for the blood sugar - lowering drugs such as glibenclamide may ameliorate oxidative stress complications in diabetic cases.

Keywords: *Securigera securidaca*; paraoxonase; glibenclamide; diabetes mellitus.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-61

Amelioration of hepatic oxidative stress and inflammation by Silymarin in mouse model of colon cancer

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Abstract

Background and Aim: Colorectal cancer (CRC) as the third most common cancer worldwide is a leading cause of cancer mortality. The pro-carcinogen, 1-2 Dimethylhydrazine (DMH), is widely used to induce CRC in rodents. DMH is metabolized in the liver and can generate serious liver damage including liver necrosis, fat infiltration, and methylation of nucleobases through the production of highly reactive electrophiles such as carbonium ions and free alkyl radicals (hydroxyl ion) leading to oxidative damage, hepatotoxicity, and liver cancer. The flavonolignan, silymarin (SMN), is well - known for its anti - inflammatory, hepatoprotective, and anti - tumor effects. Therefore, we aimed to investigate the effects of SMN in mouse model of colon cancer.

Methods: Twenty - four BALB/c male mice (25-30 g) were divided into three groups with eight mice per group (control, DMH, SMN + DMH). CRC was induced through intraperitoneal administration of DMH at the dose of 20 mg/kg b.w. once a week for ten consecutive weeks. SMN (2500 ppm) was added to the diet of the SMN + DMH group daily for eight weeks post- CRC induction. At the end of the 18th week, liver tissues were dissected. One part was frozen at -70°C for enzymatic and biochemical examinations and the other part were fixed in formalin buffer for further histopathological observations after cardiac blood sample collection and euthanasia. The serum levels of Liver function enzymes (ALT and AST) as well as the hepatic levels of superoxide dismutase (SOD), Glutathione peroxidase (GPx), myeloperoxidase (MPO), and malodialdehyde (MDA) were examined.

Results: The results showed that DMH treatment caused a significant rise in the serum levels of ALT and AST and the hepatic levels of MPO and MDA relative to the control group ($P \leq 0.05$); while a dramatic decrease in the hepatic levels of SOD and GPx was observed ($P \leq 0.05$). The addition of SMN to the diet could significantly elevate the antioxidant activity of hepatic SOD and GPx. Further, it could remarkably decline the serum levels of ALT and AST alongside the hepatic MPO and MDA levels ($P \leq 0.05$).

Conclusion: SMN could effectively alleviate DMH - induced liver toxicity signs in mice. Thus, given the documented hepatoprotective effects of SMN, it can be considered a safe herbal remedy for the reduction of chemotherapy - induced adverse effects and hepatotoxicity in clinical practice.

Keywords: Colorectal cancer; Silymarin; 1, 2-Dimethylhydrazine; hepatotoxicity.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-62

Role of adenosine receptor and its agonist and antagonist effects in breast cancer

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Abstract

Background and Aim: Adenosine receptors include four receptors; A1, A2A, A2B, and A3 Adenosine Receptor, of the G- protein- coupled receptors family and are responsible for the action of adenosine in physiological and pathological conditions. Adenosine receptors with different affinity for adenosine exist throughout the body and have other functions in various tissues. The activity of adenosine receptors in cancer cells is associated with the proliferation of cancer cells, angiogenesis, metastasis, escape of the immune system, and interference with apoptosis.

Methods: Considering the different roles of adenosine receptors in cancer cells, we intend to investigate the importance of adenosine receptors in breast cancer. Therefore; we reviewed the articles published in PubMed and Google Scholar databases regarding the change in the expression level of adenosine receptors and the effects of agonists, and antagonists of these receptors on breast cancer cells.

Results: Review of studies showed that agonists and antagonists of different adenosine receptors have different effects on breast cancer cells.

Conclusion: Examining the outcomes show that adenosine receptors and their agonists and antagonists induce or inhibit necessary actions in breast cancer cells.

Keywords: Breast Cancer; A1 Adenosine Receptor; A2A Adenosine Receptor; A2B Adenosine Receptor; A3 Adenosine Receptor.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-63

Congestive heart failure (CHF) in ischemic stroke patients

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Abstract

Background and Aim: Ischemic stroke, marked by abrupt brain blood flow loss, stems from thrombotic or embolic blockage, overshadowing hemorrhagic stroke. The Etiology of influences stroke outcomes significantly. Congestive Heart Failure (CHF), a global cause of hospitalization and mortality, elevates stroke risk 2-3 times due to inadequate blood supply. CHF-related strokes correlate with poor outcomes and higher mortality. The laboratory finding, including lipid profile, kidney biomarkers and urea, creatinine, glucose metabolism markers, count blood cells result where the valuate in stroke patients with and without CHF.

Methods: The medical records of 1,745 patients hospitalized for stroke at Imam Khomeini Hospital in the West Azerbaijan province, city of Urmia, were examined from the year 2013 to 2023. We retrospectively analyzed the demographic data, laboratory findings and mortality reports of the ischemic stroke patients using SPSS statistical package version 23.0.

Results: 1484 patients have no CHF background (85%). There is no significant associate between gender and CHF in stroke patients (p -value < 0.959). A significant age difference between the two groups is evident (p -value < 0.000) in addition to them, a significant difference in the WBC (p -value < 0.002), lymphocyte (p -value < 0.000), neutrophil (p -value < 0.001) and HB (p -value < 0.000) can be observed. The variable values that demonstrate a significant difference between stroke patients with and without CHD.

Conclusion: WBC and CBC count could be a good biomarker for diagnosis of stroke patients in terms of CHF Prevalence.

Keywords: Ischemic stroke; CHF; Congestive Heart Failure.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-64

New horizons in treatment of knee osteoarthritis: a brief look up at emerging approaches

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Abstract

Osteoarthritis (OA), which was previously known as wear and tear, is a degenerative disease involving the entire joint, including the subchondral bone, ligaments, capsule, synovial membrane, and periarticular muscles (1, 2). The term osteoarthritis is derived from the Greek words osteo (bone), arthro (joint), and itis (inflammation) (3). OA could affect any synovial joint; however, it typically occurs in the knee, hip, hand, ankle, foot and spine. The knee is the most common joint affected by OA (4). According to statistics, approximately 50% of the world population over 65 years is affected by OA (2). During the development of KOA, articular cartilage and its surrounding tissues are locally damaged. In the etiology of this condition, genetics, environment, and epigenetics play a critical role, and their interaction results in a complex pathology (5, 6). The methods for diagnosing a disease vary at each stage of the illness. Advanced machine learning and deep - learning techniques offer reliable means for early diagnosis and prognosis of osteoarthritis (7). Unfortunately, the current therapy choices for OA patients are temporarily palliative rather than curative. However, the pain and physical limitations associated with OA often cause disabilities. The administration of the drugs in combination with a non - pharmacological regimen is the most effective for OA pain management. Nonetheless, there are concerns about the adverse effects of these drugs on the human body, including liver and renal toxicity, cardiovascular and gastrointestinal disorders (8, 9). Surgery could be the last option when the pharmaceutical and non-pharmacological regimens fail to treat symptoms in individuals with severe OA (10, 11). In order to combat the progress of OA at an early stage or trigger the regeneration of articular tissues, new therapies are needed greatly (12). Recently, special consideration has been paid to the role of the immune system, metabolic pathways and regenerative medicine in new treatment strategy. This review discusses about new therapeutic horizons.

Keywords: Osteoarthritis; Mesenchymal Stem Cell; Exosome; Regeneration Medicine; Scaffold; Immunotherapy; machine learning.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-65

Topical formulation of *Boswellia* nanoemulsion as a topical delivery system in psoriasis mouse model

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Abstract

Background and Aim: Psoriasis is defined as an organ-specific autoimmune inflammatory skin disease that is persistent and immune-mediated. Psoriasis is defined as an organ-specific autoimmune inflammatory skin disease that is persistent and immune-mediated. According to pharmacological and clinical research, the gum resin of *Boswellia serrata*, or *B. serrata*, includes six different kinds of *Boswellia* Acids (BAs), which are an active herbal ingredient that block 5-Lipoxygenase (5-LO) and are important in the treatment of inflammatory illnesses. There is limited systemic bioavailability of BAs due to their steroidal (lipophilic) composition, which prevents them from solubilizing in intestinal fluid. Nano emulsions are clear, optically isotropic, thermodynamically stable mixtures of water, surfactants, and oil that have a small droplet size and a high solubility capacity for lipophilic medications.

Methods: In the present study, imiquimod (IMQ) was applied topically to the right ear pinna surface of male BALB/c mice for ten days in order to cause psoriasis-like dermatitis. As a positive control, imiquimod was treated with *Boswellia* nanogel (2% w/v) or clobetasol (0.05% w/v). Every day, measurements were made of the body weight, ear length, thickness, degree of skin inflammation, psoriatic itch, and psoriasis area severity index (PASI) score. The 10th day of the trial involved checking each ear for inflammation. Fibrosis, proliferation, using histopathological (H & E and Masson's trichrome staining) and gene expression of IL23 AND IL17.

Results: The findings verified that the psoriasis caused by IMQ persisted for five days. On the other hand, when compared to the control group, nanogel dramatically decreased the thickness, length, psoriatic itch, and skin inflammation as well as body weight.

Conclusion: All things considered, topical *Boswellia* nano gel greatly improved the macro and microscopical aspects of psoriasis. However, further clinical investigations are required to translate the effects to clinics.

Keywords: Psoriasis; *Boswellia*; autoimmune; nanoemulsion.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-66

Design and computational evaluation of quercetin- based novel inhibitors for IL-6 via Janus kinase enzymes targeting in diabetes patients: a computer- aided drug design approach

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Abstract

Background and Aim: Interleukin-6 (IL-6), a prominent inflammatory cytokine, plays a crucial role in various pathological conditions, including autoimmune diseases, cancer and diabetes. Janus kinases (JAKs) are key signaling molecules involved in the IL-6 signaling pathway. Inhibition of IL-6 signaling through JAKs has emerged as a promising therapeutic strategy. This study aimed to design and evaluate novel inhibitors for IL-6 by targeting JAK enzymes using quercetin, a natural compound with potential anti-inflammatory properties.

Methods: Computer- aided drug design (CADD) techniques were employed to identify potential binding sites and interactions between quercetin and JAK enzymes. Molecular docking simulations were performed to predict the binding affinity and stability of the quercetin- JAK complexes. This research was conducted using in silico methods. Firstly, the quercetin molecule was searched on the PubChem website, and its SMILES format was obtained. Similar molecules to quercetin were extracted using the Swiss Similarity section on the ExpASY website. The SDF format of quercetin was obtained from the ChEMBL website. Additionally, the Jak2 protein with the code 7ree was downloaded from the PDB website, and molecular docking of various derivatives of quercetin was performed with the mentioned protein.

Results: The results revealed favorable binding interactions between quercetin and JAK enzymes, indicating potential inhibitory effects on IL-6 signaling. The binding affinity and stability of the quercetin-JAK complexes were further supported by molecular dynamics simulations, which demonstrated consistent and stable binding throughout the simulation time.

Among the quercetin analogs, molecules with the codes 1779471, 1935379, 1646111 and 4069227 were compared and assessed for their binding to the active amino acids present in the protein. Among these options, molecule 4069227 (C38H26O14) showed the highest binding affinity and was introduced as the best inhibitor for the IL-6-generating enzyme, IL6 or Jak2.

Conclusion: The molecular docking and dynamics simulations revealed that quercetin and its analogs could bind to the active site of JAK2 and interfere with the IL-6 signaling pathway. Among the quercetin analogs, molecule 4069227 (C38H26O14) was identified as the most potent inhibitor of JAK2, with the highest binding affinity and stability. This molecule could be a potential lead compound for the development of new drugs for the treatment of various diseases associated with IL-6 overexpression. Further experimental validation and optimization of this molecule are warranted to confirm its efficacy and safety.

Keyword: IL-6; JAK-2; CADD; Quercetin; Diabetes.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-67

The omentin and FTO gene polymorphisms in the Iranian individuals with newly diagnosed type 2 diabetes

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Abstract

Background and Aim: Two major factors that contribute to the development of type 2 diabetes (T2D) are visceral adipose tissue fat accumulation and insulin resistance (IR). Elevated body mass index (BMI), insulin resistance, and type 2 diabetes (T2D) are associated with several polymorphisms originated from adipose tissue. It is debatable if omentin rs2274907 (Val109Asp) and fat-mass and obesity-associated (FTO) rs9939609 gene polymorphisms are linked to T2D and overweight / obesity. This study sought to ascertain the relationship between insulin resistance and the FTO rs9939609 and omentin Val109Asp polymorphisms in patients with recently diagnosed T2D.

Methods: In the case-control research, 85 healthy matched controls, ranging in age from 20 to 80, were paired with 83 recently diagnosed T2D patients. The enzyme-linked immunosorbent test and the enzymatic approach were used to measure insulin levels and fasting blood glucose, respectively. To determine insulin resistance, the homeostasis model assessment (HOMA) index was employed. To evaluate genotyping, the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was employed.

Results: Significant differences ($P = 0.011$ and $P = 0.0001$) exist between the examined individuals and the omentin Val109Asp and FTO rs9939609 polymorphisms. The FTO rs9939609 (T/A) and omentin Val109Asp genetic polymorphisms are both substantially correlated with a higher HOMA index ($P = 0.046$ and $P = 0.030$, respectively). Nevertheless, the polymorphism of omentin Val109Asp was exclusively associated with overweight or obese people. Furthermore, a significant positive correlation was found between the omentin Val109Asp and FTO rs9939609 polymorphisms and a family history of diabetes ($P = 0.046$ and $P = 0.024$, respectively).

Conclusion: The genetic variants FTO rs9939609 and omentin V109D may alter insulin metabolism and play important roles in the development of T2D by causing insulin resistance. Accordingly, type 2 diabetes may be predicted with the aid of these polymorphic regions' examination.

Keywords: Type 2 diabetes; Insulin resistance; Omentin; Fat mass - and obesity associated (FTO); Gene polymorphism.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-68

Investigation of compounds similar to capecitabine for finding compounds with less side effects using CADD

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Abstract

Background and Aim: Colorectal cancer is one of the three most common cancers worldwide and the second leading cause of cancer-related mortality in the world. Capecitabine is one of the effective drugs in the treatment of colorectal cancer. This compound is an oral fluoropyrimidine, which plays a major role in the first-line treatment of metastatic colorectal cancer. However, capecitabine has many side effects such as hand-foot syndrome, stomatitis and diarrhea. The aim of this study was to investigate the toxicity of compounds similar to capecitabine and to find compounds with fewer side effects using bioinformatics methods and ADMET LAB.2 database.

Methods: In this study, we used bioinformatics methods to evaluate the side effects and toxicity of different compounds. First, the formula and structure of capecitabine were obtained from the pubchem website in sdf format. Then, using the expasy website, the swiss similarity section, by entering the structure of capecitabine and selecting the drug option and setting the search domain on DrugBank and FP2, 50 cases of compounds similar to capecitabine were obtained in .sdf and SMILES formats. Next, by entering the SMILES format in the ADMET LAB2 website, the Services section and the ADMET Evaluation option, the toxicity of the compounds of interest, such as H-HT, DILI, Ame's toxicity, etc., were evaluated on the human body. Among the compounds that had the least toxicity, molecular docking was performed with the protein MAPK-6 with PDBCODE: 6YLC using the GOLD softwar.

Results: The top 10 compounds with the least side effects were identified and their three-dimensional structure was obtained from the RCSB PDB website. The structure of them was obtained to measure the inhibitory effect of the selected compounds on the protein MAPK-6 using the GOLD software and molecular docking between the selected drug compounds and the protein. The drug compound cytidine 5'-diphosphoglycerol with db02484 had the highest inhibitory effect and the least side effects.

Conclusion: In this study, we used bioinformatics methods and ADMET LAB.2 database to find compounds similar to capecitabine, an oral fluoropyrimidine used in the treatment of colorectal cancer, with less side effects and toxicity. We performed molecular docking with the protein MAPK-6, and identified cytidine 5'-diphosphoglycerol as the most promising candidate. This compound showed the highest inhibitory effect on MAPK-6 and the lowest toxicity on the human body. Our results suggest that cytidine 5'-diphosphoglycerol could be a potential alternative to capecitabine for the treatment of colorectal cancer.

Keywords: Colorectal cancer; Capecitabine; ADMET LAB; Toxicity.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-69

Relationship between serum small dense LDL-C and PCSK9 levels in healthy subjects

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Abstract

Background and Aim: Serum small dense LDL_c- cholesterol (sdLDL-C) value is suggested to be a remarkable risk factor for atherosclerosis. Since sdLDL-C changes may be associated with PCSK9 function, this study aimed to investigate interconnectedness between sdLDL-C, circulating PCSK9, and some lipid parameters in serum and Buffy coat fraction of healthy subjects.

Methods: The study included 124 participants who were randomly selected. The lipid profile was measured using routine laboratory methods. To calculate the serum sdLDL-C level, a heparin-related precipitation technique was used. The cellular LDL-C / protein and cholesterol / protein values were measured by lysing the cells with a methanol/chloroform binary solvent. The circulating PCSK9 level was measured using the ELISA technique.

Results: The level of circulating PCSK9 was positively correlated with LDL-C ($r = 0.29$, $p = 0.04$), but not with sdLDL-C ($r = -0.08$, $p = 0.57$). However, there were no significant correlations found between the cellular LDL-C value and the serum LDL-C level ($r = -0.12$, $p = 0.39$). Additionally, a negative correlation was observed between the value of LDL-C / protein in the cell and the estimated value of de novo cholesterol / protein ($r = -0.5$, $p = 0.001$).

Conclusion: After conducting our analysis, we have found that the sdLDL-C level in the serum is not associated with the presence of PCSK9 in the bloodstream. We suggest investigating the cellular fate of sdLDL and lipid synthesis pathways in PCSK9- targeting studies.

Keywords: sdLDL-C; LDL-C; PCSK9.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-70

High prevalence of hypovitaminosis D3 among pregnant women in central Iran

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Abstract

Background and Aim: Hypovitaminosis D3 has become an increasingly prevalent problem worldwide. Pregnant women, neonates, and breastfed infants are highly susceptible to vitamin D3 (VitD3) deficiency because of its essential role as a micronutrient. Hypovitaminosis D3 is prevalent among pregnant women in Iran. This study aimed to evaluate the Vit-D3 status of a group of pregnant Iranian women and its association with newborn Vit-D3 levels, medical and clinical indices after delivery.

Methods: This prospective, cross-sectional study evaluated 210 pregnant women referred to an educational hospital for pregnancy termination. This study aimed to assess the Vit-D3 levels in maternal and fetal samples. Blood specimens were collected from pregnant mothers and umbilical cords after delivery to determine hypovitaminosis D3, a condition characterized by low levels of Vit-D3 in the body. Mean \pm standard deviation (SD) or the orders (non-parametric tests) of variables were compared, and correlation estimations were performed to elucidate any differences or associations between groups, with a confidence interval of at least 0.95.

Results: The mean \pm SD of mothers' age and gestational age were 29.65 ± 6.18 years and 35.59 ± 1.6 weeks, respectively. Neonatal Vit-D3 levels were associated with maternal age. Using a 30 ng/mL cutoff point for serum Vit-D3 levels, 83.5% of pregnant women and 84.7% of newborns had hypovitaminosis D3. The average Vit-D3 levels of mothers and newborns at delivery time were 23.5 ± 8.07 ng/mL and 20.76 ± 9.14 ng/mL, respectively. Newborn Vit-D3 levels were positively correlated with maternal Vit-D3 serum levels ($R = 0.744$; $P < 0.001$) and gestational age ($R = 0.161$; $P = 0.022$). In newborns, head circumference was inversely correlated with bilirubin level ($R = -0.302$; $P < 0.001$) but directly associated with weight ($R = 0.640$; $P < 0.001$).

Conclusion: Hypovitaminosis D3 remains a significant challenge for pregnant Iranian women. Maternal Vit-D3 levels provide for the newborn's needs, particularly in the late stages of pregnancy. Therefore, Vit-D3 supplementation and regular monitoring are essential for pregnant women and their newborns.

Keywords: Vitamin D3; Pregnancy; Newborn; Umbilical cord; Apgar score.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Review Article

Code of Abstract: PBi-71

Non- alcoholic fatty liver disease in children that causes cirrhosis

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Abstract

Background and Aim: Chronic liver diseases like Non-Alcoholic Fatty Liver Disease (NAFLD), Non-alcoholic steatohepatitis (NASH), Cirrhosis can reduce the quality of life in children and adolescents. NAFLD is caused by the accumulation of fat in the liver. The reason for the creation of NAFLD in children can be mentioned as obesity, metabolic syndrome, diabetes and hypothyroidism. NAFLD generally doesn't have any specific symptoms, if NAFLD isn't treated, it can lead to liver cirrhosis. Liver damage caused by cirrhosis can't be compensated. High blood pressure, esophageal bleeding, malnutrition and liver cancer are complications of cirrhosis in children. Does every kind of liver cirrhosis originate from NAFLD?

Methods: We searched the international sites "Google Scholar", "PubMed", "Web of Science", "Scopus", "ISI", "ISC" and "Elsevier" with keyword "Non-Alcoholic Fatty Liver Disease", "Liver Disease", "Fatty Liver", "Cirrhosis", "Children" from the years 2002 to 2019. We used Meta - Analysis and Systematic method to write this review article. And among the articles we found in the international database, we selected 14 articles. First, we selected 90 articles and then we selected 14 of the 90 articles as references with special criteria.

Results: According to research, obese children are more prone to NAFLD, and boys are more likely to be affected than girls. But alcoholic fatty liver is not the only cause of cirrhosis in children, and a wide range of diseases can damage the liver and eventually lead to liver cirrhosis. Alpha 1 antitrypsin deficiency, Alagille syndrome (genetic digestive disorder), viral hepatitis and autoimmune hepatitis, hemochromatosis (accumulation of iron in the body) and severe overweight can also cause liver cirrhosis. The treatment of liver cirrhosis depends on the extent of liver damage. In minor injuries, the complications of cirrhosis can be reduced by weight loss, proper diet and lifestyle changes. But if the disease has progressed, one of the ways to treatment, its liver transplantation, which costs a lot of money and is not a one hundred percent solution to treat this disease and liver transplantation in children, is very dangerous and can cause death.

Conclusion: Since there isn't definitive treatment for liver cirrhosis, early diagnosis of this disease helps to control it. By observing the correct nutritional methods, healthy lifestyle, prevent the occurrence of any diseases in children, especially liver diseases, which have very bad effects on the body. Therefore, by regularly calculating the body mass index, we should prevent children from gaining weight so that they do not get non - alcoholic fatty liver disease. In this case, they will not get cirrhosis, which is a serious disease.

Keywords: Non - Alcoholic Fatty Liver Disease; Liver Disease; Fatty Liver; Cirrhosis; Children.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Review Article

Code of Abstract: PBi-72

Effect of vitamin C supplements on the result of laboratory tests

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Abstract

One of the causes of pre-analytical errors is vitamin supplements, which should be investigated as an intervention in oxidation-reduction reactions and their influence on other analytes. Vitamin C is widely used as an antioxidant, antiatherogenic, anticancer, antihypertensive, antiviral, antihistamine, and immune system modulator in different societies. The kinetics and metabolism of vitamin C include three parts, absorption from the digestive system and renal reabsorption, distribution along with metabolism, and finally excretion.

According to the pH level, absorption will mainly occur in the distal ileum by the svct1 transporter. This vitamin can interfere with redox reactions, which will cause wrong results in the measurement of analytes. It can also be placed on the surfaces of the electrodes of the electrolyte measuring device and cause problems in the measurement of electrolytes after being oxidized. Due to its structure, this vitamin can participate in cross-reactions and cause a false increase in the measurement of some analytes such as creatinine. In this study, we review the influence of vitamin C on clinical laboratory test errors. Many in-vitro and in-vivo studies investigated the interaction of ascorbic acid with biochemical analytes whose measurement method was based on oxidation-reduction reactions. For the in-vitro study, the serum of healthy people was collected, and the analytes before and after adding various concentrations of ascorbic acid have been investigated. In the in-vivo study, they checked the interference effect after the consumption of vitamin C containing supplements for one week.

The interference of vitamin C with chemical analytes can cause both false increase and decrease in the measured values. For the in-vitro study, Na, K, Cr, and Ca increased by 43%, 58%, 26% and 103%, respectively. The presence of interference for total cholesterol and TG and ammonia and lactate were undetectable. Also, there was no specific effect for BUN and GLU, phosphorus, total protein, Albumin, AMY, ALP, SGOT, SGPT, Mg, and Fe were not observed. The in-vivo results revealed an inhibition in urate and bilirubin measurements. On the other hand, vitamin C showed no interference with the measurement of TG, GLU, and Chol.

Ingestion of vitamin C has shown a greater interference effect in measuring T-Bili compared to the in-vitro condition. Vitamin supplements, especially vitamin C, are widely consumed in different societies. Therefore, there is a high possibility that the referring people have taken vitamin supplements to perform clinical tests. Due to the important role of vitamin C in producing wrong laboratory results, it seems that this factor must be considered as a potential source of pre-analytical errors in clinical laboratories.

Keywords: vitamin C; laboratory interference; chemical analytes.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-73

Aptamer based colorimetric detection of toxic mercury ions

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Abstract

Background and Aim: Mercury is one of the highly toxic heavy metals. Inhaling mercury can cause permanent lung and brain damage. Inorganic mercury can also damage the kidneys and cause blood loss. In the current research, we have developed a nano- aptasensor for rapid detection of mercury ions.

Methods: A gold nanoparticles (GNPs) RNA hybrid sensor for colorimeter detection of mercury (II) ions (Hg^{2+}) in aqueous solution was made. First, citrated gold nanoparticles were complexed with a special mercury aptamer. The specificity and sensitivity of the rapid aptasensor for Hg (II) were evaluated using optical colorimetry and spectrophotometry methods. The components of the nanoaptamer kit and its reactions were analyzed using spectrophotometry, SEM, TEM, FTIR, DLS, Zeta potential and agar gel electrophoresis.

Results: Colorimetry was the basis of the aptamer performance method. In the presence of Hg (II), the functionalized gold nanoparticles aggregate due to the formation of thymine-Hg (II)- thymine complexes, which results in the color change of GNPs from red to dark purple, which is visible to the naked eye. The detection limit of the kit was achieved about 0.5 mM.

Conclusion: The developed aptasensor with the characteristics of simplicity, sensitivity and target monitoring with the naked eye is suitable for environmental mercury monitoring.

Keywords: Aptasensor; Rapid Test; Mercury ions; Gold- nanoparticle.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-74

Development of a colorimetric label- free aptasensor for rapid detection of uranyl ions

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Abstract

Background and Aim: In recent years, aptamers show great advantages in rapid metal detection and attract increasing attentions in the field of analyte analysis. The aim of this study is to develop a label-free colorimetric aptasensor for rapid and visual detection of dissolved uranium ions.

Methods: SELEX is a powerful process of systematic evolution of ligands by exponential enrichment in vitro, which is able to produce aptamers under specific conditions. After designing the uranyl aptamer, aptamer - gold nanoparticle complex was prepared under the laminar hood. The UAPT-AuNPs complex was placed in the laboratory in a dark environment for 1 hour to perform the incubation process. Then, the uranium solution with a specific concentration was slowly added to the initial complex. After 40 minutes of incubating the complex, CTAB was added with a certain concentration to the final complex and the changes were checked. In the lateral flow aptasensor technique, the complex was loaded onto Whatman No. 1 paper and the color changes were checked.

Results: After adding the uranium solution to the complex, in the presence of uranyl ion, the coating effect of aptamer on gold nanoparticles decreased so that they became free nanoparticles. Adding CTAB salt to the complex solution, gold nanoparticles aggregated and caused a color change from bright red to dark red in the nanoparticles. These color changes were clear and obvious with naked eye. Spectrophotometry with a limit of detection (OD) of 2 mM confirmed the visual results. The detection limit of the second aptasensor was 100 mM, which is one of its advantages in reducing the amount of sample required.

Conclusion: Aptasensors based on colorimetry are very efficient and sensitive, which use the unique properties of gold nanoparticles, such as: optical properties, stability, non- toxicity, etc., to design optical sensors for the detection of uranyl ions in contaminated samples.

Keywords: Aptamer; Uranyl Ions; Nanosensors; gold nanoparticle; SELEX.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBi-75

Prevalence of depression in type 2 diabetes mellitus and ameliorating factors of it: a systematic review

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Abstract

Background and Aim: There were more than half a billion cases of type 2 diabetes (T2D) worldwide. T2D patients were more likely to suffer from depression and those who had comorbid depression had a worse prognosis. There was much observational evidence put forward the association between psychiatric disorders and type 2 diabetes mellitus. However, possible potential relationships between these two diseases require further research. In this review, we study several related factors which are associated with depression and DM Also, we investigate ameliorating factors such as medication and lifestyle improvement.

Methods: In this study, we searched related keywords in PubMed, Scientific Information Database (SID; Iran), and Google Scholar from 2019 up to June 2023. The searched keywords were Diabetes, T2D, Depression, and neuropathy.

Results: We studied genetic variations and the effects of medication and lifestyle on mood disorders in type 2 diabetes. Patients with type 2 diabetes have a higher incidence of depressive symptoms- compared to healthy individuals. It has been indicating that patients with depressive symptoms have a higher incidence of type 2 diabetes.

Conclusion: Depression is often thought to be a consequence of diabetes, perhaps due to the burden of chronic illness. Research has also suggested that depression may be a risk factor for the development of diabetes. It may be Due to the biochemical changes during depression and also the reduction in healthcare behaviors in individuals that are affected by depression. Further studies should be performed to determine the exact relationship between depression and T2DM.

Keywords: Diabetes; T2D; Depression; neuropathy.





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Venue:
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Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic review/ Meta- analysis

Code of Abstract: PBi-76

Diagnostic application of circulatory levels of long non- coding RNAs in non- alcoholic fatty liver patients

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Abstract

Background and Aim: Non- alcoholic fatty liver disease (NAFLD) is a metabolic disease refers to accumulation of triglycerides in hepatocytes and its consequences. In addition to the main risk factors, there are certain conditions and factors that make this disease more favorable. There is a new emerging molecular biomarker called long non-coding RNAs (LnRNAs) that are thought to be involved in the regulation of body metabolism, physiological and pathological processes related to non-alcoholic fatty liver disease. Therefore, in this study, we want to introduce the possible LnRNAs that has diagnostic value or can be used as a therapeutic target for non-alcoholic fatty liver disease.

Methods: The retrieved studies were searched through available databases including PubMed (MEDLINE), Google Scholar, and Scopus. The search was performed using the non- alcoholic fatty liver, non- coding RNAs, diagnostic and therapeutic values.

Results: It has been shown that some long non- coding RNAs including MALAT1, NEAT1, HULC and HOTAIR are increased in blood circulation of patient with non- alcoholic fatty liver disease. In contrast, other LnRNAs including MEG3 and FLRL2 were found whose expression is shown to decrease in fatty liver patients. Among the LnRNAs associated with non-alcoholic fatty liver disease, only HULC has been sufficiently studied and strong evidence for its mechanism of action and diagnostic value has been provided. HULC (highly up- regulated in liver cancer) was originally identified as an oncogenic and the most overexpressed long non- coding RNA in hepatocellular carcinoma. It promotes abnormal lipid metabolism by regulating multiple pathways in NAFLD.

Conclusion: Different long non-coding RNAs were introduced to be correlates with pathogenesis of non-alcoholic fatty liver disease. Among which only HULC has diagnostic value as a less invasive and new molecular biomarker for NAFLD.

Keywords: Non- alcoholic fatty liver disease; long non- coding RNAs; HULC; Diagnostic.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-77

Neuroprotective effect of Crocin in differentiated PC12: AKT/GSK3 β pathway

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Abstract

Background and Aim: Alzheimer's disease (AD) is a progressive, unremitting, neurodegenerative disorder. Saffron (*Crocus sativus* L.) as a medicinal plant has been used in traditional medicine for many years. Crocin, an active carotenoid isolated from saffron, has been considered to be promising therapeutics for neurodegenerative diseases. Herein, we aimed to identify the potential protective effects of crocin on neuronal differentiated PC12 cells by focusing on the Nrf2 upstream pathway. The AKT/GSK-3 β signaling pathway, which plays a critical role in regulating Nrf2 activity and the phosphorylation of Tau protein, is very important in AD.

Methods: PC12 cells were differentiated using nerve growth factor (NGF). Then, the dPC12 cells were transfected by application of A β ₁₋₄₂ oligomers (A β O). We evaluated the dPC12 cell viability in the presence and absence of A β O, before and after Crocin treatment (pre- and post - treatment). Firstly, Crocin (0.1-1000 μ M) were added into the dPC12 cells medium and incubated for 24 h. Then, the incubation was continued for another 24 h after adding A β ₁₋₄₂ (pre - treatment). In the second experiment, dPC12 cells were incubated with A β ₁₋₄₂ for 24 h to establish an AD model. Then, it was incubated with Crocin for another 24 h (post - treatment). The translocation of Nrf2 to nuclei was investigated with immunocytochemical analysis in dPC12 cells. To investigate the effect of Crocin treatment on the activation of the AKT/GSK-3 β pathway, some important markers in the mentioned pathway were evaluated by Western blot.

Results: The results indicated that Crocin could significantly decrease the A β toxicity. Crocin significantly increased the expression of NQO1 and AKT phosphorylation. It inactivated GSK3 β by increasing its phosphorylation, and Nrf2 translocation into the nucleus. Crocin also suppressed GSK-3 β kinase in dPC12 cells and significantly reduced Tau phosphorylation (p-Thr231). All of these effects were time dependent.

Conclusion: Crocin showed a neuroprotective effect against A β ₁₋₄₂ toxicity and an AD-like condition in dPC12 cells in both pre - treatment and post - treatment manners. This function was through AKT / GSK3 β pathway.

Keywords: Neurodegenerative Disease; Crocin; Pre - treatment; Post - treatment; Signaling Pathway.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-78

Gallic acid improves liver cirrhosis by reducing oxidative stress and fibrogenesis in the liver of rats induced by bile duct ligation

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Abstract

Background and Aim: Disturbance in the production and excretion of bile acid causes cholestatic liver disease. Liver cirrhosis is a disease that occurs if cholestasis continues. This study evaluated the protective effect of Gallic acid (GA) on liver damage caused by biliary cirrhosis.

Methods: Rats were randomly divided into 4 groups, each with 8 subjects: 1) control, 2) BDL, 3) BDL + GA 20, and 4) BDL + GA 30. The rats were anesthetized 28 days after the BDL, followed by collecting their blood and excising their liver. Their serum was used to measure liver enzymes, and the liver was used for biochemical analysis, gene expression, and histopathological analysis.

Results: Serum levels of liver enzymes, total bilirubin, liver Malondialdehyde level (MDA), expression of inflammatory cytokines and caspase-3, necrosis of hepatocytes, bile duct proliferation, lymphocytic infiltration, and liver fibrosis showed an increase in the BDL group compared to the control group ($p < 0.05$). In addition, BDL decreased the activity of liver antioxidant enzymes and glutathione (GSH) levels compared to the control group ($p < 0.05$). The groups receiving GA indicated a decrease in liver enzymes, total bilirubin, MDA, the expression of inflammatory cytokines and caspase-3, and a reduction in liver tissue damage compared to the BDL group ($p < 0.05$). The level of GSH in the BDL + GA 20 group showed a significant increase compared to the BDL group ($p < 0.05$).

Conclusion: It was found that GA, with its anti-fibrotic and anti-inflammatory properties, reduces liver damage caused by biliary cirrhosis.

Keywords: Anti- fibrotic; Bile duct ligation; Gallic acid; Liver cirrhosis; Oxidative stress.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-79

Nigella sativa extract improved prolactin levels and obstetric criteria in a rat model of hypothyroidism

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Abstract

Background and Aim: It is reported that hypothyroidism affects female reproductive system functions. Beneficial effects of *Nigella sativa* (N. sativa) on hypothyroidism related a complication has been suggested. In this study, the effects of N. sativa on serum prolactin levels and obstetric criteria were investigated in a rat model of hypothyroidism.

Methods: Hypothyroidism was induced by propylthiouracil (PTU) 0.03% in drinking water. Female rats were divided into seven groups: (1) Control, (2) Hypothyroid, (3-5) Hypothyroid groups which received 100, 200, or 400 mg/kg of the extract, (6-7) Non hypothyroid groups which received 100 or 400 mg/kg of the extract. All treatments were done 20 days before mating and during pregnancy. The weight of progenies and their dams, number of progenies and serum level of thyroxin, and prolactin in rat dams were measured.

Results: A decreased level of thyroxin was observed in PTU treated rats which confirmed a hypothyroidism status. Administration of the extract before mating improved serum thyroxin level in hypothyroid rats. Administration of all doses of the extract before mating also improved body weight of the rats versus hypothyroid group ($P < 0.001$, $P < 0.05$, and $P < 0.001$). Both 100 and 400 mg/kg of the extract also improved the weight of the control rats ($P < 0.001$). The number of offspring was significantly decreased in hypothyroid group and in the hypothyroid groups which received the extract versus the control group. The weight of progenies in the control rats treated by 400 mg/kg of the extract was higher than the control group ($P < 0.001$). The weight of progenies in the hypothyroid groups treated by 200 and 400 mg/kg extract was improved compared to the hypothyroid group ($P < 0.001$ and $P < 0.05$, respectively). There was no significant difference in serum prolactin level between control, hypothyroid and the extract treated hypothyroid rats but 400 mg/kg of the extract improved serum prolactin level in the control rats.

Conclusion: These results demonstrated that feeding of the rats with N. sativa extract before mating improved prolactin levels and obstetric criteria in a rat model of hypothyroidism.

Keywords: Hypothyroidism; *Nigella sativa*; Gestation; Progeny; Propylthiouracil; Rat; Dams.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-80

The investigation of SOCS 1 and SOCS3 mRNA expression and promoter methylation in adipose tissue from women with obesity

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Abstract

Background and Aim: Based on recent studies conducted on animal models, changes in a suppressor of cytokine signaling (SOCS) family members (mainly SOCS1 and SOCS3) are associated with the pathogenesis of obesity-related metabolic disorders. In addition, epigenetic modification can play a vital role in SOCS family transcriptional regulation. In this study, we aimed to evaluate mRNA expression and SOCS1 and SOCS3 gene promoter methylation in subcutaneous adipose tissue (SAT) of obese women compared to normal - weight subjects. In addition, we intend to identify the possible association of SOCS1 and SOCS3 transcript levels with metabolic parameters in the context of obesity.

Methods: This study was conducted on obese women (24 people) [body mass index (BMI) ≥ 30 kg/m²] and normal-weight women (22 people) (BMI < 25 kg/m²). SOCS1 and SOCS3 transcript levels were assessed by real-time PCR in SAT from all participants. After DNA bisulfite treatment, methylation-specific PCR was used to evaluate the possible methylation status of 10 CpG sites in SOCS1 promoter and 13 CpG sites in SOCS3 in SAT from obese and normal-weight women.

Results: In this study, it was observed that unlike SOCS3, whose expression pattern was associated with an increase, SOCS1 expression level was lower in obese women compared to non-obese counterparts (P-value = 0.03 for SOCS1 transcript level and P-value = 0.011 for SOCS3 transcript level). Concerning promoter methylation analysis, it was found that the methylation of SOCS1 and SOCS3 was not significantly different between obese and normal-weight subjects (P-value = 0.45 and P-value = 0.89). Correlation analysis showed that SOCS1mRNA expression transcript level was inversely correlated with BMI, hs-CRP levels, HOMA-IR, and insulin levels. However, SOCS3 transcript level positively correlated with BMI, waist - to - height ratio, waist circumference, hip circumference, hs-CRP, HOMA-IR, insulin, fasting blood glucose, and total cholesterol. Interestingly, HOMA-IR predicted SOCS1 ($\beta = -0.448$, P-value = 0.003) and SOCS3 ($\beta = 0.465$, P-value = 0.002) transcript levels in the SAT of all participants.

Conclusion: Our research findings confirm a change in transcript levels of SOCS1 and SOCS3 between the two studied groups, but this finding was not repeated in promoter methylation levels in the subcutaneous fat tissues of participants. In addition, SOCS1 and SOCS3 mRNA expression in SAT was correlated with known obesity indices, insulin resistance, and hs-CRP, suggesting the role of SOCS1 and SOCS3 in the pathogenesis of obesity - related metabolic abnormalities. However, it seems that further studies are needed to establish this concept.

Keywords: Methylation; Obesity; SOCS1; SOCS3, Adipose tissue.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-81

Effects of rosmarinic acid on methotrexate- induced nephrotoxicity and hepatotoxicity in wistar rats

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Abstract

Background and Aim: Methotrexate (MTX), used in the treatment of cancerous patients, causes toxicity in the different organs of the body. In this study, rosmarinic acid (RA) is used as an antioxidant on nephrotoxicity and hepatotoxicity induced by MTX.

Methods: Rats (n = 32) were divided into four groups: Sham; MTX; 100 mg/kg RA + MTX; 200 mg/kg RA + MTX. The amount of MTX was 20 mg/kg. 24 hours after injection of the last dose of MTX, the blood samples and kidneys and liver of rats were studied. The aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), urea, serum creatinine was assessed. Tissue antioxidant enzymes and malondialdehyde (MDA) levels were measured. The liver and kidney tissues were histopathologically examined.

Results: MTX significantly increased the urea, creatinine, ALT, AST, ALP levels, and renal MDA and significantly decreased renal catalase (CAT), hepatic glutathione (GSH), and hepatic CAT activity. MTX induced necrosis, leukocyte infiltration, eosinophilic casts, glomerular damage in kidney tissue and necrosis, degeneration and cellular vacuolization in liver tissues. RA at 100 mg/kg caused a significant decrease in ALT and AST and at two doses significantly decreased urea, renal MDA, and liver MDA. RA at 200 mg/kg significantly increased the renal CAT and liver GSH. RA in two doses significantly decreased necrosis and Leukocyte infiltration. RA caused a significant decrease in degeneration and cellular vacuolization in liver tissues.

Conclusion: RA with its antioxidant and anti- inflammatory characteristics decreased the MTX induced nephrotoxicity and hepatotoxicity.

Keywords: Hepatotoxicity; Methotrexate; Nephrotoxicity; Rat; Rosmarinic acid.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-82

Modulating the wnt signaling pathway genes in wound healing: the potential of L-carnosine, zinc sulfate, and B-complex vitamins cocktail

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Abstract

Background and Aim: The process of wound healing is a dynamic event that starts with inflammation, proliferation, and migration of various types of fibroblast cells and aims to restore the integrity and functionality of damaged tissue. One crucial signaling pathway involved in wound healing is the Wnt signaling pathway which through specific proteins, influences the behavior of various cell types, such as fibroblasts. This study aims to investigate the effects of a cocktail consisting of L-carnosine, zinc sulfate, and B-complex vitamins on the modulation of the Wnt signaling pathway during wound healing.

Methods: For preparing the cocktail, the optimal dosages of L-carnosine, zinc sulfate, and B-complex were determined using the MTT assay on human dermal fibroblast (HDF) cells. Cocktail-mediated wound healing was measured by scratch assay on HDF cells. Next, the effects of the cocktail on the expression of *SFRP1*, *SFRP2*, *SFRP4*, *MMP7*, and *RSPO2* genes involved in the Wnt signaling pathway were measured during the wound closure phenomenon by real-time quantitative PCR (RT-qPCR).

Results: The scratch assay demonstrated the wound-healing effects of the prepared cocktail on HDF cells. Additionally, the RT-qPCR results showed that the cocktail can activate the Wnt signaling pathway by down-regulating the expression of *SFRP1*, *SFRP2*, *SFRP4*, and *MMP7* and up-regulating the expression of *RSPO2*.

Conclusion: Our data suggest that L-carnosine, zinc sulfate, and B-complex vitamins cocktail exhibits wound healing properties by increasing the fibroblast proliferation via activation of the Wnt pathway.

Keywords: Wnt Signaling; Wound Healing; L-Carnosine; Zinc Sulfate; B-Complex.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Clinical Trial

Code of Abstract: PBi-83

Anti-inflammatory effects of *Boswellia* supplementation in Parkinson's disease: a randomized, double-blind, placebo-controlled trial

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Abstract

Background and Aim: Parkinson's disease (PD) is the second most common motor and neurodegenerative disorder. Dopamine replacement has been the standard treatment for years. Research indicates that inflammatory mediators are significant in PD and could be potential biomarkers for early diagnosis and treatment monitoring. Boswellic acids (BAs), the main bioactive components of *Boswellia* sp. resin, are known for their anti-inflammatory effects. BAs and incensole are the primary bioactive compounds responsible for this effect. Unlike NSAIDs, BAs can cross the blood-brain barrier. Given their anti-inflammatory properties, a randomized, double-blind; placebo-controlled pilot trial was conducted to assess these compounds as supplementary therapy in PD.

Methods: The trial included 58 patients with mild-to-moderate PD, based on UPDRS scores. Participants were randomized to either the *Boswellia* group (n = 29) or the placebo group (n = 29). The treatment dose was 400 mg K-Vie™ capsules (the main ingredient of Strowell™), taken three times daily (1200 mg/day), with matching placebos for the control group. The primary outcome measures were the Unified Parkinson's Disease Rating Scale (UPDRS) and the Montreal Cognitive Assessment (MoCA). Secondary outcomes included plasma levels of various inflammatory cytokines and chemokines (TNF- α , IL-1 α , IL-1 β , IL-2, IL-4, IL-6, IL-8, IL-10, IL-12p70, IFN- γ and MCP-1/CCL2) and prostaglandin E2 (PGE2). The trial has been registered with IRCT with the unique identifier: IRCT20170315033086N4.

Results: Out of the 58 patients, 29 were assigned to the *Boswellia* group and 29 to the placebo group, with 14 dropouts. The age of participants ranged from 43 to 83 years in the *Boswellia* group and from 46 to 80 years in the placebo group. The gender distribution was 27% female and 73% male. After 1 month, patients receiving *Boswellia* showed a significant decrease in plasma levels of several key pro-inflammatory cytokines compared to the placebo group. These cytokines included IL-6 (p = 0.0010), IL-4 (p = 0.0469), IL-1 α (p < 0.0001), IL-1 β (p = 0.0004), TNF- α (p = 0.0445), IFN- γ (p = 0.0294), and PGE2 (p = 0.0006). Additionally, the UPDRS score remained stable in the *Boswellia* group, while it significantly increased in the placebo group. No serious adverse events were observed during the trial.

Conclusion: This study suggests that a reduction in specific systemic inflammatory biomarkers, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α), correlates with improvement in brain and motor function in patients with Parkinson's disease (PD). This finding suggests that decreasing inflammation, possibly by targeting these specific biomarkers, may represent a novel avenue to effectively treat PD. Further research is needed to confirm these results and investigate the precise mechanisms by which inflammation reduction leads to functional improvement in PD patients.

Keywords: Boswellic acids; Parkinson's disease; Inflammation; Cytokines; Motor Function; Biomarkers.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Review Article

Code of Abstract: PBi-84

Atorvastatin on treatment of nonalcoholic fatty liver disease patients

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Abstract

Background and Aim: Non- alcoholic fatty liver disease (NAFLD) is a condition in which excess fat builds up in the liver, often related to obesity and insulin resistance, which can lead to inflammation and scarring of the liver tissue. While efforts have been made to develop effective treatments for NAFLD, the need for pharmaceutical interventions remains unmet. Large clinical trials investigating the association between statin use and NAFLD are scarce, leading to contradictory results. Statins play a crucial role in cholesterol synthesis in the liver. Several studies have demonstrated that statins possess anti- inflammatory, anti- thrombotic and anti- fibrotic properties. These properties make statins potentially useful in preventing the progression of NAFLD from simple steatosis to more severe forms like non- alcoholic steatohepatitis (NASH) and fibrosis.

Methods: Queries of trials were conducted in Web of science, PubMed, Scopus, and Google scholar. Only literature in the English language and published from 2010 to 2023 were screened for inclusion.

Results: The results indicate that statin use is associated with a lower prevalence of NASH and fibrosis and may have a preventive effect on NAFLD. While atorvastatin is generally safe and well- tolerated in NAFLD patients, careful dosage selection and regular monitoring of liver enzymes are essential. Future research is needed to further explore the efficacy and mechanisms of action of atorvastatin in NAFLD management.

Conclusion: By integrating atorvastatin into the treatment plan for NAFLD patients, healthcare providers can address both dyslipidemia and liver disease, ultimately improving patient outcomes and reducing the risk of cardiovascular events and liver- related complications. Based on the findings of the four aforementioned studies, a general conclusion can be drawn that the administration of atorvastatin in lower dosages over an extended duration yields more favorable outcomes compared to higher dosages.

Keywords: Nonalcoholic fatty liver disease; Atorvastatin; lipids; Oxidative Stress; inflammation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Research Article

Code of Abstract: PBi-85

The effect of wet cupping (Al-hijamah) and limonene on oxidative stress and biochemical parameters in diabetic rats

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Abstract

Background and Aim: The rate of diabetes is increasing over time and current therapeutic strategies have several side effects. So alternative treatments appear to be essential. Wet cupping is one of the complementary approaches have been used in traditional medicine, but is still under research. Limonene is antioxidant and protein glycation inhibitor.

Methods: Intraperitoneal injection of alloxan and nicotinamide were used to induce type 2 diabetes in mice. After cupping, the levels of glucose, catalase, creatinine, cholesterol, triglyceride, nitric acid, malondialdehyde, urea, HDL, GPX, SGOT, SGPT and serum, kidney and liver proteins of mice were measured.

Results: However, combination of both limonene and wet cupping methods had a significant effect on blood glucose level, significant changes in serum NO, protein, creatinine, SGPT, SGOT, cholesterol, triglyceride MDA, urea, catalase, HDL, renal GSH, MDA, catalase, liver protein, and MDA level were not been observed.

Conclusion: Based on our study, the combination of wet cupping and limonene therapy indicate effective reduction of serum glucose level in diabetic rats.

Keywords: Wet Cupping; Limonene; Oxidative Stress; Diabetes.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-86

Securigera securidaca seed extract: a new approach to diabetes mellitus treatment

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Abstract

Background and Aim: The chronic metabolic condition known as diabetes mellitus is typified by enduring hyperglycemia, which can lead to microvascular and macrovascular complications, potentially reducing lifespan. Seeds of *Securigera securidaca* are known for their high concentration of bioactive substances like flavonoids and polyphenols. This research seeks to investigate the combined impact of a hydroalcoholic extract of *S. securidaca* (HESS) and glibenclamide (G), an antidiabetic medication from the sulfonylurea class, on serum homocysteine concentrations and the phenotype of paraoxonase 1 (PON1) in a rat model of streptozotocin-induced diabetes.

Methods: Diabetes was induced by injecting streptozotocin (STZ) through i.p. route. The seeds of *Securigera securidaca* were extracted using a maceration process with 70% ethanol. The activity and phenotypes of serum PON1 were assessed using the Eckerson method (modified version) and the dual-substrate method, respectively. Oxidant and antioxidant status of serum were evaluated. Total thiols, malondialdehyde (MDA), reactive oxygen species (ROS), ferric reducing ability of plasma (FRAP) levels, blood glucose, and lipid profile were measured using spectrophotometric techniques. Statistical evaluations were performed using SPSS, version 16. A P-value below 0.05 was considered statistically significant.

Results: The administration of HESS (200 and 400 mg/kg), either alone or in conjunction with G, yielded notable improvements in blood glucose levels and lipid profiles as compared to the diabetic control group. Remarkably, a dosage of 400 mg/kg of HESS, and also its combination with G, effectively bolstered the equilibrium between oxidants and antioxidants. This was demonstrated by an elevation in total thiols and FRAP, accompanied by a reduction in ROS and MDA levels. However, no significant decrease in homocysteine levels was observed. Additionally, treatment with HESS alone (at doses of 200 and 400 mg/kg) and in combination with G provoked a transition in PON1 activity and phenotypes from feeble (AA) to intermediate (AB) and strong (BB).

Conclusion: The present investigation underscores the antioxidative potential of the hydroalcoholic extract of *S. securidaca*, which may mitigate oxidative stress-related impairment in diabetes. This implies that HESS could serve as a beneficial adjunct to conventional antidiabetic medications. Nonetheless, these findings are preliminary, and additional preclinical and clinical examinations are indispensable to corroborate the safety and therapeutic efficacy of this extract in human subjects.

Keywords: *Securigera Securidaca*; HESS; Paraoxonase-1 (PON1) phenotypes; homocysteine; diabetes.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Case Report

Code of Abstract: PBI-87

Transient hyper CKemia

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Abstract

Background and Aim: Creatine phosphokinase (CPK) is an intracellular enzyme that catalyzes the reaction of creatine and adenosine triphosphate (ATP) to phosphocreatine and adenosine diphosphate (ADP). This enzyme has three isoforms that exist in skeletal muscle (MM), myocardium (MB) and brain (BB) and damage to each of these tissues causes an increase in CPK serum levels. More than 95% of total serum CPK in healthy people is approximately CPK-MM. Drugs such as captopril, colchicine, alcohol, lovastatin, propranolol, some anesthetics, anticoagulants, aspirin, clofibrate, dexamethasone and furosemide can increase CPK levels, as well as intense physical activities, surgeries, or intramuscular injections may lead to transiently increase CPK. The amount of CPK in the serum increases 6 hours after destruction and if the destruction is not stable, it reaches its peak within 18 hours and returns to the normal level after 2 to 3 days.

Methods: The patient's blood sample was taken while fasting and the following tests were performed using an autoanalyzer. FBS (97 mg/dl), ALP (283 U/L), ALT (34 U/L), AST (93 U/L), LDH (784 U/L), CPK (12390 U/L), CK-MB (188 U/L), Troponin (< 1.5 ng/l), Na (139 mEq/L), K (4.7 mEq/L)

Results: The patient is a 34-year-old man with muscle pain and a feeling of fatigue in the lower limb area and a history of bodybuilding exercise for 9 years without a history of taking drugs or energy-generating substances, and the result of CPK was reported as 12390 UI/L. A week later, by repeating the test with a new sample, the result was 199 (U/L). After consulting the patient by cardiologists, neurologists, internal medicine, endocrinology and rheumatology doctors and checking muscle resistance and metabolic tests, the results indicated that the corresponding tests were normal. One month after the initial tests, the patient returned to the laboratory after performing intense physical activity to repeat the test, and the CPK results were normal.

Conclusion: CPK increase may be due to non-neurological, muscular diseases such as endocrine diseases, metabolic disorders, muscle trauma, drugs, malignancy, macroCK, surgery, pregnancy, infectious diseases and chronic kidney diseases (3-5). According to the clinical description and the process of increase and decrease of enzyme activity in a short period, the probability of Transient Hyper CPK is raised in this person. In this particular case, the CPK level returned to normal after a week, while the half-life of this enzyme in the body is 2 to 3 days.

Keywords: Creatine phosphokinase; Transient; muscular diseases.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-88

Comparative effects of Crocin and Losartan on RAGE, TGF- beta, TNF- alpha genes and histopathological changes in the liver tissue in rats with diabetes

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Abstract

Background and Aim: Diabetes and liver disease are linked clinically, according to preclinical and epidemiological evidence. As a result, it is critical to seek out safe and effective agents with few or no side effects. Losartan (Los) is a renin- angiotensin- aldosterone system (RAAS) blocker that is commonly used in the treatment of hype pressure. According to growing research in the field of herbal medicines as natural compounds with fewer side effects, in this study with the animal model, we compared the effects of crocin and Los on RAGE, TNF-alpha, and TGF-beta gene, as well as histopathological changes in the liver tissue in rats with diabetes.

Methods: In 40 male rats (*Rattus norvegicus*), Streptozocin (50 mg/kg, IP) was used to cause diabetes. There were five groups: diabetic and healthy groups, diabetic rats given crocin (50 mg/kg), Los (25 mg/kg), and both (crocin + Los). After six weeks, the levels of serum FBG, urea, Creatinine, and TNF-alpha were assessed. The TGF-beta, TNF-alpha, and RAGE genes in liver tissue evaluated using qPCR. To analyze the data, IBM SPSS Statistics 16.0 was used.

Results: Crocin was found to be effective in lowering FBG in diabetes group. The serum levels of ALT and AST decreased in all treated groups, but this decrease was significant in the crocin + Los group ($p < 0.05$). The relative expression of RAGE, TNF-alpha, and TGF-beta genes was significantly higher in the diabetes group compared to the healthy group. The amount of these genes decreased in groups treated with crocin and Los compared to the diabetes group, respectively, and a decrease in the RAGE gene was significant in all treated groups. TNF-alpha gene expression was reduced in all groups, but it was greatest in the Los group. Crocin + Los group showed a significant decrease in TGF-beta gene ($p < 0.05$). Histopathology results showed that the diabetic group had more bile ducts and necrosis than the healthy control group, which had no tissue changes. Hepatocyte degeneration, bile duct proliferation, inflammatory changes, and hepatocyte necrosis were mild in the treated groups, but no hepatocyte necrosis was observed in the crocin + Los group.

Conclusion: During a two- month intervention with crocin and Los, the serum levels of biochemical factors like FBG and liver function (ALT, AST) decreased in the studied animal groups. In addition, the amount of RAGE, TGF-beta, and TNF-alpha genes in liver were affected by these two drugs. This study indicated, crocin can be effective in reducing FBG levels. The levels of FBG, AST, ALT in serum, and the relative expression of these genes were also improved by the concurrent administration of crocin + Los when compared to other groups.

Keywords: Diabetes; liver disease; RAGE; TNF-alpha; TGF-beta.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-89

Evaluation of antibacterial effect of nanoparticles synthesized with *Lycium ruthenicum murray*

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Abstract

Background and Aim: Due to the alarming spread of resistance to classical antimicrobial agents, innovative therapies to combat antibiotic-resistant pathogens such as plant-derived compounds and nanoparticles seem necessary. The aim of this study was to investigate the antimicrobial properties of silver nanoparticles synthesized using *Lycium ruthenicum* extract.

Methods: In this experimental study, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Enterococcus faecalis* were studied. Aqueous extract of *Lycium ruthenicum* was prepared and silver nanoparticles were prepared in combination with *L. ruthenicum* extract. The MIC of silver nanoparticles was investigated alone and in combination with the *L. ruthenicum* plant using the broth microdilution method.

Results: In this study, silver nanoparticles biosynthesized with *L. ruthenicum* showed strong inhibitory activity with MIC 1.25 µg/ml, especially against *E. coli*, *P. aeruginosa*, *K. pneumoniae* and *E. faecalis*. Also, the highest inhibitory activity of *L. ruthenicum* extract was for *K. pneumoniae* and *E. faecalis* with MIC 2.5 µg / ml. On the other hand, biosynthesized silver nanoparticles against *E. coli* with MIC 1.25 µg/ml showed the highest inhibitory activity. In general, silver nanoparticles synthesized with *L. ruthenicum* extract had significant antibacterial effects on the studied bacteria, in comparison with silver nanoparticles by chemical method as well as the plant *L. ruthenicum* alone.

Conclusion: The results of the present study showed that silver nanoparticles synthesized with *L. ruthenicum* extract have significant antibacterial effects, which can be used as a suitable treatment option for antibiotics due to the side effects of antibiotics after further studies on animal models. He treated some antimicrobial infections

Keywords: Silver nanoparticles; Antibacterial effects; *L. ruthenicum*; minimal inhibitory concentration.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-90

Chemical composition, antioxidant and antibacterial activity of essential oil and extracts of *Scorzonera Paradoxa* Fisch & C.A.Mey

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Abstract

Background and Aim: *Scorzonera Paradoxa* is belonging to Asteraceae family that traditionally used as a vegetable in the east of Iran. This plant is rich of compounds such as flavonoid, phenolic acid derivatives, triterpenoid, sesquiterpenoid, dihydroisocoumarin and other biologically active compounds. Considering the antibiotic resistance and also the limitations of the studies conducted on the compounds and effective substances of this plant, especially the species found in South Khorasan province, the purpose of this study was to investigate the chemical compounds, antioxidant effects, and antibacterial effect of the essential oil of the leaves of *S. Paradoxa*.

Methods: In this experimental study, *S. Paradoxa* was collected from the mountainous areas of Birjand. The essential oils of the aerial parts of *S. Paradoxa* were taken out by a hydro distillation technique for 3 h and recognized using gas chromatography- mass spectrometry. Also, the total antioxidant capacity of the plant was examined by FRAP and DPPH methods. The MIC level of essential oils and extracts was evaluated on *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Enterococcus faecalis*.

Results: The compounds identified in *S. Paradoxa* essential oil were hexadecanoic acid, tetradecanoic acid and pentadecanoic acid. The highest amount of total antioxidant capacity was related to ethanolic extract, followed by methanolic extract, aqueous extract, and the essential oil of *S. Paradoxa* plant. The MIC values of the essential oil of *S. Paradoxa* on Gram- positive bacteria were 156µg/ml and *K. pneumoniae*, *E. coli* and *P. aeruginosa* were 156, 312 and 2500 µg/ml, respectively. Aqueous extract of *S. Paradoxa* was 1250 µg/ml for all bacteria examined. MIC values of ethanolic and methanolic extracts on *P. aeruginosa* bacteria were 1250 µg/ml, *S. aureus* 625µg/ml and *E. faecalis* 78 µg/ml. The MIC of the ethanolic extract for *E. coli* and *K. pneumoniae* bacteria was 1250 and 312 µg/ml, respectively. The effect of different essential oils and extracts on *E. faecalis* bacteria was better than other bacteria.

Conclusion: The methanolic extract of *S. Paradoxa* has more antibacterial effects than other extracts on the target bacteria. Also, the ability to neutralize free radicals of the ethanolic extract was higher than the other investigated extracts.

Keywords: Antioxidant; Antibacterial; extract; essential oil; *Scorzonera Paradoxa*.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-91

An overview on nanoparticles and future perspectives for drug delivery

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Abstract

Nanoparticles (NPs) with range size 1 to 1000 nanometers (nm) categorized into various groups according to their properties, shapes, or sizes. NPs exhibit improved heightened reactivity, strength, surface area, sensitivity, and stability, owing to their diminutive size. This paper provides an overview of polymeric {Dendrimer and Polymer micelle} and lipid-based {Nanostructured Lipid Carrier (NLC), and Solid Lipid Nanoparticle (SLN)} NPs including their various types, properties, methods of synthesis, potential applications, and pros & cons.

Dendrimer: Artificial NPs (approximately 5-10 nm) which consist of polymer layers surrounding a central core; methods of synthesis: divergent for producing large quantities, convergent for relatively easy purification; important applications: for catalysis, as liquid crystals to perform electrochemical reactions, and as complex anti-cancer machines. Pros: ease of manipulation of particle size and properties surface of NPs, maximum therapeutic effectiveness with minimum side effects, controlled drug release, biodegradability, and different ways of administration.

Cones: changed physical properties, highly reactive in the cellular environment, and confined drug loading.

Polymer micelle: Spherical masses of amphiphilic macromolecules (nearly 100 nm). Different types of this NPs include a monomer in low concentrations in aqueous solution and core-shell micellar structure at the critical micellar concentration (CMC) during the micellization process; Techniques of synthesis: solvent evaporation (dry process), oil in water emulsion, dialysis, filtration, and solid dispersion; the significant applications: antidiabetic effect in *in vivo*, and delivery of more anticancer agents via intravenous injection.

Pros: as drug delivery systems mainly for hydrophobic drugs, and biocompatibility.

Cones: poor drug release, high sensitivity to structural changes, and mostly low persistence in blood.

NLC: Nano-sized (50-500 nm) colloidal drug delivery systems are composed of a lipid mixture; diverse methods of preparation: hot high - pressure homogenization, cold high - pressure homogenization, high speed / shear homogenization, microemulsion, solvent diffusion and evaporation, hot melt extrusion, and solvent injection; major applications as a gene transfer system, drug targeting, and cosmetics industry.

Pros: biocompatibility, biodegradability, simple preparation, better stability, and various ways of administration.

Cones: potential cytotoxicity, and the possibility of interference by surfactants.

SLN: usually spherical with 10-1000 nm consist of a lipid core matrix which is stabilized by surfactants (emulsifiers); different techniques of preparation: formation of insoluble drug - lipid conjugate mass, high pressure homogenization, and solvent injection; crucial applications as anticancer drugs delivery systems, cosmetics industry, gene therapy, biotechnology, and nanotechnology.

Pros: simple production, biocompatibility, biodegradability, controlled and modified drug release, improving the solubility and cellular absorption of drugs.

Cones: restricted drug loading, potential challenges in NPs size and shape control, potential limitations of the molecular imaging techniques, and potential toxicity of cationic lipids.

Keywords: Nanoparticles; Dendrimers; Polymer micelle; NLC; SLN.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-92

Evaluation of anti- diabetic effects of the extract of *Dracocephalum moldavica* and silver nanoparticles containing *D. moldavica* in adult male rats diabetic with streptozocin

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Abstract

Background and Aim: Diabetes is one of the most frequent endocrine disorders, and it is linked to the development of chronic and late renal, neurological, and visual issues, as well as cardiovascular failure. *D. moldavica* and other medicinal plants are high in natural antioxidants, and phenolic compounds, which are used in traditional medicine to regulate and cure a variety of ailments. The purpose of this study was to look into the anti-diabetic effects of extract and silver nanoparticles containing *D. moldavica* in diabetic rats.

Methods: 56 male Wistar rats were randomly assigned to 8 groups in this experimental study: 1) control group as a healthy group; 2) diabetic control, groups 3 and 4 received aqueous extract at doses of 100 and 200 mg/ml; groups 5 and 6 received doses of 10, 20 mg/ml of synthesized nanoparticles; group 7 received an oral dose of 500 µg/ml of metformin; and group 8 received 10 mg/ml chemical synthesized nanoparticles on a daily basis. Oral gavage was used as an intervention every day for four weeks. A dosage of 60 mg/kg of streptozocin was used to cause diabetes. In the serum of animals, the FBS (Fasting Blood Sugar), HbA1C, Urea, Cr (creatinine), and lipid profile were assessed.

Results: The average weight in different groups at the start of the study was not significantly different ($P = 0.892$), but the average weight at the end of the study in the diabetes control group, synthesized nanoparticle with a dose of 20, aqueous extract with a dose of 100, and chemical nanoparticle was significantly lower than the healthy control group ($P < 0.05$). The mean of creatinine serum level and lipid profile did not differ substantially across the tested groups ($P > 0.05$). Compared to the healthy control group, the metformin group had a substantially higher mean serum urea level ($P = 0.004$). Serum FBS levels were considerably greater in the chemical nanoparticle group when compared to the healthy control group, and HbA1C levels were significantly higher in the metformin and diabetes control group when compared to the healthy control group ($P < 0.05$).

Conclusion: The antidiabetic effects of nanoparticles created with plant extract outperformed those of plant extract alone and chemically manufactured nanoparticles, although the difference was not statistically significant.

Keywords: Diabetes; *Dracocephalum moldavica*; Nanoparticle; Rat.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-93

Lithium and zinc levels along with oxidative status in myocardial infarction: a case- control study

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Abstract

Background and Aim: Coronary artery disease (CAD) and myocardial infarction (MI) are the most prevalent diseases globally. While several risk factors for MI are well assessed, the influence of trace elements on MI has not been thoroughly studied. This study aimed to evaluate lithium (Li) and zinc (Zn) levels in MI patients and healthy control and assess their relationship with oxidative stress (OS) parameters, such as nitric oxide (NO) and total antioxidant capacity (TAC).

Methods: This case- control study was performed on 182 patients with MI and 83 healthy subjects at Shafa Hospital in Kerman, Iran. MI patients were divided into two groups based on the angiography results: those with coronary artery block above 50 % (CAB > 50%, n = 92) and those with coronary artery block below 50% (CAB < 50%, n = 90). A flame atomic absorption spectrometer was used to detect Li and Zn levels, and biochemical indices were measured by an autoanalyzer. Also, ferric reducing antioxidant power assay and the Griess method were used to measure the amounts of NO and TAC.

Results: TAC and Li were higher in the control group than in the patient groups. Furthermore, in the CAB < 50% group, TAC and Li levels were higher than in the CAB > 50% group. In the Zn levels evaluation, higher concentration was seen in the CAB > 50% group compared to the CAB < 50% group. Moreover, Zn and NO levels were higher in both CAB groups compared to controls. In continue Li levels had a positive association with TAC and EF as well as a negative association with NO levels and Zn levels had a positive association with NO and a negative association with TAC. Li and TAC decreased the OR of MI, whereas Zn, NO increased the OR of MI. Furthermore, AUC analysis indicated that Li had the highest AUC for the diagnosis of CAB > 50% (Li < 167 ng/mL), and Zn \geq 1810 μ g/mL increased disease severity.

Conclusion: Our investigation revealed that Li had a protective effect against CAD by decreasing OS and increasing EF%. However, Zn at concentrations higher than 1810 μ g/mL was found to be cytotoxic and increased the risk of MI through increased OS. Taken together, it could be concluded that Li supplementation may decrease the risk of CAD.

Keywords: Zinc; Lithium; Myocardial infarction; Nitric oxide; Oxidative stress.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-94

The synergistic effect of Biochanin B and Dihydroartemisinin on the AML cell lines

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Abstract

Background and Aim: Overexpression of anti-apoptotic members of the Bcl-2 family proteins such as Bcl-2 and Mcl-1 is associated with enhanced cell survival and drug resistance in tumor cells. In this study, the effect of the combination of Biochanin B and dihydroartemisinin on the growth and apoptosis of AML cells was investigated.

Methods: In this experimental study, the cell survival and cell proliferation were tested by MTT assay and trypan blue staining. Cell apoptosis was assessed by Hoechst 33342 staining and caspase-3 activity ELISA assay. The mRNA levels of Mcl-1, Bcl-2, Bax and cyclin D1 were measured by qRT-PCR.

Results: Here we showed that treatment with either Biochanin B or dihydroartemisinin alone, led to significant decrease in the cell growth and survival, and triggered apoptosis in U937 and KG-1 AML cell lines. Moreover, treatment with each of the compounds alone significantly decreased the expression levels of Mcl-1, Bcl-2 and cyclin D1 mRNA, while, the expression level of Bax mRNA was enhanced. Combination of two compounds showed a synergistic anti-cancer effect.

Conclusion: In summary, the anti-leukemic potential of Biochanin B and dihydroartemisinin is exerted through the effect on cell cycle progression and intrinsic pathway of apoptosis. Therefore, they can be considered as a potential anti-leukemic agent alone or along with existing chemotherapeutic drugs.

Keywords: AML; Apoptosis; Bcl-2; Dihydroartemisinin; Biochanin B; Mcl-1.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-95

ABT-199 in combination with Dihydroartemisinin makes Human U937 and KG-1 cancer cells more sensitive to apoptosis

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Abstract

Background and Aim: Change in the balance of Bcl-2 family proteins is one of the main reasons for resistance of tumor cells to ABT-199. In this study, the effect of dihydroartemisinin on cell growth, apoptosis and sensitivity of the AML (U937 and KG-1 cancer cells line) cells to ABT-199 was investigated.

Methods: Cell proliferation and survival were assessed by trypan blue staining and MTT assay, respectively. Cell apoptosis was measured by Hoechst 33342 staining and caspase-3 activity assay. The expression levels of Bcl-2, Mcl-1 and Bax mRNA were tested by qRT-PCR.

Results: Our data showed that combination therapy significantly reduced the IC50 value and synergistically decreased the AML cell survival and growth compared with dihydroartemisinin or ABT-199 alone. Treatment with each of ABT-199 or dihydroartemisinin alone clearly enhanced the Bax mRNA expression and inhibited the expression of Mcl-1 and Bcl-2 mRNA. Inhibition of Mcl-1 mRNA by dihydroartemisinin was associated with enhancement of apoptosis induced by ABT-199 in AML cells.

Conclusion: In conclusion, dihydroartemisinin not only triggers the intrinsic pathway of apoptosis, but also can increase the sensitivity of the AML cells to ABT-199 via suppression of Mcl-1 expression.

Keywords: ABT-199; AML; Apoptosis; Bcl-2; Dihydroartemisinin; Mcl-1.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-96

Inconsistency between the results of different immunochemical methods for vitamin D in pregnant women

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Abstract

Background and Aim: Immunochemical techniques are currently employed as the predominant method in clinical laboratories for the determination of 25 hydroxy vitamin D (25 (OH) D). Currently there is no standardized guideline about the preferred method and the underlying analytical interferences for measuring 25 (OH) D, especially in pregnant women. The aim of this study was to determine the frequency of inconsistency between commonly used immunochemical methods for 25 (OH) D testing in pregnant women.

Methods: Venous blood samples were acquired from 50 pregnant women who were in the third trimester of their pregnancy. Also, to evaluate the potential influence of pregnancy on results, a total of 21 samples were collected from non-pregnant volunteers. Serum sample were separated and the level of 25 (OH) D was measured using three immunochemistry kits including Roche's Elecsys Vitamin D total for Cobas's system, Biomerieux Vidas 25-OH vitamin D total for Vidas system, and ORGENTEC's 25-OH vitamin D3/D2 for Alegria's system.

Results: The mean concentration of serum 25 (OH) D in pregnant women was 26.8, 17.13, and 21.13 ng/mL when measure by ECLIA (Roche), ELFA (Biomerieux), and ELISA (Alegria), respectively. These results indicate a statistically significant difference between serum 25 (OH) D results from three immunochemistry kits (p -value < 0.0001). The obtained results from ECLIA and ELFA showed the strongest correlation (Spearman's ρ correlation = 0.895, p -value < 0.0001). More interestingly, our findings revealed no statistically significant difference between results of 25 (OH) D when measure by kits provided from three different vendors. Accordingly, the mean concentration of 25 (OH) D was 22.14, 17.73, and 18.37 ng/mL through ECLIA, ELFA, and ELISA methods, respectively (p -value > 0.05).

Conclusion: Our results clearly showed a significant inconsistency between vitamin D results in various immunochemistry techniques. Therefore, due to the importance of accurate results for better management of patients, particularly in the pregnant women, health policy makers should determine a comprehensive guideline for vitamin D testing in this group of people.

Keywords: Immunochemistry-based techniques; Inconsistency; Uncertainty; Vitamin D.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBi-97

A review of female dietary patterns and outcomes of in vitro fertilization (IVF)

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Abstract

Background and Aim: Infertility is defined as the inability to conceive after 12 months of unprotected sex. In vitro fertilization (IVF) is considered one of the most effective infertility treatments, and many of the successes of this treatment depend on repeating this fertilization several times.

Methods: This systematic review, to identify studies aimed at the role of female dietary patterns and outcomes in vitro fertilization (IVF), search in Science Direct, Google Scholar, and PubMed databases based on the keywords Diet, In vitro Fertilization, Infertility was done. After reviewing the summary of the articles and checking the title, the irrelevant articles were removed the full text of the articles was searched and the articles related to the topic were included in the study.

Results: According to studies, infertility affects up to 15% of couples. In vitro fertilization treatment has a low success rate, but some factors associated with infertility and poor treatment outcomes cannot be modified. Who evaluated the relationship between women's dietary patterns as a changeable factor and IVF results as a contradictory result?

Conclusion: Examining more accurate and uniform methods to evaluate the relationship between women's dietary patterns and IVF results is needed, and at the clinical level, the findings of this study do not recommend any single dietary pattern to improve pregnancy or live birth rates in women. It does not support IVF treatment.

Keywords: Diet; In vitro fertilization; Infertility.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBi-98

Investigation the relationship between sleep quality and pain perception in patients with rheumatoid arthritis

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Abstract

Background and Aim: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease affecting approximately 1% of the world's population. Patients with RA experience a lower quality of life compared to the general population due to joint destruction and associated limitations in social activities and physical functions. Moreover, RA is a multifactorial disease that influenced by various factors. Numerous studies have been indicated poor sleep quality in these patients, with potential repercussions on aspects such as pain perception. The aim of this study is to explore the relationship between sleep quality and pain perception in individuals with RA.

Methods: This cross-sectional study was conducted on RA patients attending Imam Hussein Hospital. A total of 200 individuals with RA, visiting Imam Hussein Hospital in Shahroud, were selected. After obtaining informed consent and coordinating with the treating physician, patients (or their companions) were requested to respond to relevant questions. Descriptive and inferential statistics (frequency distribution, chi-square, Pearson correlation) were employed for data analysis. The normality of data was assessed using the Kolmogorov-Smirnov test. Data analysis was performed using SPSS 26 software, considering a significance level of less than 0.05 for statistical tests.

Results: The study revealed a significant statistical correlation ($p < 0.001$) between sleep quality and the duration of disease, as well as pain perception and the duration of disease ($p < 0.02$). However, no significant correlations were observed between pain perception and age, pain perception and gender, as well as sleep quality and gender, sleep quality and age. The McGill Pain Questionnaire categorized individuals into scores ranging from 1 (normal) to 5 (very severe pain). In this context, 20.4% of participants reported normal pain perception, while the majority exhibited mild to severe pain perception. Overall, the K-Square test results demonstrated a significant statistical correlation ($p < 0.001$) between sleep quality and pain perception in RA patients.

Conclusion: This study revealed the impact of sleep quality on pain perception in RA patients, suggesting a potential avenue for improving their quality of life. Enhancing sleep quality may positively influence the overall well-being of individuals with RA disorder, as indicated by the study's results.

Keywords: Rheumatoid Arthritis; Sleep Quality; Pain Perception.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Review Articles

Code of Abstract: PBi-99

A comprehensive review of biomarkers in breast cancer: diagnostic, prognostic and predictive applications

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Abstract

Background and Aim: Breast cancer biomarkers have been extensively studied for early detection, diagnosis, prognosis, prediction of therapeutic response, and monitoring of disease progression and treatment outcomes. Genetic biomarkers, such as mutations and single nucleotide polymorphisms (SNPs), have shown potential for identifying high - risk individuals and screening populations at risk for breast cancer. Biomarkers have been used to assist with breast cancer diagnosis, prognosis, prediction of therapeutic response, and surveillance during and after treatment. Tumor size, histological type, cellular and nuclear characteristics, hormonal receptors, and axillary lymph node status are routinely used biomarkers, but additional markers are needed to improve prediction and guide treatment decisions. Proteomic studies have proposed potential biomarkers, but translation into clinically useful tests has been challenging. Biomarkers have also been measured for early detection, monitoring, prognostic assessment, and prediction of therapeutic response in patients with breast cancer.

Methods: Searches were conducted for scientific papers utilizing the keywords "breast cancer" and "biomarker" in a number of reliable databases, such as PubMed, Scopus, CAB Abstracts, Cochrane Library, Web of Science Core Collection, NCRI Cancer Research Database, Google Scholar, Embase, and CINAHL.

Results: Biomarker Effects on Breast Cancer Diagnosis: 1. Identify different types of breast cancer using biomarkers: Estrogen receptor (ER), The Progesterone Receptor (PR), Human Epidermal Growth Factor Receptor 2 (HER2/neu). 2. Predicting treatment responses and deciding on appropriate treatments: Information obtained from biomarkers may be useful in predicting responses to targeted treatments or other treatments, such as hormone therapies or chemotherapy treatments. 3. Early Detection and Importance: Biomarkers can play an important role in the early diagnosis of breast cancer because they can show specific indicators of changes in cancer cells even before clinical symptoms appear. 4. Biomarker values in pre - awareness and disease prediction: These biological tools can help determine the risk of disease recurrence, changes in cancer cells, and its progression. 5. Monitoring response to treatment: Biomarkers can help monitor changes in cancer cells, respond to treatments during treatment, and play a role in the pathway to recovery.

Conclusion: A key player in the field of breast cancer research, biomarkers offer a wealth of precise and detailed data that is essential for classifying the cancer, forecasting how well a treatment will work, and enhancing the standard of care. After a thorough study, these markers reveal which patients respond best to which treatments. For lowering side effects and raising the chance that therapy will be successful, this information is extremely helpful and crucial. The application of these biomarkers is comparable to a scientific breakthrough that modifies the path of medical decision-making while simultaneously improving therapeutic outcomes. Doctors are now able to make wiser and more effective treatment decisions because of the abundance of facilities and capabilities that these new technologies have made possible. People with breast cancer may feel more hopeful as a result of these innumerable improvements in their quality of life.

Keywords: Breast cancer; Biomarkers; Diagnostic; Prognostic.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-100

MMP2 and MMP9: the inflammatory gatekeepers

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Abstract

Inflammatory processes are considered the essential hallmark of a broad range of pathological conditions. In the 21st century, lifestyle changes have laid the foundation for the emergence of a wide variety of acute as well as chronic diseases based on inflammation and inflammatory-related pathways. Matrix metalloproteinases (MMPs) are a key class of molecules primarily recruited for tissue repair and remodeling, embryonic development, and morphogenesis in the body via matrix degradation. However, alterations in this pathway can result in the emergence of diseases. In this narrative review, we summarized the recent significant findings of the available valid literature regarding the relationship between metalloproteinase 2 and 9 and inflammatory pathways and related diseases extracted from scientific databases including Scopus, ScienceDirect, and Pubmed. Recently, matrix metalloproteinases 2 and 9 have emerged as important regulatory molecules in inflammation-related pathophysiological processes such as oxidative stress. MMP9 has been found to be upregulated across an extensive range of cancers, while interestingly MMP2 is mostly found to be downregulated. MMP2 and MMP9 are also reported to be involved in the pathogenesis of autoimmune diseases, diabetes, as well as atherosclerosis. Many herbal extracts such as linalool and food supplementations including omega-3- fatty acid have been found to improve oxidative stress parameters by directly influencing the function of MMP2 and MMP9. Studying and understanding the exact mechanisms by which MMP2 and MMP9 exert their function can aid in the process of developing brand-new and novel therapeutic approaches. In this narrative review, we summarize the role of MMP2 and MMP9 in inflammation.

Keywords: Metalloproteinase 2; Metalloproteinase 9; inflammation; oxidative stress.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-101

Comparison of miR-7 and miR-29 expression in patients with Alzheimer disease and control

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Abstract

Background and Aim: Alzheimer disease (AD) is one of the most common neurological diseases in terms of frequency. The most important cause of this disease is the eextracellular plaques contain β -amyloid ($A\beta$) and intracellular fibrillary tangles. AD is a multifactorial disease in which various genetic and environmental factors play a significant role in its progress. The first manifestations of Alzheimer's include a decrease in mental abilities in the absence of impaired performance in objective cognitive tests. Also, the primary phenotype of Alzheimer's is the gradual onset and progression of amnesic symptoms and signs. MicroRNAs (miRNAs) are small non-coding RNAs that are usually made of 20 to 25 nucleotides. They mediate post-transcriptional gene repression of target RNA transcripts. Since there are no reliable biomarkers for this disease. Therefore, in this study, we decided to compare the role of two microRNAs named miRNA-29 and miRNA7 in these patients.

Methods: In this study 60 patients with Alzheimer's diagnosed by a specialist doctor were selected and 60 healthy people who were free of any neurological and metabolic diseases were selected. About 5 cc of blood was taken from each person and 16000 xg for 5 minutes in They were centrifuged at 4°C. Then, 100 microliters of the supernatant were transferred to a new tube using the serum / plasma kit to isolate total RNA, including miRNAs. First, 5 microliters of total RNA were reverse transcribed using the first strand cDNA synthesis kit. Subsequently, 2 μ L of the product was used to detect the expression of miR29 and miR7 by quantitative PCR using the miRcute miRNA qPCR Detection kit. Quality control was performed by assessing the OD ration of 260/280 nm and total RNA was quantified using ND-1000 nanodrop spectrophotometer. Data were evaluated using SPSS 16. Also, statistical analysis was done using PRISM 5.0 (GraphPad Software Inc, USA). A significant difference was defined as $P < 0.05$.

Results: Based on this study, by comparing the expression level of miR-7 in two cases, the gene expression level of this miRNA in the AD group was higher than the control group ($P < 0.001$), but compared to the expression level of miR-29 in the serum Control group and patients with AD, the mean expression level of miR-29 in patients with AD was lower than the control group.

Conclusion: Therefor, according to this experiment and the information obtained from this study, it can be suggested that the expression of miR-29 enzyme decreases in AD and the expression of miR-7 increased in AD in comparison to control group. In the central nervous system, miR-29 regulates neuronal and dendritic maturation. Dysregulation of miR-29 also has implications in aging and various neurological disorders. MiR-7 expression contributes to normal development, physiology, and neurogenesis in the central nervous system. Second, AD patients show significant downregulation of miR-7 in different regions of brain. Downregulation of miR-7 in clinical samples is associated with tau accumulation.

Keywords: Alzheimer disease; miRNA; tau.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-102

A hybrid method to optimization problems of CE-SELEX and Cell- SELEX in developing aptamers against aspartate β -hydroxylase

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Abstract

Background and Aim: Aptamers, as a new category of molecular probes, are overthrowing antibodies in molecular diagnostics. However, there are serious problems with using aptamers for this application including poor or non-specific binding in vivo conditions. Systematic evolution of aptamers is achieved through various approaches including CE- SELEX and Cell- SELEX, each suffering its inevitable weaknesses.

Methods: In our approach, the selected oligomer pool from the last cycle of CE- SELEX was sequenced and then subjected to 3 additional rounds of Cell- SELEX which provides native ASPH (CEC Hybrid-SELEX). High-throughput sequencing was applied to achieve a comprehensive sight of the enriched pools. Further confirmatory investigations on oligomers with higher copy numbers were performed using flow cytometry.

Results: Three selected oligomers, AP-CEC 1, AP-CEC 2, and AP-CEC 3, showing Kd values of 43.09 nM, 34.85 nM, and 35.92 nM respectively, were achieved based on the affinity assessment of the ASPH expressing cells.

Conclusion: Our research suggested that CEC Hybrid- SELEX could help recognize which oligomers obtained from CE- SELEX are more probably capable of binding native ASPH in vivo.

Keywords: Aptamers; SELEX Aptamer Technique; Capillary Electrophoresis; High - Throughput Nucleotide Sequencing; Aspartate β -hydroxylase.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-103

Nanoparticles and its application in medicine

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Abstract

Nanoparticles (NPs) are materials up to under 100 nanometers (nm). Some of clinical applications in modern medicine are imaging, drug carriers, gene delivery, etc. NPs are utilized in various ranges of applications based on their feature, size, method synthesis, toxicity, and surface charge. Some remarkable NPs which are discussed in recent literature including: liposome, emulsion, metallic NPs, and polymericosome.

Liposomes: Spherical vesicles composed of two-layer membranes of phospholipids. Different types of liposomes based on the layer's structure are divided into unilamellar, oligolamellar, and etc., several methods for preparing, depending on the type of liposome, are reverse phase evaporation, depletion of mixed detergent-lipid micelles, solvent injection, and heating. They are used in the diagnostic, food, and cosmetic industries as applications. The crucial medical applications include chemotherapy materials, anti-cancer drugs, antimicrobials, gene therapy, and vaccines. Some of the advantages include biocompatibility, drug delivery precision, and reduced toxicity. Some of the disadvantages include immunogenicity concerns and difficulty in targeting.

Emulsions: They are composed of immiscible liquids, are dispersed as droplets sized 0.1-100 μm into another liquid. Different types of emulsion are: water-in-oil (W/O), (O/W), (W/O/W), and (O/W/O). The methods of preparation are dry gum, wet gum, in situ soap, and mechanical methods. They are widely used in diagnostic imaging, food, cosmetic, and drug industries. As a result of stability and permeability to skin, sustained drug release and diverse drug administration, are plenty of the significant medical applications. Some of the advantages are controlled release, bioavailability, versatility, improved solubility. But, sensitivity to environmental factors, immunogenicity concerns, cost, and limited shelf life are some of the disadvantages.

Metallic NPs: With the size range of 1-100nm. Various preparation methods: sol-gel, hydrosol/magnetic fluid method, vacuum deposition, and green synthesis. A wide range of applications: drug delivery, pharmaceutical areas, cancer therapy, antimicrobial, gene therapy, imaging, and tissue engineering. Some of the advantages: biocompatibility, antimicrobial, catalytic properties, and magnetic properties. Some limitations: cytotoxicity and health concerns, biological interaction, and limited stability

Polymersome: Self-assembled polymer shells of block copolymer amphiphiles. The aqueous core can be utilized for the encapsulation of therapeutic molecules such as drugs, enzymes, proteins. The most important synthesis method is classified into two groups; solvent switching and polymer rehydration technique. They are used in drug delivery, biomedical imaging, and diagnostics. Some of the pros include: biocompatibility, high stability, versatility in encapsulation, long blood circulation, and controlled release. However, they have some cons e.g., toxicity, size distribution, and limited biodegradability.

Keywords: Emulsion; Liposome; Polymerosome; Metallic Nano particle





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-104

Elaeagnus angustifolia L. Fruit extract modulates blood biochemical parameters in rats with CCl₄- induced injury

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Abstract

Background and Aim: The liver, a vital detoxifying organ, is prone to oxidative damage. The body's antioxidant system protects the liver from oxidative stress, but excess oxidants cause liver injury. Natural antioxidants may help maintain liver function. Many plants have antioxidant phytochemicals, such as polyphenols, terpenoids, and flavonoids. *Elaeagnus angustifolia* L. fruit is one of them and can prevent oxidative damage. This study aimed to examine the effects of *Elaeagnus angustifolia* L. extract on carbon tetrachloride-induced oxidative damage in rats.

Methods: This study randomly assigned 30 male Wistar rats to five groups: control, *Elaeagnus angustifolia* L. extract, CCl₄, *Elaeagnus angustifolia* L. extract (600 mg/kg) + CCl₄, and Silymarin (100 mg/kg) + CCl₄. The rats received oral doses of Silymarin or *Elaeagnus angustifolia* L. fruit extract for 14 days, followed by an intraperitoneal injection of CCl₄ (1.0 ml/kg) on day 14. Biochemical analyses were performed on the samples collected after 48 hours. The data are presented as mean ± standard deviation. One-way analysis of variance with SPSS 16 was used for data analysis. P < 0.05 was the criterion for statistical significance.

Results: Glucose and LDL levels increased, while albumin and HDL levels decreased, due to CCl₄. *Elaeagnus angustifolia* L. extract pretreatment significantly (P < 0.05) reversed the CCl₄ effects, similar to Silymarin.

Conclusion: This study found that *Elaeagnus angustifolia* L. extract pretreatment can protect the liver from CCl₄- induced damage in rats by preserving the serum biochemical parameters, such as glucose, albumin, LDL and HDL levels. Thus, this study suggested that *Elaeagnus angustifolia* L. extract may have a preventive effect on CCl₄- induced liver damage in rats.

Keywords: Carbon tetrachloride; Oxidative stress; *Elaeagnus angustifolia* L.; Rat.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-105

From gut- dysbiosis to Parkinson's disease: highlighting the role of beta-glucan in gut microbiome reconstitution and nerve cells survival improvement in Parkinson's disease

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Abstract

Background and Aim: Parkinson's disease (PD) is a common degenerative disorder of the nervous system, affecting an estimated 1 in 500 individuals. The emerging evidence indicates that gut microbiome dysbiosis can lead to α -synuclein misfolding and accumulation which is a major pathological sign of PD. Thus, reconstitution of gut microbiome, especially those of the bacteria associated with α -synuclein, can be considered as a potential treatment for Parkinson's disease. There is evidence that beta-glucan can play an important role in reconstitution of gut microbiome. In this regard, this study reviews the evidence that shows the impact of beta-glucan on Parkinson's disease improvement.

Methods: A comprehensive collection of information was achieved from medical databases including PubMed, Scopus, and Web of Science. In order to identify related articles, keywords related to this topic including gut microbiome dysbiosis, α -synuclein, Parkinson's disease and beta-glucan were investigated and combined using Boolean operators (e.g., AND, OR).

Results: In the past five years, extensive investigations have revealed notable alterations in the compositions of gut microbiome in individuals with Parkinson's disease (PD) through various comprehensive studies comparing cases and controls. The various substances generated by gut microbiome such as hydrogen sulfide, lipopolysaccharide and magnetite are believed to trigger the process of oligomerization and aggregation of the α -synuclein protein. An earlier study on beta-glucan from yeast showed reduction in α -synuclein expression on the brain substantia nigra in Parkinson's rat model. The results of another study indicate that nanoparticles coated with glucan can promote the survival of nerve cells in PD. In addition, it has been reported that glucan particles (GPs), composed of primarily β -(1,3)-D-glucans, induced a neuroprotective humoral immune response and regulatory iTreg (CD25 and FOXP3+) cells leading to an alleviation of α -synuclein triggered pathologic alteration in a murine synucleinopathy model.

Conclusion: The healing gut dysbiosis and beneficial microbiome reconstitution that leads to reduced α -synuclein misfolding and accumulation can be a viable therapeutic target for synucleinopathies. The evidence supports that beta-glucan is able to balance the gut microbiome and amelioration of pathological changes induced by α -synuclein, which is considered beneficial in patient with PD.

Keywords: Beta-glucan; Gut microbiome dysbiosis; α -Synuclein; Parkinson's disease.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-106

Quercetin and catechin protects mice of Lep ob/ob against alloxan-induced hepatotoxicity and diabetes

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Abstract

Background and Aim: Diabetes is a metabolic disorder that considered as a chronic disease after cancer and cardiovascular diseases, and about 25% of the world's population in developing and developed countries suffers from it. Catechin is one of the antioxidants found in medicinal plants that have the potential to treat diabetes. Considering the antioxidant effects of quercetin and catechin, it seems that these compounds may be effective in reducing oxidative stress and diabetes in the liver, therefore in this study; we investigated the combined effect of quercetin and catechin on alloxan-induced hepatotoxicity and diabetes in mice of Lep ob/ob.

Methods: Thirty mice were divided into five experimental groups: group 1 (normal control, NC), group 2 (diabetic control, DC), group 3; diabetic mice treated with 150mg/kg of catechin after one week from treated with alloxan, group 4; diabetic mice treated with 150mg/kg of quercetin after one weeks from treated with alloxan and group 5; diabetic mice treated with 150mg/kg of catechin and 150mg/kg of quercetin after one weeks from treated with alloxan.

Results: The results showed that alloxan containing quercetin and catechin decreased liver enzymes, FBS, Urea, Creatinine, cholesterol, triglyceride, LDL, and TBARS levels and increased HDL, total thiol, CAT, SOD, GPx levels, and expression of PARP protein in the liver compared to the alloxan group alone ($P < 0.001$). The histopathological examinations of the liver tissue confirmed the biochemical results.

Conclusion: The findings of this study demonstrated that quercetin and catechin could be considered as an effective candidate in the treatment of hepatotoxicity and diabetes in human.

Keywords: Quercetin; Catechin; Alloxan; Hepatotoxicity; Diabetes; Mice.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-107

Caffeic acid phentyl ester (CAPE) protects mice against nicotine- induced seizures and oxidative stress

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Abstract

Background and Aim: Epilepsy is a neurological disorder in which the activity of nerve cells in the brain is disrupted and leads to frequent, unpredictable seizures. Caffeic acid phentyl ester (CAPE) is a therapeutic polyphenol that is widely present in various vegetables, fruits, and coffee. Considering the antioxidant, anti-inflammatory and anticonvulsant effects of CAPE and the role of inflammation in causing seizures, in this study the effect of caffeic acid phentyl ester (CAPE) on nicotine- induced seizures and oxidative stress in mice was investigated.

Methods: Totally thirty mice into five groups (six mice in each group) were used for the experiment. The groups were as follows: group 1 (control), group 2(single dose of nicotine 5mg/kg), group3 and 4 (CAPE 4 and 8 mg/kg for 7 days + single dose of nicotine 5mg/kg), group 5(single dose of diazepam 1mg/kg + single dose of nicotine 5mg/kg).

Results: The results showed that CAPE decreased TBARS levels and increased total thiol, CAT, SOD, GPx levels, and expression of NF-kB protein in the brain compared to the nicotine group alone (P < 0.001). The histopathological examinations of the brain tissue confirmed this result.

Conclusion: Considering the antioxidant effects of CAPE, which have been proposed in various studies, it seems that CAPE can improve seizures by reducing inflammation and inhibiting oxidative stress.

Keywords: Caffeic acid phentyl ester; Nicotine; Seizures; Oxidative stress; Mice.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-108

Quercetin and camellia sinensis leaf extracts reduce liver steatosis in high- fat diet in Lep ob/ob mice

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Abstract

Background and Aim: Fatty liver disease is defined as excessive accumulation of fat in the liver tissue, which can disrupt the normal function of the liver tissue and even lead to liver failure or cirrhosis. There is no definitive drug treatment for this disease. Considering the antioxidant effects of quercetin and Camellia sinensis leaf extract, it seems that these compounds may be effective in reducing oxidative stress and steatosis in the liver, therefore in this study we investigated the combined effect of quercetin and Camellia sinensis leaf extract on the reduction of liver steatosis in the high- fat diet in mice.

Methods: NMRI mice were randomly divided into five groups with, 6 mice in each group: the control, HFD, HFD containing quercetin, HFD containing Camellia sinensis leaf extract, HFD containing quercetin and Camellia sinensis leaf extract.

Results: The results showed that HFD containing quercetin and Camellia sinensis leaf extract decreased liver enzymes, cholesterol, triglyceride, LDL, TP, Bil and TBARS levels and increased HDL, total thiol, CAT, SOD, GPx, levels in the liver compared to the HFD group alone ($P < 0.001$). The histopathological examinations of the liver tissue confirmed the biochemical results.

Conclusion: The findings of this study demonstrated that quercetin and Camellia sinensis leaf extract could be considered as an effective candidate in the treatment of fatty liver disease in human.

Keywords: Quercetin; Camellia sinensis leaf extract; High- fat diet; Liver steatosis; Mice.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-109

Ketotifen protects mice against gentamicin- induced oxidative stress and nephrotoxicity

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Abstract

Background and Aim: Gentamicin is one of the most important and effective aminoglycoside antibiotics in treatment-resistant infections, whose frequent use leads to severe kidney toxicity. Ketotifen fumarate is a first-generation antihistamine drug and a strong stabilizer of mast cells, which has antioxidant, anti-inflammatory and anti-apoptotic properties in various models of kidney damage. The aim of this study was to investigate the protective effect of ketotifen on gentamicin-induced nephrotoxicity in mice.

Methods: In this study, the ameliorative effects of KTF (2 and 3 mg/kg, ip) on GEN (100 mg/kg, ip) model of kidney damage were evaluated in male mice. NMRI mice were randomly divided into 6 groups with 6 mice in each group. KTF and GEN were given daily for 7 days. On the eighth day, the animals were anesthetized, and their kidney tissues were removed.

Results: The results indicated that KTF can ameliorate GEN-induced the significant increase in TBARS, TNF- α and NO and decrease in the amount of total thiol, catalase, glutathione peroxidase, superoxide dismutase. The histopathological results confirmed indicated findings.

Conclusion: The findings of this study demonstrated that ketotifen is reasonably effective in nephrotoxicity gentamicin-induced in mice.

Keywords: Ketotifen; Gentamicin; Nephrotoxicity; Mice.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-110

Ketotifen protects mice against paraquat- induced oxidative stress and nephrotoxicity

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Abstract

Background and Aim: Paraquat (PQ) is the most important herbicide in the agricultural industry, which is very toxic to humans and animals and leads to disruption of many organs. Ketotifen (KTF) fumarate is a first-generation antihistamine drug and a strong stabilizer of mast cells, which has antioxidant, anti-inflammatory and anti-apoptotic properties in various models of kidney damage. The aim of this study was to investigate the protective effect of ketotifen on oxidative stress and nephrotoxicity caused by PQ in mice.

Methods: In this study, the ameliorative effects of KTF (2 and 4 mg/kg, ip) on PQ (30 mg/kg, ip) model of kidney damage were evaluated in male mice. NMRI mice were randomly divided into 5 groups with 7 mice in each group. The groups were as follows: control, PQ (30 mg/kg, Single dose on the fourth day, ip), PQ pre-treated groups that received KTF 2 and 4 mg/kg respectively, KTF (4 mg/kg, daily for 7 days, ip). On the eighth day, the animals were anesthetized, and their kidney tissues were removed.

Results: The results indicated that KTF can ameliorate PQ-induced significant increase in TBARS, TNF- α , NO and decrease in the amount of total thiol, catalase, glutathione peroxidase, superoxide dismutase. The histopathological results confirmed indicated findings.

Conclusion: The findings of this study demonstrated that KTF is reasonably effective in nephrotoxicity PQ-induced in mice.

Keywords: Ketotifen; Paraquat; Nephrotoxicity; Oxidative stress; Mice.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-111

Syringic acid protects mice against sodium arsenite- induced hepatotoxicity and diabetes

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Abstract

Background and Aim: Many studies have associated exposure to high concentrations of inorganic arsenic with an increased risk of type 2 diabetes. One of the important mechanisms of arsenic diabetogenesis is the induction of oxidative stress. Syringic acid is a flavonoid compound of hydroxybenzoic acid derivatives that acts as a free radical inhibitor and has anti-inflammatory and anti-diabetic properties. Therefore, the aim of this study was to evaluate the effects of syringic acid on sodium arsenite- induced hepatotoxicity and diabetes in mice.

Methods: 30 male mice were divided into 5 groups of 6: control: Group 1 received distilled water every day for 1 month by gavage. Group 2 received 20 mg/kg syringic acid for 7 days by gavage. Group 3 was given 3 mg/kg NaAsO₂ every day for 1 month by dissolve in drinking water. Groups 4, and 5 were co-treated with 10, and 25 mg/kg syringic acid half an hour before NaAsO₂ (3 mg/kg), respectively, daily for 7 days by gavage. After 30 days of the study, the mice were fasted overnight and on day 31, fasting blood glucose was measured and glucose tolerance test was performed. On day 32, the mice were anesthetized and a blood sample was taken from the heart. Serum factors (ALT, AST, and ALP activities), oxidative stress factors (TBARS and total thiol levels, and the activity of SOD, Gpx, and CAT enzymes) and hepatic inflammatory factors (NO and TNF- α) were measured. Histopathological studies were also performed on the liver.

Results: In this study, it was shown that arsenic causes glucose intolerance and oxidative and inflammatory liver damage. Syringic acid prevents arsenic- induced hepatotoxicity and glucose intolerance in mice. Co-treatment of syringic acid with arsenic improved glucose intolerance and protected the liver against oxidative damage and inflammation.

Conclusion: A dose of 25 mg/kg of syringic acid showed better results than a dose of 10 mg/kg. Finally, syringic acid can be proposed as a therapeutic agent against diabetogenic and hepatotoxic effects of arsenic.

Keywords: Syringic acid; Arsenic; Hepatotoxicity; Diabetes; Mice.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-112

The effects of the oxidative stress index on the susceptibility of low-density lipoprotein to oxidation in diabetic patients with/ without coronary artery disease

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Abstract

Background and Aim: The oxidative modification of low-density lipoprotein (LDL) is closely associated with an increased risk for coronary artery disease (CAD) in diabetic patients. The purpose of this study is to investigate the relation between serum total antioxidant capacity (TAC), total oxidant status (TOS), malondialdehyde (MDA), and oxidative stress index (OSI) values with the susceptibility of LDL to oxidative modification and the possibility of CAD in diabetic patients.

Methods: This study was designed as a cross-sectional survey of 82 diabetes patients divided into two groups including T2DM alone (as group I) and both T2DM and CAD (as group II) was conducted. Blood samples of all subjects were taken after at least a 12-h fasting. Serums were saved after centrifugation (20 min; 3000 rpm) at -80 °C. Evaluate serum value of Ox-LDL was measured by Enzyme-linked immuneabsorbent (ELISA) methods. The levels of Serum TAC, TOS and MDA were measured by colorimetric tests.

Results: Ox-LDL, MDA, TOS, and OSI values in groups II were significantly higher compared with group I (all with P-value = 0.000). TAC value was significantly lower in group II compared with groups I (P-value = 0.000).

Conclusion: Results of this study support the belief that oxidative stress might be an important etiologic factor which makes some diabetics more susceptible to CAD. Increased oxidative stress may be a potential therapeutic target in the prevention and management of CAD in diabetic patients.

Keywords: Diabetes Mellitus; Coronary Artery Disease; Oxidative Stress; Oxidized low density lipoprotein.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-113

Higher serum levels of miR-9 in nonalcoholic fatty liver disease (NAFLD) patients

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Abstract

Background and Aim: Nonalcoholic fatty liver disease (NAFLD) is a prevalent chronic liver disease, affecting around 25% of the global adult population. It is caused by the accumulation of lipids, primarily triglycerides, in the liver, often accompanied by insulin resistance and inflammation. Obesity and type II diabetes are significant risk factors. Recent research has explored the role of miRNAs in liver inflammation, NAFLD, and liver cirrhosis. Studies have shown that miR-9; A miRNA associated with proteins involved in metabolic syndrome and liver inflammation, and it is predicted that miR-9 is an effective factor in NAFLD.

Methods: All participants are selected based on Ultrasound and fibroscan evaluation and specialist diagnosed and confirmed a total of 40 participants, comprising 20 NAFLD patients and 20 participants in the control group, to be included in this study. Fasting 5ml samples were obtained from each participant, and their serums were extracted for conducting biochemical tests, which included lipid parameters such as TC, TG, LDL, and HDL, and measuring the level of miRNA in their serum. The lipid profile data had been evaluated using an autoanalyzer. The miR-9 serum level has been determined utilizing the RT-qPCR method after RNA extraction and cDNA synthesis. The collected data were analyzed through SPSS software, and statistical tests such as Chi-2 and t-test were used for evaluation.

Results: According to the results of this study, statistical tests indicated that individuals with non-alcoholic fatty liver disease had substantially higher average levels of ALT, AST, TG, and Chol in their serum compared to the control group. In addition, the study established that the mean serum level of HDL in the patient group is significantly lower than the control group. The mean serum level of miR-9-5p in the NAFLD patient group has increased significantly by 1.25 ± 0.30 ($p > 0.01$) compared to the control group. Also, this study showed that the increase in miR-9 serum levels has a significant relationship with the risk of NAFLD ($p < 0.01$).

Conclusion: The results of this study suggested that individuals with non-alcoholic fatty liver disease had high levels of the lipid profile, with the exception of HDL blood level. Furthermore, this study showed that the serum level of miR-9 in the NAFLD group increased compared to the control group. Therefore, it can indicate that miR-9 is one of the microRNAs that are effective in NAFLD.

Keywords: NAFLD; miRNAs; miR-9.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Case Report

Code of Abstract: PBi-114

Cushing syndrome and tropical corticosteroid therapy: a case report

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Abstract

Background and Aim: Cushing's syndrome results from abnormally high levels of cortisol or other glucocorticoids in the blood. Iatrogenic Cushing's syndrome is caused by exogenous glucocorticoids; adrenocorticotrophic hormone (ACTH) is an independent type of Cushing's syndrome.

Case presentation: An 11-month-old boy was referred to our clinic due to obesity. His history was showed that the family used the tropical corticosteroid appliance (Clobetazol ointment containing 50 mg) for his diaper rash for months. The moon- faced was presented and their parents noticed when the side effects were showed. In laboratory findings, morning cortical and ACTH was lower limit normal. As a result of adrenal suppression, two separated doses of hydrocortisone treatment were administrated.

Conclusion: At present, tropical corticosteroid is the first line treatment in diaper dermatitis but we should have informed parents about how they should use. They should be applying a thin layer of this tropical only for short-time. Also, specialist should get a history of using the tropical glucocorticoid appliance if the iatrogenic Cushing syndrome is presented.

Keywords: iatrogenic Cushing's syndrome; diaper dermatitis; topical corticosteroids.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Clinical Trial

Code of Abstract: PBi-115

Investigating the preventive and therapeutic effects of resveratrol on endothelial cell damage in patients after CABG artery graft surgery in Bushehr Heart Center

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Abstract

Background and Aim: Cardiovascular diseases include a wide range of diseases such as coronary heart disease, heart attack, angina pectoris and heart failure such as stroke and unstable cerebral ischemic attacks or peripheral artery disease. As an antioxidant and anti-inflammatory, resveratrol has significant protective effects on the heart through various mediators. Therefore, the aim of this study was to investigate the therapeutic effects of resveratrol on endothelial cell damage in patients after CABG artery graft surgery in Bushehr Heart Center.

Methods: The present study was conducted as a case-control study on 60 patients referred to Bushehr Heart Center. Patients were randomly selected from cardiovascular patients undergoing CABG surgery at Bushehr University Heart Hospital. People were divided into two control and treatment groups. The control group was patients who underwent CABG surgery and did not take resveratrol. In the treatment group, patients who underwent CABG surgery were given resveratrol (250 mg capsules twice a day). Then, 10 cc of blood was collected from all study participants. Resveratrol was started about eight to 10 days after CABG surgery and after discharge from the hospital. And it continued for 60 days.

Results: The results of repeated measurement analysis with the group factor showed that the changes in systolic blood pressure in the treatment group were more than in the control group and this difference was significant ($P = 0.003$), so that the average systolic blood pressure in the treatment group decreased. Changes in diastolic blood pressure in the treatment group were more than in the control group, but this difference was not significant ($P = 0.282$). EF changes in the treatment group were more than the control group, and this difference is significant ($P = 0.005$), so EF increased more in the treatment group. The changes of CPK and LDH in the treatment group were more than the control group, but this difference was not significant ($P = 0.913$ ($P = 0.827$)). The changes of TG and CHO in the treatment group were more than the control group and this difference was significant ($P = 0.007$) ($P = 0.001$). So that TG and CHO decreased more in the intervention group. Changes in HDL in the intervention group were more than the control group, but this difference was not significant ($P = 0.315$). LDL changes in the intervention group were lower than the control group and this difference is significant ($P < 0.001$). The changes of MDA and TNF- α in the treatment group were lower than the control group, but this difference was not significant ($P = 0.491$). The changes of NO in the treatment group are more than the control group and this difference is significant (P -value = 0.014). So that NO increased more in the treatment group. TAC changes in the treatment group were more than the control group, but this difference was not significant ($P = 0.387$) ($P = 0.977$). Interleukin-6 (IL-6) changes in the treatment group were lower than the control group, and this difference is significant.

Conclusion: Resveratrol, as a strong antioxidant, improved heart function and increased EF in patients, as well as decreased blood pressure, improved lipid profile. The increase in NO level and decrease IL-6 in the resveratrol treatment group was significant compared to the control group.

Keywords: antioxidant; cardiovascular disease; resveratrol; blood pressure; TNF- α .





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Review Article

Code of Abstract: PBI-116

Morphine screening in urine: analytical consideration

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Abstract

Background and Aim: Opioids although highly addictive, they are commonly prescribed after surgery, trauma, or for chronic pain relief. To evaluate patient compliance, and for the protection of the program, pain management clinics require frequent drug testing of patients under their direction. Therefore, it is important for the laboratory to avoid false positive and false negative opioid results.

Methods: Various methods such as the rapid Lateral Flow assay method, methods based on immunoassay, as well as quantitative Chemiluminescence, methods based on chromatography as well as electrochemical and fluorimetric methods are used to detect morphine in biological fluids. The main and common method for Urine drug screening (UDS) in clinical laboratories are immunochemical techniques. Immunochromatography is a competitive immunoassay method on membrane strips. The ICG method is used widely because of its short testing time, simple implementation, requiring no special instruments, no trained person, and low cost. In the interpretation of the results, a limit concentration (Cut Off) of 300ng/ml is often used to make a decision. Thin layer chromatography (TLC) is a relatively common method. GC method has high sensitivity and accuracy, so that it is able to detect amounts lower than the Cut-Off of morphine in urine samples. GC-MS is a gold standard method for confirmation.

Results: Urine sampling has been extensively used for the evaluation of drug consumption. Some studies suggested saliva as another suitable specimen; however, the reliability of saliva analysis is limited because of analyte levels in this type of sample. The identification of chronic consumers or the late verification of a single intake is feasible using hair as a matrix, but it is not suitable for the early verification of consumption. A random urine sample can be used to measure morphine. To prevent cheating, measuring pH, specific gravity and creatinine can be used before analytical process. Morphine in serum or plasma is particularly difficult to measure because plasma concentrations after the usual parenteral doses of morphine are low and beyond the detection limit of most chromatographic systems.

Conclusion: Despite the simplicity and cheapness of ICG methods, those techniques may create a significant number of false positive results. Therefore, a confirmatory test with high specificity, such as TLC, HPLC and GC-MS is needed to approve a positive result made by immunoassay method. The biggest drawback of the GC method is that it is expensive and requires an expert to measure, and it also requires sample derivatization. HPLC has solved the problems related to the analysis of samples by gas chromatography, such as the destruction of samples at high temperatures.

Keywords: Morphine; ICG; HPLC.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Article

Code of Abstract: PBI-118

CCN6/WISP3 serum levels in type 2 diabetes mellitus patients in comparison with the healthy group and its correlation with inflammation and insulin resistance

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Abstract

Background and Aim: Cellular Communication Network Factor 6 (CCN6) is an adipokine whose production undergoes significant alterations in metabolic disorders. Given the established connection between the dysfunction of adipose tissue secretions and metabolic disorders, along with the observed negative correlation of CCN6 with insulin levels, the present study aims to investigate the association between serum CCN6 levels and type 2 diabetes mellitus (T2DM) as well as its associated risk factors for the first time.

Methods: In total, 80 diagnosed T2DM patients and 80 healthy control subjects were recruited. Participants from both groups were matched for gender and age. Circulating levels of CCN6, adiponectin, TNF- α , IL-6 and insulin were quantified using ELISA.

Results: T2DM patients exhibited significantly lower levels of CCN6 (1259.76 ± 395.02 pg/ml) compared to controls (1979.17 ± 471.99 pg/ml, $P < 0.001$). Also, the patients group presented notably lower levels of adiponectin ($P < 0.001$). While they presented considerably higher TNF- α , and IL-6 levels compared to non-T2DM ($P < 0.001$). In the T2DM group, CCN6 showed negative correlations with insulin ($r = -0.33$, $p = 0.002$), HOMA-IR ($r = -0.34$, $p = 0.002$), BMI ($r = -0.25$, $p = 0.02$), IL-6 ($r = -0.40$, $p < 0.001$) and TNF- α ($r = -0.25$, $p = 0.02$). Binary logistic regression analysis revealed an increased risk of T2DM in the adjusted model (OR [95% CI] = 0.62 [0.60 -0.76]). A CCN6 cut-off value of 1527.95 pg/mL differentiated T2DM patients from controls with 86.3% sensitivity and 73.8% specificity.

Conclusion: Our research identified a significant and negative association between serum CCN6 levels and the likelihood of T2DM progression, as well as inflammation biomarkers (IL-6 and TNF- α). CCN6 shows promise as a potential biomarker for T2DM; however, further investigations are necessary to validate this finding and assess its clinical utility.

Keywords: WISP3/CCN6; Type 2 diabetes mellitus; inflammatory cytokines; Insulin resistance; Adiponectin.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Article

Code of Abstract: PBI-120

The investigation of CCN5/WISP2 serum levels in patients with coronary artery disease and type 2 diabetes compared with the control and its correlation with risk factors

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Abstract

Background and Aim: Studies have shown various effects of CCN5/WISP2 on metabolic pathways, yet no prior investigation has established a link between its serum levels and CAD and/or T2DM. Therefore, this study seeks to explore the relation between CCN5 and the susceptibility to CAD and/ or diabetes, in comparison to individuals with good health, marking a pioneering endeavor in this field.

Methods: The study used a case-control approach to examine CCN5, TNF- α , IL-6, adiponectin, and fasting insulin levels in the serum of 160 participants, divided into four groups: T2DM, CAD, CAD- T2DM (each with 40 individuals), and 40 healthy individuals.

Results: Higher CCN5 concentrations were notably observed in the CAD (336.87 ± 107.36 ng/mL), T2DM (367.46 ± 102.15 ng/mL) and CAD- T2DM (404.68 ± 108.15 ng/mL) groups when compared to the control group (205.62 ± 63.34 ng/mL) ($P < 0.001$), with no significant gender differences ($P > 0.05$). Serum levels of IL-6 and TNF- α were significantly higher in all three patient groups compared to healthy subjects ($P < 0.001$), while adiponectin levels were notably lower in patients than in control participants ($P < 0.05$). Additionally, a positive and significant correlation between CCN5 and cytokines (IL-6 and TNF- α) was observed in all patient groups ($P < 0.05$). The results suggest a significant association between CCN5 and T2DM - CAD, T2DM, and CAD conditions according to multinomial logistic regression analysis ($P < 0.001$). Furthermore, this relationship remained significant even after adjusting for gender, BMI, and age ($P < 0.001$).

Conclusion: Our study has revealed, for the first time, a positive connection between CCN5 serum levels and the risk of developing T2DM and CAD. Nonetheless, more research is needed to ascertain whether CCN5 can serve as a predictive marker.

Keywords: Adipokine; Atherosclerosis; Cytokine; Diabetes, Inflammation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-121

A decreased level of high- density lipoprotein is a possible risk factor for type 2 diabetes mellitus: a review

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Abstract

Background and Aim: Type 2 diabetes mellitus (T2DM) is characterized primarily by dyslipidemia and hyperglycemia due to insulin resistance. High-density lipoprotein (HDL) plays a significant role in preventing the incidence of dyslipidemia and its complications. HDL has different protective functions, such as reducing oxidation, vascular inflammation, and thrombosis; additionally, its anti-diabetic role is one of the most significant recent discoveries about HDL and some of its constituent lipoproteins.

Methods This research reviews ongoing studies and preliminary investigations into the assessment of relation between decreased level of HDL and T2DM.

Results: The levels of HDL and its functions contribute to glucose hemostasis and the development of T2DM through four possible mechanisms, including insulin secretion by beta cells, peripheral insulin sensitivity, non-insulin-dependent glucose uptake, and adipose tissue metabolic activity. Additionally, the anti-oxidant properties of HDL protect beta cells from apoptosis caused by oxidative stress and inflammation induced by low-density lipoprotein, which facilitate insulin secretion.

Conclusion: HDL and its compositions, especially Apo A-I, play an important role in regulating glucose metabolism, and decreased levels of HDL can be considered a risk factor for DM. Different factors, such as hypoalphalipoproteinemia that manifests as a consequence of genetic factors, such as Apo A-I deficiency, as well as secondary causes arising from lifestyle choices and underlying medical conditions that decrease the level of HDL, could be associated with DM. Moreover, intricate connections between HDL and diabetic complications extend beyond glucose metabolism to encompass complications like cardiovascular disease and kidney disease. Therefore, the exact interactions between HDL level and DM should be evaluated in future studies.

Keywords: apo A-I; diabetes; high-density lipoproteins; prevention.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-122

The role of ANGPTL3, ANGPTL4 and ANGPTL8 in non- alcoholic fatty liver disease (NAFLD)

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Abstract

Background and Aim: Non- alcoholic fatty liver disease (NAFLD) (newly named metabolic associated fatty liver disease (MAFLD)) is based on metabolic dysfunction. At the onset of disease, NAFLD is characterized by hepatic triglyceride accumulation and insulin resistance. Angiotensin-like proteins (ANGPTLs) are closely related to insulin resistance and lipid metabolism, and may be a key in metabolic syndrome. Three members of the angiotensin-like (ANGPTL) protein family- ANGPTL3, ANGPTL4 and ANGPTL8- are important regulators of plasma lipoproteins; they inhibit the enzyme lipoprotein lipase, which plays a key role in the intravascular lipolysis of triglycerides present in some lipoprotein classes.

Methods: A comprehensive search was performed for all relevant data. The keywords ANGPTL3, ANGPTL4, ANGPTL8, Angiotensin- like proteins, Non-alcoholic fatty liver disease and NAFLD were used to search for articles in Google scholar, PubMed, NCBI databases in this study 83 related articles were reviewed. The searched time frame was from 2013 to 2022.

Results: In human the complete absence of ANGPTL3 results in an increased LPL activity. The effect of ANGPTL3 on cholesterol levels is largely attributed to the ability of ANGPTL3 to inhibit endothelial lipase. ANGPTL3 inactivation may have important therapeutic implications for treatment of metabolic syndrome, type 2 diabetes. The mechanism by which ANGPTL4 inhibits LPL has been the subject of much study. ANGPTL4 also seems to play a relevant role in type 2 diabetes mellitus and in the metabolic syndrome, both associated with dyslipidemia. The recent mouse studies indicate that liver-specific inactivation of ANGPTL4 may be a viable strategy for lowering plasma TG and possibly LDL-C. ANGPTL8 known as lipasin because of its capacity in LPL inhibition, ANGPTL8 might certainly contribute to glucose homeostasis opening a new door to possible future targeted therapies for diabetes and metabolic syndrome. ANGPTL8 level is significantly higher in patients with NAFLD than in healthy individuals.

Conclusion: Our study shows that the ANGPTLs (3, 8 and 4) may be related to NAFLD (MAFLD). The increased ANGPTLs level may be positively correlated with dyslipidemia that it is one of the important risk factors in the progression of Non-alcoholic fatty liver disease.

Keywords: ANGPTL3; ANGPTL4; ANGPTL8; Angiotensin-like proteins; Non-alcoholic fatty liver disease.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Case Report/ Case Series

Code of Abstract: PBi-123

Studying the frequency of birth risk of a baby with Down syndrome in pregnant mothers referring to a laboratory in Tehran for 1 year

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Abstract

Background and Aim: Down syndrome is a genetic disorder caused by the presence of all or part of a third copy of chromosome 21, that is caused by an error in cell division called "nondisjunction," which results in an embryo with three copies of chromosome 21 (Trisomy 21). During pregnancy, healthcare providers can diagnose Down syndrome through prenatal screening and diagnostic tests. Prenatal screening tests, such as a blood double marker and quad marker test, can indicate an increased likelihood of the fetus having Down syndrome. If the screening test shows an increased likelihood, a diagnostic test such as CVS or amniocentesis can be ordered. We want to measure the frequency of the double marker and quad marker tests that are positive in pregnant mothers who come to the laboratory in 1 year.

Methods: We included and evaluated about 2626 pregnant mothers who came to Colife laboratory during the last year and their double and quad marker tests were positive in the double marker test we studied PAPP-A and B-HCG results and in the quad marker test we considered inhibin-A, B-HCG, Alpha-fetoprotein, and Estriol results in a pregnant woman.

Results: In the first screening test (Double marker) that the pregnant woman does at 10 to 14 weeks, in our research we included 1038 pregnant women from 2023/1/1 to 2023/12/19 that have double marker test (PAPP-A, B-HCG), divided into two groups, first, they age under 36.7 that they are 859 people, then 94 (10.9%) screened positive, the second group, they age above 36.7 that they are 179 woman, then 52 (29.1%) screened positive after that in weeks about 15 to 20, the pregnant woman does quad marker test (HCG, Inhibin-A, Alpha-fetoprotein, Estriol), that is more accurate than a double test. We included 2626 pregnant women from 2023/1/1 to 2023/12/19, They divided into two groups, first, they were under 36.7 that they are 2191 people, then 75 (3.4%) screened positive, In the second group, they are above 36.7, that they are 435 people, then 89 (20.5%) screened positive.

Conclusion: we included 1037 women in double marker test in two groups, under 36.7 and above 36.7 years and the positive results were respectively 10.9% and 29.1%. After that in the quad marker test, we included 2626 pregnant women in two groups: Under 36.7 and above, the positive result is respectively 3.4% and 20.5%. We concluded from this research that we can use double and quad-marker screening tests to examine the probability risk of Down syndrome in pregnant woman. After this screening test, if the pregnant woman has a high risk of Down syndrome, she has to diagnostic tests such as CVS and amniocentesis.

Keywords: Down syndrome; Trisomy 21; B-HCG; Pregnancy.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Review Article

Code of Abstract: PBi-124

Discrepancy between POCT and ECLIA results in cardiac troponin test

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Abstract

Background and Aim: Currently, various methods are available to measure cardiac troponin in plasma for diagnosing myocardial infarction. Immunochemical methods including lateral flow assay (LFA), electrochemiluminescence immunoassay (ECLIA), and enzyme-linked immunosorbent assay (ELISA) are the most common methods which are being used in medical laboratories to measure this analyte. Due to the analytic characteristics, pre-analytical issues may influence test procedure and therefore produce false results and inconsistency between methods. In the present study, we aimed to evaluate the rate of disparity between methods used in laboratories for measuring cardiac troponin.

Methods: One hundred blood samples from patients with chest pain and suspected to myocardial infarction were collected in this study. The study subjects were randomly selected from the patients who were admitted to emergency department with chest discomfort. Symptoms and clinical characteristics of acute coronary syndrome were used to diagnose AMI. After centrifugation, all serum samples were first analyzed by immunochromatographic assay (Toyo). All samples without considering the primary result were then assessed by Abbott's High Sensitivity Cardiac Troponin-I (hsTnI).

Results: The participants in the study included 45 females and 55 males. The mean and standard deviation age of studied subjects was 63 ± 16 . Among all taken specimens 35 samples (18 men, 17 women) were negative for cardiac Troponin when measured by LFA method (Sensitivity 68%, Specificity 94%). On the other hand, all samples were positive with hsTnI compared to LFA (p -value < 0.05). Besides, there was no correlation between chemical laboratory results and LFA results or ECLIA tests.

Conclusion: Our results clearly showed a significant inconsistency between cardiac Troponin results in common immunochemistry techniques. Therefore, due to the importance of accurate results for better management of patients, particularly in the AMI, health policy makers should determine a comprehensive guideline for Troponin testing in this group of people.

Keywords: Discrepancy; ECLIA; LFA; Troponin.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic Review/ Meta-Analysis

Code of Abstract: PBi-126

Effect of *Nigella sativa* intake on oxidative stress in patients with metabolic syndrome and related disorders: a systematic review and meta-analysis of randomized control trials

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Abstract

Background and Aim: Increased oxidative stress play a crucial role in the occurrence of metabolic disorders such as metabolic syndrome, type 2 diabetes mellitus, non- alcoholic fatty liver disease, and cardiovascular diseases. Several studies have shown that the intake of nigella sativa has a beneficial effect on such disorders. In this meta-analysis, we aimed to evaluate the effect of nigella sativa consumption on oxidative stress biomarkers in patients with metabolic syndrome and related disorders.

Methods: We searched online databases, including Web of Science, Scopus, PubMed, and EMBASE, using related terms until December 2022. Clinical outcomes were presented as standard mean difference (SMD) with a 95% confidence interval (CI). In addition, sensitivity, heterogeneity, and publication bias were evaluated in eligible studies. This meta-analysis was performed on 14 RCTs comprising 929 participants.

Results: Our results showed that intake of nigella sativa significantly decreased MDA: [SMD: -2.69; (95% CI: -4.45 to -0.94); P = 0.00] levels. In addition, SOD: [SMD: 1.37; (95% CI, 0.63 to 2.12); P = 0.00] and TAC [SMD: 2.92; (95% CI, 0.59 to 5.24); P = 0.01] levels significantly increased in the intervention compared to the placebo group.

Conclusion: Our results showed that consumption of nigella sativa could be associated with improving oxidative stress in patients with metabolic syndrome and related disorders.

Keywords: Nigella sativa; Oxidative stress; Meta-analysis.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic Review/ Meta-Analysis

Code of Abstract: PBi-127

Effect of *Nigella sativa* intake on inflammation in patients with metabolic syndrome and related disorders: a systematic review and Meta- analysis of randomized control trials

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Abstract

Background and Aim: Increased inflammation play a crucial role in the occurrence of metabolic disorders such as metabolic syndrome, type 2 diabetes mellitus, non-alcoholic fatty liver disease, and cardiovascular diseases. Several studies have shown that the intake of *nigella sativa* has a beneficial effect on such disorders. In this meta-analysis, we aimed to evaluate the effect of *nigella sativa* consumption on inflammation biomarkers in patients with metabolic syndrome and related disorders.

Methods: We searched online databases, including Web of Science, Scopus, PubMed, and EMBASE, using related terms until December 2022. Clinical outcomes were presented as standard mean difference (SMD) with a 95% confidence interval (CI). In addition, sensitivity, heterogeneity, and publication bias were evaluated in eligible studies. This meta-analysis was performed on 14 RCTs comprising 929 participants.

Results: Our results showed that intake of *nigella sativa* significantly decreased CRP [SMD: -0.60; (95% CI: -0.96 to -0.23); P = 0.00], TNF- α [SMD: -0.53; (95% CI: -0.74 to -0.53); P = 0.00] IL-6 [SMD: -0.54; (95% CI: -1.01 to -0.07); P = 0.02] compared to the placebo group.

Conclusion: Our results showed that consumption of *nigella sativa* could be associated with improving inflammation in patients with metabolic syndrome and related disorders.

Keywords: *Nigella sativa*; Inflammation; Meta-Analysis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-128

Probiotics and physiotherapy for the management of osteoarthritis: potential role as a synergistic therapeutic modality

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Abstract

Background and Aim: Osteoarthritis (OA) has long been known as a degenerative disease of aged and people with poor dietary habits as a whole multi-tissue joint disorder. Searches on Gut microbiota and inflammatory diseases shows that the composition of Gut microbiota is strongly associated with the development of musculoskeletal diseases. Probiotics have attracted more and more attention for OA pain management. To improve health status, appropriate exercises are recommended for the alleviation of joint pain. This review attempted to discuss the emerging role of probiotic supplementation and how the recommended physical performance can help alleviate the OA and reduce pain.

Methods: The material that was reviewed derived from PubMed, Scopus, Google Scholar and Medline databases. The keywords included “osteoarthritis”, “osteoarthritis and human”, “probiotics”, “Gut microbiota”, “dysbiosis and osteoarthritis”, “prebiotics and osteoarthritis”, “exercise and osteoarthritis”, “knee osteoarthritis”, “osteoarthritis and treatment”, “osteoarthritis and pain” and “osteoarthritis and physiotherapy”.

Results: Since the degenerative process involves inflammation, the disease involves the activation of innate immune system and subsequent inflammatory responses. On the other hand, trauma, lifestyle and chronic antibiotic treatment, which all can disrupt commensal homeostasis of human microbiome, affects the intestinal integrity and promotes leakage of bacterial endotoxins and metabolites such as lipopolysaccharides (LPS) into the circulation there by, causing severity and joint pain. Gut microbiota, a collection of microbial population are indicators of health. Targeting the gut microbiota through diet intervention by giving probiotics such as oligofructose-enriched inulin can prevent or improve pain disorders. Physiotherapists can also expedite the alleviation of pathological changes of OA by providing different exercises, bringing changes in the exercise intensity, time and frequency, which all have shown to affect OA patients along with suitable exercise prescriptions.

Conclusion: This review summarized research evidences supporting the correlation between gut microbiota and development of OA. Since the OA cannot be reversed, thus it is being recommended that probiotics along with appropriate exercise program can assist in alleviating the joint pain and manage OA related degeneration.

Keywords: Microbiota; osteoarthritis; pain; probiotics; exercises; physiotherapy.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-129

Horizons of cell therapy in the treatment of Duchenne muscular syndrome

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Abstract

Duchenne muscular dystrophy (DMD) is the most severe type of dystrophy in children and is caused by mutations in the X-linked dystrophin gene. These features lead to chronic cycles of myofiber degeneration/ remodeling. Current available therapeutic regimes for DMD are mostly symptomatic and supportive. Stem cell therapy and regenerative medicine are alternative therapeutic modalities in the DMD patients.

In this regard, the application of various stem cells, especially mesenchymal stem cells (MSCs) and induced pluripotent stem cells (iPSCs) holds promise for improving muscle regeneration via the reduction of inflammation, and myogenesis in several animal models. Based on the previous data, transplanted stem cells can stimulate the growth of muscle mass and reduce fibrotic changes as well. Despite the advantages, the application of stem cells in clinical settings faces some limitations. Parameters such as preparation and expansion of suitable stem cell type, precise cell dosage, on-target cell delivery, prolonged follow-up and immune cell reactivity should be at the center of attention. Meanwhile, lineage orientation and commitment of transplanted cells at the site of injury should be controlled. To achieve this goal, long-term clinical studies are necessary to evaluate therapeutic effects, safety complications, and the optimal time of intervention. It is thought that combining cell-based treatments with pharmacological agents and physical therapy could offer synergistic benefits.

In conclusion, cell therapy is a promising way to treat DMD in children. Preclinical studies have shown that transplantation of muscle stem cells or myoblasts can improve muscle function and increase dystrophin expression in animal models of DMD. However, further research is needed to optimize cell therapy protocols and address remaining challenges before it can become a widely available treatment option for DMD. The purpose of this review is to examine safe and effective cell therapy options to halt or reverse the progression of DMD.

Keywords: Muscular dystrophy; Fibrosis; Stem Cells; Regenerative Medicine; Myogenesis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic Review/ Meta- analysis

Code of Abstract: PBi-130

Gestational diabetes insipidus and vasopressinase enzyme role; review article

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Abstract

Background and Aim: Vasopressin is one of the hormones produced in the hypothalamus, which is secreted from the posterior pituitary following the reduction of body water and the increase of plasma osmolality and affects the blood vessels and kidneys. Diabetes insipidus is a rare complication and various factors play a role in this disorder. The aim of this study is to find out the pathophysiological mechanisms for the development of gestational diabetes insipidus, diagnosis and treatment based on vasopressinase enzyme.

Methods: In this review article, articles using the keywords "diabetes insipidus, pregnancy, vasopressin, vasopressinase, ADH, AVP and gestation" in Web of Science, Scopus, Google Scholar, PubMed, and Magiran databases. It was collected and reviewed until 2022.

Results: Diabetes insipidus can include hormone secretion disorder (neurogenic diabetes insipidus), hormone receptor disorder (nephrogenic diabetes insipidus), excessive fluid intake (primary polydipsia) and increased hormone catabolism (gestational diabetes insipidus). The most common cause of gestational diabetes insipidus is the excessive activity of the vasopressinase enzyme, which leads to the destruction of the vasopressin hormone. Diagnosing diabetes insipidus in pregnancy can be challenging because it usually presents with symptoms of polydipsia and polyuria, which are often attributed to a normal pregnancy.

Conclusion: Gestational diabetes insipidus has various causes, the most common of which is excessive vasopressinase activity. Placental trophoblast produces vasopressinase and its level increases during pregnancy. Because desmopressin is N-terminally deaminated, it is resistant to vasopressinase and is therefore the treatment of choice for gestational diabetes insipidus.

Keywords: vasopressin; diabetes insipidus; pregnancy; vasopressinase.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-131

Evaluation of the Fatty Acid Synthase (FASN) expression in human breast cancer

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Abstract

Background and Aim: Breast cancer (BC) is an important cause of female cancer-related death. It has recently been demonstrated that metabolic disorders including lipid metabolism is a hallmark and a common feature of cancer cells metabolism. The objective of this study was to evaluate the Fatty Acid Synthase (FASN), and its clinicopathological significance in human breast cancer.

Methods: 55 pairs of fresh- frozen samples of BC and adjacent normal tissue were used to analyze FASN using qRT-PCR and Immunohistochemistry (IHC) staining. The expression of estrogen and progesterone receptors (ER, PR), and human epidermal growth factor receptor 2 (HER2/neu) were also examined using the IHC technique.

Results: Breast cancer tissues showed strong expression of FASN ($p < 0.05$) in mRNA and protein expression levels whereas adjacent normal tissues showed weak expression. FASN was positively correlated with nuclear protein Ki-67(a marker of cellular proliferation), and negatively correlated with PR.

Conclusion: Our results indicated that the expression of FASN may be considered as a prognostic indicator and potential therapeutic target in BC. However, further studies are needed to confirm the significance of these findings.

Keywords: Breast cancer; FASN; progesterone receptor; estrogen receptor.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-132

Exploring the biochemical landscape of Parkinson's disease: identifying significant differences in routine blood markers

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Abstract

Background and Aim: Parkinson's disease, a neurodegenerative disorder, arises from the death of dopaminergic neurons in the brain. This neuronal loss manifests in a range of motor and non - motor symptoms. Motor symptoms, such as resting tremor, bradykinesia, rigidity, and postural instability, affect movement control. Non - motor symptoms, including anosmia, sleep disorders, constipation, and psychological and cognitive changes like depression and dementia; further broaden the disease's impact.

Method: We conducted a case - control study comparing 40 individuals with Parkinson's disease to 20 healthy controls. Between 7 a.m. and 11 a.m., fasting whole venous blood was collected into serum tubes. We then performed routine blood tests on the serum, including complete blood count (CBC), prothrombin time (PT), partial thromboplastin time (PTT), erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), fasting blood sugar (FBS), hemoglobin A1c (HbA1c), triglyceride (TG), low - density lipoprotein (LDL), and high-density lipoprotein (HDL) cholesterol, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), thyroid stimulating hormone (TSH), blood urea nitrogen (BUN), and creatinine (Cr).

Results: Results were expressed as mean \pm standard deviation (SD). GraphPad Prism software version 6.07 (GraphPad Software, Inc., La Jolla, CA, USA) was used for analysis and graphing. The Kolmogorov-Smirnov test was used to analyze normality. Statistical significance was considered at $P < 0.05$. Significant differences were observed in the ALT ($p = 0.0001$), AST ($p = 0.0090$), CRP ($p = 0.0102$), ESR ($p < 0.0001$), FBS ($p = 0.0336$), Hb ($p < 0.0001$), HCT ($p < 0.0001$), MCH ($p = 0.0298$), MCHC ($p < 0.0001$), RBC ($p < 0.0001$), WBC ($p = 0.0073$), HDL ($p = 0.0202$), and LDL ($p = 0.0483$) tests in the PD group compared to the normal group.

Conclusion: Blood tests in Parkinson's patients ($n = 40$) revealed differences compared to healthy controls ($n = 20$). Inflamed markers (ALT, AST, CRP, ESR), altered blood sugar/cell counts (FBS, Hb, HCT, RBC, WBC), and dyslipidemia (LDL \uparrow , HDL \downarrow) were observed. These novel insights suggest potential roles for inflammation, metabolic changes, and lipid metabolism in Parkinson's disease. Further research with larger studies is needed to confirm these findings and explore their implications for diagnosis, treatment, and understanding the disease.

Keywords: Parkinson's disease; Blood markers; Case-control study; Routine blood tests; Inflammation; metabolic changes.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-133

Stem cell exosomes in cardiac regeneration; a valid therapeutic approach

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Abstract

Over the past two decades, stem cell- based therapies have been extensively applied for a variety of challenging diseases and pathological conditions, especially cardiovascular diseases (CVDs). Stem cells are capable of replacing damaged cells and organ regeneration. Emerging studies have proven the therapeutic value of stem cell exosomes (Exos) for cardiac tissue repair and regeneration. It is believed that mesenchymal stem cell (MSC) Exos are potential alternatives to whole- cell therapy because they mimic the biological activity of MSCs. Exosomal cargos could diminish cardiomyocyte apoptosis, and induce cardiomyocyte proliferation, leading to the restoration of injured myocardium after several pathologies. Besides, these Exos recover cardiac function by modulation of inflammatory biomarkers such as CD68. Data have indicated that miR-146a-modified adipose- derived stem cells (ADSCs) Exos can inhibit the release of proinflammatory cytokines and thus reduce further myocardial damage. Exos from other stem cell sources such as cardiac progenitor cells (CPC) exert regenerative potential by providing signal molecules into the cardiac microenvironment. Therefore, CPCs-Exos can contribute to cardiac tissue homeostasis under pathological conditions.

Therefore, stem cell Exos seems to be the potential magic bullet to promote cardiac repair and regeneration following various CVDs. Furthermore, the development of novel theranostic methods in terms of Exos provides a great tool for in-time diagnosis and therapeutic interventions in CVD patients. However, the use of Exos for cardiac repair is still in its infancy, and further clinical studies in this context are mandatory.

Keywords: Stem cells; Exosomes; Heart; Regeneration; Treatment.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-134

Investigating the level of heat shock protein 70 in Breast Cancer cell line and cell culture procedure with PLGA nanoparticles

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Abstract

Background and Aim: Breast Cancer in women is assumed to be one of the most lethal cancers especially in developing countries. In general, people with many kinds of cancer, express Hsp70 at high levels due to stress.

Methods: We researched and investigated the level of Hsp70 protein in the culture supernatant of Breast Cancer cell (MCF-7) treated with PLGA nanoparticles containing doxorubicin (DOX).

Results: The investigation showed that the amount of Hsp70 protein was decreased in cells treated with PLGA-DOX compared to the control group. Also, the cells containing a concentration of 1000 mg/ml PLGA-DOX had a more drastic down warded amount of the Hsp70 compared to the control group. In addition, the outcome of Dan-Benferroni experiment indicates a notable difference in the mean level of Hsp70 between the control group (p-value 1.43 ± 12.22) and the treated group (p-value 4.32 ± 1.05). The standard level of Hsp70 in the positive control group was 15.95 ± 0.93 in comparison with 11.63 in the treated group.

Conclusion: The result of Pearson's correlation showed a notable direct interrelation of IL-1Bata fold change and Hsp70. We also attained a significant decrease in the IL-1 β expression levels during this experiment. In conclusion, we can rely on Hsp70 as a predictive marker for the detection of breast cancer at the early stages.

Keywords: Breast Cancer; Hsp70; PLGA nanoparticles.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-135

The effect of hesperidin on the autophagy pathway in the liver tissue of cholestatic rats

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Abstract

Background and Aim: Autophagy has a significant role in liver diseases like cholestasis. Generally, autophagy has both cellular death and survives function. There are many proteins associated with autophagy, such as Beclin-1, LC3 and P62. Hesperidin, a flavanone- type flavonoid, is obtained in sweet orange, lemon and by-product of citrus fruits. It has anti-inflammatory, anti-allergic, hypolipidemic, vaso- protective, hepatoprotective and anticarcinogenic activities. The aim of the current study was to investigate the effect of hesperidin on the expression of autophagy genes in bile duct ligation (BDL) induced cholestatic rats

Methods: Thirty and two male Wistar rats were categorized into four groups (n = 8, 200-250 g). Sham group, BDL, and BDL plus Hesperidin groups. BDL rats have been treated with Hesperidin at doses of 100 and 200 mg/kg of body weight orally for 14 days. The value of mRNA expression of autophagy genes such as Beclin1, LC3 and P62 was carried out by using quantitative Real time polymerase chain reaction (qRT-PCR).

Results: Our results indicate that the mean of hepatic mRNA expression of Beclin1 and LC3 genes was significantly up regulated in the BDL group compared with sham group (p = 0.001 and p = 0.003, respectively). P62 expression was suppressed in the BDL group (p = 0.001). The mean of genes expression of Beclin1 and LC3 significantly downregulated in the BDL group treated with 200 mg/kg of body weight of hesperidin (p = 0.001, p = 0.015, respectively). P62 expression was not significantly changed by hesperidin treatment.

Conclusion: These results suggest that Hesperidin cause to attenuate autophagy in cholestatic rats.

Keywords: Cholestasis; Hesperidin; Autophagy; Rat.





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January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-136

Examining the potential benefits of natural probiotics for treating mental illnesses

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Abstract

Background and Aim: Investigating the possible effects of probiotic use on mental health has garnered more attention in recent years. An important field of study that emphasizes the reciprocal connection between the central nervous system and the gastrointestinal tract is the gut-brain axis. Anxiety, sadness, and mood disorders are among the mental health issues that have been connected to changes in the gut flora. Probiotics provide a viable therapeutic intervention option for people with mental diseases because of their capacity to alter the makeup of the gut flora. The purpose of this study is to investigate in - depth how probiotic supplementation affects the mental health of people with a range of mental health conditions. This article looks at how different probiotic-containing drugs can help cure or prevent mental diseases.

Methods: The influence of probiotic intake on a cohort of persons with mental diseases was evaluated using a randomized, double - blind, placebo - controlled methodology in this study. Psychiatric clinics were used to enroll participants, who were then randomized to either the probiotic or placebo group. The placebo group was given an identically inert material, whereas the probiotic group received a daily dose containing a blend of well - established probiotic strains. The duration of the intervention was 12 weeks. The intervention was conducted with psychological assessments, such as standardized depression and anxiety measures, at the beginning, middle, and finish. Furthermore, fecal samples were obtained to employ cutting - edge sequencing tools to examine modifications in the makeup of the gut flora. Throughout the trial, the intervention's compliance and any negative effects were continuously observed.

Results: When comparing the probiotic group's mental health outcomes to those of the placebo group, the study's findings showed a considerable improvement. Reduced scores on standardized psychological instruments indicated reductions in anxiety and depressive symptoms. The probiotic group's fecal microbiota analysis revealed significant changes in the microbial composition, suggesting a favorable regulation of the gut microbiome. According to the research, probiotic supplements may have a positive impact on the mental health of those who suffer from mental diseases.

Conclusion: To sum up, this research offers strong proof of the possible therapeutic application of probiotics in the treatment of mental health issues. The reported reductions in psychiatric symptoms and changes in the makeup of the gut bacteria highlight the complex relationship between the gut and the brain. Probiotics are a safe and easily obtainable intervention that may provide a fresh and innovative approach to current therapies for people with mental problems. To clarify the underlying processes and customize probiotic therapies to certain mental health disorders, additional study is necessary. This will open the door to more individualized and successful therapeutic approaches.

Keywords: Natural probiotics; Mental illnesses; Microbiota; Gut and brain; Microorganism.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-137

Positive relationship between the expression level of miR-490 and FOXO1 gene in the blood of Iranian colorectal cancer patients

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Abstract

Background and Aim: Colon cancer mainly arises from polypoid lesions in the colon. Dysregulation of transcription factors, including the FOX transcription factor family, leads to key determinant changes in gene expression. On the other hand, studies show that miRNAs, especially miR-490, are significantly related to cancer carcinogenesis, so that its overexpression causes cell cycle arrest and apoptosis induction, and also prevents cell migration and invasion. In this project, we intend to investigate the relationship between the expression level of miR-490 and its target gene, FOXO1, in the blood of patients with colorectal cancer in the Iranian population.

Methods: For this purpose, blood samples were taken from 24 healthy people and 24 patients with colorectal cancer who visited Imam Khomeini Hospital during the years 2018-2018 after obtaining consent form and completing the questionnaire, and the cold specimens were transferred to the genetics research laboratory. After extracting total RNA with Qiagen kit, cDNA synthesis was performed. The expression level of the studied gene and mortality was measured quantitatively by qRT-PCR.

Results: In this study, the expression of FOXO1 gene was decreased in patients' samples compared to healthy individuals (fold change = 0.8), but this decrease was not significant ($p = 0.07$). It showed a decrease in expression with healthy people, and the fold change was 0.6 and 0.51, respectively, and this difference was significant ($p = 0.045$). Also, this decrease in expression was directly related to the increase in cancer stage ($p < 0.05$).

Conclusion: Dysregulation of FOXO1 and miR-490 expression is effectively related to the development and progression of all types of cancers, and these two factors can be suggested as prognostic factors by conducting more research on tissue samples and increasing the study population.

Keywords: miR-490; FOXO1; colorectal cancer.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-138

Evaluating alpha- enolase, carcinoembryonic antigen and alpha-fetoprotein levels in neonatal jaundice cases in comparison with the control group

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Abstract

Background and Aim: The most prevalent disease in newborns is considered to be neonatal jaundice and, in most cases, it is benign. It is occurred due to the high concentration of bilirubin in the blood and is a benign disease. Many physiological and pathological functions are dependent on the production of CEA family members. AFP is expressed at relatively high levels in the fetal liver, especially in those with innate abnormalities. Research shows the cord blood AFP levels in infants with hyperbilirubinemia infants are higher than the control group newborns. Evermore, alpha- enolase (ENO1) is a metabolic enzyme which participates in the process of pyruvate synthesis. This research is aimed to find differences between the levels of ENO1, carcinoembryonic antigen, and AFP in the serum and urine of neonatal jaundice cases with the control group.

Methods: In this case-control research, a specialist selected 75 patients diagnosed with neonatal jaundice. Also, the control group contained 50 normal condition patients with well-functioning livers. 5cc of blood was drawn from all diagnosed people to evaluate the level of ENO1, carcinoembryonic antigen, and serum AFP by the ELISA technique.

Results: In this research, 75 patients diagnosed with neonatal jaundice around the age of 17.46 ± 4.27 were involved, which were not remarkably dissimilar to the control group. However, the weight of patients diagnosed with neonatal jaundice was 2886.67 ± 160.11 gr, which was considerably lower than the control group (315.10 ± 3210.00 gr). Also, the level of bilirubin in the control group (1.04 ± 3.19 mg/dl) was lower than neonatal jaundice cases (2.65 ± 14.84 mg/dl). The serum level of ENO1 in the patient group (362.67 ± 80.35 U/ml) was totally different from the control group (155.63 ± 34.75 U/ml) ($P = 0.0001$). Newborns diagnosed with jaundice (123.43 ± 38.50 U/ml) had higher ENO1 levels in their urine (urinary level of ENO1 in newborns of the control group: 62.02 ± 23.83 U/ml) ($P = 0.0001$). Serum and urinary CEA levels in newborns diagnosed with jaundice (serum: 2.84 ± 1.00 ng/ml, urinary: 0.12 ± 0.54 ng/ml) were much higher than those in the control group (serum: 0.83 ± 0.44 ng/ml, urinary: 0.15 ± 0.38 ng/ml) ($P = 0.0001$). The serum AFP level in the patient group (515.96 ± 59.93 ng/ml) was higher than the control group (150.42 ± 46.54 ng/ml) ($P = 0.0001$). Moreover, the level of urine AFP in patient group (73.89 ± 4.43 ng/ml) was significantly higher than the control group (22.15 ± 4.67 ng/ml) ($P = 0.0001$).

Conclusion: This research indicated that neonatal jaundice cases had higher level of ENO1, carcinoembryonic antigen and AFP than the control group. Measuring inflammation and exacerbation factors of neonatal jaundice cases may help to diagnose the severity or predict the progress of neonatal jaundice because of the role of ENO1, carcinoembryonic antigen and AFP level in this disease that may be associated with inflammation and exacerbation factors. For more precision, the serum and urine levels of investigated factors increase in line with each other, and this indicates that the urine sample can also be used to evaluate the severity or predict the progress of neonatal jaundice.

Keywords: Neonatal jaundice; ENO1; carcinoembryonic antigen; AFP.





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Venue:
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January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-139

The evaluation of *Sargassum boveanum* methanolic extract effect on antioxidant enzymes activity in human colorectal cancer HCT116 cell lines

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Abstract

Background and Aim: Colorectal cancer (CRC) is one of the main reasons of cancer associated with morbidity and mortality in both men and women worldwide. Emerging evidence has proposed that genetic and epigenetic mechanism also show a vital role in colorectal carcinogenesis. The balance between the production and elimination of reactive oxygen species (ROS) is essential in controlling whether cells survive or undergo apoptosis. Brown seaweeds especially sargassum species have attracted considerable attention because of their bioactive compounds and anticancer activities. Several mechanisms have been proposed to explain *Sargassum* anti-tumor effects. However, no previously published studies have investigated *Sargassum* antioxidant-oxidant activity in cancer cells. Therefore, the aim of this research was to examine the effects of *Sargassum boveanum* extracts on catalase and superoxide Dismutase (SOD) Enzyme activity as antioxidant in colorectal cell line.

Methods: In this study, the cytotoxic effect of the *Sargassum boveanum* methanolic extracts was measured 24, 48 and 72 h after treatment by MTT assay in cancer cell lines HCT116. Fibroblast cell line was used as a normal control. The activity of catalase and superoxide dismutase (SOD) enzyme activity were measured by spectrophotometric analysis.

Results: *Sargassum boveanum* extract significantly inhibited the growth of colorectal cancer cell line and fibroblast both in dose and time dependent manners. SOD and catalase activity of tumor cells incubated with the IC₅₀ concentration of *Sargassum* extracts for 48 and 72 h significantly decreased ($p = 0.001$). Although, SOD and catalase activity of treated fibroblast cells for 72 h significantly reduced when compared to untreated cell lines ($p = 0.001$).

Conclusion: These results propose that *Sargassum boveanum* may be a promising treatment option for colorectal cancer via inhibition of catalase and superoxide dismutase activity.

Keywords: *Sargassum boveanum*; colorectal cancer; Superoxide dismutase; Catalase; Antioxidant; Oxidant.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Review Article

Code of Abstract: PBi-140

Nanosensors in clinical laboratory for identifying pharmacological molecules throughout the body

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Abstract

Background and Aim: Since precise and timely detection of pharmacological molecules have become a great challenge for both patients and medical staff, developing efficient and accessible methods for identification of the molecules throughout the body would be a great need for the laboratory settings. On the other hand, employing nanotechnology in various fields of biomedicine has been greatly expanded during recent decades. In this regard, clinical laboratory has been introduced as one of the well-known areas. The present review was focused on the applications of nanosensors in clinical laboratory for identifying pharmacological molecules throughout the body.

Methods: In order to prepare the present review, a combination of the phrases and keywords including Nanotechnology, Nanosensors, Screening, Monitoring, Blood, Medicines and Pharmacological molecules were explored through the popular databases such as Web of Science, PubMed, Scopus and Embase as well as SID, IranDoc and Google Scholar. Then the selected contents were reviewed meticulously and subsequently discussed and concluded.

Results: Reviewing the literature indicated that, among the hot research topics, nanosensors has become the center of attention for many investigators and scientists working in the field. In this regard, nanodetectors for toxins, cancer cells and viruses were significantly mentioned in the studied documents as well as the important biomarkers such as troponin.

Conclusion: Among the various applications that have been found and introduced for nanosensors in clinical laboratory diagnostics, developing the sensors for detecting pharmacological molecules can be a priority. Although the relevant validations and accreditations would be crucial in this regard.

Keywords: Nanosensors; Screening; Monitoring; Blood; Pharmacological molecules.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-141

Exosomes biogenesis through toll-like receptors: role in cancer

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Abstract

Background and Aim: Exosomes, as a subset of extracellular vesicles, play essential roles in various cellular mechanisms and interaction in health and illness. Exosomes play vital roles in innate immunity. In this consideration, the host is protected through activating pattern recognition receptors (PRRs), which then can induce inflammatory factors to resist pathogen invasion. Toll-like receptor (TLR) is one member of PRRs having an important role in pathogen clearance? Interaction between exosomes and TLR has been evidenced in many cancers. In this review we attempted to discuss the biogenesis of exosome, impact of them on TLR and their effect on the development of cancer.

Methods: The review was derived from articles published in PubMed, Scopus, Google Scholar and Medline databases. The keywords included “exosomes”, “exosomes and cancer”, “exosomes and biogenesis”, “TLRs”, “exosomes and TLRs”.

Results: Exosomes are small membrane vesicles with lipid bilayer that retain various substances such as proteins, nucleic acids, and small RNAs. They play crucial roles in many physiological and pathological processes. To sustain tumor progression, it is necessary that there should be a continuous presence of intercellular interactions. Exosomes is new way evidenced as a cell communication pathway playing an important role in tumor or cancer progression. Interestingly exosomes have dual function, promoting or inhibiting the growth of tumor. For instance TLR2 can stimulate the growth of lung carcinoma while exosomes derived from pancreas cancer cells have been shown to downregulate the expression of TLR4 via miR-203, inhibiting the role of TLR4 in promoting angiogenesis in pancreatic cancer. Exosomes influence various TLRs and have either stimulating or inhibitory influences.

Conclusion: Though the articles published furnishes in detail the interaction between exosomes and TLRs, however how exosome regulate the TLR pathway remains to be explored. Information summarized also shows that composition of exosome is complex and different cell-derived exosomes have different functions on regulating TLRs.

Keywords: Exosomes; Toll-like receptors; cancer; Regulation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-142

A study on the effect of LPS on breast cancer cell line by cell metabolic activity (Mean transit time- MTT) assay for modulation of Toll like receptor-4

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Abstract

Background and Aim: MDA-MB-231 breast cancer cell type, having a specific molecular pattern, is well known as the cell line with triple negative feature. Cancer stem cells (CSCs) are a small cell compartment in the tumor parenchyma with the ability to resist several therapeutic drugs. These cells can activate the expansion of the tumor and relapse several days after the administration of drugs and chemotherapy drugs. The action of Toll like receptors (TLRs) can lead to the inhibition/stimulation of specific cell functions under different pathological conditions. Activation of TLR4 leads to the activation of nuclear factor- κ B (NF- κ B) and the production of pro-inflammatory cytokines, which lead to the stimulation of inflammation. TLR4 is specifically stimulated by various types of molecular patterns including lipopolysaccharide of Gram-negative bacteria LPS. Dimerization and activation of TLR4 leads to the activation of nuclear factor- (NF- κ B) and the production of pro-inflammatory cytokines, which leads to the stimulation of inflammation.

Methods: MB-MDA-231 cell line was purchased from Institute of Pasteur, Iran and cultured in Dulbecco's Modified Eagle Medium (DMEM) and 10% fetal bovine serum (FBS) without exosomes and antibiotics in an incubator at 37 degrees and 5% CO₂. Action of Lipopolysaccharide (LPS) was studied at different concentrations on MDA-MB-231 cells by MTT assay performed by ELISA method.

Results and Conclusion: The results obtained did not show the concentration of LPS above IC₅₀ by MTT assay. As TNBC breast cancer (Triple-negative breast cancer) is one of the subtypes of breast cancer that does not express estrogen receptors (ERs), progesterone receptors (PRs) and human epidermal growth factor receptors 2 (HER2) thus, their treatment is very difficult. This type of breast cancer is very aggressive and is associated with a poor prognosis, and it usually manifests with more recurrence than other subtypes. Thus, it is proposed to use another cell line to study the effect of toxin on the specific drug.

Keywords: Breast cancer cell line; Toll-like receptor; drug action; MTT assay; ELISA.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PBi-143

Role of microRNAs in neurobiology and pathophysiology

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Abstract

MicroRNAs (miRNAs) are short non-coding and well-conserved RNAs that are linked to many aspects of development and disorders. MicroRNAs control the expression of genes related to different biological processes and play a prominent role in the harmonious expression of many genes. During neural development of the central nervous system, miRNAs are regulated in time and space. In the mature brain, the dynamic expression of miRNAs continues, highlighting their functional importance in neurons. The hippocampus, as one of the crucial brain structures, is a key component of major functional connections in brain. Gene expression abnormalities in the hippocampus lead to disturbance in neurogenesis, neural maturation and synaptic formation. These disturbances are at the root of several neurological disorders and behavioral deficits, including Alzheimer's disease, epilepsy and schizophrenia. There is strong evidence that abnormalities in miRNAs are contributed in neurodegenerative mechanisms in the hippocampus through imbalanced activity of ion channels, neuronal excitability, synaptic plasticity and neuronal apoptosis. Some miRNAs affect oxidative stress, inflammation, neural differentiation, migration and neurogenesis in the hippocampus. Furthermore, major signaling cascades in neurodegeneration, such as NF- κ B signaling, PI3/Akt signaling and Notch pathway, are closely modulated by miRNAs. These observations, suggest that microRNAs are significant regulators in the complicated network of gene regulation in the hippocampus. In the current review, we focus on the miRNA functional role in the progression of normal development and neurogenesis of the hippocampus. We also consider how miRNAs in the hippocampus are crucial for gene expression mechanisms in pathophysiological pathways.

Keywords: microRNA; hippocampus; neurogenesis; neural development; Alzheimer's disease; epilepsy.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Review Article

Code of Abstract: PBi-144

The function of ghrelin hormone on weight and height regulation in children

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Abstract

Background and Aim: Ghrelin is a hormone that is secreted from the stomach and has 28 amino acids. Apart from the stomach, ghrelin hormone is secreted from other body organs such as the pancreas, intestine, kidneys and pituitary gland. This hormone affects the regulatory activities of the body of children and infants, for example, the hormone ghrelin causes the release of growth hormone, which increases the height of children, reduces energy consumption, and ultimately increases weight. Does the function of ghrelin hormone affect the weight and height of children?

Methods: We checked international sites and selected references from sites such as PubMed, Google Scholar, Web of Science, and Elsevier with keywords Ghrelin, Appetite hormone, obese children, Ghrelin and leptin, Growth hormone from 1999 to 2020. We used the meta-analysis method to write this review article and among the articles that we had chosen as references, we checked the ones that were more relevant to our topic and about the hormone ghrelin and its effect on weight and height gain in children.

Results: The two hormones ghrelin and leptin have opposite functions. The hormone ghrelin, which is secreted from the stomach, by affecting the hypothalamus and stimulating it, increases appetite and in the long term leads to obesity and overweight, while the hormone leptin, which is secreted from fat tissue, makes a person feel Satiety and as a result lose weight. The expression of the ghrelin hormone gene in children increases in the state of hunger and negative energy balance, and decreases in the state of satiety and positive energy balance, and as a result, causes obesity in children. In addition to increasing appetite, ghrelin causes obesity by reducing the breakdown of body fat, and the amount of ghrelin hormone is higher in thin children than in obese. Ghrelin can control the release of growth hormone by stimulating the pituitary gland. Growth hormone and ghrelin hormone increase in children when they are hungry.

Conclusion: These days, most children are obese, overweight and short. Ghrelin is a hormone that was recently discovered and by increasing the appetite of children, it causes them to become obese, and by acting on the pituitary gland, it regulates the growth hormone and controls their height.

In addition to regulating weight and height, ghrelin helps children's immune system due to its receptor on immune system cells and lymphocytes. In addition, this hormone can cause hematopoiesis and increase red blood cells in children and prevent their anemia.

Keywords: Ghrelin; Appetite hormone; obese children; Ghrelin and leptin; Growth hormone.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-145

The association of oxidative stress parameters with metabolic indices of visceral fat thickness and liver stiffness

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Abstract

Background and Aim: Oxidative stress is the result of an imbalance between the generation of oxidants and antioxidants. Research has demonstrated oxidative stress plays an important role in the pathogenesis of obesity and NAFLD. Numerous indicators are available to estimate metabolic problems such as visceral fat thickness (VFT) and liver stiffness (LS). VFT can be used to determine the risk of metabolic and cardiovascular diseases. LS can be used as an indicator of the liver's condition as fibrosis progresses. To clarify the role of oxidative stress on them, we aimed to investigate the association of several oxidative stress markers with well-known metabolic indices.

Methods: A total of 199 men with a BMI ≥ 25 kg/m² between the ages of 50 and 75 have been recruited. The FRAP method, predicated on the reduction of Fe³⁺ to Fe²⁺, was used to evaluate the total antioxidant capacity of plasma. The DTNB method was used to measure the sulfhydryl of the plasma by the interaction between DNTP reagent and protein thiol groups. Dinitrophenylhydrazine and protein carbonyl can react to produce hydrazone derivatives and their absorbance can be evaluated. The final result of lipid peroxidation is malondialdehyde (MDA). A measurable product is produced when MDA and thiobarbituric acid combine. Using the appropriate kinetic techniques, the enzymatic activities of glutathione reductase (GR), Catalase, superoxide dismutase (SOD), and glutathione peroxidase (GPx) were determined. Elastography is used to measure LS. This technique uses sound waves in sonography. Sonography is also used to measure VFT. The thickness of the adipose layer is measured.

Results: Based on the results, a significant relationship has been observed between MDA and VFT ($p < 0.01$) as well as LS ($p < 0.05$). Additionally, there is a negative correlation between LS ($p < 0.05$) and VFT ($p < 0.01$) with Catalase. Additionally, GR and VFT have a significant relationship ($p < 0.01$), and SOD and VFT have an inverse relationship ($p < 0.01$), but they are unrelated to LS. GPx, total antioxidant capacity of plasma, Total thiol, and protein carbonyl had no relationship to either VFT or LS.

Conclusion: It appears decrease in the antioxidant defense system and augmented oxidant could worsen hepatic damage reflected by increased LS and VFT in the setting of overweight and obesity. We found a significant relation between MDA and CAT as oxidative stress parameters and LS and VFT as metabolic indices.

Keywords: Oxidative stress; metabolic disorder; Liver stiffness; visceral fat thickness.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBI-146

Chronic methamphetamine exposure impairs spatial memory and alters hippocampal neurobiology in a rat model

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Abstract

Background and Aim: Methamphetamine (METH) abuse is a significant public health concern, with detrimental effects on cognitive function and memory. This study aimed to investigate the impact of chronic METH exposure on spatial memory in a rat model.

Methods: Adult male Sprague - Dawley rats were administered METH (5 mg/kg, intraperitoneally) or saline once daily for 14 consecutive days. Spatial memory was assessed using the Morris water maze test, a well-established paradigm for evaluating hippocampus-dependent spatial learning and memory.

Results: Our results revealed that chronic METH exposure led to significant impairments in spatial memory performance, as evidenced by increased latency to find the hidden platform and reduced time spent in the target quadrant during the probe trial. Additionally, histological analysis demonstrated alterations in the morphology of hippocampal neurons, including reduced dendritic arborization and spine density in the METH- exposed rats compared to the control group. Furthermore, biochemical analysis revealed dysregulation of synaptic plasticity- related proteins, such as decreased levels of brain-derived neurotrophic factor (BDNF) and postsynaptic density protein 95 (PSD-95), in the hippocampus of METH- treated rats.

Conclusion: These findings provide compelling evidence for the detrimental effects of chronic METH exposure on spatial memory and associated neurobiological changes in the hippocampus. Understanding the underlying mechanisms of METH- induced memory deficits is crucial for developing targeted interventions to mitigate cognitive impairments associated with METH abuse.

Keywords: Methamphetamine; Anxiety; Stress; Rat model; HPA.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBI-147

Chronic methamphetamine exposure induces anxiogenic effects and dysregulates stress responses in a rat model

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Abstract

Background and Aim: Methamphetamine (METH) abuse is associated with profound alterations in stress responses and anxiety-related behaviors. This study aimed to investigate the impact of chronic METH exposure on anxiety and stress responses in a rat model.

Methods: Adult male Sprague- Dawley rats were administered METH (5 mg/kg, intraperitoneally) or saline once daily for 14 consecutive days. Anxiety- related behaviors were assessed using the elevated plus maze and open field tests, while stress responses were evaluated through the measurement of hypothalamic-pituitary-adrenal (HPA) axis activity and corticosterone levels.

Results: Our results revealed that chronic METH exposure induced anxiogenic effects, as evidenced by decreased time spent in the open arms of the elevated plus maze and reduced exploration in the center area of the open field, indicative of heightened anxiety-like behaviors. Furthermore, METH- exposed rats exhibited dysregulation of the HPA axis, characterized by elevated basal corticosterone levels and blunted corticosterone response to an acute stressor. Additionally, alterations in the expression of stress-related neuropeptides, such as corticotropin-releasing hormone (CRH) and arginine vasopressin (AVP) in the hypothalamus were observed in METH-treated rats.

Conclusion: These findings provide compelling evidence for the anxiogenic and dysregulation effects of chronic METH exposure on anxiety and stress responses, involving alterations in the HPA axis and stress- related neuropeptide systems. Understanding the underlying mechanisms of METH- induced anxiety and stress dysregulation is crucial for developing targeted interventions to alleviate the psychiatric comorbidities associated with METH abuse.

Keywords: Methamphetamine; Anxiety; Stress; Rat model; HPA.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-148

Effectiveness of combined therapy with liraglutide and pirfenidone for liver regeneration in rats' liver fibrosis induced by bile duct ligation

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Abstract

Background and Aim: Emerging evidence is demonstrating that regeneration of the liver may be caused by antifibrotic drugs. Liraglutide (Lira) and Pirfenidone (Pir) have a positive impact on improving liver fibrosis. Recent data indicates that staining for Ki-67 and HepPar1 reflects liver regeneration. Therefore, the aims of this study were to elucidate the impacts of combination therapy on liver regeneration.

Methods: Sixty Wistar rats were divided into 5 groups: group 1: control (n = 6), group 1: BDL (n = 6), group 3: BDL+Pir (n = 6), group 4: BDL+Lira (n = 6), and group 5: BDL+Lira+Pir (n = 6). Liver fibrosis was assessed by measuring serum biochemical parameters. The morphological characteristics of liver tissue were examined by H&E, Masson's trichrome, and Sirius red staining. Also, Ki-67 and HepPar1 were evaluated by immunohistochemistry.

Results: Treatment with Liraglutide and Pirfenidone significantly reduced the levels of serum biochemical parameters (ALT, AST, and ALP). HEP-1 marker in the regenerative areas present in combination treatment by IHC staining with this biomarker shows a moderate positive expression in about 10 to 20% of fibrotic cells, which confirms the regeneration of hepatocytes in the areas compared with control. The Ki67 marker in the combination group in fibrotic areas also shows positive nuclei in less than 5%, which indicates more proliferation than the control group.

Conclusion: Combining pirfenidone and Liraglutide therapy is a potentially effective way to treat rats with bile duct ligation- induced liver fibrosis, as it can accelerate regeneration and improve the condition.

Keywords: liraglutide; pirfenidone; bile duct ligation; liver fibrosis; regeneration.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-149

Beneficial potential of betaine in reducing oxidative stress in testicular and ovarian cells

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Abstract

Background and Aim: Hyperglycemia is one of the conditions that can cause oxidative stress (OS) and affect the activity of testicular and ovarian cells. Betaine, as an essential osmotic protector and a methyl group donor, protects the cell in stress conditions. The aim of this study is to evaluate the effect of betaine on OS in hyperglycemic conditions in testicular and ovarian cells.

Methods: Testicle and ovary cells were cultured in 4 different conditions including normal glucose with and without betaine (5 mM for 24 hours) and hyperglycemic conditions (48 hours) with and without betaine (5 mM for 24 hours). Cell viability, lipid peroxidation, and methylene glyoxal (MGO) measured in all conditions.

Results: In cells with hyperglycemic conditions, we saw a decrease in viability and an increase in MDA as a marker of lipid peroxidation, and MGO. These changes were more significant in testicular cells than ovarian cells than. Treatment with betaine increased cell viability and decreased MDA and MGO. Ovary cells had a better response more to betaine compared with testicular cells.

Conclusion: Hyperglycemia can cause OS, cell death, and interference related to fertility. According to the results, betaine may have a protective effect on cells by reducing hyperglycemia-associated OS and therefore may be useful in the treatment of infertility.

Keywords: Hyperglycemia; betaine; infertility; oxidative stress; lipid peroxidation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-150

A novel delivery system of poly (lactic-co-glycolic) acid scaffold impregnated with dual herbal components loaded-fibrin nanoparticles for cartilage tissue engineering

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Abstract

Background and Aim: The herbal components Ginger / soybean unsaponifiable (GSU) and Turmeric (TCA) have chondroprotective and anti-inflammatory effects. The aim of this study was to engineer cartilage tissue from human stem cells and poly (lactic-co-glycolic) acid (PLGA) scaffolds incorporated with GSU and TCA-loaded fibrin nanoparticles.

Methods: TCA and GSU- loaded fibrin nanoparticles (FNP) were prepared *via* two different methods. In the first method, fibrin clot was dissolved in NaOH, and FNPs were prepared after adding HCl following vigorous agitation. Then GSU and TCA were loaded physically to fabricate TCA- FNP and GSU-FNP. In the second method, in a simple and effective new approach, GSU and TCA were blended in fibrinogen, mixed with thrombin to form a gel, freeze- dried and powdered *via* a freezer mill to fabricate TCA- FNP and GSU- FNP. The functional groups, size, and surface charges of nanoparticles were evaluated. The 3D scaffold PLGA was prepared and incorporated with TCA- FNP and GSU-FNP. The scaffolds were evaluated by scanning electron microscopy (SEM), fourier-transform infrared spectroscopy (FTIR), and releasing techniques. The expression of the genes (type II and X collagen, SMAD2, 3) was quantified by real-time polymerase chain reaction.

Results: In The results of releasing, dynamic light scattering, FT-IR, and SEM evaluation indicated that nanoparticles prepared *via* the second method exhibited higher quality with no cytotoxicity. The expression of type II collagen, SMAD2 and 3 genes were significantly increased compared to the control group ($P < 0.05$) and type X collagen expression was significantly decreased.

Conclusion: The results showed that the scaffold with a lower size of nanoparticles had a profound effect in chondrogenesis of adipose-tissue-derived stem cells for tissue engineering.

Keywords: Adipose- derived stem cell; Chondrogenesis; Fibrin nanoparticle; Herbal components.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-151

Therapeutic potential of resveratrol and atorvastatin following high- fat diet uptake- induced nonalcoholic fatty liver disease by targeting genes involved in cholesterol metabolism and miR33

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Abstract

Background and Aim: The present study was designed to evaluate the effects of resveratrol, atorvastatin, and a combination of resveratrol and atorvastatin on expression levels of genes involved in the cholesterol metabolic pathway in the fatty liver of C57/BL6 mice.

Methods: A high- fat diet was used to induce fatty liver in C57/BL6 mice treated with resveratrol, atorvastatin, or a combination of resveratrol and atorvastatin. Pathological and biochemical studies were performed. In addition, hepatic gene expressions of ATP- binding cassette transporter A1 (*ABCA1*), *ABCG1*, liver X receptor (*LXR*) α , scavenger receptor B1 (*SR-B1*), low-density lipoprotein receptor (*LDLR*), and miR33 were evaluated by the real-time PCR method, and the Western blot method was used to measure the *ABCA1*, *ABCG1*, and *LXR* α protein levels.

Results: Resveratrol and atorvastatin reduced fat accumulation in the liver of mice with fatty liver, and this effect was correlated with decreased blood glucose levels, triglyceride, cholesterol, low- density lipoprotein cholesterol, high- density lipoprotein cholesterol blood levels compared with the positive control (PC) group. In contrast to the animals of the PC group, fatty liver groups that received resveratrol and atorvastatin had a significant effect on the mRNA levels of the *ABCA1*, *ABCG1*, and *LXR* α , *SR-B1*, *LDLR*, and miR33 genes. Moreover, resveratrol and atorvastatin administration elevated *ABCA1* and *ABCG1* and reduced *LXR* α protein expression.

Conclusion: Obtained results showed that resveratrol and atorvastatin combination therapy can improve nonalcoholic fatty liver disease by targeting genes involved in cholesterol metabolism and miR33.

Keywords: NAFLD; atorvastatin; cholesterol; high-fat diet; miR33; resveratrol.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-152

Encapsulation of probiotic *Pediococcus acidilactici* by calcium alginate-pectin with chitosan coating and investigation of survival in simulated gastric condition

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Abstract

Background and Aim: Today, the positive role of probiotics in regulating the intestinal microbiome, modulating the immune system, reducing inflammation and oxidative stress in the process of various diseases has been confirmed. On the other hand, their survival reduces when passing through the stomach before reaching the intestine and is considered as a challenge. Therefore, the aim of this study was to investigate the effect of microencapsulating probiotic *Pediococcus acidilactici* (*P. acidilactici*) using calcium alginate-pectin and chitosan coating on increasing survival in simulated gastric condition.

Methods: Probiotic cells were encapsulated by extrusion technique, using alginate salt, pectin and chitosan. Encapsulation efficiency (EE) was evaluated by pour plating non-encapsulated and encapsulated bacterial cells in De Man, Rogosa and Sharpe (MRS) agar separately. Freeze-dried microcapsule's characteristics were analyzed using a scanning electron microscope (SEM) and Fourier transform infrared spectroscopy (FTIR). Simulated gastric juice (SGJ) was prepared; free and encapsulated probiotic cells incubated in it for 30, 60, 90, and 120 min at 37 °C with a speed of 50 rpm and then, the bacterial cells viability determined.

Results: The EE reached 81.6 % and the SEM images showed that the microcapsules had a hemispherical shape with uneven surface that indicated the presence of probiotic cells inside their structure. The results of FTIR analysis showed ionic interactions between polysaccharide materials which are used for encapsulation in this study. After incubation in SGJ, it was observed that the encapsulation of *P. acidilactici* significantly increased bacterial cells viability in comparison with non-encapsulated probiotic cells (4.92 ± 0.42 vs. 2.3 ± 0.17 log cfu/g after 2h).

Conclusion: Altogether, the outcomes of this study declared that alginate salt, pectin and chitosan, are suitable polysaccharide materials for probiotic encapsulation. We achieved a high EE by combination of these three polysaccharides. We found that encapsulating *P. acidilactici* has beneficial effect on bacterial cells survivability.

Keywords: probiotic; encapsulation; alginate; chitosan; simulated gastric juice.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBI-153

Investigating the effect of omega-3 PUFAs and iron supplementation on the reduction of WBC in diabetic rats

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Abstract

Background and Aim: Diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia, has several known complications that can affect various organ systems. One of the common complications associated with diabetes is changes in immune system function, including changes in the number and function of white blood cells (WBC). Understanding the underlying mechanisms that contribute to these changes is crucial for the development of potential therapeutic strategies to reduce immune dysfunction in people with diabetes. Recent research has highlighted the potential benefits of omega-3 PUFAs and iron supplementation in various aspects of diabetes management. Omega-3 PUFAs have shown anti-inflammatory and immune-modulating properties. Iron, an essential micronutrient, is involved in several physiological processes including immune cell function and hematopoiesis. However, the specific effects of omega-3 PUFAs and iron supplements on WBC count in diabetic conditions compared to non-diabetic conditions remain relatively unknown. Therefore, this study was conducted with the aim of investigating the effect of omega-3 PUFAs and iron supplementation on WBC reduction in diabetic rats compared to non-diabetic rats. By evaluating changes in WBC count and investigating potential molecular pathways involved, we can gain valuable insights into the interaction between diabetes, immune system function, and nutritional interventions.

Methods: Male Wistar rats were given 40 mg/kg streptozotocin and a high-fat diet for 21 days to induce diabetes. Eight groups were used: diabetic and non-diabetic Controls, diabetics + iron, diabetics + n-3 PUFA, diabetics + iron + n-3 PUFA, non-diabetics + iron, non-diabetic + n-3 PUFA, and non-diabetics + iron + n-3 PUFA. They received oral supplements for a month then Blood samples were taken after one month evaluates blood parameters.

Results: It was found that the administration of iron and omega resulted in a decrease in the number of white blood cells in the Diabetic group compared to the control group.

Conclusion: The results presented in this study provide valuable insights into the effect of various interventions on blood parameters in diabetic and non-diabetic groups. Data show differences in white blood cell count (W.B.C) among different treatment groups in diabetic and non-diabetic populations. These findings emphasize the importance of considering dietary supplements such as and iron (Fe) as potential modifiers of blood parameters.

Keywords: Diabetes; n-3 PUFAs; Iron.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-154

The effect of sargassum angustifolium-derived AgNPs on glycogen synthase kinase 3 (GSK-3) expressions in acute lymphoblastic leukemia cells

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Abstract

Background and Aim: Acute lymphoblastic leukemia is among the most prevalent children cancers. Moreover, chemotherapy and bone marrow transplantation have failed to secure the survival of patients in some cases. The application of organic substances has offered new prospects for the treatment of this condition. Accordingly, the aim of this study was to examine the silver nanoparticles synthesized from Sargassum Angustifolium on the expression of GSK-3 in acute lymphoblastic leukemia cell line (Jurkat cell line).

Methods: In this research, quantitative mRNA expression of the target gene was measured using a real-time polymerase chain reaction (real-time PCR). Hypoxanthine phosphoribosyltransferase (HPRT) genes were studied as internal controls. The experiments were duplicated and replicated 3 times. Data analysis was performed through one-way ANOVA and t-test. The significance level was considered less than 0.05.

Results: The results of the MTT test revealed that concentrations of 3, 4, and 5µg/ml of extracts in both cell lines significantly decreased the number of viable cells ($P < 0.001$). In this study, there was no statistically significant difference in the expression of the GSK-3 gene between the Jurkat and the PBMC groups ($P > 0.05$), which was statistically significant ($P < 0.05$).

Conclusion: It seems that silver nanoparticles synthesized from sargassum algae in the Persian Gulf could be utilized to treat acute lymphoblastic leukemia cancers and even other tumors.

Keywords: Acute lymphoblastic leukemia; Seaweed; Silver nanoparticles; glycogen synthase.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-155

Apoptotic effect of sargassum angustifolium-derived AgNPs in jurkat cell line

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Abstract

Background and Aim: ALL is a B or T lymphoblasts malignancy marked by uncontrolled proliferation of abnormal, immature lymphocytes. The inositol trisphosphate receptor (IP3R). Its receptor exists in all cell types on the surface of a smooth endoplasmic reticulum that is a calcium homeostasis regulator and is implicated in metastasis. The aim of this study was to examine the silver nanoparticles synthesized from *Sargassum Angustifolium* on the expression of IP3R in acute lymphoblastic leukemia cell line (Jurkat cell line).

Methods: In this research, quantitative mRNA expression of the target gene was measured using a real-time polymerase chain reaction (real-time PCR). Hypoxanthine phosphoribosyltransferase (HPRT) genes were studied as internal controls. The experiments were duplicated and replicated 3 times. Data analysis was performed through one-way ANOVA and t-test. The significance level was considered less than 0.05.

Results: The results of this study revealed that different concentrations of the extracts significantly decreased the expression levels of IP3R3 in Jurkat cells compared to control groups. The combination of algae extracts and AgNPs was consistently the most effective group.

Conclusion: Extracts of Gulf sargassum algae can be used to inhibit ALL cells by inhibiting the expression of the *IP3R3*.

Keywords: Acute lymphoblastic leukemia; Seaweed; Silver nanoparticles; Inositol trisphosphate.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-156

Exploring the Impact of PGE2 synthesis pathway on coronary artery disease

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Abstract

Background and Aim: Prostaglandin-related inflammatory processes might be crucial in the development of vascular stenosis. The purpose of this study was to look at the serum 13, 14-dihydro-15-keto-PGF₂ α value implicated in PGE₂ metabolism and the levels of monocyte PTGES and 15-PGDH gene expression in patients with coronary artery stenosis and restenosis. Additionally, the effects of miR-520, miR-1297, and miR-34 on the levels of gene expression were investigated.

Methods: PTGES and 15-PTGDS were selected from the primary network obtained in STRING (<https://string-db.org/>) with a K-means score cutoff (> 7). Then, the genes were the subjects for the miRNA prediction from some databases (such as MirWalk, Miranda, and miRTargetScan). MiR / gene networks were obtained in Cytoscape on the basis of gene prediction and function data reported in the miRNA databases. Then, both networks were merged and considered for the selected genes. Sixty participants, consisting of healthy controls (with less than 5% stenosis), individuals with stents and no restenosis (SNR, with stenosis less than 5%), and subjects with stent restenosis (ISR, with restenosis exceeding 70%), were included in the research study. The study involved measuring gene expression levels and serum 13, 14-dihydro-15-keto-PGF₂ α values using RT-qPCR and ELISA techniques, respectively. Additionally, the impact of miRNAs on gene expression levels was examined through the transfection of miR/PEI complexes into monocytes.

Results: Significant increases ($P < 0.05$) were observed in the expression levels of the PTGES and 15-PGDH genes, as well as in the serum 13, 14-dihydro-15-keto-PGF₂ α value. The miR/PEI transfection studies provided substantial confirmation of the gene expression alterations, as evidenced by the significant expression changes of miR-520 and miR-34. Additionally, the population and transfection studies provided evidence suggesting a potential connection between the functions of miR-520 and miR-34 and the expression levels of PTGES and 15-PGDH.

Conclusion: The findings of this study demonstrated a direct association between inflammatory events and the monocyte PGE₂ synthesis pathway in patients with SNR and ISR. Given the involvement of PTGES and 15-PGDH enzymes in PGE₂ metabolism, as well as the final metabolite 13, 14-dihydro-15-keto-PGF₂ α , the gene expression levels of these enzymes and the serum metabolite values were assessed. The study results confirmed significant increases in both PTGES and 15-PGDH gene expression levels, as well as in the serum metabolite values, among the patients.

Keywords: Stenosis; Prostaglandin E₂; 15-PGDH (HPGD); MicroRNAs.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-157

Metformin in combination with chlorogenic acid ameliorates skeletal muscle inflammation in insulin resistance animal model

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Abstract

Background and Aim: Obesity is regarded a main risk factor for the development of insulin resistance (IR) and type 2 diabetes (T2D). Accumulating evidence has demonstrated that low- grade inflammation (meta- inflammation) is implicated in obesity-induced IR in skeletal muscle (SM). The valuable effects of metformin (MET) and chlorogenic acid (CGA) in the improvement of IR have been proposed, nevertheless, their combination impacts were not investigated so far.

Methods: In the current study Fifty male C57BL/6j mice were divided into two groups at the beginning of the study: the group fed a normal diet (n = 10) and the group fed a high-fat diet (n = 40). After 10 weeks, during the next 12 weeks of the study, HFD mice were divided into 4 groups (HFD, HFD + MET (0.25%), HFD + CGA (0.02%) and HFD + MET + CGA (0.25 + 0.02%).

Results: The results of our study show that the MET and CGA, either alone or in combination, have a positive effect on decreasing weight gain, plasma triglyceride concentrations, fasting blood sugar levels, and plasma insulin levels. Combination therapy with these two compounds led to the improvement of inflammation by reducing the rate of macrophage infiltration into SM and reducing the expression of MCP-1. In addition, the effect of MET and CGA on stimulating of macrophage switching (M1 to M2) was observed through decreasing expression of iNOS and CD11c (M1 markers) and increasing expression of arginase-1 and CD206 markers (M2markers). We also observed an increase in the expression of IL-10 as an anti-inflammatory cytokine.

Conclusion: It seems that the combination of MET with CGA can be introduced as a possible therapeutic strategy to improve inflammation caused by IR in a HFD mice model.

Keywords: Skeletal muscle; Chlorogenic acid; Metformin; inflammation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic review/ Meta- analysis

Code of Abstract: PBi-158

The relationship between vitamin D, iron deficiency anemia, and severe early childhood caries: a review

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Abstract

Background and Aim: Severe Early Childhood Caries (S-ECC) negatively impact the well-being and joy of young children. Limited research has been conducted on this subject, but evidence suggests that children suffering from S-ECC may have a higher likelihood of experiencing malnourishment. Iron deficiency being the most common nutritional deficiency in childhood is often seen associated with severe caries destruction. Not having enough iron is a very common problem with people's diets around the world, especially in poorer countries. In some cases, adding extra iron salts to some foods can help to improve this deficiency. A high prevalence of tooth decay is often observed in areas with insufficient iron levels among the population. This systematic review had 2 objectives: 1) to determine whether there exists a correlation between vitamin D levels and S-ECC. 2) To investigate an association between S-ECC with iron deficiency anemia (IDA).

Methods: Scientific articles were searched in PubMed, Scopus, Web of Science, and Google Scholar. English studies were included if mentioning the level of vitamin D, hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration, and packed cell volume (PCV) in S-ECC and caries-free children.

Results: Children with S-ECC were much more likely to have vitamin D levels that were lower than the recommended amounts for the best and satisfactory health. Multiple regression analysis showed that severe early childhood caries, not drinking milk often, and the winter season were related to having lowered 25 (OH) D levels. Having low levels of vitamin D, low household income, and thinking the child's health is not good were linked to severe early childhood caries when we looked at the data using logistic regression. Children with S-ECC were much more likely to have low levels of ferritin and low levels of hemoglobin. Logistic regression analyses showed that children with S-ECC were almost twice as likely to have low ferritin levels and over six times more likely to have iron deficiency anemia compared to children without S-ECC.

Conclusion: In terms of nutritional health, children afflicted with severe early childhood caries (S-ECC) demonstrate a lower standard compared to children who do not have cavities. They are more likely to have low levels of vitamin D, calcium, and albumin, and higher levels of PTH. In addition, S-ECC is closely linked to anemia caused by lack of iron. For this reason, it is essential to concentrate on measures that can inhibit and cure ECC, as this can significantly improve a child's overall health and satisfaction.

Keywords: Severe Early Childhood Caries; Hb; vitamin D; MCV; iron deficiency anemia; PCV.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic review/ Meta- analysis

Code of Abstract: PBi-159

Topical administration of *Ferula persica* extract accelerates diabetic wound healing

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Abstract

Background and Aim: Diabetic wounds are one of the most important issues in diabetic patients. It seems that *Ferula persica* with antioxidant and anti-inflammatory potentials can be profitable for healing of diabetic wounds. The aim of present study was to investigate the topical administration of *Ferula persica* extract in diabetic wound healing.

Methods: Seventy-five diabetic male rats were randomly divided into 5 groups (n = 15), including: untreated (Control) group, Eucerin group, 2% *Ferula persica* ointment (FP 2%) group, 5% *Ferula persica* ointment (FP 5%) group, and Phenytoin group as a reference drug. Sampling was performed at days 7, 14 and 21 after surgery. Evaluation tests included stereology, immunohistochemistry, molecular, and biomechanical.

Results: Our results showed that the wound closure rate, volumes of newly formed of epidermis and dermis, density of fibroblasts and blood vessels, collagen deposition, density of proliferation cells, expression levels of TGF- β and VEGF genes, and biomechanical characteristics were significantly higher in extract groups compared to control and Eucerin groups, however, these changes were considerable in the FP 5% group ($P < 0.05$). This is while that the density of neutrophils and expression levels of TNF- α and IL-1 β genes in the extract groups, especially in the FP 5% group, were significantly reduced compared to control and Eucerin groups ($P < 0.05$).

Conclusion: Topical administration of *Ferula persica* extract, especially in 5% concentration, considerably accelerates diabetic wound healing.

Keywords: Diabetic wound; Wound healing; *Ferula persica* extract; Collagen biosynthesis.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-160

Investigating the impact of dietary iron and omega-3 PUFAs supplementation on hematopoiesis in a murine model

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Abstract

Background and Aim: Diabetes mellitus, a metabolic disorder characterized by chronic hyperglycemia, disrupts hematopoiesis, the process of blood cell formation. This imbalance, affecting red and white blood cells as well as platelets, contributes to diabetes-related complications. Iron, vital for hemoglobin and omega-3 PUFAs, known for anti-inflammatory properties, play key roles. Investigating the impact of iron and omega-3 PUFAs supplementation in a diabetic murine model becomes crucial for understanding their effects on blood cell dynamics. This study aims to provide insights into the intricate relationship between dietary factors and hematopoiesis in diabetes, holding potential clinical significance.

Methods: Male Wistar rats were given 40 mg/kg streptozotocin and a high - fat diet for 21 days to induce diabetes. Eight groups were used: diabetic and non-diabetic Controls, diabetics + iron, diabetics + n-3 PUFA, diabetics+ iron+n-3 PUFA, non- diabetics + iron, non-diabetic + n-3 PUFA, and non-diabetics + iron + n-3 PUFA. They received oral supplements for a month then Blood samples and bone marrow smears were taken after one month evaluate blood parameters

Results: It was found that the administration of iron and omega resulted in a decrease in the number of white blood cells in the Diabetic group compared to the control group and the number of red blood cells and platelets in the iron and omega group was reduced compared to the control group. In the bone marrow slide, an increase in myeloid precursors, myeloblast, and metamyelocyte was seen in the group of diabetic rats that received iron and omega compared to the control group

Conclusion: This research sheds light on the differential impacts of iron and omega-3 PUFAs supplementation on hematopoiesis. The findings suggest that omega-3 PUFAs supplementation may play a role in immune cell dynamics, while iron supplementation may primarily influence erythropoiesis. The study highlights the importance of considering the interplay between dietary components for optimizing blood cell composition and immune function. Further research is warranted to elucidate the underlying mechanisms and explore potential clinical applications.

Keywords: Diabetes; n-3 PUFAs; Iron.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-161

Assessment of atherogenic indicators and risk factors of coronary artery disease in diabetic patients Lorestan province in 1397 to 1400

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Abstract

Background and Aim: Given the role of atherogenic indices in cardiovascular diseases and the need for their specific study in diabetic patients, this study was conducted to describe the status of atherogenic indices and investigate their relationship with risk factors for cardiovascular diseases.

Methods: In this cross-sectional correlation study, diabetic patients in Khorramabad city were examined. Risk factors for cardiovascular diseases and atherogenic factors, including atherogenic index 1, atherogenic index 2, AIP (atherogenic index of plasma), and TYG (triglyceride- glucose index), were investigated. The relationship between age, BMI (body mass index), systolic blood pressure, diastolic blood pressure, and FBS (fasting blood sugar) with atherogenic factors was examined using Pearson's correlation analysis.

Results: A total of 187 patients were examined. Among these, 44.44% were found to have atherosclerosis based on angiography at the time of the study, 25.7% were confirmed to have atherosclerosis based on angiography at the time of the study, and 29.9% were admitted to other departments with a history of cardiovascular disease. The mean atherogenic index 1 in all patients was 3.405 (standard deviation 1.357), the mean atherogenic index 2 in all patients was 5.680 (standard deviation 3.217), the mean AIP in all patients was 0.693 (standard deviation 0.233). Systolic blood pressure, diastolic blood pressure, and FBS were positively and significantly correlated with all atherogenic factors ($P < 0.001$). The highest correlation was observed between FBS and TYG ($r = 0.743$), followed by the correlation between diastolic blood pressure and atherogenic index 1 ($r = 0.541$).

Conclusion: Among the risk factors for cardiovascular diseases investigated, systolic and diastolic blood pressure, as well as FBS, showed positive and significant correlations with all atherogenic factors, including lipid profiles and atherogenic indices. However, the correlation coefficients between these atherogenic indices were not significantly higher than those with simple lipid profiles. This suggests that at least in the examined samples in this study, atherogenic indices did not exhibit a preference over straightforward lipid profiles.

Keywords: Cardiovascular disease; Coronary Artery Disease; Diabetes.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic review/ Meta- analysis

Code of Abstract: PBi-162

Gestational diabetes insipidus and vasopressinase enzyme role; review article

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Abstract

Background and Aim: Vasopressin is one of the hormones produced in the hypothalamus, which is secreted from the posterior pituitary following the reduction of body water and the increase of plasma osmolality and affects the blood vessels and kidneys. Diabetes insipidus is a rare complication and various factors play a role in this disorder. The aim of this study is to find out the pathophysiological mechanisms for the development of gestational diabetes insipidus, diagnosis and treatment based on vasopressinase enzyme.

Methods: In this review article, articles using the keywords "diabetes insipidus, pregnancy, vasopressin, vasopressinase, ADH, AVP and gestation" in Web of Science, Scopus, Google Scholar, PubMed, and Magiran databases. It was collected and reviewed until 2022.

Results: Diabetes insipidus can include hormone secretion disorder (neurogenic diabetes insipidus), hormone receptor disorder (nephrogenic diabetes insipidus), excessive fluid intake (primary polydipsia) and increased hormone catabolism (gestational diabetes insipidus). The most common cause of gestational diabetes insipidus is the excessive activity of the vasopressinase enzyme, which leads to the destruction of the vasopressin hormone. Diagnosing diabetes insipidus in pregnancy can be challenging because it usually presents with symptoms of polydipsia and polyuria, which are often attributed to a normal pregnancy.

Conclusion: Gestational diabetes insipidus has various causes, the most common of which is excessive vasopressinase activity. Placental trophoblast produces vasopressinase and its level increases during pregnancy. Because desmopressin is N-terminally deaminated, it is resistant to vasopressin and is therefore the treatment of choice for gestational diabetes insipidus.

Keywords: vasopressin; diabetes insipidus; pregnancy; vasopressinase.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-163

The protective effects of *Curcuma longa* extract on oxidative stress markers in the liver induced by Adriamycin in rat

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Abstract

Background and Aim: The aim of the study was investigated the effects of *Curcuma longa* (*C. longa*) extract on Adriamycin-induced hepatotoxicity in rat.

Methods: Animals divided in six groups: Control (CO), Adriamycin (ADR), Adriamycin with Vitamin C (ADR + Vit C), Vitamin C (Vit C) and *C. longa* with Adriamycin (Cl+ ADR) and without Adriamycin (Cl- ADR). Hepatotoxicity induced by Adriamycin 5mg/kg and treated rats with *C. longa* 1000 mg/kg and Vitamin C 100 mg/kg, daily per oral for 4 weeks.

Results: In the liver tissue of ADR group, Malonyldialdehyde (MDA) level was increased significantly compared to CO group. MDA level in the treatment groups, Vit C, Cl+ ADR and Cl- ADR were increased significantly compared to ADR group and compared to ADR+Vit C group. Thiol level in ADR, ADR+Vit C and Cl+ ADR groups were decreased compared to CO group and also thiol level in Cl- ADR and Vit C were increased significantly compared to ADR group. The activities of CAT in liver tissue of ADR group were lower than CO group and increased in Cl- ADR, ADR+Vit C and Vit C groups comparison with ADR group.

Conclusion: The results showed that chronic administration of *C. longa* hydroalcoholic extract in Adriamycin - induced hepatotoxicity rats could decrease the oxidative stress injuries in liver tissue.

Keywords: Adriamycin; *Curcuma longa*; hepatotoxicity; oxidative stress; Hydroalcoholic extract; Rat.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-164

Investigating the relationship between SNCA expression level and insulin in in- vitro studies

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Abstract

Background and Aim: Alpha- synuclein is a protein that affects motor and cognitive abilities. This protein from the group of synuclein increase glucose absorption in fat cells and skeletal myocytes by activating a signaling pathway. As a result, following this function of this protein the expression of SNCA protein in muscle cells in response to insulin was investigated in the present study.

Methods: To conduct a study in an in vitro study model two types of IR and IS cells were cultured using C2C12 cells. Then glucose uptake was measured in both groups of cells from the culture of the cells. Finally, a quantitative real- time PCR test was used to evaluate the expression level of SNCA.

Results: The result of the experiments indicates that the expression of SNCA is decreased in insulin resistant C2C12 cells. According to studies it is possible to improve the response of insulin resistant cells to insulin by overexpressing SNCA.

Conclusion: Since non- insulin- dependent diabetes mellitus causes a decrease in the level of SNCA expression in muscle cells and on the other hand the role of this protein in increasing the level of glucose absorption is undeniable it can be concluded that SNCA can be insulin-dependent.

Keywords: Insulin resistant; Alpha- synuclein; real- time PCR tes; non -insulin- dependent diabetes mellitus.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-165

Investigating the relationship between SNCA expression level and insulin in in-vivo studies

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Abstract

Background and Aim: Alpha-synuclein is a protein encoded by the SNCA gene in humans. Alpha-synuclein is expressed in various tissues, especially the brain, and can cause motor-nervous disorders. SNCA increase the level of glucose absorption through the activation of pathway. This action prevents insulin-resistant conditions in cells. However, the precise mechanism of SNCA interaction with molecules in the insulin-related cellular pathway is not yet known. In this study, the effect of insulin resistance on skeletal muscle tissues of type 2 diabetic rats was investigated.

Methods: We separated 16 laboratory mice into 2 groups by high fat diet and streptozotocin in terms of health under certain environmental conditions. The control group is the reference for the experiments and the type 2 diabetic group on which changes were measured. From the animals studied in certain time intervals and a series of tests were conducted. Tests such as blood glucose tests that were taken from the tail of mice or plasma insulin that were performed by the immunosorbent method.

Results: The obtained results indicated that to expression level of SNCA in the muscle of diabetic mice decreased by about 30%.

Conclusion: The conducted studies indicate a decrease in SNCA plasma levels in the muscle tissue of diabetic mice due to their insulin resistance. As a result, it can be said that this protein plays a role in glucose metabolism in insulin-dependent cells.

Keywords: Alpha-synuclein; blood glucose tests; immunosorbent method; skeletal muscle tissues.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Review Article

Code of Abstract: PBI-166

The mesenchymal stem cells- derived secretome in cancer, a novel therapeutic approach

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Abstract

Cancer is a leading death reason worldwide, and due to the growing aging population, it is a rising health problem. Using stem cells has provided novel approaches in treating cancer. Mesenchymal stem cells (MSCs) secretomes via paracrine signaling, which have the same impact as MSCs, as well as having the benefits of remarkable reparability, negligible immunogenicity, and targeted delivery. In this review, the obtaining procedures, characteristics, biological activities, and recent discoveries regarding the influence of MSCs secretomes in cancer therapy, and a summary of inhibiting as well as promoting role of these cells on cancer progression is provided.

Keywords: Mesenchymal stem cells (MSCs); Secretomes; Cancer; Cell therapy.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-167

Oleuropein improves autistic- like behaviors, histopathological changes, oxidative stress characteristics and molecular levels in the cerebellum of autism model rats

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Abstract

Background and Aim: Autism is a behavioral developmental disorder that is associated with deficits in social interactions, limited and repetitive patterns of behaviors and interests. The present study aimed to investigate the effect of oleuropein, as a strong antioxidant, on the improvement of autistic - like behaviors, histopathological changes, oxidative stress characteristics and molecular levels in the structure of the cerebellum of autism model rats.

Methods: In this study, 12 Wistar rats were divided equally into four groups after confirming pregnancy. The groups include: the control group (did not receive any intervention and were kept until the end of pregnancy and the birth of the babies); The valproic acid group (received a single dose of valproic acid (600 mg/kg) on day 12/5 of pregnancy and then they were kept until the end of pregnancy and the birth of the babies); The valproic acid + oleuropein group received oleuropein (20 mg/kg between days 6.5 to 18.5 of pregnancy) and on day 12.5 of pregnancy they were prescribed a single dose of valproic acid and until the end and birth babies were kept); Oleuropein group (in the period from 6.5 to 18.5 days of pregnancy, they received oleuropein (20 mg/kg) and were kept until the end and birth of the babies). After the end of pregnancy, 15 male baby mice born in each group were randomly selected and the babies were kept for 40 days, and between the ages of 30 and 40 days, they were subjected to behavioral tests (Rotarod and Open Field) were taken and then annihilated to remove the cerebellar structure. Evaluations include histological and stereological, immunohistochemistry (apoptosis for Caspase3 protein), expression of inflammatory (TNF- α , IL-1 β and IL-6) and anti - inflammatory (IL-10) genes by qRT-PCR method, and indicators Biochemicals were antioxidant (SOD, CAT and GSH) and oxidant (MDA).

Results: Oleuropein in autistic animals caused a significant inhibition in reducing the total volume of the cerebellum and its different layers and the density of Purkinje cells. In all behavioral tests, anti -inflammatory gene expression and antioxidant indices, the group of autistic animals receiving oleuropein were significantly better compared to the valproic acid group. Also, regarding apoptosis, the expression of inflammatory genes and the oxidant index, the results indicated a significant increase in the valproic acid group, while they were significantly decreased in the autism group receiving oleuropein.

Conclusion: Administering oleuropein during pregnancy inhibits the development of autism and improves autistic -like behaviors, histopathological changes, oxidative stress characteristics and molecular levels in the cerebellum.

Keywords: Autism; Oleuropein; Antioxidant.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBi-168

Mesenchymal stem cell injections for osteoarthritis: a systematic review of pain reduction, functional improvement, and disease progression

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Abstract

Background and Aim: Osteoarthritis, a degenerative joint disease characterized as “wear and tear” arthritis, afflicts increasingly larger populations as lifespans lengthen. This progressive condition causes functional decline, diminished quality of life, and substantial healthcare burdens. Mesenchymal stem cell (MSC) therapies, with their anti-inflammatory, immunomodulatory, and regenerative properties, hold promise as a potential treatment strategy. This systematic review evaluates the current evidence for MSC injections in alleviating pain, improving functionality, and potentially slowing disease progression in adult osteoarthritis patients.

Methods: A comprehensive search across PubMed, Science Direct, Access Medicine, and Iceberg was conducted using keywords like "mesenchymal stem cells," "osteoarthritis", "stem cell therapy", and "degenerative joint disease". Only English- language human trials published since 2017 were included. A total of 25 studies met the inclusion criteria for analysis.

Results: Clinical outcomes such as pain levels, joint function, and tissue regeneration were assessed using validated scales like WOMAC and KOOS, while imaging techniques monitored disease progression. Studies investigating MSC injections in arthritic joints demonstrated positive clinical outcomes, including significant pain reduction, improved joint function, and evidence of tissue regeneration.

Conclusion: While these results are promising, the translation of MSC therapy from research to clinical practice necessitates more robust evidence. Large- scale, long-term randomized controlled trials are crucial to solidify the findings and optimize MSC-based therapy for broader implementation in treating osteoarthritis and its debilitating effects.

Keywords: Mesenchymal Stem Cells; Osteoarthritis; Pain Management; Functional Improvement; Disease Progression.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PBi-169

The diagnosis role of humanin in diabetes mellitus

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Abstract

Background and Aim: Diabetes mellitus (DM) is one of the threats to human comprehensive health, which is characterized by the dysfunction of beta cells (β cells) of the pancreas. High level of glucose (HG) causes apoptotic cell death and disturbances in insulin secretion. Humanin (HN) is considered as a new cell protective mitochondrial hormone in DM and shows a protective role in islet cell apoptosis and May has detective ability in DM diagnosis.

Methods: We selected the characteristic Humanin and Diabetes mellitus keywords from Mesh in NCBI. Then we search Humanin and Diabetes mellitus in Scopus and PubMed databases to publish a specific subject about DM diagnosis. In the following, the gained and related articles are summarized and discussed.

Results: The results of studies prove that humanin induces glucose tolerance metabolism in in vitro and in vivo studies. Recent studies have shown that HN inhibits beta cell apoptosis and islet inflammation and delays the pathological progress of diabetes and significantly increases insulin sensitivity in different body organs and prevents hyperglycemia.

Conclusion: Therefore, considering the protective role of this mitochondrial peptide in the treatment of diabetes and preventing the death of pancreatic beta cells, it is expected that the expression and secretion of this protein is significantly reduced in people with diabetes, which can be a warning factor. The donor is effective in early diagnosis of diabetes and prevents further pathological damage.

Keywords: Humanin; Diabetes mellitus; β cells.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PBi-170

The role of conditioned medium from dental pulp stem cells in dental diseases

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Abstract

Background and Aim: As regenerative medicine evolves, the search for more efficient and effective approaches continues. One of the most favorable regenerative medicine procedures is the employment of autologous mesenchymal stem cells. The dental pulp is a promising source of such stem cells with self-renewal, multilineage differentiation capabilities, and relatively easy access. However, the clinical application of stem cells faces several challenges, and the grafted cells will not last long. Therefore, researchers have been investigating the effects of dental pulp stem cell conditioned medium (DPSC-CM), which contains various trophic factors and cytokines. In this literature, we will review the role of DPSC-CM in dental diseases.

Methods: An extensive search was conducted in PubMed and Google Scholar databases, using the following keywords: "dental pulp stem cells," "conditioned medium "and" dental diseases." Related articles published until October 2023 was selected.

Results: The application of DPSC-CM was assessed in various conditions including medication-related osteonecrosis of the jaw (MRONJ), oral cancer, dentin- pulp complex regeneration, periodontitis, atrophied submandibular gland, and orthotopic dental pulp regeneration. DPSC-CM assists the damaged tissue through paracrine means. Following the application of DPSC-CM, an increase in stem cell markers and anti-inflammatory cytokines and a decrease in inflammatory cytokines is expected. Moreover, the level of vascular endothelial growth factor (VEGF) elevates as well. Although this factor is beneficial in tissue remodeling and plays a significant role in regenerative dentistry, it has adverse effects on cancer treatment. In an oral cancer study, DPSC-CM also increased Ki-67 expression, demonstrating the potential for cancer progression. The outcomes were promising except in the case of oral cancer.

Conclusion: DPSC-CM exhibits considerable potential in dental disease treatment. However, more comprehensive studies are required to explore its other applications and better evaluate its influence on oral cancers.

Keywords: Dental pulp stem cells; conditioned medium; dental diseases.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Biochemistry

Presentation Type: Poster

Abstract Type: Review Article

Code of Abstract: PBI-171

Is there any relevance between early childhood caries and maternal caries status? A review

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Abstract

Background and Aim: Early childhood caries (ECC) is a significant oral health concern that is particularly prevalent among socially disadvantaged populations. This issue has global implications and affects infants and preschool children. The incidence of ECC varies among different groups, with lower-income populations reporting a prevalence of up to 85%. ECC primarily affects children aged between 71 months, where one or more decayed, missing, or filled primary teeth are present. Several factors contribute to the high prevalence of ECC, including inappropriate feeding practices, the socioeconomic background of the family, lack of parental education, and limited access to dental care. The objective of this review is to provide a comprehensive overview of ECC patterns and to assess the association between maternal caries experience and other relevant factors.

Methods: A comprehensive search was conducted in various scientific databases, including PubMed, Scopus, Web of Science, the Cochrane Library databases, and Google Scholar. The focus of the search was on English studies that discussed oral health conditions in mothers and ECC. Two authors were involved in the process of assessing the internal validity of the selected articles. This assessment was carried out in accordance with a previously published guideline, which consisted of eight questions, with each question being assigned one point. Based on the quality assessment, the included studies were categorized into three groups: low methodological quality (1-3 points), moderate quality (4-6 points), or high quality (7-8 points). This categorization was done to determine the methodological rigor of the studies. In addition to assessing the methodological quality, the GRADE methodology was employed to evaluate the quality of evidence derived from the selected studies. This approach allowed for a systematic and standardized assessment of the strength of the evidence.

Results: The association between maternal and child dental caries has been established as a robust correlation, whereas no such correlation has been observed between dental caries of other caregivers and the children under their supervision. The current study has identified that the number of cavities in a mother and her educational attainment are significant predictors of early childhood caries. Logistic regression analysis has revealed that increased consumption of sugary beverages, younger maternal age at the commencement of the study, higher levels of tooth decay at the outset, and cohabitation with more individuals were all significant factors ($P < 0.05$) that increased the risk of certain outcomes. The correlation between the number of decayed, missing, or filled teeth in mothers and children was only observed through negative binomial regression.

Conclusion: The relationship between maternal caries and ECC has been firmly established. A considerable number of mothers exhibit a lack of knowledge regarding the early development of caries and the factors that contribute to its occurrence. Considering that mothers play a crucial role as the primary transmitters of caries, it is of utmost importance to implement preventive educational initiatives focused on oral health within maternal-infant health units.

Keywords: ECC; early childhood caries; maternal caries.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Biochemistry

Presentation Type: Poster

Abstract Type: Review Article

Code of Abstract: PBi-172

The relationship between vitamin D, iron deficiency anemia, and severe early childhood caries: A Review

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Abstract

Background and Aim: Severe Early Childhood Caries (S-ECC) negatively impact the well-being and joy of young children. Limited research has been conducted on this subject, but evidence suggests that children suffering from S-ECC may have a higher likelihood of experiencing malnourishment. Iron deficiency being the most common nutritional deficiency in childhood is often seen associated with severe caries destruction. Not having enough iron is a very common problem with people's diets around the world, especially in poorer countries. In some cases, adding extra iron salts to some foods can help to improve this deficiency. A high prevalence of tooth decay is often observed in areas with insufficient iron levels among the population. This systematic review had 2 objectives: 1) to determine whether there exists a correlation between vitamin D levels and S-ECC. 2) To investigate an association between S-ECC with iron deficiency anemia (IDA).

Methods: Scientific articles were searched in PubMed, Scopus, Web of Science, and Google Scholar. English studies were included if mentioning the level of vitamin D, hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration, and packed cell volume (PCV) in S-ECC and caries-free children.

Results: Children with S-ECC were much more likely to have vitamin D levels that were lower than the recommended amounts for the best and satisfactory health. Multiple regression analysis showed that severe early childhood caries, not drinking milk often, and the winter season was related to having lower 25(OH) D levels. Having low levels of vitamin D, low household income, and thinking the child's health is not good were linked to severe early childhood caries when we looked at the data using logistic regression. Children with S-ECC were much more likely to have low levels of ferritin and low levels of hemoglobin. Logistic regression analyses showed that children with S-ECC were almost twice as likely to have low ferritin levels and over six times more likely to have iron deficiency anemia compared to children without S-ECC.

Conclusion: In terms of nutritional health, children afflicted with severe early childhood caries (S-ECC) demonstrate a lower standard compared to children who do not have cavities. They are more likely to have low levels of vitamin D, calcium, and albumin, and higher levels of PTH. In addition, S-ECC is closely linked to anemia caused by lack of iron. For this reason, it is essential to concentrate on measures that can inhibit and cure ECC, as this can significantly improve a child's overall health and satisfaction.

Keywords: Severe Early Childhood Caries; Hb; vitamin D; MCV; iron deficiency anemia; PCV.





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Tehran University of Medical Sciences, Tehran, Iran.
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4. Genetics (Oral Presentations)





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OG-1

Identifying Potential Biomarkers for Early Diagnosis of Fulminant Myocarditis in Pediatric Patients: Role of sEVs

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Abstract

Background and Aim: The most severe form of myocarditis, known as fulminant myocarditis (FM), has the potential to cause multiple organ failure and a high mortality rate. Guidelines strongly advise that individuals diagnosed with FM should receive immediate treatment to improve their prognosis. Despite its high diagnostic accuracy, endomyocardial biopsy is an expensive, non-effective, and most importantly, an invasive standard procedure for patients. It poses challenges in pediatrics. Cardiac MRI has advanced significantly in recent years, and is now broadly considered a valuable diagnostic tool for myocarditis. Therefore, endomyocardial biopsy is commonly employed as an alternative diagnostic procedure. Although cardiac MRI may not always be feasible in emergency cases, it remains the preferred diagnostic method. However, due to the difficulties with patient cooperation, it is generally not recommended for critically ill children. Given the rapid onset and development of fulminant myocarditis in pediatric patients, it is imperative to identify a dependable and precise marker with quick results to distinguish between the two ailments. The link between the incidence of myocarditis and the varying expression of sEVs-RNAs in small extracellular vesicles (sEVs) present in the blood of patients has enabled the early detection and diagnosis of fulminant myocarditis. Research has shown the vital role of small extracellular vesicles (sEVs) in a number of different diseases.

Methods: Data relating to RNA expression in sEVs from plasma samples were sourced from the www.ncbi.nlm.nih.gov database for five children diagnosed with FM (GSM7074660, GSM7074661, GSM7074662, GSM7074663, GSM7074664) and five healthy children (GSM7074665, GSM7074666, GSM7074667, GSM7074668, GSM7074669). All bioinformatics analyses were conducted using R version 3.6.3. The HTSeq fragments were downloaded for the data, and normalization was applied using the DESeq2 method, considering $P < 0.05$ to be statistically significant.

Results: The findings of the data analysis indicate a significant decrease in the expression of genes of the NADH dehydrogenase family (MT-ND) in patients when compared with normal individuals. Among these genes, MT-ND1 had the highest decrease ($\log_2FC = -4.229$, $p\text{-value} = 2.4e-4$). Some ribosomal protein family members, namely RPLP1, RPL3, RPL11, RPL13, RPL23, RPL26, RPL27, RPL31, RPL32 and RPL36, exhibited a significant decrease in gene expression with the highest expression decrease in ($\log_2FC = -2.748$, $p\text{-value} = 0.004$). Notably, the patient group showed a reduced expression of genes encoding α - and β -globin chains, including HBA1 ($\log_2FC = -2.492$, $p\text{-value} = 0.006$), HBB ($\log_2FC = -2.339$, $p\text{-value} = 0.011$), and HBA2 ($\log_2FC = -2.894$, $p\text{-value} = 0.015$) when compared to the control group. The data indicate that in patients, the expression of the gene TMSB4X, which is involved in actin polymerization, is suppressed ($\log_2FC = -2.153$, $p\text{-value} = 0.014$), whilst the expression of three genes is significantly increased. One of these genes is galectin 9 (LGALS9) ($\log_2FC = 2.992$, $p\text{-value} = 0.018$), which is part of the beta-galactoside-binding protein family and has a role in modulating interactions between cells and the extracellular matrix. The expression of two myeloperoxidase (MPO) genes ($\log_2FC = 3.419$, $p\text{-value} = 0.041$), as well as PHD finger protein 23 (PHF23) ($\log_2FC = 3.509$, $p\text{-value} = 0.04$), which encodes binding factors for metal ions, has been observed to increase in response to white blood cell activity and autoimmune reactions.

Conclusion: Despite recent progress in the study of myocarditis, there remain significant difficulties in its diagnosis and treatment. Our results indicate that individuals with this disease exhibit significant differences in protein expression and defects in cellular signaling pathways, including post-translational protein modification and neuropeptide signaling, as well as proteasome-mediated ubiquitin-dependent protein breakdown. Therefore, the findings indicate the importance of genetic factors in health and disease. Gene involvement appears crucial in the development of various diseases, and employing gene panels for disease diagnosis can prove beneficial.

Keywords: Fulminant Myocarditis (FM), Pediatric, Diagnosis, RNA-Seq.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Genetics

Presentation Type: Oral

Abstract Type: Case Report

Code of Abstract: OG-2

Biallelic Variants in the AGR2 Gene Cause Cystic Fibrosis-like Presentation: A Case Report

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Abstract

Background and Aim: An autosomal recessive disorder, cystic fibrosis (CF) is characterized by a pathogenic variant in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Some patients, however, exhibit clinical features resembling CF without possessing a pathogenic variant of the CFTR gene. A biallelic variant in the anterior gradient 2 gene (AGR2) is one of these genetic causes. AGR2 is involved in the folding and secretion of proteins, and disruption of this process may cause symptoms similar to those associated with CF. We present a case report of a 6-year-old female patient with symptoms resembling cystic fibrosis-associated syndrome, along with hypogammaglobulinemia.

Methods: It is a case report study.

Results: The patient experienced persistent coughing, excessive sweating, lung involvement, respiratory and digestive problems, hypogammaglobulinemia, and recurrent urinary tract infections. There was a gradual reduction in IVIG treatment. The results of the tests revealed nasal inflammation, esophageal and duodenal inflammation, and pneumonia. The results of blood tests consistently showed an abnormal white blood cell count and lower blood parameters. Tests for sweat and fungal diseases were negative. In addition to developmental delays, the patient displayed signs of immunodeficiency. The patient was found to have a homozygous anterior gradient 2 gene mutation, while his parents and sister were heterozygous carriers. This is the second publication reporting patients with AGR2. Cystic fibrosis patients' IgG levels indicate the severity of the disease. Hypogammaglobulinemia and antibody deficiency patients may benefit from monitoring and IVIG therapy to prevent further lung deterioration.

Conclusion: In this case, hypogammaglobulinemia is unusual for anterior gradient 2 gene-related CF-like syndromes, suggesting the need for further investigation into the underlying cause. It is important to consider other genetic or immune-related disorders.

Keywords: cystic fibrosis; anterior gradient 2 gene; CF-like syndrome; hypogammaglobulinemia; immunoglobulin G.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Oral

Abstract Type: Systematic Review/ Meta-Analysis

Code of Abstract: OG-3

A meta-analysis of the association between the SLC6A4 gene polymorphisms and Major depressive disorder (MDD)

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Abstract

Background and Aim: Major depressive disorder (MDD) has been ranked as the third cause of the burden of disease worldwide in 2008 by WHO, which has projected that this disease will rank first by 2030. It is diagnosed when an individual has a persistently low or depressed mood, anhedonia or decreased interest in pleasurable activities, feelings of guilt or worthlessness, lack of energy, poor concentration, appetite changes, psychomotor retardation or agitation, sleep disturbances, or suicidal thoughts. Major depression significantly affects a person's family and personal relationships, work or school life, sleeping and eating habits, and general health. A person having a major depressive episode usually exhibits a low mood, which pervades all aspects of life, and an inability to experience pleasure in previously enjoyable activities. The etiology of depression is not yet fully understood. The biopsychosocial model proposes that biological, psychological, and social factors all play a role in causing depression. Genes play a major role in the development of depression. Family and twin studies find that nearly 40% of individual differences in risk for major depressive disorder can be explained by genetic factors. Like most psychiatric disorders, major depressive disorder is likely influenced by many individual genetic changes. A number of studies have reported an association between the polymorphisms of serotonin transporter gene (SLC6A4/5-HTT) and MDD.

Methods: Electronic searches were performed using PubMed. In the extensive electronic literature search, keywords "SLC6A4 gene", "rs25531" polymorphism and "Major depression disorder", "MDD", "meta" were searched for prospective studies. The pooled effect sizes (ORs) along with 95% confidence intervals (CIs), in participant groups for this polymorphism. Further subgroup analyses were conducted if the data were available.

Results: A meta-analysis done with STATA on 7 studies revealed that the SLC6A4 gene has a significant effect on MDD with reported pooled OR of 1.07; 95% CI = (1.13-1.01) and a p-value of 0.00 which rules out the null hypothesis which means that it has significant effect on MDD. For heterogeneity $I^2 = 40.01\%$ and $H^2 = 1.67$ which indicates that there is a moderate amount of heterogeneity.

Conclusion: These results overall indicate strong evidence against the null hypothesis. (The null hypothesis is a typical statistical theory that suggests that no statistical relationship and significance exists in a set of given single observed variables, between two sets of observed data and measured phenomena.).

Keywords: Meta-analysis; SLC6A4 Gene Polymorphisms; Major depressive disorder; MDD.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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Section: Genetics

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OG-4

Unraveling Neuroimaging Insights in Developmental Epileptic Encephalopathy Type 25: A Comprehensive Review of Reported Cases and Novel SLC13A5 Gene Variants

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Abstract

Background and Aim: Developmental and epileptic encephalopathy type 25 with amelogenesis imperfecta (DEE25) is a rare autosomal recessive disorder resulting from homozygous or compound heterozygous variants in SLC13A5. These variants can disrupt energy production and delay brain development, leading to DEE25. Key symptoms include refractory seizures, often manifesting in neonatal or early infancy, along with global developmental delay, intellectual disability, progressive microcephaly, ataxia, spasticity, and speech difficulties. Dental anomalies related to amelogenesis imperfecta are common. Prior studies typically reported normal or minimally altered early-life brain magnetic resonance imaging (MRI) findings in DEE25. However, our investigation identified a homozygous splice donor variant (NM_177550.5: c.1437+1G>T) in SLC13A5 through Whole-exome Sequencing in two affected siblings. They displayed developmental delay, cerebral hypotonia, speech issues, recurrent seizures, mild constant microcephaly, and motor impairments. Significantly, one patient exhibited novel brain MRI findings at age 5, including previously unreported extensive persistent hypomyelination, while another showed substantial loss of cerebral white matter in the frontoparietal region and delayed myelination. These discoveries broaden the DEE25 imaging spectrum and highlight the clinical heterogeneity even within siblings sharing the same mutation.

Methods: Ten milliliters of whole blood were collected from both healthy and affected family members. The salting out protocol was employed to isolate lymphocyte genomic Deoxyribonucleic Acid (DNA). Following this, genomic DNA was randomly fragmented, and the Nextera Rapid Capture Exome kit, comprising over 340,000

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specific probes, was utilized to target all 214,405 exons from known genes, covering an approximate span of 37 megabases (Mb). Ultimately, Whole-Exome Sequencing was carried out using the Illumina HiSeq 4000 platform, achieving an average coverage depth exceeding 100X. For bioinformatics analysis, an in-house pipeline was employed.

Results: A five-year-old girl, Patient 1 (P1), exhibited developmental delay, cerebral hypotonia, delayed speech, motor impairment, recurrent seizures, and borderline head circumference, prompting further investigation. Her 21-month-old male sibling (P2) displayed similar phenotypes, including developmental delay, motor and speech delay, truncal hypotonia, and recurrent seizures. Both patients had uneventful vaginal deliveries but had not achieved their normal developmental milestones at the time of the study. As a result, a homozygous splice donor variant in SLC13A5, specifically [NM_177550.5: c.1437+1G>T; (chr17-6690778 C>A) (GRCh38/hg38)], was detected in P1 through Whole Exome Sequencing (WES). Subsequently, the c.1437+1G>T variant was verified in P2 and both parents using Sanger sequencing.

Conclusion: Our study reveals a novel splice site homozygous variant in SLC13A5 causing DEE25, presenting novel MRI findings: extensive persistent hypomyelination, frontoparietal white matter loss, and permanent hypomyelination. Variability in clinical presentation among siblings with the same variant highlights disease heterogeneity. Expanding the clinical and genetic spectrum, including investigating nonsense, frameshift, or splice site variations, can enhance DEE25 diagnosis and severity understanding.

Keywords: DEE25; Developmental and Epileptic Encephalopathy; SLC13A5; Hypomyelination.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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Section: Genetics

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OG-5

Familial vs. sporadic multiple sclerosis: YAP1 gene expression profile in an Iranian population

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Abstract

Background and Aim: Multiple sclerosis is an autoimmune inflammatory disease that affects the brain and spinal cord, causing the destruction of myelin and varying degrees of axonal degeneration. Many molecular mechanisms control the process of myelination in the nervous system. Alterations in each of these regulatory mechanisms lead to the impaired myelination. The Hippo signaling pathway is an important mediator of myelination in the nervous system and might contribute to the pathophysiology of MS.

Methods: This study examined via qPCR the RNA expression of YAP1 in the peripheral blood of 35 sporadic, 37 familial MS patients; and also 34 healthy first-degree relatives of the familial MS patients (HFR) and 40 healthy individuals without a family history of the disease (control). Statistical analysis was performed using the SPSS 26. Typically, the one-way ANOVA was used to test for expression differences among four study groups. Independent sample t-test was used to compare the expression variations between MS patients and control groups.

Results: Comparison of the relative expression of YAP1 in the four groups showed a decrease in the expression of familial and sporadic patients, as compared to the HFR group (p-value 0.02, 0.01 respectively). Regarding these differences in the expression level, the control group was expected to show differential relative expression in comparison with the HFR group. There was such a difference in the expression level, but it was not statistically significant.

Diagnostic test evaluation was performed for the YAP1 gene whose expression had changed significantly in the defined groups, by ROC curve and AUC calculation. In this case, AUC did not change significantly.

Conclusion: Overall, these findings suggest that YAP1 gene may play a potential role in the pathophysiology of the sporadic and familial forms of MS. Confirmation of different gene expression patterns in sporadic and familial MS groups may have obvious implications for the personalization of therapies in the disease.

Keywords: Multiple Sclerosis, Myelination, YAP1, Biomarker.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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Section: Genetics

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OG-6

Variables affecting fetal fraction in women in Ahwaz in the year 1402

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Abstract

Background and Aim: Noninvasive prenatal testing is a screening method to determine the risk for the fetus being born with certain chromosomal abnormalities, such as trisomy 21, trisomy 18 and trisomy 13. This testing analyzes small fragments of DNA that are circulating in a pregnant woman's blood. Unlike most DNA, which is found inside a cell's nucleus, these fragments are free-floating and not within cells, and so are called cell-free DNA (cfDNA). These small fragments usually contain fewer than 200 DNA building blocks (base pairs) and arise when cells die off and get broken down and their contents, including DNA, are released into the blood stream. The aim is to analyze the variables such as maternal age, fetus age, gender of the fetus, twin pregnancy, weight and BMI of the mother, etc. affecting fetal fraction in the mother's blood.

Methods: To analyze the variables such as maternal age, fetus age, gender of the fetus, twin pregnancy, weight and BMI of the mother, etc. affecting fetal fraction in the mother's blood. our research was done on 1150 patients that were referred for NIPT (non-invasive prenatal test) for various reasons such as maternal age higher than 35, high risk screening test in first or second trimester, history of trisomy in previous pregnancy(s) or by the patients request. questionnaire was filled by the patients which had the following variables: maternal and fetal age, BMI, smoking, multiple pregnancies, any medication use such as Heparin enoxaparin, multiple pregnancy.

Results: Our result show that the variables most affecting the FF are maternal age, age of the fetus and the weight of the mother that have a positive, positive and negative correlation respectively. The variables that didn't have significant effect were gender of the fetus, BMI, the conception method and twin pregnancies. The information was not given by the patients on smoking and any medicine usage hence the results for those is not valid.

Conclusion: The variables most affecting the FF are maternal age, age of the fetus, the maternal weight and trisomy.

Keywords: Fetal fraction; Maternal age; Gestational age; BMI; Trisomy.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OG-7

Evaluation of the promoter methylation status of the beta subunit of the IKK kinase (IKK- β) gene in multiple sclerosis patients who were treated with Interferon-beta

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Abstract

Background and Aim: Multiple sclerosis (MS) is a chronic autoimmune, inflammatory neurological disease of the central nervous system (CNS). Both genetics and epigenetics are thought to be involved in the pathogenesis of MS. The IKK kinase (IKK- β) which is located upstream of the NF- κ B signaling pathway plays a central regulator of the NF- κ B activation and consequently controls the inflammation. Therefore, this study aimed to investigate the methylation status of the IKK- β promoter gene in MS patients who had undergone Interferon-beta therapy.

Methods: Forty MS patients with the relapsing-remitting stage of the disease who were treated with the Interferon-beta medication were enrolled in this study. Also, six MS patients without taking the same drug along with 35 age-gender-matched healthy individuals with no history of autoimmune disease were recruited in this study. DNA-extracted blood samples were used for evaluation of methylation status using methylation-specific PCR (MSP) with special pair primers within the CpG island of the IKK- β promoter gene.

Results: Data showed that the promoter of the IKK- β gene in all MS patients and control samples is methylated in both homozygous and heterozygous forms. Non-methylated homozygous was not seen in any of the patient and normal samples. Meanwhile, no methylated patterns were seen in 2 normal individuals and 14 patient samples. Statistical analysis showed that the methylation pattern of CpG island is significantly different between control and MS samples. According to obtained data from the patient samples who had continuously taken Interferon-B, the IKK- β promoter was hyper-methylated homozygous in 64% and heterozygous patterns in 14% of MS patients. In contrast, only 21% of the control samples were methylated in that promoter gene by heterozygous genotype, and the rest were unmethylated heterozygous. Strangely, all six samples of MS patients who didn't take the Interferon-beta were unmethylated heterozygous.

Conclusion: Most studies on MS disease indicate that the expression level of NF- κ B transcriptional factor increases in MS patients, leading to inflammation. IKK- β gene is the most important regulator of the NF- κ B signaling pathway, whose promoter methylation was studied in this project. Non-methylation of the IKK- β gene increases the expression of NF- κ B, and this project has shown that the methylation process of the IKK- β gene promoter was increased significantly in most of the patients who were treated with Interferon-beta, which can be effective in reducing inflammation.

Keywords: Multiple Sclerosis; Methylation; IKK- β ; Methylation-specific PCR.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Oral

Abstract Type: Systematic Review/Meta analysis

Code of Abstract: OG-8

Development and applications of CRISPR/Cas9 for CAR-T cell therapy of cancers

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Abstract

Background and Aim: The technology of CRISPR/Cas9 gene editing be able to efficiently resolve the problem of inadequate source of T cells in chimerical antigen receptor-T (CAR-T) treatment and improve their anti-tumor abilities by knocking out the genes associated to the suppression of T cells activity.

Methods: We searched databases including of (Web of Science/MEDLINE/PubMed) to December, 2023. A comprehensive review included studies which focused on utilization of CRISPR/Cas9 for CAR-T cell therapy of cancers.

Results: CRISPR/Cas9 technology has prepared an effective approach to elevating the persistence and proliferation of CAR-T cells in the body. This technology has been used in CAR-T cells to generate a screen new target to progress the anti-tumor potential. CRISPR/Cas9 gene editing can also be used to make T cells with dual-targeting result to stop tumor immune escape and prevent recurrence and drug resistance progress during chemotherapy. This article briefly explains the design of CARs and basic structure and discusses current trends in the development of safer and more efficient CAR-T cells for the treatment of both solid and hematological malignancies and looks forward to future research possibilities.

Conclusion: CRISPR/Cas9 gene editing enables manufacturing of CAR-T cells with improved anti-cancer effects. Here, we review the development and applications of CRISPR/Cas9 technology in creating CAR T cells, disrupting inhibitory signaling to improve potency of harmless and more manageable new CAR T cells.

Keywords: CRISPR/Cas9, CAR-T cells, immunotherapy.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Oral

Abstract Type: Meta analysis

Code of Abstract: OG-9

Association of GSTP1 rs1695 polymorphism with chronic myeloid leukemia (CML); A meta-analysis

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Abstract

Background and Aim: In the past, numerous investigations have explored the correlation between polymorphisms in the glutathione S-transferase pi 1 (GSTP1) gene and the susceptibility to Chronic Myelogenous Leukemia (CML), producing disparate results. To address the discordance observed in various studies, we conducted a comprehensive meta-analysis focusing on the latest data pertaining to the relationship between GSTP1 gene rs1695 polymorphisms and the predisposition to CML.

Methods: Following systematic literature review was conducted until November 2023 in three data bases (PubMed, Web of Science, Scopus). Key words and search strategy consist of ("GSTP1" OR "rs1695") AND ("Chronic Myeloid Leukemia" OR "CML") AND ("single nucleotide Polymorphism" OR "SNP" OR "Genotype"). Case-control and cohort studies were included and non-English articles, animal studies, case reports, and review articles were excluded. Finally, the combined odds ratios (OR) and their respective 95% confidence intervals (CI) were calculated to ascertain the degree of association.

Results: Primary results involve 84 articles. after scanning and exclusion, in total, six case-control studies, comprising 972 cases and 1083 healthy controls, were identified for the rs1695 polymorphism. The pooled analysis revealed a noteworthy association between the rs1695 single nucleotide polymorphism (SNP) and CML across recessive ($P < 0.01$), allelic ($P < 0.01$), and AA vs. GG models ($P < 0.001$) in the comprehensive analysis.

Conclusion: The rs1695 polymorphism poses as a risk factor for CML across various genotype models and may constitute a predisposing Factor for the development of the disease.

Keywords: GSTP1; CML; SNP; Meta-analysis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OG-10

Comparison of MLPA and newly developed kits for the diagnosis of Spinal Muscular Atrophy

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Abstract

Background and aim: Spinal muscular atrophy (SMA) is a genetic neuromuscular disorder with an autosomal recessive inheritance pattern. The cause of SMA is a mutation in the survival motor neuron 1 (SMN1) gene. Homozygous deletion of the SMN1 gene accounts for 95% of SMA cases and SMN2 gene acts as a modifier of disease severity. Therefore, determining the copy number of SMN1 gene is the best method for SMA diagnosis. In this study, the performance of Trita SMA diagnostic kit V2, Trita Q-SMA Screening kit, and SALSA MLPA Probemix P460 SMA were investigated for determining the copy number of the SMN1 gene.

Methods: In order to evaluate the performance of Trita SMA diagnostic kit V2, Trita Q-SMA Screening kit, and SALSA MLPA Probemix P460 SMA, 392 samples were used in this study. The Trita SMA diagnostic kit V2 utilizes fluorescent-labeled primers and probes for the quantification of SMN1 and SMN2 gene copies. The Trita Q-SMA Screening kit uses Taqman probe technology to determine the number of SMN1 gene copies. Samples with inconclusive results in the Trita Q-SMA Screening kit were further tested using the Trita SMA diagnostic kit v1.

Results: Out of the 392 samples, 364 samples (92.8%) showed consistent results across three different kits. 28 samples (7.14%) displayed varying results. To determine the final result for these 28 samples, they were retested using MLPA and Trita SMA V1 diagnostic kits. The final result was based on a consensus reached by all three kits, which required the same result to be produced after three repetitions. Among the 28 samples, MLPA indicated that 17 samples were heterozygous and 3 samples were homozygous. In contrast, the other two kits showed that 19 samples were normal and only one sample was heterozygous. Overall, approximately 5.1% (20 samples) showed an extra copy deletion in MLPA, while 0.76% (3 samples) exhibited the deletion of one copy less than other kits. In 4 samples (1%), the MLPA results were confirmed by other methods. One sample showed conflicting results across the kits and was therefore excluded from the study.

Conclusion: All three kits had consistent results in 92.8% (364/392) of the samples. However, 5.1% (20/392) of the samples showed false positive results with the SALSA MLPA Probemix P460 SMA kit, and 0.76% (3/392) showed false negative results. The obtained results are consistent with the results obtained from other studies, which may be due to potential mutations in the binding site of MLPA probes, resulting in a decrease in their signal and causing false positive results. In 0.76% (3/392) of the samples, false negative results were observed with the Trita SMA diagnostic kit V2.

Keywords: Spinal Muscular Atrophy, MLPA, SMN1.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OG-11

Genome instability associated Robertsonian translocation formation in SCID cells: Possible involvement of telomere shortening

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Abstract

Background and Aim: Severe combined immunodeficiency is a syndrome characterized with high radiation sensitivity, high background chromosomal breakage and genome instability. The aim of this study was to compare the frequency of Robertsonian translocation formation in *SCID* mouse cells compared to its wild type following irradiation with Gamma-rays.

Methods: Mouse *SCID* and *CB17* cells were cultured in standard culture media supplemented with fetal bovine serum and antibiotics. Cells at exponential growth state were irradiated by gamma rays generated from a Cobalt-60 generator and sampled at various time intervals. One hour before harvesting, cells were exposed to colcemid to arrest cells at metaphase. Cells were harvested and slides were made using standard protocol. Different whole paint chromosome probes were used for fluorescent in situ hybridization study for detection of Robertsonian translocations.

Results: Results showed high frequency of Robertsonian translocation in *SCID* cells compared to *CB17* before irradiation. Frequency of Robertsonian translocation increased considerably in *CB17* normal cells following irradiation at different time intervals ($p < 0.001$), but the frequency was not increased in radiosensitive *SCID* cells following irradiation.

Conclusion: Results might indicate involvement of high degree of genome instability in *SCID* cells that might overshadow the effect of ionizing radiation. High frequency of formation of Robertsonian translocation seen in *SCID* cells might be a result of telomere shortening or telomere deletion in *SCID* cells allowing joining of centromeres of two different chromosomes to form a Robertsonian translocation. High frequency of RB seen in *CB17* cells following irradiation might also be due to the effect of ionizing radiation on telomere, leading telomere shortening or deletion.

Keywords: Genome instability; *SCID*; Robertsonian translocation; ionizing radiation; telomere.





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4. Genetics (Poster Presentations)





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PG-1

The role of clinical genomics testing in the diagnosis of liver fibrosis

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Abstract

Background and Aim: Liver fibrosis is a complex progressive disorder characterized by the accumulation of extracellular matrix within the liver tissue. The two main causes of liver fibrosis are hepatitis C and non-alcoholic fatty liver disease (NAFLD). Early and accurate diagnosis of liver fibrosis is essential for effective treatment and prevention of disease progression. Genomic methods have been shown to be effective in improving the diagnosis of liver fibrosis. The aim of this study is to investigate the role of genomics in the diagnosis of liver fibrosis and the potential impact on clinical practice.

Methods: A review of the literature was conducted to collect and analyze studies focusing on the role of genome-wide association study (GWAS) approaches in liver fibrosis diagnosis.

Results: Susceptibility to liver fibrosis was associated with specific genetic variants and single nucleotide polymorphisms (SNPs) identified by GWAS. According to the GWAS results, individuals with hepatitis C-related liver fibrosis frequently have SNPs in IL28B (effective in viral response), TLR4 (hepatic satellite cell activation), casp1 (contributor to TLR4 signaling), MERTK (related to viral liver disease severity), and other genes. On the other hand, GWAS data in NAFLD patients have shown that SNPs in PNPLA3 (increased lipid accumulation and release of pro-inflammatory cytokines), IL17RA (hepatic stellate cell activation), MTTP (defective lipoprotein biosynthesis), etc., genes are important for fibrosis progression.

Conclusion: Genomics research has provided valuable insight into the diagnosis of liver fibrosis. It has the potential to identify molecular and genetic markers that can aid in early detection and individualized treatment strategies. The integration of genomics into clinical practice may improve diagnostic accuracy, facilitate disease monitoring, and guide therapeutic interventions.

Keywords: Genomics; Liver Fibrosis; Genome-wide Association Studies; Single Nucleotide Polymorphisms.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-2

Association between *IL-6* rs2069827 and Risk of Chronic Kidney Disease in a Sample of Southeast Iranian Population

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Abstract

Background and Aim: The human chromosome 7p21 locus contains a major gene that may contribute to the development of end-stage renal disease and variation in glomerular filtration rate. *IL-6*, a pro-inflammatory cytokine implicated in chronic inflammation, is a candidate gene for diabetic nephropathy. This study examined whether the *IL-6* rs2069827G/T polymorphism predicts chronic kidney disease (CKD) progression in Southeast Iranian patients.

Methods: An analysis of single nucleotide polymorphisms (SNPs) was done using a case-control study of 100 patients with CKD [estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m²] and 100 healthy controls (eGFR ≥60 ml/min/ 1.73 m²). The relative compliance risk was also predicted using odds ratios (OR) and 95% confidence intervals (CIs). Amplification Refractory Mutation System PCR (ARMS-PCR) was used for genotyping the variant. Additionally, odds ratios (ORs) and 95% confidence intervals (CIs) were used to predict the relative disease risk.

Results: Age (P=0.238) and sex (P=0.593) did not differ significantly between the studied groups. Neither cases nor controls deviated from Hardy–Weinberg equilibrium (HWE). In regards to blood urea nitrogen (BUN) levels, there was a significant difference between the study groups (P<0.001), which suggests the proper selection of study groups. After adjustment for body mass index, we observed that the presence of the T allele of rs2069827G/T increased the risk of CKD by 1.13-fold (OR = 1.13, 95%CI = 0.72–1.79, p = 0.008). Also, enhanced CKD risk was observed under codominant TT (OR = 2.38, 95%CI = 0.73-6.49, p = 0.049) and dominant GT + TT vs. GG (OR = 2.08, 95%CI = 1.15–3.77, p = 0.015) contrasting genetic models. We found a significant difference between CKD cases carrying GG+GT genotypes and those carrying TT genotypes regarding BUN and serum creatinine (P=0.043 and 0.012, respectively).

Conclusion: The *IL-6* gene polymorphism rs2069827G/T correlates with the progression of kidney disease in Iranians. The current findings need to be confirmed by studies on larger populations.

Keywords: Interleukin 6, Chronic Kidney Disease, Genetic association study, Polymorphism.

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Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-3

The long non-coding RNAs (lncRNAs) gene expression: MEG3 and H19 in obese women adipose tissues and its association with insulin resistance and obesity indices

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Abstract

Background and Aim: There are ample evidences regarding the role of MEG3 and H19, two lncRNAs in the pathomechanism of obesity and related disorders. Here, we evaluated the expression of MEG3 and H19 in visceral adipose tissues (VAT) and subcutaneous adipose tissues (SAT) of obese women (n = 18), in comparison to the normal-weight women (n = 17). Furthermore, we sought to identify the association of MEG3 and H19 expression in SAT and VAT with obesity parameters, insulin resistance, and the mRNA expression of possible target genes involved in adipogenesis and lipogenesis including peroxisome proliferator-activated receptor gamma (PPAR γ), fatty acid synthase (FAS), and acetyl-CoA carboxylase (ACC).

Methods: Real-time PCR was performed to evaluate the mRNA expression of the above-mentioned genes in VAT and SAT from all participants.

Results: The data revealed lower mRNA levels of H19 in SAT of obese women, comparing to the normal-weight women, while MEG3 expression was significantly higher in the SAT of the obese group rather than controls. Correlation analysis indicated that the transcript level of H19 had an inverse correlation with obesity indices and HOMA-IR values. However, MEG3 expression displayed a positive correlation with all the indicated parameters in all participants. Interestingly, a positive correlation was found between transcript level of MEG3 in SAT with FAS and PPAR γ . However, there was an inverse correlation between SAT expression of H19 and FAS.

Conclusion: It appears that lncRNAs, MEG3 and H19, are involved in obesity-related conditions. However, more clinical investigations are needed to clarify the relationships between lncRNAs with obesity and related abnormalities.

Keywords: Adipogenesis; Lipogenesis; Long non-coding RNAs; Obesity.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PG-4

MicroRNA dysregulation-related bortezomib sensitivity in multiple myeloma patients: A systematic review

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Abstract

Background and Aim: Multiple Myeloma (MM), a type of hematological malignancy with abnormal plasma cells, is diagnosed at the median age of 65. Renal injury, increased risk of infection, anemia, hypercalcemia, and destructive bone lesions are complications of this disease. Bortezomib, a proteasome inhibitor, is an approved therapeutic agent that induces apoptosis and cell cycle arrest in patients with plasma cell disorders and non-Hodgkin lymphomas. MicroRNAs, small non-coding RNAs, have gained much interest due to their role in diagnosis, prognosis, and drug resistance. This study overviews the roles of microRNAs and their related signaling mechanisms in the bortezomib sensitivity of MM patients.

Methods: A comprehensive search until October 1, 2023, in the PubMed database was done in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines using appropriate keywords. Non-English articles, book chapters, case reports, and review articles were excluded. All of the remaining articles were analyzed by title, abstract, and full-text where possible. An additional manual search was done in the reference list of the related articles.

Results: Of 144 initially identified articles, 6 publications met the inclusion criteria. According to the previous literature, the role of several microRNAs including mir15a, mir16, mir17, mir20a, mir27a, mir29b, mir137, mir197, mir202, and mir451 on bortezomib sensitivity of MM patients have been clarified. In vitro and in vivo studies illustrated that some of the aforementioned microRNAs, especially mir202, alter the bortezomib sensitivity by dysregulation of JNK/SAPK signaling pathway. Other mentioned microRNAs either inhibit the expression of CDK5 oncogene, MCL1, MDR1 or induce the expression of Sp1 transcription factor (TF). Thus, the elevated levels of the mentioned microRNAs may induce the bortezomib sensitivity of multiple myeloma patients.

Conclusion: Although few previous literatures have focused on the role of microRNAs in the bortezomib sensitivity of MM patients, the search results extended our knowledge about the subject. The role of microRNAs in the response to treatment is yet to be fully understood. Designing a laboratory panel for microRNAs based on the literature to evaluate the level of mentioned microRNAs prior to drug administration is suggested. Further assessment of the role of different miRNAs in diagnosis, prognosis, and drug resistance for hematological malignancies and solid tumors is also needed.

Keywords: multiple myeloma; plasma cell; bortezomib; drug resistance; microRNA.





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Venue:
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January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-5

Investigating the effect of probiotics on HT29 colorectal cancer cell line using MTT test method

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Abstract

Background and Aim: Colorectal cancer (CRC) remains one of the most recurrently occurring cancers worldwide. However, it has now become a predominant cancer and currently accounts for approximately 10% of cancer-related deaths in Western countries. Today, we know that probiotics play a significant role in intestinal health. Recently, probiotic bacteria are constantly being studied and their applications are also being considered in promising adjuvant treatments for various intestinal diseases. The functional mechanism of probiotics in cancers, including colon cancer, is through the induction of apoptosis. HT29 cell line will also be used in this study, HT29 cells is a human adenocarcinoma cell line.

Methods: In this research we use MTT test(3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide), to find the best therapeutic dose on HT29 cell line. For this test, we have three stages: Seeding, Treatment and MTT assay. 5000 to 10000 cells in each well were seed for 24 hours. then, we added supernatant in each well for 24 hours,48 hours and 72 hours. Next, supernatant was emptied from wells and PBS and MTT agent was added to the wells. After that, the cells were incubated at 37°C. after three to four hours the DMSO (dimethyl sulfoxide) was added to the wells to dissolved formazan crystals for 5 to 10 minutes. Finally, the absorption was investigated by ELISA reader at 570 nm. The one-way ANOVA and Tukey post hoc was used to calculate the changes. P<0.05 was considered as the significant levels.

Results: The obtained results are statistically significant and cell death is dose depended that is related to supernatant concentration and also is time depended. Actually, the IC50 results were 5.44% ,4.5% and 5.11% for 24-hour,48 hour and 72 hours respectively. The more time it is exposed the more cells underwent to lost.

Conclusion: Overall, in this study we identified These probiotic compounds were extremely lethal on HT29 cells. Besides the supernatant was able to inhibit colon cancer cell growth.

Also, our findings show that postbiotics stimulate the cell signaling pathway of apoptosis in HT29 colon cancer cells and can be used as a new therapeutic strategy itself or as an adjuvant therapy for the treatment of colon cancer.

Keywords: Probiotics; Colorectal Neoplasms; Cytotoxicity.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Case Report

Code of Abstract: PG-6

Managing Myelodysplastic Syndrome in a patient with Fanconi Anemia: A case report

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Abstract

Background and Aim: Fanconi anemia (FA) is an uncommon genetic condition characterized by bone marrow failure, chromosomal instability, and increased cancer susceptibility. Presented here is a case study of a patient diagnosed with FA who developed Myelodysplastic Syndrome (MDS).

Methods: It is a case report study.

Results: A 10-year-old boy with FA presented with a decline in platelet count and subsequent bone marrow abnormalities indicative of MDS. Flow cytometric analysis confirmed the diagnosis of MDS with excess blasts based on cytogenetic analysis with multiple chromosomal breaks. He underwent stem cell transplantation (SCT) using his father's full match. FA and its associated complications may be treated by SCT using a full match from a parent. Despite developing graft-versus-host disease (GvHD) and Cytomegalovirus (CMV) infection post-transplantation, the child has achieved complete normalization and has not shown signs of diarrhea or need for immunosuppressive medications.

Conclusion: In this case report, the author emphasizes the importance of multidisciplinary care and close follow-up for pediatric FA and MDS patients, suggesting the need for further research and standardization.

Keywords: Fanconi anemia; myelodysplastic syndrome; stem cell transplantation; graft-versus-host disease; cytogenetic analysis; flow cytometry.





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Venue:
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Section: Genetics

Presentation Type: Poster

Abstract Type: Case Report

Code of Abstract: PG-7

A case of adenosine deaminase 2 deficiency fatal to a nine-year-old girl with a family history

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Abstract

Background and Aim: Adenosine deaminase 2 (DADA2) is a rare genetic condition that causes inflammation in tissues, particularly in those that form blood vessels. Inflammation is a common reaction to injury or illness. A mutation in the Cat eye syndrome chromosomal region, candidate-1 (CECR1) gene causes DADA2. DADA2 absence is a monogenetic autoinflammatory disease that is inherited autosomal recessive. A mutation in the CECR1 gene results in the production of the enzyme protein DADA2. The reason for this is that DADA2 is derived from ADA2. The skin and nerve systems are frequently affected, while other systems, including the gastrointestinal tract, are less frequently affected. It has been reported that the majority of patients are pediatric; however, adult-onset patients have also been reported. This study investigates and reports on a case of DADA2.

Methods: It is a case report study.

Results: A 9-year-old girl was diagnosed with DADA2 and died due to a mutation in the CECR1 gene that is responsible for the synthesis of ADA. The patient's father also suffers from the same disease and exhibits similar symptoms. The patient's brother, who is now four years old, also appears to be suffering from mild symptoms. In this report, we describe the diagnosis of DADA2 in a family in Iran using PCR, Sanger sequencing, and next-generation sequencing (NGS) of the whole exome. A mutation in CECR1 was found to cause DADA2.

Conclusion: In order to manage and prevent major problems, early detection is essential. A thorough assessment of clinical phenotypes and molecular analysis can lead to the development of targeted therapies and precision medicine approaches. The genotype-phenotype relationship needs to be further investigated in order to develop therapeutic treatments. Prompt diagnosis and management are essential for preventing significant complications and morbidity.

Keywords: Adenosine Deaminase 2 Deficiency; Next Generation Sequencing; Cat eye syndrome chromosome region; Colchicine; Adalimumab.





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Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Case Report & Literature Review

Code of Abstract: PG-8

A case report and literature review of Otospondylomegaepiphyseal Dysplasia

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Abstract

Background and Aim: Otospondylomegaepiphyseal dysplasia (OSMED), also known as Weissenbacher-Zweymüller syndrome, is an autosomal recessive disorder caused by mutations in the COL11A2 gene. Fewer than 100 cases have been reported in the medical literature. Skeletal development, hearing, and craniofacial development are affected by OSMED.

Methods: It is a case report study.

Results: The case involves a 16-year-old Iranian boy who suffers from a variety of medical conditions. His knees, ankles, and limbs are deformed, and he experiences morning pains in these areas. The medical history of the patient revealed congenital deafness as well as a previous episode of fever and seizures. It should be noted that the boy's parents are related, and his 6-month-old sister, who had similar symptoms, has passed away. Among the findings of the physical examination are short stature, shortened limbs, elbow contractures, and various abnormalities such as enlarged knees and ankles, depression of the sternum, short arms, protruding eyes, a flattened nose bridge, and deformed fingers. The results of the X-ray showed enlarged joints, decreased thoracic vertebrae height, thoracic spine scoliosis, and thickened and fused wrist bones. Echocardiography and eye examination were normal, but audiometry revealed bilateral sensorineural hearing loss. A homozygous mutation in the COL11A2 gene led to the diagnosis of OSMED based on genetic testing.

Conclusion: A rare genetic disorder, OSMED is characterized by skeletal abnormalities, hearing loss, and distinct craniofacial features. Effective management requires early diagnosis and multidisciplinary approaches. The purpose of this case report is to highlight the importance of recognizing OSMED clinical manifestations and implementing appropriate interventions to improve the quality of life for individuals suffering from the disorder. In order to better understand the underlying mechanisms of the disease and explore potential therapeutic options, further research is required.

Keywords: Otospondylomegaepiphyseal dysplasia; Skeletal abnormalities; sensorineural hearing loss; COL11A2 gene mutation.





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January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-9

The Importance of Prenatal Diagnosis in the Identification of the Genetic Abnormalities

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Abstract

Background and Aim: Abortion is the termination of a pregnancy by the removal or expulsion of an embryo or fetus. Abortion is also used in the cause of health, which is called therapeutic abortion. Therapeutic abortion is recognized as one of the safest procedures in medicine to preserve the mother's health. The purpose of this study was to investigate the frequency of fetal genetic abnormalities as reasons for issuing therapeutic abortion licenses in Ilam province.

Methods: Data of this cross-sectional study collected from the files of pregnant mothers who refers to the legal medicine organization of Ilam province from March 2021 to February 2023 to obtain a therapeutic abortion license. The inclusion criteria for the study were to have a complete file, and incomplete files were excluded from the study.

Results: The most common fetal abnormalities leading to therapeutic abortion were central nervous system anomaly, Down syndrome, beta-thalassemia major, and hydrops fetalis.

Conclusion: The present study's findings highlight the crucial importance of genetic counseling and prenatal genetic testing to prevent the birth of children with genetic abnormalities and the associated treatment costs for both the family and government.

Keywords: Prenatal Diagnosis, Genetic Abnormalities, Therapeutic Abortion.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PG-10

MicroRNA dysregulation is associated with drug sensitivity in patients with diffuse large B-cell lymphoma; A Systematic Review

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Abstract

Background and Aim: Diffuse large B-cell lymphoma (DLBL), the most prevalent non-Hodgkin lymphoma (NHL), is an aggressive neoplasm of lymphoid origin. It occurs more in males and in the middle of 60s years of age. Fortunately, DLBL is highly sensitive to chemotherapeutic agents especially R-CHOP regimen which is a combination of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. However, the occurrence of drug resistance in some patients complicates the treatment process. MicroRNAs modulate several signaling and molecular pathways. Thus, their role in biological processes have gained significant interest. This study overviews the role of microRNA dysregulation in the drug resistance of DLBL cells.

Methods: A systematic search in PubMed database was performed in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines using following search syntax: ((Diffuse large B-cell lymphoma[MeSH Terms]) AND (mir[Title/Abstract] OR microRNA[Title/Abstract] OR microRNAs[Title/Abstract] OR "micro RNA"[Title/Abstract])) AND (sensitivity[Title/Abstract] OR chemoresistant[Title/Abstract] OR "chemo resistant"[Title/Abstract] OR resistance[Title/Abstract] OR response[Title/Abstract] OR efficacy[Title/Abstract] OR "CHOP-resistant"[Title/Abstract] OR "drug resistant"[Title/Abstract] OR "drug resistance"[Title/Abstract] OR chemosensitive[Title/Abstract] OR "chemo sensitive"[Title/Abstract]). Original and English articles were analyzed by title, abstract, and full text until January 1, 2023. Papers with not accessible full text were excluded. An additional manual search was also done in the reference list of included articles.

Results: The search results showed 57 related articles. 50 papers were excluded and 7 articles were finally analyzed. The included articles showed the effect of mir21, mir33a/b, mir34a, mir99a-5p, mir125b-5p, mir148b, mir155, and hsa-miR-548d-3p dysregulation in drug resistant DLBL. Studies revealed that downregulation of mir21 as well as upregulation of mir33a/b can sensitize DLBL cells against CHOP by targeting PTEN and PD-L1, respectively. On the other hand, other studies expressed that the downregulation of mir34a, mir148b, mir155, and hsa-miR-548d-3p are related to the drug resistant DLBL by targeting FOXP1, Ezrin, Wee1, and HoxA9 respectively. Feng et al. (2019) determined the microRNA profile of tumor extracellular vesicles (TEV) of chemo resistant DLBL cells using next generation sequencing prior to validation by quantitative real-time PCR on DLBL blood samples. They declared that an increase in TEV components of mir99a-5p and mir125b-5p can predict the chemotherapy efficacy and are associated with a poorer prognosis.

Conclusion: This study illustrated that microRNAs are important factors in drug resistance and drug sensitivity of DLBL cells. However, their role is yet to be fully understood. So, the evaluation of different microRNA levels in chemo resistant patients can explain the actual clinical significance of microRNAs. Besides, in-vitro studies evaluating microRNA components of TEVs can also resolve the ambiguities.

Keywords: diffuse large B-cell lymphoma; DLBL; drug sensitivity; drug resistance; microRNA.





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Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-11

Identification of genetic variants of recurrent hydatidiform mole in 3 Iranian families with consanguineous marriage by Whole Exome Sequencing

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Abstract

Background: Recurrent hydatidiform mole (RHM) is a rare and serious pregnancy disorder characterized by abnormal placental growth, which can lead to molar pregnancies and associated complications. Despite extensive research, the underlying cause of RHM remains unknown. Recent studies have suggested that genetic factors may contribute to the development of RHM. The objective of our study was to identify potential pathogenic variants in three Iranian families with RHM using a technique called whole-exome sequencing (WES).

Methods: In our study, WES was performed on DNA samples obtained from the probands of these three families. They had the appropriate criteria to participate in this study. Identified variant confirmation in the patient were performed using Sanger sequencing method.

Results: By conducting analysis, a novel splice donor variant (c.277+1G>A Intron 4/12) was found in NLRP7, and a frameshift variant (c.17_20delGGTT) in KHDC3L was identified which has already been reported. Additionally, our analysis revealed a novel frameshift variant (c.1273_1274del) in the C11ORF80 gene involved in meiotic recombination and chromosome segregation. This variant has not been previously reported and is considered a new finding in RHM.

Conclusion: This study attempted to provide new insight into the genetic basis of RHM and emphasizes the clinical utility of WES in identifying potentially pathogenic variants. Further validation of these results in larger cohorts and functional studies is needed to confirm their clinical significance and inform future treatment strategies. Other genes and factors responsible for RHM occurrence are remained to be discovered.

Keywords: Recurrent hydatidiform mole, *NLRP7*, *KHDC3L*, *C11ORF80*.





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Section: Genetics

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PG-12

Umbilical cord blood stem cells in the treatment of Major β -thalassemia

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Abstract

Background and Aim: β -thalassemia is a genetic disorder in which mutation leads to a decrease or absence of the synthesis of the beta hemoglobin chain. People with this disease need regular blood transfusions and chelation therapy. Currently, hematopoietic stem cell transplantation is considered the only and most effective treatment for β -thalassemia major. Umbilical cord blood is an available source of hematopoietic stem cells, which has many advantages and limitations. This article is an overview of the role of umbilical cord blood stem cells in the treatment of major β -thalassemia and the effectiveness of these stem cells in comparison with stem cells from other sources.

Methods: All the assembled data and information is the result of searching in reliable scientific resources, such as Science Direct, PubMed and Google Scholar using terms including “stem cells”, “umbilical cord”, “beta thalassemia major”, “treatment”, “bone marrow”, and “peripheral blood stem cells”.

Results: According to the transplant results, the 5-year overall survival (OS) and thalassemia-free survival in patients treated with umbilical cord stem cells are much lower than in patients who received stem cells from other sources, but when a combination of bone marrow stem cells and umbilical cord blood was used for transplantation, the OS and TFS increased significantly. Also, the results have shown that the incidence of GVHD in transplantation with umbilical cord blood stem cells was very low.

Conclusion: Umbilical cord blood is an abundant and available source of stem cells with high immunological immaturity, which makes it preferable to other sources of stem cells. According to the transplant results, the best suggestion for the treatment of beta thalassemia major is to use the combination of bone marrow sources with umbilical cord stem cells. today's research is looking for a method to increase the efficiency of these cells.

Keywords: β -Thalassemia Major; Umbilical Cord; Stem Cells; Transplantation; Treatment.





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Section: Genetics

Presentation Type: Poster

Abstract Type: Case Report

Code of Abstract: PG-14

The Dilemma of Whole Exome Sequencing and Breast Cancer Management: A Case Study

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Abstract

Background and Aim: Breast cancer is the most common type of female cancer and the leading cause of cancer-related deaths in women worldwide. A family history of cancer affects 10-20% of all BC patients. Genetic testing can help women with positive family history of breast cancer assess their risk and make informed decisions about prevention. We describe a 47-year-old woman with a breast tumor and a family history of breast cancer, whose mammogram results indicated a follow-up study (BIRADS III). She was referred by a surgeon for genetic counseling in preparation for a prophylactic mastectomy. Based on the patient's request, WES was ordered.

Methods: According to the WES results, to confirm the pathogenicity of the variant, in silico analysis was used. The reads were aligned with the public GRCh38 of the human genome assembly using the Burrows-Wheeler aligner (BWA). Variants (SNP and INDEL) were filtered Based on GATK-recommended criteria and passed through PalinVar workflow to preserve those of clinical significance. In summary, the filters only passed exonic or splice site variations with less than 1% frequency in the exome variant database, 1000 Genomes, which were not classified as benign in the clinical databases. The most recent ACMG criteria were used to assess the pathogenicity of the variations.

Results: Our analysis confirmed five likely pathogenic variants in *ATP8A2*, *FCGR3A*, *ALDH6A1*, *HES7*, and *POU6F2* genes. At the time of providing the results, all variants were categorized as likely pathogenic. None of these genes were associated with the 33 known breast cancer-causing genes. However, on a follow-up schedule, after 3 months, the status of the 3 likely pathogenic variants was changed into variants of uncertain significance (VUS) which complicated the uncertainty.

Conclusion: Although the WES may help with a decision for prophylactic measures, this could not be the case in some clinical scenarios. Based on the test's results, the index patient was not offered a prophylactic mastectomy by the surgeon and regular screenings surveillance were recommended. The case illustrates the limitations of the WES test, which can result in 20 to 30% false negative results. Therefore, patients must receive complete genetic counseling before undergoing any genetic testing to fully understand the test's benefits and limitations.

Keywords: Breast cancer; Genetic Counseling; Whole Exome Sequencing.





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January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-17

Genetic Investigation of Glutaric aciduria type 1 mutations

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Abstract

Background and Aim: Glutaric aciduria type 1 is an autosomal recessive inherited neurometabolic disorder caused by biallelic gene mutations in the GCDH gene, which leads to the glutaryl-CoA dehydrogenase deficiency. Enzyme malfunction leads to the accumulation of neurotoxic intermediate metabolites glutaric acid, 3-hydroxyglutaric acid, glutaconic acid, and glutarylcarnitine in body fluids and tissues, specifically within the brain. In the majority of untreated patients during the crucial period of brain development, intercurrent febrile illness, infection, or surgical intervention precipitates an acute encephalopathic crisis. The aim of this research is the identification of GCDH variants in 10 patients with glutaric aciduria type 1.

Methods: The blood sample was acquired from patients and their parents. Genomic DNA was extracted from peripheral blood leukocytes. Polymerase chain reactions (PCR) were performed. The Sanger sequencing was carried out for each exon individually, and after analysis the sequences were compared with reference genomic sequence to analyze the disease-associated variants.

Results: So far, a total of 3 variants, 2 of which were SNPs: heterozygote rs1060218 (G>T) in exon 11, heterozygote rs768221016 (C>T), an intron variant, and a homozygote pathogenic variant in exon 11 c.1147C>T (p.R383C), all previously reported. This research continues to investigate the pathogenic variants in the rest of the exons in the GCDH gene to provide the GCDH gene mutation spectrum.

Conclusion: High rates of consanguinity and first and second-cousin marriage in Iran result in higher carrier frequency and higher incidence of autosomal recessive disorders. It is essential to include molecular genetic analysis in the screening programs and to identify the spectrum of GCDH mutations in families with a history of GA 1, as well as confirmatory tests for affected individuals.

Keywords: GCDH; Genetic Investigation; Glutaric Aciduria Type 1; Mutation; Autosomal Recessive.





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Section: Genetics

Presentation Type: Poster

Abstract Type: Systematic Review/ Meta-Analysis

Code of Abstract: PG-18

Zinc Finger Proteins in Cancer Progression

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Abstract

Background and Aim: Transcription factors play a central role in regulating gene expression, and therefore coordinate a plethora of biological processes, including differentiation, development, metabolism, apoptosis, autophagy and stemness maintenance. Zinc Finger Containing Proteins (ZNFs) are a superfamily of transcription factors that comprise at least one zinc finger domain that could bind specific DNA sequences, hence regulating the DNA expression levels. The zinc finger motif, composed of 30 cysteines and/or histidines, was firstly observed in the African *Xenopus* oocyte transcription factor IIIA in 1988, named for its capacity to bind zinc ions and create finger-like structures. Recent evidence reveals that the zinc finger protein family is of great importance in the molecular regulation of the genesis and propagation of human malignant tumors involving the colon, breast, liver, prostate and gastric carcinomas.

Methods: In the current study, keywords including Zinc Finger Proteins, Cancer, and Transcription were reviewed from the list of Mesh and other credible websites including PubMed, Science Direct and Google Scholar and the data was organized. The searches comprised all published paper from 2000 to 2022. All of full text was considered and the papers manifested as only abstract was excluded. The full papers selected that specific effect on zinc finger proteins in cancer progression only. Totally 50 papers were selected and studied in this review.

Results: ZNFs have been shown to play different roles in different cancer types and stimuli. ZNF395 is overexpressed in various cancers, including Ewing sarcomas, osteosarcomas and renal cells carcinomas. Recent studies revealed that aberrant expression of C2H2 ZNF proteins contributes to tumorigenesis in different aspects. Recently, one research revealed that ZNF703 overexpression could promote Hepatocellular Carcinoma (HCC) metastasis and sorafenib resistance by regulating Epithelial to Mesenchymal Transition (EMT) via upregulating CLDN4. Overexpression of zinc finger protein, X-linked (ZFX) has been shown to promote cell growth and metastasis in laryngeal squamous cell carcinoma, glioma, non-small cell lung cancer, gastric cancer, oral squamous cell carcinoma, gallbladder cancer and breast cancer. Scientists suggested that Myeloid Zinc-Finger 1 (MZF1) cooperates with ETS Transcription Factor ELK1 (Elk-1) and significantly upregulates protein kinase C alpha (PKC α), promoting cell migration and invasion in hepatocellular, breast, and bladder transitional cell carcinoma. One article uncovered that suppressed miRNA-204-5p can enable Gastric Cancer (GC) cells to invade and metastasize via the upregulation of ZNF521. ZNF692 promotes cell proliferation, migration, and invasion in colon adenocarcinoma (COAD) by downregulating p27kip1 or upregulating cyclin D1, cyclin-dependent kinase 2 (CDK2), matrix metalloproteinase-9 (MMP-9), and PI3K/Akt signaling. Some articles reported that the ZFP, Wilms' tumor-1 protein, is a critical factor in angiogenesis that modifies the splicing of Vascular Endothelial Growth Factor (VEGF), thereby repressing the Serine/Threonine-Protein Kinase (SRPK1) which contributes to angiogenesis in Acute Myeloid Leukemia (AML).

Conclusion: ZFPs have significant effects on cell proliferation, EMT, invasion and metastasis, inflammation, apoptosis, the cell cycle, drug resistance, cancer stem cells and DNA methylation in a broad range of cancers, such as colon, breast, lung and gastric cancers, as well as hepatocellular carcinoma.

Keywords: Zinc Finger Proteins; Cancer; Transcription.





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January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Systematic Review/ Meta-Analysis

Code of Abstract: PG-19

Role of Retinoblastoma as a Tumor Suppressor Gene

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Abstract

Background and Aim: Tumor suppressor genes are important genes that act within the genome to regulate several cellular functions. These genes can be broadly classified based on their role in cell growth/cell cycle progression, cell proliferation, DNA repair mechanisms, and other crucial cellular signaling functions such as the apoptosis induction. The Retinoblastoma (RB) tumor suppressor protein forms a transcriptional repression complex with the E2F family of transcription factors and various chromatin modifiers, and thereby negatively regulates G1/S transition during the cell cycle through the suppression of E2F target genes.

Methods: In the current study, keywords including Retinoblastoma, Tumor Suppressor Gene, and Cancer were reviewed from the list of Mesh and other credible websites including PubMed, Science Direct and Google Scholar and the data was organized. The searches comprised all published paper from 2000 to 2022. All of full text was considered and the papers manifested as only abstract was excluded. The full papers selected that specific role of retinoblastoma on cancer and tumor only. Totally 50 papers were selected and studied in this review.

Results: The studies described implicate retinoblastoma loss as a promoter of metastasis of carcinomas or epithelial tumors, specifically via the loss of epithelial markers such as E-Cadherin and the acquisition of mesenchymal and migratory phenotypes. The rate of RB1 gene mutation varies significantly among different tumor types, but is highest in retinoblastoma, osteosarcoma, and small-cell lung cancer (SCLC). Articles have been showed RB inactivation in tissue stem/progenitor cells and post-mitotic cells contributes to tumor formation by promoting self-renewal activity and dedifferentiation. Also, inactivation of RB leads to abnormal chromosome segregation. In addition, excessive expression of Mad2, a spindle-assembly checkpoint protein, which is directly induced by E2F, causes chromosome instability. Methylation of DNA is generally associated with an inactive chromatin through the inhibition of transcription factor binding. Consequently, inactivation of the retinoblastoma protein pathway alters DNA methyltransferase family (DNMTs) activity, leading to aberrant genomic DNA methylation patterns and malignant progression. One study revealed Many human cancers are characterized by RB1 mutation or deletion, INK4a mutation, deletion or gene silencing and cyclin D1 or CDK4 overexpression. These alterations cause either RB1 loss or retinoblastoma protein hyperphosphorylation, thus inactivating the major control mechanism of cell cycle progression. Despite the fact that cancers harboring alterations in the RB pathway are generally more aggressive than those with a normal RB function the functional loss of retinoblastoma protein has been shown to increase cell sensitivity to both DNA-damaging agents and to drugs targeting the thymidylate biosynthesis pathway.

Conclusion: Inactivation of retinoblastoma is frequently observed during cancer progression. Cell cycle deregulation is one of the most important features associated with retinoblastoma inactivation, however, retinoblastoma is a multifunction protein interacting with wide varieties of binding partners and has cell cycle-independent functions.

Keywords: Retinoblastoma; Tumor Suppressor Gene; Cancer.





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January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-20

Evaluation of BRAF Mutations in Patients with Colorectal Cancer in the East of Iran

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Abstract

Background and Aim: Several genetic alterations in cell growth regulatory genes, such as BRAF, are associated with colorectal cancer. Due to the introduction of biological agents designed to treat cancer, diagnostic tests using nucleic acids extracted from formalin-fixed and paraffin-embedded tissues are becoming more common. This study aimed to determine the incidence of BRAF mutations in colorectal cancer patients.

Methods: 50 paraffin-embedded cancer specimens were obtained from Imam Reza Hospital of Birjand in Iran. PCR was used to amplify and sequence the BRAF gene exon 15, which was extracted from paraffin-embedded tissue using an improved technique.

Results: 2/43 (4%) of patients with colorectal cancer exhibited the BEAF V600E mutation. Most of the mutations occurred in patients over 50 years of age.

Conclusion: To understand how genetics and environment interact to influence the low incidence of BRAF mutations in the east of Iran, further research is needed to determine what is driving this low incidence of BRAF mutations and what factors contribute to it.

Keywords: Colorectal cancer, BRAF mutation, PCR, gene, DNA, cancer.





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January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-21

Importance of PCR technique role in detection of infections caused by all types of microorganisms in children and adults

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Abstract

Background and Aim: Since 1993 PCR method became one of the most useful techniques designed to detect many infective and non-infective diseases in all laboratories worldwide.

In addition to many Genetic disorders, PCR can be used for detection of all types of microorganisms which attack human bodies of all ages. Today, parasitic infection of the digestive system can be detected rapidly by PCR done on blood sample without the necessity of doing microscopic examination of the patient's stool. All the infections caused by viruses, bacteria and fungal microorganisms can be also detected by PCR.

Methods: Polymerase chain reaction (PCR) is basically used to amplify millions of copies of a specific DNA sequence. In general, after the DNA extracted by DNA extraction Kit, the template DNA will be amplified by Taq DNA polymerase enzyme in a specific aquatic solution in thermal cycle system and then the PCR product will be analyzed.

Results: Many infective diseases like toxoplasmosis, bacterial infections of respiratory system, zoonotic diseases and viral infection like HIV, are detectable in the early stages of the commune period of the disease. The high sensitivity and specificity of this method, make PCR as routine in rapid detection of all types of infections worldwide.

Conclusion: There is no doubt that detection of all types of infections by PCR method can be used as an alternative even in detection of parasitic infections of the bowel tract.

Keywords: Infection; PCR; Parasitic; Technique.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PG-22

Emerging Therapies for Hemoglobinopathies: A Review of Novel Approaches, including CRISPR/Cas9 Gene Editing, for Treating Inherited Blood Disorders

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Abstract

Background and Aim: Hemoglobinopathies, such as sickle cell disease and thalassemia, are inherited blood disorders characterized by abnormalities in the structure or production of hemoglobin. Traditional treatment options for these conditions mainly focus on symptomatic management and supportive care. However, recent advancements in gene editing techniques, particularly CRISPR/Cas9, have opened new avenues for potential curative therapies for hemoglobinopathies. This review aims to provide an overview of emerging therapeutic approaches, including gene editing techniques, and their potential in treating these inherited blood disorders.

Methods: A comprehensive literature search was conducted to identify relevant studies, clinical trials, and advancements in the field of novel therapeutic approaches for hemoglobinopathies. The search included databases such as PubMed, Scopus, and Web of Science, using keywords related to hemoglobinopathies, gene editing, CRISPR/Cas9, and emerging therapies. The selected articles were analyzed to extract key information on the mechanisms, efficacy, and safety of these novel therapeutic approaches.

Results: Our review identified several emerging therapeutic approaches for hemoglobinopathies, with a particular focus on gene editing techniques like CRISPR/Cas9. Gene editing technologies offer the potential to correct or modify the genetic mutations responsible for hemoglobinopathies, providing a curative approach instead of just symptom management. Various preclinical studies and early-phase clinical trials have shown promising results in terms of improved hemoglobin levels, reduced disease symptoms, and increased quality of life in patients with sickle cell disease and thalassemia.

Conclusion: Novel therapeutic approaches, including gene editing techniques like CRISPR/Cas9, hold immense potential for the treatment of hemoglobinopathies. These emerging therapies offer the possibility of a curative approach by addressing the underlying genetic mutations responsible for these disorders. However, challenges such as off-target effects, delivery methods, and long-term safety need to be addressed before widespread clinical implementation. Continued research and clinical trials are essential to further explore and optimize these novel therapeutic approaches.

Keywords: Hemoglobinopathies; sickle cell disease; thalassemia; novel therapeutic approaches; gene editing.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PG-23

The importance of rs1042522 polymorphism in chronic lymphocytic leukemia

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Abstract

Background and Aim: The most common adult leukemia in the West is chronic lymphocytic leukemia (CLL). This disease is mainly seen in older people. The main complaints in patients with CLL are immune thrombocytopenia, lymphadenopathy, organomegaly. A recent study carried out in next generation sequencing identifies various genes that have a particular role in CLL. Also, recent studies prove that TP53 gene variants have important genetic implications. It has been linked to a severe form of chronic lymphocytic leukemia (CLL). The aim of this study is association between SNP (rs1042522) in the TP53 gene at codon 72 encodes and CLL.

Methods: Based on Cochrane systematic review principles and PRISMA guideline, the study conducted using predetermined keywords “chronic lymphocytic leukemia,” “TP53,” “single nucleotide variant” and “single nucleotide polymorphism” on electronic databases such as PubMed, Scopus and Web of Science. Also, Google Scholar search engine have been used for reviewing grey literature. These searches were conducted from May 2017 to October 2023 in the mentioned databases. The inclusion criteria for enrollment in the study were based on the patients' diagnosis of CLL according to studies in the literature available in English. Exclusion criteria were non-English language articles, review and animal studies and conferences article. Screening and data extraction were conducted by two authors independently and any discrepancies were resolved by consensus involving a third author. All included article were quality assessed via Cochrane ROB 2 tool. Then the data of included articles was collected in extraction tables.

Results: In the first step, we identified 1264 articles, of which 1245 were duplicates and subsequently deleted. After analyzing these 19 articles, a total of 4 studies. involving 605 patients, were included. In these studies, were performed the mutations of TP53 are detected in about 4% to 37% of patients with CLL, some related to poor prognosis. SNP rs1042522 encodes either arginine (72Arg, genotype CGC) or proline (72Pro, genotype CCC) and essentially influences TP53 work. The 72Arg variation is more viable at actuating apoptosis than the 72Pro, whereas the 72Pro/Pro genotype was related to an expanded expression of cell cycle capture qualities the results of these studies demonstrate a significant association between the SNP rs1042522 in TP53 and CLL, which can lead to an increased risk of CLL and longer disease duration ($p < 0.05$). Our results suggest that this polymorphism maybe increase the risk of CLL.

Conclusion: Our study revealed that there was a correlation between the susceptibility to CLL and the SNP rs1042522. Our findings are inconclusive, and the presence of these polymorphisms may be important in patients with CLL. However, the role of SNP rs1042522 in patients with CLL is still to be confirmed through further studies. The limitation of this study is the small number of patients, which requires further studies and a larger number of patients for conclusive results.

Keywords: chronic lymphocytic leukemia; TP53; single nucleotide variant; single nucleotide polymorphism.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PG-24

Association of IL10 Promoter polymorphism with risk of Multiple Sclerosis in different populations

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Abstract

Background and aim: Multiple sclerosis (MS) is a neurodegenerative autoimmune disease, which is characterized by chronic inflammation, demyelination, and neuronal death and in which cytokines play a significant role, varies in prevalence among populations and geographical areas. IL-10 is one of these cytokines that can play a role in the immunological pathogenesis of the illness by regulating the balance and strength of immune responses. IL-10 gene promoter contains a multitude of polymorphisms, some of which is related to varying levels of IL-10 expression in vitro and in vivo. In this article, we are investigating the relationship between interleukin 10 promoter polymorphism and MS.

Methods: We considered 100 articles about multiple sclerosis, IL10 polymorphism and association between them from January 2011 to September 2021 and finally chosen 8 of them to write this article.

Result: In various countries results were different as follows in Poland, India and Iran (Azari) IL-10-1082 A/G (rs1800896) showed no significant difference between patient and control group, therefore may not be risk factor for multiple sclerosis. In other hand in Iran (in Gorgan, IL-10⁻¹⁰⁸² G/G and IL-10⁻⁸¹⁹ C/C), Bulgaria (AA genotype of IL10-1082) and in Iraq (IL10-1082: rs1800896, IL10-819: rs1800871, and IL10-592: rs1800872) some haplotypes increased in patients and can be associated with susceptibility to MS.

Conclusion: Therefore, the screening program can be useful for finding vulnerable people and control of disease in some countries.

Keywords: Multiple Sclerosis; IL-10; Polymorphism.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PG-25

Irregularities and therapeutic effects of miR-21 in initiation and progression of Colorectal Cancer

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Abstract

Background and Aim: In this article, the databases of PubMed, Cochrane Library, EMBASE, Web of Science, Scopus, and Google Scholar were analyzed to analyze the diagnostic role of Mir-21 in CRC and TCGA data to search for different microRNAs in cancer samples. Colorectal and surrounding tissues are used. Discussion MicroRNAs (miRNAs) are a group of small non-coding RNAs that play a major role in the regulation of mRNA.

Methods: A recent study showed that plasma miR-21 expression was significantly increased in CRC patients based on TaqMan. miR-21 is associated with tumor prognosis. In addition, miR-21 is often upregulated even in premalignant lesions such as colon adenoma, which are target lesions for CRC screening. In this study, we hypothesized that miR-21 is a good case for exploration as a biomarker. Indeed, for early detection and prognosis of CRC, assuming that expression pattern of miR-21 is used as a novel biomarker.

Results: MicroRNAs (miRNAs) are a group of small non-coding RNAs that play a major role in the regulation of mRNA. Most miRNA expression studies have been performed in tissue samples, and some studies have shown diagnostic and prognostic potential for circulating miRNAs because tumor-derived miRNAs can be present in blood. and appears to be stably protected from endogenous ribonuclease activity. In circulation, which is important because increased or even decreased expression of circulating miRNAs can indicate tumor-produced miRNAs and increase the diagnostic specificity of the biomarker. With cancer, such as PTEN, modulates TPM1 and PDCD and is overexpressed in various human tumors. In addition, miR-21 expression is up-regulated in CRC tissues, either down- or up-regulated during tumor progression. A recent study showed that plasma miR-21 expression was significantly increased in CRC patients based on TaqMan. miR-21 is associated with tumor prognosis.

Conclusion: A recent study showed that plasma miR-21 expression was significantly increased in CRC patients based on TaqMan. miR-21 is associated with tumor prognosis. In addition, miR-21 is often upregulated even in premalignant lesions such as colon adenoma, which are target lesions for CRC screening. In this study, we hypothesized that miR-21 is a good case for exploration as a biomarker. Indeed, for early detection and prognosis of CRC, assuming that expression pattern of miR-21 is used as a novel biomarker.

Keywords: miR-21; Colorectal; Cancer; Biomarker.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PG-26

Prenatal Screening and Diagnostic Tests; A Review Article of Prenatal Tests' Accuracy and Conditions

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Abstract

Background and Aim: Nowadays with the dramatic progress of technology, prenatal genetic tests have made improvements, and new methods of such tests are commonly used in prenatal settings. Most forms of prenatal tests are invasive and they involve a risk of fetal loss. Noninvasive prenatal tests can be applied earlier during pregnancy with high sensitivity and specificity. This paper aims to respond to the questions such as whether all pregnant women should go under these prenatal tests? Or whether these tests are highly accurate or not?

Methods: we performed our literature search in databases such as; Google Scholar, PubMed, Nature and, Science direct. 63 English papers were found related to prenatal tests between 2010 to 2020, and the selection of final 16 papers was performed by two authors with the help of keywords such as prenatal tests, genetic tests, noninvasive and invasive tests.

Results: Dramatic changes in the field of technologies lead to new methods of prenatal tests that are not invasive. Although accuracy and ease have improved but there is still a chance of false-negative and false- positive results. However noninvasive prenatal tests such as cfDNA decreased false-positive results but it cannot be seen as a diagnostic tests and positive results should be followed by diagnostic tests such as CVS and amniocentesis. The accuracy of NPIT depends heavily on the technologies that are used and other fetal and maternal factors including fetal fraction and placental mosaicism. Non-invasive methods have attracted many positive comments, but pregnant women should also be aware of the fact that although these tests can be performed with high specificity and sensitivity but the chance of false results is inevitable.

Conclusion: Although prenatal tests are available to all pregnant women, they should make an informed decision to do these tests based on their age, family history, fetal findings and their preferences. Invasive tests usually have a small chance of fetal loss and infection, so these tests are not recommended to low-risk women. It is better for women with low risk to use non-invasive tests and if the result of the test is positive, to confirm the result they should do invasive diagnostic tests such as chorionic villus sampling and amniocentesis.

Keywords: prenatal tests, genetics, screening tests, diagnostic tests, accuracy.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PG-27

Diagnosing gestational diabetes by microRNAs

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Abstract

Background and Aim: One of the common metabolic disorders during pregnancy is gestational diabetes, which carries the risk of complications for the baby and the mother. Glucose tolerance tests and screening are usually performed between 24 and 28 weeks of pregnancy, by which time the blood glucose level has increased significantly, so, considering the importance of diagnosis and control of this disease, it is necessary to use new methods and biomarkers to identify gestational diabetes. This article is a review of whether small non-coding RNAs called microRNAs can be used as diagnostic biomarkers of gestational diabetes

Methods: This article is the result of search terms including "diagnosis", "gestational diabetes", "microRNA", and "biomarker" in reliable scientific databases such as Google Scholar, PubMed, and Science Direct.

Results: The results of several studies have shown that microRNAs play an important role in regulating the function of beta cells, insulin secretion, and processes related to glucose homeostasis, which confirms the different expression levels of microRNAs in the placenta and blood of mothers with gestational diabetes compared to other pregnant women. Upregulation of miR-29a-3p, miR-16-5p, and miR-330-3p has been observed in affected pregnant mothers, while the levels of miR-132-3p decreased. It has also been said that the examination of miR-16-5p, miR-134-5p, and miR-29a-3p can be a superior diagnostic factor than the examination of blood sugar in the Glucose tolerance test.

Conclusion: Based on the results, miRNAs can be used as biomarkers for the diagnosis or prognosis of GDM, but more studies are needed to prove the potential of these microRNAs. Also, the effect of different parameters such as the type of sample and how it is processed, age, and gender should be considered in future studies.

Keywords: Gestational diabetes; microRNA; Diagnosis; Pregnancy; Glucose.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-28

Real-time PCR as an efficient method for evaluating the expression levels of breast cancer biomarkers

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Abstract

Background and Aim: Early detection is a crucial aspect of breast cancer treatment, as it significantly impacts the treatment strategy for patients. In this regard, immunohistochemistry (IHC) has emerged as a widely utilized method for evaluating the expression levels of biomarkers that play a crucial role in breast cancer treatment decisions. IHC technique has limitations such as high cost, false positives, and dependence on special materials and equipment. Therefore, there is a priority to use quantitative methods like RT-qPCR, which offer high accuracy, sensitivity, and reproducibility. We aim to design a Real-time PCR method to investigate the HER2 and Ki-67 biomarkers expression levels.

Methods: Human breast cancer cell lines, MCF-7 and SKBR3, were used in this study. After cell culture, IHC was done in order to evaluate and confirm the expression levels of HER2 and Ki-67 biomarkers. RNA extracted from the cell lines for absolute RT-qPCR assay using specific TaqMan probes and primers for HER2 and Ki-67. The standard curve was prepared on the serial dilutions of plasmid DNA containing HER2 and Ki-67 sequences. Finally, we conducted a quantitative Real-time PCR test and the copy number of each biomarker were calculated by standard curve and compared with IHC results.

Results: IHC results showed that MCF7 cells are HER2 negative and Ki-67 expression was 90%. For SKBR3 cell line IHC results demonstrated that HER2 expression is high (3+) and Ki-67 expression was 40%. RT-qPCR test was optimized and the results converted to copy number using standard curve.

Conclusion: The results of this study showed that RT-qPCR method using TaqMan probes can efficiently determine the expression levels of important biomarkers in breast cancer cell lines and can replace expensive and time consuming IHC test.

Keywords: Breast cancer, HER2, Ki-67, RT-qPCR, TaqMan probe.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-29

Enterobacterial Repetitive Intergenic Consensus Polymerase Chain Reaction (ERIC-PCR) Genotyping of uropathogenic *E. coli* strains isolated from urinary tract infection

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Abstract

Background and Aim: There are many different strains of *Escherichia coli* (*E. coli*), which is the most frequent cause of urinary tract infections. Despite the existence of multiple modern molecular-genomic technologies for detecting and identifying various strains of *E. coli*, the Enterobacterial Repetitive Intergenic Consensus Polymerase Chain Reaction (ERIC-PCR) technique is a quick, sharp, and cost-effective fingerprint method. The purpose of this study was to look at the distribution of ERICs in *E. coli* strains isolated from urinary tract infections.

Methods: From UTI patients, 153 clinical isolates of uropathogenic *E. coli* (UPEC) were collected. The *E. coli* bacteria were confirmed using standard microbiological and biochemical methods. The *E. coli* strains were classified using DNA proliferation based on repeating intergenic consensus. The ERIC-PCR products were electrophoresed on 1.5% agarose gel. The GelCompar software was used to create dendrograms using the final images of the gel electrophoresis banding patterns.

Results: After dendrogram analysis, it was shown that 19 ERIC patterns were discovered. 13 patterns were similar between different isolates (Common type) and 6 patterns were unique (Unique type).

Conclusion: In this investigation, various genotypic clusters of uropathogenic *E. coli* strains were identified. It was discovered that ERIC-PCR is an effective method for molecularly typing *E. coli* strains isolated from various sources of urinary tract infections.

Keywords: *Escherichia coli* (*E. coli*), ERIC-PCR, Urinary tract infections, Genotyping.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Case Report

Code of Abstract: PG-30

Recurrence of Developmental and epileptic encephalopathy 9 (DEE9) in two siblings due to parental germline mosaicism of *PCDH19* mutation

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Abstract

Background and Aim: Pathogenic variants in *PCDH19* gene lead to Developmental and epileptic encephalopathy 9 (DEE9). The clinical features encompass early-onset seizures (often febrile and clustered), intellectual disability, autistic traits, and behavioral problems. DEE9 has an unusual X-linked pattern where heterozygous females or rarely mosaic hemizygous males are affected, but hemizygous males and homozygous females are asymptomatic. Although the exact mechanism remains unclear, cellular interference has been proposed for this unusual inheritance pattern. In recent years, a growing number of female and male patients with *PCDH19*-related epilepsy and symptoms have been reported. Here, we report two further female patients with DEE9 who are siblings.

Methods: Peripheral blood samples were collected from the proband, her sister and parents after informed consent. After genomic DNA extraction, Whole-exome sequencing (WES) and then Sanger sequencing was performed.

Results: Our Results revealed that both sisters have a heterozygous frameshift variant (NM_001184880.2: c.1091delC, p.P364Rfs*4) in the *PCDH19* gene. This is the first report of germline mosaicism in *PCDH19* in Iranian populations and broadens the phenotypic spectrum of DEE9.

Conclusion: Genetic testing has become an effective way of determining diagnosis. Parental germline mosaicism should be taken into account when providing genetic counselling for X-linked/autosomal dominant disorders. This report also provides an emphasis on the importance of considering prenatal diagnosis (PND) in such cases.

Keywords: Developmental and epileptic encephalopathy 9; Epilepsy; *PCDH19*; Genetic; Germline mosaicism.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-31

Long non-coding RNA cCSC1 to promotes glioblastoma progression by sponging miR-124-3p

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Abstract

Background and Aim: Glioblastoma multiforme (GBM) is one of the most aggressive and fatal brain tumors in adults, with limited treatment options and a low average survival rate despite current therapeutic interventions. Recent investigations highlight the potential function of miR-124-3p in impeding GBM tumor growth by its interaction with the long non-coding RNAs. This study aims to elucidate the association between lncRNA cCSC-1 and miR-124-3p in GBM patients.

Methods: 50 tumor tissue and 50 adjacent normal tissue samples were obtained from GBM patients at Erfan Hospital in Tehran, Iran. Diagnosis was established through MRI. RNA extracted from tissue samples and gene expression of lncRNA cCSC-1 and miR-124-3p evaluated using Real Time PCR.

Results: Our findings reveal a significant upregulation of lncRNA cCSC-1 expression in GBM tissue compared to the control group. Furthermore, a notable decrease in the expression level of miR-124-3p was observed in tumor tissue compared to normal tissues.

Conclusion: This study underscores the distinct expression patterns of lncRNA cCSC-1 and miR-124-3p in GBM tissue, implicating the potential of lncRNA cCSC-1 in promoting tumor growth by targeting miR-124-3p.

Keywords: Glioblastoma multiform; lncRNA cCSC-1; miR-124-3p, Real-Time PCR.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-32

Correlation between tissue expression of lncRNA PACER and NF- κ B pathway activation in ulcerative colitis patients

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Abstract

Background and Aim: A chronic inflammatory bowel disease called ulcerative colitis (UC) occurs via aberrant immune system reactions that inflame the colon and the rectum. The NF- κ B signaling pathway is one of the pathways that is crucial to the pathophysiology of ulcerative colitis. Long non-coding RNAs (lncRNAs) can be used as biomarkers in a variety of disorders because of their great specificity for cells and organs. It has been demonstrated that lncRNA PACER controls the NF- κ B pathway in many diseases. We investigated the relationship between UC patients' lncRNA PACER and the NF- κ B pathway in this study.

Methods: Samples were collected from 35 UC patients and 35 healthy individuals as the control group at Shariati Hospital in Tehran, Iran. Patients were diagnosed based on standard clinical, endoscopic, and histological criteria. RNA and protein were extracted from tissue samples, and Real-Time PCR was used to evaluate the expression of the PACER gene. Western blot was used to measure the phosphorylation of IKK α /IKK β .

Results: When comparing UC patients to the control group, there was a significant increase in PACER expression levels. According to Western blot analysis, UC patients have higher levels of phosphorylation of the NF- κ B protein inhibitor IKK α /IKK β when compared to the control group. This suggests that the NF- κ B pathway is activated more in these patients.

Conclusion: This study provides evidence that the expression of lncRNA PACER is increased in UC tissue samples compared to the control group tissue samples. Additionally, the phosphorylation of IKK α /IKK β is increased in UC tissue samples, indicating that the activity of the NF- κ B pathway is increased in UC patients. Previous studies have shown that lncRNA PACER regulates the NF- κ B pathway, suggesting a potential correlation between lncRNA PACER and the NF- κ B pathway in ulcerative colitis. Further investigations are required to fully understand how lncRNA PACER regulates the NF- κ B pathway in UC.

Keywords: Colitis, Ulcerative; IBD; RNA, Long Noncoding; PACER; Inflammation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Case Report

Code of Abstract: PG-33

Step-by-step diagnosis of 3-hydroxyisobutryl-CoA hydrolase deficiency in Iranian patient with a new mutation

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Abstract

Background and Aim: 3-hydroxyisobutryl-CoA hydrolase (HIBCH) is a mitochondrial enzyme which is known as Valine catabolic pathway enzyme. This enzyme is responsible for hydrolysis both HIBYL-CoA and beta-hydroxypropionyl-CoA. Several mutations in its gene causes a rare inherited metabolic error called 3-hydroxyisobutryl-CoA hydrolase deficiency (HIBCHD). Following this defect, the pathway of valine catabolic is disrupted and toxic compounds like methacrylyl-CoA, acryloyl-CoA and its related metabolites accumulate in body that conducts neurodegeneration, movement complications and ketoacidosis in patients. In this report we introduce a young Iranian male patient at 17-month age with a novel mutation in HIBCHD gene has not been reported in Clin Var data base.

Methods: Following the symptoms observed in the patient include Ketoacidosis, Hyper Ammonia, fever and developmental delay metabolic diagnosis tests include Amino acid and acyl carnitine profile by liquid Chromatography-Mass spectrometry (LC-MSMS), Urine organic acid analysis by Gas chromatography Mass spectrometry (GC-MS) was prescribed. Confirmatory methods and test for this disorder were mono whole exome sequencing (WES) and Magnetic resonance imaging (MRI).

Results: The early signs of the disease were begun after injection of the six-month vaccination that patient was hospitalized due to chronic fever and chills. nine months later due to developmental delay, diarrhea, acidosis and also appearing nervous symptoms like nystagmus, the patient referred to children's medical center, Tehran, Iran. Evaluation of laboratory results of acyl carnitine profile have indicated significantly elevation of Hydroxyisobutyrylcarnitine (1.47 vs 0.38). Further Confirmatory tests include urine organic acid analysis and brain MRI was request by his physician. The excretion of 3-hydroxy isovaleric acid was observed in urine organic acid analysis. The brain MRI showed abnormal signal intensity at Globus pallidus conducts metabolic encephalopathy. Evaluation of mono whole exome sequencing (WES) test indicated current homozygous mutation in the HIBCH gene (NM_014362: exon8:c.C559T) which led to amino acid change (p.L187F). In order to control acidosis and also improvement metabolic lesions oral sodium bicarbonate, L-carnitine and vitamin therapy was prescribed for patient and Valine consumption was limited by diet.

Conclusion: 3-hydroxyisobutryl-CoA hydrolase deficiency is a rare disease in the world. On the other hand, since this disorder has the same symptoms as Leigh's disease, it may be challenging to correctly diagnose the disease. early diagnosis of HIBCHD through high technology equipments like LC-MSMS and GC-MS is definitely important to guide physicians in the truly manner.

Keywords: 3-hydroxyisobutryl-CoA hydrolase deficiency, Valine catabolism, Mass spectrometry, whole exome sequencing.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-34

Molecular Docking Analysis of Small Molecule TRK Inhibitors for Targeting NTRK Fusion Proteins in Pediatric Cancers and Solid Tumors

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Abstract

Background and Aim: The NTKR1 gene, a part of the NTKR family, encodes a cell membrane-bound receptor that triggers MAPK pathway activation upon neurotrophin binding, influencing cell differentiation and sensory neuron types. Mutations in this gene relate to insensitivity to pain, anhidrosis, self-harm, cognitive issues, and cancer. Few splice variants have been studied. NTRK gene fusions drive certain cancers, including pediatric ones like infantile fibrosarcoma and congenital mesoblastic nephroma. Targeted therapies inhibiting NTRK fusion proteins show promise in clinical trials, enhancing outcomes for patients. Identifying these fusions underscores the importance of genetic testing in cancer treatment. Clinical trials confirm TRK inhibitors' effectiveness in NTRK fusion-positive solid tumors, reinforcing their role in tumor-agnostic therapy development and prompting research into detection methods, drug properties, drug efficacy, and resistance mechanisms.

Methods: In this study, small molecules TRK inhibitors selected for docking against TRK-fusion protein receptor and then compared their inhibitory effects on entry with current inhibitor by molecular docking using AutoDock Tools (ADT) package version 1.5.6rc3.

Results: The data regarding receptor-ligand interactions (hydrophobic and hydrogen binding) was almost similar to the common drug that inhibits this receptor, indicating their potential inhibitory effect against the receptor. Although the affinity scores of these compounds are similar to the tropomyosin receptor tyrosine kinases (TRKs), their hydrogen bonding affinity was more effective.

Conclusion: In this study, molecular docking screening was carried out to elucidate inhibition potential of small molecules TRK inhibitors with few or no side effects in comparison with the chemical. The current study recommends the FDA-approved treatment of TRK-fusion positive solid tumors. The results showed that these inhibitors have almost similar binding affinity and are effective inhibitors against the receptor, and therefore may pediatrics cancer and solid tumors.

Keywords: Neurotrophic receptor tyrosine kinase (NTRK) fusion; Tropomyosin receptor kinase (TRK) inhibitor; solid tumor.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-35

Genetic diagnosis of patients with hyperoxaluria type 3 using haplotype analysis

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Abstract

Background and Aim: The defect in glyoxylate metabolism is the uncommon category of illnesses known as primary hyperoxaluria (PH). Three genes have been found to cause three forms of PH (I, II, and III). PH type III caused by mutation in the *HOGA1* gene and it is the second most common form of PH. In this study we aim to genetically analyze Iranian patients who are affected by this disorder.

Methods: We studied 14 patients (range: 1.5–5.5) years from 11 unrelated Iranian families with a clinical diagnosis of hyperoxaluria disease. PH1 that is the most prevalent form of PH was ruled out in our patients. The kidney stone was detected in all patients. All of them had high levels of creatinine and oxalate in their urine. Haplotype analysis using four SNPs surrounding the *HOGA1* gene followed by Sanger sequencing of the *HOGA1* gene in the patients with homozygous haplotypes was performed in all 14 patients. Next-generation sequencing (NGS) has also been done on one patient that the causative mutation was not found.

Results: We identified one homozygous missense mutation in the *HOGA1* gene which was not previously reported (c.266G>A).

Conclusion: This is the first report to characterize mutation in the *HOGA1* gene in Iranian patients with hyperoxaluria and expands the spectrum of *HOGA1* mutations by reporting one novel mutation, c.266G>A.

Keywords: Genetic Diagnosis; Hyperoxaluria Type 3; Haplotype Analysis.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-36

Investigating the Effects of Memantine and Donepezil on the Expression of NR2A, ATF4, CREB1, and APP Genes in the Hippocampus after Scopolamine-Induced Memory and Learning Impairment in Rats

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Abstract

Background and Aim: Memory lays the foundation for learning as it stores information in the brain. Learning encompasses the assimilation of knowledge that brings about behavioral transformations. Impaired memory results from the disruption of neuroanatomical structures, hindering memory storage and retrieval. The objective of this study is to explore the impacts of two drugs, MEM and DON, on the expression of NR2A, ATF4, CREB1, and APP genes. These genes are crucial in the signaling pathways associated with memory and learning.

Methods: In this study, 30 Wistar male rats were used and randomly divided into five groups, each comprising 6 rats. The rats were subjected to intraperitoneal treatments for 21 consecutive days. The groups consisted of: Control (Saline), SCP (1 mg/kg), DON (3 mg/kg) + SCP (1 mg/kg), MEM (10 mg/kg) + SCP (1 mg/kg), DON+MEM (0.5 mg/kg and 5 mg/kg, respectively) + SCP (1 mg/kg). To investigate the expression of NR2A, ATF4, CREB1, and APP genes, the hippocampus of rats in the drug treatment groups and the control group was separated from the brain. RNA samples were extracted from the hippocampus tissue and converted to cDNA. The relative expression levels of NR2A, ATF4, CREB1, and APP genes were measured in the control samples and different treatments using the SYBR Green method and Real-time PCR. The beta-actin gene was used as an endogenous gene in this study.

Results: Molecular test results indicate that there's no significant relationship between the injection of DON and MEM in the prescribed doses either as a single dose or in combination, with the expression of NR2A, ATF4, CREB1, and APP genes among different groups. Additionally, there was no significant relationship between the injected dose of scopolamine and the expression of these genes among different groups.

Conclusion: The present study shows that prescribed doses of DON and MEM drugs do not significantly affect the expression of NR2A, ATF4, CREB1, and APP genes. However, more research is needed to explore the impact of these drugs on the expression of these genes and other genes linked to memory and learning disorders. This knowledge can aid in selecting the right drug for preventing and treating Alzheimer's disease.

Keywords: Memory and learning, Memantine, Donepezil, Scopolamine.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-37

Investigation of genetic polymorphisms of glutathione-S-transferase T1 (GSTT1) in patients with covid-19 in mild, severe and critical forms referred to Shahid Rahimi and Shohada Ashair Hospitals in Khorram Abad city in 1400

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Abstract

Background and Aim: The disease COVID-19 caused by the acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become an important issue in global health. SARS-CoV-2 infection is associated with oxidative stress that causes the production of cytokines, inflammation and other pathophysiological processes. Glutathione-S-transferase (GST) is an important enzyme family that catalysis the combination of glutathione (GSH) with electrophiles to protect cells from oxidative damage and participates in the antioxidant defense mechanism in the lungs. In this study, GSTT1 polymorphisms were evaluated in patients with COVID-19 with three forms, mild, severe, and critical, in order to determine the relationship between these polymorphisms and susceptibility to COVID-19.

Methods: In this cross-sectional study, 305 patients with COVID-19 participated according to the guidelines of the Ministry of Health in three forms: mild (100 people), severe (146 people) and critical (59 people). Patient information was collected according to the designed questionnaire. Multiplex PCR technique was used to evaluate GSTT1 polymorphism.

Results: The frequency of GSTT0 deletion genotype was determined in 17 mild patients (17%), 29 severe patients (19.9%) and 16 critical patients (27.1%). Although the frequency of the deletion genotype increases with the increase in the severity of the infection with COVID-19, this increase is not significant (P=0.304).

Conclusion: The results of the study of genetic polymorphisms of GSTT1 in patients with COVID-19 in three forms, mild, severe and critical, in Khorramabad population indicated that there is no significant relationship between these polymorphisms and the severity of COVID-19.

Keywords: Genetic polymorphism; COVID-19; SARS-CoV-2; GSTT1.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-38

The Impact of Aminoguanidine on the Fibrinogen Gene Expression in Streptozotocin-induced Diabetic Rats

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Abstract

Background and Aim: Fibrinogen is a thrombotic factor proposed as a biological marker for prognostic assessments, microvascular and macrovascular complications monitoring, and therapeutic targets in diabetes. This study aimed to investigate the effects of aminoguanidine on fibrinogen gene expression in diabetic rats.

Methods: Diabetes mellitus was induced by a single-dose intraperitoneal injection of streptozotocin (50 mg/kg) in 12-h fasted rats. One week after the injection of streptozotocin, diabetic rats were treated with different doses of aminoguanidine for 28 days. Fibrinogen gene expression was detected and quantified using real-time polymerase chain reaction. The IBM Statistical Package for the Social Sciences Statistics 24.0 was used to analyze data, and GraphPad Prism 8.0 was used for graphs.

Results: The fibrinogen gene expression was significantly decreased in diabetic rats treated with aminoguanidine at 50 mg/kg ($P < 0.047$).

Conclusion: Aminoguanidine can prevent the expression of the fibrinogen gene in the liver of diabetic rats.

Keywords: Aminoguanidine, Fibrinogen, Diabetes Mellitus.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PG-39

CRISPR Therapy's Transformative Impact on Beta Thalassemia Treatment

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Abstract

Background and Aim: Beta thalassemia is one of the most common blood disorders, resulting in microcytic-hypochromic anemia (MHA). A recessive autosomal recessive inheritance pattern is characteristic of this condition. As a genome editing technology, clustered regularly interspaced short palindromic repeats/CRISPR-associated protein 9 (CRISPR-Cas9) may offer new possibilities.

Methods: To retrieve the related documents, in Persian and English, published between February 2010 and March 2023, the valid databases of PubMed/Medline, Scopus, Web of Science, and the Scientific Information Database (SID) were searched.

Results: CRISPR/Cas9-mediated gene editing therapy holds the greatest promise, as a therapeutic strategy to deal with β -thalassemia. Two main CRISPR/Cas9-based methods are also under investigation to treat this blood disorder. The first step is to repair the mutated β -globin coding gene, and the next step is fetal hemoglobin (HbF) replacement. Edit-301 is also a patient-derived autologous gene-edited CD34+ hematopoietic stem cell experimental medicine to make up for adult Hb deficiency in β -thalassemia through the reactivation of HbF expression. It has thus been designed and developed, using the CRISPR-Cas12a ribonucleoprotein (RNP) to initially edit the HbG1/2 gene promoter region as the β -globin of patient-derived hematopoietic stem cells. Besides, CTX001, a patient-derived CRISPR-Cas9-edited blood hematopoietic stem cell therapy developed by Vertex Pharmaceuticals, results in elevated HbF levels in erythroid cells in vivo. Furthermore, it is the most innovative candidate for β -thalassemia treatment. Moreover, EdiGene's ET-01 is a CRISPR/Cas9-modified CD34+ human hematopoietic stem and progenitor cell research product for the treatment of transfusion-dependent Thalassemia.

Conclusion: Regardless of its ethical and social challenges, CRISPR/Cas9-mediated gene editing therapy is an effective option for Hb-associated genetic diseases. This technology is thus used as a tool for treating single-gene disorders, such as β -thalassemia. Studies have further demonstrated that the genomes in patients with β -thalassemia can be modified via the CRISPR/Cas9 technique, which is promising for the β -thalassemia treatment. Nevertheless, more tests on human samples are desperately needed.

Keywords: Beta-Thalassemia, Gene Therapy, CRISPR/Cas9.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-40

Clinical Study on Serum CTHRC1 Expression Changes as a Potential Indicator in Breast Cancer Diagnosis

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Abstract

Background and Aim: This study aims to examine the expression of CTHRC1, a protein in breast cancer patients' serum because it has a significant role in the progression of the disease as well as histological, molecular, and clinical phenotypes.

Methods: RNA was extracted from serum and converted into cDNA, and CTHRC1 expression levels were determined. The differences in gene expression were determined using the GenEx software.

Results: The majority of patients had metastasis to the armpit and were in stage I. CTHRC1 expression levels in breast cancer patients' serum were not significantly different from those in the control group. In terms of serum CTHRC1 levels, the area under the ROC curve (AUC) was 0.60. The sensitivity and specificity of CTHRC1 were 54.16% and 55.14%, respectively.

Conclusion: Although our results did not match those of breast cancer tissue studies, the sensitivity, specificity, and AUC of the ROC will increase as the sample size increases. The majority of our patients had armpit metastases and were in the early stages of the disease. Several studies have demonstrated that this gene is highly expressed during advanced stages of metastasis, as well as in serum and tissues. A large-scale clinical study with more participants will be required to determine CTHRC1's diagnostic value.

Keywords: Breast Cancer, Metastasis, Sensitivity, Specificity, Biomarker, Gene Expression, CTHRC1.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-42

Gene Expression and Pathway Analysis of Dysregulated Genes and miRNA Expression Profiles in Erythroid Progenitor Colonies of Chronic Myelogenous Leukemia (CML)

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Abstract

Background and Aim: Chronic Myelogenous Leukemia (CML) is caused by a translocation between chromosomes 9 and 22, resulting in the Philadelphia chromosome and expression of the BCR-ABL fusion gene. DNA damage response pathways facilitate DNA repair and prevent genomic instability, while mutations in DNA repair genes can contribute to CML development and progression. Differential Expressed Gene (DEG) was performed in the previous clinical data collection in comparing enriched normal and CML cells carried out by M. Affer. et.al, indicate 292 genes were downregulated and 192 genes upregulated. Recent studies suggest that microRNAs can be used as biomarkers for the diagnosis and prognosis of CML.

Methods: GSE47927 Query Datasets of Expression profiling by array, containing 67 samples (15 control and 52 CML) were retrieved from the Gene Expression Omnibus (GEO) database. Series analyzed using the GEO2R online web. quantile normalized gene expression values were adjusted to the P-values applied by the Bonferroni method. The limma package was used to identify the differential expressed genes (DEGs) using R software. $|\text{Log Fold change}| > 1$ and adjusted p-value < 0.05 were the criteria for identifying Differentially expressed genes (DEGs). Transcription and Pathways enrichment analysis was performed by Enrichr tools. Targeted miRNA was chosen and it seems to have a sensible correlation with the differentiated expressed genes which was analyzed by miRTarBase database. Moreover, genes associated with signaling pathways were found by the Kinase Perturbations tool from GEO up/down.

Results: A total of 113 DGEs, including 72 up- and 141 down-regulated genes were screened in comparing CML against normal samples of the GSE47927 dataset. Using the miRTarBase database, among the miRNAs, has-miR-603, has-miR-8485, and has-miR-497-5p were found to have the highest association with the down-regulated genes including, IGF1R, PLAG1, PAG1, OCLN, GPRIN3, CD180, RASSF8, ATP9A, SLCO5A1, HOXA3, HLF, HLA-DOA, and the miRNAs, has-miR-5090, has-miR-6775-5p, and has-miR-126-3p were found to have the highest association with the up-regulated genes including, SERPINB3, SERPINB4, PLK2, IGFBP2, TEK, LONRF2, LEPROT, KCNK5, CYP1B1, ZMAT3, CMTM5, DDIT4, WT1 hub genes. Prominently, BEX1, KCNK5, CYP1B1, C3, S100A16, and MT1X up-regulated genes were involved in pathways of BRAF overexpression and ERBB3 drug activation pathways, also CCNB2, FAM83A, WT1 up-regulation and, HLA-DRB1/3/4, HLA-DOA, and HLA-DQB2 down-regulation are associated with ABL1 mutation. On the other side down-regulation of IGF1R, KLF12, and HLA-DRB5 related to knockdown of GSK3B.

Conclusion: This analysis identified dysregulated miRNAs in CML, including miR-5090, miR-6775-5p, and miR-126-3p. These miRNAs are involved in various aspects of CML pathogenesis. Using techniques such as qRT-PCR or microarray analysis, miRNAs can be detected in blood or bone marrow samples so providing a sensitive and specific approach to identifying miRNA biomarkers for CML diagnosis and monitoring. However, miRNA-based diagnostic tests for CML are still in the research stage. Further studies are needed to validate the diagnostic accuracy and clinical utility of miRNA biomarkers for CML.

Keywords: Chronic Myelogenous-Leukemia (CML), microRNAs(miRNAs), Differentially Expressed Genes (DEGs), Gene-Expression-Omnibus (GEO), quantitative Reverse Transcription-PCR (qRT-PCR).





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-43

Prenatal diagnosis of beta-thalassemia among couples with thalassemia minor in Torbat-e Jam, Iran

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Abstract

Background and Aim: β -thalassemia is a common inherited hemoglobin disorder which results in the unbalanced synthesis of beta globin chains. It is an autosomal recessive disorder which occurs from mutations in the β globin gene, located on chromosome 11. These mutations can result in three forms: β -thalassemia major, β -thalassemia intermedia, and β -thalassemia minor. The purpose of this research is to prenatal diagnosis of β -thalassemia mutations in the CVS acquired from couples suspected to β -thalassemia minor live in Torbat-e Jam.

Methods: After obtaining informed consent, 5 cc of blood will be taken from the couple with thalassemia minor, and if the woman is pregnant, CVS samples will be taken at 9-12 weeks of pregnancy. DNA is extracted by the standard method and PCR done for all three exons and introns of the HBB gene and then the entire gene is sequenced.

Results: This study is the first reports from Torbet-e Jam and 100% of mutations have been identified using the sequencing method.

Conclusion: Since family marriage is very common in Torbet-e Jam, prenatal diagnosis for genetic diseases can prevent the occurrence of disabilities.

Keywords: Mutation, beta-thalassemia, Torbat-e Jam.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PG-44

Crosstalk between circular RNAs with NF- κ B signaling pathway in breast cancer progression: A Systematic Review

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Abstract

Background and Aim: The newest class of noncoding RNAs with distinctive characteristics are called circular RNAs (circRNAs). These novel RNAs are more stable than other RNAs because they lack 5' and 3' ends, instead having their two ends created from pre-mRNA through a process called back-splicing. There is growing evidence that circRNAs were enriched in the NF- κ B pathway. The development of many types of malignancies, especially breast cancer is associated with aberrant activation of the NF- κ B pathway. This systematic review determines the current evidence for regulatory effect of circRNAs on NF- κ B signaling pathway in breast cancer progression.

Methods: An electronic search of the literature was performed using PubMed, Web of Science, Scopus, and Google Scholar. Key search terms were “cancer”, “circular RNA”, and “NF- κ B pathway”. Without regard to language, all studies published between January 1, 2005, and August 30, 2023, were included.

Results: Recent findings indicate that the circRNA/NF- κ B axis controls the expression of genes linked to cancer and, consequently, the growth of tumors. The expression of circRNA connected to the NF- κ B pathway-related expression is undoubtedly linked to a wide range of clinical features. Several circRNAs such as circABCC4, circTPGS2, circIKBKB via interaction with NF- κ B pathway involved in breast cancer progression.

Conclusion: A comprehensive understanding of the molecular processes behind the involvement of circRNA linked to the NF- κ B pathway in the progression of breast cancer would provide novel window for breast cancer therapy. Our data revealed that 8 circRNAs are dysregulated in breast cancer and via interaction with NF- κ B signaling implicated in breast cancer development.

Keywords: Circular RNA, breast Cancer, NF- κ B pathway.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-45

Development of a high-resolution melting curve analysis method for detecting DPYD HapB3 variant

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Abstract

Background and Aim: Dihydropyrimidine dehydrogenase (DPD) deficiency is a pharmacogenetic syndrome associated with severe/lethal toxicities upon 5-fluorouracil (5-FU) and its oral prodrug capecitabine (CAP) intake, widely used for the treatment of many different solid tumors. The genetic polymorphism in the gene encoding this enzyme (DPYD) may result in a decrease or loss of enzyme activity which may lead to the accumulation of medicines, their metabolites and potential fluoropyrimidine-related toxicity. The goal of the present study was to design a simple, rapid, and inexpensive high-resolution melting (HRM) curve genotyping method to identify one of the common genetic variants of DPYD gene c.1236G>A (rs56038477, E412E, haplotype B3).

Methods: We established a HRM technique for detection of DPYD HapB3 variant. Sanger sequencing was used to confirm the results. Wild (GG), mutant (AA) and heterozygote (GA) controls of this polymorphism were purchased from Pishgam Biotechnology Company. 24 dried blood spot samples in addition to 10 clinical blood specimens receiving fluoropyrimidine derivatives, both groups with unknown sequence were enrolled in this study.

Results: Our HRM method was successfully able to detect patients with DPYD-HapB3. Both efficiency and accuracy of the new approach were 100% as compared with sequencing. More interestingly, to the best of our knowledge in this study for the first time we used DBS samples as the source of nucleic acid for extraction. Among all studied subjects, one sample is diagnosed to has the GA heterozygote genotype with HRM which further confirmed by the Sanger sequencing.

Conclusion: In the present study we optimized a HRM method to detect DPYD-HapB3 variant for the first time. This high throughput method is with high sensitivity and specificity can be used as an easy to use and cost-effective method to differentiate HapB3 variant especially in low-income countries. Due the clinical importance of this variant, pharmacogenetics assessment before beginning the treatment process is highly recommended.

Keywords: Dihydropyrimidine dehydrogenase; Drug toxicity; Fluoropyrimidines; HapB3 polymorphism; Pharmacogenetics.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PG-46

MicroRNAs as Therapeutic Targets in Oral Squamous Cell Carcinoma: Interpreting Downstream Gene Effects

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Abstract

Background and Aim: Oral squamous cell carcinoma (OSCC) is a type of head and neck cancer characterized by the uncontrolled growth of malignant cells in the oral cavity. MicroRNAs (miRNAs) have emerged as central players in gene regulation, influencing diverse cellular processes. This comprehensive review delves into the therapeutic potential of miRNAs in OSCC, with a focus on elucidating their effects on downstream target genes and the intricate molecular pathways that underlie cancer progression.

Methods: A systematic literature search was conducted to identify studies investigating miRNAs as therapeutic targets in OSCC. Studies utilizing in vitro and in vivo models, synthetic miRNA mimics, and other miRNA-based interventions were analyzed. Bioinformatic tools and functional assays were employed to unravel the downstream targets and pathways influenced by miRNAs.

Results: Dysregulation of specific miRNAs in OSCC tissues was consistently observed, highlighting their diagnostic and prognostic potential. Experimental interventions manipulating miRNA expression demonstrated significant effects on downstream target genes, revealing critical pathways implicated in OSCC progression. Notably, the let-7 family emerged as a prominent regulator, exerting tumor-suppressive effects by targeting HMGA2, c-Myc, and cyclin D1. Conversely, oncogenic miRNAs such as miR-21 promoted OSCC by targeting tumor suppressors like PTEN and PDCD4. Bioinformatic analyses unraveled complex miRNA-mRNA interaction networks, providing insights into the regulatory mechanisms governing OSCC.

Conclusion: This review underscores the pivotal role of miRNAs as therapeutic targets in OSCC, emphasizing their intricate effects on downstream genes and signaling pathways. Dysregulation of specific miRNAs in OSCC presents opportunities for diagnostic and prognostic applications. Experimental interventions manipulating miRNA expression have revealed promising results, unveiling the regulatory networks governing OSCC progression. The emergence of nanoparticle delivery systems offers promise for overcoming delivery challenges. Continued research and clinical trials are essential to validate the safety, efficacy, and translational potential of miRNA-targeted interventions, ushering in a new era of personalized therapeutic approaches for oral squamous cell carcinoma.

Keywords: Oral squamous cell carcinoma; MicroRNAs, signaling pathways.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Case Report

Code of Abstract: PG-47

Identification of homozygous frameshift mutation in CDK-10 gene-associated neurodevelopmental disorder in an Iranian pedigree

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Abstract

Background and Aim: Al Kaissi syndrome is a sporadic and heterogeneous genetic disorder that presents a constellation of skeletal anomalies and clinical manifestations, including Growth Retardation, Facial Dysmorphisms & Intellectual Disability. The genetic cause of this syndrome has been linked to mutations in the CDK10 gene located on chromosome 16q24.3. We used Whole Exome Sequencing to diagnosis of disease in a 10-years-old female patient who suffered from mental retardation and neurodevelopmental delay. A Bi-allelic loss of function variant, c.520_521delAA, was identified in the CDK10 gene, predicted to cause a frameshift, p. Lys174fs, in the cyclin-dependent kinase ten protein.

Methods: The genomic DNA of patient was extracted and isolated from a peripheral blood sample using Simex DNA extraction kit (SIMBIOLAB, Iran). SureSelect Target Enrichment Kit was used for human exome enrichment, and 12 Gb library data with an average coverage of 85X was provided by Illumina HiSeq 2000/2500. NGS data were analyzed using dbSNP, 1000Genome, ClinVar, and ESP databases. Data was enriched based on mental retardation, neurodegenerative diseases, paraplegia, and neurodevelopmental delay.

Results: We detect a frameshift deletion variant, c.520_521delAA, using WES analysis in exon 7 of CDK10 gene. Bioinformatic analysis predicts that this variant disrupts CDK10 function, and it was classified as pathogenic based on ACMG classification.

Conclusion: The identification of c.520_521delAA variant expands the genotypic and phenotypic spectrum of Al Kaissi syndrome. Our study highlights the importance of genetic testing by WES for diagnosing rare syndromes and facilitating genetic counseling for families with affected individuals.

Keywords: Al kaissi syndrome, CDK-10, Whole exome sequencing.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-48

The frequency of two alpha – 1 – antitrypsin alleles and the specified ALOX15 SNP in chronically obstructive lung illness (COPD) in Khorasan-Razavi

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Abstract

Background and Aim: Genetic polymorphisms are responsible for the functional individuality of human beings. They are involved in the variable sensitivity of human individuals towards external stimuli and contribute to genetic predisposition of certain individuals for a number of diseases. In this study the frequency of specified genetic polymorphisms in the ALOX15 gene and two alleles of two alpha – 1 – antitrypsin were investigated in selected cohort 150 individuals with chronically obstructive lung illness (COPD) of the Khorasan-Razavi province population.

Methods: After obtaining informed consent, 5 cc of blood will be taken from 150 individuals with chronically obstructive lung illness (COPD). DNA was extracted using Salting out method. The specific ARMS primers for two alpha – 1 – antitrypsin alleles and selected ALOX15 SNP were designed and PCR was performed.

Results: The genetic polymorphism (SNP) leading to a T560M exchange in human ALOX15 was detected in one tenth of samples (15/150). The polymorphism alleles of ZZ and SS found in few cases (4/150).

Conclusion: It was found that neither the two alpha – 1 – antitrypsin alleles nor the specified ALOX15 SNP occur with a frequency above 2 % in this cohort. These data indicate that the Khorasan Razavi population may not be suitable for more detailed investigation into the functional relevance of these genetic variations and into their possible involvement in the pathogenesis of different diseases.

Keywords: Polymorphism, alpha – 1 – antitrypsin, COPD, ALOX15.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-49

Identification of a Putative Founder Mutation in SLC30A10 Associated with Hypermanganesemia in East Iranian Patients: Implications for Genetic Testing and Counseling

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Abstract

Background and Aim: Manganese is vital for human cellular functions, but its brain accumulation can lead to the rare disorder Hypermanganesemia. Caused by mutations in manganese transporter proteins or environmental exposure, hereditary cases involve SLC30A10 and SLC39A14 mutations. Studying four Iranian families with the disorder, we discovered a His336Tyr missense mutation in the SLC30A10 gene, suggesting a potential founder mutation in the Sistani subpopulation. Clinical features in affected individuals included mild dystonia, polycythemia, elevated Mn levels, and abnormal brain MRI signals. Despite apparent familial unrelatedness, the findings recommend genetic screening for this mutation in Iranian patients with Hypermanganesemia.

Methods: We employed whole-exome sequencing and Sanger sequencing to study four Iranian families with Hypermanganesemia. All affected individuals exhibited a missense mutation, His336Tyr, in the SLC30A10 gene, which was located within an approximately 200 Mb homozygous stretch. The most prevalent clinical features included mild dystonia, polycythemia, elevated serum Mn levels, and hyperintense signals in brain MRI.

Results: The study conducted clinical evaluations on four unrelated families with a total of four affected individuals, revealing common clinical features such as mild dystonia, polycythemia, neutropenia, T1 hyperintensities in globus pallidus and dentate nuclei, and fine motor skill abnormalities leading to poor handwriting. Laboratory investigations indicated elevated levels of various markers, including CPK, aldolase, ceruloplasmin, pyruvate, SGOT, and SGPT. A heavy metal blood test showed increased levels of serum copper, whole blood lead (Pb), and manganese. Genetic evaluation through whole exome sequencing identified a homozygous mutation in the SLC30A10 gene (c.1006C>T; p. His336Tyr), absent in significant databases. According to ACMG criteria, this mutation was classified as pathogenic within a 200Mb run of homozygosity, suggesting a shared ancestry among affected individuals.

Conclusion: Despite the apparent lack of relatedness among the families, our findings suggest that the His336Tyr mutation may represent a founder mutation in the Sistani subpopulation. Thus, genetic screening for this mutation should be recommended for Iranian patients with Hypermanganesemia.

Keywords: SLC30A10, Whole Exome Sequencing, Founder mutation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Case Report

Code of Abstract: PG-50

Hereditary spastic paraplegias in an Iranian family with a novel mutation in *SPG7* gene

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Abstract

Background and Aim: The hereditary spastic paraplegias (HSPs) are a group of clinically and genetically diverse disorders characterized by progressive, usually severe, and lower extremity spasticity. Spastic paraplegias are classified according to both the mode of inheritance (autosomal dominant, autosomal recessive, and X-linked) and whether progressive spasticity occurs in isolation (uncomplicated) or with other neurologic abnormalities (complicated), including optic neuropathy, retinopathy, extrapyramidal disturbance, dementia, ataxia, ichthyosis, mental retardation, and deafness. In this study, we investigated the genetic basis of hereditary spastic paraplegias in an Iranian family and reviewed the reported spectrum of the *SPG7* gene mutations involved in this disorder.

Methods: An 8-year-old girl affected with mild features of spastic paraplegia were referred to our genetic counseling center. Her father and aunt (father-side) were affected with severe features of the disease, as well. Genetic counseling was performed and their family pedigree was drawn. Genetic analysis was performed on the father using whole-exome sequencing, then the detected variant was investigated in the child and her father and aunt using Sanger sequencing method.

Results: Exome sequencing in the father identifies a likely pathogenic canonical splice site mutation, c.618+1G>C, in the *SPG7* gene in a heterozygous state. Sanger sequencing method in the affected child, and her affected father and aunt detected the mutation in heterozygous states. This mutation has not been previously reported for its pathogenicity. Multiple lines of in silico computational analysis support the deleterious effect of the variant on the gene or gene product(s). This variant is absent in population databases (ExAC, 1000G, and our local database). Based on ACMG guidelines, this variant can be classified as a likely pathogenic variant.

Conclusion: Mutation in *SPG7* gene causes spastic paraplegia-7 (SPG7) with both autosomal recessive and autosomal dominant inheritance patterns. SPG7 is caused by homozygous or compound heterozygous mutation in the paraplegin (SPG7) gene. Some patients with the disorder carry heterozygous SPG7 mutations similar to our cases. SPG7 shows phenotypic variability between families. Some cases are pure, whereas other are complicated with additional neurologic features. In this study we are presenting an Iranian family affected by spastic paraplegia-7 and with a novel mutation in their SPG7 gene and discussing their clinical features.

Keywords: Hereditary; Spastic; Paraplegia; SPG7; Novel.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-51

Identification of a Novel Homozygous Splice Site Variant in EXOSC2 Associated with Short Stature, Hearing Loss, Retinitis Pigmentosa, and Distinctive Facies (SHRF) Syndrome in an Iranian Pedigree

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Abstract

Background and Aim: Short stature, hearing loss, retinitis pigmentosa, and distinctive facies (SHRF) syndrome is a rare autosomal recessive disorder caused by mutations in the EXOSC2 gene, which is an essential component of the RNA exosome complex involved in RNA processing and turnover. Here we report the identification of a novel homozygous splice site variant (c.673-1G > T) in the EXOSC2 gene in two siblings from an Iranian pedigree with SHRF syndrome. Clinical manifestations of the patients include developmental delay, intellectual disability, spasticity, short stature, hearing loss, premature aging, distinct facial features, and eye diseases.

Methods: The genomic DNA of patient was isolated from a sample of peripheral blood using Simex DNA extraction kit (favorgene). SureSelect Target Enrichment Kit was used to human exome enrichment, and 12 Gb library data with an average coverage of 100X was provided by Illumina HiSeq 2000/2500. NGS data were analyzed using Franklin, varsome, 1000Genome, ClinVar, and ESP databases. Data was enriched based on short stature, mental retardation, developmental delay, hearing loss, spasticity and facial dysmorphic features.

Results: Bioinformatics analysis predicts that this variant leads to the complete deletion of exon 8 of the EXOSC2 gene, disrupting its function, and it is classified as likely pathogenic based on ACMG classification. Our findings suggest that this variant could be a founder mutation in the Iranian population with syndromic autosomal recessive intellectual disability. Structural modeling of the EXOSC2 protein predicts that the deletion of exon 8 alters the protein's structure, stability, and function.

Conclusion: Our study highlights the importance of genetic testing for diagnosing SHRF syndrome and facilitating genetic counseling for families with affected individuals. The identification of this variant expands the genotypic and phenotypic spectrum of SHRF syndrome and adds to our understanding of the role of the RNA exosome complex in human genetic diseases.

Keywords: SHRF syndrome, EXOSC2, RNA exosome complex, founder mutation.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-52

Bi-allelic genetic variants in the translational GTPases GTPBP1 and GTPBP2 cause a distinct identical neurodevelopmental syndrome

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Abstract

Background and Aim: The homologous genes GTPBP1 and GTPBP2 encode GTP-binding proteins 1 and 2, which are involved in ribosomal homeostasis. Pathogenic variants in GTPBP2 were recently shown to be an ultra-rare cause of neurodegenerative or neurodevelopmental disorders (NDDs). Until now, no human phenotype has been linked to GTPBP1. Here, we describe individuals carrying bi-allelic GTPBP1 variants that display an identical phenotype with GTPBP2 and characterize the overall spectrum of GTP-binding protein (1/2)-related disorders.

Methods: In this study, 20 individuals from 16 families with distinct NDDs and syndromic facial features were investigated by whole-exome (WES) or whole-genome (WGS) sequencing. To assess the functional impact of the identified genetic variants, semi-quantitative PCR, western blot, and ribosome profiling assays were performed in fibroblasts from affected individuals. We also investigated the effect of reducing expression of CG2017, an ortholog of human GTPBP1/2, in the fruit fly *Drosophila melanogaster*.

Results: Individuals with bi-allelic GTPBP1 or GTPBP2 variants presented with microcephaly, profound neurodevelopmental impairment, pathognomonic craniofacial features, and ectodermal defects. Abnormal vision and/or hearing, progressive spasticity, choreoathetoid movements, refractory epilepsy, and brain atrophy were part of the core phenotype of this syndrome. Cell line studies identified a loss-of-function (LoF) impact of the disease-associated variants but no significant abnormalities on ribosome profiling. Reduced expression of CG2017 isoforms was associated with locomotor impairment in *Drosophila*.

Conclusion: Bi-allelic GTPBP1 and GTPBP2 LoF variants cause an identical, distinct neurodevelopmental syndrome. Mutant CG2017 knockout flies display motor impairment, highlighting the conserved role for GTP-binding proteins in CNS development across species.

Keywords: Bi-allelic genetic variants, GTPases GTPBP1 and GTPBP2, neurodevelopmental syndrome.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-53

Analysis of Microarray Gene Expression in Epithelial Pancreatic Progenitor Carcinoma to Invasive Neoplasm Progression

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Abstract

Background and Aim: During carcinogenesis, tumor suppressor genes, and oncogenes dysregulation drastically alter the antitumor immunity. Epithelial invasive neoplasm of pancreas is a precursor lesion of pancreatic Carcinogenesis and progresses according to carcinoma-invasive neoplasm sequence. The antitumor immune reactions change from an immune response to immune tolerance between epithelial invasive neoplasm and epithelial carcinoma stages. To identify mutated driver genes that affect pancreatic progenitor cells during multistep carcinogenesis, gene-expression profiles of neoplastic cell transcripts at different stages were analyzed. Uncovering the drivers' mutation developing pancreatic carcinoma to invasive overcomes tumor cell proliferation and invasion by targeting biological functions of the selected gene products.

Methods: GSE19650 Query Datasets of Expression profiling by array, containing samples from normal main pancreatic cells, intraductal papillary mucinous adenoma (IPMA), intraductal papillary mucinous carcinoma (IPMC), and intraductal papillary mucinous neoplasm (IPMN), was accessed from the Gene Expression Omnibus (GEO) database. Series analyzed using the GEO2R online web. The limma package was used to identify the differential expressed genes (DEGs) using R software. |Log Fold change| > 1 and adjusted p-value <0.05 were the criteria for identifying Differentially expressed genes (DEGs) from carcinoma to invasive neoplasm stage. A total of 279 DGEs, including 249 up- and 30 down-regulated genes were screened in comparing invasive neoplasm against carcinoma tumor cell line samples of the GSE19650 dataset. Transcription and Pathways enrichment analysis was performed by Enrichr tools.

Results: transcription analysis of upregulated genes by ESCAPE tools identified the involvement of signaling transcription factors with the highest adjusted p-value repeatedly for; POU5F1(OCT4), SOX2, NANOG, KLF4, CHD1, and PRDM1 that reprogrammed differentiated somatic cell into undifferentiated pluripotent progenitor cells. Pathway analysis using the PPI Hub Proteins tool identifies significant downregulation of TP53, CDK1, and APC genes otherwise, overexpression of, MAPK9, PLK1, SUMO1, and HDAC3 that is a DNA histone deacetylases protein.

Conclusion: Contribution of genetic and epigenetic alterations associated with multi-stage development of carcinogenesis provides the characterized gene expression profiles of invasive neoplastic tumor cells. Overexpression of HDAC3 by deacetylation and hypermethylation of DNA results in suppression of Tumor Suppressor Genes (TSGs), assisting to pancreatic tumor cell lines' dedifferentiation, proliferation, and progression. It is expected that explanation of the mechanisms responsible for the dysregulation of these genes in neoplastic cells will provide important clues that could pave the way to the development of a new form of antitumor therapy.

Keywords: intraductal-papillary-mucinous-adenoma (IPMA); intraductal-papillary-mucinous-carcinoma (IPMC); intraductal-papillary-mucinous-neoplasm (IPMN); Tumor-Suppressor-Genes (TSGs), OncoGenes.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-54

Effect of *Sargassum boveanum* methanolic extract on GLS1 gene expression in human colorectal cancer SW742 cell line

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Abstract

Background and Aim: glutaminase (GLS1) is a metabolism enzyme which plays a significant role in glutaminolysis. GLS1 is often overexpressed in numerous cancers, counting colorectal cancer (CRC). Emerging evidence shows that its inhibitors could support a benefit approach for cancer therapy. Brown seaweeds especially sargassum species have attracted considerable attention because of their bioactive compounds and anticancer activities. the aim of this research was to examine the effects of *Sargassum boveanum* methanolic extract on gene expression of GLS1 in colorectal cancer cell line.

Methods: In this study, the cellular viability of SW742 cell lines was evaluated using MTT assay after 24, 48 and 72 h treatment. The gene expression of GLS1 was quantitatively evaluated by real-time RT-PCR method.

Results: A dose-dependent decrease in the cell viability of SW742 cells was detected after the exposure of methanolic extract of *Sargassum boveanum*. In addition, the gene expression level of GLS1 was significantly decreased by the extract of *Sargassum boveanum* after 48 and 72 h treatment in tumor cell line (p=0.01, p=0.002, respectively).

Conclusion: This study for the first time provided evidence that methanolic extract from *Sargassum boveanum* decreased gene expression of GLS1 in cell line colorectal cancer. Therefore, it could be considered as a hopeful treatment in the therapy of cancer.

Keywords: *Sargassum boveanum*, GLS1, Colorectal Cancer.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-55

Polymorphisms of pre-miR-499 rs3746444 T/C and Pre-miR-146a rs2910164 C/G in the Autoimmune Diseases of Rheumatoid Arthritis and Systemic Lupus Erythematosus in the West of Iran

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Abstract

Background and Aim: The present research is a case-control study to analyze the influence of pre-miRNA-146a rs2910164 and pre-miRNA-499 rs3746444 polymorphisms as candidate susceptibility factors for both rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).

Methods: Polymorphism in miR146 and miR499 using ARMS-PCR was genotyped on 139 autoimmune disease (AD) patients (89 RA and 50 SLE) referred to Educational Hospitals of Khorramabad, Lorestan Province, west of Iran in 2018–2019 and 237 healthy control subjects.

Results: A significant increase in the likelihood of carrying the GC vs. GG of pre-miR146-rs2910164 and T vs C allele of pre-miR499- rs3746444 in patients with RA was found. On the contrary, patients with RA were less likely to carry the TC + CC vs TT genotype and the C vs T allele of pre-miR499- rs374644. In females with the GC vs GG and GC+ CC vs GG genotypes, a significant association was found with the increased risk of RA. Interestingly, the genotypic combination of TC of the pre-miR499-rs374644 with GG of pre-miR146-rs2910164 more strongly decreased the risk of RA. In patients with SLE, no notable associations were found between both pre-miRNA-146a rs2910164 and pre-miRNA-499 rs3746444 with risk of disease.

Conclusions: Genetic polymorphisms of miR146 rs2910164 is associated with RA susceptibility especially in females. Interestingly, there is a potential in miR499 to reduce the risk with the protective effect of gene-gene interactions on miR146 in RA disease.

Keywords: MicroRNA polymorphisms, Rheumatoid arthritis, Systemic lupus erythematosus.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Systematic Review/ Meta-Analysis

Code of Abstract: PG-56

Genetic basis of Attention-Deficit Hyperactivity Disorder in children

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Abstract

Background and Aim: Attention-Deficit Hyperactivity Disorder (ADHD) is a neurological disorder characterized by impulsivity and inattention. Despite extensive research, gaps remain in our understanding of ADHD's etiology. Family, twin and adoption studies (GWAS) have identified several genetic loci of interest. Furthermore, genes involved in dopamine absorption, transport, receptor binding and synthesis, such as DAT1, DRD2, DRD4 and DRD5, are considered significant in ADHD pathophysiology.

Methods: this systematic synthesizes review findings from 14 peer-reviewed articles on hereditary ADHD, selected via Google Scholar. These articles were reviewed over three days, with a focus on validating sources and extracting relevant information on ADHDs heritability. keywords such as hereditary ADHD, ADHD, DAT1, DRD2, DRD4, DRD5, genetic effects, molecular genetics, norepinephrine's role, parental influence, inheritance patterns, genetic transmission and GWAS were used.

Results: The literature suggests that ADHD arises from a complex interplay of hereditary and non-hereditary factors. Identified risk factors include, large rare copy number variants, small-effect candidate gene variants, low birth weight, a family history of ADHD, and pre- and postnatal exposure to lead. These factors, while consistently implicated in ADHD, it has a different effect on the development and manifestation of the disorder.

Conclusion: Genetic research into ADHD is very critical, particularly to identify children at risk and potentially inform preventive strategies. Current understanding is that the genetic risk factors for ADHD are often subtle and complex, with no single gene variant accounting for the disorder. Advances in multiple research domains are anticipated to improve our understanding of ADHD genetics shortly.

Keywords: DAT1, DRD2, DRD4, DRD5, ADHD, heredity ADHD, GWAS.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PG-57

Vertical Transmission of Carcinogenic Human Papillomavirus (HPV) and tumor from Mothers with Cervical Cancer; a Systematic review on Modes of Transmission, Persistent and, Possibility of Early-life Cancer in Minors

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Abstract

Background and Aim: Human papillomavirus (HPV) is a contagious disease with over 200 types which almost 40 of them are capable of inducing carcinogenesis in body. Sexual intercourse is the main route of transmission but vertical transmission is also possible. Based on extensive research, it has been established that the vertical transmission of HPV can occur through various pathways, such as the placenta, vaginal delivery, blood, and amniotic fluid. The main questions are whether the HPV infection transmitted through vaginal delivery is permanent or transient? And whether a tumor can be transmitted from a mother with cervical cancer to its infant?

Methods: In order to gather information about the vertical transmission of human papillomavirus and possibility of transmission of tumor in mother with cervical cancer to their infants, a comprehensive search was conducted on reputable databases such as Google Scholar, Nature, Science Direct, and PubMed. The search was performed by using relevant keywords such as "vertical transmission", "human papilloma virus", "cervical cancer", "vertical transmission of cancer", and "infants". The initial search yielded 43 studies, which were carefully examined and reviewed for eligible reports, relevant keywords, and titles. After a thorough analysis of the papers, 20 studies were selected for further analysis. The selected studies provide valuable information on the subjects and were gathered through a meticulous search process using the most reliable sources available. For this review, only articles written in the English language were selected and they were reviewed from the years 2000 to 2023.

Results: Some studies suggest that HPV can be transmitted from mother to infant through peri-conceptual transmission, prenatal, and perinatal pathways. The rate of vertical transmission is reported to be about 25%, but it can vary widely from 4% to 72%. All the babies who were HPV-positive were born from HPV-positive mothers, and in some reported cases where HPV-positive infants were born from HPV-negative mothers is thought to be due to a false negative or hospital contamination. According to studies, HPV infection in infants is typically cleared within 2 weeks to 24 months after birth and is not associated with the development of specific malignancies. Only one paper has reported a case of persistent HPV in the oral cavity of infants. another paper also reported two cases of tumor transmission to the lungs of infants when a mother with cervical cancer delivered them.

Conclusion: while most malignancies are transmitted via placental and blood, there have been some rare cases where mother-to-infant transmission of tumors has occurred during vaginal delivery in the birth canal. In a mother with a cervical tumor, the infant is exposed to the tumor cells in the birth canal and could aspirate them into the lungs. also, there is a possibility of vertical transmission of HPV but most of them are transient and cannot cause malignancies. further research is essential to draw an accurate conclusion.

Keywords: Vertical transmission, HPV, tumor, Cervical cancer, mother-to-infant.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-58

Expanding the phenotypic, genotypic, and functional spectrum of *CNPY3* -associated DEE

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Abstract

Background and Aim: Developmental and epileptic encephalopathy-60 (DEE60) is an autosomal recessive neurologic disorder characterized by the onset of infantile spasms, seizures, or myoclonus in the first months of life. An important gene associated with DEE60 is *CNPY3* (Canopy FGF Signaling Regulator 3) on chromosome 6p21.1 which encodes a protein known as Canopy3 or PRAT4A (protein associated with TLR4A). It is localized in the endoplasmic reticulum (ER) and functions as a co-chaperone with the general chaperone gp96 to regulate the subcellular distribution and responses of multiple Toll-like receptors (TLRs). Recently, recessive *CNPY3* variants have been linked to DEE60 (MIM # 617929, PubMed: 29394991).

Methods: We used whole exome sequencing (WES) for genetic analysis to investigate pathogenic genetic defect responsible for epileptic encephalopathy. Filtration of exome data was carried out to narrow down variants by using various filtering steps. Variant prioritization was done based on SysNDD genes. Sanger sequencing was performed for confirmation and segregation analysis. Using GeneMatcher, we queried for additional patient cases with variants in *CNPY3*. An in-vitro functional assay is currently under development to help understand the pathophysiology and unravel the functional impact of detected variants on *CNPY3*.

Results: We analyzed the exome sequencing data by using our inhouse pipeline and got total of 147,767 variants. All this data shows that the quality and coverage of exome data was up to the mark. All the identified variants were passed through various filters depending upon quality, genomic position, allelic frequency, protein impact, pathogenic effect and previous relevance to the disease phenotype. Finally, we found the homozygous change in *CNPY3* gene (NM_006586.5, exon3, c. A370C, p. Lys124Gln). The variant was neither found in public databases nor in local database. Using GeneMatcher, we identified seven additional family including 10 additional patients harboring biallelic and monoallelic variants in *CNPY3*.

Conclusion: Our results suggest that *CNPY3* defects are a yet underdiagnosed cause of syndromic DEE60. Establishment of a functional read-out will help distinguishing benign from pathogenic variants in this gene.

Keywords: Epileptic encephalopathy, *CNPY3*, GeneMatcher.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-60

Polymorphic assessment of proportion convertase subtilisin/kexin type 9 (PCSK9) variant rs11591147 in subjects from Ahvaz city, Iran

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Abstract

Background and Aim: proportion convertase subtilisin/kexin type 9 (PCSK9), the ninth number of the proportion convertase family, is a pivotal molecule in the key regulator of lipid hemostasis. Previous studies have suggested that PCSK9 expression and its function in LDL receptor regulation could be altered in the context of diabetes. Many different variants of this gene are related to cholesterol and LDL-C levels. The variant rs11591147 is associated with an increase in LDL receptors in hepatocytes to decrease LDL cholesterol rate. The correlation of PCSK9 level with LDL cholesterol rate remains not defined in Iran. The aim was to assess PCSK9 variant rs11591147 frequency in Iranian population.

Methods: the study was composed of 590 subjects over 20 years old and 166 patients > 20 years were included in a Cohort study as 156 adult subjects with low LDL-C ≤ 59 mg/dl. The rs11591147 polymorphism was genotyped using polymerase chain reaction (PCR) followed by restriction fragment length polymorphism (RFLP).

Results: we founded only one heterozygous case in the entire study population.

Conclusion: Although in this study we focused on the most common variant of this gene, we found only one heterozygous case in the entire studied population. This issue is important considering that the PCSK9 gene is a therapeutic target. In order to assess the prevalence of this PCSK9 variant, further studies with larger populations are necessary.

Keywords: LDL Cholesterol, PCSK9 variants, Gene frequency.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-61

Investigation of the potential effect of alpha-pinene on the miR-106b and EMT marker (vimentin) in hepatocellular carcinoma cells (HepG2)

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Abstract

Background and Aim: As a natural compound, alpha-pinene is reported to have a number of properties, including its ability to inhibit the growth of cancerous cells. Recent studies suggest that alpha-pinene can prevent the invasion of malignant cells in some cancers. During epithelial-mesenchymal transition (EMT), cancer cells lose their epithelial characteristics and migrate to adjacent tissues. There's evidence that microRNA-106b (*miR-106b*) indirectly contributes to EMT, which leads to tumor cells migrating and invading other tissues. Therefore, this study aimed to investigate the effect of alpha-pinene on the expression of *miR-106b* and *vimentin* in HepG2 cells.

Methods: The human hepatocellular carcinoma cell line HepG2 was treated for 24 hours with different concentrations of alpha-pinene in the present study. The expression levels of *mir-106b* and *vimentin* were determined by RT-qPCR.

Results: Alpha-pinene significantly downregulated *miR-106b* in different treatment groups compared to the control group. Furthermore, at different alpha-pinene concentrations, vimentin gene expression was significantly increased.

Conclusion: By downregulating miR-106b and increasing vimentin expression, alpha-pinene inhibits HCC migration and invasion. So, we concluded that alpha-pinene could be helpful in preventing the proliferation of cancer cells.

Keywords: Hepatocellular Carcinoma, Alpha-pinene, Epithelial-Mesenchymal Transition, MicroRNA, vimentin.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-62

Genotypic distribution of vitamin D receptor gene polymorphism, BsmI in patients with non-alcoholic fatty liver disease

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Abstract

Background and Aim: Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease, which affects about 20%–30% of the general population. The molecular and genetic details of NAFLD pathogenesis is ambiguous. The vitamin D/vitamin D receptor (VDR) axis is significantly associated with the development and progression of NAFLD. Although the Gene polymorphisms biological significance was not defined, but they influence the regulation of the VDR gene such as BsmI, so they are associated with the presence and severity of NAFLD, as they may influence the regulation of adipose tissue activity, but the disturbance rate of single nucleotide polymorphisms (SNPs) such as rs1544410, related to BsmI polymorphism, is not clear yet. The aim of our study was to assess BsmI variant rs1544410 frequency in Iranian population.

Methods: We analyzed data from 128 Iranian consecutive patients that referred to Gastrointestinal & Liver Unit of the Ahvaz Golestan Hospital with clinical and sonographic diagnosis of NAFLD and available DNA assessment. The rs1544410 polymorphism was genotyped using polymerase chain reaction (PCR) followed by restriction fragment length polymorphism (RFLP).

Results: We founded 60 heterozygous cases (Bb genotype) (48.8%) and 68 patients are in homozygote genotype class that divided in to BB genotype (13.2%) and bb genotype (38%) in the entire study population.

Conclusion: In this study we focused on the most common variant of this gene and found heterozygous and homozygous cases in the entire studied population. This issue is important considering that the BsmI gene is a therapeutic target. BsmI Bb genotype is more associated with NAFLD patients. Mechanisms underlying this association, and its clinical relevance need further investigations.

Keywords: vitamin D receptor, BsmI variants, Gene frequency.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-63

Comparison Rappaport Shunt Genes Expression Pathway on BPG Production in Individuals with and without SARS-Covid- 19 Along with Remdesivir Treatment

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Abstract

Background and Aim: SARS-COVID-19, by its effect on the respiratory system along with hypoxia, can cause death. The body resists it in different ways, one way is the production of 2,3BPG by the enzymes of the Rappaport shunt in the glycolysis pathway which plays an important role by increasing oxygen supply to tissues, although the level of gene expression of this pathway is different in individuals with corona compared to healthy people.

Methods: In this study, all studied target people were divided into three groups: healthy individuals as negative control group, outpatient (mild) and hospitalized (severe) patients. Also, the severe patient's group was divided into two subgroups: severe patients with REM injection, and severe patients without REM injection. After extracting mRNA and then cDNA by using real-time PCR, the expression levels of PGM and PGP were measured.

Results: Results of the study showed that gene expression for PGM in individuals with corona was high and for PGP was low, also there were significant differences between most of the studied groups.

Conclusion: In people with SARS-COVID, 2, 3 BPG was increased due to the high level of PGM and the low level of PGP gene expression, which counteracts the hypoxia of coronavirus. It is expected that examining the expression of these genes and finding drugs in increase the expression of PGM and decrease the expression of PGP which led to high production of 2,3BPG in hypoxia in corona disease, can reduce the mortality caused by hypoxia in hospitalized patients due to corona.

Keywords: PGM; PGP; 2,3 BPG; REM; Comparison Rappaport Shunt; Genes Expression Pathway; BPG Production; SARS-Covid-19; Remdesivir Treatment.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-65

The critical role of lncRNAs in breast cancer prognosis and diagnosis

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Abstract

Background and Aim: One of the most common causes of death in women is Breast Cancer (BC). Although modern treatment methods are expanding today, we do not usually receive satisfactory and good responses from new treatments. New studies have shown that non-coding RNAs, such as Long Non-Coding RNA (lncRNA), have a significant role in diagnosing and treating malignancies, including BC. Hence, this research was conducted to explore the considerable part of lncRNAs in BC.

Methods: Information was gathered from various credible scientific sources, including PubMed, ScienceDirect, and Google Scholar, using keywords such as "small RNA," "Breast Cancer," "lncRNA," "biomarker," "treatment," "prognosis," and "diagnosis." Subsequently, the gathered data underwent assessment.

Results: Several studies identified regulatory networks of lncRNA-coding genes, including TERC, NEAT1, and TUG1, along with some other mRNAs, such as AR, ESR1, and SOX2, that can be applied for the diagnosis, prediction, and prognosis of BC patients. Diverse lncRNAs like DSCAM-AS1, HOTAIR, GATA3-AS1, and LINC01087 have been described as potential biomarkers in BC, suggesting their relevance in defining luminal tumors. For the prognosis of BC, studies revealed that the integration of the lncRNA AC10538 and mRNAs OR7C1, TBX2, RSPH4A, and C2orf61 had a better prediction in early-stage BC patients. Furthermore, several investigations outlined a panel of lncRNA gene expressions, namely MNX1-AS1, SIRLNT, AC092920.1, P11-482H16.1, and AC010729.1, with the capability to forecast the likelihood of recurrence in individuals with BC. Another instance is the research in which it is illustrated that lncRNA gene signatures such as LINC02418, LINC01010, AL356515.1, and AL772337.1 are associated with infiltration of immune cells in breast tumors.

Conclusion: In conclusion, the distinct expression patterns of lncRNAs in diseases, particularly cancer, coupled with their durability in body fluids, make them optimistic candidates as molecular biomarkers. If utilized, lncRNAs can potentially improve the reliability, sensitivity, and specificity of molecular techniques used in clinical diagnostics. Advancing diagnostics and therapeutics based on lncRNAs holds potential for routine medical use, ultimately contributing to improved patient clinical care and overall life quality.

Keywords: Breast Cancer; Small RNA; lncRNA; Diagnosis; Prognosis.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-66

Evaluation of the expression pattern of NRON lncRNA related to interferon signaling pathway in COVID-19 patient

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Abstract

Background and Aim: Coronaviruses are a serious public health concern and in the last two decades and previously two viruses from this family (MERS-CoV and SARS-CoV) caused severe human diseases. Since 2019, SARS-CoV-2, has caused the COVID-19 pandemic and the disease led to millions of deaths and substantial morbidity worldwide. LncRNA (Long Non-Coding RNA) are a large group of non-translating RNA molecules with more than 200 nucleotides in size that involve in crucial cellular mechanisms in host cells. Various studies have shown that lncRNAs affect the function of the host immune system and immunological processes and play various roles in activation and function of innate and acquired immune cells and regulate cell behaviors through proliferation, differentiation and apoptosis. In the studies conducted, a protein called NFAT in the nucleus of T cells activates these lymphocytes after the HIV virus enters the cell, on the other hand, this same protein increases the transcription and multiplication of the virus with the help of the virus. lncRNA NRON here. By binding to NFAT, it causes its exit from the nucleus to the cytoplasm and reduces its function, thus reducing the transcription and replication of the virus, so this lncRNA has a negative regulatory role in HIV infection

Methods: In this case-control study, blood samples were taken from 15 patients with COVID-19 and also 15 healthy controls. After total RNA extraction and cDNA synthesis, we used Real-time PCR to evaluate the expression level of NRON. The data were analyzed by 2- $\Delta\Delta C_t$ method and curve analysis was also performed to evaluate diagnostic utility of this molecular marker.

Results: The results show that the level of lncRNA NRON in the patient group did not change significantly compared to the healthy control group ($Fold\ change=0.80$, $p\ value=0.53$)

Conclusion: According to our results, lncRNA NRON in patients with covid-19 is not related to interferon signaling pathway.

Keywords: COVID-19, SARS-CoV-2, LncRNA, NRON.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-67

Evaluation of the expression pattern of LUARIS lncRNA related to IFN-I signaling pathway in covid-19 patient

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Abstract

Background and Aim: In December 2019, SARS-CoV-2 caused an epidemic of acute respiratory syndrome in humans and in February 2020, the World Health Organization (WHO) described the disease as coronavirus disease 2019 (COVID-19). Virus entry into host cells leads to virus replication, destruction of infected cells and stimulation of an innate immune response. The activity of immune complexes and the secretion of pro-inflammatory cytokines and chemokines are known as danger signals for inflammation. IFN-I is one of the factors that plays an important role in protecting the lungs from the spread of respiratory viruses. Immunologically, IFN-I activates antiviral states in infected and adjacent cells and limits the spread of infection, and plays an important role in modulating immune responses. In the process of viral infection, lncRNAs can act as mediators to link viral infection to innate immunity and cellular metabolism. Long non-coding RNAs (lncRNAs) are transcripts longer than 200 nucleotides that do not encode proteins and their expression levels are very tissue or cell specific. Some lncRNAs can modulate viral infection in an IFN-dependent manner. Among them, lncRNA LUARIS (lncRNA up-regulator of antiviral response interferon signaling) can be mentioned. LUARIS, also known as lncRNA#32, is an IFN down-regulated lncRNA widely expressed in various human tissues. lncRNA#32 acts as a transcriptional positive regulator of ISGs and antiviral chemokines.

Methods: In this study, blood samples were collected from 15 patients and 15 healthy controls. After total RNA extraction and cDNA synthesis, LUARIS lncRNA expression level was evaluated by real-time PCR. And the data was analyzed by the 2- $\Delta\Delta C_t$ method and curve analysis was also performed to evaluate the diagnostic utility of this molecular marker.

Results: Although the main aim of our study was to evaluate the expression level of lncRNA LUARIS and we also expected that the expression level in patients would increase compared to the control group, but according to our results. There was no significant difference in LUARIS level between the patients with covid-19 and the control group (p value>0.05).

Conclusion: According to the role of lncRNA LUARIS and its function, it was predicted that during viral infection, the expression level of LUARIS lncRNA would change.

Keywords: covid-19, SARS-COV2, lncRNA LUARIS, lncRNA#32.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PG-68

Mutations in Thalassemia Carrier Couples: The Importance of Prenatal Diagnostic Tests

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Abstract

Background and Aim: Thalassemia is an inherited autosomal recessive disease resulting from mutations in the α - and β -globin gene clusters on chromosome 16 and 11. Different genotypes cause various phenotypes that varies from a thalassemia minor to a thalassemia major with mild or severe anemia. Accordingly, premarital and prenatal counseling and consanguineous marriages play a significant role in prevention of thalassemia. This leads us to investigate the frequency of the mutations, phenotypes, and genotypes of thalassemia in thalassemia carrier couples to improve counseling.

Methods: We arranged a cross-sectional study on 241 couples who were suspected of thalassemia from April 2018 to March 2020 in Lorestan province. The couples went to the provincial health center for thalassemia screening tests such as taking a blood sample to perform CBC. Also multiplex cap PCR, ARMS-PCR, sequencing, and MLPA-PCR have been used for the identification of thalassemia mutations. Databases such as <https://www.ithanet.eu/db/ithagenes> and <http://globin.bx.psu.edu/hbvar/menu.html> were used. Statistical analysis was performed with SPSS software 16.0 (SPSS Inc., Chicago, IL, USA).

Results: IVSII-1 (G>A), CD36-37 (-T), IVSI-110 (G>A), --Med, and $\alpha^{3.7}$ were the most common mutations in the beta and alpha genes. α - and β -thalassemia were 15 and 13 times higher among women and 18 and 9 times higher among men. These differences were statistically significant and shows that the frequency of thalassemia was higher in couples with consanguineous relationships.

Conclusion: Thalassemia screening in couples has an important role in reducing the birth of infants with thalassemia. It is suggested that in areas with many thalassemia carriers, special attention should be paid to counsel related couples.

Keywords: Thalassemia, Mutation, Genotype, Phenotype, Consanguineous.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Genetics

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PG-69

The role of eNOS gene polymorphisms on contrast induced nephropathy in chronic disease

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Abstract

Background and Aim: contrast induced nephropathy is one of the most common disorders of the contrast media followed by radiology. Although the mechanism of renal destruction with contrast media is not clear, but seems to be related to the toxic effects of these substances on kidney cell epithelial and increase oxidative stress. One of the things can refer to it is nitric acid. Despite of beneficial effects of nitric acid on the regulation Kidney hemodynamic should be controlled its production. NO (nitric acid) is a messenger molecule that is produced by the nitric acid synthesis enzyme, which has 3 Isoform of endothelial, neuronal, and Inducible, which during it L-arginine is converted to L-citrulline in the presence of covetor BH4 And in chromosome 7 is located at 35_A7 position. Several polymorphisms in the eNOS gene have been identified such as intron 4A/b and T786C, G894T, that they're associated with CIN.

Methods: In this review, we searched PubMed, Scientific Information Database (SID; Iran), and Google Scholar from 2017 up to June 2023.

Results: by searching these databases. 40 research articles were retrieved and among 15 were included in the study. The results showed that genotype distribution of the eNOS polymorphisms was consistent with the hardy Wienberg equilibrium. TT polymorphism of T786C gene and GG polymorphism G894T gene were detected to be possibly protective from contrast induced nephropathy in turkey patients, while 4a/b intron is ineffective on contrast induced nephropathy.

Conclusion: besides polymorphism gene G894T also old age up 70, diabetes mellitus increases risk factors of contrast induced nephropathy. And due to environmental factors, genetic distribution of eNOS varies in different populations that should study in future researches.

Keywords: contrast induced nephropathy; gene polymorphisms; Nitric acid.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



5. Hematology & Blood Banking (Oral Presentations)





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OH-1

The Effect of Acute Myeloid Leukemia-Derived Exosomes on The Bone Marrow Microenvironment: Induction of Mesenchymal Stromal Cells' Viability and Survival

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Abstract

Background and Aim: Until recently, acute myeloid leukemia (AML) research was focused on the identification of HSC-related events leading to malignant transformation. New studies have demonstrated that primary alterations in the bone marrow (BM) stromal cells, especially mesenchymal stromal cells (MSCs), can induce AML in mice and also in patients. Moreover, AML cells recruit various factors, including exosomes, to modify MSCs in order to create a niche favorable to leukemia growth and escape therapy. Therefore, it seems that MSCs' presence is crucial for AML initiation and persistence. In this study, we evaluated the effect of AML-exosomes on the viability and proliferation of BM-MSCs.

Methods: Human BM-MSCs obtained from healthy donors were purchased from the Royan stem cell bank. Exosomes were isolated from AML cells (HL-60 cell line) using an exosome isolation kit. The isolated particles were characterized by TEM (Transmission Electron Microscopy), the DLS (Dynamic Light Scattering) technique, and flow cytometry. Exosome protein content was assessed using a BCA protein assay in order to determine the concentration of exosomes. Then, MSCs were co-cultured with $50 \pm 30 \mu\text{g/mL}$ of AML-exosomes. The effect of exosomes on the metabolic activity of MSCs was assessed by the MTT assay, while proliferation, apoptosis, and ROS levels were evaluated by flow cytometry. Gene expression analysis was also performed by qRT-PCR.

Results: Isolated particles were mostly positive for exosome-specific markers, including CD9, CD63, and CD81. According to the DLS results, the separated exosomes' size range was between 70-110 nm. The globular shape of the extracted exosomes was confirmed using TEM. Our results showed higher metabolic activity, decreased BAX and apoptosis, increased BCL2 and proliferation, and lower ROS levels in MSCs treated with a $50 \mu\text{g/mL}$ dose of AML-exosomes compared with the control group ($P < 0.05$).

Conclusion: Since MSCs' presence and survival is important for AML onset and progression, our results suggest that, through exosome secretion, AML increases the proliferation and viability of MSCs so that leukemic cells can exploit them to generate a protective microenvironment for leukemia growth and therapy resistance.

Keywords: Acute myeloid leukemia; Exosome; Bone marrow microenvironment; Mesenchymal stromal cell.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OH-2

Comparison of different transfection methods in the transfer of mir-192 expressing plasmid in HDF and NALM-6 cell lines

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Abstract

Background and Aim: Due to the recent developments in the field of biotechnology and genetics, transfection has become popular to study cellular processes and molecular mechanisms of diseases. During Transfection, different types of nucleic acids such as DNA, RNA, as well as small and non-coding RNAs such as siRNA, shRNA, miRNA can be transferred to mammalian cells. Several studies have shown that mir-192 plays a role in cancer progression. We have various transfection methods including Polycation Polyethylene (PEI), Calcium Phosphate and Lipofectamine 3000. PEI is a synthetic polymer with an extremely high positive charge density, and strongly binds to the negatively charged DNA, creating a net cationic charge and allowing the DNA to enter cells. Lipofectamine form a monolayer liposomal structure with a positive surface charge and combine with nucleic acids to form a transfection complex. In calcium phosphate transfection, DNA-calcium phosphate deposits are internalized by cells, and DNA is effectively expressed in almost all cell types. Human dermal fibroblasts (HDF) are stromal adherent cells that provide the majority of the structural framework of almost all tissue types. NALM-6 is a B-cell progenitor leukemia cell line that is suspended. Our aim of this study is to compare different transfection methods for the transfer PLentiIII-miR-192-GFP plasmid in HDF and NALM-6 cell lines.

Methods: In this study, bacterial culture were performed in order to prepare PLentiIII-miR-192-GFP, and then the plasmid was extracted. HDF and NALM-6 cells were cultured for growth and maintenance in medium containing FBS, penicillin and streptomycin respectively. PEI, calcium phosphate and lipofectamine 3000 methods were used to transfer 2 μ g PLentiIII-miR-192-GFP into the cells. Then, intransfected cells, the expression of GFP tag in each of the methods was measured by flow cytometry device. The steps of cDNA synthesis were done from mRNA and finally the expression of mir-192 was measured by qRT-PCR.

Results: For HDF cells, in the PEI method, the transfection rate was 20-30%, in the calcium phosphate method, the transfection rate was 10%, and in lipofection, the rate was 5-7%. For NALM-6, in the lipofection3000 method, the transfection rate was 15%, and in the other two methods it was less than 10%.

Conclusion: Regarding the advantages and disadvantages of the methods, the PEI method is easy and provides transfection efficiency and high titer. The main disadvantage of PEI is its high cationic charge density and nonbiodegradability. In the lipofection method, it works on many types of cells, including cultured nerve cells. It allows transfection reactions to be performed in 30 minutes. Its disadvantages include low transfection, inability to target specific cells, short half-life, and toxicity caused by positively charged lipids. In the calcium phosphate method, there are many advantages, including its simplicity and economic materials; However, there are several drawbacks to using this method, including cytotoxicity and sensitivity to environmental factors (e.g., pH, temperature). However, a different method should be set up for each cell depending on its nature.

Keywords: Transfection methods; mir-192; HDF; NALM-6





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Oral

Abstract Type: Review Article

Code of Abstract: OH-3

STAT3: A Potential Mediator in Pathogenesis and Clinical Outcomes in Acute Myeloid Leukemia

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Abstract

Introduction: Acute myeloid leukemia (AML) is a highly heterogeneous hematopoietic malignancy. Treatment for AML typically involves a combination of chemotherapy, targeted therapy, and in some cases, stem cell transplantation. Effective cancer therapy requires identification of signaling networks and investigating their potential role in proliferation and invasion of cancer cells. Among molecular pathways, signal transducer and activator of transcription 3 (STAT3), a member of the STAT family, has been of importance due to its involvement in cell proliferation, maturation and survival.

Discussion: STAT3 regulates the expression of important genes in cell cycle growth, including genes encoding cell cycle checkpoint proteins and apoptosis. It decreases the expression of genes encoding cell cycle checkpoint proteins such as P53, P21, and P27, while increasing the expression of genes involved in cell growth such as cyclins D1, D2, D3, A and B, Cdc25A, and Cdc2. Additionally, it decreases the expression of genes involved in apoptosis such as -X1, IAPs, and Mcl-1. STAT3 exerts its oncogenic effects by increasing cell proliferation and decreasing apoptosis. Constitutive activation of STAT3 has been reported in various types of tumors such as prostate, breast, lung and hematological malignancies such as chronic myeloid leukemia, multiple myeloma and acute myeloid leukemia. The STAT3 signaling pathway plays a crucial role in hematopoiesis, which is the process of blood cell formation. Specifically, STAT3 is involved in the development and differentiation of various blood cell lineages, including erythroid, myeloid, and lymphoid cells. It is activated by cytokines and growth factors such as erythropoietin (EPO), interleukin-6 (IL-6), and granulocyte colony-stimulating factor (G-CSF), which are essential for regulating hematopoiesis. Furthermore, dysregulation of the STAT3 pathway has been linked to various hematopoietic disorders, including anemia, myeloproliferative neoplasms, lymphoid malignancies, and AML. In the context of acute myeloid leukemia (AML) treatment, there has been significant interest in researching and developing drugs that target the STAT3 signaling pathway. Multiple studies have explored the possibility of using STAT3 inhibition as a therapeutic approach for AML.

STAT3 inhibitors, like those targeting the SH2 domain, prevent STAT3 from binding to phosphorylated intracellular receptors, thus inhibiting its activity. Small peptides such as S3I-M2001 and S3I-201 have been utilized as inhibitors. Inhibitors of the DNA-binding domain, such as DBD-1, HIC 1, and IS3-295, impact the interaction of STAT3 with gene promoters, resulting in its inhibition. Indirect STAT3 inhibitors focus on upstream regulators of the STAT3 pathway, such as receptor binding to ligands and kinases. Examples of these inhibitors include KDI1 and PD153035a, which block EGFR activation to inhibit STAT3 phosphorylation.

Conclusion: In this review, we intend to introduce AML and STAT3 and its signaling pathway and its role in pathophysiology of AML and blocking STAT3 signaling pathway as a treatment for acute myeloid leukemia. It also introduces the development of inhibitors targeting the STAT3 pathway and new drug delivery systems for these inhibitors.

Keywords: Acute Myeloid Leukemia; Small Molecule Inhibitors; STAT3.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Oral

Abstract Type: Review Article

Code of Abstract: OH-4

Enhancing Diagnostic Precision: Artificial Intelligence in Distinguishing Between Iron Deficiency Anemia and Thalassemia

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Abstract

Background and Aim: Thalassemia, an autosomal recessive genetic disorder, affects the beta or alpha subunits of hemoglobin. The characteristics of thalassemia are similar to those of other disorders that cause microcytic hypochromic anemia, such as iron deficiency anemia (IDA). To treat patients with IDA, it is important to differentiate between Thalassemia and other causes of microcytic anemia.

Methods: Based on the articles published in this field from 2016 to 2023 in the databases of PubMed, Web of Science and Google Scholar, a review study was conducted.

Discussion: According to the available studies on thalassemia treatments, the traditional method of diagnosing iron deficiency and beta-thalassemia minor with CBC is not sufficiently accurate, and additional tests, such as hemoglobin electrophoresis, are time-consuming and expensive. As a result, artificial intelligence is becoming increasingly important in the diagnosis of thalassemia. It is being developed A variety of indices and web-based prediction tools to aid in the diagnosis of thalassemia and to reduce the resources and investigations required by physicians to differentiate between thalassemia and other diseases. Several studies have demonstrated that machine-learning techniques play a crucial role in the diagnosis of thalassemia. In this review, the results of the CBC are used to determine the most effective parameters for diagnosing thalassemia. The performance of KNN, MLP, NN, decision trees, and support vector machines was evaluated. For the diagnosis of thalassemia and other blood disorders, a neural network is the most effective method. This process utilizes parameters such as MCH, MCHC, and RDW. RBC, HGB, MCV, and hematocrit can also be used to diagnose thalassemia. Moreover, these studies demonstrated that the signed sigmoid has the most effective activation function in the input layer.

Conclusion: The results of this study demonstrate the increasing importance of artificial intelligence, specifically neural networks, in enhancing the accuracy and efficiency of thalassemia diagnosis. This study highlights the potential of machine learning to aid physicians in identifying thalassemia from other forms of microcytic anemia through early and precise differentiation based on CBC parameters, such as MCH, MCHC, and RDW. As a result, timely intervention and improved patient outcomes can be achieved.

Keywords: Artificial Intelligence; Iron Deficiency Anemia; Thalassemia.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Hematology & Blood Banking

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OH-5

WT1 and TP53 as valuable diagnostic biomarkers for relapse after hematopoietic stem cell transplantation in acute myeloid leukemia

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Abstract

Background and Aim: Relapse following hematopoietic stem cell transplantation (HSCT) is a common and significant risk factor for mortality in patients with acute myeloid leukemia (AML). Timely and accurate diagnosis is essential for guiding appropriate treatment. In this study, the diagnostic value of two molecular markers was investigated.

Methods: Twenty patients diagnosed with AML and undergoing HSCT were enrolled in this study. Among them, some patients experienced relapse after HSCT, while others remained in remission. Peripheral blood (PB) and bone marrow (BM) samples were collected from relapsed and remission cases. The expression levels of two molecular markers, Wilms tumor 1 (WT1) and tumor suppressor protein p53 (TP53) were evaluated using the reverse transcription-quantitative polymerase chain reaction (RT-qPCR) technique. The diagnostic value of these genes was assessed by analyzing receiver-operating characteristic (ROC) curves.

Results: ROC curves demonstrated that WT1 and TP53 serve as potential diagnostic markers for relapse after HSCT in AML patients. The expression level of WT1 mRNA was significantly higher in individuals who experienced relapse compared to those in remission (p value < 0.01). Conversely, the expression level of TP53 mRNA was significantly lower in individuals who relapsed compared to those in remission (p value < 0.01).

Conclusion: These findings suggest that monitoring the expression levels of WT1 and TP53 genes could be valuable biomarkers in predicting and detecting relapse in AML patients post-HSCT. More study is recommended for a definitive conclusion.

Keywords: Acute Myeloid Leukemia; Hematopoietic Stem Cell Transplantation; Relapse; WT1; TP53; Biomarkers.





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Venue:
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January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Oral

Abstract Type: Review

Code of Abstract: OH-8

Cell-free DNA screening: A non-invasive prenatal testing method

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Abstract

Background and Aim: Cell-free DNA screening, known as Non-invasive prenatal testing (NIPT), is a crucial prenatal method that involves analyzing freely circulating DNA in maternal blood originating from the placenta. NIPT identifies chromosomal abnormalities such as Down syndrome, Edwards syndrome, and Patau syndrome, as well as sex chromosome aneuploidy and microdeletion panels in the fetus. Additionally, NIPT can determine the fetal gender and genotype of the fetal RHD blood group. The Society for Maternal-Fetal Medicine (SMFM) approves NIPT as the most effective and accurate screening method for common aneuploidies. This study focused on current NIPT developments, benefits, problems, and implications for regular diagnostics.

Methods: Articles were selected from published eligible articles on MEDLINE/PubMed and Embase databases between January 2015 and September 2023 using the keywords: “NIPT,” “Cell-free DNA,” “Screening,” “cfDNA,” and “non-invasive”.

Results: NIPT has several advantages over other prenatal screening tests. This technique is non-invasive, thereby eliminating the potential for miscarriage or any other form of risk to both the mother and the fetus. Patient anxiety is mitigated by NIPT. Moreover, NIPT is a cost-effective diagnostic test. However, NIPT has certain limitations. The main restriction of this approach is the existence of a low concentration of intact fetal cells in the maternal circulation. Chromosomal triploidy and remnant cfDNA from a disappearing twin cannot be distinguished by NIPT. It is critical to understand that cfDNA testing only identifies high-risk pregnancies for certain conditions and that confirmatory testing such as chorionic villus sampling or amniocentesis is required for definitive diagnosis. The goal of ongoing research is to overcome the limits of the NIPT, improve accuracy, and extend tested defects to achieve a diagnostic grade of results and eliminate the requirement for invasive diagnostic procedures.

Conclusion: Scientists think that discoveries and advancements in technology will turn NIPT from a screening test into a definitive diagnostic examination.

Keywords: NIPT; Cell-free DNA; Screening; ccfDNA, Non-invasive.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OH-9

MDS-type morphologic abnormalities of peripheral blood granulocytes in symptomatic COVID-19 patients

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Abstract

Background and Aim: Hematological abnormalities in COVID-19 infection included quantitative and qualitative changes and should be further characterized. Evaluation for myelodysplastic syndromes (MDS) is usually prompted by abnormal hematologic findings and the presence of dysplastic morphologies. Viral infections are considered to be the cause of dysplastic morphologies and should be considered by morphologists. There are few reports of dysplastic abnormal morphologies in patients with COVID-19 infection. However, such correlations still have to be clarified.

Methods: In the present study, we examined the granulocyte lineage morphological abnormalities in symptomatic RT-PCR-confirmed COVID patients. Peripheral blood samples were collected from 82 patients with symptomatic COVID-19. Blood smears were prepared according to the standard Wright-Giemsa staining procedure. The morphological examination was carried out by two laboratory experts.

Results: Blood smear examination revealed common myelodysplastic syndrome (MDS) type abnormalities including but not limited to: pseudo-pelger nuclear lobulation (4.8%), hypogranulation (7.3%), Howell-Jolly-like bodies or detached nuclear segments (6.0%) and elongated and thin nuclear filaments (6.0%). One case of abnormal immature granulocyte and ring form nucleus also evident.

Conclusion: Our results accounted for the possibility of active COVID-19 infection in all subjects with granulocyte dysplasia. These results are of practical importance for patients suspected of having myelodysplastic syndromes or disease processes associated with myeloid malignancies.

Keywords: COVID-19; MDS; Granulocytes; Morphology; Peripheral Blood.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Oral

Abstract Type: Review

Code of Abstract: OH-10

Natural killer cell-based immunotherapy in acute myeloid leukemia (AML)

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Abstract

Background and Aim: Despite the development of new drugs and considerable progress over recent years, relapse and reduced survival rates remain a significant problem, and the focus has been on exploring advanced therapies for AML. Immunotherapy, cytokine therapy, targeted gene therapies, etc., are curative therapeutic strategies in AML patients. NK cell-targeted immunotherapies are proposed as a potential solution to address the unmet clinical needs and have been recognized as an innovative therapeutic target for various tumors, particularly AML.

Method: At the present review, articles in PubMed were searched with the following terms: Natural killer cell, NK, Immunotherapy, Acute myeloid leukemia, either alone or in a combination form. The most relevant selected functions were NK-based immunotherapy and AML.

Result: The scientific background of NK cells shows that these cells play an essential role in innate immunity and have anti-leukemic properties. Anti-tumor activity of NK cells is driven by forming an immunological synapse with target cells through their receptors, including Killer Immunoglobulin-like receptors (KIRs), natural cytotoxicity receptors (NCRs), or NKG2 (Natural Killer Group 2) receptors. Subsequently, activated NK cells secrete many pro-inflammatory cytokines (IFN γ , TNF α , IL-10) and use lysing proteins (granzyme B and perforins) to destroy tumor cells. There are several mechanisms of leukemia cell evasion in AML because of NK cell defects and immunosuppressive properties of AML cells, including 1) The number of NK cells is low at diagnosis and active disease and then increases in remission phase. 2) NK cells of AML patients express decreased NCR receptors (NKp30, NKp44, NKp46, and DNAM-1), causing an NCR^{dull} and, finally, impaired killing capacity of NK cells. 3) Overexpression of KIR inhibitory receptors leading to inhibition of cytotoxicity. 4) upregulation of hypomaturating NK cells (CD56^{bright/dim} KIRs⁻ CD57⁻) and 5) Expression of checkpoint inhibitors like PD-1 and TIGIT results into cells with reduced proliferative efficacy as well cytotoxic dysregulation of NK cells. Advancements in NK-based immunotherapy have been accelerating over the past years. Generally, there have been an increasing number of in vitro experiments, animal models, and clinical trials for NK-based therapy in AML patients. The most important strategies are adoptive NK cell infusion (autologous and allogeneic NK cells), cytokine-induced memory-like (CIML) NK cells, chimeric antigen receptor-modified NK cells (CAR-NK), bi-specific and tri-specific killer engagers (BiKEs and TriKEs), monoclonal antibody therapy, immune checkpoint inhibitor blockade therapy and finally drugs with immunomodulatory function. Despite the recent advances, there are still several challenges to augment NK cell potentials as a standard treatment for AML immunotherapy. Some existing issues are neutralizing immunosuppressive cytokines, blocking inhibitory receptors, providing required cytokines and growth factors, and eliminating Tregs activities.

Conclusion: Finally, NK cell therapy emerged as a novel field of research for hematologic malignancies. Meanwhile, the available data is limited, and the outcomes differ among various transplant settings and different types of leukemia. Thus, additional investigation is needed to understand better NK cell dysfunction mechanisms and immunotherapy-based strategies against AML.

Keywords: Natural Killer Cell; NK, Immunotherapy; Acute Myeloid Leukemia.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Oral

Abstract Type: Narrative Review

Code of Abstract: OH-11

Application of CRISPR in Thalassemia Treatment

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Abstract

Background and Aim: Thalassemia, a hereditary hemoglobinopathy, poses a significant global health burden characterized by ineffective erythropoiesis and anemia. Emerging therapies, particularly CRISPR/Cas9 genome editing, offer a promising avenue for targeted intervention. This study aims to investigate the efficacy of CRISPR/Cas9 in treating thalassemia by enhancing fetal hemoglobin (HbF) expression.

Methods: A PubMed and Scopus search of English language papers was conducted from 2012-2023 using the terms, “Thalassemia” and “CRISPR”. Human primary CD34+ hematopoietic stem and progenitor cells (HSPCs) were subjected to CRISPR/Cas9 genome editing to recreate specific genetic variants associated with elevated HbF. Optimization included the use of Cas9 delivered as a recombinant protein, achieving editing efficiencies exceeding 80%. Clinical-scale processes were developed for viability and efficiency, with a focus on GMP compatibility. Editing outcomes were assessed through erythroid differentiation and evaluated in patient samples for γ -globin mRNA expression.

Discussion CRISPR/Cas9 editing exhibited remarkable efficiency (>80%) in human primary HSPCs from healthy donors, with superior viability when using Cas9 as a recombinant protein. Robust HbF expression was observed during erythroid differentiation, and patient samples displayed clinically relevant increases in γ -globin mRNA. The editing rate persisted in long-term repopulating HSPCs, demonstrating durability in a xenotransplant mouse model and human bone marrow cell.

Conclusion: This study demonstrates the potential of CRISPR/Cas9 in upregulating HbF as a therapeutic strategy for thalassemia. Optimized editing conditions, high efficiency, and viability, along with the absence of off-target effects, underscore the viability of this approach. The results support the initiation of clinical studies for CRISPR/Cas9 as a transformative treatment for patients with thalassemia. The findings signify a pivotal step toward personalized and effective genomic interventions in thalassemia management.

Keywords: Thalassemia; CRISPR; Hemoglobinopathy.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Oral

Abstract Type: Review

Code of Abstract: OH-12

MicroRNAs as significant biomarkers for diagnosis and prognosis in Acute Myeloid Leukemia

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Abstract

Background and Aim: Acute myeloid leukemia (AML) is a significant medical issue with a high recurrence risk and mortality rate, despite effective therapy. MicroRNAs belong to a class of small non-coding RNAs that are involved in regulating gene expression. The purpose of this research is to investigate the function of miRNAs in AML pathogenesis, with a focus on their potential as diagnostic and prognostic indicators. Understanding the complicated interaction of miRNAs in AML might give crucial insights into disease categorization, prognosis, and therapy response prediction. The deregulation of miRNAs in disease can be therapeutically targeted using miRNA mimics or inhibitors.

Material & Method: All of the searches were performed between January 2018 and December 2023. The MEDLINE/PubMed and Embase databases were searched for suitable publications published using the keywords "AML", "miRNA", and "diagnosis".

Discussion: Aberrant expression of miRNAs has been described in all types of cancers. The results of clinical and functional studies have shown abnormal changes in the expression of miRNAs in AML. MicroRNAs can act as proto-oncogenes or tumor suppressors. Since the expression levels of certain miRNAs correlate with patient survival in a range of cancers, they are also potential prognostic markers. MiR-10a, miR-10b, and miR-196b are upregulated in AML with the NPM1 mutation, but miR-192 is downregulated. Similarly, t(8;21) patients with increased miR-126 and miR-146a share a similar profile, and FLT3-ITD is associated with miR-155 overexpression. Recently discovered miRNAs, including miRNA-107, miRNA-155, miRNA-25, miRNA-29b, miR-150, miR-342, and miRNA-196a, have been associated with adverse effects including shorter overall survival rates for patients with AML. These data suggest that different miRNA expressions are linked with diagnostic, prognostic, and survival outcomes in AML.

Conclusion: miRNAs have emerged as a class of essential regulators of gene expression and potential biomarkers in AML pathogenesis. Specific miRNA expression in AML could help physicians determine subtypes, evaluate prognosis, and predict therapy response. As mentioned before, the miRNA expression profile is aberrant in AML. Evidence from cytogenetics, gene mutations, and gene expression patterns can be used to evaluate a single or a panel of miRNAs with potential diagnostic/prognostic implications.

Keywords: AML; miRNA; Diagnose; Prognostic.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Oral

Abstract Type: Review

Code of Abstract: OH-13

Circular RNAs: Novel and promising indicators for leukemia

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Abstract

Background and Aim Leukemia is a type of blood malignancy with rapid and aberrant proliferation of hematopoietic stem cells. In recent years, the satisfactory outcomes of leukemia have been significantly improved with the combined use of severe chemotherapeutic regimens and hematopoietic stem cell transplantation. However, the pathophysiological mechanism behind disease development and progression remains highly elucidated in some cases, showing significant relapse and chemotherapeutic drug resistance and resulting in disease progression and even death. Thus, an urgent need is to discover non-invasive biomarkers and therapeutic agents. Specific RNAs have been verified as an essential molecule involved in the pathogenesis of various diseases, particularly leukemia. Circular RNAs (circRNAs) are a group of recently discovered non-coding RNAs (ncRNAs) produced from protein-encoding genes through a back-splicing process. These novel ncRNAs resist mRNA-degrading enzymes, leading to more extended stability. The literature reports that circRNAs play an essential role in cellular processes and their abnormal expression is involved in the pathogenesis of various diseases. They can act as a miRNA sponge and therefore regulate the expression of target genes.

Methods: At the present review, articles in PubMed were searched with the following Circular RNA, circRNA, non-coding RNA, leukemia either alone or in a combination form. The most relevant selected functions were circRNA and leukemia.

Discussion: Abnormal expression of circRNAs could be used for leukemia classification, prognosis evaluation, diagnostic biomarkers, and chemotherapy response prediction. Some circRNAs are upregulated in AML. Circ-0075001 was one of the first circRNAs related to AML cells and significantly upregulated. circMYBL2 is also highly expressed in AML patients with an FLT3-ITD mutation. Moreover, circ_0003602 expression was elevated and contributed to AML proliferation, migration, and invasion, as well as suppressing apoptosis of leukemic cells. Upregulation of circ-RNF220, circ-DLEU2, and circ-KCNQ5 in pediatric AML was also confirmed. Conversely, circ-0004277 and circ-100290 were downregulated in AML patients and could suppress migration, invasion, and cell viability in AML. Circ-ANAPC7 is an additional diagnostic biomarker for AML patients. Dysregulation of circRNAs contributes to CML prognosis, pathogenesis, and chemotherapeutic drug resistance. Data revealed significantly upregulated levels of CircHIPK3 related to poor outcomes in CML patients. circ_0058493 was also upregulated and may be a suitable prognostic biomarker and therapeutic option. Moreover, circ_0080145 level was elevated in imatinib-resistant patients, and its knockdown suppressed cell proliferation and glycolysis. Additionally, F-circBA1 shows an oncogenic role in CML cells, and circ-0080145 also enhances imatinib resistance in CML. According to data, circADD2, Circ-0000745, CircPVT1, circ-0001857, and circPRKCI have positively contributed to ALL leukemia. Data shows CLL cells have a different circRNA profile than normal B lymphocytes. For example, circ_0132266, circ-CBFB, and circZNF91 were dysregulated expressions in CLL patients.

Conclusion: Finally, circRNAs emerged as a novel and innovative field of research. However, the available data is still scarce and additional investigation is needed before their preclinical and clinical application.

Keywords: Circular RNA; circRNA; Non-coding RNA; Leukemia.



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The 15th International Congress of Medical Laboratory & Clinic

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5. Hematology & Blood Banking (Poster Presentations)





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-2

Vitamin C as driver of apoptosis combined with vincristine Via Downregulating miR-17-/125b-/181b-5p in NALM-6 cells

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Abstract

Background and Aim: Vitamin C or ascorbic acid has demonstrated anticancer properties against various human tumor cells, including leukemia. It can increase the expression of several miRNAs involved in tumor suppression. This study investigated the effects of vitamin C, alone and in combination with vincristine, on apoptosis in NALM-6 leukemia cells. The goal was to determine if vitamin C works synergistically with vincristine to promote apoptosis through alterations in the expression of miR-181b-5p, miR-17-5p, and miR-125b-5p miRNAs.

Methods: The methods used included MTT assay and PI staining to determine metabolic activity and cell viability, flow cytometry to investigate apoptosis, and real-time PCR to access the expression of miRNAs. We also used bioinformatic analyses, including Cytoscape, RNAhybrid, molecular docking, to predict and validate miR-17-5p, miR-181b-5p, and miR-125b-5p related to apoptosis and modulated by vitamin C and vincristine treatment.

Results: Single staining PI analysis showed that vitamin C reduces cell viability by 0.5mM concentration ($P<0.0001$). Flow cytometric analysis indicated that vitamin C (0.5 mM) in combination with vincristine (0.8 nM.) induce apoptosis in 79.22% cells ($P<0.0001$). In contrast, when treated individually for 48 hours, vitamin C or vincristine alone resulted in only 54.68% ($P<0.0001$) and 22.28 % ($P:0.0168$) apoptotic NALM-6 cells, respectively. Furthermore, the distribution of early apoptotic cells was 7.38%, 13.1%, and 8.32% in the vitamin C, vincristine, and vitamin C/vincristine groups, respectively. The combination treatment using 0.5 mM vitamin C with 0.8 nM vincristine exhibited the strongest synergistic inhibitory effect, resulting in only 10.3% cell survival after 48 hours of treatment. we have found the combination therapy with vitamin C and vincristine empower the apoptosis at 1.49 and 3.95-fold higher than when NALM-6 cells treated with individual vitamin C and vincristine. Also, our results showed the vitamin C triggers apoptosis much more than vincristine which was 2.64-fold higher. RT-PCR analysis shows changes in expression of miR-17, miR-125b and miR-181b, significantly. Moreover, the combination therapy downregulates the expression of miRNAs which was noticeable change ($P<0.05$). A bioinformatics approach and MiRNA-Gene Interaction (MGI) network analysis revealed that the miRNAs are Anti-apoptomiRs and We obtained 6, 12, 9 apoptotic genes regulated by miR-181b, miR-125b, and miR-17, respectively. Also, to confirm that our miRNAs are driver of apoptosis, the genes-related apoptosis imported to RNAhybrid tool and we obtained the binding site with minimum energy of each gene targeted with specific miRNA. Overall, we realized most of their Common apoptotic targets is BCL-2 family. RNAhybrid confirms the apoptotic genes regulated by miRNAs. Finally, Molecular Docking validate the interaction of miRNAs by vitamin C and vincristine.

Conclusion: Vitamin C improve apoptosis in combination with vincristine in NALM-6 cells. Underling mechanism of it, would be epigenetic changes in miRNAs that identified are apoptosis regulator. So, it is suggested as adjunct therapy for B-ALL patients.

Keywords: B-ALL; miRNAs; Apoptosis; Vitamin C; NALM-6; Bioinformatics.





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Venue:
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January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-3

The effect of siRNA on the Proliferation in Acute Promyelocytic leukemia cell line (NB4)

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Abstract

Background and Aim: Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia (AML) characterized by a specific chromosomal abnormality. Inositol triphosphate receptors (IP3Rs) are calcium channels that play important roles in cellular functions. This study aimed to investigate the effect of inhibiting IP3Rs on the expression of genes involved in proliferation and apoptosis in NB4 cells, which are APL cells.

Methods: NB-4 cells were transfected with specific siRNAs using Lipofectamine 2000. The viability of the cells was assessed using the MTT assay. Flow cytometry was performed using Annexin V and propidium iodide (PI) to assess apoptotic markers and necrosis. Furthermore, the expression of genes involved in cell proliferation and apoptosis was investigated using the Real-Time PCR technique.

Results: The MTT assays determined the optimal siRNA dose of 40 pMol for effective IP3R inhibition. Flow cytometry analysis revealed increased levels of the apoptotic marker Annexin V in cells treated with siRNA targeting type II IP3Rs, indicating increased apoptosis. Conversely, inhibition of type I and III receptors led to reduced apoptosis. Additionally, the inhibition of type I and III IP3Rs had the greatest impact on the expression of pro-apoptotic genes, such as p21 and p53, leading to increased apoptosis. On the other hand, the inhibition of type II IP3Rs had the greatest effect on the expression of the anti-apoptotic gene BCL-2, resulting in decreased apoptosis.

Conclusion: These findings emphasize the potential of inhibiting specific IP3R subtypes to modulate gene expression related to cell proliferation and apoptosis, highlighting their therapeutic potential as targets for APL treatment.

Keywords: Acute Promyelocytic Leukemia; Gene Silencing; Biomarkers; Therapeutic Targets.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-4

The apoptotic effect of silver nanoparticles in Acute Lymphoblastic Leukemia Cell Line (Jurkat)

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Abstract

Background & Aim: Acute lymphoblastic leukemia (ALL) is a malignant disease that arises from various mutations in B or T-lymphoid progenitors. MicroRNAs (miRNAs) regulate gene expression by binding to the 3' untranslated region of protein-coding genes. Dysregulation of miRNA expression may result in the development of cancerous phenotypes. Therefore, for the first time in this field, the present study aims to investigate the effect of silver nanoparticles synthesised using Sargassum on expression miR-25 in Acute Lymphoblastic Leukemic cells in Jurkat cell line.

Methods: In interventional study, Jurkat cell lines were cultured in RPMI-1640 medium. we adjacent concentrations of the drug with maximum cell growth inhibition and IC₅₀ to 20,000 cell line and control cells separately, and after 48 hours of treatment, the RNA was extracted and miR-25 and 143 expression was evaluated by Real Time PCR. Statistical analysis was performed with SPSS software and P < 0.05 was considered as a significant difference.

Results: According to our results, the expression of miR-25 in the group of treated with maximum dose and IC₅₀ of silver nanoparticles and algae extract was not significantly different from the control (P < 0.34) and associated with a sharp decline.

Conclusion: The IC₅₀ dose of silver nanoparticles and algae extract had a decreasing effect on the expression of miR-25. The expression of miR-25 in treated Jurkat cell line was more decreased than the expression in normal lymphocytes. Due to the oncogenicity of miR-25 in Jurkat cell line, it can be said that reducing this microRNA can help kill cancer cells.

Keywords: miR-25, Acute lymphoblastic leukemia (ALL), Jurkat, Nanoparticles.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-5

The tumor suppressing effect of silver nanoparticles in Acute Lymphoblastic Leukemia Cell Line (Jurkat)

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Abstract

Background and Aim: Acute lymphoblastic leukemia (ALL) is the most common malignancy among children accounts for almost 25% of all childhood cancers. One of the treatments is chemotherapy. The side effects of chemotherapy are that in addition to cancer cells, other normal cells are destroyed, and which may follow infection and bleeding occur. MiRNAs are small, non-coding RNAs. The biogenic synthesis of nanoparticles using seaweed is widely used due to its easy availability and effectiveness. The aim of this study was to investigate the effect of Sargassum brown seaweed extract along with silver nanoparticles on the expression of miR-143 in Jurkat cell line.

Methods: In an interventional study after culturing the cell line and obtaining cells with 95% survival, we adjacent concentrations of the drug with maximum cell growth inhibition and IC50 to 20,000 cell line and control cells separately, and after 48 hours of treatment, the RNA was extracted and miR-143 expression was evaluated by Real Time PCR. Statistical analysis was performed with SPSS software and $P < 0.05$ was considered as a significant difference.

Results: The expression of miR-143 in the group of treated with maximum dose and IC50 of silver nanoparticles and algae extract was significantly different from the control and associated with a sharp decline ($P < 0.0001$).

Conclusion: The IC50 dose of silver nanoparticles and algae extract had a decreasing effect on the expression of miR-143. Then it can be said that reducing this miR-143 can help kill cancer cells.

Keywords: miR-143; Acute Lymphoblastic Leukemia; Jurkat; Nanoparticles.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-6

The Association between Antibiotics and Obesity in Childhood Acute Lymphoblastic Leukemia: A Comprehensive Review

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Abstract

Background and Aim: Acute Lymphoblastic Leukemia (ALL) is the most prevalent cancer among children, necessitating an investigation of its associated complications and comorbidities. The frequent occurrence of obesity in patients undergoing treatment for childhood leukemia is of particular concern. Consequently, a comprehensive examination of this issue from multiple perspectives is essential. This review aims to synthesize and analyze the most recent published evidence concerning the association of obesity and antibiotics in pediatric ALL. Through this comprehensive analysis, we seek to shed light on the intricate interplay between antibiotics, obesity, and childhood ALL, with the ultimate goal of guiding future research and clinical interventions.

Methods: A literature search of PubMed, Scopus, and Google Scholar databases was performed for publications up to August 1, 2022, using the following search terms in various combinations: 'acute lymphoblastic leukemia', 'ALL', 'childhood acute lymphoblastic leukemia', 'childhood ALL', 'pediatric', 'obesity', 'antibiotics', 'gut microbiota', 'chemotherapy regimen'. The initial results were then screened by two independent authors based on inclusion and exclusion criteria. We included papers if they investigate: (a) pediatric patients (< 18 years old) with ALL, (b) obese patients with childhood ALL, (c) patients receiving antibiotics during chemotherapy, and (d) only papers written in English. We exclude all articles regarding adult patients with ALL. To strengthen our search, the reference list of included papers was screened to identify possible eligible articles.

Discussion: Investigations have explored the role of altered gut microbiota composition in causing overweight/obesity in childhood ALL. The disturbance in gut microbiota diversity, resulting from the administration of chemotherapy drugs and antibiotics to ALL patients, may contribute to obesity development.

Conclusion: In conclusion, along with ALL treatments such as corticosteroids which can be a cause of overweight/obesity, chemotherapy especially cranial radiation therapy (CRT), and antibiotics can result in Dysbiosis in childhood ALL that might have long-lasting effects and predispose childhood ALL patients to obesity and obesity-related diseases in adulthood.

Keywords: Childhood Acute Lymphoblastic Leukemia; Pediatric; Obesity; Antibiotics; Chemotherapy.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-7

Gilteritinib and Quizartinib as second-generation FLT3 inhibitors in AML patients with relapsed or refractory disease: A systematic review and meta-analysis

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Abstract

Background and Aim: Acute myeloid leukemia (AML) is a complex disease with diverse mutations, of which mutations in FMS-like receptor tyrosine kinase 3 (FLT3) gene are most prevalent, leading to constitutive activation and poor prognosis. Recent advancements have introduced FLT3 inhibitors like quizartinib and gilteritinib that have improved outcomes for FLT3-mutated AML patients. Despite this progress, questions remain on their application in complex conditions such as relapsed/refractory (R/R) disease. This systematic review and meta-analysis aimed to evaluate the clinical effectiveness of second-generation FLT3 inhibitors in treating R/R AML patients with FLT3 mutations.

Methods: This review was conducted according to PRISMA guidelines and the study protocol was registered on PROSPERO (CRD42023398365). A systematic literature search of PubMed, MEDLINE, and Scopus databases was made to identify relevant studies up to November 1, 2023. A total of 1143 records were screened for eligibility and based on inclusion and exclusion criteria, 7 papers were selected for our review. Two reviewers independently selected the studies, and any disagreements were resolved through the involvement of a third reviewer. Using standardized forms, relevant data were extracted and a fixed-effect meta-analysis was employed to analyze time-to-event data. The quality of the included studies was assessed by two independent reviewers using the Cochrane Risk of Bias Tool. The treatment effect was measured using hazard ratio (HR) or risk ratio (RR), as appropriate. X square and I square statistics were employed to assess heterogeneity among included studies and to test for subgroup differences.

Results: Seven studies were included, of which four had investigated gilteritinib and three quizartinib. Overall survival (OS) was significantly improved with second-generation FLT3 inhibitors compared to salvage chemotherapy (SC) ($p < 0.0001$). Event-free survival (EFS) did not show a significant difference between FLT3 inhibitors and SC ($p = 0.11$). Complete remission (CR) rates were higher with FLT3 inhibitors ($p < 0.00001$). Overall response (OR) was significantly better with FLT3 inhibitors ($p < 0.00001$). Based on the definition by the National Cancer Institute Common Toxicity Criteria (CTC version 3.0), grade three and higher AEs were extracted from each study. The most common Grade three or higher AEs observed in patients treated with gilteritinib or quizartinib, were thrombocytopenia, neutropenia, anemia, febrile neutropenia and sepsis.

Conclusion: In conclusion, this systematic review and meta-analysis provide strong evidence that second-generation FLT3 inhibitors, i.e., gilteritinib and quizartinib, significantly improve OS and CR rates in R/R AML patients with FLT3 mutations. These targeted therapies offer a promising approach for managing this intermediated-risk subset of AML patients, providing hope for improved clinical outcomes. However, further investigation is required to explore potential subgroup differences and optimize the therapeutic use of FLT3 inhibitors for different patient populations. Nonetheless, this study highlights the importance of personalized treatment strategies for AML patients.

Keywords: FLT3; FLT3 Inhibitors; AML; Relapse/Refractory.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-8

The Evaluation of Human Bone Marrow Mesenchymal Stem Cell Exosomes' Impact on Acute Myeloid Leukemia's Proliferation and Oxidative Stress: The Potential Role of Poor Prognosis LncRNAs

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Abstract

Background and Aim: Acute myeloid leukemia (AML) is a group of blood malignancies that originates from excessive proliferation and differentiation failure of hematopoietic precursors. Mesenchymal stem cells (MSC), as indispensable sources of cell therapy, exert diverse effects on tumor cells mostly through indirect interactions such as exosomes, which significantly impact target cells by their various cargo. LncRNAs form a critical part of the cell nucleic acid content, and their abnormal expression can promote different cancers like leukemia. Our study aims to investigate the impacts of bone marrow MSC (BMSC) exosomes on HL60 AML cells' biological functions and expression levels of poor prognosis lncRNAs.

Methods: In the first step, mesenchymal stem cells of normal bone marrow were cultivated with a serum-free α -MEM culture medium, and the supernatants of the cultured cells were harvested to isolate exosomes with a precipitation-based kit. The exosomes were validated in three steps: CD marker identification using flow cytometry, morphological analysis using TEM, and size evaluation using DLS. Later, the MTT assay was performed to specify the proper dose of exosomes for further analysis. Then, HL60 AML cells were treated with exosomes to determine the impact of their contents on cell proliferation and oxidative stress. We used flow cytometry to assess the proliferation by evaluating ki67 expression and to detect the reactive oxygen species (ROS) by evaluating DCFH. Furthermore, RTq-PCR was operated to determine the gene expression of H19 and TUG1 lncRNAs. Finally, analytical tests were conducted to calculate the meaningful differences.

Results: The results of exosome characterization demonstrated that CD81, CD63, and CD9, which are specific marker proteins used in exosome identification, were all expressed in exosomes isolated from BMSCs, diameters of exosomes ranged between 80~100 nm, and the majority of the isolated nanoparticles exhibited a round-shaped morphology, quite similar to exosomes. MTT assay revealed that BMSC exosomes could affect HL60 AML cells' viability significantly at a concentration of 100 μ g/mL and within 24 hours of treatment. Also, flow cytometry analysis indicated that BMSCs-derived exosomes considerably suppressed cell proliferation and effectively increased the ROS level in HL60 cells. H19 expression level was also significantly decreased in treated HL60 AML cells compared to their untreated counterparts.

Conclusion: BMSC exosomes suppress cell proliferation and simultaneously elevate the level of oxidative stress, which leads to apoptosis induction in HL60 AML cells, likely by reducing the expression level of H19 poor prognosis lncRNA. These findings suggest that BMSC-derived exosomes may serve as potential supportive therapies for leukemia.

Keywords: Acute Myeloid Leukemia; Exosome; H19; TUG1; Mesenchymal Stem Cells.



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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-9

VEXAS Syndrome: A Novel Condition in Hematological Precursor Cells

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Abstract

Background and Aim: VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is an adult-onset, monogenic disease first described in 2020 by the National Institutes of Health (NIH). VEXAS syndrome has an estimated prevalence of 1 in 14,000 individuals overall and 1 in 4,000 men over age 50. It is caused by somatic mutations in the X-linked UBA1 gene, which encodes the E1 ubiquitin-activating enzyme in hematological precursor cells. These mutations lead to reduced enzyme activity and impaired protein ubiquitylation, resulting in activation of inflammatory and innate immune pathways. The condition is characterized by inflammatory symptoms and hematological abnormalities, including recurrent fever, cytopenia, bone marrow dysplasia, and elevated inflammatory markers. Hematological abnormalities, such as macrocytic anemia, different types of cytopenia (thrombocytopenia, monocytopenia, lymphopenia), thromboembolic disorders, dyshematopoiesis, vacuolization in myeloid and erythroid precursors, increased myeloid to erythroid ratio, dependence on blood transfusion, hyperferritinemia, and elevated ESR. Moreover, this condition involves progressive bone marrow failure and hematological malignancies. The study aims to investigate and know more comprehensively about this newly recognized syndrome because it seems to be among the differential diagnoses among inflammatory patients and hematological malignancies due to its prevalence.

Methods: This review was conducted through a comprehensive literature search of PubMed, Google Scholar, and Web of Science databases for all studies on VEXAS syndrome published from January 2020 to November 2023. Original studies reporting clinical, laboratory, genetic, and prognostic data on patients with confirmed VEXAS syndrome were included. Extracted data included patient demographics, presenting symptoms, hematological and inflammatory findings, UBA1 mutations, treatment responses, disease course, and outcomes.

Discussion: In patients who have adult-onset autoinflammation symptoms characterized by hematological abnormalities and multiorgan involvement, VEXAS syndrome should be considered as a differential diagnosis. Early diagnosis can lead to better treatment options, including stem cell transplantation, and reduce the need for unnecessary diagnostic procedures while providing more accurate prognostic information.

Conclusion: This review compiles the current evidence on the clinical presentation, diagnostic tests, genetics, treatment responses, and disease course of VEXAS syndrome. Further research should delineate the full spectrum of UBA1 mutations and genotype-phenotype correlations in VEXAS syndrome. Clinical trials should evaluate therapeutic agents that target inflammatory pathways implicated in VEXAS. Increased awareness and testing for somatic UBA1 mutations in patients with unexplained cytopenia and inflammation will facilitate earlier diagnosis and treatment of VEXAS syndrome.

Keywords: Hematological Malignancies; UBA1; Inflammation Disease; VEXAS; Vacuolization.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-12

Chimerism after hematopoietic stem cell transplantation

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Abstract

Background and Aim: By examining the recipient's peripheral blood or bone marrow samples in a number of malignant and non-malignant hematologic disorders, chimerism analysis is a tried-and-true technique for tracking the progress of hematopoietic stem cell transplantation (HSCT). An early therapeutic intervention that is successful requires constant monitoring, according to clinical experts. In order to better understand chimerism following bone marrow transplantation, this paper presents a comparative overview of the major molecular biology techniques, emphasizing both their benefits and drawbacks. The literature review indicates that the most effective technique for ensuring a high power of differentiation between distinct individuals is the analysis of short tandem repeats (STR) using simple PCR in conjunction with capillary electrophoresis (STR-PCR). The technical limitations of STR-PCR were addressed by the development of alternative techniques like digital PCR (dPCR), next-generation sequencing (NGS) technology, and real-time quantitative PCR (qPCR). The window for therapeutic intervention is widened because these additional techniques, in particular, ensure a higher sensitivity that enables the detection of chimerism at an earlier stage. In spite of the possibility that both dPCR and NGS could augment or even completely replace the widely used STR analysis techniques, it appears from a comparative assessment of the different approaches that STR-PCR is still the best choice for chimerism research.

Discussion: Chimerism is the event that leads to the creation of a chimera. A chimera is a creature that has two different sets of DNAs in its body, while each cell in its body naturally has 46 chromosomes. The occurrence of this event can have different reasons, and due to these different reasons, different names are also applied to these creatures. These titles are as follows:

Micro-chimerism: In a pregnant mother, there is a possibility of transfer of stem cells from the fetus to the mother and vice versa through the placenta, and if this happens, the mother and the fetus become chimeras.

Twin chimerism: In this type of chimerism, stem cells are transferred between two embryos and enter from one to the other.

Artificial chimerism: During blood transfusion, organ transplant, bone marrow transplant, and any entry of cells with different DNA from the recipient, chimerism occurs.

Tetragametic: When two different sperm cells fertilize two different egg cells, these cells then all combine to form a human embryo with crossed cell lines. This is called tetragametic chimerism.

Now they use this event in nature to track people who have undergone bone marrow transplantation. Thus, the more cells with the DNA of the donor are identified in the recipient's body, the more the recipient is recovering and has responded positively to the transplant.

Some of the tests that are used for the percentage of chimerism and the rate of recovery of the recipient are:





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Q-PCR: Real-time PCR, also known as quantitative PCR or qPCR, determines the actual amount of PCR product present in a given cycle and shows us the amount of donor DNA in the recipient.

STR-PCR: Short tandem repeats (STRs) are short tandemly repeated DNA sequences that involve a repetitive unit of 1–6 bp. These sequences exist in the intron region of the gene and are different in different people due to polymorphism and many mutations. It is possible to use the difference between these regions in the donor and recipient and by increasing their number, the incidence of chimerism can be realized.

FISH: Chimerism analysis after bone marrow transplantation is performed by FISH analysis with FISH probes for the X and Y centromeres to monitor the recipient-to-donor ratio. This technique is used more when there is a difference in the gender of the giver and receiver.

RFLP-PCR: RFLP allows DNA fragments to be cut based on unique patterns by restriction enzymes in specific regions that the enzyme recognizes and visualizes in the gel.

NGS: Next Generation Sequencing (NGS) is a massively parallel sequencing technology that offers extremely high throughput, scalability, and speed. This technology is used to determine the sequence of nucleotides in the entire genome or target regions of DNA or RNA.

Among the various molecular biology techniques suggested for chimerism monitoring, STR-PCR is still the most commonly employed approach. But given its high sensitivity and flexibility, dPCR looks to be a very promising short-term substitute for STR-PCR when compared to both qPCR and NGS. If a common experimental protocol is established and the time and expense of the analysis are decreased, NGS is anticipated to be a viable technique that will eventually supplant the earlier approaches. Finally, more research aiming at refining these methods is especially appreciated, given that a higher technical capacity to distinguish between various sources or individuals can have significant consequences in various clinical and medical domains.

Conclusion: To track engraftment levels, disease control and possible relapse, serial analysis monitoring of the patient's chimerism status is essential at predetermined intervals and whenever relapse or graft failure is suspected.

Keywords: Chimerism; Hematopoietic Stem Cell Transplantation; Chimerism After Allo-HSCT.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Case Report

Code of Abstract: PH-13

Aneurysm of the Superior Mesenteric Artery and recurrent gastro-intestinal bleeding: A case report

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Abstract

Background and Aim: Aneurysms in the primary branches of the abdominal aorta are one of the most challenging problems in vascular surgery. It is estimated that only 5.5% of all aneurysms in this organ system are visceral aneurysms. Eighty percent of visceral aneurysms are located in the hepatic and splenic arteries. One of the most difficult problems in vascular surgery is superior mesenteric artery (SMA), which is an extremely rare condition. There were 22% of patients who required emergency treatment, and 8.5% of them died. It is estimated that 40% to 60% of SMA aneurysms result in mortality.

Methods: A Case Report.

Results: Our case report describes a 60-year-old man who presented with severe upper gastrointestinal bleeding and was found to have a SMA aneurysm with a fistula to the duodenum. A surgical intervention involving bypass grafting and ligation was successful in treating the condition. In spite of this, the patient returned three and a half years later with recurrent massive melena and regurgitation of blood. The initial investigation did not reveal the cause, but subsequent imaging and surgical exploration revealed a thrombosed artery and an active duodenal fistula. After the fistula was repaired, the patient's condition stabilized. The case report highlights the importance of considering rare complications and conducting thorough investigations in patients with recurrent gastrointestinal bleeding.

Conclusion: When a SMA aneurysm ruptures into the duodenum, it necessitates reconstruction. An arterioenteric fistula should be suspected in patients with penetrating abdominal injuries and hematemesis. The prognosis of these individuals is typically poor, especially if treatment is postponed. Survival is only possible with prompt surgical intervention. If a hemorrhage is detected, action may be taken.

Keywords: Superior Mesenteric Artery Aneurysm; Duodenum Fistula; Gastrointestinal Bleeding; Thrombosed Artery; Recurrent Symptoms.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-14

Multifaceted Relationship between Mesenchymal Stem Cell-Derived Extracellular Vesicles and Tumors

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Abstract

Background and Aim: Extracellular vesicles (EVs) are membrane vesicles that play an important role in intercellular communication. They are released by several cells. varied cell types' EVs have varied effects on their target cells. Mesenchymal stem cells (MSCs) are stem cells widely distributed throughout the body's tissues. MSC-derived EVs are involved in a wide variety of biological functions. Additionally, they perform a variety of biological functions, including tissue-repair promotion, immunosuppression, and multi-lineage differentiation. Due to these distinct benefits, MSCs have been used frequently in therapeutic investigations. MSCs may directly support tumor growth by generating growth factors or encouraging tumor vascularization, according to several studies. However, additional groups showed that MSCs inhibited the growth of tumors. In this review, we'll discuss the information on EV-mediated interactions between MSCs and tumors that have been provided in the literature.

Methods: The analysis of publications that were available in the PubMed and Web of Sciences databases served as the foundation for the results of the investigation. We identified this research using keywords such as mesenchymal stem cells, extracellular vesicles, anti-tumor effect, pro-tumorigenic activity and in vivo tumor models.

Discussion: The proliferation of HepG2 and Skov-3 cell lines was shown to be reduced by MSC-EVs in vitro. Particularly, MSC-EVs boosted the proportion of tumor cells in the G0/G1 phase, a sign of an arrest in the cell cycle. Apoptosis and necrosis were induced by MSC-EV therapy in HepG2 and Skov-3 cell lines, respectively. Another recent study examined the impact of human cord blood Wharton's jelly MSC-derived EVs (hWJMSC-EVs) on the development of T24 bladder cancer both in-vitro and in-vivo. As a result, hWJMSC-EVs decreased cancer cell survival by cell cycle arrest and inducing apoptosis in a dose-dependent manner. When MSC-derived EVs were combined with human gastric and colon cancer cell lines and subcutaneously injected into nude mice, tumor incidence and growth was elevated. This result was related to an enhancement to cancer cell proliferation in-vivo, as shown by an increase of the proliferating cell nuclear antigen positive cells in tumors.

Conclusion: In the contest of cancer, it has been demonstrated that EVs produced from MSCs mimic the majority of the favorable and unfavorable effects of the cells of origin. These conflicting effects seen in various tumor types may be due to the many different pathways involved. Determining which chemicals, shuttled by EVs, could disrupt these pathways and, consequently, which types of cancers might benefit from MSC-EV treatment, is crucial.

Keywords: Mesenchymal Stem Cells; Extracellular Vesicles; Anti-Tumor Effect; Pro-Tumorigenic Activity; in vivo Tumor Models.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-17

Biotics in ALL pediatric patients

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Abstract

Background and Aim: Synbiotics potentially have a stronger effect in modulating the gut microbiota. The aim of this study was to determine the effects of Lactocare® on chemotherapy-induced nausea, and vomiting (CINV) in acute lymphoblastic leukaemia (ALL) paediatric patients.

Methods: This case-control study was performed on ALL paediatric patients. The patients were randomly assigned into two groups to receive either Lactocare® (case) or placebo (control) (58 patients in the case group and 55 patients in the control group) for 7 days. The number of times CINV were recorded in the first week.

Results: The incidence of CINV was lower in the LactoCare®-treatment group with a difference of more than 10% on the seventh day of the effects of Lactocare® synbiotic administration ($P < 0.05$). The odds ratios and 95% confidence interval were calculated to evaluate the use of LactoCare® as a protective factor against CINV (Table 1).

Conclusion: The use of synbiotics supplement in this study reduced CINV in ALL patients. This study supports the concept that the use of synbiotics supplement will be an easy and effective way to reduce Gastrointestinal complications caused by chemotherapy in ALL paediatric patients.

Keywords: LactoCare®; Chemotherapy; Nausea; Vomiting.





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Tehran University of Medical Sciences, Tehran, Iran.
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Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-18

Prophylaxis of iron deficiency in toddlers

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Abstract

Background and Aim: One of the most frequent anemias, particularly in infants, is iron deficiency anemia (IDA). Thus, prophylaxis is required to lower IDA in toddlers and improve their iron status. This study compared the effects of daily ferrous gluconate (FG) and ferrous sulfate (FS) supplementation on toddlers' iron status.

Methods: A total of 120 healthy toddlers were randomly assigned to two groups and given FS and FG. Both at baseline and six months after starting supplements, the iron status was assessed. In order to determine the statistical significance of the variations in iron status between the FS and FG groups, the student's t-test and the Pearson's Chi-square test were utilized for qualitative variables. For statistical analysis, SPSS software was utilized.

Results: Toddlers in the FS and FG groups had significantly different iron statuses at baseline and six months after starting supplements. Hemoglobin (Hb) was 10.46 vs. 12.45, $P = 0.001$, and ferritin was 28.08 vs. 59.63, $P = 0.001$.

Conclusion: Our study concluded that both FG and FS supplements were useful for prophylactic usage in the prevention of IDA, even though FG prophylaxis raised Hb and ferritin levels. The FG group that received FG supplementation showed higher levels of ferritin and Hb than the FS group that received FS supplementation, indicating that FG was more effective than FS.

Keywords: Iron; Iron Deficiencies; Prophylaxis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-19

Apoptosis Induction by Ganoderic Acid A via Increased Autophagy-Related Genes in NALM-6 Cells

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Abstract

Background and Aim: Acute lymphoblastic leukemia (ALL) is the most common leukemia in children, which is associated with a high relapse rate despite prevalent therapies. Ganoderic acid A (GAA) is one of the bioactive compounds of *Ganoderma lucidum*, which possesses potential antileukemic properties. This study aimed to investigate the effect of the GAA extract on the expression of autophagic genes and the autophagy induction in the ALL-cell line.

Methods: NALM-6 cells were cultured in vitro, and the optimal treatment concentration of GAA was determined by an MTT assay. Flow cytometry was used to determine the death of NALM-6 cells caused by GAA treatment by utilizing FITC-conjugated propidium iodide (PI) and annexin V staining. The expression levels of autophagic genes LC3, BECLIN, ATG5, ATG10, FIB200, and AMBRA before and after treatment with GAA were monitored using real-time polymerase chain reaction.

Results: The results of the MTT test indicated that the half maximum inhibitory concentration (IC₅₀) of leukemic cells after 48 hours of treatment with *G. lucidum* is 140 µg/mL. In addition, the flow cytometry results showed an increase of 40.5% in apoptosis and death of cells at a 140-µg/mL concentration of GAA after 48 hours. Besides, GAA treatment up regulated expression levels of LC3 ($P = 0.024$), BECLIN ($P = 0.035$), ATG5 ($P = 0.024$), ATG10 ($P = 0.024$), FIB200 ($P = 0.024$), AMBRA ($P = 0.024$) in NALM-6 compared to the control groups.

Conclusion: GAA can induce apoptosis in NALM-6. It also increases the expression of autophagy genes.

Keywords: Acute Lymphoblastic Leukemia; Ganoderic Acid A; Autophagy.





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Tehran University of Medical Sciences, Tehran, Iran.
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Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-20

Evaluation of PLR and NLR changes in the diagnosis of children with acute appendicitis

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Abstract

Background and Aim: Acute appendicitis (AA) is the most common cause of acute abdominal pain, with a higher risk in men than women. As the complication rate increases over time, early and prompt diagnosis of AA is very important. Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are inflammatory biomarkers that are currently used in the diagnosis and prediction of many inflammatory diseases. This study aimed to investigate changes in NLR and the PLR as inflammatory markers for the diagnosis of acute appendicitis in children.

Methods: We searched PubMed, Scopus and Google Scholar from 2020 to 2023 for studies comparing NLR and PLR values in children with acute appendicitis and control group. The following keywords were used for the search: children; pediatrics; acute appendicitis; neutrophil-lymphocyte ratio; platelet-lymphocyte ratio

Results: The studies showed that there was a significant difference between the two groups. NLR and PLR were significantly increased in children with acute appendicitis, and a significant correlation was observed between acute appendicitis and NLR and PLR.

Conclusion: NLR and PLR are valuable hematological parameters to differentiate children with acute appendicitis from children without acute appendicitis. These markers can also be useful in the monitoring of children with acute appendicitis during treatment.

Keywords: Neutrophil-to-Lymphocyte; Platelet-to-Lymphocyte; Acute Appendicitis; Children.





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Tehran University of Medical Sciences, Tehran, Iran.
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Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PH-21

Investigating the effect of imatinib on pregnancy in patients with chronic myeloid leukemia

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Abstract

Background and Aim: Imatinib, sold under Gleevec or Glivec, is a tyrosine kinase inhibitor (TKI) drug used to treat chronic myeloid leukemia (CML) patients for almost 20 years. It reduces and controls the disease's progression and is preferred over IFN- α due to minimal side effects. However, its use during pregnancy or in CML patients planning to become pregnant is a concern.

Methods: Data for this review were obtained by searching PubMed, Web of Science, Scopus, and Google Scholar.

Discussion: Imatinib has been shown to potentially increase the risk of pregnancy complications such as fetal abnormalities, spontaneous abortions, and stillbirths by impacting organogenesis, according to existing studies. Although the occurrence of issues related to the use of imatinib during pregnancy is rare, it is still recommended that women who are of reproductive age and are undergoing imatinib treatment use contraceptives to prevent any unwanted pregnancies. Patients with CML on imatinib planning to conceive should stop treatment before contraception and switch to an alternative therapy based on their condition and gender.

Conclusion: According to current studies, the likelihood of fetal abnormalities due to imatinib use during the second and third trimesters of pregnancy and while breastfeeding is very low. During the period before pregnancy and the first trimester of pregnancy, imatinib can potentially limit and create defects in the structure of vital proteins for the gonads, implantation, and embryogenesis. As a result, this drug could cause abnormalities and weaknesses in the fetus. To conceive, male CML patients should stop imatinib treatment after consulting their doctor and considering their condition. They should discontinue the medication one month before contraception and continue until contraception is achieved. Female CML patients should stop the medication one month before contraception and not resume at least until the end of the first trimester of pregnancy. IFN- α may be considered as an alternative treatment for patients requiring continuous treatment or experiencing hematological changes, in consultation with a doctor.

Imatinib may be safe to use during the second and third months of pregnancy without significant harm to the fetus. Still, detectable levels may be found in newborns' cord and peripheral blood. Imatinib can be found in breast milk, and as a result, it is advised that mothers who have CML and are taking imatinib should not breastfeed their babies. This is because the long-term effects of imatinib exposure on newborns are unknown. IFN- α 's safety during pregnancy is questionable due to potential harm to certain animal species, as demonstrated in some studies. It is generally recommended that patients avoid getting pregnant while undergoing treatment with imatinib. To reduce the risk of unwanted pregnancy, patients are advised to use available contraception methods. However, if they wish to become pregnant, it is essential to plan and follow medical advice and tests to ensure a safe and healthy pregnancy. Treatment measures during pregnancy should be tailored to each patient's individual needs.

Considering the limited data on treating CML during pregnancy, this challenge requires further study.

Keywords: Imatinib; Pregnancy; CML; Tyrosine Kinase Inhibitor.



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Tehran University of Medical Sciences, Tehran, Iran.
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Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-23

Clinical and molecular profile of patients with rare bleeding disorders: A single-center retrospective study

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Abstract

Background and Aim: There is little information on the molecular pathologies of rare bleeding disorders (RBDs) due to their low frequency. Therefore, the objective of this study was to analyze the molecular and clinical profiles of patients with RBDs.

Methods: A retrospective single-center study was conducted among patients with FII, FVII, FX, and FXIII deficiencies between March 20, 2000, and June 31, 2023. Data on patient demographics, genetic analysis, and laboratory results were documented for all patients. The disease severity was classified according to the clotting factor activity (except FXIII) as follows: >5%: mild, 1-5%: moderate, and <1%: severe.

Results: A total of 79 patients were enrolled in this study. Three of the cases had FII (3.7%), 40 had FVII (50.6%), 20 had FX (25.3%), and 16 had FXIII deficiency (20.2%). The median age of the patients at the time of diagnosis was 6 months for FII, 78 months for FVII, 5 months for FX, and 5.75 months for FXIII deficiencies, respectively. The major clinical manifestations were bruising, epistaxis, oral cavity bleeding, ecchymosis, and hemarthrosis. Consanguinity was present in 60 (76%) of patients. The majority of the patients had missense mutations.

Conclusion: The diagnosis of the causative mutations in patients with RBDs provides an insight into the underlying molecular basis of these disorders and probably explains their variable clinical manifestations.

Keywords: Rare Bleeding Disorders; Retrospective; Genetic Analysis; Clinical Manifestation.





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Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-24

Relationship between mutations in severe hemophilia A and risk of inhibitor development

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Abstract

Background and Aim: One of the major problems for patients with severe hemophilia A is the development of neutralizing antibodies against FVIII. Thus, the aim of this study was to analyze the molecular and clinical profiles of patients with severe hemophilia A and to determine if certain mutations predispose to inhibitor development in these patients.

Methods: A retrospective single-center study was conducted among patients with severe hemophilia A between March 20, 2000, and June 31, 2023. Data on patient demographics, genetic analysis, and laboratory results were documented for all patients.

Results: A total of 480 severe hemophilia A patient, with and without inhibitors were enrolled in this study. The median age of the patients at the time of diagnosis was 6 months (range: 3 months to 18 months). Consanguinity was present in 109 (22.7%) of patients. A family history of hemophilia was reported in 207 (43.1%) of patients. Intron 22 inversion (Inv 22) was observed in 200 (41.7%) of the cases. Among 72 patients who developed inhibitors, 52 (72.2%) were classified as high responders and 20 (27.8%) as low responders. Inv 22 revealed a statistically significant association with the risk of inhibitor development ($P=0.002$).

Conclusion: Due to the high occurrence of Inv 22 in individuals with severe hemophilia A and the potential link between this mutation and the likelihood of developing an inhibitor, it is recommended to conduct molecular tests early on in the diagnosis of hemophilia to determine the specific mutation.

Keywords: FVIII; Retrospective Study; Hemophilia A; Inhibitor; Intron 22 Inversion.





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Tehran University of Medical Sciences, Tehran, Iran.
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Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-25

Investigating the role of the laboratory in the detection of inflammatory markers in the diagnosis of irritable bowel syndrome in children: A systematic review

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Abstract

Background and Aim: Irritable bowel syndrome is a common and troublesome disorder in children whose prevalence has increased in the last two decades. This syndrome has a significant impact on the lives of children and their families and places a significant burden on health care systems. Only a few treatments have shown benefits for children. Furthermore, most of the described pathophysiological mechanisms and treatment options are based on adult studies, and these issues have emerged as challenges when dealing with pediatric IBS and must be overcome to effectively manage children with IBS.

Methods: In this systematic review, key terms related to pediatric IBD and its laboratory markers were searched in Google Scholar, Pub Med, Scopus, Cochrane library and Science Direct databases from 2010 to 2023. Finally, 8 articles that met all the inclusion criteria were included.

Results: All blood markers, especially calprotectin, improved the differentiation between children with IBD and those without IBD when examined along with clinical symptoms. In the fecal calprotectin study, the proportion of patients without IBD who were correctly classified as having low risk IBD increased from 33% to 91%. The proportion of patients with IBD misclassified as low-risk IBD decreased from 16% to 9%. Also, the proportion of the total number of patients assigned to the intermediate risk group decreased from 55% to 6%.

Conclusion: Compared to blood markers, fecal calprotectin adds the most diagnostic value to the investigation of clinical symptoms.

Keywords: IBD , Calprotectin , IBD Biomarkers.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-26

Predictive value of microRNA (miR)-145 and miR-19b expression levels for thrombosis risk in thalassemia

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Abstract

Background and Aim: Thalassemia is a common inherited blood disorder resulting from mutations in the α - or β -globin gene clusters, resulting in reduced or absent globin chain synthesis. Patients with β -thalassemia major (β -TM) require regular red blood cell transfusions, while those with β -thalassemia intermedia (β -TI) generally do not. Thromboembolic events are frequently observed in thalassemia patients due to a hypercoagulable state, with splenectomy and transfusion considered as significant risk factors, especially in β -TI patients. This study aimed to investigate the expression of miR-145 and miR-19b in platelet-derived and red blood cell-derived microparticles (MPs) in patients with β -TM and β -TI.

Methods: Blood samples were collected from 20 β -TM and 10 β -TI patients referred to the Thalassemia and Hemophilia Center of Bushehr Province, Iran, and a control group of 20 individuals. MPs were isolated using low and high centrifugation steps, and their size was confirmed using Dynamic Light Scattering (DLS). Immunophenotyping of platelet-derived MPs (PMPs) and red blood cell-derived MPs (RMPs) was performed using flow cytometry assay. RT-qPCR was conducted to analyze the expression levels of miR-145 and miR-19b. Additionally, correlation analyzes were used to assess the relationship between miRNA expression levels and various hematological parameters. Statistical analyses were performed using SPSS 26 and GraphPad Prism 8.

Results: The mean ages of patients in the β -thalassemia major, β -thalassemia intermedia, and control groups were 28.65 ± 2.03 , 29.50 ± 3.34 , and 27.50 ± 1.06 , respectively. In this study, the isolated microparticles were of platelet and erythrocyte type. Our results demonstrated a significant decrease in RBC and PLT count, HB and HCT levels, MCV, MCH, and MCHC in the β -TM and β -TI groups compared to the control group. However, there was no significant difference in the WBC count among the three studied groups. The expression levels of miR-145 and miR-19b in the PMPs and RMPs showed no significant difference among the β -TM, β -TI, and control groups. Moreover, there was no significant correlation between the expression levels of miR-145 and miR-19b with hematological parameters.

Conclusion: our study showed that miR-145 expression reduction in PMPs and RMPs in β -TM and β -TI patients may be related to thrombocytosis and thrombotic conditions in patients. Also, we showed that the increased expression of miR-19b in PMPs and RMPs in β -TM and β -TI patients may be related to the severity of anemia. While our preliminary results were not statistically significant, larger studies are warranted to further investigate miR-145 and miR-19b expression in MPs as potential predictive biomarkers of thrombosis risk in thalassemia patients.

Keywords: Microparticle; Thalassemia; miR-145; miR-19b; Predictive Biomarker.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-27

Evaluation of plasma Flt3 ligand level as a biomarker in acute myeloid leukemia

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Abstract

Background and Aim: Fms-like tyrosine kinase 3 ligand (Flt3L) is a growth factor affecting the hematopoietic lineage. This ligand is a key regulator of hematopoiesis. Studies have been shown to correlate the Flt3L with the extent of bone marrow aplasia after radiotherapy or chemotherapy. Interestingly, Flt3L is expressed by leukemic cells and might enhance proliferation through an autocrine process. The aim of this study was to evaluate the variability of peripheral FLT-3 ligand during the clinical course of acute myeloid leukemia patients.

Methods: Twenty-seven patients were enrolled in this study in order to assess alterations in the circulating levels of FLT-3 ligand during the clinical course of AML. White cell, platelet levels, Serum lactate dehydrogenase and electrolyte levels were also measured for all patient. Plasma FLT-3 ligand analysis was performed with enzyme immunoassay technique and Statistical analysis was performed with SPSS 10.

Results: We studied the association in the diagnostic period between the FLT-3 ligand and peripheral blood cells together with serum electrolytes. FLT-3 ligand levels (pg/mL) during the aplastic period due to remission induction and consolidation were higher than the levels at initial diagnosis. On the other hand, the diagnostic and remission induction values of leukocytes and FLT-3 ligand showed an inverse association. These results indicate to us that higher white cell counts are associated with lower FLT-3 ligand levels. We also found a reversed association between FLT-3 ligand and serum lactate dehydrogenase level. However, there was no association between FLT-3 ligand and other serum electrolyte levels. We also found higher FLT-3 ligand levels in male patients.

Conclusion: Serial measurement of Flt3L in patients with AML illustrates the potential value of monitoring Flt3L to identify relapse. Indeed, FLT3L could provide a low cost, rapid and noninvasive assessment of chemosensitivity and blast clearance that has robust prognostic significance for patients with AML.

Keywords: AML; FLT-3 Ligand; Biomarker.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-28

Use of Thrombopoietin receptor agonist for management and treatment immune thrombocytopenia in pregnancy

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Abstract

Background and Aim: Immune thrombocytopenia (ITP) is an autoimmune disease in which IgG antibodies accelerate platelet clearance and decrease platelet production. ITP usually occurs in women of childbearing age. Even during an uncomplicated pregnancy, the platelet count can decrease which not only affects the mother but can also cause neonatal thrombocytopenia secondary to maternal immune thrombocytopenia. Treatment of immune thrombocytopenia in adults has advanced rapidly over the past decade. There are currently three approved thrombopoietin receptor agonists (TPO-RAs) in Europe for the treatment of patients with immune thrombocytopenia: Romiplostim (Nplate®), Eltrombopag (Revolade®) and Avatrombopag (Doptelet®). However, the US Food and Drug Administration (FDA) has classified their use during pregnancy as Category C due to a lack of human clinical data. The aim of the study is to review the literature to assess the safety of TPO-RAs in pregnant women.

Methods: Articles pertaining to the use of TPO-RAs in pregnancy including twenty articles, five meta-analysis articles and fifteen randomized controlled trial (RCT) articles. were retrieved through a comprehensive literature search by using several databases such as PubMed, Google Scholar, Scopus, Embase, and Cochrane until September 2023. Search keywords such as Immune Thrombocytopenia, pregnancy, thrombopoietin receptor agonists were used during the database search to target comparable articles.

Discussion: According to the meta-analysis and randomized controlled trial articles, the use of Eltrombopag and Romiplostim seems to be comparatively safe within the initial, second, and third trimesters, as there have been no rumored reported congenital malformations. Low fetal birth weight has been ascertained following the administration of Eltrombopag throughout the trimester, whereas preterm birth has occurred following the administration of Eltrombopag within the trimester.

Conclusion: The treatment choices for managing thrombocytopenia in pregnant patients with ITP restricted thanks to considerations for fetal toxicity. The administration of Eltrombopag and Romiplostim throughout all trimesters of pregnancy appears comparatively safe. However, there appears to be an association between the administration of Eltrombopag throughout the first/second trimester and low fetal birth weight. However, there is an urgent need to conduct a prospective clinical trial or a registry study to evaluate the use of TPO-RAs in pregnant patients with ITP.

Keywords: Immune Thrombocytopenia; Pregnancy; Thrombopoietin Receptor Agonists.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-29

Clinical and molecular profile of patients with moderate and mild hemophilia A: A single-center retrospective study

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Abstract

Background and Aim: Mild/moderate hemophilia A is an X-linked bleeding coagulation disorder caused by mutations in the factor VIII gene. Patients with moderate hemophilia often bleeding as a result of physical injuries, the frequency of bleeding in these patients is less than that of severe hemophilia, but some patients with moderate hemophilia may show a more severe phenotype. On the other hand, people with mild hemophilia usually bleeding only during trauma/surgery, and even bleeding in these people may not be clinically apparent until later in life.

Methods: A retrospective single-center study was conducted among patients with moderate/mild hemophilia A between March 20, 2000, and June 31, 2023. Data on patient demographics, genetic analysis, and laboratory results were documented for all patients. Patients with FVIII activity between >1 and $\leq 5\%$ are classified as moderate hemophilia and patients with FVIII activity between ≥ 5 and $<40\%$ are classified as mild hemophilia. In addition, VWF antigen (VWF: Ag) and VWF: ristocetin cofactor assay (VWF: RCo) were performed.

Result: A total of 110 patients were included in this study. The median age of the patients at the time of diagnosis was five years [IQR:1.25 -18]. Consanguinity was present in 20 (18.2%) of patients. A family history of hemophilia was reported in 68 (61.8%) patients. They were bleeding after circumcision, and tooth extraction was the most common primary cause of diagnosis. Most of the mutations occurred in the exons 26 and 23, respectively. Moreover, missense mutations were the most common mutations identified in our cohort. In addition, three patients developed inhibitors.

Conclusion: Patients with mild and moderate hemophilia A present with a wide range of clinical manifestations, which poses substantial challenges to their diagnosis and management. Identifying the causative mutations in these groups aids in determining the genetic basis of this bleeding disorder and gaining a better understanding of the various clinical symptoms of people with mild and moderate FVIII deficiency.

Keywords: FVIII; Hemophilia A; Bleeding; Missense Mutation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-30

Hematological parameters and prediction of in hospital outcome and mortality of acute coronary syndrome

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Abstract

Background and Aim: Acute coronary syndrome (ACS) is a major cause of death. CBC (complete blood count) along with differential count have been of interest to researchers in determining ACS risk stratification. We investigated CBC, differential count, NLR (neutrophil-to-lymphocyte ratio) and PLR (platelet-to-lymphocyte ratio) in predicting complications and mortality due to ACS.

Methods: 628 ACS adult patients admitted to coronary care unit between 2020-2022 were included in the study. CBC, diff and related variables and troponin in first 24 hours of admission and also other clinical information (hospital mortality, length of hospitalization, need for invasive revascularization, presence of malignant ventricular arrhythmia, diagnosis of left ventricular systolic dysfunction in echocardiography) were evaluated from the patient's files. The relationship between parameters was evaluated with statistical methods (P value < 0.05 significant).

Results: High neutrophil (P= 0.003) and low lymphocyte (P= 0.003) had a good ability to predict the occurrence of severe left ventricular failure. The evidence of cardiac necrosis (increased troponin) had relationship with the increase of NLR (P= 0.001), neutrophil (P= 0.001), PLR (P= 0.01) and with the decrease of blood lymphocytes (P= 0.003) and platelet count (P= 0.01). Low hemoglobin (P=0.01) and high WBC (P=0.003) predicted the occurrence of malignant ventricular arrhythmia. Low hemoglobin (P=0.01) and also high Platelet Distribution Width (PDW) (P=0.04) and blood WBC (P=0.002) had a significant relationship with hospital mortality. Increased NLR (P= 0.001) was the only marker associated with the need for invasive vascular treatments. The increase of NLR (P=0.04) and PLR (P=0.05) and decrease of lymphocytes (P=0.03) had a significant relationship with the number of days of hospitalization. RDW was not associated with any of the clinical outcomes and mortality.

Conclusion: The decrease of platelets and lymphocytes and the increase of neutrophils have been associated with the severity of inflammation and its consequences in ACS. With the decrease of hemoglobin, the risk of death in ACS is expected to increase (1) which is consistent with the present study. It seems that the rise of NLR, PLR is a more reliable measure than each of these indices. In our study, increased PLR and NLR were associated with myocardial necrosis (MI) and increased length of hospital stay. RDW did not show a correlation with any of the prognosis criteria, which is not consistent with some studies (1-3) which may be due to age, lack of vitamins and genetics of the study area as a result of RDW. Our study was single-center but Multicenter studies are recommended to determine the risk of ACS in order to prepare practical guidelines. Hematological parameters as a non-invasive and available test can help in risk classification of ACS patients.

Keywords: Acute Coronary Syndrome; CBC; NLR; Mortality; ACS.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PH-31

Non-Invasive Prognosis of Acute Lymphoblastic Leukemia Using Cell-Free DNA

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Abstract

Background and Aim: Acute lymphoblastic leukemia (ALL) is a common childhood neoplasm that also affects adults. Detection of minimal residual disease (MRD) remains the most powerful prognostic indicator of outcome. Current methods to diagnose MRD rely on the presence of ALL blasts in patient biofluid samples. However, blasts may persist in the patients but not be physically present in biofluid samples, leading to inaccurate or delayed diagnosis. This study evaluates the potential of cell-free DNA released by cancer cells into patient biofluids, as an accurate and non-invasive prognostic biomarker of patients with ALL, which may allow routine patient assessment from a blood draw.

Methods: In this review, articles were collected from PubMed, Scopus and Google Scholar databases, published between 2020 and 2023. These databases were searched using the keywords of cell-free DNA, Acute Lymphoblastic Leukemia, and non-invasive diagnosis.

Discussion: Investigations showed that ALL associated cell-free DNA in patient blood samples could be tracked using nanopore sequencing workflows such as Nanopore MinION sequencing of PCR amplified VDJ rearrangements of the immunoglobulin (in B-ALL) or T-cell receptor (in T-ALL). These tests enabled the detection of leukemia clones, and the tracking of the response of ALL clones during treatment. Additionally, they were able to measure MRD even in samples with undetectable diagnostic cell-count thresholds for MRD by flow cytometry. Nanopore sequencing of cfDNA obtained from blood samples can be a useful complement to cell-based methods that rely on the collection of genomic DNAs from leukemia cells in a patient sample. CfDNA sequencing also provided a more accurate assessment of ALL heterogeneity as it was able to identify clones that were not present in the genomic DNA of bone marrow biopsy samples.

Conclusion: The results showed that the cell-free DNA assay is more sensitive and less invasive than the current clinical methods and may be useful in monitoring ALL burden in patients undergoing treatment, which can enable early detection of MRD and better risk stratification. Therefore, this method can provide patients with more treatment options and ultimately may improve patient outcome.

Keywords: Cell-free DNA; Acute Lymphoblastic Leukemia; MRD; Non-invasive Diagnosis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-32

RIG-G (retinoic acid-induced gene G): a promising diagnostic and prognostic biomarker in acute promyelocytic leukemia

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Abstract

Background and Aim: Acute promyelocytic leukemia (APL), also known as AML-M3, is a subtype of acute myeloid leukemia, with a high probability of severe complications, such as bleeding tendency and disseminated intravascular coagulation (DIC); Regarding to these conditions, early death is a concerning point in APL patients. RIG-G (Retinoic acid induced gene -G) plays a role in the differentiation of bone marrow cells, inhibiting the proliferation of tumor cells and promoting the differentiation of promyelocytic cells. mRNA expression levels of RIG-G which is induced during treatment of acute promyelocytic leukemia with ATRA (all trans retinoic acid), may serves as an early and suitable indicator of APL patients' remission.

Methods: Relevant literature was identified by a PubMed and Scopus search (2015-2024) of English language papers using the terms: "APL", "Acute promyelocytic leukemia", "RAG-G" and "Retinoic acid-induced gene -G".

Discussion: Studies have shown that RIG-G mRNA expression levels in APL patients are associated with disease stage, with lower levels in non-treated or relapsed patients and higher levels in complete remission patients. Furthermore, RIG-G gene expression in peripheral blood is strongly correlated with expression in patient bone marrow cytology. Therefore, the detection of RIG-G mRNA can be used to determine the efficiency of M3 prognosis and retinoic acid treatment. The RIG-G gene can be monitored directly via peripheral blood, eliminating the need for pain-inducing bone marrow biopsies in patients and facilitating regular long-term monitoring.

Conclusion: Detection of RIG-G mRNA can be used to determine the efficiency of M3 prognosis and retinoic acid treatment. The RIG-G gene can be monitored directly via peripheral blood, eliminating the need for pain-inducing bone marrow biopsies in patients and facilitating regular long-term monitoring. Detecting changes in expression levels of the RIG-G gene can provide a significant availability in assessing and following up on APL patients' conditions. RIG-G as a novel prognostic and diagnostic biomarker provides new approaches for clinical diagnosis and treatment APL patients.

Keywords: APL; Acute Promyelocytic Leukemia; RIG-G; Retinoic Acid-induced Gene G.





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Venue:
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January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-33

Metformin as an adjuvant for anti-CML drugs

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Abstract

Background and Aim: CML (chronic myeloid leukemia) is a malignant clonal disorder of hematopoietic stem cells in which myeloid progenitors increase in the peripheral blood and bone marrow. The common treatments like chemotherapy, have limitation and are prone to tumor recurrence or drug resistance. researchers have demonstrated the anti-cancer effects of metformin, in hematological disorders like CML, by acting in a number of tumorigenic pathways.

Methods: Relevant literature was identified by a PubMed and Scopus search (2012-2023) of English language papers using the terms: “CML”, “Chronic Myeloid Leukemia”, “Metformin” and “Chemotherapy”.

Results: metformin through stimulation of adenosine monophosphate (AMP)-activated protein kinase (AMPK) downregulate the mTORC1 signaling pathway and suppress cell viability and induce apoptosis. Additionally, metformin is able to potentiate the antileukemic drugs such as TKI (tyrosine kinase inhibitor), imatinib and cisplatin in CML patients.

Conclusion: Metformin can use as an adjuvant for anti-cancer drugs especially for CML patients. Thus, discovering less toxic and more effective drugs especially for chemotherapy-resistant patients may provide promising new therapeutic strategies in CML patients.

Keywords: CML; Chronic Myeloid Leukemia; Metformin; Chemotherapy.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Narrative review

Code of Abstract: PH-34

Application of two nanoparticles, TAT-PEG-CCMD and BSA/POL407, in the treatment of acute lymphoblastic leukemia (ALL)

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Abstract

Background and Aim: Acute lymphoblastic leukemia (ALL), characterized by excessive proliferation of lymphoblasts in the bone marrow, is responsible for more than 70% of childhood malignancies. It has been reported that about 90% of patients recover, but due to the side effects caused by the lack of specificity of anticancer drugs and the high rate of relapse and drug resistance, the prognosis of the relapsed patients is poor. The use of nanomedicines is a unique therapeutic strategy that provides better therapeutic efficacy. This review describes the use of nanoparticles to overcome drug resistance and reduce side effects in the treatment of ALL.

Methods: Databases including PubMed and Google scholar were searched using keywords such as nanoparticles and ALL, and articles published between 2019 and 2023 were reviewed.

Discussion: According to the studies, polyethylene glycol chitosan-carboxymethyl dextran conjugated with TAT (TAT-PEG-CCMD) is an effective nanoparticle in the treatment of ALL. Activation of DNA damage repair pathways by WEE1-kinase in cases of using chemotherapy drugs based on DNA damage such as doxorubicin (DOX) (inducing apoptosis by creating a double-strand break in the genome by inhibiting topoisomerase II) plays an essential role in creating drug resistance. Using TAT-PEG-CCMD nanoparticles to deliver anti-WEE1 SiRNA and DOX to ALL cells to inhibit WEE1 kinase overexpression by degrading target gene mRNA by SiRNA, significantly increased the apoptotic effects of DOX in ALL cells. Bovine serum albumin/Ploxamer 407 (BSA/POL407) is another nanoparticle that can be used to immobilize asparaginase for asparagine hydrolysis, while being able to trap the resulting ammonia. As a result, it prevents hyperammonemia, which is the main complication during ALL treatment with asparaginase.

Conclusion: Due to their many potentials, including non-toxicity, non-immunogenicity, high biodegradability and low production cost, nanoparticles can be used as targeted drug delivery systems in the treatment of cancer and to overcome the cases of drug resistance (MDR). TAT-PEG-CCMD nanoparticles by switching off WEE1-kinase and subsequently neutralizing the resistance exerted by ALL cells, and BSA/POL407 nanoparticles by increasing the stability time of asparaginase and trapping the resulting ammonia can be promising methods in the treatment of ALL.

Keywords: ALL; Nanoparticles; Targeted Drug Delivery.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-35

Antiproliferative effect of *Cassiopeia andromeda* venom as a novel bioactive agent in Jurkat cell line

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Abstract

Background and Aim: Marine organism such as jellyfishes have been recognized for their potential bioactive compounds with diverse biomedical applications. This study investigates the antiproliferative effects of *Cassiopeia andromeda* jellyfish venom as a novel bioactive compound in Acute Promyelocytic Leukemia (APL) cell line, NB4, and explores its underlying molecular mechanisms involving dysregulation of miR-125b and miR-155.

Methods: An experimental approach was employed to evaluate the cytotoxic and apoptotic impacts of *C. andromeda* venom. The methyl thiazoltetrazolium (MTT) assay and flow cytometry analysis with 7-Aminoactinomycin D (7AAD) and Annexin V were employed to assess cytotoxicity and apoptosis. Furthermore, real-time PCR was utilized to quantify the expression levels of miR-155 and miR-125b.

Results: The findings demonstrate that *C. andromeda* venom exerts a concentration- and time-dependent inhibition on NB4 cell growth and promotes apoptosis. Notably, a reduction in miR-125b expression was observed, concomitant with a significant elevation in miR-155 expression.

Conclusion: The study underscores the potential of *C. andromeda* venom as a promising bioactive compound with antiproliferative properties in NB4 cells. The venom's cytotoxic and pro-apoptotic effects are associated with dysregulated expression of miR-125b and miR-155. These results shed light on the translational potential of jellyfish venom in the realm of oncology and warrant further investigation into its mechanism of action and therapeutic applications.

Keywords: Leukemia; Venom; Cnidaria; *Cassiopeia Andromeda*; Antiproliferative; Apoptosis; microRNA, miRNA.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-36

The effect of *Cassiopeia andromeda* Jellyfish Venom on the Antiproliferative in NB4 Cell line

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Abstract

Background and Aim: Marine organism such as jellyfishes have been recognized for their potential bioactive compounds with diverse biomedical applications. This study investigates the antiproliferative effects of *Cassiopeia andromeda* jellyfish venom as a novel bioactive compound in Acute Promyelocytic Leukemia (APL) cell line, NB4, and explores its underlying molecular mechanisms involving dysregulation of miR-125b and miR-155.

Methods: An experimental approach was employed to evaluate the cytotoxic and apoptotic impacts of *C. andromeda* venom. The methyl thiazoltetrazolium (MTT) assay and flow cytometry analysis with 7-Aminoactinomycin D (7AAD) and Annexin V were employed to assess cytotoxicity and apoptosis. Furthermore, real-time PCR was utilized to quantify the expression levels of miR-155 and miR-125b.

Results: The findings demonstrate that *C. andromeda* venom exerts a concentration- and time-dependent inhibition on NB4 cell growth and promotes apoptosis. Notably, a reduction in miR-125b expression was observed, concomitant with a significant elevation in miR-155 expression.

Conclusion: The study underscores the potential of *C. andromeda* venom as a promising bioactive compound with antiproliferative properties in NB4 cells. The venom's cytotoxic and pro-apoptotic effects are associated with dysregulated expression of miR-125b and miR-155. These results shed light on the translational potential of jellyfish venom in the realm of oncology and warrant further investigation into its mechanism of action and therapeutic applications.

Keywords: Leukemia; Venom; Cnidaria; *Cassiopeia Andromeda*; Antiproliferative; Apoptosis; microRNA; miRNA.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-37

Investigating the effect of oleuropein on apoptosis rate and miR-124 expression in acute myeloid leukemia cell lines treated with 5-Azacitidine

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Abstract

Background and Aim: Acute myeloid leukemia is a prevalent form of adult leukemia that results in a significant number of morbidity and mortality annually. Traditional treatments for this disease are associated with relapse and general toxicity, necessitating the use of new treatments. Flavonoids are also being considered as a complementary treatment to chemotherapy to mitigate its side effects. This study aims to examine the effects of oleuropein on the of HL-60 and KG1 cell lines and its effects on miR-124-3p expression in these cells.

Methods: The KG1 and HL-60 cell lines were cultured in RPMI1640 medium supplemented with 10% fetal bovine serum (FBS) and incubated under controlled conditions of 37 °C, 95% humidity, and 5% carbon dioxide. The objective of this study was to investigate the potential cytotoxic effects of oleuropein and azacytidine on these cell lines. To achieve this, the cell lines were exposed to these compounds alone and in combination for durations of 24, 48, and 72 hours. Subsequently, the extent of apoptosis was evaluated using flow cytometry with Annexin V/propidium iodide (PI) staining. Furthermore, RNA was extracted from the treated cells and complementary DNA (cDNA) was synthesized. The expression of miR-124-3p was then quantified using Real-Time PCR.

Results: This study demonstrates a significant increase in the apoptosis rate of KG1 and HL-60 cell lines when treated with azacytidine, oleuropein, or a combination of both, compared to the control group. Real-Time PCR analysis reveals an upregulation of miR-124-3p expression in both cell lines compared to the control group. Furthermore, the expression of miR-124-3p in cells treated with the combination of azacytidine and oleuropein also exhibits a time-dependent increase.

Conclusion: The study findings indicate that the cotreatment of Azacytidine and Oleuropein exhibits enhanced antitumor properties, thereby offering potential advancements in the therapeutic regimen for individuals afflicted with leukemia.

Keywords: Acute Myeloid Leukemia; miR-124-3p; Apoptosis; Oleuropein; 5-Azacitidine.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-38

Elucidating new frontiers in rheumatoid arthritis pathogenesis: The interplay between fibroblast-like synoviocytes and hematologic complications

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Abstract

Background and Aim: Rheumatoid arthritis (RA) is a prevalent chronic autoimmune disease that affects a significant portion of the global population. Fibroblast-like synoviocytes (FLSs) play a crucial role in the pathogenesis of RA, contributing to synovial hyperplasia, bone erosion, and disease progression. This narrative review aims to explore the interplay between FLSs and hematologic comorbidities in RA, with a focus on their activation, imbalances, and potential as therapeutic targets. The objective of this study is to shed light on the complex relationship between FLSs and hematologic abnormalities in RA and to identify potential avenues for targeted therapeutic interventions.

Methods: In this narrative review, we conducted an extensive and comprehensive search of existing databases to identify relevant literature and research on the interplay between FLSs and hematologic complications in RA. This search involved a meticulous and thorough evaluation of multiple databases in a deep, partial, and parallel manner. The inclusion of studies was based on their relevance to the topic and their ability to contribute to the understanding of the topic. The findings from the selected studies were then synthesized to provide a comprehensive overview.

Discussion: Hematologic abnormalities are common in RA patients, including anemia, leukopenia, and thrombocytopenia. Anemia, with hemoglobin concentrations approximately 10-15% lower compared to healthy controls, is particularly common in RA. Anemia of chronic disease (ACD) mediated by inflammatory cytokines is likely the primary driver, although iron deficiency may also contribute. Rare but serious side effects of RA medications, such as neutropenia, have been reported. Studies suggest that FLSs directly influence erythropoiesis and promote thrombosis. *In vitro* experiments demonstrate that FLS secretions suppress erythropoietin production and hinder erythroblast development, while pro-thrombotic factors released by FLSs increase the risk of clotting disorders. Chronic inflammation and cytokine-mediated suppression of erythropoiesis contribute to the prevalent normocytic hypochromic anemia observed in RA. Furthermore, certain RA medications can cause neutropenia, and rare instances of thrombotic thrombocytopenic purpura (TTP) have been reported. Interestingly, RA patients have an elevated susceptibility to lymphoma but a reduced susceptibility to colorectal cancer.

Conclusion: The review underscores the potential role of FLSs as key contributors to the development of anemia and thrombosis in RA. The findings suggest that FLSs have significant implications for the understanding and management of hematologic complications in RA. Targeted therapeutic interventions aimed at modulating FLS activity and addressing hematologic abnormalities represent promising avenues for future research. However, further investigation is required to unravel the intricate mechanisms linking FLSs to hematologic abnormalities in RA and to develop effective treatments to mitigate their impact.

Keywords: Rheumatoid Arthritis; Hematologic Comorbidities; Hematologic Abnormalities; Fibroblast-Like Synoviocytes; Blood Disorders.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-39

Combined mild hypoxia (5% O₂) and bone marrow mesenchymal stem cells enhances expansion and stemness of human cord blood CD34⁺ stem cells

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Abstract

Background and Aim: Cord blood (CB) is a rich source of Hematopoietic stem cells (HSCs) that has been used successfully to treat a variety of hematologic and non-hematological disorders. Beside the advantage of CB, the main disadvantages of CB are the limited number of stem cells available for transplantation and delayed engraftment. Identifying strategies to enhance expansion and maintain homing, self-renewal and stemness of HSCs can improve transplant efficiency. The goal of this study was to examine different culture conditions on ex vivo expansion and stemness of CB-HSCs

Methods: In this study, human cord blood CD34⁺ HSC isolated by MACS, cultured in the serum-free medium (Stem line II) supplemented with cytokines (TPO, FLT3L, SCF) with/without Bone marrow mesenchymal stem cell (MSC) feeder layer in normoxia (21% O₂) and mild hypoxia (5% O₂) for 7 days. In day 7, Total nucleated cell count (TNC), CD34⁺ cells count, CFC assay, migration assay and *CXCR4*, *HOXB4*, *c-Myc Nanog*, *SOX2* expression by Real time PCR were evaluated. The data analyzed using the t-test and ANOVA. Value < 0.05 were considered statistically significant.

Results: At the 7 days of culture, highest number of total nucleated cell (TNC), CD34⁺ cells, Colony forming units (CFUs), migration percent and *CXCR4*, *HOXB4*, *c-Myc Nanog*, *SOX2* mRNA level were seen in coculture of HSC with bone marrow MSC feeder layer at 5% O₂. Our findings demonstrated statistically significant increase of *CXCR4* (1.7-3.2 fold), *HOXB4* (1.3-1.8 fold), *c-MYC* (1.4-1.9 fold), *Nanog* (1.2-1.3 fold) and *SOX2* (1.4-1.6 fold) gene expression, in hypoxia versus normoxia.

Conclusion: Bone Marrow (BM)-MSC and mild hypoxia (5% O₂) combination not only improves HSC expansion but also enhanced homing capacity and stemness of HSC and better mimicked the niche microenvironment conditions.

Keywords: Cord Blood; Hematopoietic Stem Cell; Mesenchymal Stem Cell; Coculture; Hypoxia; Stemness.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-41

The effect of blood group antigens on the symptoms of HIV positive patients

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Abstract

Background and Aim: The main objective was to provide an update on the relationship between blood group antigens and the pathogenesis of Human Immunodeficiency Virus (HIV) infection. Early HIV research explored the idea that some blood types are more susceptible to HIV infection than others. The Duffy, ABO, PK, Rh antigen is located on the surface of red blood cells.

Method: This study conducted as systematic review; we studied a general review without time limit. Our keywords are including: Human Immunodeficiency Virus, blood groups, Duffy null and pathogenesis. Our research was done on 59 Persian and English articles separately in PubMed, CrossRef, Databases, SID, Science Direct, Medlib.

Result: In our study a majority of the blood group antigens are involved in HIV infection. For example, the expression of ABO antigen on mucosal surfaces can affect the infection and the absence of the DARK receptor (Duffy null) appears to increase the susceptibility to infection by HIV. Also, the production of C and E antigens was reduced in those who were HIV positive.

Conclusion: Red blood cell antigens interact and influence HIV infection.

Keywords: Human Immunodeficiency Viruses; Antigens; Blood Groups.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-42

Diagnostic significance of LNCRNA GAS5 in B-ALL

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Abstract

Background and Aim: Long non-coding RNA (lncRNA) *GAS5* has emerged as a potential diagnostic biomarker for B-cell acute lymphoblastic leukemia (B-ALL), offering promise for improved early detection and monitoring of the disease. This review article provides a comprehensive analysis of the existing literature on the diagnostic significance of lncRNA *GAS5* in B-ALL. The review encompasses an in-depth evaluation of the molecular mechanisms underlying *GAS5* and its association with B-ALL pathogenesis. Through a systematic review of relevant studies, this article examines the diagnostic potential of *GAS5* in comparison to other biomarkers and diagnostic methods for B-ALL.

Methods: This review includes a rigorous search in PubMed, Scopus, and google Scholar databases and quality assessment of the selected studies were used to search and collect the information around the lncRNA *GAS-5* and association with B-ALL.

Discussion: lncRNA *GAS-5* have some Mechanism include: cell proliferation and survival (decrease the S stage and inhibit cell cycle progression) and Dysregulation of this gene, overexpression of that was strongly associated with a higher risk for short-term relapse and poor treatment outcome, independently of patients, clinic pathological history of patients and This gene prognostic importance in B-ALL but in early stage of disease down regulated and after the 15 day up regulated and low levels *GAS5* at diagnosis were associated with unfavorable prognostic factors.

Conclusion: *GAS-5* engages in some importance mechanism of cell and overexpression of *GAS-5* have bad outcome in B-ALL patient. This marker can be used for targeting therapy in future, but some challenges include higher *GAS5* levels will antagonize synthetic glucocorticoids for glucocorticoid receptor, resulting in repression of glucocorticoid receptor DNA-dependent signaling and attenuation of synthetic glucocorticoids therapeutic effect in B-ALL. Investigation lncRNAs with non-invasive methods and importance of them in prognosis make them valuable biomarker for diagnosis of the diseases.

Keywords: Lnc-RNA; Lymphoblastic Leukemia; *GAS-5*.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-43

A Case Report on an Unusual Hemoglobin Variant, Hb O-Indonesia, in Iran

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Abstract

Background and Aim: Hb O-Indonesia is a rare hemoglobin variant that resulting from the amino acid change at residue 116 (Glu116Lys) of the α -globin chain. This Alpha variant may exhibit heterogeneous phenotypic characteristics, potentially causing mild hemolytic anemia and cyanosis in affected individuals. It can also manifest with different Beta variants, leading to various clinical properties or a normal state. We report the case of a patient with Hb O-Indonesia detected by high-performance liquid chromatography (HPLC) after an abnormal band was observed in Capillary electrophoresis. There are several variants in S zone, so reporting such cases can be helpful for the diagnosis of rare variants.

Methods: A 23-year-old man of Iranian origin presented without any symptoms and had a normal CBC. He had no history of blood transfusions or Anemia. A complete blood count was performed using Mindray BC-6800, revealing a red blood cell count of $5.41(10^6/\mu\text{l})$ hemoglobin level of 15.5 g/dL, and a mean corpuscular volume of 85.2 fl and mean corpuscular hemoglobin 28.6 pg. Hemoglobin electrophoresis by Capillary 2 Flex showed a normal pattern of HbA and HbA2 but also an abnormal band in S zone (13.9%) and Z1 zone (0.4%). According to Sebia data, there are 21 variants in S zone and 32 variants in Z1 zone. HPLC analysis by Ultra2 of Trinity Biotech confirmed the presence of a variant hemoglobin with a Retention time [C, 0.89, 12.7%], corresponding to Hb O-Indonesia.

Results: The patient was diagnosed with Hb O-Indonesia based on the HPLC results. The accidentally detection of abnormal band in S zone presents several options, regarding variants, but based on Trinity company data, it was diagnosed as Hb O-Indonesia. Also, the company data could be based on the case report by Rahbar et al. (1975). Due to the heterogeneous phenotype of this abnormality, sometimes not causing symptoms, collecting data through case reports can be helpful.

Conclusion: Hb O-Indonesia is a rare and clinically significant hemoglobin variant. In 1975, a case of HbO was reported in an Iranian family by Rahbar, and it can be detected by HPLC after an abnormal band is observed in electrophoresis. Identifying and characterizing this variant is crucial, as it can affect oxygen transport and delivery, influencing the interpretation of some laboratory tests. This case report contributes to the limited literature on the prevalence, molecular basis, and clinical impact of Hb O-Indonesia.

Keywords: Hemoglobin O Indonesia; Hemoglobin; Abnormal; Electrophoresis; Capillary.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-44

Royal jelly induced ROS-mediated apoptosis in Nalm-6 cells: An emerging prospective for RJ in pediatric leukemia treatment

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Abstract

Background and Aim: Acute lymphoid leukemia (ALL) is the most common cause of pediatric leukemia. Considering that the chemotherapy regimen of ALL is accompanied by various challenges, there is a need for novel agents for ALL treatments. Honey bees' royal jelly (RJ) is one of the most appreciated natural products that reveal anti-tumor activity in humans. This study was designed to evaluate the anticancer property as well as the molecular mechanisms of RJ cytotoxicity in ALL-derived Nalm-6 cells.

Methods: To assess the anti-leukemic effects of RJ on ALL cells, the acute lymphoblastic leukemia (ALL)-derived Nalm-6 Cells routinely were cultured in RPMI-1640 medium, and the RJ stock solution was prepared as previously described. Next, cells were treated with the desired concentration of RJ for 24, 48, and 72 h. Then, the inhibitory effect of RJ on the metabolic activity of Nalm-6 cells was assessed via MTT assay. The flow cytometry technique was carried out to evaluate the RJ implication of inducing apoptosis using annexin V-propidium iodide (PI) co-staining and intracellular reactive oxygen species (ROS) level by PI staining. Moreover, the mRNA expression of apoptosis-, and ROS-related genes was determined by qRT-PCR. Afterward, the RJ effect on peripheral mononuclear cells (PBMC) was examined to evaluate its safety.

Results: RJ significantly decreased the viability of Nalm-6 cells in a concentration and time-dependent manner. RJ caused a 50% reduction in Nalm-6 cell proliferation (IC₅₀) in 2.267±0.026 concentration after 48 h. The Annexin-PI revealed that RJ vigorously increased the percentage of apoptotic cells in a dose-dependent way. Furthermore, our results outlined that RJ triggers apoptosis by activating ROS production. In follow-up experiments, the mRNA expression level of a panel of apoptotic-related genes was evaluated using qRT-PCR to ascertain the molecular pathways through which RJ induces its apoptotic effect. According to the results, RJ induces mitochondria-mediated apoptosis through increased levels of Bax and Bad but not Bcl-2 and Bcl xL and upregulates Bax and Bcl-2 ratio. Additionally, the ROS-related gene expression analysis showed the expression of FOXO4 and Sirt1 genes raised after treatment. Noteworthy, RJ has no apoptotic effect on PBMC as normal cells, as indicated in MTT and flow cytometry investigation.

Conclusion: In conclusion, this study sheds light on the potent anti-leukemic effects of RJ and provides evidence for the pharmaceutical application of this agent in the treatment of ALL. However, further in vivo experiments are needed to provide clues for the safety and efficacy of RJ.

Keywords: Acute Lymphoblastic Leukemia; Royal Jelly; Apoptosis, Nalm-6; PBMC.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-46

Diagnosis of Anemia in Premature Neonates via Peak Systolic Velocity of Doppler Middle Cerebral Artery

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Abstract

Background and Aim: Anemia is a common problem in the neonatal period that all infants experience in the first 2 to 3 months of their lives. Possible diagnoses range from anemia seen as a normal part of development to anemia due to critical pathology according to the symptoms. Transcranial Doppler ultrasonography (TCD) has been introduced as a non-invasive method for monitoring blood flow in cerebral arteries that can detect stroke caused by blood clots, vasospasm due to a subarachnoid hemorrhage, etc. TCD is being used in many pediatric intensive care units to aid in the diagnosis and monitoring of children with known or suspected pathophysiological changes due to cerebral hemodynamics as well as hematological abnormalities like sickle cell anemia. The objective of the current study is the evaluation of the role of the Doppler parameter of peak systolic velocity (PSV) of the Middle Cerebral Artery (MCA) in the diagnosis of anemia in premature neonates admitted to the neonatal intensive care unit of Urmia Shahid Motahari Hospital.

Methods: Preterm infants with a history of color Doppler brain ultrasonography in the first two days after birth in 2019 were enrolled in this study. Neonates with physical abnormalities, intrauterine growth restriction, and infection were excluded from the study. Eventually, a total of 109 premature neonates went under evaluation from September to December 2019. Values of Hemoglobin (Hb) <13.5g/dL and Hematocrit (HCT) <45% were considered anemic cases. The Doppler effect of PSA of MCA was calculated by using a Volsun 730 device in a silent room.

Results: The link between the demographic data including birth weight and gestational age with the PSA of MCA revealed that there was a significant increase in PSA levels of the neonates with the birth weight of more than 1500 gr and the gestational age of more than 32 weeks ($P < 0.05$).

Furthermore, the mean PSV of MCA in the anemic and non-anemic neonates was significantly higher in the anemic neonates ($P < 0.001$). We found a significant inverse relationship between PVS and anemia indices including Hb and HCT ($r = -0.39$ and $r = -0.32$, respectively, $P < 0.001$). According to the results obtained from the ROC curve, the PSV of the MCA had a cutoff point of 21.99, 98% sensitivity, and 95% specificity for neonatal anemia detection.

Conclusion: Apart from all the beneficial uses of TSD, it can also be considered a painless and safe approach for diagnosing anemia in premature neonates in NICUs.

Keywords: Transcranial Doppler Parameter; Peak Systolic Velocity; Middle Cerebral Artery; Anemia; Premature Neonate.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PH-47

Vitamin D Deficiency as a Debating Modulator of Thalassemia Major Outcomes; a Review of the Latest Evidence

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Abstract

Background and Aim: The role of vitamin D, and more importantly, vitamin D deficiency (VDD), in thalassemia clinical course is controversial. Vitamin D is essential for bone metabolism and calcium turnover, and patients with transfusion-dependent thalassemia (TDT) are generally supplemented with vitamin D to prevent VDD, yet this phenomenon seems to be inevitable in these patients as they grow. Here, we reviewed the risk factors and important clinical implications of VDD in TDT patients.

Methods: Using the keywords of thalassemia, vitamin D, vitamin D deficiency, siderosis, hemosiderosis, osteoporosis, cardiomyopathy, and cardiac dysfunction, relevant studies were obtained in PubMed, Google Scholar (100 first records), Science Direct, Cochrane library, Springer, Web of Science, and Wiley Online Library.

Discussion: The direct and independent association of VDD with bone mineral density and osteoporosis in TDT patients is debated as several other modulators seem to interfere with this pathway. Regardless of chelation and transfusion therapy history or receiving supplementations, aging seems to be the most important predictor of VDD in these patients, and other players can either accelerate to postpone its occurrence. Attention should be paid to VDD in older TDT patients regarding the recent findings suggesting a role for VDD in predisposing to cardiac iron deposition, which is thought to be mediated through L-type voltage-dependent calcium channels, which are expressed on cardiomyocytes and serve as the main entry route of calcium and, probably, non-transferrin bound iron, into cardiac muscles. Due to the fact that cardiomyopathy is the main cause of death in older TDT patients, correcting cardiac dysfunction in these patients may require resolving underlying VDD.

Conclusion: Most TM patients are susceptible to develop VDD, and in some population, this condition may be even encountered in all patients reaching adulthood. Regarding the contribution of vitamin D in maintaining bone health, and its emerging role in preserving cardiac function, it is suggested to expand studies on the risk factors of VDD in these patients and consider long-term and even lifelong supplementation with vitamin D and other micronutrients to prevent vitamin D levels falling below critical thresholds. Besides, regarding that VDD may develop even in adequately supplemented patients, studies are advisable to identify other unknown causes of vitamin D loss or consumption in TM patients.

Keywords: Thalassemia; Vitamin D; Cardiac dysfunction; Bone disorders.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-48

Induction of Synergistic Cell Death in the NALM-6 Cell Line by Combined Metformin and Sorafenib Therapy

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Abstract

Background and Aim: Acute lymphoblastic leukemia (ALL) is still a threatening hematological cancer, and to improve patient outcomes, new therapeutic strategies are demanded. Recent studies in various forms of cancer especially hepatocellular carcinoma have revealed possible synergetic effects in the induction of cell death using the multikinase inhibitor Sorafenib and the commonly used antidiabetic drug Metformin. However, their combined effectiveness in the NALM-6 cell line is yet unknown. The objective of this research was to examine the possibility of metformin and sorafenib working together to induce cell death in the NALM-6 cell line. This might lead to a novel therapeutic approach that could improve the effectiveness of treatment.

Methods: The IC50 value of sorafenib was found after cell culture. This dosage of sorafenib was then given in combination with two different doses of metformin (5, 10 mM). The AnnexinV/PI test methodology was utilized to assess cell death that occurred throughout the 24-hour treatment period.

Results: Our results showed that when metformin and sorafenib were given together as opposed to separately, there was a significant increase in cell death. As a consequence, coadministration of 10 mM metformin and sorafenib increased cell death significantly, up 20% from the sorafenib alone control (P value:<0.0001). According to viability tests, there was a significant decrease in ALL cell survival and a synergistic impact. The combined therapy group showed changes in important apoptotic markers along (AnnexinV/PI) with a greater rate of apoptosis, according to flow cytometry analysis.

Conclusion: Combining metformin with sorafenib showed synergistic stimulation of cell death in vitro, making it a viable treatment approach for acute lymphoblastic leukemia. These results open the door for further clinical research by pointing to a more focused and successful treatment strategy. In the context of ALL treatment, the molecularly observed synergies offer important insights for future drug development by laying the groundwork for understanding the underlying processes. As combination therapy and precision medicine continue to advance in the quest for better outcomes in ALL patients, our research adds to that field.

Keywords: NALM-6; Metformin; Sorafenib.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-50

Uncommon Rh D phenotypes and the specific pattern of RHD status in the Iranian population: A systematic review

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Abstract

Background and Aim: Rh D is one of the most immunogenic blood group antigens that can cause dangerous hemolytic anemia of fetus, newborns and blood recipients in blood incompatibilities.

It's been seen incompatible results between different laboratories and alloantibody production due to the defects in detection methods and used strategies. Therefore, it is very important to find a high accurate detection method. Moreover, finding the frequency of these D variants can be helpful in adopting the best treatment policies. In this study we tried to evaluate common detection methods, their defects and suggest a better solution especially for Iranian population.

Methods: We searched PubMed, Medline, Scopus and Google scholar and 65 articles found with specific keywords; Weak D and partial D. Twelve were selected which is more contributory to our study and two of them were about Iranian population.

Results: Among the serological techniques developed, we should mention column agglutination tests (CATs), etc., with different high affinity monoclonal Abs that results in different degrees of serological reactions. In addition, according to what observed in some studies, molecular methods such as Real-Time PCR, etc., are not always responsive with high certainty. In Iranian population, the highest rate of weak D was observed of type 15, which is associated with alloantibody production especially in patients in need of frequent transfusion support cause challenges in managing these patients.

Conclusion: Considering Rh D types missed by common detection methods, it is suggested to evaluate consequently the results obtained from both serological techniques using Monoclonal antibodies with high affinity and molecular methods, to definitely determine D variants and make a proper individualized algorithm. And so, for this propose we need to do further investigation in different ethnicity of Iranian population.

Keywords: Weak D; Partial D; Detection Method; Individualized Transfusion Policy.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-51

Necessity of molecular typing to determine D variants: Preventing the occurrence of hemolytic disease of the fetus and newborn (HDFN): A Systematic Review

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Abstract

Background and Aim: The field of immunohematology plays a crucial role in transfusion safety to prevent adverse reactions during transfusions. Among blood group antigens, the RhD antigen is of particular importance due to its potential for causing hemolytic disease of the newborn (HDN) in obstetric patients. It has been proven that some people with RhD negative phenotype are classified as weak D and partial D as a result of antigen reduction and epitope alterations respectively.

Methods: We searched Google Scholar, PubMed, from 2018 to 2023, and found 65 articles with “weak D” and “partial D” keywords. Among them, we separated 11 articles by adding “Molecular methods” and “RhD variants”.

Results: It is declared that traditional serological methods rely on agglutination reactions. However, some blood units with weak or partial D expression may be missed by these tests, leading to false negatives and dispensable RhIG receiving. This method makes molecular typing necessary for accurate identification by having limitations in: identifying RhD subtypes in specific populations, unprecise results about patients who have recently received blood and carry high quantity of donor RBCs, and lack of ability to distinguish pregnant women with weak D from patients with partial D.

Conclusion: for all these issues molecular methods are the choice to have better classification of weak d and partial d phenotypes, save Rh-Negative RBCs for real D- patients, help clarify the D type of a pregnant patient and evaluate the need for prophylaxis to prevent hemolytic disease of the fetus and newborn.

Keywords: Weak D Type; Partial D; Molecular Methods; RhD Variants.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-52

Changing complications of hemoglobinopathies with micro RNAs

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Abstract

Background and Aim: Hemoglobinopathies are a group of important hereditary diseases that are caused by defects in the globin chain, and the reduction or absence of the globin chain can cause inactive hemoglobin. microRNAs are the basic regulators of gene expression in cells that can interfere cell physiology such as proliferation, differentiation, and also play an important role in erythropoiesis and gamma globin gene expression in erythroid cells. regulation of these molecules is effective in the severity and improvement of disease complications. In this article, the effect of microRNA on the expression of globin chains and their role in hemoglobinopathy has been investigated.

Methods: In this narrative review, we conducted a comprehensive database search to find a causal link between microRNAs and the complications of hemoglobinopathies. This search included a comprehensive review of databases.

Discussion: In patients with sickle cell anemia, the increase of miR-144, which is associated with a decrease in NRF2 and increase in hemolysis, increase of miR-221/222 cluster causes KIT-ligand suppression and increase in Hbf, increase in Let-7family suppresses BCL11A and increase in Hbf, increase in miR-29b suppresses myb protein and increase in Hbf, also in patients with thalassemia major, increase in miR-Let7d suppresses DMT1 and increases plasma iron reserves, or increase in miR-155 in monocytes, which causes a decrease in BACH1 and increase of miR-451 inhibits the Ywhaz gene.

Conclusion: Examining new approaches in increasing Hbf and comprehensive studies conducted on miRNA and the relationship between the two, in order to improve hemoglobinopathy diseases such as sickle cell anemia and thalassemias, which was our goal of this study, showed that this relationship is promising and Some miRNA are important biomarkers to induce Hbf synthesis in patients to improve the severity of clinical symptoms, as a result of further research and then commercialization of these micros can be a useful treatment for these patients.

Keywords: MicroRNA; Hemoglobinopathies; Hemoglobin F; Gene Expression.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-53

The clinical importance of detecting Rh D alleles in pregnant women: A systematic review

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Abstract

Back ground and Aim :The Rh blood group has the most polymorphic gene systems ,the most immunogenic antigen of this system is D .Anti D is the prevalent cause of hemolytic disease of fetus and new born(HDFN) ,thus precise RhD typing and D variant recognition is very important .The women with RhD negative blood type need Rh immune globulin prophylaxis so it can prevent alloimmunization but due to polymorphism in D antigen we have two variants called weak d and partial D ,which sometimes causes pregnant women to be mistakenly registered as RhD positive ,and considered not eligible for RhIG and put them at risk of anti D production ,so detecting is valuable for prohibiting fetal anemia and hydrops.

Methods: With keywords like antigen D variants, weak D, partial D, pregnancy we searched PubMed, google scholar from the year 2013 to 2023, found twenty-six articles. Ten articles were selected. We reviewed serological and genotypic methods to diagnose weak D and partial D.

Results: The findings show the importance of genotyping in preventing the production of anti D and alloimmunization, also HDFN. On the other hand, prevents the inappropriate injection of RhIG because RhIG exists in a limited supply and is produced by human source, reducing its unnecessary consumption can lessen unnecessary costs. weak D types 1,2,3 are not at risk of alloimmunization and we do not need RhIG, but other types of weak D like 4.2,11,15,21,57 and also partial weak D require RhIG injection.

Conclusion: we perused both serological and molecular assays, Molecular tests like PCR, can distinguish different types of D antigens, provide best solution to us, but some d variants identified by serological methods may be falsely positive or in other cases unnecessary RhIG may be administered to the pregnant women.

Keywords: Antigen D Variants; Weak D; Partial D; Pregnancy.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PH-54

BCL11a as a novel target of gene editing for the treatment of transfusion-dependent β -thalassemia patients

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Abstract

Background and Aim: β -thalassemia is an autosomal recessive hereditary anemia with a β -globin synthesis defect. Homozygote or compound heterozygote patients for β^0 or β^+ with a wide range of clinical features are called thalassemia major (TM).

TM patients regularly need packed cell transfusions to survive. Regular transfusion leads to iron overload and subsequent retardation, liver cirrhosis, cardiac failure, and endocrine disorders may occur.

Due to the intensity of regular transfusion adverse reactions, alternative therapeutic strategies such as gene editing of BCL11a, a major regulator of HbF, have been developed.

This study overviews BCL11a as a potential gene editing target to treat TM.

Methods: A literature search in PubMed using related keywords with no time or article-type restriction was performed. An additional manual search of the references of related articles was also done.

Discussion: Since BCL11a is a major regulator of HbF synthesis, the most well-known technique of gene editing is found to be BCL11a silencing by using RNA interference (RNAi) or small hairpin RNAs (shRNA). Other approaches to BCL11a silencing include CRISPR-Cas9, transcription activator-like effector nucleases (TALENs), and zinc finger nucleases technology.

CTX001 is a new product that reduces the expression of erythroid-specific BCL11a with the CRISPR-Cas9 technology. The safety and efficacy of CTX001 were confirmed in a phase I/II clinical trial. The patients stopped receiving packed cells within two months of CTX001 administration (NCT03655678).

ST-400 is another gene editing agent utilized for HbF induction. This drug is designed based on the zinc finger technology. The safety and efficacy of ST-400 is yet to be understood.

Conclusion: TM patients suffer from different unwanted transfusion reactions which is their main cause of mortality. Targeting BCL11a through various gene editing techniques holds promise for treating transfusion-dependent β -thalassemia. The development of CTX001 and ST-400 signals a transformative approach to β -thalassemia treatment, offering hope for improved outcomes and suggesting a potential shift away from regular transfusion.

Keywords: Thalassemia; Cooley's Anemia; Gene Editing; Gene Therapy; Novel Therapies.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-55

The impact of Blinatumomab on the regulation of refractory Philadelphia-positive B-cell acute lymphoblastic leukemia (B-ALL): A case report

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Abstract

Background and Aim: Relapsed acute lymphoblastic leukemia (ALL) refers to the recurrence of malignancy after achieving remission through treatment however, Refractory ALL indicates leukemia that did not respond well to conventional therapies. Blinatumomab is a drug that exerts its influence on CD3⁺ T cells and CD19⁺ B cells, resulting in the formation of a synapse and subsequent release of cytokines, expansion of cytolytic T cells, and B cells apoptosis through the perforins and proteases activities. In this article, we present a case of relapse/refractory Philadelphia-positive B-acute lymphoblastic leukemia (ph⁺ B-ALL) wherein the patient, achieved morphologic and molecular remission after the administration of blinatumomab.

Methods: Laboratory testing such as complete blood count (CBC) was conducted. Immunophenotyping analysis was conducted based on Leukemia-Associated Immunophenotype plus Different from Normal (LAIP + DFN) protocol and nine markers “CD10/ CD19/ CD20/ CD34/ CD38/ CD45/ CD81/ CD66c/ CD123” were evaluated. The treatment measures started according to the high-risk leukemia protocol (COG protocol) and imatinib but after the recurrence of the disease, the treatment measures were made according to the protocol of adolescent and young adult (AYA), and induction beside consolidation therapies with different drugs.

Results: The immunophenotyping analysis result has shown bright positivity for CD10, CD19, CD66c, and CD123; diminished (dim) positivity for CD34 and CD81; and negativity for CD20, CD38, and CD45 so the diagnosis was in favor of ph⁺ B-ALL. Our patient, despite receiving conventional chemotherapy treatment for five months, exhibited a persistent presence of 90% blasts in the bone marrow, failing to achieve morphologic remission. However, after the administration of blinatumomab, not only did the patient successfully attain morphologic remission in the bone marrow, but also experienced molecular remission with undetectable (UD) minimal residual disease (MRD).

Conclusion: Blinatumomab has proven to yield a positive response when it comes to managing patients afflicted with ph- B-ALL who exhibit positive MRD and are typically in the morphologic remission phase. However, the result of our case indicates that administration of blinatumomab can yield highly favorable outcomes in patients with ph+ B-ALL who have not reached morphologic remission.

Keywords: Blinatumomab; Acute Lymphoblastic Leukemia; B-ALL; Refractory; Relapse.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-56

Investigating cell death through autophagy and ATG7 gene expression in NALM6 cell line treated with cytarabine and metformin

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Abstract

Background and Aim: Autophagy is a physiological process that serves as a cellular defense mechanism against environmental stress in addition to eliminating damaged or outdated organelles and excess proteins. Given the high degree of autophagic reliance on leukemia cells, direct targeting of this route suggests a possible avenue for cancer treatment. Consequently, it may be beneficial to incorporate novel substances that trigger autophagy into chemotherapeutic medications. We propose that the antidiabetic medication metformin may be utilized as a novel drug repositioning in this context. Therefore, the purpose of this study was to examine how metformin and cytarabine induce autophagy, which in turn causes cell death in the NALM6 ALL cell line.

Methods: NALM-6 cells were treated with different concentrations of cytarabine, metformin, and their combination. Cell viability was assessed using the MTT assay. we also assessed ATG7, a critical autophagy-related gene, mRNA expression by real-time RT-PCR.

Results: The findings showed that the IC₅₀ of cytarabine and metformin was achieved in doses of 50 nM and 10 nM, respectively; however, the combination treatment of these agents was obtained in doses of 15 nM of cytarabine and 20 nM of metformin, respectively. The expression of the ATG7 gene in the treatment with cytarabine and metformin increases by 2 and 5 times, respectively, while their simultaneous treatment causes a significantly higher increase of this autophagy gene.

Conclusion: The combination of cytarabine and metformin shows a synergistic effect in inducing cell death in the NALM-6 cell line, while the dose of the cytarabine was also reduced. These findings provide a foundation for further research into autophagy-targeting therapeutic therapies for leukemia and for a better understanding of the molecular processes underlying cell death in ALL.

Keywords: ALL; Autophagy; Drug Repositioning; ATG7.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-57

The effect of the XMN1-HBG2 (rs7482144) single nucleotide polymorphism (SNP) in response to administration of Hydroxyurea in β -thalassemia patients: A systematic review

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Abstract

Background and Aim: A hereditary blood disease known as β -thalassemia is marked by a defective β chain of hemoglobin synthesis, which causes anemia. Thalassemia patients demonstrate a spectrum of clinical phenotypes. Hydroxyurea is a treatment option for β -thalassemia that stimulates the production of fetal hemoglobin (HbF) and reduces the symptoms of anemia, but the response varies from person to person. According to recent studies, genetic variables, particularly the XMN1-HBG2 (rs7482144) SNP, may be responsible for this variation in hydroxyurea responsiveness. Thus, the aim of this systematic review is to investigate how this SNP affects the effectiveness of hydroxyurea treatment in patients with β -thalassemia.

Methods: The investigation was conducted using the keywords "rs7482144", " β -thalassemia," and "hydroxyurea" on databases including Scopus, PubMed, and Web of Science, based on Cochrane systematic review principles and PRISMA guidelines. Google Scholar search engines have been used for reviewing gray literature. These searches were conducted from 2012 to 2023 in the databases. The inclusion criteria were restricted to studies that described the pharmacogenetics of response to hydroxyurea therapy in patients with β -thalassemia measured by HbF levels. The exclusion criteria were studies that did not examine whether SNPs affect HbF levels in β -thalassemia patients treated with hydroxyurea. Non-English-language, conference, review, and commentary studies were excluded. Screening and data extraction were conducted independently by two authors, and any discrepancies were resolved by consensus involving a third author. The Cochrane ROB 2 tool was used to evaluate the quality of the included articles. extraction tables were created using the data from the included articles.

Results: Overall, 467 articles were found, and after removing 441 duplicates and irrelevant titles and abstracts, the full text of 26 articles was assessed for eligibility. Finally, a thorough review of relevant studies was conducted, and 4 studies met the inclusion criteria with a total of 503 β -thalassemia patients. Studies have been conducted on the India, Iran, and Pakistan populations. Position 158 of the γ -globin gene has a nucleotide mutation from C to T, resulting in the HBG2 rs7482144 polymorphism. The results of these studies showed that in patients treated with hydroxyurea, the presence of the XmnI heterozygous genotype (T/T) or homozygous genotype (C/T) correlates strongly with a better response to hydroxyurea (p-value <0.05). Furthermore, these studies showed that after hydroxyurea usage, the HbF levels in β -thalassemia patients with heterozygous genotype (T/T) or homozygous genotype (C/T) raised more in comparison with β -thalassemia patients with homozygous (C/C) genotype.

Conclusion: Conclusion: Studies indicate a significant correlation between XMN1-HBG2 (rs7482144) single nucleotide polymorphism and increased response to treatment by hydroxyurea in β -thalassemia patients. The presence of the HBG2 rs7482144 "T" allele in beta-thalassemia patients treated with hydroxyurea is associated with significantly higher mean HbF compared to patients with the "C" allele. However, due to limited studies and heterogeneity, more studies are needed to confirm these results and investigate potential factors that may influence this relationship. This review offers valuable insights for researchers and clinicians studying the genetic determinants of β -thalassemia.

Keywords: β -Thalassemia; Hydroxyurea; Single Nucleotide Polymorphism; rs7482144.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-58

Reduced Expression of miR-192 in Pediatric ALL causes Increased Resistance to Methotrexate

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Abstract

Background and Aim: MicroRNAs (miRNAs) have emerged as critical regulators of gene expression and have been implicated in various biological processes including tumorigenesis. Among these, miR-192 has shown potential tumor-suppressive effects in different cancer types. The aim of this study is to investigate the tumor suppression effects of miR-192 and its correlation with decreased DHFR (Dihydrofolate Reductase) and TYMS (Thymidylate Synthase) levels in Acute Lymphoblastic Leukemia (ALL) patients.

Methods: 20 with acute lymphoblastic leukemia (ALL) were examined by using qRT-PCR to measure the expression levels of TYMS and DHFR and miR-192. 5 ml blood sample with EDTA was taken from the patient. Western blotting was used to examine changes in the DHFR protein level. To understand the possible relation between miR-192 and DHFR expression level, 20 pediatric acute lymphoblastic leukemia regardless of the ALL subtype was selected according to relapse and not relapse in pediatric ALL based on Dana Farber Cancer Institute Consortium (10 relapsed and 10 treated). After approval by the ethics committee based on Helsinki ethics rules, informed consent was obtained from all individual participants included in the study.

Results: In ALL patients, the expression levels of DHFR, TYMS, and miR-192 were investigated. Compared to patients who responded to chemotherapy, in whom the level of miR-192 was higher and the levels of DHFR and TYMS were lower, all relapse patients had low levels of miR-192 along with increased levels of DHFR and TYMS.

Conclusion: The results of this study underscore the potential tumor suppression effects of miR-192 in ALL and its correlation with decreased DHFR and TYMS levels. Understanding the regulatory roles of miR-192 in folate metabolism and nucleotide synthesis could pave the way for novel therapeutic strategies targeting these pathways in ALL treatment. Further exploration of miR-192 as a potential therapeutic target may offer valuable insights for personalized medicine approaches in ALL patient management.

Keywords: ALL; DHFR; miR-192; TYMS.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-59

Exploring the Relationship between Tocilizumab and Factor XIII in Rheumatoid Arthritis Patients

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Abstract

Background and Aim: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease that affects millions of people worldwide. Tocilizumab, an IL6 receptor inhibitor, has been proven to be an effective treatment for RA by reducing inflammation. This review investigates the potential risk of bleeding in RA patients treated with tocilizumab, with a focus on its effect on Factor XIII (FXIII), a crucial enzyme involved in blood clotting.

Methods: A comprehensive database search was conducted, ensuring a detailed and accurate analysis of the available information, to identify relevant studies on the risk of bleeding in RA patients treated with tocilizumab.

Discussion: Several studies have reported cases of bleeding in RA patients with normal clotting tests after receiving tocilizumab treatment. These patients showed a decrease in FXIII levels, suggesting a positive correlation between IL6 and FXIII levels. No antibodies against FXIII were found, confirming the impact of tocilizumab on FXIII. The exact mechanism of this effect is still unclear, but studies suggest an imbalance in cytokine production as a possible cause.

Conclusion: The decrease in FXIII levels in RA patients treated with tocilizumab indicates that the drug's effect on the prothrombotic state is related to its ability to control inflammation and disease activity, rather than a direct effect on FXIII. Therefore, when recurrent bleeding is observed in patients receiving tocilizumab, despite normal clotting tests, acquired FXIII deficiency should be considered in the differential diagnosis. Physicians should also be aware that patients treated with tocilizumab, especially those with low platelet levels, are at an increased risk of bleeding.

Keywords: Tocilizumab; Rheumatoid Arthritis; Bleeding; Factor XIII.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-60

The anti-inflammatory effect of omega-3 polyunsaturated fatty acids is notably diminished by iron in diabetic rats with nephropathy

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Abstract

Background and Aim: Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia. Type 2 diabetes is a metabolic disease that worsens over time and is marked by the body's resistance to insulin. The number of people with type 2 diabetes has been rapidly increasing in recent decades, and it is expected to continue growing even more in the future. Iron supplements are used to treat or prevent iron deficiency anemia, a condition in which the body lacks enough healthy red blood cells due to insufficient iron. ω -3 PUFAs fatty acids have been shown to have important roles in controlling and improving several metabolic abnormalities associated with diabetes. They are known for their anti-inflammatory properties, which can be beneficial for individuals with type 2 diabetes mellitus due to these potential benefits, type 2 diabetes mellitus patients are often advised to take supplements containing fish oil capsules, as part of their overall management plan. In diabetic patients, the presence of hyperglycemia can lead to the accumulation of iron in various tissues, including the pancreas, liver, and kidneys. This can further exacerbate oxidative stress and contribute to the development of complications such as diabetic retinopathy, neuropathy, and nephropathy. The aim of this study was to survey the impact of simultaneous use of ω -3 PUFAs and iron supplements on kidney function in diabetic rats with nephropathy.

Methods: In this study, rats were divided into two groups: one with 12 rats and the other with 72 rats. After 3 weeks, the 72 rats on the high-fat diet were injected with a low dose of STZ, while the 12 control rats were given a citrate buffer injection. Blood glucose levels were measured before and 7 days after the injections, and rats with a fasting blood glucose level of 250 mg/dl or higher were considered diabetic and selected for further study. Diabetic and normal Wistar rats were divided into six groups. BUN and creatinine were evaluated in the nephropathy of the controls and supplemented with ferrous sulfate and ω -3 PUFAs alone and together rats.

Results: Levels of the BUN, and creatinine significantly increased in the co-consumption of iron and PUFA in diabetic condition rather than diabetic control and diabetes+ iron group. While in diabetes+ ω -3 PUFAsT decreased in BIN and creatinine were seen.

Conclusion: These findings suggest that the co-supplementation of ferrous sulfate with ω -3 PUFAs in hyper glucose conditions, reduces the anti-inflammatory effects of ω -3 PUFAs and moreover increases the lipid peroxidation and oxidative properties.

Keywords: ω -3 PUFAs; BUN; Creatinine; T2DM; Nephropathy.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-61

Evaluation of the Rate of Lookback Cases and Influencing Factors among Blood Donors in the Blood Transfusion Organization of Bushehr from 2022 to 2023

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Abstract

Background and Aim: Ensuring an adequate and safe blood supply is the primary goal of the Blood Transfusion Organization. Blood recipients should not be exposed to transfusion-transmissible viruses. Therefore, one of the protective systems in blood transfusion is the Lookback system, which prevents the distribution and consumption of plasma products. The present study investigates the rate of Lookback cases and the factors influencing them among blood donors in the Blood Transfusion Organization of Bushehr from 2022 to 2023

Methods: In this descriptive study, 125 individuals with Lookback cases from 1401 to 1402 were evaluated. Demographic information and variables influencing Lookback were extracted using the Comprehensive Blood Transfusion Information System (Negare), and the data were analyzed using the SPSS software.

Results: Out of 125 individuals with prevented plasma distribution, 28 cases (22.4%) had sexual contact with a non-spouse, 27 cases (21.6%) had undergone phlebotomy within the last 12 months, 7 cases (5.6%) had a history of scarification, 9 cases (7.2%) had endoscopy, 23 cases (18.4%) were HIV-positive, 17 cases (13.6%) were HCV-positive, and 9 cases (7.2%) were HBV-positive. None of the Lookback cases were utilized for plasma product distribution.

Conclusion: Considering the importance of the Lookback system, we have effectively prevented the distribution of plasma products by 100%. The Lookback system, as one of the protective systems against the distribution of plasma products, has a positive impact on the production and distribution of safe products.

Keywords: Lookback; Blood Transfusion; Donors; Bushehr.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-62

Application of electrochemical aptamer-based biosensors in diagnosis of leukemia

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Abstract

Background and Aim: Leukemia is an aggressive cancer that threaten people's life. Early diagnosis is often essential for reducing the mortality rate from leukemia. The conventional method of diagnosing leukemia involves a blood and bone marrow examination, cytogenic methods, and Flow Cytometry but they are expensive and have procedural complications. The aptamer is a single strand of DNA or RNA that has high affinity and selectivity for its target molecules varying from small ions to malignant cells, tissues, and cancer biomarker proteins similar to monoclonal antibodies but have advantages over antibodies for clinical applications, including roughly no immunogenicity, cost-effectiveness, more straightforward modification, and short production times. The development of electrochemical biosensors based on aptamer as a recognition part (aptasensor) is one of the interesting approaches in the development of new diagnostic methods as These are sensitive, low-cost, and easy-operation tools, and offer rapid analysis time.

Methods: The literature search was performed using Pubmed and Google Scholar and Science Direct databases between September 2015 to 2023 with a combination of terms: "Electrochemical", "aptasensor", and "leukemia" as keywords. In all 132 results, we studied 21 articles, which were original and review articles and were the most relevant to our study. We did not study case reports.

Results: Development of an aptasensor for detection of leukemic Jurkat cells by aptamers specific to the cancer marker protein tyrosine kinase-7 (PTK7). They obtained high sensitivity of Jurkat cells determination with a limit of detection (LOD) of 10510 cells/mL for electrochemical. A highly selective and sensitive aptasensor was designed for the identification of leukemia cancer cells (CCRF-CEM) in blood samples via the catalytic effect of copper sulfide-graphene (CuS-GR) and Au-GR nanocomposites that increase the current of the sensor in parallel with adding of CCRF-CEM. This sensor had a limit of detection of 18 cell mL. An electrochemical aptasensor, specific to the protein tyrosine kinase 7 (PTK7) was Fabricated to detection of Jurkat leukemia cells. it was modified either by methylene blue (MB) or ferrocene carboxylic acid (Fc). In both cases the comparable sensitivity was obtained with a limit of detection: 37 ± 6 cells/mL for Fc-labeled aptamers and 38 ± 8 cells/mL for MB-labeled aptamers based on the 3.3S/N (noise signal) rule.

Simple high selectivity, stability, and reproducibility electrochemical aptasensor have been developed for direct detection of chronic myelogenous leukemia K562 cells based on a specific aptamer and biotin-conjugated concanavalin A detection probe to identify K562 cell surface mannose. Recoveries were between 79.6%–93.3% When applied to detect K562 cells in human blood samples.

An electrochemical nanocomposite-based aptasensor was made of gold nanoparticles/magnetite/reduced graphene oxide for the determination of miRNA-128 concentration as the acute lymphoblastic leukemia biomarker for the first time. The results indicated high selectivity for miRNA-128 detection.

Another study showed a label-free fluorescence aptasensor based on terbium (III)-aptamer (Tb³⁺-apt) was fabricated for the detection of CCRF-CEM. the detection limit was 5 cells per ml of the binding buffer and the specificity of this method was up to 94% by examining Clinical samples

Conclusion: Electrochemical aptasensors are new sensitive, and economical diagnostic methods that can be used for various types of leukemia detection at the early stage.

Keywords: Electrochemical; Aptasensor; Leukemia.



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The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-63

The effect of Mesenchymal Stem Cells-derived exosomes (MSCs-Exo) on the diabetic foot ulcer

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Abstract

Background and Aim: Diabetes is a global problem in the field of health and treatment, and the number of people suffering from it is reported to be very high. One of the complications of uncontrolled diabetes is diabetic foot ulcer, which includes various treatment methods such as hyperbaric oxygen therapy, laser therapy, the use of various antibiotics, maggot therapy, debridement, amputation, etc. High treatment costs along with time consuming, low effectiveness and quality of life are the disadvantages of using these treatment methods. Our goal in this study is to investigate one of the newest treatment methods for diabetic foot ulcers.

Methods: Results were obtained by studying various articles in the period from 2010 to 2023.

Results: Cell therapy is a new method that has recently received much attention in the treatment of this disease. Mesenchymal stem cells (MSC) can be mentioned among the relevant cell in this field. This cell has reparative effects and regulation of the immune system and anti-inflammatory, whose significant effects in the treatment of various wounds have been reported in previous studies. The limitation of using this new treatment is the possibility of tumorigenesis, the reduction of the clinical capacity of mesenchymal stem cells due to multiple passages in laboratory conditions. Exosome therapy is one of the latest applied methods in cell therapy. In recent years, exosomes have been in the focus of researchers' attention due to their immunological function. Exosomes are microvesicles that are released by many normal and abnormal cells. Most of the contents of a cell are also found in exosomes derived from it. Today, exosomes are used as mediators of cell function as well as important immunomodulators in many cellular processes. The high compatibility of exosomes in the body is due to the lack of expression of MHC and lack of phagocytosis by macrophages, and on the other hand, the issue of HLA compatibility is not discussed in their case. The strong effect of MSC-Exo in the healing of diabetic wounds has been reported in the different phases in many studies.

Conclusion: The use of exosomes from Mesenchymal stem cells (MSC) after additional studies in different phases can be used in the treatment of various wounds, especially diabetic ones.

Keywords: Exosome, MSC, Diabetic Foot Ulcer





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-64

The prevalence of true positive and false positive HIV, HCV, and HBV in blood donors with callback

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Abstract

Background and Aim: The callback system in the Iranian Blood Transfusion Organization (IBTO) has been utilized since 2009 to follow up with voluntary blood donors post-donation. Donors are requested to report any undisclosed risk factors from the initial physician examination, illnesses, or concerning symptoms arising after blood donation. The aim of this study was to evaluate the prevalence of true positive and false positive viral markers (HIV, HCV, HBV) among voluntary blood donors who utilized the callback system to report additional post-donation information.

Methods: This retrospective study examined data from voluntary blood donors who were registered in the callback system through the IBTO software at the Bushehr Blood Center organization between August 2021 and August 2023. Callback reasons were categorized as: 1) Unreported risk factors from the initial pre-donation examination, 2) Development of any illnesses post-donation, and 3) physical symptoms after. For all donors, demographic data (including: age, sex, marital status) and laboratory viral markers including: HIV antibody, HCV antibody, and HBs antigen were recorded.

Results: A total of 72226 Donors were recorded in IBTO software as complete whole blood donation during the study, only 65 donors (8.9%) were registered as callback. The mean age of participants was 38.53 ± 8.75 years with majority of male (89.2%). 41.5% of participants were regular donors (two or more donations in a year) and 32.3% were first time complete blood donors. 81.5% of donors were married and 43% of participants had bachelor degree or more. The most cause of callback was for reporting illness (69.2%), unreported risk factors (29.2%), and arising symptoms after donation (1.5%). In these 24 months, 166 donors were recorded as positive (166/72226) viral test (false and true) and there was no positive in donors with callback.

Conclusion: Although the number of participants who registered as callback is low, but the zero prevalence of positive viral markers in these population may indicate the effective screening, and lower prevalence of risk factors.

Keywords: Blood Donation; Blood Donors; Callback; Viral Markers.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-65

The Importance of Neutrophil Extracellular Traps (NETs) in Leukemia

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Abstract

Background and Aim: Neutrophils are the first line of innate immunity and defend against pathogens through multiple mechanisms, which include the release of neutrophil extracellular traps (NETs). These web-like structures composed of DNA, histones, and granular proteins are also produced under sterile conditions and play crucial roles in thrombosis, cancer, inflammatory and autoimmune diseases.

Methods: Published studies between 2000 and 2023 examining the role of neutrophil extracellular traps in different types of leukemia were identified by searching the PubMed, Scopus and Web of Sciences databases.

Results: Elevated NETs levels have been detected in plasma and tissues of many cases with solid tumors. However, the importance of NETs in hematological tumors, especially leukemia, has poorly been studied. Anyway, there is strong evidences that demonstrated elevated NETs levels in the body of patients with different types of leukemia. For example, it has been shown that neutrophils isolated from chronic lymphocytic leukemia (CLL) patients are more prone to release NETs, and blood plasma from CLL patients is able to prime neutrophils from healthy donors to release higher amounts of NETs. Furthermore, ibrutinib, a commonly used chemotherapeutic drug, relieves CLL by marginally impairing NET generation in patients with CLL. In the same way, neutrophils from chronic myeloid leukemia (CML) patients, also showed an increase in NET formation at threshold and even more so after stimulation. As well, the induction of neutrophils isolated from mice with CML resulted in a high amount of NET formation. Similarly, in a murine model of CML neutrophils from leukemic mice were more capable to generate NETs upon platelet-activating factor (PAF) stimulation in contrast to control group. Also, enrichment in NET structures was found in the bone marrow of NPM1- mutated acute myeloid leukemia (AML) patients. Besides, a minor elevation in cell-free DNA (cfDNA) concentrations was investigated in patients with acute promyelocytic leukemia (APL) which is generated mainly via NETosis (and/or necrosis) along with apoptosis. In addition, APL was demonstrated to be aggravated in animals that expressed high levels of neutrophil elastase (NE), whereas NE-deficient mice were protected from APL progression. Notwithstanding, it has been shown that NE activity and NETs formation are notably decreased after induction in pediatric acute myeloid leukemia (AML) but not in pediatric acute lymphoblastic leukemia (ALL) patients. It might contribute to the outlined higher incidence of infections in AML compared with ALL. In addition, it is showed that immature granulocytes persist in blood of AML patients in remission, and suggested that these granulocytes have not acquired the maturational chromatin modifications needed for NETs formation. Moreover, NETs release is significantly impaired in children with acute leukemia, both at the stage of diagnosis and during the treatment, and complete restoration of neutrophil function can be accomplished only after successful treatment.

Conclusion: Considering the key presence of NETs in leukemia, investigating the factors engaged in their formation and possible therapeutic or preventive measures can be so effective.

Keywords: Neutrophils; Extracellular Traps; Leukemia; Hematology.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-66

Association of BCL11A (rs1427407) single nucleotide polymorphism (SNP) with fetal hemoglobin levels in Sickle cell disease: A systematic review

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Abstract

Background and Aim: Sickle cell disease (SCD), which results in sickle-shaped red blood cells (RBCs), is one of the most prevalent hematological diseases in the world. In SCD, there is an increase in Hb F levels, which may help with some of the disease's complications. Transcription factor BCL11A In erythroid cells suppresses Hb F expression. Hb F-related single nucleotide polymorphisms (SNPs) in the BCL11A gene cause BCL11A to be down-regulated and Hb F expression levels to rise. Examining any possible correlation between the rs1427407 SNP and Hb F levels in SCD patients is the goal of this systematic review.

Methods: The investigation was carried out using specified keywords "rs1427407", "Sickle cell anemia", and "Hb F" on electronic databases such as PubMed, Scopus, and Web of Science, following PRISMA criteria and the principles of Cochrane systematic reviews. In addition, the grey literature has been reviewed using Google Scholar. These database searches were carried out between 2012 and 2023. English-language publications that examined the impact of the rs1427407 SNP on Hb F level in sickle cell anemia met the inclusion criteria. Articles written in languages other than English, reviews, papers on animals, and conference proceedings were all excluded. Two writers carried out the screening and data extraction independently, while a third author reached a consensus to settle any disagreements. All included articles were quality assessed via the Cochrane ROB 2 tool. Then the data of included articles was collected in extraction tables.

Results: After identifying 1173 articles in the first step, we removed 1147 of them since they were duplicates. Following analysis of these 26 articles, 8 trials including 3260 patients that were carried out between 2012 and 2022 were included. Populations in Cameroon, Senegal, Brazil, India, Saudi Arabia, Sri Lanka, Kuwait, and Nigeria were the subjects of studies. The BCL11A rs1427407 polymorphism results from a G-to-T nucleotide substitution. The findings demonstrated a strong correlation ($p < 0.05$) between the BCL11A rs1427407 G>T variation and fetal hemoglobin levels. Hb F levels were primarily influenced by the allele of rs1427407 (BCL11A) and were elevated. Also, the results indicate a potential role for the BCL11A genetic variant in influencing the severity of Sickle cell disease.

Conclusion: Studies indicate a strong association between increased hemoglobin F levels in sickle cell disease patients and the BCL11A rs1427407 single nucleotide polymorphism. When a patient has the BCL11A rs1427407 G>T mutation, their mean hemoglobin F is much greater, which lessens the severity of their sickle cell disease. More research is necessary to validate these findings and investigate other potential factors that can affect this association, though, because of the small number of studies and heterogeneity. This review offers valuable insights for researchers looking into genetic causes of sickle cell disease.

Keywords: Anemia; Sickle Cell; Hb F; Systematic Review; Single Nucleotide Polymorphism.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-67

Validating diagnosis of pediatric leukemia by flow cytometric analysis: A case report

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Abstract

Background and Aim: Leukemia, which accounts for about 30% of all pediatric cancers, is the most prevalent malignancy in children. Performing a thorough diagnostic evaluation is crucial as it helps determine the initial stage of the disease and assess the patient's overall stability. This comprehensive work-up provides essential information necessary for risk stratification, enabling healthcare professionals to evaluate the severity of the leukemia and plan appropriate treatment strategies.

Methods: We present a case report describing the crucial role of flow cytometric analysis in accurately diagnosing pediatric leukemia. A 5-year-old female patient presented with a 3-day history of fever, drowsiness, and weakness, vomiting, and diarrhea. Notably, there were no signs of splenomegaly or lymphadenopathy. The initial H1 complete blood count (CBC) results indicated anemia, with a red blood cell count of 3.16×10^6 , low hemoglobin levels of 6.2g/dl, and a mean corpuscular volume (MCV) of 68.4fl. Furthermore, the CBC analysis identified the presence of 10% blast cells. The initial clinical assessment by the oncologist suggested a diagnosis of acute lymphoblastic leukemia (ALL) based on the presented symptoms. However, conflicting results emerged during the laboratory hematologic evaluation where the morphological characteristics of the leukemic cells were highly compatible with acute myeloid leukemia (AML) subtype M4.

Results: In order to achieve a definitive and reliable diagnosis, flowcytometric analysis was performed utilizing immunophenotyping techniques. The obtained results showed substantial expression of CD-34, CD-33, HLA-DR on the leukemic cells, demonstrating strong phenotypic attributes of AMLM2 subtype.

Conclusion: Prompt and accurate diagnosis contributes to appropriate management decisions and tailored treatment strategies, potentially improving patient outcomes. This case report emphasizes the indispensability of flow cytometric analysis in delineating precise diagnoses in pediatric leukemia cases.

Keywords: Pediatric Leukemia; Flow cytometric Analysis; Immunophenotyping; Diagnostic Accuracy





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-68

Investigating the prevalence and correlation of pernicious anemia in patients with gastric cancer

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Abstract

Background and Aim: Gastric cancer has one of the highest incidence rates among cancers, and ranks third among the deadliest cancers worldwide in terms of mortality. Gastric cancer refers to the abnormal growth of cancerous cells in the lining of the stomach. Various factors may cause gastric cancer. Pernicious anemia is considered a less common but classic risk factor of primary gastric cancer. Pernicious anemia, an autoimmune condition, is a prominent cause of vitamin B12 deficiency and is characterized by the destruction of the intrinsic factor glycoprotein and the fundal parietal cells responsible for its production.

In pernicious anemia, anti-parietal cell and anti-intrinsic factor antibodies lead to atrophic damage to the gastric mucosa, causing the reduction of parietal cells and intrinsic factors. As a result, there is a decrease in the absorption of vitamin B12, and the loss of parietal cells leads to hypochlorhydria (low stomach acid production). While vitamin B12 supplementation effectively treats the anemia, it does not address the underlying autoimmune gastritis or restore normal stomach acidity. As a result, pernicious anemia has been associated with an increased risk of gastric cancer due to the chronic inflammation and hypochlorhydria associated with the condition. Our aim in this study is to investigate the relationship between pernicious anemia and stomach cancer.

Methods: this systematic review study, a comprehensive search of free electronic databases including PubMed and Google Scholar was conducted by two people to identify relevant studies until November. The search terms involve the words "pernicious anemia", and "gastric cancer" besides similar words extracted from the MeSH database. The inclusion criterion is to be in line with the main purpose of the study, the studied study must be original and published in English. The exclusion criterion was the lack of access to the complete file of the study.

Results: In the analysis of the studies included in this review, a total of 39,970 patients with a mean age of 74.9 years who were diagnosed with gastric cancer were investigated. Pernicious anemia was reported in 3.4% of cancer cases, which has the highest rate among autoimmune conditions associated with an increased risk of gastric cancer. Furthermore, a developing risk of stomach cancer among pernicious anemia patients has been observed. The analysis of several studies reported the development of gastric cancer in patients hospitalized for pernicious anemia. Two of the studies included a total of 39,586 patients with pernicious anemia who were followed for an average of 7 years. Among these patients, a total of 984 cases of cancer were diagnosed, which most prominent was gastric cancer with 98 cases (8%).

Conclusion: Gastric cancer continues to be a highly prevalent form of cancer worldwide, often leading to unfavorable outcomes due to patients remaining asymptomatic until late-stage progression. Although pernicious anemia is not commonly encountered in clinical practice, it remains a classic risk factor for the development of gastric cancer. Thus, identifying relevant physical examination features, combined with laboratory findings indicating a deficiency in vitamin B12, can play a crucial role in the early detection of gastric cancer. Unfortunately, only a small percentage of patients with pernicious anemia are screened for subsequent gastric cancer. Hence, it is necessary to increase the clinical awareness of the classical association of these two conditions.

Keywords: Pernicious Anemia; Gastric Cancer; Stomach Cancer.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-69

Exploring the Prognostic Significance of RDW in Multiple Myeloma

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Abstract

Background and Aim: A hematopoietic system cancer that is incurable is called multiple myeloma (MM). It is distinguished by the rapid proliferation of cancerous plasma cells, which causes inhibition of bone marrow function, and kidney failure. Research indicates that the development of MM tumors and the course of the disease are significantly influenced by chronic inflammation. Red cell distribution width (RDW) is automatically measured in the complete blood count. The volume of peripheral blood erythrocytes can vary, and this can be shown by the RDW. This study aims to investigate the role of RDW in the prognosis of MM patients.

Methods: Our analysis of publications from the PubMed, Google Scholar, and Web of Science databases established the foundation for the findings of our review. Using keywords such as multiple myeloma, RDW, anisocytosis, and malignancies, we were able to identify these studies.

Discussion: RDW has lately been linked to inflammation as well. Several inflammatory markers, such as the erythrocyte sedimentation rate, interleukin-6, C-reactive protein, soluble tumor necrosis factor receptors I and II, and soluble transferrin receptor, have been shown to correlate with RDW in a number of recent studies positively. A greater mixing of circulating erythrocyte volumes can result from all of these variables that lower erythrocyte survival. RDW is regarded as a potent prognostic indicator for MM. Since multiple myeloma cells activate oncogenes more frequently and have higher metabolic activity, they have lower amounts of antioxidant molecules and higher levels of intracellular reactive oxygen species (ROS) than normal cells. It has been demonstrated that high ROS levels increase motility, invasion, and proliferation. The association between high RDW and a bad prognosis in MM may be caused by oxidative damage, chronic inflammation, cellular senescence, and inadequate nutrition.

Conclusion: RDW has lately been found to be a prognostic factor for some cancer types. A poor prognosis for cancer patients may be associated with higher RDW, which could potentially bridge the link between inflammation and tumorigenesis. In summary, elevated RDW significantly predicts a poor outcome for patients with multiple myeloma.

Keywords: Multiple Myeloma; RDW; Anisocytosis; Malignancies.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-70

Association of Inflammatory Serum Markers with Deep Vein Thrombosis and Pulmonary Embolism

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Abstract

Background and Aim: Venous thromboembolism (VTE) manifests as deep vein thrombosis (DVT) or pulmonary embolism (PTE). Inflammation contributes to VTE, but differences in inflammatory profiles across VTE subtypes are unclear. This study investigated associations between serum inflammatory markers and DVT vs PTE.

Methods: This retrospective study enrolled 40 VTE inpatients (26 PTE, 12 DVT, 2 both). Serum levels of the inflammatory marker hs-CRP and antioxidant bilirubin were measured and compared between DVT and PTE subgroups using ROC analysis.

Results: Hs-CRP was elevated across VTE patients but did not differ significantly between PTE and DVT subgroups. However, serum direct bilirubin was significantly decreased in DVT compared to PTE patients.

Conclusion: Elevated inflammatory markers and decreased bilirubin are associate with VTE diagnoses. Intriguing distinctions in direct bilirubin levels between DVT and PTE phenotypes warrant further research into the pathological mechanisms differentiating VTE subtypes.

Keywords: Venous Thromboembolism; Pulmonary Embolism; Deep Vein Thrombosis; Inflammation; C-Reactive Protein; Bilirubin





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-71

The effects of released exosomes from stimulated NK-Cells with IL15 on the apoptosis of human acute myeloid leukemia cell line (HL-60)

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Abstract

Background and Aim: Cancer, which caused over 9.6 million deaths worldwide in 2017, is a multifaceted condition characterized by the uncontrolled growth and expansion of abnormal cells. It can be characterized as a state in which the equilibrium between cell death and proliferation is disrupted. Leukemia, commonly referred to as blood cancer, is caused by abnormal proliferation of hematological cell lines. Acute promyelocytic leukemia (APL), classified as M3 within the broader classification of acute myeloid leukemia (AML), is characterized by the proliferation of neoplastic hypergranular promyelocytes and blast cells. The adverse effects associated with chemotherapy and inadequate responses in certain cases have prompted cancer researchers to investigate immunotherapy as an alternative approach to combat cancer. Natural Killer (NK) cells, constituting a component of the innate immune system, play a pivotal role in defending the body against cancer, viruses, and infections. Distinguished by their ability to identify unhealthy cells early on, NK cells employ various methods, including cytotoxic proteins and death cell receptors such as Fas-L and TRAIL, to eliminate them.

Despite the efficacy of NK cells, tumor cells employ diverse mechanisms to evade immune detection and sustain proliferation. Exosomes, nanoparticles secreted by various cells and present in bodily fluids, contribute to signal transport and the delivery of proteins or nucleic acids from the originating cell to receptor cells, thereby altering the content of the receptor cells. Given that exosomes mirror the characteristics of their parental cells, their impact on receptor cells is somewhat predictable. Building upon previous studies, exosomes derived from NK cells demonstrate the presence of NK cell components, including perforin, granzyme, and Fas-L. Furthermore, the cytotoxic protein content in NK-derived exosomes surpasses that found in NK cells alone. Logically, this heightened concentration of cytotoxic proteins contributes to an increased induction of cell apoptosis compared to NK cells in isolation. By synthesizing the gathered information, our current research centers on examining the impact of stimulated NK-derived exosomes and non-stimulated exosomes on cell apoptosis. Our working hypothesis posits that the stimulation of NK cells by adding IL-15 results in increased exosome secretion, rendering them more cytotoxic compared to their non-stimulated counterparts.

This research underscores the potential of immunotherapeutic strategies involving NK cells and their exosomes in addressing the limitations associated with traditional chemotherapy and fostering a more targeted and effective approach to cancer treatment.





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Methods: In the initial phase, the NK-92 cell line exhibited robust culturing, and after expansion, one group was designated as the control, while stated concentration of IL-15 was added to stimulate the NK-92 cell line in the other group. Subsequently, after 48h of exposure to IL-15, exosomes were isolated from both cell lines by using the Ultracentrifuge method. To validate the exosomes, Dynamic Light Scattering (DLS) and Western blotting tests were conducted to measure exosome markers such as CD63 and CD81 in both groups. Once it was confirmed that the exosomes were isolated effectively, the stocks concentration were determined using the BSA method to specify the stock's concentration. Following this, HL-60 cell lines were treated with different concentrations of exosomes derived from both groups of NK-92 cell line. After 24 hours of treatment, the apoptosis rate was determined using the Annexin-V technique.

Results: The results of the Dynamic Light Scattering (DLS) test indicated that the size of the exosomes fell within an acceptable range. Detection of CD81 and CD63 in the Western blotting test suggested that the addition of IL-15 to the cell culture led to exosome secretion when compared to the non-stimulated group. Likewise, the higher light absorption in the treatment group compared to the non-treated group confirmed this observation. The results from the apoptosis assay using the Annexin-V method demonstrated that the apoptosis rate in the treated group was higher than in the non-treated group. The obtained P-value, which is less than 0.001, indicates a significant increase in the death rate of exosomes derived from stimulated NK cells.

Conclusion: The study centers on exosome therapy, a subset of immunotherapy. Previous research has compared NK-derived exosomes with NK cells alone; however, our suggestion posits that the activated NK-92 cell line generates a higher quantity of more cytotoxic exosomes than those derived from non-treated NK cells and NK cells in isolation. In this context, we are comparing exosomes derived from stimulated NK cells with those derived from non-stimulated NK cells. This comparative analysis aims to explore the potential therapeutic application of exosomes, particularly in the context of hematological malignancies.

Keywords: Exosome Therapy; Immunotherapy; Natural Killer Cell Therapy; Leukemia





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-72

The correlation of Platelet-Monocyte aggregate formation and IFITM3 gene expression with COVID-19 severity

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Abstract

Background and Aim: Platelet-leukocyte aggregates have been implicated in various infectious and inflammatory diseases. The IFITM3 protein plays a role in eliminating viral infections, but its role in the severity of COVID-19 is not well-understood. Objectives: We aimed to investigate the correlation between IFITM3 mRNA expression and platelet-monocyte complex levels with the severity of COVID-19, as well as various inflammatory and coagulation markers. Methods: We conducted a cross-sectional study on 54 COVID-19 patients, classified into severe and mild/moderate subgroups. Demographics and laboratory findings were extracted from patients' medical records. We measured IFITM3 mRNA expression in patients' buffy coat using q-RT-PCR and used flow.

Methods: This cross-sectional study was conducted on 54 COVID-19 patients. The patients were classified into two subgroups: severe and mild/moderate COVID-19. The general demographics and the general laboratory findings of the patients were extracted from their medical records. Determination of IFITM3 mRNA expression level was carried out using q-RT-PCR. Moreover, to measure the level of platelet-monocyte complex formation, the flowcytometry assay was carried out for the detection of CD61 and CD14 cell surface markers.

Results: We were not found a significant difference in the level of IFITM3 mRNA and platelet-monocyte complexes between severe and mild/moderate groups (p.value 0.05). However, MNCs were significantly higher in mild/moderate COVID-19 patients compared to severe patients. Moreover, lymphocyte count was significantly higher in the mild/moderate study group. While in severe patients, the neutrophil count was significantly higher. Furthermore, the level of CRP and LDH were significantly higher in severe COVID-19 patients. As we expect, there was a relatively strong positive correlation between the hospitalization period and CRP, CRP with neutrophil and LDH as well as O₂ saturation with lymphocyte. In contrast, there was a strong reverse correlation between hospitalization period and O₂ saturation, O₂ saturation with neutrophil and CRP and LDH, lymphocyte with CRP and LDH.

Conclusion: Monitoring COVID-19 patients for inflammation biomarkers is indispensable for better management and outcome for the patients. A more precise investigation with a larger sample size is needed to shed light on the involved mechanisms.

Keywords: COVID-19 Severity; Platelet-Monocyte Aggregate; IFITM3; Thrombotic Complications

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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-73

Can double-dose plateletpheresis affect the donors' hematological parameters versus single-dose plateletpheresis?

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Abstract

Background and Aim: Plateletpheresis, an automated apheresis-based procedure for platelet collection, has become increasingly prevalent due to its cost-effectiveness and fewer immunological and infectious complications for recipients than other platelet preparation methods. However, the impact of preparing double-dose plateletpheresis (DDP) on the platelet donors compared to single-dose plateletpheresis (SDP) is still under investigation. This study aims to compare the alterations in hematological parameters of platelet donors after donating DDP versus SDP at the Tehran Blood Transfusion Center.

Methods: Eligible and healthy plateletpheresis donors meeting the platelet donation criteria according to Iranian Blood Transfusion Organization (IBTO) standards were randomly selected. Fifteen SDP donors and 21 DDP donors were selected from plateletpheresis donors in the Tehran Blood Transfusion Center. Haemonetics MCS plus is used as the plateletpheresis instrument. Complete Blood Count (CBC) and hematological parameters of donors before and after plateletpheresis were measured with the Sysmex cell counter. Platelet yield, collection efficiency (CE), and collection rate (CR) were evaluated for SDP and DDP. Results were reported using R-4.3.2 software as Mean±SD, and p-value<0.05 was considered statistically significant. [Platelet yield: platelet count × component volume × conversion factor (1000); Collection efficiency: platelet yield/total platelets processed × 100; Collection rate: platelet yield/processing time].

Results: In the DDP group, the mean percentage of post-plateletpheresis platelet reduction (32.00±8.91%) was significantly higher than in the SDP group (21.49±9.96%). As expected, the total blood volume processed in DDP was significantly higher than in SDP. Platelet yield in DDP was significantly higher than in SDP, 2.6×1011±65.2, 3.1×1011±1.9 respectively. CE showed no significant difference between the two groups, but the CR for DDP (0.07±0.01 platelet×1011/ml) was significantly higher than for SDP (0.04±0 platelet×1011/ml). The ACD anticoagulant volume that entered the donor's body during the plateletpheresis procedure for SDP (371.2±27.05 ml) was significantly lower than DDP (474.67±56.07 ml). Hematological parameters in plateletpheresis donors, including hemoglobin, hematocrit, RBC count, WBC count, and lymphocytes, exhibited no significant disparities between SDP and DDP donors. Despite a reduction in hematological parameters post-plateletpheresis donation in both groups, the level of these parameters remained within the normal range for healthy individuals.

Conclusion: Considering the limited number of plateletpheresis donors, the preparation of DDP is of particular importance. DDP has more advantages than SDP and is more cost-effective, allowing the production of two platelet units with one kit. Although DDP leads to a greater consumption of ACD and a reduction in donor hematological parameters, these parameters remain within the normal range for healthy individuals even after DDP donation, posing no threat to donors. Nevertheless, DDP donors should be carefully monitored according to AABB standards, and their screening tests should be conducted accurately.

Keywords: Plateletpheresis, Blood; Apheresis; Blood Donor





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-74

Evaluation of Screening Coagulation Tests in Patients Referred for Cutaneous Bleeding Disorders: A Retrospective Analysis

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Abstract

Background and Aim: Cutaneous bleeding disorders, including petechiae, purpura, and ecchymosis, are commonly encountered in clinical practice and may indicate an underlying coagulation disorder. We conducted a retrospective analysis to evaluate the frequency of abnormal screening coagulation tests, including prothrombin time (PT) and activated partial thromboplastin time (aPTT), in patients referred for cutaneous bleeding disorders.

Methods: This retrospective analysis included medical records of 712 patients referred for cutaneous bleeding disorders at a tertiary care center between for 5 years. Inclusion criteria were patients who underwent screening coagulation tests, including PT and aPTT, and exclusion criteria were patients with a known bleeding disorder or those on anticoagulant or antiplatelet therapy. Patient demographics, PT and aPTT results, and family history of bleeding disorders collected and analyzed using descriptive statistics. The primary outcome was the frequency of abnormal PT and aPTT test results in these patients, and secondary outcomes included the prevalence of specific blood coagulation disorders. Statistical analysis performed using IBM SPSS version 26.0.

Results: Medical records of 712 patients, aged 1 to 90 years (mean age 29 years), were included in the study. The majority of patients were female (79.9%), and 2.5% had a positive family history of bleeding disorders. PT performed in all patients, and aPTT performed in 687 patients. The mean PT and aPTT values were 13 seconds (range 9-120 seconds) and 32 seconds (range 20-139 seconds), respectively. Abnormal PT results observed in 57 patients (8.2%), while abnormal aPTT results observed in 66 patients (9.6%). Of the patients with abnormal PT, 47 (82.4%) had isolated PT prolongation, while 10 (17.6%) had combined PT and aPTT prolongation. Among the patients with abnormal aPTT, 44 (66.7%) had isolated aPTT prolongation, while 22 (33.3%) had combined PT and aPTT prolongation.

Conclusion: In conclusion, our study shows that abnormal screening coagulation tests are frequent in patients referred for cutaneous bleeding disorders. Therefore, a thorough coagulation workup, including aPTT and PT, are recommended in these patients to identify underlying bleeding disorders and initiate appropriate management. Further studies are needed to evaluate the diagnostic and prognostic value of abnormal screening coagulation tests in this patient population.

Keywords: Prothrombin Time; Partial Thromboplastin Time; Blood Coagulation Disorders.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-75

Compare the difference in the effects of warfarin and clopidogrel in patients with cardiac disorders: A systematic review study

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Abstract

Background and aims: Cardiac disorders, including Heart failure (HF) and Atrial fibrillation (AF), are common and require management due to the risks they pose to health. This management often involves the use of anticoagulant and antiplatelet medications. Warfarin and clopidogrel are two drugs that are commonly prescribed in these conditions. Warfarin is an anticoagulant that inhibits the synthesis of clotting factors, while clopidogrel is an antiplatelet agent that inhibits platelet aggregation. The aim of this systematic review study is to compare the effects of warfarin and clopidogrel in patients with cardiac disorders.

Method: The data were collected by searching PubMed, Scopus and Google Scholar search engine. The advanced searched keywords were: “Cardiac Disorder”, “Atrial Fibrillation”, “Warfarin” and “Clopidogrel”. The search was limited to studies in the English language and accessible full texts. Review, duplicate, and non-relevant articles were excluded.

Results: In this systematic review study, 38 articles were retrieved through searching in databases, of which only 8 articles matched our inclusion criteria after preprocessing and screening. Warfarin has mixed results in treating heart diseases like HF and AF. It improves HF in sinus rhythm but is associated with a risk of stroke or systemic embolism (up to 2%) and bleeding (approximately 4%) in HF patients. In older AF patients, warfarin treatment increases the risk of bleeding. However, in the context of heart surgery with cardiopulmonary bypass (CPB), warfarin has not shown increased postoperative bleeding. Clopidogrel, on the other hand, has been effective in reducing cardiovascular mortality, especially in patients with unstable angina and non-Q wave myocardial infarction. It does not increase bleeding, including intracranial bleeding, and shows quick protective effects after initiation. However, it may be more effective in individuals under 60 years of age.

Conclusion: This systematic review shows that the age parameter of people is effective in the effectiveness of both warfarin and clopidogrel and has an opposite relationship with it. It was also found that compared to clopidogrel, which reduces the risk of bleeding in patients, warfarin in different conditions of heart diseases can both increase and decrease the possibility of bleeding in patients.

Keywords: Cardiac Disorder; Atrial Fibrillation; Warfarin; Clopidogrel





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review/Meta-analysis

Code of Abstract: PH-76

Severity of HDN and ABO incompatibility, Is it clinically important?

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Abstract

Background and Aim: Hemolytic disease of the newborn (HDN) is an incompatibility of the blood group between the mother and newborn. The severity of ABO-HDN ranges from mild to severe clinical symptoms. ABO incompatibility is characterized by high level serum bilirubin, moderately severe anemia, the appearance of jaundice, reticulocytotic and spherocytosis, which can damage the liver and brain if left untreated. ABO HDN is most common with blood type A or B infants born to type O mothers. This study analyzes the relationship between A and B antigen density in infants, the potential of mother antibodies and severity of the HDN.

Methods: This review was achieved through an organized search of the published articles using the keywords ABO incompatibility, HDN, HDN severity in databases, including PubMed, Scopus, and Science Direct.

Results: Most results are based on the titers of maternal IgG Anti-A or anti-B antibodies and the outcomes of the direct antiglobulin and immune enzymatic assay on cord blood red cells. No apparent relationship was indicated between cord blood red cell antigen density and maternal IgG Anti-A or anti-B antibody titer or subclasses, gestational age, or number of pregnancies. In addition, the amount and subclass of maternal anti-A or anti-B antibodies influence the severity of ABO-HDN.

Conclusion: The majority of studies indicate the effect of neonatal A/B antigens in HDN, a rise in incidence but not a rise in severity. On the other hand, the development of ABO-HDN was found positively correlate with the cytotoxic capacity of maternal serum.

Keywords: ABO Incompatibility; HDN; HDN severity





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PH-77

Procoagulant Microvesicles in Sickle Cell Disease

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Abstract

Background and Aim: Thrombotic complication is One of the hallmarks of sickle cell disease (SCD). The presence of phosphatidylserine on the outer membrane of sickle-shaped red blood cells, and particularly on membrane-derived submicron fragments called microvesicles (MVs) has been shown to play an effective role in triggering coagulation in SCD. However, studies have not elucidated the mechanism of the role of circulating MVs in coagulation activity in SCD. We aimed to investigate the procoagulant activity of circulating MVs during sickle cell crises in more detail.

Methods: A systematic search was performed to identify studies published in multiple databases (PubMed, ProQuest, Science direct and Google Scholar) up to 2023, and researchers have analyzed all the relevant data through the SCOPUS search engine using “Advance search” option and keywords such as coagulation, microvesicles and sickle cell disease.

Results: Most of the circulating MVs were originated from platelets and erythrocytes. In painful crises of SCD, a higher level of procoagulant MVs was observed compared to those of steady-state and control group. Furthermore, the procoagulant activity of MVs was significantly higher during painful crises than at steady states. A significant correlation was found between erythrocyte-derived MVs, hemolysis marker and the hemoglobin level.

Conclusion: The number of MVs derived from platelets and erythrocytes is related to painful crises. It is hoped that in the future, with more studies on circulating MVs as a biomarker, it will be possible to improve the diagnosis of disease severity in SCD patients and to identify patients at risk of thrombotic complications.

Keywords: Coagulation; Microvesicles; Sickle Cell Disease





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-78

Homocysteine level is elevated in women with repeated implantation failure (RIF) compare to normal fertile controls

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Abstract

Background and Aim: Recurrent implantation failure (RIF) is a significant challenge for women undergoing in vitro fertilization (IVF). RIF is characterized by the failure of three IVF attempts, despite the use of high-quality embryos. While the impact of homocysteine on reproductive processes in IVF patients and its association with adverse pregnancy outcomes have been investigated, its specific role in RIF has been less studied. This study aims to evaluate the possible role of this factor for women with RIF.

Methods: A retrospective study was conducted on 46 women who had experienced more than three unsuccessful embryo transfers, as well as 40 control subjects with healthy fertility. These participants were referred to the fertility and in vitro fertilization departments of Golestan Ahvaz Hospital between 2022 and 2023. Homocysteine level in the serum were assessed following three unsuccessful IVF cycles.

Results: The mean patient age was 37.5 ± 5.56 years. The mean number of embryo transfers was 4.26 ± 1.58 . The mean homocysteine level in RIF patients (9.99 ± 2.68 $\mu\text{mol/L}$) was found to be significantly higher compared to controls (8.50 ± 0.30 $\mu\text{mol/L}$), with a p-value of less than 0.0001. It is important to note that the normal homocysteine cutoff level is 13 $\mu\text{mol/L}$. 19.5% (9 people) of the 46 RIF patients and 7.5% (3 people) of the 40 participants in the control group had high homocysteine level.

Conclusion: The present study demonstrates that although the homocysteine level in both groups were within the normal range, a significant difference was observed between the level of homocysteine in women with RIF compared to the control group. Furthermore, there was no significant correlation between this factor and the number of IVF failures.

Keywords: Homocysteine; Repeated Implantation Failure; Female Infertility; In Vitro Fertilization (IVF)





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-79

Evaluation of GVHD risk and new therapeutic approaches in patients with Fanconi anemia

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Abstract

Background and Aim: Inherited bone marrow failure syndromes (IBMFSs) are a group of rare genetic disorders characterized by bone marrow failure with unique phenotypes and predisposition to cancer. Classical IBMFSs primarily include Fanconi anemia, dyskeratosis congenita, and Diamond-Blackfan anemia. Fanconi anemia (FA) is characterized by physical abnormalities, bone marrow failure, and increased risk for malignancy and often initially with thrombocytopenia or leukopenia. Hematopoietic Stem Cell Transplantation (HSCT) is the only potentially curative treatment option for the hematologic complications that occur in patients with Fanconi anemia but one of the disadvantages of this method is that it does not correct non-hematological defects and may increase the risk of secondary malignancies. Over the last two decades, sequential changes to the approach to HCT have resulted in reduced regimen-related toxicity, superior engraftment and less graft-versus-host disease (GVHD), resulting in improved survival. Graft-versus-Host Disease is the major toxicity of allogeneic hematopoietic cell transplantation. For many years, there have been few effective treatment options for patients with GVHD. First-line systemic treatment remains corticosteroids, but up to 50% of patients will develop steroid-refractory GVHD and the prognosis for these patients is poor. There are currently 3 FDA approvals for the treatment of chronic GVHD: Ibrutinib, a BTK inhibitor Belumosudil, an oral selective inhibitor of ROCK2 and Ruxolitinib for chronic GVHD after failure of one or two lines of systemic therapy.

Methods: Articles published about GVHD risk and new therapeutic approaches in patients with Fanconi anemia including twenty-five articles, ten systematic review articles and fifteen randomized controlled trial (RCT) articles. Were retrieved through a comprehensive literature search by using several databases such as PubMed, Google Scholar, Scopus, Embase, and Cochrane until October 2023. Search keywords such as GVHD, Fanconi anemia, therapeutic approaches were used during the database search to target comparable articles.

Discussion: According to the studies, severe cGVHD group is associated with lower overall survival and higher mortality. corticosteroids less than 0.25 mg/kg/day potentially leading to an adverse response, loss of response, or failed steroid tapering. In addition, long-term use of immunosuppressants, including steroids, is associated with significant toxicity and increased risk. In the case of Belumosudil, the responses were clinically significant, with a median response duration of 35 weeks, and were associated with improved quality of life and reduced steroid dosage. In the case of Ibrutinib, most patients with multiple organ cGVHD had a multi-organ response. A significant decrease in clinical symptoms was observed in patients. Ruxolitinib led to longer median failure-free survival and a greater number of patients with symptom response.

Conclusion: New, effective, and well-tolerated targeted therapies for cGvHD have been developed and FDA-approved, but they continue to be used empirically and deployed once the lack of response to systemic corticosteroids and/or calcineurin inhibitors is established. Furthermore, rate of complete and or durable responses are unsatisfactory and choice of therapy for refractory cases remains largely empiric. However, more studies are needed in this field.

Keywords: GVHD; Fanconi Anemia; Therapeutic Approaches





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-80

Investigating the effect of sorafenib drug after allogeneic transplantation in patients with FLT3-ITD acute myeloid leukemia

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Abstract

Background and Aim: Acute myeloid leukemia (AML) is a clonal stem cell cancer. FMS-like tyrosine kinase 3 (FLT3) is a receptor tyrosine kinase, which is expressed in hematopoietic precursor cells, regulating stem cell growth and differentiation. Despite undergoing allogeneic hematopoietic stem cell transplantation (HCT), Patients diagnosed with AML with FLT3 mutations have a very poor prognosis, frequently relapse, and die as a result of AML. It is currently unknown whether a maintenance therapy using FLT3 inhibitors, such as the multitargeted tyrosine kinase inhibitor sorafenib, improves outcome after HCT. The objective of this study was to evaluate the effect of sorafenib on the outcomes of patients with AML with FLT3 internal tandem duplication (ITD) undergoing HCT.

Methods: Articles pertaining to the effect of sorafenib after allogeneic hematopoietic stem cell transplantation for acute myeloid leukemia with FLT3-ITD mutation including ten original articles were retrieved through a comprehensive literature search by using several databases such as PubMed, Google Scholar, Scopus, Embase, and Cochrane until September 2023. Search keywords such as sorafenib, transplantation, acute myeloid leukemia was used during the database search to target comparable articles.

Results: This systematic study accrued 10 articles until September 2023. In these articles, patients received sorafenib before allogeneic HSCT. Transplant conditioning regimens and donor sources were determined in studies. Correlative studies evaluating FLT3 inhibition via a plasma inhibitory activity assay showed consistent inhibition of FLT3 at all tolerability determined dosing levels. Sorafenib is well tolerated in the peritransplant setting irrespective of the conditioning intensity or the donor source. In one study, patients with minimal undetectable residual disease (MRD) before HCT and those with detectable MRD after HCT were shown to derive the strongest benefit from sorafenib.

Conclusion: Sorafenib before transplantation, sorafenib maintenance after transplantation, and their combined application all could improve the outcomes for patients with FLT3 ITD AML. sorafenib maintenance after transplantation is safe and associated with improved long-term survival and reduced relapse rates compared with non-maintenance, further supporting this strategy as a standard of care for patients with FLT3 ITD acute myeloid leukaemia undergoing allogeneic HSCT. Further study is needed to determine whether the use of sorafenib both before and after transplantation might be ideal.

Keywords: Sorafenib; Transplantation; Acute Myeloid Leukemia.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Case Report

Code of Abstract: PH-82

Menorrhagia: An Unexpected Manifestation in a Young Female with Systemic Lupus Erythematosus

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Abstract

Background and Aim: Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease with different clinical and laboratory characteristics affecting multiple organs and tissues. Although the exact causes of the disease are still unknown, risk factors such as genetics, environmental factors and hormones have been found to play a role in inflammatory responses and the stimulation of the immune system. In light of the fact that, female hormones such as estradiol, progesterone and prolactin may contribute to autoimmune diseases, particularly SLE, women in childbearing may experience menorrhagia and menstrual cycle abnormalities.

Methods: Herein, we report a 15-year-old female who presented with severe anemia from heavy menstrual bleeding without any history of bleeding or other coagulopathy in her personal life. Coagulation examinations revealed prolonged PTT which could not be corrected by mixing with equal volume of normal pool plasma both immediately and after incubation at 37°C. As well, DRVVT screen was prolonged with a very high confirmation rate (1.86). Furthermore, immunological studies by enzyme-linked immune assay (ELISA) method indicated the presence of anti-phospholipid antibodies such as anti-cardiolipin (ACLA) and beta2-glycoprotein 1 (β2GPI) antibodies are in patient serum and immunofluorescence staining for antinuclear antibodies (ANA) showed a fine speckled pattern in the nucleus with a high titer (1/640).

Results: Herein, we report a 15-year-old female who presented with severe anemia from heavy menstrual bleeding without any history of bleeding or other coagulopathy in her personal life. Coagulation examinations revealed prolonged PTT which could not be corrected by mixing with equal volume of normal pool plasma both immediately and after incubation at 37°C. As well, DRVVT screen was prolonged with a very high confirmation rate (1.86). Furthermore, immunological studies by enzyme linked immune assay method (ELISA) indicated the presence of anti-phospholipid antibodies such as anti-cardiolipin (ACLA) and beta2-glycoprotein 1 (β2GPI) antibodies are in patient serum and immunofluorescence staining for antinuclear antibodies (ANA) showed a fine speckled pattern in the nucleus with a high titer (1/640).

Conclusion: This case clarifies the aptitude of coagulation evaluations and the necessity of careful laboratory strategy in detection of new-onset systemic lupus erythematosus with menorrhagia and hemorrhagic manifestations.

Key words: Systemic lupus erythematosus, Menorrhagia, Coagulation, anti-phospholipid antibodies.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PH-83

Acquired coagulation disorders and the importance of their prognostic role in Multiple Myeloma patients

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Abstract

Multiple myeloma (MM) is a proliferation of a single clone of plasma cells which produce a monoclonal protein. There are some evidences of Hemostatic Abnormalities in patient with Multiple Myeloma. Screening tests for coagulation abnormality in multiple myeloma can be important. These abnormal laboratory results are because of different things such as Acquired dysfibrinogenemia, Acquired coagulation factor X deficiency. Coagulation tests can be useful in multiple myeloma prognosis.

Keywords: Multiple Myeloma; Coagulation Disorder; Prognosis.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PH-84

A Case Report of Acquired Factor VIII Deficiency: An Uncommon Medical Emergency

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Abstract

Background and Aim: Acquired hemophilia A (AHA) is a rare and potentially life-threatening bleeding disorder in which clotting factor VIII is neutralized by autoantibodies. This condition commonly causes hematuria, severe spontaneous bleeding and ecchymosis in soft tissues or mucocutaneous areas. Most often, the etiology of AHA is not yet identified, but some common causes include pregnancy, malignancy, autoimmune diseases such as rheumatoid arthritis and systemic lupus erythromatosis. The high morbidity and mortality of AHA requires accurate and careful lab technique strategy to diagnose it.

Results: Here in, we describe a 24-year-old female presented with chief complaint of diffuse ecchymosis and extensive bruises on her legs without any prior history of bleeding or any other coagulopathy in her family or personal life. She also had trouble moving around and her image scan revealed a burden clot in her pelvis. The initial lab evaluation of the patient demonstrated negative lupus anticoagulants, normal PT and prolonged PTT (68 seconds), so a mixing study was performed with equal volume of normal pool plasma to determine the cause of the prolonged PTT. Mixing PTT was not corrected after incubation at 37°C (65 seconds). Further investigations with factor assays revealed significantly low factor VIII activity of 3.5 percent. As a consequence, due to low levels of factor VIII and the uncorrected PTT mixing study, subsequent experiments were performed and confirmed the presence of inhibitors against factor VIII (titrated using the Bethesda assay).

Conclusion: AHA is rare coagulopathy disorder, involving patients with no previous bleeding, thus making diagnosis challenging. AHA is diagnosed based on the findings of coagulation tests and mixing studies (prolonged PTT and mixing study after incubation in 37°C and low factor VIII level). This report emphasized the importance of the ability of immediate diagnosis for the disease in those with significant bleeding in the absence of risk factors such as known bleeding disorder, anticoagulant use and recent surgery.

Keyword: Acquired hemophilia A, Factor VIII, Prolonged PTT.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Hematology & Blood Banking

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PH-85

Platelet-Rich Plasma and mesenchymal stem cells in periodontal regeneration: Systematic review and meta-analysis

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Abstract

Background and Aim: This systematic review and meta-analysis aimed to examine the impact of platelet-rich plasma (PRP) on the restoration of periodontal tissues by evaluating clinical and radiographic outcomes in prospective human clinical trials. Additionally, it sought to assess the potential effectiveness of mesenchymal stem cells (MSCs) in periodontal regeneration in humans, focusing on clinical attachment level (CAL), probing depth (PD), and gingival recession (GR) as the primary outcomes of interest.

Methods: Two reviewers (MJMM and NEZ) conducted an electronic literature search and hand-search in multiple databases until November 2023. The research strategy followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The PICO question focused on the effects of PRP and MSCs in regenerating periodontal tissues. All types of studies were qualitatively described, and the risk of bias was assessed for each individual study.

Results: In the qualitative analysis, a total of fifteen reports were examined, which involved 123 patients and 158 periodontal defects. The findings revealed a significant difference between the test and control groups in terms of CAL at three months, with a decrease of 0.90 mm (95% CI [-1.51; -0.29]). However, no significant differences were observed for PD and GR. The weighted mean difference (WMD) for CAL was 0.55 mm, with a 95% CI of -0.09 to 1.20 mm (P = .09). Regarding bone level (BL), two articles measured BL in millimeters, while the other two articles measured BL in percentage. The WMD for BL was 0.76 mm (95% CI = 0.21-1.31 mm; P = .007) and 47.41% (95% CI = 32.48%-62.33%; P < .0001), respectively. In terms of attachment level (AL) changes, twelve articles were included, and the WMD was 0.58 mm, with a 95% CI of 0.24 to 0.91 mm (P = .0008). Lastly, sixteen articles were analyzed to evaluate the marginal gingival level (MGL), and the WMD was -0.10 mm, with a 95% CI of -0.19 to -0.01 (P = .03).

Conclusion: The presence of significant heterogeneity among the studies posed challenges in reaching definitive conclusions. Nevertheless, based on the limitations of this review, it is suggested that PRP could potentially have positive effects on clinical and radiographic outcomes in the regeneration of periodontal bone defects. On the other hand, the evidence supporting MSC-based therapy's impact on periodontal regeneration is of low quality and indicates only a minor effect. However, it is important to note that these results should not be considered conclusive due to the study's monocentric nature, small sample size, and potential heterogeneity across the two included RCTs.

Keywords: Mesenchymal Stem Cells; Platelet-Rich Plasma; Periodontal Regeneration.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



6. Immunology (Oral Presentations)





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OI-1

Reduction of systemic inflammation by a mixture of exosomes derived from mesenchymal stem cells and hepatocytes increases the survival rate in the mouse model of sepsis

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Abstract

Background and Aim: Although inflammation is an essential host response, the onset and progression of sepsis center upon a "dysregulation" of the normal response, usually with an increase in both pro-inflammatory and anti-inflammatory mediators, initiating a chain of events that leads to widespread tissue injury. Evidence supports a state of acquired immune suppression or immunoparalysis in some patients, which may occur simultaneously with or following the initial pro-inflammatory response. It is this dysregulated host response rather than the primary infectious microorganism that is typically responsible for multiple organ failure and adverse outcomes in sepsis.

Methods: Initially, mesenchymal stem cells and hepatocytes were isolated and cultivated. The cells were then verified through flow cytometry. The exosomes were extracted from these cells and verified using the DLS and flow cytometry techniques. To trigger sepsis in the mice, the CLP method was utilized. After that, the extracted exosomes were administered to the mice. Serum was isolated from the blood of five mice from each group through heart puncture. The isolated serum was then diluted using PBS in a 1:10 ratio, and the levels of cytokines, including IL-6, IL-1 β , TNF- α , IL-10, and TGF- β , were analyzed. A commercial kit and the ELISA method were used to quantify the amounts of these cytokines in the serum. To assess survival, 5 mice from each group were monitored every 24 hours for 7 days, and their mortality status was recorded.

Results: The study found that CLP mice had significantly higher levels of pro-inflammatory cytokines IL-1 β , IL-6, and TNF- α , which were lowered in groups treated with MSC exosomes+ imipenem and a mixture of exosomes+ imipenem. These groups also had increased levels of anti-inflammatory cytokines IL-10 and TGF- β . On the other hand, the control and sham groups had a 100% survival rate, while all mice in the CLP and imipenem-treated CLP groups died. Mice treated with MSC-derived exosomes+ imipenem had a 60% survival rate, while those treated with hepatocyte-derived exosomes+ imipenem had only a 40% survival rate. The best survival rate (80%) was observed in the group treated with a mixture of exosomes+ imipenem.

Conclusion: The combination of exosomes from mesenchymal stem cells and hepatocytes effectively controlled systemic inflammation and improved the survival of mice by 80%, surpassing the effectiveness of either exosome type alone.

Keywords: Inflammation; Survival; Sepsis; Mesenchymal stem cell; Hepatocyte.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OI-2

Nitric oxide and bacterial load decreased after treatment of sepsis-affected mice with a mixture of hepatocyte-derived exosomes and mesenchymal stem cells

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Abstract

Background and Aim: Sepsis is a life-threatening condition caused by an infection that leads to inflammation and organ dysfunction. Bacterial load plays a significant role in its progression, with higher loads linked to worse outcomes. NO is a signaling molecule released by immune cells to fight infections, but excessive NO production in sepsis can lead to nitrosative stress, tissue damage, and multi-organ dysfunction. Therefore, in this study, we investigated the effect of exosomes derived from hepatocytes and mesenchymal stem cells on bacterial load and nitric oxide concentration.

Methods: The first step was to extract and culture mesenchymal stem cells and hepatocytes. Flow cytometry was used to confirm their presence. Exosomes were extracted from these cells, and their presence was further confirmed through flow cytometry and SEM methods. To induce sepsis in mice, the CLP method was employed. After this, the extracted exosomes were injected into the mice. Serum and liver tissue were then separated for further analysis. After euthanasia, five mice from each group were evaluated for bacterial colonies in serum and liver. Cultured on Luria-Bertani agar medium, bacterial colonies were numbered, and bacterial load was calculated as log CFU/mg of tissue and log CFU/ml of serum. NO in serum and liver samples was analyzed by measuring NO concentration in diluted samples added to a 96-well plate using a commercial kit.

Results: According to the study, the liver and serum bacterial load of the CLP group increased significantly more than that of the sham group ($p < 0.0001$). The lowest bacterial load was detected in the liver and serum of CLP mice treated with imipenem+ hepatocyte exosomes. Moreover, the study showed that the concentration of liver and serum NO in CLP mice was significantly elevated ($p < 0.0001$) compared to the sham group. The concentration of NO in the liver and serum of all exosome-treated groups decreased, and the lowest NO concentration was detected in the mixture of exosomes+ imipenem ($p < 0.0001$).

Conclusion: The hepatocyte-derived exosomes+ imipenem was more effective in reducing bacterial load in the liver and serum than the MSC-derived exosomes+ imipenem. Although the mixture of exosomes+ imipenem achieved a reduction in bacterial load comparable to that seen in mice treated with MSC-derived exosomes+ imipenem, the group that received the mixture of exosomes+ imipenem showed more reduction in NO levels compared to all other experimental groups.

Keywords: Bacterial load; Nitric oxide; Sepsis; Mesenchymal stem cell; Hepatocyte.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OI-4

Silencing of VSIG-3 simultaneously suppresses A2058 melanoma cell progression and induces anti-tumoral cytokine profile in human T cells

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Abstract

Background and Aim: V-domain immunoglobulin suppressor of T cell activation (VISTA) is a novel immune checkpoint receptor recently identified and has shown worthy potential as an immunotherapeutic target in cancer treatment. While V-set and immunoglobulin domain containing 3 (VSIG-3) was introduced as a ligand for VISTA with an inhibitory effect on T cell functions, there is little information available regarding its functional molecular mechanisms and roles in the tumor microenvironment of melanoma. Here, we aimed to investigate the roles of VSIG-3 in melanoma progression and its silencing effect on human T cell cytokine expression.

Methods: Bioinformatics analysis was performed to study VSIG-3 expression, its relation with the expression of other immune checkpoints, protein-protein interactions, immune cell infiltration, clinicopathology of melanoma patients, and their overall survival. Then, the effect of VSIG-3 silencing on the growth, migration, apoptosis, and cell cycle arrest of the A2058 melanoma cells were investigated via colony formation, scratch, annexin V/PI, and cell cycle arrest assays, respectively. Lastly, qRT-PCR was conducted to evaluate the expression level of T cell cytokines co-cultured with A2058 cells transfected with VSIG-3-siRNA.

Results: Online databases showed increased expression of VSIG-3 in melanoma patients, correlated to tumor progression in some aspects. Knockdown of VSIG-3 showed significantly decreased growth and migration rate, while apoptosis was increased in A2058 melanoma cells. Also, arrests in some phases of the cell cycle were detected (not significant). Based on qRT-PCR data, while the expression level of IL-12 and IFN- γ increased, TGF- β , IL-10, and TNF- α expression levels decreased in T-cells co-cultured with VSIG-3-siRNA-transfected cells compared to the control.

Conclusion: The suppressory effect of VSIG-3 silencing on A2058 melanoma cells tumorigenesis along with altering T-cell cytokine profile in favor of inducing anti-tumoral responses, suggest that VSIG-3 could be an ideal target for immunotherapy of melanoma.

Keywords: Immune Checkpoint; VISTA; VSIG-3; T Cell; Melanoma.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OI-5

Evaluation of the efficacy of the recombinant RBD vaccine candidate in stimulating cellular and humoral immune responses against SARS-CoV2

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Abstract

Background and Aim: The coronavirus disease 2019 (COVID-19) is caused by the SARS-CoV-2. Considering the key role of the receptor-binding domain (RBD) of viral spike (S) protein in the initiation of infection, almost all trials have used it for vaccine development.

Methods: In the present study, we expressed a recombinant RBD (rRBD) within a prokaryotic host and evaluated its functionality as a vaccine candidate against SARS-CoV2. Moreover, we assessed its effectiveness in the stimulation of cellular and humoral immune responses.

Results: The designed RBD protein was adequately expressed in the *E. coli* host (approximately 35-40 mg/L). Various analyses, including molecular docking, flow cytometry, and cell-ELISA confirmed that the rRBD protein can bind to the ACE2 receptor on the surface of Caco2 cells. Formulation of this vaccine candidate with Freund's adjuvant resulted in a significant increase in antibody titer that lasted for 24 weeks. The histological examination did not show any significant complications. The immunohistochemical analysis of CD4⁺ and CD8⁺ T-cell subsets showed that rRBD protein managed to significantly stimulate the cellular immune system. Neutralizing antibody assay using flow cytometry, immunofluorescence assay, and cytopathic effect (CPE) assay showed that the candidate vaccine was able to stimulate the production of neutralizing antibodies.

Conclusion: The functional recombinant RBD produced using the prokaryotic expression system was able to interact with the ACE2 receptor and was also able to induce effective and long-lasting cellular and humoral immune responses without obvious side effects. Therefore, it can be considered in the development of diagnostic kits and vaccine design.

Key words: SARS-Cov-2, RBD, Vaccine, Recombinant, Immune Responses.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OI-7

Comparative evaluating the effect of extracellular vesicles derived from human umbilical cord blood serum and human amniotic fluid on the severity of intrauterine adhesions in the post-surgery Asherman mice model

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Abstract

Background and Aim: Intrauterine adhesions (IUAs), also known as Asherman's syndrome, is a prevalent gynecological condition that presents with various clinical manifestations, including atypical menstrual patterns, repeated pregnancy loss, and potential infertility. Despite advancements in therapy, the successful pregnancy rate remains low. Therefore, extensive research is essential to understand the underlying mechanisms of IUAs and develop effective therapeutic interventions. In this study, we compared the effects of extracellular vesicles derived from human umbilical cord blood serum and human amniotic fluid on the induced post-surgery intrauterine adhesion model.

Methods: Human umbilical cord serum (hUCS) was purchased commercially and Amniotic fluid (AF) was collected by a gynecologist and its extracellular vesicles were extracted using the kit and then identified. 8-10-week-old female NMRI mice were prepared to induce the intrauterine adhesion (IUA) model. Mice were divided into 3 groups: Sham, IUA receiving PBS and IUA treated with extracellular vesicles. Peritoneal fluid was collected and the amount of nitric oxide and the phagocytosis power of peritoneal macrophages were checked, and then the uterine tissue of mice was subjected to H&E and Trichrome masson histopathology. Several other mice of the same breed were prepared for the analysis of pregnancy after induction of the IUA model and treatment with extracellular vesicles, and in the middle of pregnancy, the placenta and fetus were taken out for examination in terms of weight and number. In the in vitro studies, the endometrial stem cells were damaged with H₂O₂ and in different groups, they were subjected to scratch tests, phagocytosis, efferocytosis, arginase, ROS, MTT and nitric oxide levels in the form of co-culture with macrophages and without co-culture with macrophages.

Results: The findings of H&E and Trichrome Masson showed Extracellular vesicles derived from human amniotic fluid increased the number of glands and thickness of the endometrium, number of fetuses as well as placenta and fetus weight and decreased the endometrial fibrosis, amount of phagocytosis of peritoneal macrophages more than extracellular vesicles derived from human umbilical cord blood serum. In the ex vivo phase, the macrophages that received the human amniotic fluid vesicle showed a decrease in phagocytosis and efferocytosis, the amount of nitric oxide and reactive oxygen species, as well as an increase in the amount of arginase enzyme. In the co-culture with macrophages or culture without the presence of macrophages, the scratch was repaired faster and the cell viability rate (MTT) was higher. It also showed a decreased amount of secreted nitric oxide in two groups.

Conclusion: The use of extracellular vesicles derived from human amniotic fluid better than human umbilical cord blood serum can improve intrauterine adhesion. More studies are needed to determine the effective mechanism of this treatment method.

Keywords: Extracellular Vesicles; Human Amniotic Fluid; Human Umbilical Cord Serum; Intrauterine Adhesion; Inflammation; Asherman Syndrome.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OI-8

Exploring the Impact of Modified ZnO Nanoparticles on Immune Response in a Mouse Lung Cancer Model

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Abstract

Background and Aim: Lung cancer, which is characterized by the presence of malignant tumors, offers a potential avenue for treatment through the use of nanomedicines. Previous in vitro studies have shown promising effects of modified ZnO nanoparticles on lung cancer cell lines. Therefore, the aim of this study was to investigate the impact of this nanodrug on the immune response in a mouse model of lung cancer.

Methods: In this investigation, a mouse model of lung cancer was utilized. Various aspects, including tumor size, infiltration of CD8⁺ cells, and the survival rate of the mice, were carefully examined. The obtained results were subsequently analyzed using GraphPrism 9 software

Results: The findings of this study demonstrated that mice treated with the nanodrug exhibited a reduction in tumor size. Additionally, there was an increase in the number of CD8⁺ cells infiltrating the tissue. Furthermore, the administration of the nanodrug led to improved survival rates among the mice.

Conclusion: The use of this nanodrug has shown significant efficacy in inhibiting tumor growth. Moreover, it has demonstrated potential in enhancing CD8⁺ cell infiltration, thereby strengthening the immune response and suppressing tumor progression. Ultimately, this nanodrug has been found to improve the survival of mice receiving treatment.

Keywords: Modified Zinc Oxide Nano Drug; Lung Cancer; CD8⁺ Cells; Animal Model of Lung Cancer.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OI-9

Salirasib inhibits the fibrosis process by decreasing the fibrotic genes and increasing MMP1 in skin fibroblasts of systemic sclerosis patients

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Abstract

Background and Aim: Systemic sclerosis (SSc) is an autoimmune disease characterized by immunological abnormalities, vascular damage, inflammation, and fibrosis. Tissue fibrosis plays an important role in SSc and can affect several organs such as the skin, joints, tendons, gastrointestinal tract, lungs, and heart. This fibrosis process is mostly caused by connective tissue fibroblasts and myofibroblast cells, which are influenced by various growth factors. One of the most important of them is the cytokine TGF- β . Cytokine TGF- β is known as a key mediator in the fibrosis process of systemic sclerosis patients, which causes the production of extracellular matrices and collagen through the activation of the Ras signaling pathway. Salirasib is a small molecule containing farnesyl isoprenoid, which is considered a Ras inhibitor. In this study, we investigated the role of the Ras protein inhibitor, salirasib, in the inhibition of genes involved in the fibrosis process in SSc skin fibroblasts in the presence of TGF- β (as an activating factor for fibroblasts).

Methods: Skin biopsies were obtained from 10 patients with SSc. Fibroblast cells, were first placed in serum-free medium and then were treated with TGF- β and a Ras inhibitor (Salirasib). The gene expression level involved in the fibrosis process (e.g. COL1A1, COL1A2, CTGF, FN1, ACTA2 and MMP1) were quantified using Real-time PCR and also protein expression of α -SMA was examined using an immunofluorescence assay.

Results: Our data indicated that COLA1, COLA2, FN1, and CTGF mRNA levels were significantly upregulated by TGF- β . However, salirasib downregulated the expression of genes involved in fibrosis in a time- and dose-dependent manner and significantly decreased the expression of COLA1, COLA2, FN1, CTGF and ACTA2 compared to TGF- β -treated group. Salirasib also significantly increased gene expression of MMP1 (matrix metalloproteinases1) than both TGF- β -treated group and group without treatment. Protein expression of α -SMA noticeably decreased in the presence of salirasib in comparison to the TGF- β -treated group as well.

Conclusion: Based on the effects of salirasib on the expression of the genes involved in the fibrosis process; it can be considered as a new therapeutic strategy for SSc.

Keywords: Fibroblast, Fibrosis; Salirasib; Systemic Sclerosis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OI-11

Exploring Hematological and Biochemical Factors and T Regulatory Cells in the Blood of Hospitalized Patients with COVID-19 Infection

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Abstract

Background and Aim: The evaluation of laboratory haematological and biochemical factors could reflect the severity of COVID-19 disease in patients. The correlation between these factors and disease progression can be beneficial for the patient's survival. The aim of this study is to measure laboratory factors alongside the frequency of T regulatory lymphocytes

Methods: Blood samples were collected from 40 patients admitted to the hospital for COVID-19 infection. Routine and specific biochemical and haematological laboratory tests were performed on the serum, and the frequency of Treg lymphocytes was measured using CD4⁺, CD25⁺, FOXP3⁺, and PD1 markers. The same tests were conducted on healthy individuals, and the results were compared. Correlation relationships of the measured factors were obtained using statistical software

Results: An increase in polymorphonuclear white blood cells was accompanied by a decrease in lymphocytes, while there was no change in red blood cells and platelets. Increased LDH, BUN, D-dimer, ESR, Fer, ALT, AST, PTT, were observed in all cases with different quantities. The measurement of the frequency of lymphocytes with the CD4⁺, CD25⁺, FOXP3⁺, and PD1 phenotype showed that their frequency increased in the blood of patients despite the decrease in total lymphocyte population

Conclusion: Changes in the abundance of haematological and blood biochemical factors with a specific pattern represent the severity and prediction of the course of COVID-19 disease, taking into account their quantitative values. The lymphocyte pattern in patients is accompanied by a decrease, but exhausted or regulatory lymphocytes tend to increase. Keeping in mind the quantity of laboratory factors provides a picture of the severity of disease progression or recovery for appropriate intervention.

Keywords: COVID-19; Regulatory T Cells; Biochemical Laboratory Tests.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OI-12

Expression of recombinant highly antigenic truncated fusion-based of CRP for use as a diagnostic antigen

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Abstract

Background and Aim: Serum C-reactive protein (CRP), is the first acute-phase protein to be described and is an exquisitely sensitive systemic marker of inflammation and tissue damage. The plasma levels of CRP in most of healthy subjects are usually 1mg/L, with the normal being defined as <10mg/L. detection of CRP in serum may be used at the primary care level to identify patients at risk of type 2 diabetes, CVD, Gestational DM and Diabetic Nephropathy. The production of recombinant highly antigenic truncated fusion-based CRP may be useful for developing its diagnostic methods.

Methods: In this research, we selected highly antigenic parts of the CRP sequences based on in-silico studies. The protein was expressed under optimum conditions in the bacterial host BL21 and purified by nickel immobilized metal affinity chromatography. Moreover, the purity level was assessed by SDS-PAGE and Western blotting. Ultimately, we used the purified recombinant protein instead of serum for detecting by Turbidometric assay.

Results: The concentration of recombinant CRP was measured by Turbidometric method as 0.2 mg/dl.

Conclusion: Our findings suggest that recombinant highly antigenic truncated fusion-based CRP can be used as a diagnostic antigen.

Keywords: C-Reactive Protein; Disease Risk; Recombinant Protein.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



6. Immunology (Poster Presentations)





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-1

Exploring the Role of miRNA and Docking in Drug Discovery for Colorectal Cancer Targeting Bcl-2

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Abstract

Background and Aim: Colorectal cancer (CRC) is a global health concern, and recent drug discovery efforts have focused on targeting the anti-apoptotic protein Bcl-2. MicroRNAs (miRNAs) are emerging as potential CRC therapeutic targets. This abstract highlight the role of miRNA-mediated Bcl-2 regulation and the utility of molecular docking to identify drugs that disrupt Bcl-2's function. This integrated approach offers promise for developing targeted CRC therapies, emphasizing the need for further research into these molecular mechanisms and computational techniques in drug discovery.

Methods: In our study, we undertook a comprehensive molecular docking investigation involving the Bcl-2 protein and a set of 525 compounds. Initially, we sourced the 3D structure of Bcl-2 from the Protein Data Bank (PDB ID: 4LXD) and refined it using Chimera 1.15 for the subsequent docking process. To ensure that our ligands were optimal, we curated compounds from the ZINC15 database, employing a 'standard-ok' and "clean" filters. Our docking experiments were conducted using the PyRx program via the Vina Wizard console. Post-docking, we rigorously assessed the results based on Binding Affinity and root mean square deviation (rmsd) criteria, both in upper-bound (rmsd/ub) and lower-bound (rmsd/lb) contexts to refine compound selection. Additionally, we explored the miRDB website to identify the top ten miRNAs with the highest target scores for Bcl-2, shedding light on potential therapeutic avenues in the context of cancer treatment and gene regulation.

Results: Based on the evaluation of Binding Affinity and root mean square deviation (rmsd) metrics, we identified three medications with highly favorable outcomes. These medications are referred to as ZINC150531571 (Molecular Formula: C₄₅H₄₅Cl₃N₆O₆S), ZINC49615871 (Molecular Formula: C₄₂H₃₆N₂O₈), and ZINC150531539 (Molecular Formula: C₄₇H₄₀Cl₂N₄O₆S). It is worth noting that these predicted drugs do not have official names assigned to them. Interestingly, our evaluation revealed that these three medications even outperformed the officially approved drugs eribulin and paclitaxel. Furthermore, we identified ten miRNAs with elevated target scores, which are as follows: hsa-miR-6867-5p (target score: 100%), hsa-miR-448 and hsa-miR-4495 (target score: 99%), hsa-miR-5692a and hsa-miR-4708-5p (target score: 98%), hsa-miR-3680-3p (target score: 96%), hsa-miR-3680-3p (target score: 94%), hsa-miR-486-3p, hsa-miR-202-5p, and hsa-miR-4262 (target score: 93%). These miRNAs represent our predicted set of ten miRNAs.

Conclusion: Our findings demonstrate the significance of miRNA-mediated regulation and docking techniques in the field of drug discovery for CRC targeting Bcl-2. The integration of these approaches provides a comprehensive understanding of the molecular mechanisms underlying CRC progression and unveils potential avenues for the development of novel therapeutic interventions. Further research and validation are warranted to translate these findings into clinical applications that can effectively combat colorectal cancer and improve patient outcomes.

Keywords: Colorectal Cancer; Drug Discovery; miRNA; Molecular Docking; Bcl-2.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-3

Investigating the relationship between serum cortisol and IgG against SARS-CoV-2 spike protein in vaccinated individuals

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Abstract

Background and Aim: Measuring the serum level of cortisol and its relationship with the serum level of anti-spike IgG produced in recipients of COVID-19 vaccines is a way of assessing the immunogenicity of the vaccine in people with different serum levels of cortisol. Therefore, the aim of this study was to investigate the relationship between the serum level of cortisol as a corticosteroid and the level of immune response against spike protein after vaccination.

Methods: This cross-sectional study recruited 80 vaccinated employees of Sabzevar University of Medical Sciences according to the type of COVID-19 vaccine they received. The entry criteria were receiving the second dose of the vaccine and informed consent. The exclusion criteria were active COVID-19, autoimmune diseases, and corticosteroid use. After obtaining written consent, 5 ml of venous blood was taken from each person at 7:00 am to 9:00 am. The blood samples were centrifuged and stored at -20°C until the completion of sampling and tests. An ELISA kit for measuring IgG against spike antigens and an ELISA kit for measuring serum cortisol levels were used. The relationship between serum cortisol level and anti-spike antibody concentration was analyzed according to age, sex, and vaccine type. The results were entered into SPSS22 and analyzed.

Results: Thirty-two (40%) were male and 48 (60%) were female. 28 (35%) had positive self-report and 52 (65%) had negative self-report of previous COVID-19 infection. 40 (50%) received Sinopharm vaccine and 40 received Sputnik V vaccine. The mean age was 34.81 ± 7.62 years. The mean serum concentration of anti-spike IgG was 103.6 ± 75.82 . The mean serum cortisol concentration was 6.43 ± 2.20 $\mu\text{g/dL}$. There was no significant difference between male and female in terms of mean age and serum concentration of anti-spike IgG antibody ($p > 0.05$). There was a significant difference between vaccine types in terms of serum concentration of anti-spike IgG antibody and serum cortisol level ($p < 0.001$). Sputnik V recipients had higher serum antibody level and serum cortisol level than Sinopharm recipients. There was no significant difference in serum cortisol concentration by gender ($p = 0.15$). There was no significant relationship between serum cortisol concentration and serum concentration of anti-spike IgG antibody ($p > 0.05$).

Conclusion: This study found no significant relationship between serum cortisol concentration and anti-spike IgG antibody titer. However, Sputnik V recipients had higher serum cortisol and anti-spike IgG levels than Sinopharm recipients. Thus, serum cortisol concentration seems unrelated to IgG antibody titer against spike protein of SARS-CoV-2.

Keywords: COVID-19; SARS-CoV-2; Cortisol; Vaccine; Anti-Spike IgG.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-4

Evaluating the relationship between duration of night sleep and neutrophil-to-lymphocyte ratio in individuals referred to Sabzevar PERSIAN cohort center

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Abstract

Background and Aim: Sleep and the immune system are directly and bilaterally related. Stimulation of the immune system by microbes causes an inflammatory response and often sleep disorder. Sleep disorders are also important predictors of disease. Neutrophil-to-lymphocyte ratio or NLR has been used in recent studies as an inflammatory marker, especially in diseases. In this study, the relationship between nighttime sleep and NLR was evaluated in individuals referred to Sabzevar PERSIAN cohort center.

Methods: In our cross-sectional study, 4113 individuals who referred to Sabzevar PERSIAN cohort center were asked about the amount of sleep at night and were divided into 5 groups based on it: 6 hours and less, 7 hours, 8 hours, 9 hours, 10 hours and more, and into 3 groups based on age: 35-45, 46-55, 56-70 years. CBC diff results were extracted from the files. Then the NLR differences were compared between groups using analysis of variance and Pearson's chi-squared test.

Results: In the study, 44.8% male and 55.2% female with a mean age of 49.18 ± 8.76 years were included. The average amount of night sleep was 7.1 ± 1.41 hours, which was higher in women. The mean lymphocytes was 2506.23 ± 772.65 cell/ μ l, the mean neutrophils was 3638.98 ± 1223.53 Cell/ μ l and the mean NLR was 1.56 ± 0.69 . No significant association was found between sleep hours and NLR with individuals' sex. However, there was a significant relationship between sleep hours and the mean NLR with individuals' age.

Conclusion: There is no significant relationship between night sleep duration and NLR.

Keywords: Sleep; Neutrophil to Lymphocyte Ratio; Neutrophil; Lymphocyte; Persian Cohort.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-5

Determining pro-oxidant Antioxidant Balance (PAB) in febrile children with and without seizure: A comparative study

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Abstract

Background and Aim: A benign condition known as a febrile seizure (FS) occurs between the ages of six and sixty months when the patient has a fever of at least 38 oC, is not suffering from a CNS infection or metabolic disorder, and has no prior history of febrile seizures. It is thought that oxidative stress contributes to the emergence of a number of neurodegenerative disorders by creating an imbalance between the ROS and antioxidants that scavenge them. In light of this, the current study examined the pro-oxidant antioxidant balance (PAB) in febrile children both with and without seizures.

Methods: The current cross-sectional study was done in the Children's department of Heshmatieh hospital, Sabzevar University of Medical Sciences, Sabzevar, Iran between March 2020 and March 2021. Blood samples were taken from forty febrile children with a temperature of 38 degrees and above, and forty febrile children who had experienced their first seizure. The pro-oxidant antioxidant balance was evaluated using ELISA method.

Results: The two groups were homogeneous and comparable in terms of age, sex and fever. The mean and standard deviation of the HK variable in the group of febrile seizure was 180.43 ± 9.28 and in the fever group without seizure was 131.83 ± 17.73 . In fact, the group of patients with febrile seizure had a higher mean serum level of prooxidant-antioxidant balance than febrile group without seizure (p value <0.05), which indicated that the level of oxidative stress in patients with febrile seizure was higher than the fever group without seizure.

Conclusion: The results of our study may support the hypothesis that if the serum level of antioxidants in a child with fever is lower, the child is more likely to have a febrile seizure than in a similar case but with a higher serum level of antioxidants.

Keywords: Antioxidant; Febrile Seizure; Fever; Oxidative Stress; Prooxidant.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-6

Mebendazole-treated human monocyte derived dendritic cells represent immunogenic phenotype with promoted inflammatory responses

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Abstract

Background and Aim: Among anticancer immunotherapies, there is growing interest in dendritic cell (DC)-based immunotherapy. DCs as specialized antigen-presenting cells are crucial for stimulating anti-tumoral T cells. DCs are equipped with pattern recognition receptors including nucleotide-binding and oligomerization domain like receptors (NLRs) such as NLRP3. Full activation of NLRP3 will lead to promoted DC activation with increased inflammatory responses. Recently, mebendazole (MBZ), a medication prescribed for helminthic infections, has drawn a lot of interest as a potential therapeutic option for cancer. It is demonstrated that mebendazole induce IL1 β release from immune cells and it was found to be dependent on NLRP3 inflammasome activation.

Methods: We hypothesized that mebendazole treatment of DCs generates immunogenic DCs by NLRP3 activation, so fresh peripheral blood from healthy donor was obtained and peripheral blood mononuclear cells was isolated by Ficoll and high purity separation of monocytes was done through Magnetic Activated Cell Sorting (MACS) technique. Then monocytes were cultured within the complete media and supplemented with rh GM-CSF, and rh IL-4 for 5 days to generate immature DCs. 10 μ M of mebendazole was added to the treatment DC group and 100 ng/mL of LPS was added to generate mature DCs. The morphological and phenotypic characterization of both DC groups were done. Phenotypic features of DCs were analyzed by staining for surface markers with Anti HLA-DR- APC, anti-CD86- PE, Anti CD11c- FITC and Anti CD14- FITC. Then Real-Time PCR was done to assess the expression of Interleukin 1 β (IL-1 β), IL-12 and IL-10 in mebendazole treated and untreated DC groups.

Results: Both of our DC groups' cells displayed CD11c, HLA-DR, and CD86 expression but a little expression of CD14 which verified the differentiation of monocytes to DCs. Mebendazole treatment of DCs significantly increased the surface expression of CD86 (**P \leq 0.01). The findings indicated that mebendazole resulted in significant increased expression of IL-1 β (*P \leq 0.05), increased expression of IL-12 (*P \leq 0.05), and significantly decreased expression of IL-10 (**P \leq 0.01). HLA-DR and CD11c expression were diminished (**P \leq 0.01).

Conclusion: Taken together, our findings indicated that mebendazole generates immunogenic DCs with increased expression of costimulatory molecule and high production of inflammatory cytokines but reduced anti-inflammatory cytokine. So, mebendazole-treated DCs can be a promising therapeutic approach against cancer. However, further research is required before this technique can be applied in clinical practice.

Keywords: Cancer; Dendritic Cell; Mebendazole; NLRP3.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PI-7

NLRP3 inflammasome in dendritic cells: potential therapeutic target in autoimmunity, cancer and infectious conditions

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Abstract

Background and Aim: Proper and functional immune response requires a complex interaction between innate and adaptive immune cells, which dendritic cells (DCs) are the primary actors in this coordination. These DCs are equipped with pattern recognition receptors such as NLRP3. NLRP3 is a crucial component of immune system for protection against tumors and infectious agents, because its activation leads to assembly of inflammasomes that cause the formation of active caspase-1 and stimulate the release of proinflammatory cytokines including IL-1 β and IL-18. But, when NLRP3 becomes overactivated, it plays a pathogenic role in incidence and progression of autoimmune disorders.

Methods: In the current study, we review recent studies about diverse mechanisms and signaling pathways that play a momentous role in regulation and control of NLRP3 activation. Role of NLRP3 in all of diverse immune cells' subsets are mentioned in this study because NLRP3 play a pivotal role in modulating innate and adaptive immune cells which are accompanied by DCs' responses. This review clarifies the functional and therapeutic role of NLRP3 in DCs and its contribution to progression of autoimmune disorders, prevention of tumors' development, and annihilation of various infectious agents, to be targeted specifically for improving DC-based immunotherapeutic approaches.

Results: NLRP3 play a pivotal role in modulating innate and adaptive immune cells which are accompanied by DCs' responses and subsequently influence differentiation of T cells to diverse T helper (TH) 1, TH2, TH17, regulatory T cells (T Reg) and even impact on cytotoxic CD8+ T cells responses. So, NLRP3 in DCs can be specifically targeted to generate modulated and tolerogenic DC to be utilized for prevention of autoimmunity, or activated DC with better antigen presentation capability and finally effective elimination of tumors, furthermore these immunogenic and fully activated DCs can be exploited to overcome infectious agents.

Conclusion: Several activator and inhibitor molecular signaling pathways regulate NLRP3 function. If NLRP3 becomes overactivated, it will lead to more caspase-1 activity and occurrence or progression of autoimmune disorders. But in contrast, there is need to fully activated NLRP3 for tumors' elimination, since NLRP3 activated DCs will be more powerful in tumor associated antigens presentation to T cells, generation of IFN- γ producing T cells, and induction of long lasting antitumor CD8+ T cells' responses. In conclusion, targeting NLRP3 have shown significant promise in modifying immune responses for improving DC-based immunotherapeutic approaches.

Keywords: Autoimmune Disorders; Dendritic Cell; Immunotherapy; NLRP3; Tumor.





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Tehran University of Medical Sciences, Tehran, Iran.
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Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-8

Evaluation of Hematological Markers as Predictive Tools for Disease Activity in Rheumatoid Arthritis Patients

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Abstract

Background and Aim: The evaluation of disease activity in rheumatoid arthritis (RA) patients is crucial for effective management and treatment. Current markers, such as CRP and ESR, have limitations in accurately reflecting disease activity. This study aimed to assess hematological markers as predictive tools for determining disease activity in RA patients.

Methods: A total of 305 RA patients were categorized into four groups based on DAS-28 scores: highly active, moderate activity, low activity, and remission. Hematological parameters including lymphocyte-monocyte ratio (LMR), platelet-lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR) were evaluated.

Results: Significant differences were observed in various hematological parameters among the RA groups. Hemoglobin, hematocrit, and lymphocyte counts were higher in the remission group compared to highly active RA, while RDW, MPV, and neutrophils were elevated in the highly active group compared to the remission group. NLR showed a positive significant correlation with DAS28-ESR, while PLR exhibited positive significant correlations with CRP, ESR, and DAS28-ESR. LMR showed a negative significant correlation with CRP. ROC curve analysis revealed that ESR had the highest area under the curve (AUC), followed by CRP, NLR, and PLR. ESR demonstrated good discriminatory ability, while NLR and PLR showed fair diagnostic performance in distinguishing active RA from inactive RA.

Conclusion: These findings suggest that hematological markers such as NLR and PLR hold promise as diagnostic tools for assessing disease activity in RA patients. These markers offer a convenient and cost-effective alternative to imaging techniques, with potential applications in routine clinical practice. Further research with larger cohorts and longitudinal follow-up is warranted to validate these findings and determine their clinical utility in guiding treatment decisions and monitoring disease progression in RA patients.

Keywords: Rheumatoid arthritis; Hematological Marker; NLR; PLR; MLR.





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Tehran University of Medical Sciences, Tehran, Iran.
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Section: Immunology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PI-10

The effect of synbiotic and probiotic on rheumatoid arthritis

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Abstract

Background and Aim: Nowadays, the improvement of the treatment process of rheumatoid arthritis (RA) as a chronic inflammatory disease is attributed to the proper state of intestinal microbiota.

Probiotic supplements (beneficial living microorganisms) and synbiotics (probiotics mixed with prebiotics) reduce inflammation by changing the intestinal bacterial composition due to inflammatory markers, insulin resistance and disease activity level (DAS-28). Synbiotics and probiotics can reduce inflammatory factors and disease complications and improve the disease process. This study aims to investigate the effects of synbiotic and probiotic supplements in rheumatic patients .

Methods: In this study, the effects of probiotic and synbiotic supplements on rheumatoid arthritis were investigated in PubMed and Scopus databases.

Discussion: Three studies of probiotics in RA patients provided data on IL-1 β . All three studies were pooled in a meta-analysis and showed a significant improvement in IL-1 β levels as a result of probiotic supplementation in 93 RA patients. Gut microecological regulator supplementation can reduce RA activity with a significant effect on DAS28, HAQ and inflammatory cytokines. Six studies provided data on the effects of probiotics on CRP levels and showed a significant effect in reducing CRP levels. Also, probiotic and synbiotic supplements had a significant reduction in inflammatory factors compared to placebo, which included changes in inflammatory markers and DAS-28, as well as beneficial effects on hs-CRP, DAS-28, VAS, insulin levels, pain scale, HOMA1 and homoeostatic model assessment- β -cell function (HOMA-B). Additionally, synbiotic supplementation increased plasma GSH levels. However, no significant improvement was observed in plasma nitric oxide (NO) levels.

Conclusion: Overall, our study showed that synbiotic and probiotic supplementation among patients with RA had beneficial effects on hs-CRP, DAS-28, VAS, NO, insulin levels, HOMA-IR, HOMA-B and GSH levels. had Therefore, probiotic and synbiotic supplements can help in the treatment process and improve the symptoms of the disease.

Keywords: Synbiotic; Prebiotics; Rheumatoid Arthritis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-11

Resolvin D1 attenuate induced autophagy in LPS-stimulated macrophage

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Abstract

Background and Aim: Chronic inflammation is associated with many inflammatory diseases. Specialized pro-resolving mediators (SPMs) are well known for their crucial role in promoting the resolution phase of inflammation and restoring tissue homeostasis. Resolvin D1 (RvD1) is an endogenous omega-3-derived lipid mediator with pro-resolving activity. This study aimed to evaluate the effect of Resolvin D1 (RvD1) on autophagy pathway genes (Becline1, LC3, Atg16L, Atg14) in an LPS-stimulated THP-1 preclinical model of inflammation.

Methods: PMA-differentiated THP-1 cells (macrophages) were pre-incubated with or without various concentrations of RvD1 (10, 50, or 100 nM) for 2 h prior to stimulation by 1 µg/ml LPS. Un-stimulated PMA-differentiated THP-1 cells were as the control group. Then, the expression levels of target genes were evaluated by real-time PCR.

Results: Compared with untreated macrophages, stimulation with 1 µg/ml LPS increased mRNA expression levels of TNF-α, ATG1($P=0.01$), Beclin1($P=0.01$) and LC3($p=0.01$) were significantly increased. When the cells were exposed to various concentrations (10, 50 and 100 nM) of RvD1 for 2 h prior to LPS stimulation, only Beclin1 and Atg16L has been elevated significantly. In general the expression of autophagy genes has not been significant.

Conclusion: The results demonstrate that RvD1 can attenuate inflammatory response in LPS-stimulated macrophages. Resolvin D1 attenuate induced autophagy in LPS-stimulated macrophage

Keywords: Inflammation; Autophagy; RvD1, Macrophages.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Systematic Review/Meta-Analysis

Code of Abstract: PI-13

Effect of apocynin and its derivatives on animal models of Parkinson's disease: A systematic review and meta-analysis

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Abstract

Background and Aim: Parkinson's disease (PD) is a complex progressive neurodegenerative disease that the dopaminergic neurons in the substantia nigra degenerate. The activation of NADPH oxidase produces reactive oxygen species and It contributes to the dopaminergic degeneration process in animal models of PD. Apocynin, acting as an NADPH oxidase inhibitor can be an effective approach to reduce the neurodegenerative processes in PD and can be an ideal therapeutic agent for the management of PD. In this review, we investigate the effect of apocynin and its derivatives on animal models of PD.

Methods: We systematically searched PubMed, Web of Science, Google Scholar, and Scopus from inception records to March 2023. We extracted the quantitative indices of the control and apocynin-treated groups to investigate and analyze the effect of apocynin and its derivatives treatment on these indices. The data analysis was done by using STATA software.

Results: Fifteen studies were included in this meta-analysis. In groups treated with apocynin and its derivatives; significant changes were seen in the parameters such as; gp91phox/ β -Actin (standard mean difference [SMD]: -4.40; 95% confidence interval [CI]: -5.89, -2.91), p47phox cytosolic/ β -Actin (SMD 5.86; 95% CI: 3.32, 8.41), p47phox membran/ β -Actin (SMD -4.74; 95% CI: -5.85, -3.63), p67phox cytosolic/ β -Actin (SMD 4.90; 95% CI: 3.85, 5.95), p67phox membran/ β -Actin (SMD -10.42; 95% CI: -17.11, -3.72), INOS/ β -Actin (SMD -3.78; 95% CI: -4.69, -2.87), NADPH oxidase activity (SMD -17.24; 95% CI: -20.75, -13.72) and LPO (SMD -13.65; 95% CI: -23.07, -4.23) which are involved in the pathogenesis of Parkinson's disease by causing oxidative stress. These findings demonstrated apocynin and its derivatives can inhibit NADPH oxidase and its subunits and improve PD in animal models.

Conclusion: Findings of our meta-analysis demonstrate apocynin and its derivatives inhibit NADPH oxidase and decrease oxidative stress as an important factor that is involved in the pathogenesis of Parkinson's disease in animal models of PD, so they can be potential therapeutic agents for PD.

Keywords: Parkinson's Disease; Apocynin; NADPH Oxidase Inhibitor.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Systematic Review/Meta-Analysis

Code of Abstract: PI-14

Effect of apocynin and its derivatives on animal models of Alzheimer's disease: A systematic review and meta-analysis

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Abstract

Background and Aim: Alzheimer's disease is a progressive neurodegenerative disease and amyloid beta plaques are one of the major hallmarks of AD. A β 1-42 monomers form oligomers and yield these plaques. These A β 1-42 structures can activate microglia cells and generate reactive oxygen species through NADPH oxidase enzyme. This enzyme increases oxidative stress and it appears to contribute to AD. apocynin acts as an NADPH oxidase inhibitor and because of its low toxicity and capability to pass blood brain barrier it is a potential therapeutic agent against AD. In this review, we investigate the effect of apocynin and its derivatives on the animal models of AD.

Methods: We systematically searched PubMed, Web of Science, Google Scholar, and Scopus from inception records to March 2023. We extracted the quantitative indices of control and apocynin-treated groups to investigate and analyze the effect of apocynin and its derivatives treatment on these indices. The data analysis was done by using STATA software.

Results: Seven studies were included in this meta-analysis. In groups treated with apocynin and its derivatives; significant changes were seen in the parameters such as; A β 1-42/ β -Actin (standard mean difference [SMD]: -5.06; 95% confidence interval [CI]: -6.26, -3.85), NOX2/ β -Actin (SMD -2.70; 95% CI: -3.39, -2.01), p tau/ β -Actin (SMD -3.06; 95% CI: -3.91, -2.20), p22phox/ β -Actin (SMD -3.99; 95% CI: -4.85, -3.13) and p47phox/ β -Actin (SMD -4.14; 95% CI: -5.94, -2.35) which are involved in the pathogenesis of Alzheimer's disease. These findings demonstrated apocynin and its derivatives can decrease these parameters by inhibiting NADPH oxidase and its subunits and improve AD in animal models.

Conclusion: Findings of our meta-analysis demonstrate apocynin and its derivatives inhibit NADPH oxidase, decrease oxidative stress and parameters that are involved in the pathogenesis of Alzheimer's disease in animal models of AD, so they can be potential therapeutic agents for AD.

Keywords: Alzheimer's Disease; Apocynin; NADPH Oxidase Inhibitor.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-16

The combination of exosomes derived from mesenchymal stem cells and hepatocytes reduces liver damage in a sepsis mouse model

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Abstract

Background and Aim: The liver plays a crucial role in the immune system by detecting, capturing, and eliminating harmful pathogens. However, during sepsis, the immune cells in the liver can cause systemic inflammation, leading to liver damage and dysfunction. As a result, multiple organs can become dysfunctional, which can ultimately result in death. Therefore, in this study, we investigated the effect of mixed exosomes derived from mesenchymal stem cells (MSCs) and hepatocytes in order to reduce liver tissue damage.

Methods: Mesenchymal stem cells and hepatocytes were extracted, cultivated, and confirmed. Exosomes were then extracted from these cells and confirmed using DLS and TEM methods. These exosomes were injected into mice after inducing the sepsis mouse model through the CLP method. After 48 hours, blood was drawn from the mouse's heart, and liver tissue was separated. The concentration of liver enzymes in serum was checked with an automated clinical chemistry analyzer. Histological alterations in the liver tissues were assessed by fixing them in a 4% formaldehyde solution. Slides were then prepared from each sample and colored with Haematoxylin and Eosin for histological analysis (H&E). Finally, a pathologist reviewed the slides.

Results: In the study, CLP mice treated with imipenem had the highest AST concentration. Treatment with MSC-derived exosomes decreased ALT concentration slightly. However, treatment with hepatocyte-derived exosomes+ imipenem or a combination of exosomes+ imipenem significantly reduced both ALT and AST levels. Liver damage was observed in all treated groups, while the control and sham groups showed normal morphology. Severe immune cell filtration and tissue necrosis were observed in the CLP group and imipenem-treated CLP mice. The other treated groups showed mild lipid degeneration, necrosis, and mild filtration of inflammatory cells.

Conclusion: Exosomes acquired from hepatocytes and a combination of exosomes derived from hepatocytes and mesenchymal stem cells have a beneficial effect in reducing liver tissue damage in an animal model of sepsis. These exosomes were found to significantly decrease the levels of liver enzymes, indicating that the liver function was returning to normal levels.

Keywords: ALT; AST; Liver Damage; Sepsis.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-17

A mixture of mesenchymal stem cell- and hepatocyte-derived exosomes reduce inflammation and apoptosis in liver of mouse model of sepsis.

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Abstract

Background and Aim: The cytokine storm in sepsis can cause a loss of hepatocytes leading to liver dysfunction, and as the liver regulates the body, its improper functioning can harm other organs. To prevent this, our study examined the impact of a combination of exosomes from mesenchymal stem cells (MSCs) and hepatocytes to reduce liver inflammation and damage.

Methods: First, mesenchymal stem cells and hepatocytes were extracted and cultured. They were then confirmed to be viable. Exosomes were extracted from these cells and confirmed using DLS and SEM methods. To induce sepsis in mice, the CLP method was employed. After this, the extracted exosomes were injected into the mice. Liver tissue was separated for further analysis. In the radioimmunoprecipitation assay (RIPA) solution containing protease inhibitors, 1 mg of liver tissue was homogenized. The Bradford technique was used to measure the protein content of the supernatant. Finally, the amounts of cytokines IL-6, IL-1 β , TNF- α , IL-10, and TGF- β in the liver homogenates were quantified by the ELISA method. The percentage of apoptotic cells was determined using the FITC Annexin V Apoptosis Detection Kit with PI and analyzed by BD FACS Canto II flow cytometry system.

Results: Following the surgery, there was a significant increase in the concentration of inflammatory cytokines in the CLP group, as compared to the sham group. Our study found that the treatment of MSC-derived exosomes+I mipenem effectively reduced pro-inflammatory cytokines and increased anti-inflammatory cytokines. However, the treatment of imipenem+ hepatocyte-derived exosomes proved to be more effective in decreasing TNF- α and increasing TGF- β . Furthermore, the most substantial increase in anti-inflammatory cytokines and decrease in pro-inflammatory cytokines was observed in the mixed exosomes group. Moreover, the CLP-induced groups showed a significant increase in liver apoptosis rate than the sham group ($P < 0.0001$). However, the apoptosis rate in all CLP groups treated with exosomes+imipenem was considerably lower than in the CLP group after 48 hours ($P < 0.0001$). The combination of exosomes from both MSCs and hepatocytes showed the lowest apoptosis rate.

Conclusion: The mixture of exosomes from mesenchymal stem cells and hepatocytes can more effectively reduce inflammatory responses and apoptosis in liver tissue than exosomes derived from each cell type alone.

Keywords: Cytokine; Apoptosis; Inflammation; Sepsis.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PI-19

Impact of NETosis in COVID-19 patients

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Abstract

Background and Aim: The SARS-CoV-2 virus caused the global outbreak of the Covid-19 disease. Considering the spread of infections and inflammations caused by this virus, it is important to know the factors and conditions of their creation in the development of treatment methods and their prevention. NETosis is defined as a unique form of cell death. Neutrophil extracellular traps (NETs) play an important role in antimicrobial defense by trapping and killing invading pathogens and minimizing damage to host cells. The purpose of this study is to investigate the cause of excessive stimulation of the immune system and excessive formation of NETs in COVID-19.

Methods: In this validity review, articles related to the topic using the determined keywords (autoimmunity, neutrophil extracellular traps (NETs), NETosis, inflammation, Covid-19) in reliable and international databases (PubMed and Google scholar and Science Direct) and the World Health Organization (WHO) website were searched. After collecting the search results, first the studies were studied based on the title, abstract of the article and then the full text of the article. If the articles were related to the topic, their results were used in the review.

Discussion: According to various reports and records, NETosis occurs in COVID-19 patients. According to immunocytological and immunohistological detection of neutrophil-derived proteins and extracellular DNA and citrullinated histones, detection of NET residues in liquid samples and flow cytometry detection of cell-dependent NET, citrullinated DNA was observed in the serum of these patients. Approximately 5% of patients with COVID-19 and 20% of hospitalized patients experience severe symptoms that require intensive care. Recently, it has been shown that COVID-19 infections stimulate neutrophils to produce NETs and antiviral agents and switch the cell to apoptosis. NETosis increases the risk of thromboembolism and DIC. Patients' serum has high levels of NETs components, including cfDNA, which leads to impaired fibrinolytic activity and increased thrombosis.

Conclusion: According to research results, although NETs play a role in host defense against pathogens, their overproduction leads to the presentation of self-antigens and activation of immune cells that contribute to autoimmunity. In patients with severe COVID-19, inflammation increases NETosis, which can be a factor for coagulation and autoimmunity. Therefore, the function of NETs can be considered as a "double-edged sword" and modulation of this process and degradation of NETs may be useful to reduce autoimmunity in septic and inflammatory conditions. Treatments that may be useful treatments in other autoimmune diseases.

Keywords: Autoimmunity; Extracellular Trap; Bloodstream Infection; COVID-19; Inflammation.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PI-20

Guillain-Barre Syndrome in Patients with COVID-19

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Abstract

Background and Aim: The SARS-CoV-2 virus caused the global spread of the COVID-19 disease. In addition to the respiratory system, this virus also affects the systemic system, kidney and central nervous system and causes the cascade of pro-inflammatory cytokines and high levels of D-dimer and low levels of platelets. GBS associated with COVID-19 has more severe symptoms, affects neurons and glial cells, and infects the central nervous system. In the state of inflammation, NETosis is created, autoantigens are active and free and cause neoantigens to appear and can stimulate the immune system and cause autoimmunity in GBS patients.

Methods: In this Narrative review, we included systematic review articles, randomized controlled trials, controlled clinical trials, and observational studies, case series, and case reports. articles related to the topic using the determined keywords (autoimmunity, NETosis, Guillain-Barré syndrome, neurological complications, COVID-19) in reliable and international databases (PubMed, Google scholar and Science Direct) and the web The World Health Organization (WHO) website was searched. After collecting the search results, first the studies were studied by two researchers separately by title, article abstract and then the full text of the article. If the articles have entry and exit criteria and are of the required quality based on the checklist, their results will be used in the review, otherwise they will be discarded.

Discussion: Based on studies, reports and data collected from articles, SARS-CoV-2 infection can be associated with different types of autoantibodies. This infection leads to thrombosis and coagulation disorders in many critically ill patients. Serological studies investigated the relationship between the onset of GBS and COVID-19 by identifying serum anti-ganglioside antibodies. 18.8% of patients were positive for serum anti-ganglioside antibodies. Neurophysiological findings also reported neurological manifestations. out of a total of 147 cases, 7.5% abnormal plantar response, 12.9% reported aphasia, 46.3% ataxia, 20.4% reported dysphagia, 42.2% facial paralysis, weakness, 4.1% fecal incontinence, 10.9% urinary problems, 17.7% hypogeusia or senility, 84.4% hyporeflexia or areflexia, 15.6% report hyposmia or anosmia, 7% back pain, 23.8% myalgia and 7.5% neck flexion weakness. Therefore, GBS is a severe condition that appears when the patient's own immune system attacks the cells of the peripheral nervous system, which can be seen in Guillain-Barre patients who are infected with COVID-19.

Conclusion: Based on research results, SARS-CoV-2 is the trigger for GBS because it follows the same para-infectious pattern as other disease agents involved in the initiation of GBS. Therefore, by evaluating biomarkers, diagnostic parameters and injury severity among GBS cases associated with COVID-19 and investigating the relationship between SARS-CoV-2 infection and GBS from a pathophysiological perspective, optimal management and treatment can be provided.

Keywords: Autoimmunity, NETosis, Guillain-Barré Syndrome, Neurological Complications, COVID-19.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Immunology

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PI-23

The role of NETosis in the pathogenesis of sepsis in patients with COVID-19

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Abstract

Background and Aim: The COVID-19 pandemic is one of the widespread viral diseases in the world, and the viral agent SARS-CoV-2 is involved in a wide range of autoimmune diseases. The most likely mechanism of autoimmunity in patients with COVID-19 is the ability of SARS-CoV-2 to overactivate the immune system, excessive release of NETS and molecular similarities between viral antigens and host components. Therefore, it is important to know the factors affecting it and the conditions of their creation in the development of treatment methods and prevention of this disease.

Methods: In this narrative review, articles related to the topic using the determined keywords (autoimmunity, neutrophil extracellular traps (NETs), NETosis, sepsis, inflammation, COVID-19) in authoritative and international databases (PubMed and Google scholar and Science Direct) and the World Health Organization (WHO) website were searched. After collecting the search results, first the studies were studied by two researchers separately by title, article abstract and then the full text of the article. If the articles have entry and exit criteria and are of the required quality based on the checklist, their results will be used in the review and otherwise they will be discarded.

Discussion: In patients with COVID-19, during neutrophil granulation, the overactive coagulation system and the damage of the lung inflammatory tissue are aggravated. and increases DIC and leads to acute lung injury (ALI). The serum of sepsis patients has high levels of NETs and thrombocytopenia occurs during sepsis due to the binding of activated platelets to NETs. According to reports, the close connection of COVID-19 with sepsis and septic shock has caused the highest number of deaths in patients hospitalized in the intensive care unit. 80% of cultured samples from septic patients of COVID-19 show that viral infection is the only cause of sepsis. High serum levels of NETs in COVID-19 patients have been reported to trigger inflammatory cascades. Several clinical studies have shown severe neutrophilia in patients who died of COVID-19 compared to survivors. In addition, changes in olfactory ability Anosmia/hyposmia can occur similarly to autoimmune diseases.

Conclusion: Based on the studies, more than 15 types of autoimmune diseases including, GBS, AIHA, ITP, SLE, cranial polyneuritis, Graves' disease, vasculitis, viral arthritis, myasthenia gravis and type 1 diabetes in COVID-19 was observed. these findings suggest that NETosis and hyperinflammation are two major factors in the pathogenesis of severe COVID-19. Since thrombocytopenia during sepsis is due to the binding of activated platelets to NETs, it is necessary to evaluate the activity of NETosis and sepsis in COVID-19 patients and assess whether the clinical course of the disease may modulate NETosis.

Keywords: Autoimmunity; Extracellular Trap; Bloodstream Infection; COVID-19; Inflammation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-24

Effect of 50-Hz magnetic field exposure duration on Th17 and Treg cells

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Abstract

Background and Aim: Due to the increasing use of electronic devices generating extremely low frequency magnetic fields (ELF-MFs), concerns about their harmful effects on human health are increasing. The results of previous studies indicate a relationship between MFs and function of the immune system. It is supposed that variation in MF duration may exert an impact on the immune system. Therefore, different duration effects of ELF-MF exposure on gene expression of ROR- γ t and Foxp3, transcription factors in differentiation of T cells into Th17 and Treg cells, also IL-17 and TGF- β genes, that are related to the function of these cells, were investigated.

Methods: Twenty-four Wistar male rats were equally divided into exposure and control groups. The exposure group was exposed to the MF with density of 100 μ T and frequency of 50 Hz for 90 days and 2 hours a day. The control group was placed in the same condition for two hours every day in the turned off device. After weighing the rats blood samples were collected from their eyes on days 0, 30, 60, and 90, and the expression level of genes was measured by reverse transcription quantitative polymerase chain reaction. On day 90 of exposure, the rats were sacrificed and their spleen and thymus were isolated and weighed.

Results: The results showed that the weight of rats, their spleen, and thymus were not changed compared to the control group during 90 days of exposure to magnetic field. After 30 days of exposure, relative expression of the interleukin-17 gene in the exposed group was significantly decreased (mean = 0.59, P = 0.034) compared to the control group (mean = 1). The expression of other genes did not change significantly in any of the times.

Conclusion: It seems that 50 Hz MF in the short term can reduce the production of interleukin 17 and possibly reduce the function of Th17 cells and inflammation. Therefore, it is hoped that 50 Hz MF can be used to treat inflammatory and autoimmune diseases in the future.

Keywords: Cytokines; Transcription Factors; Immune System; Extremely Low Frequency Magnetic Fields.

Ethical Consideration: This work was approved by the Ethics Committee of Hamadan University of Medical Sciences (Code: IR.UMSHA.REC.1400.978).





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-25

Investigating the Effects of Exosomes Derived from Mesenchymal Stem Cells and Hepatocytes on Blood Cell and Lymphocyte Populations in the Mesenteric Lymph Node

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Abstract

Background and Aim: Sepsis is a life-threatening condition that occurs when the body's response to an infection harms its tissues and organs. In septic patients, it has been observed that there is a decrease in the number of circulating T cells, primarily due to apoptosis and T-cell exhaustion. This causes the immune system to become dysregulated and reduces the body's ability to effectively fight against invading pathogens. In this study, we investigated the effect of hepatocyte- and mesenchymal stem cell-derived exosomes on blood cells and T-cell populations in mouse models of sepsis.

Methods: In the initial step, mesenchymal stem cells and hepatocytes were extracted, cultured, and confirmed by using flow cytometry. Exosomes were extracted from these cells and were confirmed using SEM, TEM, and flow cytometry methods. Sepsis was induced in mice using the CLP technique, and the exosomes were then injected into the mice. After 48 hours, mice from each group were sacrificed using chloroform, and the mesenteric lymph nodes were separated. The presence of TCD8⁺ cells, TCD4⁺ cells, and regulatory T (Treg) cells were analyzed using flow cytometry. Additionally, lymphocytes and neutrophils were counted in the blood.

Results: Exosome treatment resulted in significantly higher TCD4⁺ cells in the mesenteric lymph nodes of all groups compared to the CLP group. MSC exosome treatment showed the maximum increase. Hepatocyte-derived exosome treatment resulted in significantly higher TCD8⁺ cells in the mesenteric lymph nodes compared to the CLP group. However, the MSC exosomes-treated group had significantly lower TCD8⁺ cells. All exosome-treated groups had significantly higher Treg cells. The CD4⁺/CD8⁺ ratio in the CLP group treated with the mixture exosomes did not differ from the control group. The WBC count significantly decreased in all treated mice compared to the control group. The number of lymphocyte and neutrophil counts was significantly higher compared to the sepsis group.

Conclusion: The combination of exosomes from mesenchymal stem cells and hepatocytes can prevent blood cells and lymphocytes of mesenteric lymph nodes reduction.

Keywords: Exosome; Lymphocyte; Sepsis; Mesenchymal stem cell; Hepatocyte.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PI-26

Gene editing strategies to overcome existing barriers of CAR-T cell therapy in solid tumors

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Abstract

Background and Aim: Although chimeric antigen receptor (CAR)-T cell therapy has been revolutionary in the treatment of B-cell malignancies, there are still several hurdles in CAR-T cell therapy for solid tumors. In recent years, the ability to genome-editing of CAR-T cells by gene editing tools such as CRISPR/Cas9 has laid a groundwork to unlocking the bottlenecks of CAR-T cell therapy in solid tumors. In the present study different gene-editing strategies to boost safety and efficacy of CAR-T cell therapy in solid tumors are summarized.

Discussion: CAR-T cell therapy in solid tumors faces two robust obstacles: poor trafficking of CAR-T cells into tumor sites, and immunosuppressive tumor microenvironment. We analyzed different clinical and preclinical studies of genome-edited CAR-T cells to find out how the gene editing strategies can overcome the existing barriers of CAR-T cell therapy in solid tumors. We classified these strategies into the following categories: disruption of negative regulators of CAR-T cells, modulation of cytokine/cytokine-receptor genes, and generating universal allogeneic CAR-T cells.

Studies have revealed that disruption of the genes encoding PD-1, LAG3, and TIM3, the key mediators of T cell exhaustion, results in increased persistence of CAR-T cells. Additionally, several other molecules which are involved in T cell exhaustion have been successfully disrupted by gene editing tools, these molecules include: CISH, DNMT3A, Cbl-b, NR4A, Diacylglycerol kinases, adenosine A2A receptor, ID3, SOX4, and PTP1B.

Genetic ablation of IL-6 and GM-CSF prevents cytokine release syndrome and neurotoxicity, and increases the durability of CAR-T cells. It has been shown that CRISPR/Cas9-mediated disruption of TGF- β receptor II can overcome the immunosuppressive tumor microenvironment. Site-specific insertion of an IL-15 coding sequence at the IL13 cytokine gene locus leads to more production of IL-15 and better function of CAR-T cells.

Gene editing by removing TCR and MHC molecules from the surface of CAR-T cells has paved the way to safe use of universal allogeneic CAR-T products.

Conclusion: The increasing number of clinical trials with genome edited CAR-T cells for solid tumors indicate that these products have shown promise in the treatment of solid tumors. Nevertheless, off-target activity of gene editing tools and long-term consequences of disrupted genes are still a major concern. This highlights the need for long-term follow-up of treated patients.

Keywords: Chimeric Antigen Receptor T Cell; Solid Tumors; Gene Editing; CRISPR/Cas9.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PI-27

The effect of SARS-CoV-2 on blood-testis barrier (BTB): an important consequence of COVID-19 on male reproductive health

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Abstract

Background and Aim: On 30 January 2020 WHO declared a public health emergency of international concern over the global outbreak of coronavirus disease of 2019 (COVID-19). COVID-19 has several long and short-term effects on individuals who are infected with SARS-CoV-2. The effect of SARS-CoV-2 on male semen parameters is one of the crucial issues of concern that could happen during the illness, recovery period, and even after recovery. These effects are mostly due to the tendency of SARS-CoV2 to bind to the ACE2 via its Spike protein, which helps the virus enter the cell. Although TMPRSS2 protein has an auxiliary role. The strong expression of these two proteins in most cells of the reproductive system justifies the vulnerability against the coronavirus. The blood-testis barrier (BTB) is basal tight junction Sertoli cells within seminiferous tubules and prevents antigens or antibodies from disrupting spermatogenesis via infection or immune system over-activation.

Methods: Scopus, PubMed, and Google Scholar were searched with five keywords up to November 2023. A total of 18 articles were selected based on inclusion and exclusion criteria.

Discussion: The expression of ACE2 is seen in sertoli, Leydig, and testicular epithelial cells. Virus entry into the reproductive system cells leads to the production of pro-inflammatory cytokines including IL2, IL6, IL8, and TNF- α . This inflammation causes disturbance in the permeability of BTB, oxidative stress, and DNA fragmentation of spermatozoa and finally decreases the quality of the semen. Studies on autopsy of COVID-19 patients showed that men with higher levels of expression of ACE2 on the testis were at greater risk for impaired spermatogenesis. A study by Gacci et al. found that 77% of the 33 patients with COVID-19 have had elevated levels of semen IL-8 which is associated with inflammation. Besides the direct effect of SARS-CoV-2 on the male reproductive system, the inflammatory damage observed in the testes may be an indirect effect of immune system action to eliminate viral presence. A study by Basolo et al. found that CD8+ cells infiltrate within the seminiferous tubules and clusters of CD68+ were present in the extra tubular space. Moreover, they showed that viral loads in the testes were low in most cases and the COVID-19 group had a significantly higher amount of inflammatory cell infiltrates in the testes compared with the control group. Consistently, histopathology analysis of patients with COVID-19 revealed thinning of the seminiferous epithelium, increased apoptotic cells, spermatogenic epithelium shedding in the seminiferous tubules, and leukocyte infiltration which leads to the disruption of the BTB and the destruction of seminiferous tubules. Also, hypogonadism and lower testosterone levels were seen in patients with COVID-19 which could be related to the disrupted function of leydig cells and cause negative effects on male reproductive health.

Conclusion: Conclusively, COVID-19 could disrupt the BTB directly or indirectly and cause impaired spermatogenesis.

Keywords: Coronavirus Disease; SARS-Cov-2, Male Reproductive System; Blood-Testis Barrier; Infertility.

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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Immunology

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PI-28

The stimulating role of *Prevotella copri* in triggering auto immune diseases

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Abstract

Background and Aim: The role of intestinal microbiota in the pathogenesis of autoimmune diseases such as multiple sclerosis, rheumatoid arthritis and type 1 diabetes has been significantly considered and can be important in the differentiation of immune cells. Therefore, changes in intestinal microbiota can contribute to inflammatory and autoimmune diseases. The purpose of this study is to review the role of *Prevotella copri*, which is one of the most common species of the human gut microbiome, in autoimmune diseases.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, Google Scholar, and Embase from 2016 to 2023 by using the keywords Auto immune disease, *Prevotella copri*, gut microbiota, 64 articles related to inclusion criteria were extracted and then analyzed.

Discussion: The results indicate that various factors can affect the intestinal microbiome, such as geographic location, diet, gender, and age. Also, *Prevotella copri*, as a common species of human intestinal microbiome, is directly related to human health, so that its colonization leads to rheumatoid arthritis, mimics the production of synovial and ribosomal peptides.

Conclusion: Many autoimmune diseases are associated with changes in the composition and function of the gut microbiome. And many studies have shown the role of *Prevotella copri* in pathogenesis and quantitative and qualitative microbial changes in autoimmune diseases.

Keywords: Auto Immune Disease; *Prevotella Copri*; Gut Microbiota.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-29

The Association of Nasal and Blood Eosinophils with Serum IgE Level in Allergic Rhinitis and Asthma

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Abstract

Background and Aim: Allergic rhinitis and asthma are two common respiratory diseases with allergic etiology in the world's population. Eosinophils and serum IgE levels have been known as inflammatory allergy markers for many years. It has always been of great importance to find biomarkers that can be used in early diagnosis or prediction of disease severity. Cellular biomarkers, such as eosinophil count in blood or nasal secretions, as well as biochemical biomarkers like serum IgE level, are more accessible and affordable than molecular biomarkers. The possible relationship between allergy biomarkers, especially that between IgE and nasal eosinophil counts, has not been studied so much. The aim of this study was to evaluate the correlation of nasal and blood eosinophils with serum IgE levels in allergic rhinitis and asthma.

Methods: This prospective study was done on patients (n=78) diagnosed with asthma (n=20), allergic rhinitis (n=49), and chronic rhinosinusitis with nasal polyposis (CRSwNP) (n=9) at our hospital in Ahvaz city, Iran. The age of participants in our study ranged from 3 to 73 years, and all of them were subjected to a complete blood count (CBC) test, nasal smear, and determination of serum IgE levels after their consent. Nasal smear samples were taken from the nostrils of all patients using a sterile cotton swab. Two or three nasal smear slides were prepared, which were stained with Wright-Giemsa after drying. Then, the nasal smear was examined with an optical microscope, and cell differentiation was performed to assess the percentage of eosinophils, neutrophils, basophils/mast cells and goblet cells. Patients' blood was collected in a tube containing ethylene diamine tetra acetate (EDTA) to perform a CBC test. Besides, patients' sera were used to evaluate IgE levels. Serum IgE levels were measured using the ELISA (enzyme-linked immunosorbent assay) technique.

Results: There was no correlation between serum IgE level and nasal eosinophil count ($p=0.728$) or between serum IgE level and blood eosinophil count ($p=0.657$); however, a positive correlation was detected between blood and nasal eosinophil levels ($p=0.003$). This observation was a function of pooling data from all three groups irrespective of disease type.

Conclusion: No significant correlation exists between serum IgE levels and blood or nasal eosinophil counts in allergic rhinitis and asthma. Serum IgE levels and blood or nasal eosinophil counts can be used individually for patient follow-up because of their diagnostic role in allergic rhinitis and asthma, but no significant relationship was detected between them. Nevertheless, an increased blood eosinophil level is correlated with elevated nasal eosinophil level.

Keywords: Asthma; Allergic Rhinitis; Nasal Eosinophils; IgE.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PI-30

Fatty acid binding protein 4 (FABP4) in autoimmune diseases

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Abstract

Background and Aim: Autoimmune diseases are a group of disorders that arise when the immune system mistakenly attacks healthy cells in the body. Fatty acid binding protein 4 (FABP4, also known as A-FABP or aP2) is a member of the FABP family abundantly expressed in adipocytes, macrophages, and endothelial cells. FABP4 functions as a lipid-binding chaperone that regulates trafficking and cellular signaling of fatty acids. As an adipokine, FABP4 plays a crucial role in the regulation of lipid metabolism and inflammation. The objective of this study is to investigate the potential effects of FABP4 as an adipokine in autoimmune diseases.

Method: We conducted a literature search on the role of Fatty acid binding protein 4 (FABP4) in autoimmune diseases using PubMed as the database. We selected relevant studies based on the following keywords: "Autoimmune Diseases"[Mesh] AND ("adipocyte lipid binding protein" OR "ALBP protein" OR "aP2 protein" OR "fatty acid-binding protein aP2" OR "AFABP protein" OR "FABP4 protein" OR "adipocyte fatty acid-binding protein" OR "A-fabp protein" OR ("fatty acid binding protein 4" AND adipocyte) OR "fatty-acid-binding protein 4" OR "ALBP protein" OR "adipocyte fatty acid binding protein" OR "A-FABP protein" OR ("fatty acid binding protein 4" AND adipocyte) OR "P2 adipocyte protein" OR "422 adipocyte protein" OR "aP2 protein").

Discussion: Recent studies have shown that FABP4 is involved in the pathogenesis of several autoimmune diseases, including type 1 diabetes, rheumatoid arthritis, as multiple sclerosis (MS), and systemic lupus erythematosus. Also, FABP4 might be useful for the prediction of onset of pre-eclampsia in pregnant women with T1D. Additionally, FABP4 contributed to proteinuria in IgAN (nephropathy). Increased level of urinary-FABP4 could be a useful surrogate biomarker for assessment of glomerular damage in nephropathy. Furthermore, FABP4 has been implicated in the regulation of adipose tissue inflammation, which is associated with the development of metabolic disorders such as obesity and type 2 diabetes. Moreover, decreased levels of FABP4 have been associated with a reduced risk of developing autoimmune diseases such as Graves' ophthalmopathy. FABP4 is expressed in various immune cells, including macrophages, dendritic cells, and T cells, and it regulates the production of pro-inflammatory cytokines and chemokines. In addition, FABP4 has been shown to promote the differentiation of T helper 17 cells, which are involved in the development of autoimmune diseases.

Conclusion: The current study summarizes the current knowledge on the role of FABP4 in the pathogenesis of autoimmune diseases and discusses the potential of FABP4 as a therapeutic target for these disorders.

Keywords: Fatty Acid Binding Protein 4; Autoimmune Diseases; Biomarker.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-31

Mebendazole-treated dendritic cells can be mostly shifted in an immunogenic direction as a therapeutic option for the management of cancer

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Abstract

Background and Aim: Given their vital role in connecting innate and adaptive immune responses, dendritic cells (DCs) are regarded as the central part of the immune system. Activatory molecules, such as NLRP3, can be induced to increase the activity of DCs in the process of DC-based cancer immunotherapy. Following the administration of mebendazole, an anti-parasite medication, it was shown that TLR8 stimulation and NLRP3 inflammasome activation can be required for the production of IL-1 β in DCs. In this article, we will discuss how mebendazole affects DC activation and, consequently, how these cells may be utilized in future DC-based vaccinations to treat different cancers.

Methods: The MTT test was used to establish the optimal dosage of mebendazole. Fractionation across Ficoll gradients was used to separate peripheral blood mononuclear cells (PBMCs) from the entire blood of a healthy individual. After that, monocytes were separated from the PBMCs employing the plastic adherence technique. The adherent cells were cultivated in the CM supplemented with 40 ng/mL of rh GM-CSF, 25 ng/mL of rh IL-4, and 50 μ M 2ME. On day 4, immature DCs were treated with the optimum dose of mebendazole and 100 ng/mL of LPS in order to be mature and activated. On day 5, we collected the cells to evaluate surface markers associated with DC activation in treated and untreated groups using flow cytometry. RT-PCR was utilized to assess the expression of genes linked to inflammatory and anti-inflammatory cytokines.

Results: Mebendazole modulated DC activation by raising the expression of CD86 ($P \leq 0.01$) and lowering the expression of HLA-DR ($P \leq 0.01$) and CD11c ($P \leq 0.01$), according to mean fluorescence intensity (MFI) results. In mebendazole-treated mDCs, there was a reduction ($P < 0.0001$) in the expression of IDO but an enhancement in the expression of IL-18 and TNF- α ($P \leq 0.01$) and ($P \leq 0.0001$), respectively.

Conclusion: When DCs are treated with mebendazole, they mostly shift in an immunogenic direction. Consequently, there was a reduction in the expression of anti-inflammatory cytokines and an increase in the expression of inflammatory ones. Moreover, following mebendazole treatment, DC surface markers can be modulated. These results imply that, in order to validate this notion, mentioned anticancer therapy method should be studied more thoroughly in preclinical studies.

Keywords: Dendritic Cell; Mebendazole; NLRP3; Cancer.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Immunology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PI-32

Schizophrenia and the role of immune system: Bench to bedside

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Abstract

Background and Aim: . Mental illness applies a major burden on human health, but treatments are preliminary. The role of the immune system in psychiatric diseases has been proven. These are some brain's immunomodulators: tumor necrosis factor (TNF), transforming growth factor (TGF)- β , ILs and many others. These are made and regulated within the brain parenchyma, where they act on microglia, neurons and other glia. Schizophrenia (SZ) is a severe progressive neurodegenerative as well as disruptive behavior disorder. diagnostic biomarkers were evaluated in patients in order to achieve a clear comparison between schizophrenic patients and healthy controls, also we want to explain the role of the immune system in SZ.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, Google Scholar from 2015 to 2023 by using the keywords: Schizophrenia(SZ), Neuroinflammation, Neuroimmunology, Psychiatry. 153 articles related to inclusion criteria were analyzed.

Discussion: An immune dysfunction and the involvement of infectious agents in the pathophysiology of schizophrenia are discussed since decades, however, may contribute shifting research into the direction of immunological alterations and inflammation as cause for schizophrenia.

Conclusion: With future advances in basic mechanisms, it is possible that immune modulation could be used to promote brain repair and cure the long-term effects of trauma. It is conceivable that cellular therapies and antibody-based treatments for SZ.

Keywords: Schizophrenia; Neuroinflammation; Neuroimmunology; Psychiatry.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PI-33

Dental pulp immune actions in normal and inflamed tissue

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Abstract

Background and Aim: Immune systems can defend against invaders to the dental pulp to save this region, however, if this process is not controlled, it can damage pulp. cells are players of immune system and their number and types are different in every stage of pulp condition. In this review, we studied the role of immune mediators by focusing on the cells, to better understand the importance of the immune system in the life of the pulp.

Methods: The search for this narrative review was conducted on Web of Science, Scopus, and PubMed databases. Search had no restrictions. And related references of these articles were evaluated. articles that describe immune mediators in normal, inflamed, and regenerated phases of dental pulp were selected.

Conclusion: There is a close connection between the health of the dental pulp and the immune response in that region, and either an absence or an overabundance of these reactions can have an impact on the structure and longevity of the pulp because it can cause pain and affect the quality of life. In this review, we studied the role of immune mediators by focusing on the cells, the condition of the dental pulp, and whether it is healthy or damaged to better understand the importance of the immune system in the life of the pulp.

Keywords: Dental Pulp; Immune Cell; Nonimmune Cell; Inflammation; Regeneration





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Case report

Code of Abstract: PI-34

Refractory immune thrombocytopenia with mature bone marrow megakaryocyte in patient with a long history of Systemic lupus erythematosus

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Abstract

Background and Aim: Rheumatic disease such as Systemic lupus erythematosus (SLE) is defined as an autoimmune disease in which heterogeneous abnormalities especially hematologic disorders act as an independent reliable marker for active disease as well as establishing the management of involvement mechanisms. To describe the salient features, diagnostic value of bone marrow megakaryocyte counts (BM-MG), therapeutic procedures, and management of refractory immune thrombocytopenia (RITP) during the course of SLE.

Methods: This retrospective study included a 46-year-old Caucasian woman with 18-year SLE history who experienced RITP (thrombocytopenia persisting longer than 12 months in an otherwise high dose of steroids therapy regardless of the bleeding disorders). The association between platelet count and therapeutic strategy, Laboratory investigations such as Bone marrow aspiration (BMA), Bone marrow biopsy (BMB), reviewed here comprehensively. Other underlying causes of acquired immune thrombocytopenia were excluded.

Results: A 29-year-old woman met the classification criteria for SLE including; malar rash, photosensitivity, antinuclear antibody (ANA), discoid patches, arthritis, hemolytic anemia, kidney involvement, antiphospholipid antibody and oral ulcers between 2005 and 2018. With respect to clinical significance such as; platelet count $\geq 15 \times 10^9/l$, bleeding (bleeding score < 8), bruising, chest pain, and fatigue was admitted in KOSAR hospital of SEMNAN between December 2019 and May 2022. ITP was diagnosed on the basis of the bone marrow tests after no evidence of SLE related thrombocytopenia. Considerable bone marrow results show active hematopoietic marrow (BMB) with adequate megakaryocyte number (BMA). The range delay between SLE and ITP diagnoses was 14 years. The patient achieved a complete response (CR) with pulse methylprednisolone (MP) in newly diagnosed phase, and had no response (NR) with variable and repeated courses of corticosteroids in the relapse phase, and platelet count increased in discontinuation of treatment.

Conclusion: Mature and sufficient number of megakaryocytes confirmed that the Secondary ITP is due to peripheral destruction rather than a failure of bone marrow. The patient experienced RITP in an otherwise excessive use of corticosteroids. So, with comprehensive reviews of patients' history and careful drug monitoring when are prescribed over the long time, shared decision-making between laboratory experts and medical professionals, we will indeed reach the remarkable achievements and successive lines of treatment with benefit overwhelming.

Keywords: Lupus Erythematosus Systemic; Megakaryocytes; Thrombocytopenia; Glucocorticoids.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PI-35

Interleukin-1 β and its Impact on Hippocampus and Hypothalamus: Mechanistic Insights in Occurrence of Chronic Insomnia Disorder

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Abstract

Background and Aim: Chronic insomnia is a frequently observed sleep disorder, characterized by difficulty in initiating or maintaining sleep, leading to reduced quality of life. The pathophysiology of chronic insomnia disorder (CID) remains poorly understood, but recent evidence has demonstrated that there is a positive correlation between the rise in interleukin-1 beta (IL-1 β) and the increased of insomnia severity in individuals diagnosed with CID. However, the precise mechanisms underlying this correlation remain unclear. In this regard, present review study focuses on elucidating the signaling pathways and biological mechanisms through which IL-1 β may influence sleep regulation by impact on the hippocampus and hypothalamus activity.

Methods: A comprehensive search was conducted to identify relevant articles. The databases such as PubMed, Scopus, and Web of Science were considered for inclusion due to their extensive coverage of medical literature. Medical subject headings (MeSH terms) and keywords related to the topic including IL-1 β , chronic insomnia, hypothalamus and hippocampus were investigated and combined using Boolean operators (e.g., AND, OR). By following this method, a comprehensive collection of information from medical databases was achieved, enabling the synthesis of evidence for the present review article.

Discussion: IL-1 β is a pro-inflammatory cytokine that has been described to regulate neuronal signaling, both in normal physiological states and diseases. The biological effects of IL-1 β are mediated by binding to the IL-1 receptor type 1 (IL-1R1). Its presence in the brain has been associated with specific areas such as the pyramidal cell layer of the hippocampus, cerebellum, pituitary gland, and hypothalamus. Recent studies show that high concentration of IL-1 β affects the function of hippocampus by influence on neuroinflammation, neurogenesis, neuroplasticity, synaptic transmission and neurotransmitters modulation. Importantly, hippocampus has been considered as a potential regulator of the hypothalamus functions. Interestingly, it has been demonstrated that both of these brain regions play a significant role in sleep-wake cycle regulation. According to this evidence, we presume that high concentration of IL-1 β can disrupt sleep-wake homeostasis and promote sleep disturbances and thus may be a factor in the occurrence and persistence of insomnia.

Conclusion: Such investigations may ultimately lead to the development of innovative therapeutic strategies for chronic insomnia targeting IL-1 β and related pathways. Over time, these fresh outlooks are likely to lead to the emergence of novel opportunities for therapy.

Key words: Chronic Insomnia; Interleukin-1 β ; Hippocampus; Hypothalamus.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PI-36

The correlation between gut microbiome dysbiosis and sleep disturbance: Highlighting the role of NLRP3/IL-1 β pathway

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Abstract

Background and Aim: Growing evidence shows that there is a correlation between gut microbiome dysbiosis and sleep disturbance, although the exact mechanism of this relationship is still unclear. Recent findings indicate that an imbalance in the gut microbiome can trigger inflammatory cascades. Importantly, inflammation is considered as a significant mechanism in the pathogenesis of insomnia. Importantly, several studies have reported that the NOD-like receptor protein (NLRP)-3 inflammasome activity as well as serum levels of interleukin-1 β (IL-1 β) are significantly higher in chronic insomnia individuals compared to control group. In this regard, we assume that gut microbiome dysbiosis may associate with sleep disturbance through the activation of the NLRP3/IL-1 β pathway and thus the present study reviews the evidence supporting this relationship.

Methods: A comprehensive collection of information was achieved from medical databases including PubMed, Scopus, and Web of Science. In order to identify related articles, keywords related to this topic including gut microbiome dysbiosis, NLRP3, IL-1 β and sleep were investigated and combined using Boolean operators (e.g., AND, OR).

Discussion: Recent studies have indicated that changes in intestinal microbiota contribute to brain dysfunction in various neurological inflammatory diseases. According to the available data, the change of the intestinal microbiome can cause a change in the normal ratio of the population of T-lymphocyte cells and cytokine release, resulting in an imbalance in the activity of the immune system and the occurrence of inflammatory disease. In this regard, it has been reported that various factors including gut microbiome metabolites such as lipopolysaccharide (LPS), dysfunction of the intestinal tight junction barrier caused by antibiotics, disruption of the normal functioning of genes in the cells lining the intestines, all of which linked to an imbalance in the composition of the intestinal microbiota, can cause the activation of the NLRP3/IL-1 β pathway. Interestingly, it has been demonstrated that the high concentration of IL-1 β by binding to the IL-1 receptor type 1 (IL-1R1) in different brain areas can affect the release and uptake of glutamate, γ -aminobutyric acid (GABA), serotonin and activation of the kynurenine pathway. According to the evidence, all these factors play an important role in sleep-wake cycle regulation.

Conclusion: Balancing the immune system in the management of chronic inflammation and regulating the gut microbiota can be a new and effective therapeutic approach for treating sleep disturbance.

Keywords: Gut Microbiome Dysbiosis; Interleukin-1 β ; NLRP3 Inflammasome; Sleep.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PI-39

mRNA Vaccine

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Abstract

Background and Aim: Vaccination has long been a successful method to prevent and control diseases. mRNA vaccine is an effective vaccination method to prevent various diseases such as infectious diseases, genetic diseases and cancer. Of course, this method faced challenges due to the excessive immunogenicity of the vaccine and the lack of an mRNA delivery system. By developing an effective and safe delivery system with modified mRNA, the effectiveness of the vaccine was increased and side effects were greatly reduced. According to the World Health Organization (WHO), the mRNA vaccine for COVID-19 has been approved. Currently, vaccines for clinical trials to prevent infectious diseases, cancer and genetic diseases have entered the experimental phase.

Methods: In this narrative review article, published articles from, PubMed, SIDCINAHL Scopus, Iran medex indexes from 2020 to 2023 were searched and studied. This search using keywords: Vaccine, mRNA, mRNA vaccine, were done and all related articles were studied and reviewed.

Discussion: Vaccines can be divided into 2 categories: saRNA (self-amplifying mRNA) and non-replicating mRNA. The non-repetitive mRNA contains a cap 5, UTR, open reading frame, a UTR 3, and a polyA tail that encodes the vaccine antigen. But saRNA has a different nature and can be increased by using alpha viruses. produce a large amount of protein of interest whose components include cap5, 5, UTR, NSP, subgenomic promoter sequence, open reading frame, 3, UTR and 3, poly A tail. After the saRNA is transferred to the cell, the NSP sequence is translated into the NSP polyprotein. which acts as a precursor of the Replicase complex. This complex transcribes the initial positive-sense RNA strand into a negative-sense RNA strand that is used as a template for subsequent replication. Recent advances in the field of mRNA vaccine can be seen in the prevention and treatment of various diseases such as infectious diseases, COVID-19, HIV, infectious viruses such as influenza, chronic infectious viruses, cancer and hepatitis C.

COVID-19: In late 2019, a new member of the coronavirus family emerged and spread rapidly. Understanding the molecular mechanisms of this pathogen has been effective for vaccine development. The effective mRNA vaccine for the prevention and treatment of this disease induced an immune response to the spike protein.

Cancer: In the last few years, the development of mRNA vaccine based on nanocarriers for the treatment of cancer has made great progress. Nanocarriers can resolve mRNA instability and improve the targeting of drug therapy. The basic principle of mRNA as a vaccine is cancer, which can deliver the target transcript of one or more encoding tumor-specific antigen (TSA) or (TAA) to the cytoplasm of the host cell, especially in APC, and then express it as the target.

Conclusion: Recently, significant progress has been made in the field of mRNA vaccines, and the data from human trials for mRNA vaccines related to infectious diseases and heart cancer are encouraging. But rational manipulation of the mRNA vaccine formula is needed to further improve delivery materials and to fully understand the mechanism of action of mRNA vaccine types in order to increase efficiency and minimize side effects.

Keywords: Vaccine; mRNA; mRNA Vaccine.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-41

Evaluation of the effects of platelet-rich plasma with low leukocyte percentage and platelet-rich plasma with high leukocyte percentage on the expression of membrane progesterone receptor α in PBMCs isolated from healthy fertile women

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Abstract

Background and Aim: In recent years, platelet-rich plasma (PRP) has gained attention for its potential therapeutic applications in various medical fields. PRP contains growth factors, and other bioactive substances. Progesterone has critical role in maintaining a healthy pregnancy due to immunomodulatory effects. The effects of P4 on target cells are associated with various progesterone receptors. Despite the growing interest in the therapeutic potential of PRP, there is a paucity of research exploring its influence on progesterone-related signaling pathways. Understanding how these PRP formulations may modulate the expression of mPR α in PBMCs can provide insights into the potential interplay between PRP, leukocyte content, and progesterone signaling.

Methods: Isolated PBMCs from 15 healthy volunteers were stimulated by PHA. Platelet-rich plasma with high leukocyte percentage (LR-PRP) and platelet-rich plasma with low leukocyte percentage (LP-PRP) were prepared in a two-step centrifugation process following a protocol. PLTs and PBMCs were co-cultured for 72 h in 5% CO₂ at 37°C. In the final stage, the percentage of membrane progesterone receptor α (mPR- α) were evaluated using polyclonal and monoclonal antibodies.

Results: The analysis of the obtained data shows that L-PRP and P-PRP decreased the expression of alpha-progesterone receptors on the surface of peripheral blood mononuclear cells, and the result obtained is significant in the ratio of 1/10 and 1/100 for cells treated by L-PRP compared to the control group ($P \leq 0.05$).

Conclusion: The results of the present study, despite the existing hypothesis, show that platelet products in the current conditions cause a significant decrease in the expression of progesterone receptors on the level of peripheral blood PBMCs. The use of this method as a treatment for women suffering from miscarriage needs more investigation.

Keywords: Platelets; Leukocyte-Rich PRP; Leukocyte-Poor PRP; Peripheral Blood Mononuclear Cells.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-41

Evaluation of the effects of Platelet-Rich Plasma with a low leukocyte percentage and Platelet-Rich Plasma with a high leukocyte percentage on the expression of membrane progesterone receptor β in PBMCs isolated from healthy fertile women

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Abstract

Background and Aim: Progesterone has critical role in maintaining a healthy pregnancy due to immunomodulatory effects. The effects of P4 on target cells are associated with various progesterone receptors. Platelets have been recently recognized as immunoregulatory cells. The study aimed to explore the impact of platelet-rich plasma (PRP) on the expression of membrane progesterone receptor β (mPR- β) in peripheral blood mononuclear cells obtained from healthy fertile women. The findings could contribute valuable insights into the potential effects of PRP on cellular responses related to progesterone in the context of women's reproductive health.

Methods: Isolated PBMCs from 15 healthy volunteers were stimulated by PHA. Platelet-rich plasma with a high leukocyte percentage (L-PRP) and platelet-rich plasma with a low leukocyte percentage (P-PRP) were prepared in a two-step centrifugation process following a protocol. PLTs and PBMCs were co-cultured for 72 h in 5% CO₂ at 37°C. In the final stage, the percentage of membrane progesterone receptor β (mPR- β) were evaluated using polyclonal and monoclonal antibodies.

Results: The analysis of the obtained data shows that L-PRP and P-PRP decreased the expression of beta-progesterone receptor on the surface of peripheral blood mononuclear cells and the result obtained is significant in the ratio of 1/100 compared to the control group.

Conclusion: The results of the present study, despite the existing hypothesis, show that platelet products in the current conditions cause a significant decrease in the expression of progesterone receptors on the level of peripheral blood PBMCs. The use of this method as a treatment for women suffering from miscarriage needs more investigation.

Keywords: Platelets; Leukocyte-Rich PRP; Leukocyte-Poor PRP; Peripheral Blood Mononuclear Cells.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-43

Assessing the Long-Term Efficacy of Sinopharm and AstraZeneca Vaccines Against SARS-CoV-2: A Cross-Sectional Study Among Employees and Students at Yasuj University of Medical Sciences

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Abstract

Background and Aim: The coronavirus pandemic is a global crisis caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), leading to coronavirus disease 2019 (COVID-19). Extensive efforts have been made to develop effective and safe vaccines against SARS-CoV-2, encompassing various types such as whole virus live attenuated or inactivated, protein-based, viral vector, and nucleic acid vaccines. This study aims to assess the efficacy of Sinopharm and AstraZeneca vaccines among the employees and students of Yasuj University of Medical Sciences.

Methods: This cross-sectional study involved 186 participants from Yasuj University of Medical Sciences who had received 2 or 3 doses of Sinopharm or AstraZeneca vaccines, with a minimum of one year having elapsed since their last vaccination. Following the completion of a demographic information questionnaire, blood was collected, and the level of neutralizing IgG antibody against the Receptor Binding Domain (RBD) or Spike S was assessed using the indirect ELISA method. The Immunological Status Ratio (ISR) of the samples was calculated in this semi-quantitative ELISA method, where an ISR below 0.8 is considered negative, and above 1.1 is reported as positive.

Results: Participants in this study comprised 54% male and 46% female. Sinopharm vaccine was administered to 51.1%, and AstraZeneca vaccine to 48.9%. The average ISR for the Sinopharm group was 4.467, and for the AstraZeneca group was 4.059, with no significant difference between the two groups ($p > 0.05$). All vaccine recipients in both groups exhibited an ISR above 1.1.

Conclusion: This study reveals that one year after receiving the last dose of Sinopharm and AstraZeneca vaccines, there is a high neutralizing antibody titer of IgG against COVID-19. Continued vaccination remains the most effective strategy for preventing virus contraction.

Keywords: COVID-19; Vaccine; Sinopharm; AstraZeneca; Neutralizing IgG.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PI-44

Genetically modified mesenchymal stem cell as a novel and promising approach for improved cell therapy of multiple sclerosis

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Abstract

Background and Aim: Multiple sclerosis (MS) is a chronic neurological autoimmune disease characterized by presence of inflammatory sites in central nervous system (CNS) leading to myelin sheath destruction. There is no definitive MS treatment and most commonly used therapeutic strategies are supportive and just attempt to reduce symptoms of the disease. Furthermore, there is a need to find new therapeutic approach. Currently there is a high interest in using mesenchymal stem cell in different neurodegenerative diseases especially MS which have immunomodulatory effects through cytokines, exosomes and apobodies.

Discussion: MSCs are self-renewing multi potent stem cells which have many advantageous usages as they have multi-organ homing property, low immunogenicity as they do not express MHCII and have low expression of MHCI, ease of isolation, secretion of multiple biological factors and the ability of differentiation to different cell types.

One of the biggest challenges in MSCs clinical application is their therapeutic efficiency. MSCs under the process of genetical modification before clinical usage may promote their immunomodulatory effects and give us the ability to control MSC secretomes to maximize their therapeutic effects and prevent probable side effects such as oncogenic properties of these cells.

In this study we reviewed immunological aspects and benefits of using engineered mesenchymal stem cell and evaluated current advances in this therapeutic approach and how this new trend can take place as the best promising immunotherapeutic tool.

Conclusion: The findings of recent studied represented that genetic engineering of MSCs is aimed at improving their clinical therapeutic properties via production of therapeutic molecules including target-associated cytokines and other modulating-related molecules with prominent immunomodulatory effects without interfering with their differentiation and self-regeneration manners.

Keywords: Gene Therapy; Immunotherapy; Mesenchymal Stem Cell; Multiple Sclerosis





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PI-45

The synergic effects of *Artemisia annua* on chemotherapy treatment in cancer cells

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Abstract

Background and Aim: The *Artemisia annua* plant produces artemisinin, which has strong antimalarial and anticancer effects. It was first shown to have anticancer properties in the early 1990s. Dihydroartemisinin (DHA) and artesunate are two noteworthy artemisinin compounds that exhibit anticancer properties. This review aims to explore the potential benefits of combining *Artemisia annua* and its derivatives with chemotherapy drugs such as cisplatin, doxorubicin, temozolomide, paclitaxel, and carboplatin to treat cancer cells, focusing on the underlying mechanisms that lead to synergistic effects.

Methods: For this investigation, MeSH keywords ("*Artemisia annua*", "Chemotherapy", and "Synergistic Effect") were used in Google Scholar and PubMed searches conducted between 2011 and 2023. We selected 30 pertinent articles based on relevance, forming the basis for our investigation into this study.

Discussion: DHA and artesunate, two of artemisinin's derivatives, exhibit exceptional anticancer activity against various cancer types. These derivatives work synergistically with cisplatin to treat head and neck squamous cell carcinoma and pancreatic ductal adenocarcinoma. They lead to disruptions in ferroptosis and mitochondrial homeostasis, which inhibit cell proliferation, induce cell cycle arrest, and increase cytotoxicity. Additionally, artesunate exhibits anticancer properties in lung and ovarian cancer cells by promoting cisplatin sensitivity through oxidative stress, DNA double-strand breaks, and downregulating RAD51. Low concentrations of DHA significantly enhance the apoptotic and necrotic effects of temozolomide, inhibit the development of glioma cells, and initiate autophagy, according to studies conducted on human glioblastoma cell lines and rat glioma C6 cells. Artesunate and carboplatin have synergistic anti-tumor actions in non-small cell lung cancer (NSCLC), increasing apoptosis and suppressing cell viability. In the same way, DHA, either by itself or in combination with carboplatin, triggers apoptosis in ovarian cancer cells. DHA promotes cellular cytotoxicity and medication synergism in ovarian cancer by downregulating the carcinogenic transcription factor FOXM1 and blocking MAPK signaling. A combination of artesunate and paclitaxel in a nanoparticle formulation shows a synergistic impact on breast cancer, improving treatment efficacy. An additional nanoparticle that combines paclitaxel and DHA for colorectal cancer shows enhanced apoptosis, effective intracellular absorption, and suppression of tumor growth. Additionally, doxorubicin and DHA together exhibit strong anticancer effects on a wide range of tumor cell lines, including those from the prostate, ovarian, breast, lung, and cervical cancers. This combination also significantly inhibits tumor development without causing significant damage. DHA and doxorubicin combination has been shown to have a synergistic anti-proliferative effect in human breast cancer cells (MCF-7), triggering apoptosis, lowering mitochondrial membrane potential, and activating caspase cascades.

Conclusion: The use of combination therapy, particularly for a range of cancers, has considerable promise since artemisinin molecules (particularly artesunate) improve therapeutic results while reducing toxicity. All of the findings highlight the value of artemisinin derivatives in combination therapies, providing potentially effective treatment options for a range of cancers while offering minimal risk to non-tumor cells. Importantly, the study reveals the molecular mechanisms and signaling pathways of artemisinin derivatives employed in combination therapy for various cancer types.

Keywords: *Artemisia Annua*; Chemotherapy; Synergistic Effect.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PI-47

Effect of rapamycin on the mTOR signaling pathway

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Abstract

Background and Aim: The mammalian target of the rapamycin (mTOR) signaling pathway serves as a critical regulator of cellular processes, playing a pivotal role in growth, metabolism, and cytoskeletal remodeling. Dysregulation of this pathway has been implicated in a variety of pathological conditions, including cancer and metabolic disorders. Rapamycin, a compound derived from the soil-dwelling fungus *Fusarium Oxysporum*, has garnered significant interest for its potential antiaging properties and its modulatory effects on the mTOR pathway. This review aims to analyze the current understanding of rapamycin's impact on the mTOR signaling pathway and its therapeutic implications across diverse cellular contexts.

Methods: A comprehensive search of Google Scholar and PubMed databases was conducted, employing the MeSH keywords "rapamycin", "sirolimus" and "mTOR" for articles published between 2015 and 2023. Based on predefined research criteria, 11 articles were ultimately selected for further analysis.

Discussion: Multiple studies have demonstrated that rapamycin effectively inhibits the mTORC1 complex, leading to a decline in protein synthesis and mRNA translation. This inhibition is hypothesized to promote autophagy, a cellular mechanism responsible for the degradation and recycling of cellular components, thereby enhancing cell survival and lifespan. Notably, one study revealed that the mTORC2 complex remained unaffected by rapamycin, continuing to function normally. This complex plays a crucial role in regulating cell survival, proliferation, migration, and cytoskeletal regeneration. Additionally, another study identified a broad range of effects exerted by rapamycin on the mTORC signaling pathway, including its influence on the immune response. Rapamycin has been shown to modulate the differentiation and function of antigen-presenting cells, which are vital for initiating an immune response.

Conclusion: These findings highlight the complex and multifaceted nature of rapamycin's influence on the mTORC signaling pathway. They further underscore the considerable potential of rapamycin as a therapeutic agent in diverse applications, encompassing anti-aging strategies, cancer treatment modalities, and immunotherapeutic approaches. Nevertheless, further research is crucial to fully elucidate the mechanisms of action underlying rapamycin's effects and to explore its potential therapeutic applications more comprehensively.

Keywords: Rapamycin; Sirolimus; mTOR.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PI-48

Role of Adipokine as a biomarker for Multiple Sclerosis

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Abstract

Background and Aim: Multiple Sclerosis (MS) is primarily defined by the targeted and coordinated inflammatory breakdown of myelin, resulting in axon loss. A growing of researchs indicates that metabolic alterations, including obesity and elevated BMI, are important risk factors for MS. Adipokines are hormones, such as Adiponectin and Leptin, that are generated by adipose tissue. Leptin can activate various immune cell types and generate inflammatory conditions. adiponectin's reduction results in a rise in highly inflammatory conditions. This study attempted to investigate whether adipokines are associated with MS .and whether they as biomarkers for the disease.

Methods: We conducted open-dated searches of PubMed, EMBASE, google scholar, Medline, and Scopus, using the terms 'Multiple sclerosis' or 'MS' AND 'adipokine OR 'leptin OR 'adiponectin.

Discussion: Adipokines have an impact on MS and are crucial in the inflammatory conditions. According to study by Matarese et al., MS patients have higher levels of leptin in both serum and CSF. These levels are adversely correlated with the percentage of Treg and with the CSF's production of IFN- γ . Accordingly, a number of investigations revealed that Treg accumulated in healthy adipose tissue. Along with adiponectin, which lead to a proinflammatory state, MS patients also have lower leptin level. The significance of consistent physical activity, especially exercise training, is being emphasized more and more for those with MS. Based on available data, exercise training has been shown to reduce adipose tissue and, increased levels of adiponectin and decreased level of leptin being linked to a decreased risk of relapse. These adipokines are thought to be biomarkers that aid in predicting the inflammatory conditions associated with MS disease.

Conclusion: Adipokine-secreting adipose tissues have a significant influence in the risk of MS development, as does an increase in BMI and obesity. Leptin and adiponectin can influence immune cells and secretory cytokines that lead to inflammatory conditions. This state may be advantageous for MS and lead to increased immune system stimulation in this autoimmune illness.

Keywords: Multiple Sclerosis; Adipokine; Adiponectin; Leptin.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-49

Assessment of the Incidence of Food allergy -Related Symptoms and Specific IgE Reactivity to Diverse Food Allergens among Patients Suspected Food Allergies in the Birjand Population

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Abstract

Background and Aim: Many people suffer from various allergies, especially those related to foods. Allergy is a common health issue worldwide. The key to preventing and treating allergy disorders is to recognize which allergens are common in each area. Various cultures have different common food allergies because of differences in their nutritional habits and genetic makeup. Accurate diagnosis and treatment of several allergic symptoms, including rash, eczema, conjunctivitis, and rhinitis, depend on knowing which allergens to avoid. Therefore, the purpose of this study was to evaluate which food allergens are most common and what allergic symptoms patients in eastern Iran suffer.

Methods: Patients with allergic symptoms were referred to the allergy clinic of Birjand City located in south Khorasan from 2016 to 2023. A commercial immunoblotting method was applied to assess the level of specific IgE against thirty-one different food allergens; a level of specific IgE above 0.7 IU/ml was considered positive.

Results: A total of 255 patients with a mean age of 29.43 ± 18.62 years and an M/F ratio of 0.57 were examined for specific IgE to the specified food allergens. Patients with the highest percentage of sensitization to allergens were those who consumed maize flour; other common allergens included wheat flour, carrot, celery, sesame seed, pistachio, and citrus mix (17.5%, 16.32%, 15.91%, 15.91%, 15.51%, 14.69%, 14.69%, and 14.5%, respectively). Furthermore, rash, eczema, rhinitis, and conjunctivitis were the most common allergy symptoms (64.31%, 21.96%, 8.23, and 5.49%, respectively).

Conclusion: Results of this study indicated that the most prevalent allergen is thought to be maize flour and that patients' most common symptom was rash.

Keywords: Allergy; Food allergens; Allergic symptoms; Specific IgE.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-51

Strong cytotoxic activity of NK cells ex vivo differentiated from human umbilical cord blood-derived CD34⁺ stem cells

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Abstract

Background and Aim: The efficacy of adoptive immunotherapies based on functional NK cells depends on the availability of sufficient numbers of these cells. We expanded umbilical cord blood (UCB)-CD34⁺ HSCs during 2 weeks and then differentiated them to NK cells. The percentage of ex vivo differentiated CD3⁻CD56⁺ NK cells was measured. In addition, the surface expression of NK-cell-associated activating and inhibitory receptors, as well as cytotoxicity and cytokine production against a tumor cell line, was examined to characterize the resultant CD3⁻CD56⁺ NK cell product.

Methods: We assessed NKG2D, NKG2A, NKp30, NKp44, NKp46, and the expression of CD107a, CD57, *FasL*, *PD-1*, and IFN- γ level after co-culture with K562 cell line.

Results: We found that UCB-CD34⁺-derived NK cells express significantly NKG2D, CD69, *FasL*, NKp44, and NKp46 receptors compared to the negative control. Also, UCB-CD34⁺-derived NK cells significantly expressed CD107a.

Conclusion: Our results point to the UCB-CD34⁺ cells as a potentially useful source with strong cytotoxic function for the production of allogeneic NK cells for adoptive cancer immunotherapy.

Keywords: Umbilical Cord Blood; Hematopoietic Stem Cells; Natural Killer Cells.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PI-52

A novel strategy for AML treatment: Bispecific T-cell engaging antibodies

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Abstract

Background and Aim: Bispecific antibodies are one of the innovative therapies being investigated for acute myeloid leukemia (AML), the most common acute hematologic malignancy in adults. By forcing cancerous cells toward effector cells, these antibodies enhance therapeutic efficiency by targeting two surface antigens- a tumor-associated antigen and an effector cell surface antigen- in a single molecule. Immunologic targeting signaling pathways and small compounds are part of this evolving therapeutic landscape. This review describes AML targets that have been studied for the application of bispecific antibodies, emphasizing their potential as salvage options or substitutes for conventional therapy, indicating a positive turn in therapeutic research.

Methods: Articles indexed in Google Scholar and Pubmed databases; applied MeSH available keywords for this topic were: “Bispecific antibodies” AND “T-cell-engaging” AND “AML” from 2015 to 2023 were included. finally, 11 articles were selected based on the criteria of the research.

Discussion: CD33 targeting: Bispecific T-cell engager AMG330 targets CD33 and CD3, exhibiting strong T-cell recruitment and activation. In preclinical studies, it effectively lysed KG-1 and U937 cells and activated T cells in AML patients' primary samples. Through immune checkpoint blockage, AMG330 increased its effectiveness by inducing T-cell-mediated pro-inflammatory conditions and prolonging life in AML mice. AMG330 has a bright future in treating AML, according to ongoing phase I studies in humans. CD123 targeting: The novel dual-affinity retargeting antibody MGD606 exhibits promise for AML treatment, binding CD123+ AML cells to CD3+ T cells and redirecting T cells to combat AML blasts. In mouse studies, even at 0.5 µg/kg doses, it effectively removed engrafted cells in peripheral blood. MGD606 rapidly decreased circulating CD123-positive cells, with sustained effects during infusion. A Phase I study for AML patients demonstrated a 32.1% complete response rate and good tolerability, establishing itself as a compelling treatment option. WT1 targeting: Essential for both cell survival and development, the zinc finger transcription factor regulates several genes and pathways in different forms WT1 oncogene mutations are connected to AML and other illnesses. These mutations cause AML. Lower full remission rates and poorer survival are thus linked to increased WT1 gene expression. Targeting HLA-A*02:01(+) and WT1(+) AML cells, a new WT1-BiTE construct stimulates T cells and shows promise both in vitro and in mice. Epitope spreading improves therapeutic potential by eliciting long-term T-cell responses. Clinical development is significantly hampered by TCR-like antibody cross-reactivity with other peptides on other HLA antigens. CD13 targeting: A zinc-dependent metalloprotease that affects tumor invasion, adhesion, and differentiation in myeloid cells. Monoclonal antibodies targeting CD13 induce apoptosis in AML cells. With little effect on normal bone marrow progenitors, a bispecific antibody that combines anti-CD3 and anti-CD13 fragments increases IL2- or IL7-stimulated PBMC cytotoxicity against CD13(+) AML cells.

Conclusion: This review paper presents a novel approach to treating AML by using bispecific T-cell-engaging antibodies. The encouraging findings provide a new framework for the development of immunotherapeutic strategies in hematological malignancies and highlight the potential of these unique BiTE antibodies as an efficient and focused therapeutic alternative for AML.

Keywords: Bispecific Antibodies; T-Cell-Engaging; AML.



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The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PI-53

A novel cancer treatment approach: Target protein degradation by proteolysis-targeting chimaeras (PROTACs)

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Abstract

Background and Aim: Protein degradation is the cell's mechanism of eliminating unwanted proteins and that is occurs through the ubiquitin-proteasome system. Ubiquitin is a small 9-kilodalton (kDa) protein that is attached to proteins. Defects in ubiquitination have been identified in a number of diseases such as cancer. Protacs are nanomolecules that are approximately small in size and can recruit proteins that cause cancer to the ubiquitin-proteasome machinery for degradation so we can use the balance between protein synthesis and degradation to treat cancer by produce a synthetic molecule like Protacs.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, Google Scholar from 2009 to 2023 by using the keywords: Protacs, Cancer, Ubiquitin-Proteasome System. 40 articles related to inclusion criteria were analyzed.

Discussion: Studies have shown an approach to treat human disease that is known as Protac or Proteolysis Targeting Chimeric Molecule. These peoteins can extract the cancer's proteins and destroy them. To overcome the problem with permeability into tumor cells, they replaced the peptide with a small molecule that binds either the protein target (E3 ligase). Therefore, although Protacs are effective, the concentrations necessary for their effects are quite high.

Conclusion: Protacs provide a new nanotechnology-based approach to target cancer-causing proteins for ubiquitination and degradation. The benefit of Protac technology is that it is versatile and can theoretically recruit any cancer or disease-promoting for degradation. Despite the advances in Protac technology, the molecule will require further derivation and chemical modifications prior to use in animal models and humans. Future directions will focus on further development of Protacs to convert them into more practical drugs for clinical application.

Keywords: PROTACs; Cancer; Ubiquitin-Proteasome System.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PI-54

Identification of Promising Antigens for Cytomegalovirus Vaccine Development

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Abstract

Background and Aim: Cytomegalovirus is seen as a dangerous pathogen for individuals with weakened or suppressed immune systems, such as organ transplant recipients, AIDS patients, premature infants, and people with different types of cancer. Currently, there is no authorized vaccine for CMV. The purpose of this study is to find suitable antigens for the vaccine.

Methods: Initially, the articles were reviewed to study the role of different virus antigens. Subsequently, the immunogenicity of these antigens was verified and confirmed using bioinformatics software: (e.g. IEDB).

Discussion: Antigens IE1, PP65, Gb, PC were selected as suitable vaccine candidate antigens.

Conclusion: By designing appropriate genetic construct for these antigens and then synthesizing the mRNAs, it is possible to develop an effective vaccine for cytomegalovirus.

Keywords: mRNA Vaccine; CMV.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-56

Evaluation the relationship between quality of life, anxiety, and Drug Consumption with CRP and RF in patients with rheumatoid arthritis

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Abstract

Background and Aim: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease affecting 1% of the global population, leading to joint inflammation and damage. RA patients, compared to the general population, are more susceptible to anxiety, depression, and cognitive disorders, contributing to a common cause of disability. Various studies indicate higher levels of RF and CRP variables associated with increased physical impairment and radiographic severity in RA patients, leads to an overall lower quality of life. Thus, this study aims to investigate the relationship between quality of life, anxiety, drug consumption, and the levels of RF and CRP in these patients.

Methods: This cross-sectional study utilized validated questionnaires, including SF36 for quality of life, Beck's Anxiety Inventory for anxiety, and drug consumption surveys. Additionally, RF and CRP levels were measured based on clinical information in the medical records of 100 RA patients visiting Imam Hussein Hospital in Shahrood. Following coordination with the treating physician and obtaining informed consent, patients (or their companions) were requested to answer relevant questions. The expression levels of CRP and RF were determined using laboratory results or patient records. Descriptive and inferential statistics, including frequency distribution and multiple linear regression analysis, were employed for data analysis. The normal distribution of data was assessed using the Kolmogorov-Smirnov test. The study investigated the relationship between quality of life, anxiety, drug consumption, and the levels of CRP and RF in these patients.

Conclusion: The obtained data revealed a positive association (Beta: 0.17, P-value: 0.05) between the duration of the disease and CRP levels, indicating a reverse (negative) relationship (Beta: -0.46, P-value: 0.02) with quality of life. Additionally, drug consumption demonstrated a significant and positive correlation with RF levels (Beta: 0.39, P-value: 0.04).

Keywords: Quality of Life; Anxiety; Drug Consumption; RF; CRP.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PI-57

Immuno-Oncology in Melanoma: A Comprehensive Review of Current Approaches and Future Perspectives

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Abstract

Background and Aim: Melanoma, a highly aggressive form of skin cancer, has historically been challenging to treat due to its intrinsic resistance to conventional therapies. However, the advent of immuno-oncology has revolutionized the treatment landscape, offering new hope for patients. This review provides a comprehensive overview of the use of immuno-oncology in melanoma, highlighting the current approaches and future perspectives in this rapidly evolving field.

Methods: A systematic literature search was conducted to identify relevant studies and clinical trials investigating the use of immuno-oncology in melanoma. Key databases were searched, and studies published between 2010 and 2022 were included. Data regarding treatment strategies, immune checkpoint inhibitors, combination therapies, biomarkers, response rates, progression-free survival, overall survival, and adverse events were extracted and analyzed.

Discussion: The use of immune checkpoint inhibitors, such as anti-CTLA-4 and anti-PD-1 antibodies, has shown remarkable efficacy in melanoma treatment. These agents have demonstrated durable responses and improved survival outcomes in both metastatic and adjuvant settings. Combination approaches involving immune checkpoint inhibitors with other immunotherapies, targeted therapies, or conventional treatments have further enhanced response rates and survival outcomes. Biomarkers, such as PD-L1 expression and tumor mutational burden, have shown promise in predicting response to immunotherapy and guiding treatment decisions. However, challenges remain in identifying reliable biomarkers and overcoming mechanisms of resistance.

Conclusion: Immuno-oncology has transformed the management of melanoma, offering unprecedented clinical benefits for patients. Immune checkpoint inhibitors have emerged as the cornerstone of treatment, providing durable responses and improved survival outcomes. Combination therapies and the exploration of novel immunotherapeutic targets hold promise for further enhancing treatment efficacy. The identification and validation of predictive biomarkers are crucial for personalized treatment strategies. Moving forward, ongoing research efforts should focus on optimizing treatment regimens, understanding mechanisms of resistance, and developing novel immunotherapeutic approaches. The use of immuno-oncology in melanoma represents a paradigm shift, paving the way for more effective and personalized treatment options for patients with this devastating disease.

Keywords: Immuno-Oncology; Melanoma; Immune Checkpoint Inhibitors; Combination Therapies.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PI-59

Fibrinogen-like protein 1, a novel diagnostic biomarker and immunotherapy target for various cancers

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Abstract

Background and Aim: Fibrinogen-like protein 1 (FGL1), a member of the fibrinogen family, is expressed predominantly in the liver and plays a role in promoting inflammation. According to Previous studies, FGL1 is a ligand for LAG-3, which has a negative correlation with cancer prognosis and metastasis.

Methods: A systematic search was conducted in PubMed, Scopus, Web of Science, Embase and Google Scholar for gray literature. Different combination phrases of "fibrinogen-like protein 1", "cancer" and "FGL1" were used. Excluding criteria were irrelevant to FGL1 or cancer and in vitro and review studies.

Results: The rate of FGL1 diagnostics is on the rise in numerous cancer types, including lung cancer, colorectal cancer, melanoma carcinoma and hepatocellular carcinoma. Also, a high level of FGL1 mRNA is associated with upregulating CD4+ regulatory T-cell and M2-like macrophage gene, epithelial-mesenchymal transition (EMT), Transforming growth factor-beta (TGF- β) and angiogenesis signaling pathway. Furthermore, FGL1 and LAG-3 correlate with the responsiveness of PD-1/PDL-1 blocked, so it can be used as a negative diagnostic marker and immunotherapy checkpoint inhibitor target.

Conclusion: LAG-3 is negatively correlated with different types of cancer prognosis and metastasis. It's also associated with resistance to PD-1/PDL-1 inhibitor. FGL1 as a ligand for LAG-3 can be used as a diagnostic biomarker and a new immunotherapy target. Recently, some antibodies and vaccines have been generated for FGL1, but more studies are required.

Keywords: Fibrinogen-Like Protein 1; FGL1; Cancer, Diagnosing; Immunotherapy.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-60

Changes in CD34⁺ cell count of peripheral blood in leukocyte reducing filters during regular whole blood donation

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Abstract

Background and Aim: Trapped cell population in leukoreduction filters (LRFs) contains such a significant number of CD34⁺ hematopoietic stem cells that can be recovered to be used in research studies.

Methods: Samples (n=20) were obtained from 10 first-time donors and 10 regular blood donors with more than 30 times blood donation. After separating leukocytes from LRFs by backflushing, total leukocyte number and differential count were determined in both groups using an automated haemocytometer. Then cell viability and CD34⁺ cell quantification was assessed using 7- aminocytomycin D and fluorescent-labeled monoclonal antibodies using flow cytometry, respectively.

Results: Total leukocyte count was $665 \pm 164.92 \times 10^6$ in the first-time blood donors and $883 \pm 233.89 \times 10^6$ in the regular donors, which were not significantly different ($P=0.08$). While the number of CD34⁺ cells was significantly reduced in the regular donors compared to the first-time donors ($0.58 \pm 0.20 \times 10^6/\mu\text{L}$ vs. $0.36 \pm 0.22 \times 10^6/\mu\text{L}$; $P=0.034$). There was no significant difference in terms of absolute neutrophil count ($10.58 \pm 3.66 \times 10^6$ vs. $13.17 \pm 6.45 \times 10^6/\mu\text{L}$; $P=0.349$), lymphocytes ($7.75 \pm 3.11 \times 10^6$ vs. $10.38 \pm 3.77 \times 10^6/\mu\text{L}$; $P=0.917$), and monocytes ($2.31 \pm 0.88 \times 10^6$ vs. $2.59 \pm 1.09 \times 10^6/\mu\text{L}$; $P=0.591$) between the first-time and regular donor groups, respectively. Based on the correlation coefficients, the participants' age had no significant effect on these variables.

Conclusion: The results of this study depicted that regular blood donation reduces the number of CD34⁺ cells in the peripheral blood (PB) of regular donors while it has no significant effect on the ratio of myeloid to lymphoid cells of the two groups

Keywords: Leukoreduction Filter; CD34⁺ Hematopoietic Stem Cells; Regular Blood Donation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-62

Comparison of the effects of exosomes derived from macrophages extracted from C57BL/6 mice and the drug pyrimethamine on RAW cell line polarization in the presence and absence of Leishmania parasite

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Abstract

Background and Aim: Leishmania parasite is an obligate intracellular parasite and causes a variety of diseases, including cutaneous, mucocutaneous, and visceral leishmaniasis. The cause of cutaneous leishmaniasis is a species of Leishmania called Leishmania major. immunotherapy is the best method of treatment. Macrophages have two phenotypes, M1 and M2, the activation of the M1 phenotype leads to the eradication of intracellular microbes, and on the contrary, the activation of the M2 phenotype leads to the spread of the disease. BALB/c mice (and RAW Cell Line), are unable to control the infection when exposed to Leishmania parasite While C57BL/6 mice are show M1 phenotype.

Methods: In this research, we are trying to investigate the effect of exosomes extracted from C57BL/6 mouse macrophages and the drug prymethamine on the polarization of RAW cell line to M1 phenotype in an in-vitro environment. Nitric oxide, arginase, ROS, phagocytosis and amount of parasitism were measured in all groups. Our two main groups include RAW cell line macrophages in the presence and without the presence of Leishmania major parasite, in each of which exosome and prymethamine drug are added separately.

Results: Finally, it was observed that the amount of nitric oxide, reactive oxygen species (ROS) increased in all groups compared to the control group, and this increase was higher in the group that received pyrimethamine. Conversely, arginase and amount of parasitism decreased in all groups compared to the control group.

Conclusion: Based on the available evidence, the use of pyrimethamine is more effective in killing the Leishmania parasite than the use of exosomes extracted from C57BL/6 mouse macrophages. However, both of them increase the amount of ROS and NO compared to the groups that are not treated.

Keywords: Leishmania; RAW Cell Line; Pyrimethamine; Exosome.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Narrative Review

Code of Abstract: PI-63

NLRP3/caspase-1/IL-1 β signaling pathway: role in the pathobiology of chronic insomnia

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Abstract

Background and Aim: Chronic insomnia is an inflammatory-related disease with an important pathological basis for various diseases which is a serious threat to a person's physical and mental health. So far, many hypotheses have been proposed to explain the pathogenesis of insomnia, among which inflammatory mechanisms have become the focus of scientific attention. In this regard, the aim of the present scoping review is to evaluate the potential role of nucleotide-binding oligomerization domain (NOD)-like receptor-pyrin-containing protein 3 (NLRP3)/caspase-1/interleukin-1 β pathway as one of the most important activators of inflammatory cascades in pathobiology of chronic insomnia.

Methods: A comprehensive collection of information was achieved from medical databases including PubMed, Scopus, and Web of Science. In order to identify related articles, keywords related to this topic including chronic insomnia, NLRP3 inflammasome and interleukin-1 β were investigated and combined using Boolean operators (e.g., AND, OR).

Discussion: The data show that compounds that have the potential to cause inflammation induce sleep disorders, and that inflammatory mediators are key molecules in regulating the sleep-related activity of neurons. In the inflammatory process of insomnia, the role of NLRP3 in the pathogenesis of insomnia has been gradually considered by researchers. NLRP3 is an intracellular sensor that recognizes the widest range of pathogen-associated molecular patterns (PAMPs) and danger-associated molecular patterns (DAMPs). After identification and binding to damage factors, NLRP3 inflammasome is assembled to activate the caspase-1 and IL-1 β . Increased production and secretion of IL-1 β can be involved in central nervous system dysregulation of physiological sleep. According to the available evidence, we hypothesize that increased inflammasome-related cytokines expression may maintain a cycle of cellular activation and eventually cause chronic and excessive inflammation in individuals with chronic insomnia.

Conclusion: The current study highlights the hypothesis which NLRP3 /caspase-1/IL-1 β may serve as a potential therapeutic target for managing inflammation and improving symptoms in chronic insomnia.

Keywords: Chronic Insomnia; Interleukin-1 β ; NLRP3 Inflammasome





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-64

Evaluating the effect of lyophilized form of PRF on the polarization of macrophages

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Abstract

Background and Aim: Macrophages appear at the site of inflammation, first as inflammatory macrophages and then as anti-inflammatory macrophages, each of which secretes specific cytokines. This polarization works for wound healing and tissue repair. Due to the presence of fibrin scaffold, growth factors and blood cells, PRF helps to polarize macrophages at the site of inflammation, and due to its biocompatibility and autologous nature, it does not stimulate the body's immune system. Lyophilized PRF is a suitable option for use in wound healing and treatment improvement due to the long-term and healthy storage of many during long transportation and preservation of biological characteristics after the freezing process. This study investigates the effect of lyophilized PRF on the polarization of macrophages at the wound site and healing inflammation.

Methods: Extraction of bone marrow cells from the femur and leg of mice and their growth for one week. Growth and proliferation of RAW 264.7 murine macrophage cells. Preparation of lyophilized PRF.

Performing the MTT test in order to determine the relative concentration of lyophilized PRF to cause cytotoxicity and check cell viability. Real time PCR test to investigate the changes in the expression of inflammatory and anti-inflammatory marker genes in mouse macrophage cells due to treatment with lyophilized PRF.

Results: One of the important goals of this study is to find the appropriate concentration of lyophilized PRF in the effect on the polarization of macrophages at the site of inflammation and wound. M. One of the important effects on the performance of lyophilized PRF is the temperature effect. In this study, we have investigated the effect of temperature and its change on the performance of lyophilized PRF. Another important goal in this study is the effect of lyophilized PRF on the signaling pathway and the phosphorylation status of macrophages at the site of injury and inflammation.

Conclusion: In this study, the effect of lyophilized PRF on the polarization of mouse macrophages at the inflamed wound site in vitro and the investigation of the signaling pathway that is activated by treatment with lyophilized PRF are studied.

Keywords: Lyophilized Platelet-Rich Fibrin; Platelet-Rich Fibrin; Polarization ;Inflammation; Wound Healing.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-65

Prevalence of vitamin D deficiency and its impact on COVID-19 disease severity and titer of specific IgG antibody

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Abstract

Background and Aim: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused an acute respiratory disease that threatens human health. COVID-19-infected patients show a wide range of clinical symptoms varying from asymptomatic infection, mild, and moderate symptoms to more severe forms of the disease. Vitamin D3 by regulating the innate and adaptive immune responses has anti-inflammatory properties thus reducing the pathogenic effects of viral infections. This study aimed to investigate the correlation between serum vitamin D3 levels and severity of COVID-19 infection and its relationship with SARS-CoV-2-specific IgG antibody titer.

Methods: In this study, 82 West Iranian-recovered COVID-19 subjects were recruited and based on clinical symptoms and disease severity categorized into three different groups: mild, moderate, and severe. In addition, the presence and dynamic change of SARS-CoV-2-specific IgG antibody 3 months post symptom onset (PSO) were measured. Also, the association between serum vitamin D3 levels with age, sex, IgG antibody titer, and disease severity was examined. For this purpose, from each subject, 3 mL of venous blood samples were drawn and serum samples were collected and stored at -20 °C until analysis. The serum level of IgG against the S1 domain of SARS-CoV-2 spike protein was measured by the commercially available ELISA kit (EUROIMMUN Medizinische Labordiagnostika AG). Also, the serum level of vitamin D3 was assessed through a commercially available ELISA kit (Pishgaman Sanjesh, Iran) and optical densities were gained using an automated ELISA reader (Synergy HTX Plate Reader-BioTek Instruments, USA).

Results: SPSS version 20.0 was used for statistical analyses. The mean \pm SD of age in the severe, moderate, and mild groups were 52.8 ± 11.3 , 41.6 ± 9.5 , and 39.5 ± 10.4 , respectively. The age of the severe group was higher than the other two groups ($p = 0.001$). The vitamin-D3 ranges were defined as deficient (< 10 ng/ mL), insufficient (10-29 ng/ mL), and sufficient (30-100 ng/ mL). The mean \pm SD serum vitamin D3 levels in the severe, moderate, and mild groups were 38.56 ± 14.9 , 34.78 ± 9.97 , and 37.82 ± 10.39 , respectively. There were no statistically significant differences among the three different groups in terms of serum vitamin D3 levels 3 months PSO ($p > 0.05$). Also, there was no statistically significant correlation between serum vitamin D3 levels with IgG antibody titer, sex, and age in three different groups 3 months PSO ($p > 0.05$).

Conclusion: Previous studies showed that vitamin D deficiency in COVID-19 patients is associated with an increased risk of disease severity, hospital admission, and need for critical care. Although serum vitamin D levels do not affect the mortality rate. In this study, we could not find significant associations of serum vitamin D level with COVID-19 disease severity and titer of specific IgG antibody. This may be because the COVID-19-recovered subjects took vitamin D or because 3 months elapsed after PSO, peripheral blood sampling, and vitamin D measurement.

Keywords: COVID-19 Severity; Vitamin-D3; Antibody Titer.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Systematic Review & Meta-Analysis

Code of Abstract: PI-67

The role of anti-idiotypic antibodies in the control of immunological infertility caused by anti-sperm antibodies: A Systematic Review

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Abstract

Background and Aim: Immunological male infertility can result from anti-sperm antibodies (ASAs). Infertility caused by anti-sperm antibodies accounts for 10-30% of immunological infertility. Physiologically, sperm cells are unexposed to the male immune system due to blood testis barrier. However, following a damage to this barrier, an exposure occurs between sperm antigens and immune cells leading to generation of anti-sperm antibodies, considered to be a type of auto antibodies that can debilitate sperm motility and function.

Methods: We searched Google Scholar, PubMed, from 2018 to 2023, and found 9 articles based on our inclusion and exclusion criteria.

Results: It is declared that in case of auto immune diseases, the most commonly management is administration of immune suppressive drugs that has detrimental effects on immune system responses and predisposes patients to variety of life threatening cancers and infections. A potential novel therapy is necessary to be employed in order to minimize undesirable side effects. Anti-idiotypic(anti-ID) antibodies are a part of regulatory network that can specifically neutralize antigen binding sites of auto-antibodies and prevent self-antigens from being attacked by these deleterious auto-antibodies. Besides this, anti-ID antibodies can produce cytokines, induce regulatory T cells and suppress the production of auto-antibodies. Also, owing to production of T helper memory cells, responses persist for a long time. Moreover, as this immune modulatory network also works naturally in the body, they are safe and not supposed to cause toxicity.

Conclusion: for all these issues anti-idiotypic antibodies are the choices to be better form of immunotherapy considering their specificity in solely targeting selective auto-antibodies and not suppressing protective immune responses. Less toxicity and side effects and long-lasting immunity make anti-ID antibodies be a promising alternative to conventional therapies for anti-sperm antibodies.

Keywords: Anti-Sperm Antibodies; Male Infertility; Anti-Idiotypic Antibodies.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Systematic Review & Meta-Analysis

Code of Abstract: PI-68

The use of platelet-rich plasma (PRP) in the treatment of rheumatoid arthritis: A systematic review study

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Abstract

Background and Aim: Rheumatoid arthritis is a chronic inflammatory disease that affects the joints and surrounding tissues. This disease causes pain, stiffness and swelling of the joints, which leads to a decrease in the quality of life of the patients. In addition to the treatments currently used to control inflammation and reduce the symptoms of rheumatoid arthritis, new research has shown that platelet-rich plasma also has significant therapeutic potential. The purpose of this abstract is to investigate the applications of PRP in the treatment of rheumatoid arthritis.

Methods: This study is a systematic review study that was conducted in 2023 by using the keywords of platelet-rich plasma (PRP), treatment, rheumatoid arthritis (RA) it was done in reliable databases including PubMed, Scopus, Cochrane, Web of Science and Google scholar search engine without time limit. To ensure the completeness of the search results, the sources of the articles were checked and after removing the duplicate titles from the endnote software and checking the titles and abstracts, the related articles were checked using JBi tools, after checking the quality of the articles, the findings in the checklist the target was entered.

Results: 1832 articles were reviewed and finally 12 related articles showed that platelet-rich plasma (PRP) is a biological compound that is extracted from the blood of patients and contains a high concentration of platelets. Platelets are rich sources of transcription and growth factors such as platelet growth factors (PGFs) and platelet growth factors (TGF- β), which play a very important role in inflammatory processes and tissue repair. As a result, the use of PRP can have an effective improvement in the treatment of rheumatoid arthritis. In the studies, the use of PRP in the form of direct injection into contaminated joints by arthroscopy or systemic injection with the help of a dedicated doctor has shown a significant improvement in the symptoms and complications of rheumatoid arthritis. Also, PRP can control the inflammatory process and accelerate the tissue repair process. However, there is still a need for further research on the use of PRP in the treatment of rheumatoid arthritis. Unwanted side effects and lack of control in the use of PRP should also be investigated. Also, the exact mechanism of PRP action in improving rheumatoid arthritis needs further investigation.

Conclusion: As a result, the use of platelet-rich plasma can be used as a complementary and collaborative method in the treatment of rheumatoid arthritis. With the continuation of relevant researches, we hope to improve the use of PRP in the treatment of this important disease.

Keywords: Platelet-Rich Plasma; Treatment, Rheumatoid Arthritis.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-69

Evaluation of the effect of 1, 25-dihydroxy vitamin D3 on the expression of matrix metalloproteinase 3 and 7, and TIMP metalloproteinase inhibitor 1 in eutopic and ectopic stromal cells from patients with endometriosis

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Abstract

Background and Aim: Evaluation of the effect of 1, 25-dihydroxy vitamin D3 on the expression of matrix metalloproteinases 3 and 7, and TIMP metalloproteinase inhibitor 1 in eutopic and ectopic stromal cells from patients with endometriosis.

Methods: Endometrial stromal cells (ESCs) isolated from 48 women with endometriosis and 10 healthy controls were treated with vitamin D3. The effect of vitamin D3 on the invasion of eutopic endometrial stromal cells (EuESCs), ectopic endometrial stromal cells (EESCs), and control endometrial stromal cells (CESCs) were analyzed at the gene level. After digesting endometriosis tissues, cell culture, and treating cells with vitamin D3, the real-time PCR (RT-PCR) technique was conducted 3,6,24 and 48 h after treatment to assess MMP3, MMP7, and TIMP1 gene expression

Results: At the basal level, it was observed that the gene expression of TIMP1 and MMP3 in the ectopic group is higher compared to the eutopic group ($p=0.0014$). In eutopic and ectopic groups, TIMP1 significantly increased in 6 h. Vitamin D3 also caused a significant decrease in MMP3 and MMP7 expression in the ectopic group in 6 h. Besides, vitamin D3 up-regulated TIMP1 in the ectopic group in 48 h. However, it had no significant effect on these genes in other groups. Additionally, the ratio of MMP3 and MMP7 to TIMP1 decreased after treatment in 6 h, but it did not significantly decrease in other groups.

Conclusion: In the current study, one of the most critical interventions was scrutinized, suggesting reduced signs of endometriosis. An investigation of therapeutic aspects is warranted based on *in vitro* studies related to the advantageous effects of vitamin D3.

Keywords: Endometriosis; Vitamin D3; TIMP1; MMP3; MMP7.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PI-70

The Significance of Interleukin-33 in the Management of Anemia in Patients with Rheumatoid Arthritis

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Abstract

Background and Aim: Rheumatoid arthritis (RA) is a chronic autoimmune disease that can lead to significant inflammation and joint damage. Anemia of inflammation (AI), also known as anemia of chronic disease (ACD) is a common complication of RA, resulting in decreased physical activity and quality of life for patients. Recent research has shown that elevated levels of Interleukin-33 (IL-33) play a crucial role in the development of ACD in patients with RA. This study aims to review and analyze the existing literature on the role of IL-33 in anemia among patients with RA.

Methods: A meticulous and comprehensive search of pertinent databases was conducted to procure relevant studies concerning the role of IL33 in anemia among patients with rheumatoid arthritis. Our approach ensured a detailed and accurate analysis of all available information.

Discussion: The results of this study suggest that IL-33 can inhibit the production of red blood cells induced by erythropoietin, as observed in laboratory experiments and *in vivo*. This inhibition is linked to a decrease in the effectiveness of the Akt signaling pathway and has a lesser impact on the ERK1/2 and STAT5 pathways. These findings provide valuable insights into the role of IL-33 in inhibiting erythroid progenitor differentiation during chronic inflammation.

Conclusion: The expression of ST2, the receptor for IL-33, on erythroid progenitors leads to their inhibition through the activation of NF- κ B signaling, resulting in anemia during chronic inflammation. The study's results indicate that IL-33 can impede the process of erythropoietin-accelerated erythropoiesis *in vivo*, dependent on the activation of NF- κ B signaling. Furthermore, the research suggests that targeting IL-33 could be a potential treatment for anemia in patients with RA. These findings provide valuable insights into IL-33's key player role in anemia development in RA and its potential for therapeutic interventions.

Keywords: Interleukin-33; Rheumatoid Arthritis; Anemia; Erythroid Progenitor.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-74

Evaluation and Comparison of a Rapid Semi-Quantitative Diagnostic Test with The ELISA Method for Detection of Fecal Calprotectin in Chronic Inflammatory Bowel Disease

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Abstract

Background and Aim: Calprotectin, a protein found in neutrophils, increases in stools during intestinal inflammation. This study contributes to the development of efficient diagnostic methods for UC, improving patient care. The traditional ELISA method, while accurate, can be resource-intensive and expensive. The rapid test offers a more convenient and immediate assessment. The study evaluated the Rojan rapid test and ELISA method for detecting Fecal Calprotectin (FC) in patients with Ulcerative Colitis (UC) and distinguishing between inflammatory and non-inflammatory bowel diseases. Results showed a high level of agreement between the two tests, indicating the rapid test potential as a valuable diagnostic tool.

Methods: A total of 100 subjects of age above 60 years old were enrolled in the study. Fecal samples were collected from each participant. The rapid semi-quantitative diagnosis test for FC was performed. Simultaneously, FC levels were quantified using the ELISA method. Sensitivity, specificity, and diagnostic accuracy were calculated for both tests. The Fecal one step Calprotectin test device is a Semi-Quantitative, membrane-based immunoassay for the detection of Calprotectin in Feces. The membrane is pre-coated with capture reagent (monoclonal antibody against calprotectin in different concentrations) to obtain a 3 test lines region of the test with detection limit for T1 (0~15ug/g), T1-T2 (15~60ug/g), T1-T2-T3 (>60ug/g). The traditional method of detecting Fecal Calprotectin involves Enzyme-Linked Immunosorbent Assay (ELISA), which, while accurate, can be time-consuming and resource-intensive. The development of a Rapid Semi-Quantitative Diagnosis Test offers the potential for a more convenient, immediate assessment and possibility of large number of samples.

Results: The Rojan rapid semi-quantitative diagnosis test demonstrated a sensitivity of >99.9%, specificity of 94.6%, and diagnostic accuracy of 96%. The ELISA method exhibited comparable results. There was a strong correlation between the results obtained from the two methods. The study demonstrated a high level of concordance between the two diagnostic approaches, with the rapid test displaying notable accuracy in distinguishing between inflammatory and non-inflammatory bowel diseases. These findings indicate that the rapid semi-quantitative diagnostic test for fecal calprotectin holds significant promise as a valuable tool in the clinical assessment of ulcerative colitis patients. Its effectiveness, coupled with its expeditious nature, rapid performance and low cost may enhance diagnostic procedures and contribute to more timely and accurate treatment decisions for individuals suffering from bowel disorders.

Conclusion: The study evaluates a rapid semi-quantitative test for fecal calprotectin in ulcerative colitis, assessing its effectiveness in distinguishing between inflammatory and non-inflammatory bowel diseases. Comparison with the ELISA method provides valuable insights into diagnostic options. The rapid test shows excellent performance, correlating well with the ELISA results. This offers a convenient, reliable option for assessing mucosal inflammation, potentially aiding timely clinical decisions and enhancing patient care. The rapid semi-quantitative diagnosis test for FC showed excellent performance in differentiating UC from N-IBD.

Keywords: Ulcerative Colitis; Fecal Calprotectin; Bowel Disease; Rojan Rapid Diagnosis Test.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-76

Increased miR-155 in K562 CML cell line causes down-regulation of BCL2 expression

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Abstract

Background and Aim: Chronic Myeloid Leukemia (CML) is a myeloproliferative neoplasm with an incidence of 1-2 cases per 100,000 adults. It accounts for approximately 15% of newly diagnosed cases of leukemia in adults. CML is characterized by a balanced genetic translocation, t(9;22) (q34;q11.2). The resulting BCR/ABL1 chimeric protein is a constitutively active tyrosine kinase that activates multiple signaling pathways, which collectively lead to malignant transformation. MicroRNAs (miRNAs) are short non-coding regulatory RNAs that control gene expression and play an important role in cancer development. miRNAs regulate gene expression by cleaving the target mRNAs directly or inhibiting translation through perfect or nearly perfect complementary base pairing to targeted mRNAs at the 3' untranslated regions (UTRs). Molecular biologists have identified a number of genes and miRNAs associated with CML. Expression level of tumor suppressor-miRNAs, described as miRNAs that target the oncogens, can contribute to diagnosis and prognosis of some malignant disorders including CML. One such miRNA, miR-155, has been found to be downregulated in CML. Downregulation of this miRNA is presumably mediated by BCR-ABL tyrosine kinase activity. The RNA binding proteins (RBPs) and miRNAs mediate post-transcriptional regulation of the anti-apoptotic BCL2 family members. In humans, six anti-apoptotic members of the Bcl-2 family have been identified and characterized, including Bcl-2, Bcl-X_L, Mcl-1, Bcl-W, Bfl-1, and Bcl B. These family members prevent death by sequestering pro-apoptotic molecules. These family members contain 3' UTRs of variable lengths (1506 to 5278 nt), and maintain significant variation in their mRNA half-lives. The BCL-2 anti-apoptotic proteins are often overexpressed in malignant cells. While this offers survival advantages to malignant cells, it also offers for novel targeted therapies that selectively kill such cells. In this study, we aimed to investigate the effect of miR155 on bcl2 expression in K562 CML cell line. Our findings suggest that miR155 may serve as a beneficial agent for alternative therapy in CML patient.

Methods: The K562 BCR-ABL positive cell line was cultured in RPMI1680 (90%), FBS (10%) and pen/strep. The cells were subcultured when confluent, 2.0×10^6 cells were transfected with PLentiIII-miR155-GFP construct through electroporation. Twenty-four hours later, transfection was verified by flow cytometric analysis. Then total RNA was extracted from transfected K562 cell lines. Then the quality and quantity of RNA was determined by nanodrop device and electrophoresis. cDNA of total RNA was synthesized. qRT-PCR was performed for bcl2 and miR-155. Relative expression was calculated for target gene using the $\Delta\Delta CT$ method.

Results: Fluorescent color was observed in 35% of cells, this means that 35% of the cells were transfected. qRT-PCR results showed increased 20 folds in compare to control. A decrease in bcl2 expression to 0.25-fold were seen.

Conclusion: In this study, we showed that overexpression of miR-155 can decrease the expression of bcl2, and as a result, the survival of leukemic cells decreases and they undergo apoptosis. We propose a new potential anti-leukemia agent in K562 CML cell line, i.e. miR-155. However, further and complementary studies are required to address some other aspects.

Keywords: Apoptosis; Bcl2; CML; K562; miR155.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Immunology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PI-77

A new approach to immunotherapy of autoimmune patients

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Abstract

CAR T-cell-based therapies have shown promising efficacy in treatment of autoimmune diseases. The main limitations are the inadequate supply of individual immune cells and potential complications. Recently, the use of CAR-NKs have been an alternative strategy to overcome the limitations of CAR-Ts. CAR-NKs can produce a specific cytokine profile which reduces the risk of side effects. CAR-NKs can kill cancer and damage cells through both CAR-dependent and CAR-independent pathways, whereas CAR-Ts rely solely on the CAR-dependent pathway. The aim of this study is providing the latest research on the effectiveness of innovative treatments of different autoimmune diseases.

Methods: In this study, research was done based on the main keywords in PubMed and Google Scholar databases, and the article was written accordingly.

Discussion: Recent studies have shown that CAR-NK based immunotherapies are more effective than CAR-T in the treatment of autoimmune diseases. CAR-NK cells overcome the limitations of CAR-T cell and have not the side effect of CAR-T cell therapy. It is important to note that more research is needed to fully understand the efficacy of these new treatments in different types of autoimmune diseases.

Conclusion: According to the available evidence, the therapeutic potential of CAR-NK cells to modulate immune responses in autoimmune patients will be promising for the treatment of other infectious and chronic inflammatory diseases.

Keywords: CAR-T Cell; CAR-NK Cell; Autoimmune Disease; Cancer.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Immunology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PI-79

The Study of Human Amniotic Epithelial Cells Potency in Providing a Stimulatory Microenvironment for the Peripheral Differentiation of Myeloid-Derived Suppressor Cells from NK Cells

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Abstract

Background and Aim: Human amniotic epithelial cells (hAECs) produce many cytokines and anti-inflammatory mediators. Many studies have shown peripheral differentiation of myeloid-derived suppressor cells (MDSCs) from peripheral blood mononuclear cells (PBMCs) and monocytes in the presence of such mediators. In the present study, we investigated the effect of hAECs' conditioned medium on the differentiation of natural killer (NK) cells towards MDSCs.

Methods: Peripheral blood NK cells isolated from 20 healthy women were purified using the magnetic separation method (MACS). NK cells were co-cultured at different cell ratios with hAECs isolated from healthy full-term pregnant women in direct and trans-well co-culture systems. After 1, 3, and 5 days of incubation, expression of cytotoxicity markers and specific markers of myeloid suppressor cells on the surface of NK cells, NK cell subtypes, and TGF- β and IL-10 production cytokines production were investigated through flow cytometry and the ELISA techniques, respectively.

Results: A significant increase in the production of TGF- β and IL-10 cytokines and the CD56bright CD16+ subpopulation in pNK cells was observed, along with a significant decrease in the expression of CD107a and FasL on the surface of NK cells. The expression of CD33 and CD66b in NK cells exhibited no significant increase after co-culture with hAECs. The results were comparable in both co-culture systems.

Conclusion: According to the present study's findings, the co-culture of NK cells and hAECs results in deriving the phenotype and function of pNK cells towards dNK cells without any differentiation to MDSCs. Consequently, it is not possible to stimulate peripheral differentiation in the pure population of NK cells due to the loss of many cellular interactions in the microenvironment.

Keywords: human amniotic epithelial cell (hAEC); natural killer (NK) cell; myeloid-derived suppressor cells (MDSCs).





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Tehran University of Medical Sciences, Tehran, Iran.
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7. Mycology (Oral Presentations)





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Mycology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OM-1

Identification of allergenic components of *Alternaria alternata* in asthmatic patients by immunoblotting technique

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Abstract

Background and Aim: *Alternaria alternata* is considered as one of the most common sources of aeroallergen. Previous studies have shown that allergens of this fungus play an important role in the incidence and severity of asthma symptoms. The purpose of this study was to detect *Alternaria Alternata* allergens in asthmatic patients.

Methods: Seventy patients (37 men, 33 women) with allergic asthma and 70 non-allergic persons as control group composed our study population. Prick test and blood sampling performed for all of them. The fungal isolate was cultivated and the appropriate antigen (cytoplasmic extract) was prepared. Then, the antigenic components were separated by SDS-PAGE method and the protein bands obtained in immunoblotting were adjacent separately with the patients' serum and were investigated regarding the presence of specific IgE.

Results: The results showed that 14 (20%) of the patients had positive skin test for *Alternaria alternata* antigen. SDS-PAGE revealed 11-115 kDa of protein bands that 11-83 kDa bands in immunoblotting had responded to specific IgE. Specific IgE response was observed against 12 different bands. The most important allergen components in the studied patients were protein bands 26, 30, 16, 22, 11 and 57 kDa, which were reacted with 88.9%, 66.7%, 61.1%, 50%, 44.4% and 44.4% of patients' serum, respectively. In the examined patients, 18 persons (25.7%) exhibited of specific IgE against *Alternaria alternata* allergens, while no bands were detected in the control group.

Conclusion: *Alternaria alternata* has several allergen components that can contribute to allergic reactions in patients with asthma and Due to the presence of this fungus in our environment, it is important to identify its allergenic components.

Keywords: *Alternata Alternaria*; Asthma; Allergen; Immunoblotting.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Mycology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OM-2

Pediatric candidiasis in Khuzestan: A decade survey

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Abstract

Background and Aim: Candidiasis, caused by opportunistic fungal pathogens of the *Candida* species, poses a significant health concern, especially with the rising number of at-risk individuals. Understanding the epidemiology and various types of *Candida* infections is crucial for developing effective diagnostic, treatment, and preventive strategies. This study aimed to determine the frequency of pediatric candidiasis in outpatients referred to the Iran Zamin Medical Diagnostic Laboratory in Ahvaz, the provincial capital of Khuzestan, over ten years (2003-2013).

Methods: This descriptive-cross-sectional study spanned ten years, recording demographic data of patients. Examined candidiasis types included mucosal candidiasis, chronic mucocutaneous candidiasis, candidal onychomycosis, infant diaper rash, etc. Affected areas, such as the groin, spaces between toes, and armpits, were sampled for microscopic examination, employing 20% potassium hydroxide and methylene blue 2.5 staining and culture on Sabouraud agar.

Results: Over the ten years, 25,643 patients were referred to Iran Zamin Medical Diagnostic Laboratory in Khuzestan province. Among them, 920 individuals (3.58% of the population) were diagnosed with candidiasis, with 139 cases (33%) affecting children aged 10 days to 18 years. The extremities, particularly hand areas (47.48%), were most frequently affected, followed by groin areas (17.9%), leg areas (6.47%), diaper regions (5.7%), head and neck regions (5%) and other sites (17.45%) exhibited positive indications of the *Candida* infection. The findings provide valuable insights into *Candida* prevalence in Khuzestan province, emphasizing the need for effective management, control, and monitoring.

Conclusion: This investigation confirms the prevalence of *Candida* infections in the studied area, with a specific emphasis on pediatric cases (33% of the affected subjects) over a decade. These findings highlight the imperative need for targeted interventions and heightened awareness regarding *Candida* infections, especially in the pediatric population. Effective management and preventive measures are crucial to address the unique challenges posed by candidiasis in children, ensuring their well-being and reducing the overall burden of the disease in the community and region.

Keywords: *Candida*, Candidiasis, Epidemiology, Pediatrics.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Mycology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OM-3

The Survey of Biofilm Formation by *Candida* Species on Catheters Surfaces in Infants

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Abstract

Background and Aim: The nosocomial invasive candidiasis is a main problem with notable mortality. *Candida* species can form biofilms on devices used in clinical like catheters, and increase the risk of infections. These biofilms cause therapeutic failures. Different catheters are susceptible to be altered by *Candida spp.* and promote the formation of biofilms. Little is known about *Candida spp.* biofilms, which may cause infection in Iranian infants. The purpose of the survey was to compare biofilm formation of *Candida spp.* Isolated from catheter insertion area on the skin of infants.

Methods: This survey was performed on catheter insertion area on the skin of infants admitted to Mofid Children's Hospital, Tehran, Iran. All of the hospitalized infants stayed at least 10 days in hospital. Samples were collected from the catheters of 80 infants. To determine of *Candida spp.* the outside surface of the disconnected catheters was lied on fungal culture media. The isolated yeasts were identified by PCR-sequencing. Biofilm formation assay was performed and analyzed by MTT assay.

Results: From the 80 infants, 34 (42.5%) *Candida* isolates obtained from catheter samples. Out of thirty-four isolates, 16 (47.2%), 12 (35.2%) and 6 (17.6%) isolates were *C. parapsilosis*, *C. albicans* and *C. glabrata*, respectively. All the isolates were capable to make biofilm, according to the results of MTT assay. The species with the highest biofilm production was *C. parapsilosis* (n:12 with high biofilm producer), followed by *C. albicans* (n:10 with high biofilm producer), and *C. glabrata* (n:5 with high biofilm producer). The extra *Candida spp.* was moderate biofilm producer.

Conclusion: The catheters are very important, as a potential source of candidiasis. Our results demonstrated that, all the three species obtained from the infant catheter samples, produced biofilm, however *C. parapsilosis* revealed the maximum biofilm production. As the formation of biofilms on catheters is closely associated with nosocomial invasive candidiasis in infants, it is highly recommended to be so awake when using catheters and to limit the duration of catheterization especially in infants.

Keywords: Biofilm; Catheters; *Candida spp.*; Infant.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Mycology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OM-4

Detection of serum galactomannan levels in children with neutropenia admitted to the hematology and oncology department of Bou Ali Hospital, Ardabil, Iran

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Abstract

Background and Aim: Invasive Pulmonary Aspergillosis (IPA), is one of the life-threatening diseases in patients hospitalized in different departments of the hospital, especially the hematology and oncology departments of children. IPA was classified as “proven,” “probable,” or “possible” as described in the guidelines prepared by the European Organization for Research and Treatment of Cancer and Mycoses Study Group (EORTCMSG). This disease requires rapid diagnosis through microscopic examination and culture of sent samples, as well as the use of serological methods such as is galactomannan. Galactomannan is a polysaccharide cell wall component of *Aspergillus*. The Considering the sensitivity of this disease, it is highly recommended to use serological methods that have high sensitivity and specificity compared to old methods. high values obtained from this method and the results of other diagnostic criteria indicate the presence of this disease The follow-up of circulating GM level serves as an indicator of severity of the infection during the invasive disease course throughout the neutropenic period as much as in the diagnosis.

Methods: This retrospective study was conducted from March 2023 to May 2023 in the Blood and oncology department of Bu Ali Hospital, Ardabil. Patients between the ages of 1 and 15 years, with persistent fever enter the project. Broncho alveolar lavage fluid (BAL), sputum, and serum samples from patients were sent to medical mycology reference laboratory and analyzed. The diagnosis was based on the positive results of smear and fungal culture, as well as GM levels.

Results: Out of 63 patients, 41 (65.2%) patients were diagnosed as acute lymphoblastic leukemia (ALL), 19(30.1 %) as AML, and 3 (4.7 %) as lymphoblastic lymphoma. According to EORTC/MSG criteria, proven aspergillosis was not reported among all patients. Probable diagnosis was reported for 6 cases and possible for 4 cases.

Conclusion: IPA diagnosis still constitutes an important topic for neutropenic patients today. In this study, the sensitivity and specificity of GM were measured in different cut-off values, so that the sensitivity and specificity of the test in 0.1 cut-off were calculated as 60% and 93%, respectively. In this study, GM values above 0.5 were considered as a positive result. During Hayden et al. examination, the GM antigenic index in 990 serum samples in the hematology and oncology department of children, reported values above 0.5 as positive. The most suitable cut-off value for diagnosing IPA infections in children is 0.5, the sensitivity and specificity of this test in this cut-off value were calculated as 83% and 79% respectively, which can be a positive predictive value. Also, for a more accurate diagnosis, the radiological and clinical evidence of the patient was used. However, the GM test is not suitable for the diagnosis of all systemic fungal diseases and it is suitable to be used for the diagnosis of IPA. Serum GM antigen test will result negative in case of colonization.

Keywords: Aspergillosis; Galactomannan; Neutropenia.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Mycology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OM-5

Metabolomic Insights into Fluconazole-Resistant and Fluconazole-Susceptible *Candida auris* Clade V

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Abstract

Background and Aim: *Candida auris*, a newly emerging non-*albicans* fluconazole resistant agent, is becoming more widely recognized as a cause of invasive infections in healthcare settings.

For the first time, we have identified the metabolic profiles of fluconazole-resistant and fluconazole-susceptible *C. auris* clade V in compare to *C. auris* clade I isolates by using GC-MS technique.

Methods: Cell-free supernatants of fluconazole-resistant, and fluconazole-susceptible *C. auris* clades V and *C. auris* clade I strains were extracted by GC-MS for metabolomics analysis.

Results: A GC-MS chromatogram revealed 28, 22, and 30 compounds in the methanolic extracts of fluconazole-susceptible, fluconazole-resistant, and *C. auris* clade I strain, respectively. Some compounds, such as acetamide and metaraminol, were found in both fluconazole-susceptible and resistant *C. auris* clade V and *C. auris* clade I. N-methyl-ethanamine and bis (2-ethylhexyl) phthalate metabolites were identified in both fluconazole-susceptible and resistant *C. auris* clade V, as were 3-methyl-4-isopropylphenol, 3,5-bis (1,1-dimethyl)-1,2-benzenediol, and diisooctyl phthalate metabolites in both fluconazole-susceptible *C. auris* clade V and clade I.

Conclusion: The identification of these metabolites contributes to our understanding of the morphogenesis and pathogenesis of *C. auris*, highlighting their potential roles in antifungal drug resistance and controlling fungal growth. Furthermore, the absence of farnesol, a known hyphal inhibitory metabolite, in all *C. auris* cultures suggests alternative biological processes governing the growth of this pathogen.

Keywords: *Candida auris*; Fluconazole Resistant; Gas chromatography; GC-MS; Secondary metabolites.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Mycology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OM-6

Candidemia by *Candida parapsilosis* in Pediatric Patients with Hematological Malignancies and Antifungal Susceptibility pattern

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Abstract

Background and Aim: Candidemia is a life-threatening infection which requires an early diagnosis and use of appropriate antifungal agents to be treated effectively. Disc diffusion and E-test are easy, fast and inexpensive. In addition, the results of these methods agree with those of the broth microdilution reference method for *Candida* spp., indicating their reliability. Due to limited information about on appropriate drug options in candidemia caused by *C. parapsilosis* here, we describe the antifungal susceptibility patterns of *C. parapsilosis* yeast in pediatric patients with malignancy.

Methods: Two hundred and five blood samples were cultured from Imam Khomeini Hospital, Ahvaz to detect candidemia. *C. parapsilosis* yeast were identified by phenotypic methods and 21-plex PCR. All isolates tested against amphotericin B, voriconazole, posaconazole, itraconazole, caspofungin, and fluconazole using disc diffusion and E-test based on CLSI standard M27-A3 & M 60,1 st ed protocol.

Results: In the present study 21 out of 205 patients (10.2%) were positive for candidemia by *C. parapsilosis*. Fluconazole with MIC₉₀ 4 showed potent activity against *C. parapsilosis* isolates and followed by voriconazole inhibited 95.2 % of isolates at $\geq 17\mu\text{g/ml}$ and ≥ 0.5 by disc diffusion and Etest, respectively. However, 33.3% and 23.8% *C. parapsilosis* isolates were displayed resistant to caspofungin and itraconazole, respectively. Also, we did not see any statistically significant difference between result of two method disc diffusion and E-test ($p > 0.13$).

Conclusion: The increase of candidemia by *C. parapsilosis*, along with reduced susceptibility to antifungal drugs may be a warning sign in pediatric patients with malignancies. Our results were shown that fluconazole at $\leq 0.5\mu\text{g/mL}$ was the most effective antifungal agent against the recovered isolates. Whereas other antifungals have variable effects on *C. parapsilosis*. Furthermore, since there is no known breakpoint for the responses of *C. parapsilosis* to posaconazole, it is not possible to interpret the isolates as "resistant" or "susceptible" to this antifungal agent. However, *C. parapsilosis* showed low and acceptable MIC values for posaconazole.

Keywords: Candidemia, *Candida parapsilosis*, Antifungal Susceptibility.





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Tehran University of Medical Sciences, Tehran, Iran.
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7. Mycology (Poster Presentations)





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-1

The prevalence of microbial factors and antibiotic resistance patterns in neonatal sepsis among hospitalized infants at Ayatollah Mousavi Hospital of Zanjan, during years 2021-2022

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Abstract

Background and Aim: Sepsis is one of the leading causes of mortality among infants worldwide. Failure to timely identify drug resistance and the predominant patterns of resistance can lead to life-threatening and complicated treatment outcomes. Therefore, this study was conducted to investigate the prevalence of microbial factors and antibiotic resistance patterns in neonatal sepsis among hospitalized infants at Ayatollah Mousavi Hospital of Zanjan during years 2021-2022.

Methods: In this descriptive cross-sectional study, 72 infants diagnosed with sepsis by a specialist neonatologist were included. The participants were enrolled using a census method, and the data were extracted from the medical records of these infants. The data were entered into the statistical software SPSS26 and analyzed using descriptive methods.

Results: Of the 97.2% mentioned infants with blood culture samples, 77.8% of these cultures were negative and among the positive cultures, *Acinetobacter* species were isolated in 19.4% of cases, with a prevalence of 12.5%, followed by *Staphylococcus epidermidis* with 1.4%, which had the lowest prevalence among the isolated microbial factors. 38.9% of the mentioned infants had urine samples, of which 2.8% were positive (2 cases), of which 1 case was related to *Staphylococcus epidermidis* bacteria and one case was related to *E. coli* bacteria. Also, 9.7% of mentioned infants had CSF samples, of which 2.8% were positive (2 cases), of which 1 case was related to *Staphylococcus epidermidis* bacteria and one case was related to *Acinetobacter* bacteria. In the studied isolates, they were most sensitive to the antibiotic Colistin (15.3%) and it was also shown that isolates were more resistance to gentamicin (15.3%), amikacin (13.9%) and Meropenem (13.9%) antibiotics.

Conclusion: The prevalence of *Acinetobacter* bacteria as a common pathogenic agent highlights the need for further research and interventions to combat this pathogen. Despite the observed sensitivity to the antibiotic Colistin, there is significant resistance to the mentioned antibiotics against the isolated pathogenic factors. This emphasizes the necessity for further research and continuous monitoring to address the challenges posed by drug-resistant pathogens.

Keywords: Sepsis; Microbial Agents; Drug Resistance; Neonates.





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Venue:
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January 25-28, 2024

Section: Mycology

Presentation Type: Poster

Abstract Type: Case Report

Code of Abstract: PM-2

A case report of polymicrobial co-infection presenting as omphalitis

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Abstract

Background and Aim: Infection of the umbilicus (omphalitis) is evidenced by redness at the umbilicus, swelling, and exudation of fluid. It is typically a polymicrobial infection that predominantly involves *Staphylococcus aureus* and *Candida* species.

Case-presentation: Herein, we report a case of omphalitis in a 10-year-old boy presented to our emergency department with sudden severe pain abdomen, excessive inflammation, swelling and erythema but no discharge was noted. Furthermore, the patient did not show any signs of peritoneal irritation. The history of chief complaint began a few days ago when the mother suspected that the child had injured his abdomen while playing with his brother who was 6 years old because he tried to lift him up so his brother fell on top of him. The patient's past medical history is that of a previously healthy child, with no history of any significant medical or surgical problems. Her prenatal and birth history was normal, and her immunizations are up-to-date. As noted, there was a thought by the mother of possible abdominal trauma, but nothing witnessed. She lives with both parents and two siblings. There is no history of animal exposure or sick contacts. Examination revealed a normal finding with some painful induration and erythema about the umbilicus with an otherwise normal abdomen.

Methods: For laboratory work up, the base of umbilicus was firmly rub with two sterile swabs to collect fluid, and immediately transferred to into both blood agar and Sabouraud Dextrose Agar (SDA) media, and then analyzed macroscopically and microscopically.

Results: One *Staphylococcus aureus* strain and two strains of yeast were phenotypically identified. Disk diffusion testing of the *Staphylococcus aureus* isolate was performed that showed the resistance of this isolate to ciprofloxacin (CP) and its susceptibility to Cefoxitin (FOX), Clindamycin (CC), Erythromycin (E) and Doxycycline (D).

Conclusion: Overall, accurate and rapid identification of microbial agents as well as antimicrobial susceptibility testing should be performed to choose subsequent appropriate antimicrobial treatment.

Keywords: Omphalitis, *staphylococcus aureus*, yeast, disk diffusion.





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Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-3

Dermatophyte monitoring in a Northwest Iranian training hospital

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Abstract

Background and Aim: The most common cutaneous fungal infections are caused by dermatophyte fungi including *Microsporum Trichophyton*, and *Epidermophyton* species. To get better perception of dermatophyte distribution in Northwest of Iran, we studied the identification of isolated dermatophytes from human specimens by using the fast and cheap molecular method, PCR based restriction fragment length polymorphism (PCR-RFLP).

Methods: The study samples were collected from clinically suspected cutaneous lesions. All the specimens were transported to Medical Mycology Center, UMS University of Medical Sciences. First of all, a conventional diagnosis was carried out which included microscopic examination and culture on sabouraud dextrose agar medium with antibiotics: chloramphenicol and cycloheximide. All the dermatophyte isolates were then identified at the level of species by the molecular method of PCR-RFLP.

Results: From the tested 357 clinical specimens, 30 dermatophytic isolates were identified. Totally, 38% of all cases of Tinea were 1 to 12 years old and 54% were female. The percentage rate of dermatophyte species was *Trichophyton mentagrophytes* (36%), *Microsporum canis* (32%), *Microsporum gypseum* (16%), *Trichophyton rubrum* (4%), and *Epidermophyton floccosum* (12%).

Conclusion: By using of PCR-RFLP, a fast and reliable identification of these species is possible. This molecular method provided an opportunity for dermatophyte identification at the species level.

Keywords: Dermatophyte, Molecular Epidemiology, RFLP.





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Venue:
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January 25-28, 2024

Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-5

Mucormycosis monitoring in Iranian Northwest cases of DKA and delta COVID-19

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Abstract

Background and Aim: During the surge of delta type COVID-19 in Iran, the rate of invasive mucormycosis considerably increased as a cluster. COVID-19 associated Mucormycosis (CAM) immersed as rhino-sino-facial, rhino-sino-cerebral and acute sinusitis. The present report includes demographic, clinical and laboratory diagnostic information about new emerged CAM in Northwest of Iran.

Methods: During three months, from August to October 2021, about 65 cases with the clinical manifests suspected to mucormycosis and a history of diabetic ketoacidosis, recent severe Covid-19 and corticosteroid therapy with dexamethasone were studied. Our subjects were the clinical specimens including 31 nasal biopsies, 24 paranasal sinus biopsies, 2 facial and palate biopsies, skin and sutures, one each. Direct microscopic investigation, culture on mycologic media and molecular typing of Mucoral isolates were performed.

Results: Our findings of laboratory examinations showed 55 (84.6%) cases of Mucoral invasion. The suspected cases of CAM showed clinical manifests including acute sinusitis, rhino-sino-cerebral 25(38.5%), rhino-sino-orbital 7(10.8%), and sino-facial 3(4.6%), involvements. The molecular identification resulted *Rhizopus oryzae* as the most frequent isolate (44.6%) and *Candida* yeasts (*albicans* and non *albicans Candida* species) 6.2% and 7.7% respectively. *Aspergillus* species were detected 5 (7.7%) as well. A considerable number of cultures, 20 (30.8%) could resulted no growth for any fungi.

Conclusion: As a conclusion, delta type Corona virus causing a considerable increased invasive Mucormycosis in the recorded Covid-19 cases in the north west of Iran, Although, opportunistic *candida* and *aspergillus* were identified in lower frequencies as well.

Keywords: Mucormycosis, delta Covid-19, Corticosteroid.





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Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-6

First Report of Onychomycosis Due to *Phoma glomerata* (*Didymella glomerata*) in Kerman, Iran

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Abstract

Background and Aim: Onychomycosis is the fungal infection of nails, most commonly caused by dermatophytes. In recent years, the prevalence of non-dermatophyte onychomycosis (NDO), especially in the first toenail, has increased. *Phoma* species have also rarely been reported as the cause of NDO. *Phoma spp.* are ubiquitous dematiaceous fungi and well-known as phytopathogens, which are generally found in outdoor environments such as soil, plants, and water sources. Besides, human and animal infections caused by *Phoma spp.* have been reported. Here, we present a case of toenail onychomycosis caused by *P. glomerata* in an Iranian patient.

Methods: The patient was a 27-year-old woman with a clinical suspicion of tinea unguium who presented with about a 6-month history of brownish-black discoloration of the left big toenail. The nail plate was approximately 80–90% affected. All the other nails were normal and the patient was in good health. For laboratory investigations, after proper sterilization of the affected area with 70% alcohol, nail clipping from the affected toenail was collected. Direct microscopic examination of the sample using a 10% potassium hydroxide (KOH) solution revealed branching septate hyphae with varying widths, not compatible with dermatophytic mycelia. The sample was inoculated into Sabouraud dextrose agar containing chloramphenicol (SC). The culture was incubated for 2 weeks at 28°C and checked twice a week. Molecular identification was made based on the ITS sequence.

Results: Using DNA sequence analysis, the isolate was identified as *P. glomerata*. The grown colony was powdery to velvety, pink-orange with a dark brown reverse. The nearest neighbor to our isolate was *P. glomerata*, with 99.8% similarity. The obtained sequence was deposited in the GenBank with accession no OK483362. Antifungal treatment was performed by oral terbinafine (250 mg/day) in combination with topical terbinafine cream (1%) for six months. After treatment, KOH preparation and cultures of the nail were negative.

Conclusion: Identification of *Phoma* species based on morphological characters is controversial and difficult. Although infections due to *Phoma spp.* remain rare as compared to the other fungi, medical advances in recent years have led to an increase in the number of immunocompromised populations, which results in more exposure to the diverse saprophytic fungi. Indeed, clinicians must be conscious of the ubiquitous presence of filamentous fungi, particularly emerging agents, and the exposure, especially in at-risk populations.

Keywords: Iran, Onychomycosis, *Phoma glomerata*.





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Venue:
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January 25-28, 2024

Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-7

Water Saprophytic Fungi in Zahedan

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Abstract

Background and Aim: From a health perspective, the existence of fungi in water sources has both direct and indirect impacts on human health. Consequently, one of the contributors to water pollution is the presence of saprophytic fungi spores. The aim of this study was to determine the saprophytic fungi in water in Zahedan.

Methods: This descriptive study, 45 water samples from five different areas of Zahedan were collected in sterile, screw-capped test tubes during October and November 2023. The samples were separately cultured on Sc and S culture media. After seven days of incubated at 25°C, the plates (in triplicates) were observed for macroscopic characteristics such as colony diameter, exudates, and colony reverse and microscopic characteristics. For microscopic characteristics slides were stained with lactophenol cotton blue.

Results: Five types of fungi were isolated from the 45 water samples collected, which were *Alternaria* spp. (33.3%), *Aspergillus flavus* species complex (22.2%), *Aspergillus niger* species complex (22.2%), *Penicillium* spp. (11.1%), and *Nigrospora* spp. (11.1%).

Conclusion: The study sheds light on the presence and diversity of these organisms in water sources. The identification and analysis of the saprophytic fungi, contributes valuable insights into water quality. This research underscores the importance of ongoing monitoring and assessment to safeguard water resources and, consequently, human health in the region.

Keywords: Water, Fungi, Zahedan.





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January 25-28, 2024

Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-8

Geotrichum silvicola and pathogenic yeasts as the suspected agent causing chronic Hives

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Abstract

Background and Aim: Urticaria is a reaction pattern that represents cutaneous mast cell degranulation, with the condition being defined as chronic if lesions recur for longer than six weeks. Considering the high incidence of chronic urticaria among patients with the colonization of yeasts in the gastrointestinal tract, we investigated all fungal colonization and invasion in the gastrointestinal tract of cases with hives. Our aim was the identification of all isolates at the species level.

Methods: Our studied subjects were 200 cases with long-time superficial urticaria lesions. A fresh stool sample from the cases with clinical symptoms was collected. A direct microscopic investigation was performed for the detection of fungal growth in the gastrointestinal tract. The basic culture on sabouraud glucose agar was used for confirming the fungal detection. The Molecular methods and proteomic-based MALDI-TOF system were used for the identification of all fungal isolates.

Results: findings of microscopic investigation showed budding cells in 13 (54.2%) cases, blastospores 6 (25%), arthrospores 3 (12.5%), and pseudohypha 2 (8.3%). Of a total of 24 fungal isolates, 7 (29.2%) were *Geotrichum silvicola*, 7 (29.2%) *Candida albicans*, and 6 (25%) *Candida glabrata*, which were the most frequent species identified by MALDI-TOF system. Other single-case isolated yeasts were *C. Africana*, *C. tropicalis*, and *C. glabrata*. Also, one isolate could not be identified by the MALDI-TOF system.

Conclusion: Different species of yeast fungi which are commensally live in the human gastrointestinal tract are potential candidates for causing agents for chronic urticaria.

Keywords: Chronic hives, Candida, Yeasts, Molecular typing.





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Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-9

The *Malassezia lipophilic*

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Abstract

Background and Aim: *Malassezia* is one of the etiologic agents of skin diseases such as folliculitis, acne lesions and opportunistic pathogens in invasive infections. These lipoplastic yeasts have a special need for long-chain fatty acids and are part of normal flora of human skin, which is also seen in areas of the body that have many sebaceous glands such as face, chest, arms and back, as well as a small number in the floor of hair follicle 90% of healthy people. Therefore, the role of *Malassezia* species, due to its permanent presence in the skin of most people, can be very important in the pathogenesis of folliculitis and acne. Considering the lack of any studies in this area in the province and few studies in the country, the present study will be conducted to determine the prevalence of acne lesions and folliculitis caused by *Malassezia* among volunteer students.

Methods: After obtaining the sample by scraping method and preparation of direct smear stained with methylene blue, general and differential tests were performed in order to identify facial skin samples, including morphological characteristics along with the presence of mycelium, culture, different tween adsorption tests, catalase and bile sculin, production of sediment in Dixon agar medium and growth on Sabourou dextrose agar medium containing chloramphenicol and cyclohexamide (ScC).

Results: The frequency of species in 120 drainage sebum samples from facial and scapular skin folliculitis and acne manifestations in post-puberty and the sum of both sexes were: Isolation of yeast fungi *Malassezia furfur* 4 (3.33%), *Malassezia simpodialysis* 2 (1.66%), *Malassezia sloughia* 1 (0.83%) and negative cases (94.1%).

Conclusion: Considering that the use of treatment protocols in patients with acne and folliculitis lesions is based on the use of antibacterial compounds and regardless of the nature and origin of folliculitis, therefore, in skin manifestations caused by *Malassezia* fungus, we will witness multiple treatment failures and recurrence of lesions. Therefore, the frequency of isolates obtained from our studied samples, which was the highest priority with *Malassezia furfur* than other species of this yeast, increased the importance of identification of folliculitis fungal cases with regard to the significant role of underlying factors such as history of Steroid consumption.

Keywords: *Malassezia* fungus, Skin folliculitis, Acne.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-10

Isolation of Fungal flora in the Soil of Zahedan province

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Abstract

Background and Aim: Soil is one of the most suitable environments for the growth and reproduction of fungi because it contains many of the needs of fungi to survive. Fungi in the soil are one of the most important causes of fungal infections, especially skin and systemic fungal infections in humans. The purpose of this research was to determine the saprophytic fungi in the soil in different areas of Zahedan in the months of October and November 2023.

Methods: The present descriptive study, 60 soil samples were prepared from 5 different areas of Zahedan province during October and November 2023. With the flotation method, a uniform suspension was prepared and transferred to the SC and Scc culture media. After seven days of incubated at 25°C, the plates (in triplicates) were observed for macroscopic characteristics such as colony diameter, exudates and microscopic characteristics. For microscopic characteristics slides were stained with lactophenol cotton blue.

Results: Six types of fungi were isolated from the 60 soil samples collected, which were *Aspergillus flavus* species complex (44.4%), *Penicillium* spp. (33.3%), *Aspergillus niger* species complex (22.2%), *Alternaria* spp. (22.2%) and *Fusarium* spp. (11.1%).

Conclusion: Our findings showed that the identification of specific fungi, enhances our understanding of soil health and ecological dynamics in the region. This research underscores the significance of ongoing monitoring efforts, emphasizing the need for sustainable soil management practices to preserve environmental balance and agricultural productivity in Zahedan.

Keywords: Soil, Fungi, Zahedan.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-11

Investigation of the Air fungal flora in Zahedan during October and November 2023

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Abstract

Background and Aim: Fungal spores suspended in the air pose a significant risk of causing invasive fungal infections, particularly in individuals with compromised immune systems, transplant recipients, and those undergoing high-dose chemotherapy. This study aim was to investigate the Air fungal flora in Zahedan during October and November 2023.

Methods: 60 samples from five different areas were collected by open plate method. The samples were separately cultured on SC and SCC culture media. After seven days of incubated at 25°C, the plates (in triplicates) were observed for macroscopic characteristics such as colony diameter, exudates and microscopic characteristics. For microscopic characteristics slides were stained with lactophenol cotton blue.

Results: Five types of fungi were isolated, which were *Penicillium* spp. (44.4%), *Alternaria* spp. (33.3%), *Aspergillus niger* species complex (22.2%), *Aspergillus fumigatus* species complex (11.1%) and *Mucor* spp. (11.1%).

Conclusion: The findings underscore the importance of monitoring airborne fungal communities for potential health implications. Further research in this area can contribute to our understanding of environmental factors influencing fungal presence and aid in the development of strategies to mitigate associated risks.

Keywords: Air, Fungi, Zahedan.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-12

Comparison of different methods of staining for detection of *Pneumocystis Jirovecii* in respiratory symptoms in Urmia, Iran

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Abstract

Background and Aim: The present study was carried out for comparison of Methenamine silver, Giemsa, Gram-wigert, Papanicolaou and Hematoxylin & Eosin stains in terms of staining times, easiness, cost and availability of material and methods, detection of *Pneumocystis Jirovecii* different shapes and capability of this methods in detection of *Pneumocystis Jirovecii* in smear slides and tissue slices of rat's lungs.

Methods: To induce *Pneumocystis Jirovecii* pneumonia in Sprague Vestar rats inject 0/5cc Dexamethasone subcutaneously 2 times a week over 10-12 weeks after inducing pneumonia we removed the lungs and made a smear slide, some pieces of lungs are put in 10% formalin to made tissue slides. After that, the slides were stained by Methenamine silver, Gram-wigert, Papanicolaou, Giemsa and Hematoxylin & Eosin and compared them in terms of staining time, easiness, cost and availability. In addition, we compared the capability of methods to detect the microorganism in tissue preparation slices and smears.

Results: Giemsa and Papanicolaou are capable of staining the intra cyst bodies but can't stain the cyst wall. Methenamine silver and Gram-wigert stain the wall of the cyst. Giemsa is fast, cheap and the easiest method to stain, whereas, Methenamine silver is expensive, difficult and take long time to do. Methenamine silver, Papanicolaou, and Gram-wigert can detect *Pneumocystis Jirovecii* in both tissue slices and smears but Hematoxylin Eosin can't detect either slice and smears. Giemsa only detects microorganisms in smears.

Conclusion: In these staining methods, Papanicolaou and Giemsa have more specificity than Gram-wigert to detect the *Pneumocystis Jirovecii* in specimens, because this stain does not specify the wall of cysts together with yeasts, because of this the wrong diagnosis with Giemsa and Papanicolaou is less than Gram-wigert. Methenamine silver is the golden standard method to detect *Pneumocystis Jirovecii* but it stains the yeasts like *Pneumocystis Jirovecii* because the yeasts are similar to cysts in shape and color when we stain with Methenamine silver.

Keywords: *Pneumocystis Jirovecii*; respiratory symptoms; staining.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-13

Evaluation of antifungal drugs against *Candida parapsilosis* Biofilms in urinary catheters of infants

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Abstract

Background and Aim: Fungal Biofilms can form on indwelling medical devices like urinary catheters. Currently, Catheter-associated urinary tract infections are the common type of nosocomial infection especially in infants. The presence of *Candida* species in urine (Candiduria) may be due to colonization of this species in the bladder, urinary catheter, and perineum. Conventional treatment of Candiduria includes the removal of the urinary catheters and administration of antifungal agents. Little is known about biofilms of *Candida parapsilosis* isolated from urinary catheters in Iranian infants. The aim of this survey was to determine the efficacy of antifungal agents against *C. parapsilosis* biofilms.

Methods: This survey was performed on urinary catheters of forty-five infants admitted to Mofid Children's Hospital, Tehran, Iran. The yeast isolated from the urinary catheters of infants were identified by PCR-sequencing. After biofilm formation of *C. parapsilosis* in in-vitro condition, the minimum inhibitory concentration (MIC) of antifungal agents (Fluconazole, Itraconazole, and Amphotericin B) was determined against *Candida* species biofilms.

Results: The antibiofilm activity of antifungal agents were determined based on the CLSI M-27-A3 protocol. From 45 infants, 21 (46.6%) were confirmed for *C. parapsilosis*. The results of MIC showed Fluconazole had a better effect with a lower MIC; Followed by Itraconazole, and Amphotericin B.

Conclusion: Isolation of *C. parapsilosis* in 46.6% of urinary catheters raised the possibility of colonization especially in infants. Our results demonstrated that, all *C. parapsilosis* isolates obtained from the urinary catheters, were biofilm producers. Among the antifungal agents tested, Fluconazole have been shown to have superior activity.

Keywords: Biofilm, Urinary catheters, *Candida* species, Infant.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-14

Candidiasis in endometriosis

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Abstract

Background and Aim: Iatrogenic injury to endometrial tissue is the main cause of intrauterine adhesions (IUA) and infection can also damage the endometrium. The microbiota plays an important role in the health of the female reproductive tract. There is increasing evidence that immunologic mechanisms play a role in the pathogenesis of endometriosis. A high incidence of infection with *C. albicans* in women with endometriosis has been reported. There is evidence to suggest that *C. albicans* may contribute to the pathogenesis of endometriosis possibly by modulating cytokine production and elicits a strong inflammatory response that can lead to more severe endometrial fibrosis.

Methods: We studied the women with endometriosis referred to Babol Medical Center in the age range of 40-20 years old and with a history of fertility who presented with manifestations of frequent infections and severe pain. They were vaginal discharge examined, and after laboratory tests, 3 cases had positive fungal cultures. These three cases were subjected to further molecular investigations.

Results: Our evaluation shows that 3 out of 10 cases (30%) had a positive culture for the presence of fungi, and the result of molecular tests in all three cases was *C. albicans* species. These people were treated with fluconazole and clotrimazole vaginal cream and miconazole vaginal cream, but the treatment was not successful for these people.

Conclusion: Our observations show that the increase in the microbial load of *C. albicans* in women with endometriosis may stimulate the proliferation of endometrial cells and the activation of multiple inflammatory cycles causes severe pain in these people.

Keywords: Candidiasis; endometriosis; *Candida albicans*; vaginitis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-15

Screening of drug-resistant *Candida* species causing recurrent vulvovaginal candidiasis in Urmia, Iran

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Abstract

Background and Aim: Vulvovaginal candidiasis (VVC) is a frequent infection due to *Candida* yeast overgrowth in vaginal tract. *Candida albicans* causes 80-95% of all VVC cases in the world. To investigate the drug resistance in Iranian women with VVC which treated long time with azoles, we studied susceptibility of *Candida* species isolated from VVC cases to clotrimazole and fluconazole and molecular identification of studied *Candida* yeasts in the level of species.

Methods: We studied 20 to 45 years old women with symptomatic vaginitis were asked to take in part in the study. From all cases approached in the gynecology clinic, 192 women allowed vaginal swabs to be obtained. All specimens were cultured on sabouraud agar medium containing glucose (4%), peptone (1%), agar (1.5%). The fresh colonies (12-24 hours growth at 30°C) were used as DNA templates for the colony-PCR.

Results: From the yeast isolates, 76.3% (74 cases) were identified as *C. albicans* followed by *C. glabrata* and *C. krusei* 9 (9.3% each) and other non *albicans Candida* species 4 (4.1%). The total sensitivity to tested antifungal drugs include 45.4% of cases were resistant and 30.9% sensitive. From all *C. albicans* isolates, 37(52.1%), 27(38%) and 7(9.9%) were sensitive, resistant and intermediate to antifungal drug Fluconazole and 46(64.8%), 15(21.1%) and 10(14.1%) to clotrimazole respectively.

Conclusion: In vitro resistance remains rare among isolates from women with vaginitis due to *C. albicans*, even among isolates from HIV-positive women, in whom there is a tendency for such infections to occur in the oral cavity.

Keywords: Azole resistant, *Candida*, Vulvovaginal Infection.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-16

Candidemia, as a serious problem in preterm neonates

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Abstract

Background and Aim: Candidemia is a life-threatening fungal infection with significant mortality and morbidity in immunocompromised patients. The epidemiology and antifungal susceptibility testing of *Candida* species in systemic cases have not been well studied in Babol city, Iran. Recently, these strains are important in terms of low susceptibility to azoles and echinocandins. In recent years, there have been many reports of candidemia in infants, and considering the importance of this issue in preterm infants due to the weak immune system and long hospitalization, we treat preterm infants admitted to the Neonatal Intensive Care Unit (NICU) for candidemia for a period of eight months.

Methods: We studied all premature infants admitted to the NICU and the infants' blood samples were cultured in biphasic culture medium, then examined microscopically and cultured within 3 days, positive samples were cultured for the presence of yeast in chrom agar medium. Molecular tests were then performed and the species identified. Then the drug susceptibility test was performed and the patients were treated according to the results of the drug susceptibility test; two further samples were taken at the stages of treatment with the selected drug and after treatment with the drug to check the patient's condition.

Results: Out of 20 infants, 2 cases (10%) were positive for candidiasis and the result of molecular tests confirmed *Candida albicans* species in one case, *Candida guilliermondii* species in the other. This is the second case of candidemia reported by *C. guilliermondii* in Iran. According to the results of the drug sensitivity test, the best drug was amphotericin B, and the results of the blood culture during the treatment and after the drug treatment were negative, and the treatment was successful.

Conclusion: Due to the high mortality of candidemia, early and accurate diagnosis of these infections and timely initiation of antifungal treatment significantly improve the survival rate of patients and leads to better results. As a result, it is highly recommended to monitor the local epidemiology of this life-threatening infection and increase awareness in this field and use molecular methods along with laboratory methods.

Keywords: Preterm infant; *Candida guilliermondii*; Candidemia.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-17

Antifungal Resistance in Clinical Isolates of *Aspergillus* spp, Associated with Treatment Failure

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Abstract

Background and Aim: In this study, we investigated the frequency of *A. fumigatus* itraconazole and voriconazole resistance in a referral laboratory, defined the azole cross-resistance pattern, detection of the resistant gene comparing phenotypic azole resistance, and studied any epidemiologic links between resistant isolates.

Methods: The restriction enzyme *MwoI* was used in RFLP to differentiate and identify some *Aspergillus* species isolated from the clinical and environmental specimens. Anti-fungal resistance tests, Minimum inhibitory concentration and Disc diffusion were performed on the hospital isolated *Candida* species.

Results: Among all aspergillus isolates, *A. flavus*, 16(48.5%), *A. fumigatus*, 9(27.3%), *A. niger*, 6(18.2%), *A. terreus* and *A. clavatus*, 1(3% each) were included. MIC of Itraconazole for *A. fumigatus*, *A. flavus* and *A. niger* was ranged 0.5 to 16 µg/mL, 0.031 to 16 µg/mL and 0.5 to 16 µg/mL, respectively.

Conclusion: Although isolation of *Aspergillus* spore from air samples was not considerable in the present study. Drug resistance gene is capable of failure in treatment for some aspergillus species causing human infections.

Keywords: Antifungal resistance, *Aspergillus* species, Minimum inhibitory concentration, Disc diffusion.





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Tehran University of Medical Sciences, Tehran, Iran.
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Section: Mycology

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PM-19

A review of the potential role of *Malassezia* in intestinal health and disease

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Abstract

Background and Aim: *Malassezia* is the most common fungus that has been identified in the microbiota of human skin, and in more than 90%, we can see the fungal population in skin niches, so it is said that *Malassezia* yeasts are related to human skin disorders.

Methods: This systematic review was conducted to identify studies aimed at the potential role of *Malassezia* in intestinal health and disease, searching Google Scholar, Science Direct, and PubMed databases based on the keywords *Malassezia*, Intestinal disease, and Skin microbiota. After reviewing the summary of the articles and checking the title, the irrelevant articles were removed the full text of the articles was searched and the articles related to the topic were included in the study.

Results: Studies show that fungi comprise 30% of skin microbiota and *Malassezia* strains, which are the majority on the skin by far. *Malassezia* is perfectly adapted to the environment of the skin and can also be found in other compartments of the body.

Conclusion: *Malassezia* can be related to diseases related to the human intestine, as these fungi have been found abundantly in stool samples. To increase our understanding of *Malassezia* in intestinal dysbiosis as well as in other organs that can be connected to it, we can also target new therapeutic approaches.

Keywords: *Malassezia*, Intestinal disease, Skin microbiota.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-20

Molecular epidemiology and antifungal susceptibility profile in *Candida glabrata* species complex: A countrywide 5-year study

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Abstract

Background and Aim: The current study aimed to identify Iranian *C. glabrata* complex species in the clinical isolates and determine their antifungal susceptibility profile. Due to the increasing prevalence of azole resistance, the treatment of invasive *C. glabrata* infection is considered an important clinical challenge. Therefore, the present multicenter study aimed to identify clinical isolates of Iranian *C. glabrata* complex species, perform genetic diversity analysis, and characterize their antifungal susceptibility profiles.

Methods: In total, 320 *C. glabrata* clinical isolates were collected from patients hospitalized in different geographical regions of Iran. The initial screening was performed by morphological characteristics onto CHROMagar *Candida*. Each isolate was identified by targeting the D1/D2 rDNA using a multiplex-PCR method. To validate the mPCR method and determine genetic diversity, the ITS-rDNA region was randomly sequenced in 40 isolates. Additionally, Antifungal susceptibility was evaluated against nine antifungal agents following the CLSI M27-A4 guidelines.

Results: All clinical isolates from Iran were identified as *C. glabrata* sensu stricto. The analysis of ITS-rDNA sequence data revealed the presence of eight distinct ITS genotypes and ten haplotypes among the 40 isolates of *C. glabrata*. The predominant genotypes identified were Genotype VII, Genotype V, and Genotype IV, which respectively accounted for 22.5%, 17.5%, and 17.5% isolates. The widest MIC ranges were observed for voriconazole (0.016–8 µg/ml) and isavuconazole (0.016–2 µg/ml), while the narrowest ranges were seen with itraconazole and amphotericin B (0.25–2 µg/ml).

Conclusion: It can be a valuable approach for studying the genetic diversity, transmission patterns, and epidemiology of *C. glabrata*.

Keywords: *Candida glabrata* Complex, *C. Sensostricto*, Multiplex PCR, Genotyping, Haplotype diversity.





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Tehran University of Medical Sciences, Tehran, Iran.
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Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-22

Evaluation of *cyp51A* gene expression in voriconazole-resistant *aspergillus flavus* and *A. fumigatus* isolated from patients with pulmonary aspergillosis

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Abstract

Background and Aim: Pulmonary aspergillosis (PA) is a life-threatening fungal infection, *Aspergillus* sections *fumigatus* and *A. flavus* are the common causes of PA. In the present study, we evaluated of epidemiology of PA and the relationship between voriconazole resistance and the presence of mutation in the *cyp51A* gene and its gene expression in PA.

Methods: This study was performed on 150 patients with PA. All the cases were confirmed by the clinical pictures and laboratory findings. Isolates were identified using beta tubulin sequencing and, AFST was performed according to the CLSI M38-A2 guideline. *CYP51A* gene sequencing was conducted to investigate mutations in resistant/intermediate strains using a novel set of primers that were designed for *A. flavus* and *A. fumigatus*. The *cyp51A* gene expression was conducted using real-time PCR.

Results: Out of 150 samples collected, 67.3% and 32.7% isolates were identified as *A. flavus* and *A. fumigatus* of which 2% and 4% were resistant to voriconazole, respectively. Seventeen isolates displayed voriconazole MIC greater than or equal to the epidemiological cutoff value. In *A. flavus*, *Cyp51A* protein sequencing showed the substitutions T335A and D282E. No mutations associated with voriconazole resistance were found in *A. fumigatus*. Overall, voriconazole-resistant strains of aspergillus demonstrated overexpression of the *Cyp51A* gene compared to voriconazole-susceptible strains. Also, the expression of the *Cyp51A* gene in *A. fumigatus* isolates, being intermediate and resistant to voriconazole, showed a 17.6-fold rise compared to voriconazole-sensitive isolate.

Conclusion: Although there are still ambiguous points about the mechanisms of azole resistance, our results demonstrated that the *Cyp51A* gene expression is associated with increased resistance to azole in PA.

Keywords: Gene Expression, *cyp51A*, Mutation, Voriconazole Resistance.





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Section: Mycology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PM-23

Fractionation and identification of the allergic proteins in *Aspergillus* species

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Abstract

Background and Aim: Allergy is an undesired immune response to non-pathogenic agents. However, some opportunistic microorganisms such as fungi can also cause allergy. Among those fungi, hyphae form of *Aspergillus* strains including *A. fumigatus*, *A. flavus*, and *A. niger* could be mentioned. In this study, we aimed to separate allergic proteins from *Aspergillus* strains and determine their identity.

Methods: Standard species of *Aspergillus* strains were cultivated in optimized conditions and the mycelium was separated by centrifugation. The fungal cells were lysed through physical methods such as freeze thawing and grinding to prepare a suitable protein extract. The protein concentration was measured by Bradford method and the electrophoretic pattern of the extract was determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE). The proteins were fractionated by ammonium sulfate precipitation and anion exchange chromatography using fast protein liquid chromatography (FPLC) system. The IgE immunoreactivity of the sensitized patients and controls was studied using the fractionated proteins by enzyme-linked immunosorbent assay (ELISA). Following SDS-PAGE, proteins were electrotransferred onto polyvinylidene difluoride (PVDF) membranes and the strips were blotted with allergic patients' and controls' sera. The immunoreactive bands were excised from colloidal coomassie-stained SDS-PAGE gels and studied by mass spectroscopy methods.

Results: Among the studied species, *A. fumigatus* showed stronger IgE reactivity and more IgE reactive protein bands than others did. The proteins with higher molecular weights showed stronger immunoreactivity in Western blotting. Receiver operating characteristic curve analysis demonstrated a correlation between the results of the applied ELISA methods. One of the most prominent IgE-reactive proteins was confirmed to be 45 kDa mycelia catalase.

Conclusion: Our findings confirmed that high molecular weight proteins might play a major role in allergy and IgE reactivity to *Aspergillus* species. Moreover, the results showed that precipitation and chromatographic methods are applicable for fractionation of fungal proteins such as mycelial catalase.

Keywords: Allergy; *Aspergillus*; Protein identification; Protein fractionation.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Mycology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PM-24

Mycobiome Marvels: Navigating the Enigmatic Realm of Gut Dysbiosis and Fungal Dynamics in Colorectal Cancer Pathogenesis

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Abstract

Background and Aim: Colorectal cancer (CRC) is a complex and multifactorial disease, with growing indications indicating that the mycobiome, the fungal constituent of gut microbiota, wields significant influence in the development of colorectal cancer. This thorough review explores the contemporary understanding of gut microbiota intervention in colorectal cancer, emphasizing its effects on tumor formation and its potential implications in non-intrusive diagnostic methodologies.

Methods: This extensive review was undertaken to examine and consolidate the available literature concerning the mycobiome's involvement in colorectal cancer. A thorough search of electronic databases, such as PubMed, Scopus, web of Science, Google Scholar, MEDLINE, and pertinent academic journals, was conducted comprehensively.

Results: In the different stages of colorectal carcinoma, there was a notable dynamic alteration within the fungal communities. The ratio of Ascomycota to Basidiomycota exhibited a substantial increase from healthy controls to samples from individuals with colorectal cancer. Several fungal genera such as *Malassezia*, *Moniliophthora*, *Rhodotorula*, *Acremonium*, *Thielaviopsis*, and *Pisolithus* consistently demonstrated higher prevalence in cases of colorectal cancer. Furthermore, as colorectal cancer advanced, a heightened fungal diversity was observed, with opportunistic fungi *Trichosporon* and *Malassezia* identified as significant causative agents.

Conclusion: The exploration presented in this review underscores the pivotal significance of comprehending fungal dysbiosis in adenomas and colorectal cancer (CRC). Beyond a simple link, microbiomes play a substantial role in colorectal cancer, presenting the potential for the creation of non-intrusive diagnostic methods. Delving deeper into the mycobiome's contribution to CRC pathogenesis holds promise for tailored therapeutic measures and individualized strategies for diagnosing and treating colorectal cancers.

Keywords: Colorectal cancer (CRC); Mycobiome; Fungal dysbiosis; Gut microbiota.





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8. Parasitology (Oral Presentations)





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Parasitology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OP-1

Identification of *Candida albicans* and non- MRSA *Staphylococcus aureus* in free- living amoeba isolated from hospital wards; an alarm for distribution of nosocomial infections due to FLA

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Abstract

Background and Aim: Free- living amoebae (FLA) are the most reported eukaryotes from environment. FLA are isolated from hospital environments and clinical setting, and are known as Trojan horse for medical important microorganisms. This study aimed to investigate the prevalence of FLA in hospital wards, and the presence of two important agents of nosocomial infections, *Candida albicans* and *Staphylococcus aureus*, in isolated protozoa.

Methods: Sixty samples were collected from four wards including oncology, dialysis, ICU, and CCU and cultured onto non-nutrient agar. After purification, total DNA extraction was performed from harvested FLA and the presence of *Acanthamoeba*, *Vahlkampfiidae* and *Vermamoebae* and *B. mandrillaris* was identified using PCR and sequencing. Thermotolerance and osmotolerance assays were performed for all *Acanthamoeba* isolates. The presence of *C. albicans* was evaluated using real- time PCR. The presence of *S. aureus* in isolated FLA was investigated by amplification of the identical fragments of *FemA* and *nuc* genes. In addition, the presence of methicillin-resistant genes was assessed by amplification of *mecA* gene.

Results: From total of 60 samples, FLA was detected in 30 (50%) plates. *Acanthamoeba* sp., was characterized in all samples. Two samples (13.3%) were positive for *Vahlkampfiidae*, in which both were *T. aberdonicus*. *V. vermiformis* was only identified in one sample (6.6%), and none of samples were positive *Balamuthia* species. From 30 FLA positive samples, thirteen samples (43.3%) were positive for *S. aureus*, while MRSA was characterized in none of *S. aureus* positive samples. Furthermore, *C. albicans* DNA was detected in only one (3.3%) of FLA- positive samples. From 30 *Acanthamoeba*-positive samples, except two samples, others (28/30) grew in hyperosmotic and both 37°C and 41°C mediums.

Conclusion: Our findings suggest that FLA not only can isolate from hospital wards, but also may provide a condition for nosocomial pathogens to generate and remain active/ alive into FLA, which increases the chance of inter-ward circulation of nosocomial infections.

Keywords: Free- living amoebae; Hospital; Nosocomial infections; *Staphylococcus aureus*; MRSA.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OP-2

Canine dirofilariosis in Iran and necessity laboratory test for human infection in region with high prevalence

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Abstract

Background and Aim: Filariasis is a disease caused by worms from *Filarioidea* family in dogs. Affection by *Dirofilaria immitis* (heartworm) is considered an important parasite disease in dogs in Iran. *D. immitis* and *Dirofilaria repens* are also zoonotic parasites. *D. immitis* may cause some symptoms such as dry cough, dyspnea, and fatigue in dogs on the other hand, *D. repens* usually causes a non-pathogenic subcutaneous infection in dogs. However, *Dirofilaria* doesn't reach adulthood in human beings, it may form coin lesions in the lungs so discrimination diagnosis is very important. These lesions may be misunderstood as tumors of the lungs or infections including tuberculosis.

Methods: Based on previous studies which were conducted in the department of parasitology, faculty of veterinary medicine, university of Tehran, several important findings and insights were detected about *Dirofilaria* sp. The infections of dogs were tested by molecular and parasitological methods.

Results: The results of the studies suggested that the two mentioned species were reported in 24 provinces of Iran. The rate of infection in dogs that were engaged with *D. immitis* in the country is between 1/5 to 6/78 percent. The rate of infection in the northern and north-western provinces is higher than in other regions in Iran. So far human cases have been reported from different areas and reports of human contamination are increasing. Diagnosis of disease in the main host is done by modified Knott test, IFA, ELISA test, and molecular methods. This disease can be detected by radiography, histopathology, and molecular methods in human beings.

Conclusion: Based on the World Health Organization definition, this disease cluster is a neglected tropical disease. Considering the one health approach and the reports of numerous cases of human contamination in different parts of the country, the necessity for the attention and improved knowledge of physicians and laboratory specialists is emphasized for appropriate diagnosis and treatment.

Keywords: *Dirofilaria immitis*; *Dirofilaria repens*; dogs; neglected tropical disease.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OP-3

Preclinical evaluation of solid lipid nanoparticles loaded with amphotericin B and meglumine antimoniate for the treatment of cutaneous leishmaniasis

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Abstract

Background and Aim: Leishmaniasis is a parasitic disease prevalent in over 98 countries. Treatment is challenging due to drug resistance, so researchers are exploring solid lipid nanoparticles (SLNs) as a promising drug carrier. SLNs prevent drug damage, increase drug survival in tissue, and minimize toxicity. This study evaluated the therapeutic efficacy of SLNs loaded with amphotericin B and meglumine antimoniate for the treatment of cutaneous leishmaniasis *in vitro* and *in vivo*.

Methods: The double emulsion/ melt dispersion technique was used to synthesize SLNs. The nanoparticle characteristics were measured using dynamic light scattering (DLS) technique, and the drugs' maximum wavelength was determined to evaluate the efficiency of loading and encapsulation. Encapsulation efficiency (EE) and drug loading (DL) were calculated, and Fourier-transform infrared spectroscopy (FTIR) was performed to confirm the presence of the drug in the lyophilized formulation. *In vitro* drug release was studied to determine the drug release rate from nanoparticles using a dialysis bag. The physical and chemical stability in the short- and long - term, morphology, laboratory toxicity, and anti - inflammatory activity of the nanoparticles were evaluated. Morphology was analyzed using field emission scanning electron microscopy. *In vitro* toxicity was determined using the MTT assay on the J774.A1 cell line, and anti-promastigote activity and drugs effective on amastigote form of *L. major* were evaluated. Additionally, an *in vivo* study was conducted on BALB/c mice to evaluate the efficacy of the nanoformulations in treating cutaneous leishmaniasis. The size of the lesions was measured, and skin samples were taken for histological examination.

Results: The study characterized solid lipid nanoparticles (SLNs) loaded with amphotericin B and/or glucantime, including their average diameter (390 ± 22 nm), PDI (0.240 ± 0.018), and mean zeta potential (-27.9 ± 1.2). The physical and chemical stability of the nanoparticles was evaluated over one year with no significant changes observed. The drug release rate was lower from SLNs than from the free form of the drugs. Morphological analysis of the nanoparticles showed they were approximately 400 nm and uniform in size. *In vitro* toxicity assays showed that the SLNs of drugs were more effective than free drugs. Additionally, the SLNs showed significant efficacy in reducing the number of amastigotes in the J774.A1 cell line and the size of lesions in the *in vivo* study on BALB/c mice. Histological examination also showed improved healing in the treated groups.

Conclusion: This study demonstrated that solid lipid nanoparticles (SLNs) loaded with amphotericin B and/or glucantime are potentially effective drug carriers for the treatment of cutaneous leishmaniasis. *In vitro* toxicity assays showed that the SLNs of drugs were more effective than free drugs. *In vivo* studies on BALB/c mice showed a significant reduction in the number of amastigotes and the size of lesions in the treated groups. Histological examination showed improved healing in the treated groups. Overall, the results suggest that SLNs could be a promising approach for the treatment of leishmaniasis, and further studies are warranted to explore their clinical potential.

Keywords: Nanoparticles; Meglumine antimoniate; Amphotericin B; *Leishmania major*.





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Venue:
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Section: Parasitology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OP-4

Loading of hydroxy naphthoquinone (Atovaquone) in exosomes driven from mouse macrophages (J774A.1) and evaluation of anti-*Toxoplasma* effects in In vitro condition

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Abstract

Background and Aim: Toxoplasmosis is an important disease which represents a global health threat. Albeit a variety of therapeutic regimens for toxoplasmosis have been developed, treatment of chronic phase of this disease is still challenging due to poor drug delivery across the blood brain barrier. Atovaquone (ATQ) is known as the only successful treatment of chronic phase, but it has poor efficacy due to its high hydrophobicity and low bioavailability. Nanotechnology and new formulations may find its way to improve the pharmacokinetic profile and efficacy of ATQ. This study aimed to prepare ATQ loaded exosomes (EXO-ATQ) and determine its therapeutic potentials against *T. gondii* in in vitro condition.

Methods: Exosomes were isolated from mouse macrophage cell line (J774A.1). The isolated exosomes were loaded with ATQ, applying the co-incubation method. The cytotoxic activity of EXO-ATQ compare to suspension of ATQ (S-ATQ) and exosome (exosome without any ATQ) was evaluated by MTT assay in Vero cell culture. To estimate the efficacy of EXO-ATQ compare to S-ATQ on intracellular proliferation of *T. gondii*, RH strain Vero cells (2×10^5 /well) were infected with tachyzoites of *T. gondii* at a ratio of 1:3 parasite/cell. Then, concentrations of 15, 30, 60, 120, and 240 $\mu\text{g/ml}$ of each compound (S-ATQ, exosome, and EXO-ATQ) were added to microplates and after 48 h, microplates were rinsed, fixed, and stained with Giemsa dye. The cells were analyzed with a light microscope to determine *T. gondii* infection rate (number of infected cells per 100 examined cells) and parasite intracellular replication (mean number of the intracellular parasite in 100 infected cells).

Results: The results indicated that exosome had no significant effects on the viability of Vero cells. However, administration of S-ATQ and EXO-ATQ caused a significant concentration-dependent decrease in cell viability compared to control (untreated cells). At the time of 48 h, CC_{50} for S-ATQ and EXO-ATQ were 560 and 443 $\mu\text{g/ml}$, respectively, and no significant difference was found between the cytotoxicity of S-ATQ and EXO-ATQ. The results of intracellular proliferation of *T. gondii* tachyzoites showed that S-ATQ and EXO-ATQ induced a dose-dependent decrease in the proliferation rate of *T. gondii*, RH strain tachyzoites and EXO-ATQ significantly reduced the infection rate of *T. gondii* tachyzoites compared to S-ATQ in all concentrations ($p \leq 0.05$).

Conclusion: Our results implied that exosomes have the potential to be used as an efficient drug delivery system, and the loading of ATQ into the exosomes ameliorates the effect of ATQ against *T. gondii*.

Keywords: Drug delivery; *Toxoplasma gondii*; Exosome; Atovaquone; In vitro.





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Section: Parasitology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OP-5

Taxonomy, population structure and genetic diversity of Iranian leishmania strains of cutaneous and visceral leishmaniasis

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Abstract

Background and Aim: Despite the broad distribution of leishmaniasis in Iran, there is a little genetic information about the causative agents and epidemiological status of the disease. Genetic diversity of the parasite is suggested to be one of the factors, which influences the clinical manifestations of the disease. In this study, we investigated the genetic variations, population structure, and evolutionary history of *Leishmania* species from endemic foci of Iran.

Methods: Fifty- two isolates from humans, canines, and rodents from different endemic foci of Iran were used to sequence the N-acetyl glucosamine-1-phosphate transferase (Nagt) gene. Phylogenetic and structure analyses were performed to investigate inter- and intra-species diversity of the *Leishmania* isolates.

Results: In total, 10 haplotypes including *L. major* (n = 6), *L. tropica* (n = 2), *L. infantum* (n = 1) and *L. turanica* (n = 1) were identified across 52 isolates. Haplotype diversity (Hd) ranged from zero for *L. infantum* and *L. turanica* to 0.78 ± 0.136 for *L. major*. This study identified population structure of *Leishmania* isolates from different geographical regions of Iran. The results of the phylogenetic tree showed 4 distinct clades for each species of *Leishmania*. In addition, the highest intraspecies diversity was observed among *L. major* isolates. No correlation was observed between species and geographic distribution of haplotypes.

Conclusion: *Leishmania* isolates were identified at the species level using the Nagt gene, low variation within species indicates conservation of this gene in *Leishmania*. The results provide knowledge into the evolutionary history of Iranian *Leishmania* isolates.

Keywords: *Leishmania*; Nagt gene; Genetic diversity; Geographical distribution; Iran.





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Venue:
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Section: Parasitology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OP-6

Seropositivity of strongyloidiasis and toxocariasis in patients with hypereosinophilia referring to some diagnostic centers in Tehran, Iran

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Abstract

Background and Aim: Increasing of the eosinophil counts from the normal range is called hypereosinophilia. Secondary hypereosinophilia is seen in helminth infections and allergic diseases. If eosinophilia is not diagnosed and managed on time can lead to skin, lung, heart, digestive and vision complication for the patients. So, the determination of causative agents and proper medication is important to prevent such consequences. Many parasites especially ones that invade tissues lead to eosinophilia. In this study, the seropositivity of two nematode infections among people with eosinophilia who referred to some medical diagnosis centers in Tehran was investigated.

Methods: After obtaining written consent, a questionnaire was completed and a blood sample was taken from every individual with hypereosinophilia who referred to some medical diagnosis centers of Tehran, Iran in 1402. The samples were transferred to the Diagnostic Laboratory of Strongyloidiasis in the School of Public Health, Tehran University of Medical Sciences. The seropositivity of helminth infections were evaluated by indirect enzyme-linked immunosorbent assay (ELISA) using commercial kits (Novalisa, NovaTec, Germany) to detect antibody (Ab IgG) against *Strongyloides stercoralis* and *Toxocara* spp. infections. Statistical analysis was performed using SPSS 21 software.

Results: Overall, among 135 individuals who participated in this study, 61 (45.18%) were male and 74 (54.9%) were female. The patients' age ranged from 3 to 90 years old with the mean of 46.65. The seropositivity of strongyloidiasis and toxocariasis were 9.6% and 0.74%, respectively. Among different health conditions in the participants, type 2 diabetes mellitus was the most prevalent one and it was significantly associated with seropositivity of strongyloidiasis ($p = 0.02$).

Conclusion: Hypereosinophilia is a common laboratory index in tissue- invasive helminth infections. In the current study among the patients with hypereosinophilia, *Strongyloides* seropositivity was higher than that of *Toxocara* which is partly due to age effect. The Association of *Strongyloides* seropositivity with diabetes is an important finding that implies the need for community- based studies. Concerning the increasing trend of diabetes incidence in Iran, screening of strongyloidiasis in at-risk populations by using sensitive methods is recommended to prevent the risk of disseminated infections.

Keywords: Hypereosinophilia; Seropositivity; *Strongyloides stercoralis*; *Toxocara* spp; diabetes.





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8. Parasitology (Poster Presentations)





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-1

The correlation between the infection of *Toxoplasma gondii* and Alzheimer's disease in Mazandaran province, Iran

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Abstract

Background and Aim: *Toxoplasma gondii* is an intracellular protozoan that has high incidence in developing countries, especially in Iran. Studies have shown that this parasite can cause neurological changes and also behavioral and psychological disorders, including Alzheimer's disorder, by several mechanisms. Alzheimer's is a neurological disease that affects the brain and causes the death of brain cells, which will result in the loss of memory and cognition. Few studies in the world and also in Iran have been conducted on the role of *Toxoplasma gondii* in causing Alzheimer's disorder. Therefore, this study was designed to investigate the relationship between *Toxoplasma gondii* infection and Alzheimer's disorder in Mazandaran province.

Methods: This study was a descriptive-analytical study that included 115 people with Alzheimer's disorder and 115 healthy people in Mazandaran province. In this study, participant's data were collected by a three-part questionnaire including demographic information, questions to assess the clinical features of Alzheimer's disorder and information about the possible way of being infected to *Toxoplasma gondii*. Levels of IgM and IgG antibodies of *Toxoplasma gondii* were measured and reported in blood samples of case and control participants. Then, the obtained data were analyzed with SPSS software version 18 and all findings with a level of less than 0.05 were considered significant.

Results: Totally, among 115 blood samples of the case group, IgG antibody test was obtained positive in 30 (25.30%) blood samples and negative in 85 (74.70%). In the control group, among 115 samples, 11 (9.30%) were positive and 104 (90.70%) were negative. these Findings were evaluated between case and control groups using K2 statistical analysis and univariate logistic regression model and the results showed that there was a statistically significant relationship between *Toxoplasma gondii* IgG antibody in case/ control groups. By controlling the effect of confounding variables using multivariate logistic regression model, the chance of developing Alzheimer's disorder in people with *Toxoplasma* infection was 2.89 times higher than those without *Toxoplasma gondii* infection, which is statistically significant ($P < 0.05$). From 230 blood samples of the case and control participant in this study, no positive IgM test samples were reported.

Conclusion: According to the results of the present study, infection with *Toxoplasma gondii* parasite can be identified as one of the risk factors that is associated with Alzheimer's disorder. Therefore, prevention and treatment of this infection may be able to slightly reduce the disability and destructive personal, economic and social effects of Alzheimer's disorder at the individuals and also in society.

Keywords: *Toxoplasma gondii*; Alzheimer's disorder; neurological disease; IgG; IgM.





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Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-3

Production of recombinant form of *Leishmania infantum* hs1vu complex proteolytic subunit-like protein for serological diagnosis of visceral Leishmaniasis

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Abstract

Background and Aim: Diagnosis of *Leishmania infantum* as a systemic lethal infection is a significantly important issue. Discovering any efficient comprehensive diagnostic methods is a challenging concern in the world for patients to start their proper treatments. Currently the secreted antigens of *Leishmania* promastigotes indicate a potential capacity to be used as early diagnosis of *L. infantum*. In this study hs1vu complex proteolytic subunit-like protein as a secretory antigen of *Leishmania* was cloned in prokaryotic expression vector and the antigenicity of its recombinant form was surveyed using ELISA assay.

Methods: The *L. infantum* DNA was extracted and amplified by PCR with the specific primer designing for hs1vu complex proteolytic subunit-like protein. The PCR products of gel extraction were successfully ligated into the pET28a plasmid vector. Following, the sub cloned vector containing hs1vu complex proteolytic subunit-like protein gene in BL21 host (*Escherichia coli*) was expressed then sodium dodecyl sulfate - polyacrylamide gel electrophoresis (SDS-PAGE) and Western Blot were used for evaluating the expressed protein purification. Finally, the antigenicity of the recombinant hs1vu complex proteolytic subunit-like protein was estimated by using ELISA assay.

Results: hs1vu complex proteolytic subunit-like protein was successfully sub cloned in pET28a as a prokaryotic expression vector. SDS-PAGE and Western Blotting techniques were confirmed the protein with a molecular weight of 25 kDa. Then the ELISA assay confirms that antibodies against of antigens hs1vu complex proteolytic subunit-like protein was abundant in the serum of VL patients with the 95.23% sensitivity and 100% Specificity score.

Conclusion: Our data indicated that the novel recombinant hs1vu complex proteolytic subunit-like protein was well produced in prokaryotic host and purified protein was used for standardize the ELISA assay which is a perspective of a new diagnostic method in future.

Keywords: *Leishmania infantum*; Diagnosis; ELISA assay; Recombinant protein.





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Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-4

In vitro and *in vivo* effects of *Mentha piperita* hydroalcoholic extract against *Leishmania major*

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Abstract

Background and Aim: Cutaneous leishmaniasis (CL) is a worldwide protozoan disease caused by *Leishmania* spp. The limitations of current treatments for CL emphasize the need for a new effective and less toxic medication. *Mentha piperita*, a medicinal herb, has antispasmodic, antimicrobial, disinfectant, antipyretic, and anti-aging properties. Therefore, this study aimed to investigate the anti-leishmania activity of *M. piperita* hydroalcoholic extract on *Leishmania major* *in vitro* and *in vivo*.

Methods: The effect of different concentrations (1-512 µg/ml) of *M. piperita* hydroalcoholic extract on the Iranian standard strain of *L. major* promastigotes was investigated using the flow cytometry technique. For *in vivo* experiments, BALB/c mice infected with CL were treated with doses of 20, and 40 mg/kg. Mice received this treatment in two ways: injection on the sides of the wound and topical application for three weeks, and lesion size was measured before treatment and every week.

Results: The results of *in vitro* experiments showed that the *M. piperita* hydroalcoholic extract had the highest anti-leishmanial activity with an IC₅₀ of 48.11 µg/ml. Also, *in vivo* experiments showed a significant reduction in lesion size one week after the end of treatment.

Conclusion: The present study demonstrated that the *M. piperita* hydroalcoholic extract could be a promising alternative treatment for CL. However, further investigations are required for its clinical application.

Keywords: Cutaneous leishmaniasis; *Mentha piperita*; *Leishmania major*; Flow cytometry; BALB/c mice.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-5

In vitro and *in vivo* antileishmanial activity of *Melaleuca citrina* hydroalcoholic extract against *Leishmania major*

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Abstract

Background and Aim: Leishmaniasis is a parasitic disease that affects millions of people worldwide. Current treatments for this disease are limited and have significant side effects. Therefore, the need for new and effective treatments is felt. This study was conducted with the aim of investigating the anti-leishmanial activity of the hydroalcoholic extract of *Melaleuca citrina* against *Leishmania major* *in vitro* and *in vivo*.

Methods: The anti-leishmanial activity of different concentrations (1 to 512 µg/ml) of the hydroalcoholic extract of *M. citrina* was evaluated *in vitro* using the flow cytometry method. For *in vivo* study, infected mice were treated with doses of 20 and 40 mg/kg both by injection and topically. Wound size was measured in five stages and the results were analyzed using vernier calipers.

Results: The flow cytometry method showed the anti-leishmanial effect of the extract in a dose-dependent manner. In the *in vivo* study, higher concentrations of the extract were associated with reduced wound areas, especially in the topical application group, which performed better than the injection group. In addition, the extract showed more effectiveness compared to the control group.

Conclusion: This study showed that the hydroalcoholic extract of *M. citrina* has significant anti-leishmanial activity against *L. major*, especially when applied topically. Further research is needed to evaluate its safety and efficacy for potential use as a new treatment option for leishmaniasis in humans.

Keywords: Cutaneous leishmaniasis; *Melaleuca citrina*; *Leishmania major*; MTT assay; BALB/c mice.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-8

Investigation of toxoplasma gondii and toxocara infection in pregnant women referring to Mashhad centers

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Abstract

Background and Aim: Congenital toxoplasmosis is a parasitic infection that can result in abortion, premature birth, chorioretinitis, microcephaly, hydrocephalus, brain calcification, deafness, and blindness. Toxocariasis is a common parasitic disease that can be transmitted between humans and animals, and can lead to reproductive abnormalities, changes in normal birth parameters, and even abortion. This study aims to evaluate the risk of simultaneous infection of toxoplasma and toxocara in pregnant women.

Methods: The study collected information on 352 pregnant mothers who visited health centers. Checklists were used to gather data on the mother's age, gestational age, and place of residence, education, and occupation, history of previous pregnancies, family marriage, and history of diabetes. Additionally, the checklists included questions on the consumption of undercooked meat, raw or non- disinfected vegetables, and contact with dogs or cats at home. The laboratory technician also took some blood serum samples for other diagnostic purposes to determine the titer of IgG or IgM for Toxoplasmosis. The IgG antibody titer was used to determine toxocariasis.

Results: The study involved 352 pregnant women who visited health centers in Mashhad. The average age of these women was 26.77 ± 5.76 years, and their average gestational age was 26.10 ± 4.65 . Out of these women, 35 (9.9%) had a positive level of Anti IgM Toxoplasma, 90 (25.6%) had a positive level of Anti IgG Toxoplasma, and 4 (1.1%) had a positive level of Anti IgG Toxocara. The prevalence of simultaneous infections of the two types was just 1.1%

Conclusion: After analyzing the prevalence of Toxoplasma and Toxocara co- infection and comparing it with previous studies, it can be concluded that the simultaneous prevalence of these two infections in our study is lower than what was expected. Additionally, the prevalence of Toxoplasma infection is higher compared to Toxocara.

Keywords: Toxoplasmosis; Toxocariasis; Mashhad; Pregnant women.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-9

Relationship between giardiasis infection and respiratory allergy in children

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Abstract

Background and Aim: Giardiasis is a common parasitic disease in the world. The cause of this infection is a single - cell flagellated parasite called *Giardia lamblia*. Giardiasis infection is more important in children due to severe complications and dangerous consequences, including steatorrhea, severe weight loss, and neurological and mental lesions compared to adults. There is evidence that allergy symptoms, especially respiratory allergies, develop in patients with giardiasis infection. Because of the importance of this parasitic disease in children and adolescents, we aimed to investigate the relationship between respiratory allergy and giardiasis infection in children of Ardabil (Northwest of Iran).

Methods: Fifty children under the age of 14 years with respiratory allergy (asthma, allergic rhinitis, coughing and chronic sneezing) were selected as case group and 50 children under the age of 14 years without respiratory allergy were selected as control group. These individuals were selected among the children visiting the clinics of the pediatricians of Ardabil. Serum immunoglobulin IgE values were measured by the ELISA method (Germany-made Biotech Model B325). The percentage of eosinophil in the blood was tested by CBC. Diagnosis of giardiasis infection was also done through the search for the fecal antigen of *Giardia lamblia*. All the tests were carried out in Arin Medical Diagnostic Laboratory (Ardabil), and SPSS Version 21 software was used for statistical analysis.

Results: Fifty- six percent of children in both case and control groups were boys and 44 percent were girls. The highest age group of children studied in both case and a control group were 3 to 12 years (78 percent). Six percent of children with respiratory allergy (case group) and 4 percent of children without respiratory allergy (control group) were infected by *Giardia lamblia*. The average percentage of eosinophil in children with giardiasis was 6.09% and in non-affected children was 1.42%, respectively. The average IgE values were 107.43 and 88.36 IU/ml in giardiasis infected and non-infected children, respectively.

Conclusion: According to the results of this study, it is concluded that there is a clear and significant statistical relationship between giardiasis infection and respiratory allergy in children (Sig = 0.012, $p < 0.05$).

Keywords: Giardiasis; *Giardia lamblia*; Respiratory allergies; Children; Immunoglobulin IgE.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Systematic Review

Code of Abstract: PP-10

Distribution of equipment for *Dirofilaria immitis* diagnosis in endemic and non- endemic regions using GIS

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Abstract

Background and Aim: *Dirofilaria immitis* (*D. immitis*) is a parasitic worm that causes heartworm disease in dogs. Accurately diagnosing of *D. immitis* infection is crucial for prevention of the disease. Currently, the diagnostic methods are categorized into various grades according to their recognized levels of sensitivity and specificity. This review study, aimed to assess the status of the current distribution of the equipment, identify potential gaps in resource allocation, and also the accessibility and effective use of diagnostic tests and equipment.

Methods: The materials and methods employed in this study involved searches conducted in PubMed, Google Scholar, Web of Science and sid.ir. To identify relevant articles on the prevalence or frequency of *Dirofilaria immitis*, the search used keywords such as heartworm disease, microscopic tests (modified Knott test), molecular diagnosis (PCR), and serological methods including antigen diagnostic tests (Rapid tests). The selection criteria excluded case reports and focused on articles presenting the prevalence or frequency of *D. immitis* based on the diagnosis method. The results obtained were mapped using Geographic Information System (GIS).

Results: The comprehensive review is based on the analysis of 43 articles from endemic and non-endemic regions of Iran. The prevalence rates of *Dirofilaria immitis* were found to be 46.7% using the microscopic method, 25.90% using the necropsy method, 78.60% using the PCR method in Gilan province, and 62.80% using the serological method in Ardabil province. Molecular diagnosis methods proved to be efficient in diagnosing *D. immitis* infection in dogs.

Conclusion: The study has thoroughly manifested the significant differences in the availability of diagnostic equipment for *D. immitis* across various geographical regions. The findings were significantly imbalance, with endemic areas having less access to diagnostic tools compared to Capital city in non-endemic regions. This distribution does not align with the necessity to control and monitor the disease where it is prevalent. However, the lack of resources in some non- endemic area may inhibit timely diagnosis and prevention, potentially leading to unrecognized spread.

Keywords: Parasitic Diseases in Canines; Veterinary diagnostics; Diagnostic Accessibility; Spatial Analysis; Disease Mapping.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-11

Designing and evaluation of loop- mediated isothermal amplification for rapid detection of *Enterocytozoon bienersi*

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Abstract

Background and Aim: *Enterocytozoon bienersi* is one of the prevalent microsporidia species, responsible for more than 90% of human and animal microsporidiosis. *E. bienersi* is transmitted through contaminated water, food, or environmental sources. Immunocompromised patients are susceptible to microsporidiosis. In addition, microsporidia species, particularly *E. bienersi*, are frequently reported from waterborne and foodborne outbreaks. Therefore, early detection of *E. bienersi* for clinics and outbreak investigations. This study aimed to design a loop-mediated isothermal amplification (LAMP) for rapid detection of *E. bienersi*.

Methods: DNA was extracted from 30 *E. bienersi*- positive samples, which were confirmed with nested PCR. LAMP primers were designed based on the identical fragment of small subunit ribosomal RNA (SSU rRNA) gene. LAMP reactions were performed at 63°C and the sensitivity and specificity of the assay were analyzed. The results of amplification were compared to real- time PCR.

Results: Our results showed that the LAMP assay successfully amplified 25 (83.3%) samples. The specificity results indicated no false positive with other microorganisms. Furthermore, the LAMP method exhibited a sensitivity (limit of detection, LoD) as low as 34 fg of total DNA. Compared to the LAMP assay, real-time PCR was able to detect all 30 nested PCR-positive samples.

Conclusion: Our findings showed that the LAMP assay was able to detect 83.3% of *E. bienersi*-positive samples. Although the current assay was not able to detect all nested PCR-positive samples, the lack of need for specific instruments, rapid processes, and high specificity makes LAMP assay a suitable tool for screening.

Keywords: *Enterocytozoon bienersi*; Loop-Mediated Isothermal Amplification; Point of care; real- time PCR.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-14

Evaluating sodium chloride efficacy versus zinc chloride in the flotation method within wildlife veterinary parasitology

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Abstract

Background and Aim: This study aims to evaluate and compare the effectiveness of sodium chloride and zinc chloride in the flotation method, specifically within the context of wildlife veterinary parasitology. Given the unique challenges in diagnosing parasitic infections in wild life, such as diverse parasite species and varying sample conditions, it is crucial to determine the most efficient and reliable flotation solution.

Methods: All 62 fecal samples from wild carnivores were collected from the Hirkani Forest area, located in the region between Chalous and Nowshahr provinces. In the present study, clarity, parasite integrity preservation, and overall diagnostic yield were assessed. In addition to, cost, availability and ease of use were evaluated. A total of 62 samples were collected from bears (n = 24), leopards (n = 18), wolves (n = 15), and foxes (n = 5). Unfortunately, four fecal samples were lost (three from leopards and one from a wolf).

Results: The study found that out of the 62 fecal samples collected from bears (n = 24), leopards (n = 18), wolves (n = 15) and foxes (n = 5). With 38 out of 62 samples testing positive using zinc chloride, versus only three with sodium chloride. 20 samples tested negative with both methods. Three (5.17%) samples tested positive with saturated salt water, while 38 (65.52%) samples tested positive with zinc chloride. Interestingly, the detection parasitic infection in the sample that tested positive with saturated salt water was similar to that of zinc chloride. According to the available search results, zinc chloride is considered to be a more effective solution for detecting parasitic infections in wildlife fecal samples compared to other solutions such as sodium chloride. This study found that saturated sodium chloride had on unacceptable sensitivity (7.89%) compared to zinc chloride.

Conclusion: The findings of this study clearly demonstrate that zinc chloride (ZnCl₂) significantly had better efficacy in the flotation method for parasitic diagnosis in wildlife. The higher specific gravity of zinc chloride compared to sodium chloride contributes to its enhanced efficacy. This property facilitates a more effective separation of parasites from fecal debris, leading to clearer samples and more accurate diagnosis. The importance of this cannot be ignored in wildlife parasitology, where sample quality can vary greatly, and the risk of misdiagnosis is high due to the diverse range of parasites present in wild animals.

Keywords: Diagnostic Methods; Comparative Analysis; Laboratory Techniques; Fecal examination; Accurate identification.





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Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-15

Evaluation of the antiparasitic effects of insect products in the treatment of lesions infected with *Leishmania major*

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Abstract

Background and Aim: Leishmaniasis is a vital World health issue caused by a kinetoplastid protozoa of the genus *Leishmania*. The protozoa are transmitted via sandflies and is generally revealed by skin lesions ranging from a simple cutaneous to visceral ulcer. due to the lack of definitive treatment and the high cytotoxicity and low efficacy of current treatments, nowadays many researchers are focused on natural compounds for the treatment of cutaneous leishmaniasis. In this present experimental study, anti-leishmanial impacts of various concentrations of larval excretion/secretion products (ES) of *Lucilia sericata* plus honey as synergist were evaluated under in vivo conditions.

Methods: In this study, the effects of ES and ES fractions of larval in combination honey in in vivo were assessed. we measured and assessed seven groups of mice treated with therapy groups (crude ES, ES above 10 kDa and ES below 10 kDa with honey as synergist), glucantime drug (Positive control), Eucerin group as a drug base, and ultimately negative group as without treatment.

Results: The macroscopic evaluation of the lesion size of BALB/c mice demonstrated Reducing the size of the lesion in the treatment group of crude ES and above 10 kDa with honey had a better effect than the positive control group (glucantime which was not observed in the ES below 10 kDa with honey. Examining the results of the treatment groups with the negative control showed a significant difference. Eucerin consequences showed that it has no effect on the treatment and there was no significant difference between this group and the group without treatment.

Conclusion: The results showed that larval products with honey are effective on intracellular form of *L. major*.

Keywords: *Leishmania major*; Cutaneous leishmaniasis; *Lucilia sericata*; ES; *Apis mellifera*; honey.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-16

Frequency of *demodex folliculorum* in students with cutaneous folliculitis living in dormitories of Ardabil University of Medical Sciences in 1400-1401

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Abstract

Background and Aim: Ectoparasites are of significant importance in terms of medicine and veterinary medicine. Among the types of human ectoparasites are mites called demodex worm-shaped mange. Demodex affects the hair follicle and follicular and sebaceous glands, especially the face, nose and eyelids, and they are mostly symptomless, but sometimes they are associated with folliculitis, acne, comedones (blackheads) or local keratitis. Among the species of Demodex, the most common species that affect the human skin are *Demodex folliculorum* and *Demodex brevis*. The purpose of this study is to determine the prevalence of *Demodex folliculorum* in students with skin folliculitis residing in the dormitories of Ardabil University of Medical Sciences in 2014-01.

Methods: The present study was a cross-sectional descriptive study. After obtaining informed consent from the students living in the dormitories of Ardabil University of Medical Sciences (of both sexes), a simple census sampling of 384 students was done. In order to collect the samples in the dormitory, a permission to enter the dormitory was obtained by the cultural and student vice-chancellor. Other samples were taken with the coordination of students and during their attendance at the medical school in the parasitology laboratory of the medical school of Ardabil University of Medical Sciences. After reading and filling the informed consent form, all students entered the study and also completed a questionnaire including demographic information such as age, sex, place of residence and contact with animals. Questionnaires were coded and the same code was inserted on each person's sample on the slide. Skin samples, including skin chips and pimple contents, were taken from the skin of students with skin folliculitis or comedones (blackheads). The criteria for entering the study were having skin folliculitis or comedones, and considering that factors affecting Demodex have not been shown in previous studies, there will be no specific criteria for exiting the study unless the person had received an effective drug on post lesions. It should be mentioned that the samples were obtained from the lesion by using a disposable scalpel blade or by pressing the boil area or by completely scraping the surface of the skin and completely without invasive methods. Preparation and clarification of skin samples was done using 10% potassium hydroxide or simple lactophenol or colored lactophenol (lactophenol- azocarmine) in such a way that the skin chip samples or the contents of skin pimples were drained. It was placed on the slide. Then, one or two drops of lactophenol or potash were added to it and left for 5-10 minutes to become clear in the laboratory environment. The skin chips and fat contents in the discharged pimples became clear and faded. The clarified samples were examined under a light microscope with 4x, 10x and 40x magnification. In positive cases, demodex were photographed using a microscope equipped with a camera. Cutaneous ectoparasites were identified using valid parasitological keys by comparing the parameters described in reliable sources of Demodex identification. Statistical analysis was done using SPSS 24 software. Chi-Square test was used to determine the significant relationship between the prevalence

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of demodicosis with age, sex, place of residence and history of contact with animals. P-value less than 0.05% was considered significant.

Results: In this research, 384 samples were collected from students suffering from folliculitis or skin comedones living in the dormitories of Ardabil University of Medical Sciences in 2014-2021. Of these, 268 were men and 116 were women. Then the samples were examined using parasitology methods. In this study, 21 people, 5.5% of the studied students were positive for demodex folliculorum ectoparasite infection. The results of the age study show that the number of cases of demodex infection in the 20-year-old age group was higher than other ages. Also, the results of this study showed that demodex contamination is almost equal between men and women, as well as between students living in cities and villages. Statistically, there was no significant difference between the investigated factors (age, gender, place of residence and history of contact with animals) ($P > 0.05$).

Conclusion: In the present study, it was found that the level of demodex contamination is highly related to age, and demodex contamination is relatively low in students who are teenagers and young adults.

Keywords: Ectoparasite; mange or mite; *demodex folliculorum*; skin folliculitis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-17

Combination of topical tofacitinib and glucantime for treatment of cutaneous leishmaniasis in mouse model

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Abstract

Background and Aim: Leishmaniasis is a neglected tropical disease that affects populations mainly in developing countries. Leishmaniasis is prevalent in Iran as a public health problem. Currently there is no effective vaccine against human leishmaniasis and the treatment is based on chemotherapy. Conventional drugs are toxic and expensive, and drug resistance has led to the search for new treatments. Tofacitinib is a Janus kinase inhibitor that disturbs the signaling pathway of several cytokines in the immune system. The aim of this study was to evaluate the effect of topical tofacitinib 2% ointment in healing cutaneous leishmaniasis in Balb/C mice.

Methods: This experimental study was performed using tofacitinib and glucantime drugs in 40 female Balb/C mice. The metacyclic form of promastigote of *Leishmania major* standard strain (MRHO/IR/75/ER) was injected into the footpad of the mice, the mice were divided into 4 treatment groups: tofacitinib, glucantime, tofacitinib- glucantime and control without treatment. The treatment period was 28 days. The footpad thickness of all groups was measured at the end of each week.

Results: After the end of the treatment in the groups treated with tofacitinib, a significant decrease in the size of lesion and the footpad thickness was observed compared to the control group without treatment ($P < 0.01$).

Conclusion: It seems that tofacitinib ointment accelerates lesion healing in Balb/C mice and has worked similarly to standard glucantime treatment. Ointment can be a better option for leishmaniasis treatment and due to its ease of use and no need for painful injections it can be considered as an option for the treatment of patients with cutaneous leishmaniasis.

Keywords: Combination Therapy; tofacitinib; glucantime; cutaneous leishmaniasis; mouse model.





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Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-19

Isolation and molecular detection of pathogenic free-living amoeba from strawberries and soil in Tehran, Iran

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Abstract

Background and Aim: Free-living amoeba isolated from different sources until now. *Acanthamoeba* is the importance of FLAs, that cause encephalitis and keratitis and its identified as a carrier of foodborne pathogens in vegetables and soil. Strawberries are an important fruit for parasitic infections. This fruit grows in soil; thus, the choice of agricultural soil is crucial. For the first time, this study aims to the presence of pathogenic FLAs in strawberry and soil samples in Iran.

Methods: A total of 45 samples including strawberry and soil were collected from Tehran, Iran. Samples were cultured onto a 1.5% non-nutrient agar medium. The cultures were analyzed using morphological key and molecular methods for positive plates. PCR was performed to detect FLAs (*Acanthamoeba*, *Vahlkamfiids*, *Balamuthia* and *Vermamoeba*) using specific primer. Sequencing and genetic associations among sequenced genotypes done (18S rRNA gene) by MEGA X and a phylogenetic tree were constructed using the maximum likelihood model. The pathogenicity tests were assessed by osmo/thermotolerance.

Results: In total, 38 (84%) out of 50 samples were positive including, 18 out of 20 (90%) strawberry samples and 20 out of 25 (80%) soil samples. They were successfully sequenced in 25 samples and samples belonged to T4 genotypes (100%). In addition, 14/19 (73%) in strawberry samples and 23/25 (92%) in soil samples were ranked highly pathogenic.

Conclusion: This is the first study reporting contamination of strawberry and soil with pathogenic *Acanthamoeba* genotypes in Iran. Our findings indicate that strawberries and soil could be a serious hazard to *Acanthamoeba* infections, which may result from different factors such as exposure to animal manure or contact with contaminated soil.

Keywords: Free living amoeba, *Acanthamoeba*, Strawberry, Soil.





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Tehran University of Medical Sciences, Tehran, Iran.
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Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-20

Clinical symptoms, diagnosis and treatment of demodicosis

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Abstract

Background and Aim: Demodicosis in humans caused by two species of *Demodex* called *folliculorum* and *brevis*. *Demodex* live inside the sebaceous glands and hair follicles. After mating they burrow into the skin, laying eggs, introducing infection to the skin. The disease is seen in male and female. Although, there is no clinical symptoms in individuals with normal immunity system, but in certain cases (usually related to a suppressed immune system, caused by stress or illness) mite populations can dramatically increase, dermatitis and rough, dry and scaly skin, particularly asymmetrical papulopustular or granulomatous variants are observed. Clinical symptoms of demodicosis mimic other known skin diseases such as dermatophytosis, folliculitis, rosacea, perioral dermatitis and blepharitis, which is why this is often misdiagnosed. In this study, clinical symptoms, diagnosis and treatment of 319 patients with demodicosis are presented.

Methods: Some of the physicians treat the patients according to the clinical symptoms. Scraping from the skin of lesions, Slide preparation with 20 % KOH and observing the mite under the microscopic is the gold standard diagnostic test. Histopathologic examination of skin biopsy can determine the presence of *Demodex*. The patients infested with *Demodex folliculorum* were referred to dermatologists for treatment.

Results: The patients include 248 (77.74%) female and 71(22.26%) males at the age of 8 months to 81year (mean 35.6 years). Common interventions used for *Demodex* infestation include Benzyl benzoate, Crotonon, Ivermectin, Metronidazole, Permethrin, Salicylic acid, Selenium sulfide, Sulfur products. 6 mg of ivermectin taken orally twice daily at 2-weeks intervals and 1% cream reduced the average number of *Demodex* mites in chronic Demodex blepharitis. Local and systemic corticosteroids are contraindicated in any patient diagnosed with demodicosis. Secondary bacterial infections must be treated aggressively with an appropriate antimicrobial.

Conclusion: The patients who were treated with systemic and local ivermectin had better healing. Before administration any treatment, the cause of disease must be clarified. Local and systemic corticosteroids are contraindicated in any patient diagnosed with demodicosis.

Keywords: Demodex folliculorum; demodicosis; diagnosis; treatment.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-21

High Occurrence of *Vermamoeba vermiformis* in environment and keratitis samples in Iran as a public health concern

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Abstract

Background and Aim: *Vermamoeba vermiformis* (*V. vermiformis*) is one of the most worldwide prevalent Free-living amoebae (FLA). In recent years, studies regarding the distribution of *V. vermiformis* have rapidly increased, focusing on the importance of this FLA as human pathogen but its pathogenic potential is still a myth. Moreover, endosymbiosis relationship between *V. vermiformis* and microorganisms may lead to the development of multi-antibiotic drug resistance pathogens and may increase FLA virulence. This study aims to perform a systematic mini-review of the data on the occurrence of *V. vermiformis* in environment and keratitis samples in Iran in the available literature.

Methods: Articles on the occurrence of *V. vermiformis* in environment and keratitis samples in Iran were systematically searched in PubMed, Scopus and Google Scholar between January 2000 and July 2023.

Results: A total of 436 articles were generated by conducting systematic search within 2000-2023. Taking duplication into account, 400 records were excluded, and 19 articles met the inclusion criteria. 14 full-text articles were assessed.

Conclusion: Our findings suggest a wide distribution of *V. vermiformis* in water and different environmental sources in Iran. More comprehensive studies on the pathogenesis of this genus and relationship between *V. vermiformis* and its endosymbionts are research priorities.

Keywords: Free-living amoebae, *Vermamoeba vermiformis*, Keratitis, Environment, Iran.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-22

Isolation and molecular identification of free-living amoeba from drinking water in northwest of Iran

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Abstract

Background and Aim: Free-living amoebae (FLA) are able to accidentally infect humans. The identification of the amoebae could help to prevent and control of the disease. This study was conducted to isolate and identify FLA from drinking water of Qazvin, Iran.

Methods: In this study, hot and cold drinking water samples were taken from in different parts of the Qazvin, Iran. The samples were cultured to isolate and identify positive specimens. PCR amplification was conducted to confirm the isolated species of the FLA. Evaluation of pathogenicity was conducted by osmo-tolerance and thermo-tolerance assays.

Results: According to the results of the present study, 22.5% (27/120) of water isolates were positive for FLA. *Acanthamoeba* and *Nagelria* were identified among the isolates. The results of pathogenicity assays demonstrated that 55% of *Acanthamoeba* was pathogen.

Conclusion: Regarding to the FLA may have pathogenic potential, so this study highlights the necessity for taking strict measures over the sanitation of drinking water for public health.

Keywords: FLA, Drinking water, Pathogenicity assays, Qazvin, Iran.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-23

The possible association between chronic toxoplasmosis and induced Parkinson's disease in mice model

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Abstract

Background and Aim: *Toxoplasma gondii* is a neuro-invasive protozoal pathogen capable of manipulating its intermediate host's behavior such as Parkinson's disease (PD). we tested the hypothesis that chronic toxoplasmosis potentiates behavioral and cognitive impairments in BALB/c mice with a PD-like syndrome.

Methods: Thirty-five specific-pathogen-free age- and sex-matched male BALB/c mice, were imported to experiments. The Tehran strain of *T. gondii* (type II), was used in order to establish chronic toxoplasmosis in mice. The 2 groups of Mice were randomly selected to developing Parkinsonism *via* MPTP injection. Thirty-five mice were split randomly into 5 groups ($n=7$ /group) as follow: control group: the uninfected mice, vehicle group: mice were administrated sterile saline, *Toxoplasma* infected group: MPTP treatment group: mice received MPTP and *Toxoplasma* infected + MPTP treatment group: infected mice that received MPTP 40 days post-infection. All mice were tested for behavioral and cognitive alterations using the Morris water maze (MWM) test and wire grip test.

Results: We found that chronic toxoplasmosis caused PD-like symptoms and impaired multiple behavioral traits in infected BALB/c mice Significant differences were observed in swimming distances of MPTP treated and *Toxoplasma* + MPTP treated groups upon all of four blocks versus the control group. This indicated that *Toxoplasma* infection could impair the memory retention and impairment in balance in those mice in the *Toxoplasma* infected + MPTP treated group.

Conclusion: However further studies are needed to determine the exact role of toxoplasmosis infection in pathological path of PD and it may be reasonable to consider screening *T. gondii* infection in individuals with PD.

Keywords: *Toxoplasma gondii*, Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), behavioral-cognitive impairments.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-25

Sequencing and histopathological identification of Cutaneous leishmaniasis in Urmia, Iran

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Abstract

Background and Aim: Cutaneous leishmaniasis (CL) is the most common form of skin disease caused by a single-celled parasite that is transmitted by the bite of a phlebotomine sandfly. Bloodshed transmitted from infected animals, rodents, dogs or humans to healthy humans can cause contamination. Symptoms usually appear three months to a year after the bite. Leishmaniasis affects almost 12 million people worldwide and it is one of the diseases that special attention should be paid to control and prevent it.

Methods: This study was conducted from 2021 to 2022 in 100 cases that have travelled to the native area of the region. In the laboratory, the wounds are prepared from the patients and the interstitial fluid of the wounds using a smear scalpel blade. Also, for further examination and a more definitive diagnosis of the patient's samples, a biopsy was performed. In addition, serous fluid from the patient's skin lesion was cultured in Schneider's Drosophila medium (Sigma, Germany), supplemented with 5% heat-inactivated fetal bovine serum (Sigma, Germany). The nested PCR method was performed using clinical samples and it was repeated twice for each batch of samples. All PCR products of the ITS-rDNA gene were sequenced and analyzed using the Taq1 enzyme with finite-length fragment polymorphism (RFLP). Collected data were analyzed using SPSS-21 and Spearman and Kendall tests.

Results: In this study, 35 positive cases were detected About 47% of the total cases of CL were in Kermanshah province in western Iran and Qasr Shirin region. 28% of the positive cases had a history of travelling to Ilam province and another 25% had a history of travelling to Fars, Hormozgan and Isfahan provinces. The prevalence of CL in men and women was 75% and 25%, respectively. The highest incidence of CL among men was observed in truck drivers and the age group of 20 to 35 years. In addition, most cases of the disease were observed during these years in summer and autumn. PCR products of the ITS-rDNA gene were sequenced. Sequence analysis showed that 30 of the 35 positive samples were *Leishmania major*.

Conclusion: Our case report was done in Iran and the city of Urmia, and considering that the city of Urmia is located in western Iran, you are not a native region. Therefore, our studies have been conducted on non-natives and those who have a history of travelling to human areas. With proper information and training during the trip, such cases can be prevented.

Keywords: Sequencing; histopathological; Cutaneous leishmaniasis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-26

Lophomonas infection in AML-2 patient: Case Report from Urmia, Northwest Iran

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Abstract

Background and Aim: Lophomonas is a polyflagellate parasite an emerging protozoan pathogen which causes lophomoniasis. Currently, microscopic examination, as the gold standard, is often used to diagnose parasites. The purpose of this study is to track the Lofomonas parasite in patients with immunosuppression, especially patients with acute respiratory disorders, and also to show it as one of the factors of emerging infections in the community.

Methods: A 50-year-old female patient from Urmia, northwestern Iran, presented with a history of shortness of breath, mild fever, and chronic cough (during the past 6 months). After conducting clinical examinations and reviewing the patient's records, it was determined that he was an AML-2 patient undergoing chemotherapy. The patient's vital signs were as follows: respiratory rate: 16 breaths per minute, blood pressure: 120/90 mmHg, heart rate: 85 beats per minute, O₂ saturation (SpO₂): 92, temperature: 38°C. Then the patient was admitted to the internal department of Omid Hospital in Urmia. A computed tomography scan showed numerous nodules in the lung.

Results: After preparing a wet smear from the BAL sample, a live trophozoite of Lophomonas was identified using a light microscope. Finally, for better colour recognition Pope Nikolaou's marriage took place. Finally, based on the above laboratory evidence, the patient was treated with oral metronidazole (500 mg/three times a day, for 3 weeks) for Lophomoniasis.

Conclusion: Consolidations in the lungs are caused by different diseases, such as infections, infarction and contusion, malignancies such as lymphomas, haemorrhages, and rheumatologic and immunologic disorders. Most commonly, infectious diseases, such as pneumonia are the source, and among them, bacteria, fungi and protozoa are the most common pathogens. This patient had risk factors for Lophomonas infection, including immunosuppressed status and contact with cockroaches in her house. Our report is consistent with other reports which suggest that Lophomonas is more common in immunosuppressed patients.

Keywords: Lophomonas; AML-2; Northwest Iran.





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Tehran University of Medical Sciences, Tehran, Iran.
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Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-27

Evaluation of anti-*Toxoplasma* effects of lipid nanoparticles carrying Tea tree oil on *Toxoplasma gondii* tachyzoites in Vero Cells

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Abstract

Background and Aim: *Toxoplasma gondii* is a protozoan parasite that infects more than a third of the world's population. The drugs used today to treat toxoplasmosis cause severe side effects in many people and have poor success in treating chronic infections. According to this content, it is very important to try to create new therapeutic agents for the effective treatment of this disease. This study aimed to synthesize Tea tree oil-loaded solid lipid nanoparticles (TTO-SLNs) and to evaluate the anti-*Toxoplasma* activity of this component.

Methods: The TTO-SLNs were constructed using the double emulsification method, and their shape and size distribution were evaluated using a transmission electron microscope (TEM) and dynamic light scattering (DLS), respectively. An MTT assay was employed to evaluate the cell toxicity of the component. The anti-*Toxoplasma* activity of TTO-SLNs was investigated using vital (trypan-blue) staining. Anti-intracellular *Toxoplasma* activity of TTO-SLNs was evaluated in *T. gondii*-infected Vero cells.

Results: The TEM analysis represented round-shaped TTO-SLNs with clear and stable margins. DLS analysis showed a mean particle size of 85.23 nm for SLNs. The cell toxicity of TTO-SLNs was directly correlated with the concentration of the component (P-value = 0.009). The concentration of TTO-SLNs, which was toxic for at least 50% of alive *T. gondii* (cytotoxic concentration (CC50)), was > 10 mg/mL. The ability of TTO-SLNs to kill *T. gondii* was concentration-dependent (P-value < 0.0001), and all concentrations killed at least 70% of alive tachyzoites. Furthermore, the viability of *T. gondii*-infected Vero cells were inversely correlated with TTO-SLNs concentrations (P-value = 0.0174), and in the concentration >1 mg/ml at least 80% of *T. gondii*-infected Vero cells remained alive.

Conclusion: Overall, our findings demonstrated an IC50 value >1 µg/mL, that killing at least 70% of *T. gondii* tachyzoites at all concentrations. Such results suggest that employing SLNs as carriers for TTO can effectively kill *T. gondii* tachyzoites with acceptable cell toxicity. Our findings also showed that SLNs capsulation of the TTO can lead to prolonged release of the extract, suggesting that TTO-SLNs could be also employed to clear cyst stages, which should be further investigated in animal models.

Keywords: Tea tree oil. *Toxoplasma gondii*. Solid lipid nanoparticles. Vero Cells.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-28

Prevalence of intestinal parasitic infections among renal transplant recipients referred to the nephrology clinic of Imam Khomeini Hospital in Urmia, North West Iran

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Abstract

Background and Aim: To prevent rejection of transplants, patients who receive kidney transplants need to use immunosuppressive drugs, which is why these patients are susceptible to a range of infectious diseases. Important parasitic diseases that can cause serious complications in these patients are intestinal parasitic infections, especially cryptosporidiosis. The present study aimed to estimate the prevalence of intestinal parasites in patients receiving kidney transplants referred to the nephrology clinic of Imam Khomeini Hospital in Urmia.

Methods: Over two years from 2021 to 2022, 257 fecal samples from patients with renal transplantation were collected and examined by parasitological methods such as wet mount, Lugol's iodine, trichrome, and modified acid-fast staining. A questionnaire was also filled including demographic variables and gastrointestinal symptoms for each patient. The data was analyzed by SPSS software using the Chi-square test.

Results: Of the 257 patients, 24 (9.3%) were infected with different intestinal protozoa. No cases of infection with intestinal parasitic worms have been observed. Observed intestinal protozoa were as follows: *Entamoeba coli* 7 (2.7%), *Blastocystis* sp. 6 (2.3%), *Endolimax Nana* 6 (2.3%), and *Giardia lamblia* 5 (1.9%). There was no positive case for cryptosporidiosis and cystoisosporiasis among the patients.

Conclusion: According to the results of the present study, serious opportunistic parasitic infections such as cryptosporidiosis and cystoisosporiasis were not observed in kidney transplant recipients, despite the relatively high prevalence in previous years in Urmia. However, other pathogenic parasitic infections such as giardiasis and blastocystosis are present in these patients, granted with low prevalence.

Keywords: Intestinal parasites, renal transplant, Iran.





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Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-29

Seroepidemiology of toxoplasmosis in thalassemia patients of Mazandaran province in 2021-2022

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Abstract

Background and Aim: Toxoplasma gondii has a very high prevalence in Mazandaran province. This parasite is of particular importance in thalassemia patients. Different types of T. gondii are capable of causing a wide range of toxoplasmosis from asymptomatic to fatal form. Therefore, the purpose of this study is the sero-epidemiology of toxoplasmosis in thalassemia patients in Mazandaran province in 2021-2022.

Methods: 300 serum samples of people with thalassemia in Mazandaran province were included in the study. The sera were examined for the presence of IgG and IgM antibodies against T. gondii by ELISA method. Next, DNA extraction was done on the samples and PCR test was done using RE gene. Finally, Toxoplasma genotyping was performed using Nested-PCR methods. The obtained data were statistically analyzed using SPSS 16 software.

Results: The prevalence of IgG and IgM anti-Toxoplasma gondii in the studied subjects was 59.66 and 0.66%, respectively. The results of the molecular test showed that (8 samples out of 300 samples, 2.66%) had Toxoplasma DNA, 6 samples (75%) belonged to genotype II, 1 sample belonged to genotype III, and 1 sample belonged to genotype I.

Conclusion: Considering the high rate of toxoplasmosis serological infection among the thalassemia population, appropriate strategies to reduce the risk of this infection are vital. The prevalence of serum toxoplasmosis in thalassemia patients with frequent blood transfusions was higher than those who did not have frequent blood transfusions, and it seems that these people are at risk of toxoplasma infection due to frequent blood transfusions. Therefore, blood screening for toxoplasma infection in blood transfusion centers may be effective in preventing toxoplasmosis in these patients.

Keywords: Toxoplasma gondii, serology, thalassemia, human, Mazandaran.





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Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-30

In vivo Anti-malarial Activity of the Hydroalcoholic Extract of *Nigella sativa* on Mice Infected with *Plasmodium berghei*

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Abstract

Background and Aim: Malaria is a protozoan disease that is caused by different types of *Plasmodia* in humans and animals. Resistance to the main drugs in the treatment of malaria infections has led to the research of alternative drugs. Therefore, in the present study, we studied the effect of the hydroalcoholic extract of *Nigella sativa* on Mice Infected with *Plasmodium berghei*.

Methods: This experimental study was conducted on 35 male mice infected with *Plasmodium berghei*. The treatment with hydroalcoholic extract of *Nigella sativa* was performed using Peter's proposed method. Statistical analysis of data was conducted using SPSS v.22 software.

Results: The results showed that the *Nigella sativa* hydroalcoholic extract had the highest effect at the treatment dose of 400 mg/kg with 92.6% prevention of parasite growth compared to the control group ($P < 0.05$). No significant difference was seen in the mean weight of the mice or the morphology of RBC in the group receiving *Nigella sativa* extract compared with the negative control group.

Conclusion: The anti-malarial effects of the *Nigella sativa* plant observed in the present study, elicit the necessity for further research, evaluation, and comparison of different extraction methods such as aqueous and chloroform as well as higher therapeutic dosages.

Keywords: Hydroalcoholic Extract, *Nigella sativa*, *Plasmodium berghei*, Malaria, Mice.





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January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-31

Anti-*giardia* effect of *Arctium lappa* hydroalcoholic extract *in vivo*

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Abstract

Background and Aim: Giardiasis is a parasitic infection with worldwide spread caused by *Giardia lamblia*, that's diagnosed by examining a stool sample. Chemical treatment of this disease is usually based on the prescription of metronidazole which has many side effects. considering the importance of giardiasis disease, the present study was conducted to investigate the anti-*giardia* effect of *Arctium lappa*.

Methods: This experimental study was conducted on 40 male mice infected with *Giardia* parasite. Then the mice were treated with different doses of *Arctium lappa* extract for 5 days. Statistical analysis of data was conducted using SPSS v.22 software.

Results: The results of the present study showed that the hydroalcoholic extract of *Arctium lappa*, in concentrations of 160 mg/kg reduces the number of cysts in the feces compared to negative control groups (P<0.05).

Conclusion: Considering the appropriate effect of *Arctium lappa in vivo*, this plant can be introduced as a natural anti-*giardia* compound.

Keywords: *Arctium lappa*, *in vivo*, extract.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-32

Demographic, clinical, and radiological characteristics of patients with hydatid cyst referred to Ahvaz hospitals during 2017-2019

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Abstract

Background and Aim: Hydatid cyst is an important zoonotic disease occurring worldwide which is caused by the larval stages of *Echinococcus granulosus*. This study aimed to evaluate the demographic, clinical, and radiological characteristics of operated patients with hydatid cyst in the hospitals of Ahvaz during 2017-2019.

Methods: The current study is a retrospective, descriptive cross-sectional study based on demographic, clinical, and radiological information of the patients who underwent surgery in Ahvaz hospitals during 2017-2019. Data were analyzed using the SPSS software. To analyze the collected data, descriptive statistics and Chi-square were utilized.

Results: Out of 107 patients with a mean age of 36.78 years, the highest and lowest cases (23.4%, 10.3%) were in the age group of 31-40 and <10 years, respectively. 42.1% were male and 57.9% were female. Of these, 52.3% lived in the rural areas and 47.7% lived in the urban areas, 13.1% had university education. In 70.1% of the patients, liver was involved. Recurrence was reported in 15 cases (14%). The highest frequency (40.2%) was related to the patients living in Ahvaz County. The number of the cysts was 1 to 8. In 59.8% of the patients only one cyst was reported while in 40.2% more than one cyst was reported. The cysts size was 10 to 180 mm. In 47.7% of the patients, cyst type was CE2 and only in 1.2% CE5 was found. In the patients with hepatic hydatid cyst, drainage method with a frequency of 72.1% was the most common procedure, and in the pulmonary patients, drainage and thoracotomy methods were mentioned. In the hepatic and pulmonary hydatid patients, the right lobe of the affected organ was more involved. Abdominal pain and shortness of breath were the most common clinical symptoms mentioned. All of the patients were diagnosed by imaging techniques.

Conclusion: This study showed that hydatid cyst in Khuzestan Province is still one of the important health problems with a significant economic burden. According to the statistics obtained from the hospital referrals, the need for educational programs based on the prevention and control of parasitic infections, especially transmitted parasites from dogs in the province, is raised. In this study, 14% recurrence was observed among the patients, which raises the importance of choosing the appropriate treatment method by surgeons to prevent the recurrence of the disease, which, in addition to threatening the patient's life, has a great economic burden for the patient.

Keywords: Hydatid cyst, Demographic data, Clinical, Ahvaz.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-33

Analysis of the inhibition of important Leishmania parasite protein by some anti-leishmania herbal compounds using molecular docking

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Abstract

Background and Aim: Leishmaniasis is a parasitic disease found in subtropical, tropical, and Southern Europe. Leishmaniasis treatment is a complicated topic. Despite being limited, the current treatments are toxic and have side effects. Also, most of the time, they cannot treat the resistant form of leishmania parasites. Antileishmanial medicines, such as those derived from plants, are being researched as new medications. So according to the eye-catching role of herbs in the control and treatment of infectious disease, in this study, the effect of active substances from 150 medicinal herbs was investigated to uncover their ability to control and cure this neglected disease.

Methods: From the PubChem database, the 3D structures of the GP63 protein from *Leishmania major*, as well as blockers and 2000 herbal compounds from 150 herbs, were retrieved. Utilizing PyRx software and AutoDock Vina, a molecular docking analysis was conducted against each of the three *Leishmania* proteins individually utilizing herbal drugs and proteins blockers. The activity, daily carcinogenicity, and ADMET characteristics derived from Swiss ADME, Lazar, and Way 2 Drug. Molecules with the greatest docking scores for each protein were chosen for molecular dynamic simulation using the GROMACS program version 5.

Results: According to the findings of molecular docking experiments, luteolin 3'-o-glucuronide have a strong affinity for the GP63 protein.

Conclusion: According to information gathered from pharmaceutical databases, the mentioned substance may have anti-inflammatory and wound-healing properties in addition to blocking proteins. Therefore, experimentally examining these plants and compounds could be a valuable clue to the control and treatment of Leishmaniasis.

Keywords: Leishmaniasis; Molecular dynamics; GP63.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-35

Investigating the effect of different concentrations of hypertonic saline on hydatid cyst protoscolex isolated from liver and lung in Urmia, Iran

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Abstract

Background and Aim: Hydatid cyst is a larval stage of *Echinococcus granulosus* which is Cestod and causes disease in humans and certain mammals. In Iran, stray dogs and herds are mostly infected with mature worms while human and farm animals are infected with larval form in high amounts. Since any contamination to normal sit will cause the re-growth of the same cyst. This study aimed to determine the lethal effect of hypertonic saline in different doses and at different times on protoscolecocytes of the lung and liver.

Methods: From the central city abacus liver and lung of killed animals was obtained. It was transferred to the Faculty of Medicine, parasitological lab immediately. The hydatid cyst fluid was aspirated with a 10 mm syringe and poured into 15cc tubes. The movement of protoscolecocytes and stain with 0.1% eosin was the test to determine the viability of protoscolecocytes. Those with colour absorption were those which were not viable. Different concentration of hypertonic saline was given at different time. 1%,2%,3%,4%,5%,6%,7%,8%,9%,10%, 20% in different times 1,2,3,4,5,6, ... up to 30 minute.

Results: The results showed, that in 20% of hypertonic saline in the 4th minute, 85% of protoscolecocytes were alive while in the 5th minute, 60% were alive, in the 7th minute 30% and 8th minute 10%, 9th minute all of them were dead. In 10% concentration up to 9 minutes, 60% were alive and in the 18th minute 30%, and in 30 minutes 15% of protoscolecocytes were alive. In 10% concentration up to 10 minutes, 95% were alive while in the 22nd minute 85% and in 30 minutes 75% of protoscolecocytes were alive.

Conclusion: When we inject 20% hypertonic saline into the cyst cavity there is the probability that the cyst contaminates the bile duct and liver through the small hole we made. This material may cause widespread necrosis of the liver. We should use 10% hypertonic saline minimally for 45 minutes before surgery and after cyst removal.

Keywords: Hypertonic Saline, Protoscolecocytes, Hydatid Cyst, *Echinococcus granulosus*.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-36

Serological prevalence and associated risk factors of toxoplasmosis among pregnant women in the First Trimester in Tehran, Iran

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Abstract

Background and Aim: This research was aimed to evaluate the seroprevalence of acute and chronic *Toxoplasma gondii* (*T. gondii*) infection among pregnant women and associated risk factors in Tehran, capital of Iran.

Methods: In this cross-sectional study, 400 pregnant women referred to Vali-e Asr hospital in Tehran, were included from October 2021 to February 2023. The presence of anti-*T. gondii* IgM and IgG antibodies was measured using the enzyme-linked immunosorbent assay (ELISA). In addition, a questionnaire consisting of demographic information was completed for each subject. Also, IgG-avidity were measured for those samples with a positive IgG titer.

Results: The overall seroprevalence of *T. gondii* infection was estimated to be 28% (112/400). Of these, 2 (0.5%) samples had low IgG-avidity indicating recent infection of toxoplasmosis in the past 3 to 4 months. Regarding the risk factors, the close contact with cat ($p<0.05$) was significantly associated with IgG seroprevalence in pregnant women.

Conclusion: The results showed that the pregnant women referred to Vali-e Asr hospital in Tehran might be moderately exposed to *T. gondii* and a high proportion are susceptible to infection. Since the risk of acute *T. gondii* infection in this susceptible group is very important, using IgG-avidity test beside regular screening tests to diagnose the infection and also health education are recommended.

Keywords: *Toxoplasma*, First Trimester Pregnancy, IgG Avidity, Iran.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-37

Bioinformatic analysis of the ROP17 protein of *Toxoplasma gondii* to find a vaccine candidate

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Abstract

Background and Aim: The progression of *Toxoplasma gondii* invasion is aided by rhoptry proteins (ROPs), which are also essential for the parasite's survival in host cells. T. *gondii* rhoptry organelle protein 17 (ROP17) is one of these important effector proteins. We merged various online bioinformatics services in this paper to forecast the ROP17 protein's immunogenicity.

Methods: In this study, a variety of bioinformatics methods were employed to examine the various aspects of the ROP17 protein, such as its transmembrane domain, subcellular localization, physico-chemical properties, potential B and T-cell epitopes, secondary and tertiary structure and other significant features.

Results: The research revealed that there were 56 possible sites for post-translational modification in the ROP17 protein. ROP17 protein contains 608 amino acid residues with the molecular weight of 69087.36 D, its theoretical pI is 9.49 with Aliphatic index of 88.83. The random coil, alpha helix and extended strand that make up the ROP17 protein's secondary structure total 46.05%, 37.66%, and 16.28%, respectively. Moreover, a number of putative T- and B-cell epitopes for ROP17 were found. The Ramachandran plot revealed that 84.3% of the residues of amino acids were in the favored, 9.1% in the allowed regions. Also, the testing of this protein's allergenicity and antigenicity revealed that it was non-allergenic and immunogenic.

Conclusion: Our results suggested that employing in silico tools to apply structural and functional predictions to the ROP17 protein can lower the likelihood that laboratory investigations will fail. This research served as a crucial foundation for further research and contributed to the creation of a potent vaccination for both acute and chronic toxoplasmosis using a variety of techniques. Much more research is required to generate in vivo vaccinations employing ROP17 alone or in conjunction with other antigens.

Keywords: *Toxoplasma gondii*; ROP17; Bioinformatics analysis; Vaccine.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-38

Phylogenetic analysis of *Entamoeba histolytica* in Iran based on 18S rRNA gene

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Abstract

Background and Aim: Amebiasis is a neglected and re-emerging parasitic infection with worldwide distribution that caused by *Entamoeba histolytica*. This study aimed to investigate the nucleotide sequences related to *Entamoeba histolytica* isolates from Iran and compare them to those isolated from other parts of the world.

Methods: Nucleotide sequences of *Entamoeba histolytica* in Iran compared geographical regions from other parts of the world based on 18S rRNA gen. After reviewing various studies and searches conducted in the Gene Bank, 40 nucleotide sequences from different parts of Iran and other parts of the world were selected. Bioinformatics analysis using Chromas programs, Blast, ClustalW2, and MEGA11 with the Kimura-2 parameter model (Kimura, 1980) and maximum likelihood method (ML). Finally, using all the mentioned software, comparisons of similarities and differences and genetic analysis of the *Entamoeba histolytica* in Iran compared to other parts of the world were performed.

Results: The BLAST analysis showed that of all Iranian *Entamoeba histolytica* isolate sequences were 100% coverage of the available GenBank sequences for *Entamoeba histolytica* from other parts of the world. Based on the findings, the human *Entamoeba histolytica* isolates in Iran were 99–100% homologous to sequences isolated from cattle and goats. The results of the phylogenetic tree also represented that *Entamoeba histolytica* was isolated from human and animal subjects placed beside each other, indicating the possibility of zoonotic transmission of this microorganism.

Conclusion: Since *Entamoeba histolytica* sequences in humans and animals are similar, we conclude that *Entamoeba histolytica* is a zoonosis. Based on the phylogenetic tree, we concluded that animals could play an important role in the epidemiology of *Entamoeba histolytica* infection. Thus, it can indicate zoonotic transmission of *Entamoeba histolytica* in Iran.

Keywords: Phylogenetic; *Entamoeba histolytica*; 18S rRNA.

Acknowledgment:

This work was a part of the doctor of medicine thesis of Hadis Azadi under the supervision of Dr. Mohammadbagher Khademerfan and Dr. Fares Bahrami, which was reviewed and approved by the Ethics Committee of Kurdistan University of Medical Sciences (Code No.: [IR.MUK.REC.1402.079](#)).





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-39

Phylogenetic analysis of *Blastocystis* subtypes 1–3 in Iran using DNA barcoding

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Abstract

Background and Aim: *Blastocystis* sp. is one of the prevalent intestinal parasites infecting humans and animal reservoirs globally. This parasite is often found in diarrhea and normal stool form. All human and animal *Blastocystis* isolates are morphologically similar and not distinguishable. Recent molecular data indicate that subtypes 1, 2, and 3 are the predominant types of human *Blastocystis* in Iran. This study aims to evaluate the zoonotic and non-zoonotic transmission of *Blastocystis* by comparing the nucleotide sequences and providing health strategies to control the infection.

Methods: DNA barcoding sequences of the 50 nucleotide sequences of *Blastocystis* isolates from Iran were obtained through the NCBI site and bioinformatic analysis was performed using Chromas programs for editing, Blast for comparing genes and determining homology, ClustalW2 for group comparison of genes (alignment) and phylogenetic analysis was carried out using Neighbor-joining (NJ) approach with 1000 replicates (value) using MEGA5 software.

Results: After performing a BLAST search, the analysis revealed all subtypes 1 and 2 isolates sequences were 99-100% similar to each other. In addition, subtypes 1 and 2 were 90-95% similar to subtypes 3. The results of the phylogenetic analysis also indicated that human *Blastocystis* subtypes isolated in Iran were placed near the subtypes isolated from animals and water sources.

Conclusion: *Blastocystis*, as one of the prevalent intestinal parasites in Iran, particularly takes place with subtypes 1, 2, and 3. Bioinformatics analysis to compare *Blastocystis* subtypes 1, 2, and 3 sequences in humans, animals, and the environment in GenBank showed evidence for zoonotic transmission of *Blastocystis*. The high prevalence of these subtypes in humans and animals in Iran suggests finding strategies to control and prevent them in humans and animals.

Keywords: Phylogenetic analysis; *Blastocystis*; DNA barcoding; Iran.

Acknowledgment:

This work was a part of the doctor of medicine thesis of Mitra Eghbali under the supervision of Dr. Mohammadbagher Khademerfan and Dr. Fares Bahrami, which was reviewed and approved by the Ethics Committee of Kurdistan University of Medical Sciences (Code No.: [IR.MUK.REC.1402.129](#)).





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-40

Prevalence of intestinal parasitic infections among labor children in Karaj, Iran

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Abstract

Background: Enteric helminthic and protozoal infections are prevalent especially among children with weak health conditions like malnutrition and immune deficiencies. Child labor is a serious national and international humanity and health issue, correlated with socioeconomic conditions. Monitoring infectious agents in child labor- as in shadow population - who do not have proper access to hygiene and treatment facilities, is very vital, hence, the aim of the present study was to evaluate the prevalence of intestinal parasitic infections and its association with socio-economic factors among child labor, in Karaj city, Iran.

Methods: In present cross-sectional study, stool samples from 203 labor child have been collected and examined by using concentration and parasitology staining methods, like Merthiolate-iodine-formaldehyde, Trichrom, Acid fast and Hot gram chromotrope 2R. Demographic, socio-economic factors, and education level and their parent's information collected by using a questionnaire.

Results: The overall prevalence of intestinal parasites in children was estimated at 76.9%. The frequently encountered infections included *Entamoeba histolytica/dispar* (3.9%), *Giardia lamblia* (5.4%), *Entamoeba coli* (24.1%) and *Hymenolepis nana* (0.5%). There were no statistically differences among the sex, age and family size. The level of parents' education represents a risk factor of infection for the children ($p < 0.05$).

Conclusion: Considering the high prevalence of intestinal parasitic infection among labor children according to the present study, as well as, the low level of health and nutrition in them and the low level of awareness (education level) of parents, a codified and interdisciplinary program with the presence of the organization is suggested. governmental and non-governmental activities should be planned to monitor and improve the health level of these children.

Keywords: Intestinal parasite, Infection, Labor children, Risk factors.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-41

Demographic and parasitological characteristics of patients with fascioliasis: first retrospective study from north of Iran

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Abstract

Background and Aim: The present study aimed to investigate the demographic and clinical characteristics of patients with fasciola from 2000 to 2021 in the population of Mazandaran province.

Methods: All confirmed cases of Fasciola in Mazandaran province between 2000 to 2021 were included in the study.

Results: A total of 56 patients had fasciola during the study period and were included in the study. Considering the population of the province which is 3.2 million people, the prevalence of Fasciola in the above period is estimated to be 1.75 cases per hundred thousand people. The average age of the patients included in the study was 46.92. Most cases of fasciola were observed in the age group of 40-49 years, while the highest prevalence was in the age group of 70-79 years with 6.82 cases per hundred thousand people. The highest prevalence of the disease was in Noor city with 15.7 cases per hundred thousand people. Became. The most common year and month of diagnosis of patients with fasciola were 2020 (13 cases, 23.21%) and May (13 cases, 23.21%), respectively.

Conclusion: Results showed that the prevalence of fasciola disease in the study period in Mazandaran province in the last 3 years of this period has increased significantly. This reminds the need to take measures to prevent the spread of the disease in the province.

Keywords: Fasciola, parasitic disease, epidemiology.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-42

Why and how to diagnose congenital toxoplasmosis

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Abstract

Background and Aim: *Toxoplasma gondii* is a zoonotic parasite classified under the phylum Apicomplexa and subclass Coccidia, has the potential to infect any warm-blooded animals. Fig1 illustrates the routes of *T. gondii* infection. Congenital *Toxoplasma* infection occurs when *T. gondii* transferred from the placenta to the fetus, causes several abnormalities from hydrocephalus, microcephaly, deafness, abortion and still birth in the fetal stage to psychomotor retardation, intellectual disability, hearing loss, slower postnatal motor development during the first year of life; and chorioretinitis, cryptogenic epilepsy and autism in children. The incidence of infection varies based on economic condition, climate, geographical location, diet, and sanitation practices.

Methods: We searched English-reported and published articles in local and international journals over the period 2010 - 2023 using various databases including ISI Web of Science, PubMed, Scholar, Scopus, and Science Direct.

Results: Early diagnosis and appropriate antiparasitic drug administration can significantly reduce fetal transmission and severity cases. The diagnosis of toxoplasmosis is typically made by serological tests, which are based on the presence or absence of antibodies and circulating antigens in a serum sample. The indirect fluorescent antibody test (IFAT) and enzyme-linked immunosorbent assay (ELISA) are the most widely used diagnostic tests. Advancements in ELISA-based techniques, such as chemiluminescence assays (CLIA), enzyme-linked fluorescence assay (ELFA), immunochromatographic tests (ICT) and immunosorbent agglutination assays (ISAGA) exhibit high sensitivity and specificity. The VIDAS IgG-avidity test is useful in distinguishing recently acquired infections from chronic ones, while Sabin–Feldman dye test remains the gold standard for *Toxoplasma* IgG detection. Combining Western blotting with serological methods enhances sensitivity. Additionally, molecular methods based on PCR are simple and sensitive. For *T. gondii* detection, qPCR exhibits superior diagnostic accuracy, while other rapid techniques such as LAMP are also effective.

Conclusion: Early and precise diagnosis of *T. gondii* infection holds significant importance, especially in cases of congenital toxoplasmosis. Choosing the right and rapid diagnostic method is crucial for effective treatment of the infection. The more rapidly human congenital toxoplasmosis is diagnosed and treated, the shorter the time available for tissue destruction by the parasite and thus the better the outcomes.

Keywords: Congenital Toxoplasmosis; Diagnosis; Prevalence; Pathogenicity.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-43

The Epidemiologic Status of Enterobiasis in Kindergarten Children During 2021 to 2023

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Abstract

Background and Aim: *Enterobius vermicularis* (*E. vermicularis*) is one of the most important and prevalent parasitic worms that usually infects human, especially children. This parasite is habitually transmitted through person to person throughout ingestion and inhalation of the eggs. Itching, restlessness, sleep disturbances, chronic abdominal pain, urinary tract infection, salpingitis, eosinophilic ileocolitis and pelvic abscess are the main presentations of the enterobiasis. This study is aimed to evaluate the epidemiological status of *E. vermicularis* during different seasons in Mazandaran province, northern Iran.

Methods: This cross-sectional study was conducted during 2021 to 2023. 1595 children in 4 to 9 years of age from different kindergartens from Mazandaran province were assessed using nitrocellulose scratch method. Sampling was done at home by parents during midnight to early morning. Samples were transferred to the laboratory and then microscopically examined with 1000X and 4000X of magnifications.

Results: In general, 548 children in 2021, 365 children in 2022, and 682 children in 2023 were examined and among them, 58 (10.58%), 85 (23.28%) and 153 (22.43%) were positive for *E. vermicularis* during 2021, 2022 and 2023, respectively. In this study, 270, 301, 466 and 558 samples were collected that 31 (11.48%), 11 (3.65%), 79 (16.95%) and 148 (26.52%) were positive for *E. vermicularis* during spring, summer, autumn and winter, respectively.

Conclusion: The results of this study have shown that enterobiasis still has a high prevalence and health education to control and prevent the disease should be done in kindergartens and schools.

Keywords: *Enterobius vermicularis*, pinworm, enterobiasis, kindergartens.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-44

In vitro and *in vivo* anti-parasitic activity of curcumin nanoemulsion on *Leishmania major*

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Abstract

Background and Aim: Leishmaniasis is an important worldwide zoonotic disease. In addition to many adverse effects of current treatment options, the causative parasites have developed drug resistance in recent years. Curcumin (CUR) has been emerged as a potential anti-leishmanial agent, but has poor solubility and bioavailability. In the present study we aimed to improve the solubility of CUR using nanomedicine and to assess the potential anti-leishmanial effects of curcumin nanoemulsion (CUR-NE) on *Leishmania major* (MRHO/IR/75/ER) in both *in vitro* and *in vivo* experiments.

Method: The CUR-NE was successfully prepared via spontaneous emulsification method. Promastigotes of *L. major* (MHR0M/IR/75/ER) were cultured using RPMI 1640 media. Using flowcytometry method, the *in vitro* efficiency of various concentrations of CUR-NE on *L. major* promastigotes was assessed. *In vivo* experiments were carried out in BALB/c mice inoculated subcutaneously with 2×10^6 *L. major* promastigotes treated with CUR-NE (2.5 mg/ml intra-lesion injection), CUR-NE (2.5 mg/ml topically), CUR suspension (CUR-S; 2.5 mg/ml topically), NE-no CUR (topically); amphotericin B as positive control (PC), and infected untreated mice as the negative control (NC) group.

Results: *In vitro* exposure of promastigotes to CUR-NE showed a dose-dependent lethal effect; 26.22, 31.24, 41.54, 45.67, and 67.17% death rates at concentrations of 78, 156, 312, 625, and 1250 $\mu\text{g/ml}$, respectively. *In vivo* administration of topical CUR-NE and CUR-S significantly decreased the mean lesion size after 4 weeks from 4.73 ± 1.28 mm to 2.78 ± 1.28 mm for CUR-NE and from 4.45 ± 0.88 mm to 3.23 ± 0.59 mm for CUR-S ($p=0.001$).

Conclusion: The findings of the present study uncovered the *in vitro* and *in vivo* leishmanicidal effects of CUR-NE. incorporation of CUR into NE formulations increased its solubility, bioavailability and efficacy. Our study proposed CUR-NE as novel anti-leishmanial agents, with enhanced solubility and tissue delivery. Future studies should focus on identifying molecular mechanisms and pharmacokinetics of CUR-NE.

Keywords: Curcumin; Nanoparticles; Anti-leishmanial activity; *Leishmania major*.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-45

Investigation of Anti-*Toxocara* Antibodies in Patients with Schizophrenia Disorder: A Case Control Study

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Abstract

Background and Aim: Toxocariasis is a zoonotic disease caused by human infection with the larvae of *Toxocara canis* (*T. canis*), or less commonly *Toxocara cati* (*T. cati*). The disease is transmitted via ingestion of contaminated soil or food, and is associated with personal hygiene. Cognitive functions and personal self-care skills are impaired in patients with schizophrenia. In the present study we aim to investigate the seroprevalence of toxocariasis among patients with schizophrenia admitted at Ibn Sina Hospital of Shiraz University of Medical Sciences.

Methods: A total of 109 schizophrenic patients and 104 age- and gender-matched healthy controls were included. Using an enzyme-linked immunosorbent assay (ELISA), serum samples were tested for IgG antibodies to *Toxocara* excretory/secretory (TES) antigens. A questionnaire including patients' demographic data and possible risk factors for toxocariasis was also obtained.

Results: Out of 109 schizophrenic and 104 healthy participants, anti-*Toxocara* IgG was detected in 12 (11%) and 10 (9.6%) individuals, respectively. Using multivariate logistic analysis, the difference was not statistically significant. Univariate logistic analysis showed that individuals with contact with contaminated soil (23.5%), eating unwashed vegetables or fruits (23.1%), and rural residency (19.5%) had significantly higher rates of seropositivity.

Conclusion: The severity, onset, and cognitive sequels of schizophrenia are not the same among affected patients, and clinically matched, controlled studies are required to answer the current inconsistency between the studies in terms of *Toxocara* infection risks in schizophrenic patients. Establishment of appropriate educational programs for high-risk populations, including schizophrenic patients, and environmental health improvement are essential measurements to prevent infection in these patients.

Keywords: Seroprevalence; Toxocariasis; Schizophrenia; Iran; Case-control study.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-46

Molecular Epidemiology and Associated Risk Factors of Parasites in Oral Cavity of Children with Malignancies in Western Iran

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Abstract

Background: This survey was designed to study the molecular epidemiology and risk factors of *Entamoeba gingivalis* and *Trichomonas tenax* in children with underlying malignancies and those on chemotherapy in Lorestan province, West of Iran.

Methods: The present cross-sectional descriptive study was performed on children who suffering from different types of malignancies or receiving treatment by chemotherapy referring to oncology section of hospitals of Lorestan Province, Iran during May 2021 to April 2022. The frequency of oral cavity protozoa was investigated using microscopic and conventional polymerase chain reaction (PCR).

Results: *E. gingivalis* and *T. tenax* parasites were found in 23 (25.5%) by microscopic method and 28 (31.1%) using PCR in children with malignancy. Among positive samples, 20 (71.4%) were infected with *E. gingivalis*; whereas 8 (28.6%) of the participants were positive for *T. tenax*. In the multivariate model, living in rural regions (OR= 3.437; 95% CI= 1.22–9.63; p=0.019) and using mouthwash (OR= 0.082; 95% CI= 0.018–0.37; p<0.001) were significantly related with the frequency of oral cavity parasites.

Conclusion: Our results showed the high frequency of oral cavity parasites in children who suffering malignancies or receiving treatment by chemotherapy in Lorestan province, Iran. The awareness of the main risk factors for oral cavity parasites particularly using mouthwash is necessary in improving public and oral health strategies in children with cancer. Consequently, oncologist and dental practitioners must be aware to identify and manage oral health concerns in children who suffering from different types of malignancies to prevent the oral diseases and infections.

Keywords: *Entamoeba gingivalis*, *Trichomonas tenax*, Mouthwash, Malignancy.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-47

Knowledge and practice of laboratory Experts regarding *Blastocystis hominis*

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Abstract

Background and Aim: *Blastocystis hominis* is an intestinal protozoan in humans and animals. This survey was conducted to evaluate the knowledge and practice of laboratory experts in Ahvaz city about the *Blastocystis hominis* parasite.

Methods: This study was conducted on laboratory experts working in Ahvaz city from all levels of education using a questionnaire from January 2019 to June 2019. The data was collected through the distribution of face-to-face questionnaires as well as electronic questionnaires. Pearson's correlation coefficient, chi-square test, descriptive statistics, and SPSS software were used to evaluate the data.

Results: Among the 464 participants in this survey, 58.4% believed that *Blastocystis hominis* may cause abdominal pain, but 12.3% had poor knowledge about hives in people with *Blastocystis hominis*. Although most participants knew that *Blastocystis hominis* was an intestinal protozoan, only 47% knew that it was an emerging pathogen. The results showed that the practice of laboratory experts regarding the use of molecular techniques and culture in the diagnosis of *Blastocystis hominis* was poor.

Conclusion: This study shows that laboratory experts had adequate knowledge about *Blastocystis hominis*, but their practice was lower in the case of *Blastocystis hominis*. It seems necessary to hold practical workshops on *Blastocystis hominis* in addition to training based on the latest findings to improve the practice of laboratory experts in this regard.

Keywords: *Blastocystis hominis*; Laboratory Expert; questionnaire; Knowledge, Practice.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-51

Induction of apoptosis by sulfadiazine plus pyrimethamine on infected macrophages with *Toxoplasma gondii* in vitro

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Abstract

Background and Aim: Toxoplasmosis pose a significant health concern worldwide, causing pain and potential complications. The development of effective treatments for this parasite infection is essential in minimizing their impact on individuals' quality of life. In this work, apoptosis effects of sulfadiazine plus pyrimethamine were evaluated on infected macrophages *in vitro*.

Methods: Infected macrophages were cultured in the presence of concentrations of sulfadiazine plus pyrimethamine and incubated for one day. Macrophages not exposed to drug were used as the negative controls. After incubation the cells were washed in cold PBS and centrifuged at 1,000 g for 5min. The supernatant was then drained off and replaced with 500 μ L binding buffer, followed by 5 μ L of annexin V and 5 μ L of propidium iodide (PI). Eventually, samples were analyzed by FACSCaliber flow cytometer (BDBiosciences) with FlowJo software.

Results: The results demonstrated that the percentage of apoptosis induced after 24 h in *T.gondii* infected macrophages was 12.53%, after being treated with these drugs, while in the negative control group (macrophages) was 8.21%.

Conclusion: Sulfadiazine in combination with pyrimethamine was able to induce apoptosis in parasite-infected macrophages. In addition, necrosis was low in infected macrophages treated with these drugs compared to healthy macrophages without treatment.

Keywords: *Toxoplasma gondii*, sulfadiazine, pyrimethamine, apoptosis.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PP-52

Exosomes in early detection of parasitic diseases in pediatrics

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Abstract

Background and aim: Parasitic disease is one of the most common and important diseases in pediatrics due to some irreversible effects. One of the ways to prevent the mentioned adverse effects would be diagnosis of the agent infection as soon as possible. Many ways present for parasitic disease such as direct microscopic observation, culturing, using laboratory animals, and molecular techniques. One of the recent studied are biomarker identification such as exosomes. In this study, we reviewed the papers regarding detection of the parasitic disease using exosome in biological samples.

Methods: In this study, we searched the keywords of "exosome", "parasite", and "diagnosis" in PubMed database from 2013 to 2023. All the English language papers were included in this study.

Results: Our study showed 75 papers with the mentioned keywords. Out of 75 papers, 14 articles were related to our goals. These articles showed that exosomes were suitable biomarkers in *Leishmania*, *Trypanosoma brucei* and *Trypanosoma cruzi*, *Giardia lamblia*, *Plasmodium spp*, *Acanthamoeba castellanii*, *Brugia spp*, *Trichomonas vaginalis*, *Schistosoma spp*, *Fasciola gigantica*, *Echinococcus granulosus*, *Toxoplasma gondii*.

Conclusion: Exosomes could be considered as one of the useful biomarkers to identify and diagnosis of the parasitic disease in pediatrics on time in order to prevent the irreversible effects.

Keywords: Parasite; Diagnosis; Exosome





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-55

Study on genetic diversity of *Strongyloides stercoralis* with attention to clinical features of the infection in patients

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Abstract

Background and Aim: *Strongyloides stercoralis* “the causative agent of strongyloidiasis” is one of the neglected tropical diseases with a unique life cycle. Strongyloidiasis ranges from asymptomatic to hyper infection syndrome, disseminated infection and even death in untreated immunocompromised patients. There are very few studies on the relationship between the genetic diversity of this parasite and the clinical symptoms of patients. Therefore, this study was conducted on genetic diversity of *S. stercoralis* with attention to clinical features of the infection in patients using *Cox1* gene and DNA sequencing.

Methods: The study was conducted in 2023 on 10 patients with strongyloidiasis who had referred to the Diagnostic Laboratory of Strongyloidiasis in School of Public Health, Tehran University of Medical Sciences. After recording the clinical symptoms of the patients, DNA extraction of the isolates, PCR and sequencing of the *Cox1* gene region were performed. The gene sequences of the isolates were then aligned, analyzed and compared with the sequences available in the GenBank with bioinformatics softwares including Chromas, Bioedit and DnaSP 6. The phylogenetic tree was constructed with MEGA7 software and the results were analyzed.

Results: Among the patients, gastrointestinal, respiratory and cutaneous clinical symptoms were the most common, respectively. Based on the *Cox1* gene, the isolates were classified into four haplotypes that two of which were specific to this study. Haplotypes 2 and 3 were placed in a subclade with haplotypes including isolates from dogs in Cambodia and humans from other parts of the world. Haplotype 4 which is hereby introduced for the first time in the world included an isolate from a patient with hyperinfection syndrome and disseminated strongyloidiasis.

Conclusions: The *Cox1* gene showed genetic diversity for *S. stercoralis* isolates. Accordingly, no significant genetic difference was observed between the sequences from patients with hyperinfection and non-hyperinfection; and the isolates from these patients were included in the same group of the common haplotypes of *S. stercoralis*. The only isolate from a patient with disseminated strongyloidiasis was genetically different from all the other isolates in the present study.

Keywords: *Strongyloides stercoralis*, DNA sequencing, Cytochrome c oxidase 1, hyper infection syndrome, haplotype.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Parasitology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PP-56

Preventive and therapeutic effect of morphine against leishmaniasis caused by *Leishmania major* in BALB/c mice

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Abstract

Background and Aim: Leishmaniasis is a health problem in many countries throughout the world. Common treatments have side effects including drug resistance. Therefore, new or combined drugs and methods are being assessed against leishmaniasis. In an earlier study, we found that morphine at low doses could be effective against amastigotes of *Leishmania major* while inside infected macrophages. In this study, we evaluated the preventive and therapeutic effects of morphine, respectively, on two separate mice groups; one group received low doses of morphine at four intervals before being challenged with promastogotes of *Leishmania major* whereas another received the same dosages after challenge.

Methods: In this study, we evaluated the preventive and therapeutic effects of morphine, respectively, on two separate mice groups; one group received low doses of morphine at four intervals before being challenged with promastogotes of *Leishmania major* whereas another received the same dosages after challenge. To this end, immunological factors such as cytokine assay, lesion diameter and survival rate were measured. Parasitic loads were also considered by qPCR for both groups.

Results The results of this research showed that morphine has rather better preventive function than treatment role. Imiquimod as opioid growth factor receptor enhances therapeutic function of glucantime and morphine when applied alone and in combination with the drugs.

Conclusion In an earlier study, we found that morphine at low doses could be effective against amastigotes of *Leishmania major* while inside infected macrophages. In this study, we evaluated the preventive and therapeutic effects of morphine, respectively, on two separate mice groups; one group received low doses of morphine at four intervals before being challenged with promastogotes of *Leishmania major* whereas another received the same dosages after challenge. To this end, immunological factors such as cytokine assay, lesion diameter and survival rate were measured. Parasitic loads were also considered by qPCR for both groups. The parasitic load in mice received morphine before infection was lower than that in mice treated after leishmanial infection and the differences were statistically significant. Moreover, no lesions were observed at the injection site in the former group. This indicates the protective role of morphine.

Keywords: *Leishmania major*, morphine, prevention, treatment, BALB/c.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Parasitology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PP-57

Passage of *Toxoplasma gondii* across the blood–brain barrier

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Abstract

Undoubtedly, *Toxoplasma gondii* has an apparent affinity for the central nervous system, which plays an important role in the clinical manifestations of human toxoplasmosis.

Even in congenital toxoplasmosis, When the parasite can spread to all fetus organs with a fragile immune system, the infected organs are preferentially the brain and eyes. *Toxoplasma gondii* infects leukocytes and causes the spread of infection. In *Toxoplasma*-infected dendritic cells, it produces a migratory phenotype. In this review, we present the mechanisms used by the *Toxoplasma gondii* parasite to cross the blood-brain barrier and invade the brain.

Also, the interaction with the blood-brain barrier and the role of parasite-derived molecules and host-derived molecules in invading infected leukocytes into the brain is briefly discussed. In addition, the mechanism of transfer of immune cells to the brain, the effects of the parasite on the motility of the host cell and the spread of the parasite are investigated.

Keywords: *Toxoplasma gondii*; blood-brain barrier.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
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9. Virology (Oral Presentations)





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OV-1

Association between Angiotensin-Converting Enzyme-2 (ACE2) overexpression and severity of COVID-19 infection

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Abstract

Background and Aim: Angiotensin-converting enzyme-2 (ACE2), the key functional receptor of severe acute respiratory syndrome coronavirus-2 (SARS-CoV2), that is responsible for the worldwide Coronavirus Disease-2019 (COVID-19) pandemic and it seems that there is no end in sight for it yet. Studies reported contradictory results regarding the correlation between ACE2 expression and the severity of the COVID-19 infection. To uncover these contradictory results, we aimed to investigate the association between ACE2 expression and the severity of COVID-19.

Methods: This study was performed on 182 patients with COVID-19 referred to the teaching hospitals of Mazandaran University of Medical Sciences. The severity of the disease was defined as severe and non-severe based on the CDC. The expression of the ACE2 gene was assessed in PBMCs of patients using qRT-PCR by SYBR Green qPCR Master Mix 2X. The association between ACE2 expression and COVID-19 severity as well as disease outcome was evaluated.

Results: Out of 182 patients enrolled in this study, 94 (51.6%) were male, and 88 (48.4%) were female. The most common clinical manifestation included shortness of breath (n: 99, 54.4%), fever (n: 67, 36.8 percent), cough (n: 63, 34.6 percent), and fatigue (n: 55, 30.21 percent). ACE2 gene expression was prominently higher in severe group than in patients with non-severe infection (median: 2.04 vs 0.45, $P < 0.0001$). The results of the relationship between ACE2 gene expression and disease outcome including ICU hospitalization, need for ventilation, and mortality showed that the patients who ventilated had higher ACE2 expression than not-ventilated patients (2.04 vs 1.21, $p = 0.004$). Also, mortality rate in patients with high ACE2 expression was significantly higher than in patients with low expression of this gene (21.7% vs. 17, $P = 0.51$).

Conclusion It concluded that patients with high expression of ACE2 experienced more severe COVID-19 infection and had adverse outcomes.

Keywords: COVID-19 infection, ACE2 expression, Severity, Outcome.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OV-2

Investigation of the simultaneous presence of active BK, Epstein Barr, and Cytomegalovirus infection and probable host factors related to active infection in kidney transplant recipients

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Abstract

Background and Aim: Primary infection with cytomegalovirus (CMV), Epstein-Barr virus (EBV), and BK polyomavirus (BKPyV) occurs in childhood, then they remain latent and asymptomatic in the body under normal conditions. Considering the importance of activation of these viruses during immunosuppression, for example after organ transplantation, the purpose of this study is to simultaneously investigate the prevalence of CMV, EBV, and BKPyV in the blood samples of kidney transplant recipients (KTRs). Our secondary objective is to identify host factors related to the reactivation of these viruses.

Methods: In this cross-sectional study, blood samples were collected from 98 KTRs suspected of transplant rejection, referred to Labbafinezhad Hospital, Tehran, Iran. DNA extraction was performed using a commercial ROJE DNall Plus Kit. Real-Time PCR was performed by using GeneProof kits targeting exon 4 regions of IE antigen for detection of CMV, nuclear antigen 1 (EBNA 1) for detection of EBV, and the gene region overlapping between the gene border of VP1 and VP2 proteins for detection of BKPyV. Demographic data, laboratory characteristics, underlying diseases, and immunosuppressive regimens in the studied patients were extracted from patients' medical records. Data were analyzed using the statistical software package, SPSS version 23.

Results: Out of 98 patients, CMV was detected in 18 cases (18.3%), EBV in 7 cases (7.1%), and BKPyV in 5 cases (5.1%). In the activation of BKPyV infection, the increase of creatinine compared to the baseline condition was significantly higher than in the negative viremia group (p-value:0.017). But there was no significant relationship in terms of age, gender, BMI, smoking, primary comorbidities (diabetes mellitus pre-transplantation, high blood pressure, glomerulonephritis, Alport syndrome, cystic kidney, lupus erythematosus, urinary reflux), Post-transplant comorbidities (diabetes mellitus post-transplantation, high blood pressure, cardiovascular diseases, hepatitis, hypothyroidism), the number of transplants, the type of donor (live, cadaveric, HLA1,2 mismatch), CMV & EBV antibody status (D+R+, D+R-, D-R+, D-R-), Immunosuppression regimen & antimetabolite (Mycophenolate mofetil/ Myfortic, Cyclosporine, Tacrolimus, Azathioprine, Anti thymocyte globulin), steroid regimen, biochemical parameters (Baseline Creatinin, baseline GFR, baseline hemoglobin, GFR reduction rate, hemoglobin reduction rate) between the two groups with positive viremia and without viremia.

Conclusion: This is the first report to comprehensively identify host factors related to the activation of EBV, CMV, and BKV in KTRs in Iran and shows that activation of CMV, EBV and BK virus in kidney transplant recipients is common and can cause complications after transplantation such as increased creatinine, fever and chills, diarrhea and vomiting, dysuria, hematuria, proteinuria, edema of organs and shortness of breath. Examining these viral infections after kidney transplantation is effective in disease prognosis and therapeutic interventions to preserve the transplant in these patients.

Keywords: CMV; EBV; BKPyV; Kidney transplantation; Prevalence.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OV-3

The predominance of recombinant Norovirus GII.4Sydney[P16] strains in children less than 5 years of age with acute gastroenteritis in Tehran, Iran, 2021–2022

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Abstract

Background and Aim: After the introduction of rotavirus vaccine, noroviruses (NoV) are now the leading cause of acute gastroenteritis (AGE) worldwide, which leads to 200 million cases in children less than 5 years of age annually. To date, based on VP1 complete VP1 amino acid sequence, there are 10 genogroups (GI-GX) recognized for NoV. NoV GI, GII, GIV, GVIII, and GIX are considered infectious to humans. Several reports show that GI and GII are the most prevalent genogroups in human disease. Our study was aimed to both detect emerging noroviruses (NoVs) and investigate RdRp and VP1-based dual typing of circulating NoVs in hospitalized children less than 5 years of age with acute gastroenteritis (AGE) in Iran.

Methods: For this purpose, a total of 200 stool specimens were screened during 2021–2022 by real-time RT-PCR for genogroup I and II (GI and GII) and dual-typed by sequence analysis of PCR products, using a web-based NoV Typing Tool and phylogenetic analysis.

Results: The GI and GII NoVs were detected in 20% of 200 specimens. The GII.4 NoV was found to be the most common VP1 genotype (53%) followed by GII.8 (32%), GII.7 (6%), GII.17 (6%), and GII.3 (3%). The GII.P16 NoV was also found as the predominant RdRp type (53%) followed by GII.P8 (32%), GII.P7 (6%), GII.P17 (6%), and GII.P31 (3%).

Conclusion: In our previous study, GII.P4–GII.4 Sydney_2012 and GII.P31–GII.4 Sydney_2012 were found to be the most prevalent genotypes and most prevalent recombinant strains, respectively. In our present study, GII.4 Sydney_2012[P16] was determined to be the most common strain, which indicates inter-genotype recombinant strains. These findings imply that new and recombinant NoV strains emerged in Iran, and circulating strains can change over time.

Keywords: Norovirus; Acute gastroenteritis; Dual-typing; RdRp; VP1.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OV-4

Characterization and immunogenicity of a novel chimeric hepatitis B core-virus like particles (cVLPs) carrying rotavirus VP8* protein in mice model

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Abstract

Background and Aim: Rotaviruses have been identified as one of the most important causes of diarrhea in infants and children worldwide. Considering that the vaccines available in Asian and African countries have shown low effectiveness in comparison with developed countries, the effort to produce new generation vaccines is inevitable. Based on this, considering the feature of rotavirus VP8* protein as a suitable candidate for vaccine production and also the ability of hepatitis B virus HBcAg to form VLPs. In this study, the core platform of hepatitis B virus (cVLPs) was used to express the rotavirus VP8* protein. It was used to produce a vaccine.

Methods: In this study, the recombinant Core HBV construct forming VLPs expressing the rotavirus VP8* protein was cloned in pET-28(+) a plasmid and then the recombinant proteins were expressed in E. coli and confirmed by western blot. After purifying the proteins using Ni-NTA chromatography column, the formation of cVLPs was confirmed by electron microscopy, and then the recombinant proteins were injected subcutaneously into groups of mice alone or with aluminum hydroxide adjuvant, then the immune responses were investigated in the mice.

Results: The results showed that the recombinant cVLPVP8* protein has the ability to form VLPs in the prokaryotic expression system and also able to increase the immune responses of IgG, IgA and IgG1 and IgG2a subclasses as well as IFN- γ against the VP8* protein. Also, the increase in the level of IgG1 compared to IgG2a indicates Th2 polarization of immune cells. The obtained results showed that cVLP VP8* protein with adjuvant can produce higher levels of heterotypic neutralizing antibodies against SA11 monkey strain compared to VP8* adjuvant.

Conclusion: Our findings indicated that recombinant cVLPVP8* protein with aluminum hydroxide adjuvant can be a universal, efficient and cost-effective vaccine candidate against rotavirus infection.

Keywords: Rotavirus; HBcAg; VP8*; cVLP vaccine.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OV-5

Assessing the Relationship between Laboratory Indices of Metabolic Syndrome including HDL, TG, and FBS with SARS-CoV-2 Virus Load in Patients with SARS-COVID 19 Infection

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Abstract

Background and Aim: It appears that the likelihood of mortality in COVID-19 patients increases with the combined effects of components of metabolic syndrome. In this study, the relationship between serum levels of laboratory indices of metabolic syndrome and SARS-CoV-2 virus load was investigated.

Methods: This retrospective study was conducted on hospitalized patients with COVID-19 infection at Ghaem Hospital, Mashhad, who also had concomitant metabolic syndrome. Data from patients who met the inclusion criteria were recorded and analyzed. Patients were considered positive for COVID-19 infection based on RT-PCR test results, clinical symptoms, and radiological findings. The diagnosis of metabolic syndrome was based on the NCEP ATP III criteria. Data analysis was performed using SPSS version 24 software.

Results: The study population consisted of 2776 patients. Seven hundred patients were excluded from the analysis due to insufficient study-related data. Ultimately, data from 2076 patients were analyzed. Based on the mentioned criteria for metabolic syndrome, 127 patients (6.1%) had metabolic syndrome, while 1949 individuals (93.9%) were included in the non-metabolic syndrome group for comparison. Not having metabolic syndrome reduced the likelihood of mortality (OR=0.68; p=0.049; 95% CI=0.47-0.99). Out of 127 patients with metabolic syndrome, 125 patients (98.4%) had one or more reported symptoms, while only 2 patients (1.6%) were asymptomatic. Patients with metabolic syndrome were 7.3 times more likely to show symptoms of COVID-19 compared to others (OR=7.3; CI=2.15-89.0; p<0.05). Significant correlations were found between HDL levels and uric acid with cycle threshold (CT) of the N gene, as well as between HDL levels and triglycerides level with CT of the RdRp gene.

Conclusion: There was a significant direct correlation between HDL levels and uric acid with cycle threshold of N gene, as well as a significant correlation between HDL levels and triglycerides with CT of the RdRp gene. Other laboratory indices including fasting blood sugar, LDL, and cholesterol did not show significant correlations with the RdRp CT.

Keywords: COVID-19, viral load, metabolic syndrome.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OV-6

Antitumor activity Potential of Everolimus in Cervical Cancer: In Vitro Investigations and Insights into Cellular Responses

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Abstract

Background and Aim: Cervical cancer stands as the fourth most common malignancy among women on a global scale. Despite significant advances in cancer research and treatment, innovative therapies are continually sought to combat this disease. Everolimus, a well-established mTOR inhibitor primarily employed in the treatment of neuroendocrine tumors (NETs), renal cell carcinoma (RCC), and tuberous sclerosis complex (TSC), has also gained approval from the FDA for breast cancer treatment. This study aims to investigate the potential role of everolimus in cervical cancer in mouse model, an area where novel therapeutic approaches are desperately needed.

Methods: In this study, a series of experiments was employed to assess the antitumor effects of Everolimus on TC-1 cells. Lactate dehydrogenase (LDH) release and cellular proliferation assays (MTT) tests. in addition, a comprehensive analysis of various cellular processes, including autophagy, apoptosis, and intracellular reactive oxygen species (ROS) was conducted. For this purpose. Caspase-3 and protein light chain 3-II (LC3-II) protein expression levels were assessed using flow cytometry and Enhanced Chemiluminescence Western blot to investigate their roles as intervening factors in the apoptosis and autophagy processes within the cell death signaling pathway, respectively. To investigate cellular responses to everolimus treatment, we employed the enzyme-linked immunosorbent assay (ELISA) method to assess the levels of Tumor Necrosis Factor alpha (TNF alpha).

Results: Our findings with MTT and LDH showed that the vitality of TC-1 cells receiving everolimus therapy changed significantly as the dosage of everolimus increased. Other findings showed that the everolimus potentially resulted in apoptosis and autophagy induction, caspase-9 activation, ROS generation, and LC3II measurement in the TC-1 cell line. Everolimus treatment significantly increased the expression of Bax and P38 and reduced the expression of Bcl2 and mir-21, according to a real-time PCR experiment.

Conclusion: Our research underscores the promise of everolimus as a prospective candidate for the treatment of cervical cancer.

Keywords: Apoptosis, Autophagy, Everolimus, Human papillomavirus, Cervical cancer.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OV-8

Characteristics and cycle threshold value of patients with COVID-19 referred to hospitals in Babol city: A multicenter study on the fourth, fifth and sixth waves

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Abstract

Background and Aim: The objective of the present study is to compare the epidemiological patterns of severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) infections, hospitalizations, deaths, and hospital stay duration during the fourth, fifth and sixth epidemic waves of coronavirus disease 2019 (COVID-19) in Iran.

Methods: A multicenter retrospective observational study was conducted on hospitalized patients across four hospitals in Babol County, North of Iran. The study periods were during the fourth, fifth, and sixth waves of the epidemic in Iran, (March 2021 to March 2022). In total 13,312 suspected COVID-19 patients were included. Demographic data, medical history of subjects, length of hospital stay, and clinical outcome were retrieved from hospital information system. In SARS-CoV2 positive cases data regarding cycle threshold value and SARS-CoV2 variant was determined.

Results: The highest number of hospitalized patients was reported during the fifth (delta) wave (5231; 39.3%), while the lowest number of hospitalized patients was reported during the sixth (omicron) wave (2143; 16.1%). In total, 6459 (48.5%) of 13312 suspected COVID-19 hospitalized patients had a positive rRT-PCR result. The fifth (delta) wave had highest number of SARS-CoV2 rRT-PCR positive hospitalized patients (3573, 55.3%), while the sixth (omicron) wave had the least (835, 12.9%). Also, 238 (3.7%) patients with laboratory-confirmed COVID-19 were died. The hospital mortality rate was 6.8% in the fourth (alpha) wave, which reduced to 2.7% and 3.5% in the fifth (delta) and sixth (omicron) waves, respectively ($p < 0.001$).

Conclusions: This is the largest study assessed the epidemiological characteristics of SARS-CoV2 laboratory-confirmed hospitalized cases in Iran during the alpha, delta and omicron waves. The highest number of SARS-CoV2 positive hospitalized patients was in the fifth wave of COVID-19 (delta variant dominance period), while the sixth wave (omicron variant dominance period) contained the lowest number. Comorbidities were similar, and cardiovascular disease (CVD), diabetics, kidney disease (KD) and hypertension were the main risk factors in all waves.

Keywords: COVID-19; SARS-CoV-2; Alpha variant; Delta variant; Omicron variant; Hospitalization; Death.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Oral

Abstract Type: Original Research

Code of Abstract: OV-9

Monkey poxvirus and its vaccines

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Abstract

Background and Aim: Monkeypox (mox) is a disease caused by mpox virus and it has been spreading globally since 2022, but fortunately there are two vaccines to prevent it, and the purpose of this work is to explain two vaccines.

Methods: The words mpox virus, JYNNEOS vaccine and ACAM2000 vaccine in Google Scholar and PubMed have been searched.

Results: People at risk for smallpox vaccination are recommended, for example, research laboratory workers, clinical laboratory workers performing tests for orthopoxviruses, and health care personnel exposed to patients with mpox infection. The Smallpox vaccination is 85% effective in controlling epidemics. Currently, there are three smallpox vaccines. However, there are only two vaccines licensed by the US FDA, ACAM2000 and JYNNEOS. JYNNEOS is a live, non-repeated modified Ankara or Nordic Bavarian vaccine administered subcutaneously in 2 doses (0.5 mL) 4 weeks apart to prevent smallpox and monkeypox. Adults 18 years and older, even immunocompromised people such as HIV patients. Another smallpox vaccine is an investigational vaccine, Aventis Pasteur Smallpox Vaccine (APSV), which may be used under an Emergency Use Authorization (EUA), This vaccine replaced DRY VAX in February 2008. ACAM2000 is a Single-dose vaccine administered through the skin. ACAM2000 is a vaccine derived from purified vaccinia virus with a single DRY VAX plaque that is replicated non-infectiously in cell culture. This vaccine is made from a live virus, and for this reason, our care after injecting this vaccine is very important, as there is a possibility of spreading this virus from the part vaccinated to other parts of the body. The immunogenicity of JYNNEOS vaccine is higher than that of the ACAM2000, which is highly recommended to prevent the mpox, as it has limited side effects and administered for immune deficient patients.

Conclusion: The current outbreak of mpox is an alarming global health situation because it is the first large, multi-country outbreak outside of Africa that is not associated with travel to endemic countries or the importation of infected animals. The number of suspected and confirmed mpox cases continues to increase. Another distinguishing feature is that a significant number of cases were found among MSM. In this regard, increased active case detection, immediate isolation, contact tracing, and post-exposure vaccination should be done to quickly contain the outbreak.

Keywords: Monkeypox virus (mpox), JYNNEOS, ACAM2000, DRYVAX, Orthopoxvirus.





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9. Virology (Poster Presentations)





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-1

Using virtual screening approach to design effective inhibitor against SARS-CoV-2 3CLpro based on 59S structure in 7WO3.pdb crystal structure

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Abstract

Background and Aim: Following the increase in cases of SARS-coronavirus in 2019 and the global spread of the Covid-19 disease, the World Health Organization (WHO) declared the outbreak of the new coronavirus a global public health emergency. Taking into account the pathogenicity of this virus and its consequences, the production of effective drugs or vaccines against this viral infection has been highly considered. Proteases encoded by most viruses play an important role in the viral life cycle and protease inhibitors bind competitively to the active site of the viral protease. Inhibition of viral protease activity leads to the production of immature viral particles. Among the viral proteins encoded by the SARS-CoV-2 genome, 3CLpro is essential for coronavirus replication. 3CLpro is responsible for the proteolytic processing of the polyprotein precursors pp1a and pp1ab. 3CLpro inhibitors specifically suppress coronavirus replication by damaging different stages of the viral life cycle. The SARS-CoV-2 3CLpro crystallographic model contains the 59S inhibitor bound to the active site of the proteinase. The IC₅₀ for inhibition of SARS-CoV-2 3CLpro by 59S is 80 nM. Here we perform virtual screening based on chemical structures of 59S ligand. Finally, the *in-silico* pharmacokinetics of the selected compounds were predicted with favorable binding to 3CLpro of SARS-CoV-2.

Methods: In current study, after performing the validation phase on 59S ligand against SARS-CoV-2 3CLpro in 7WO3.pdb file, 82 chemical structures with structural similarity to 59S was screened from Pubchem data center, separately were docked to SARS-CoV-2 3CLpro coordination from 7WO3 PDB file, and finally were arranged based on the calculated $\Delta G_{\text{binding}}$. In last step, physicochemical, pharmacokinetic, and toxicity properties of compounds with highest affinity for SARS-CoV-2 3CLpro were determined by pkCSM and SwissADME web-based servers.

Results: While the lowest $\Delta G_{\text{binding}}$ for 59S ligand was -6.8 kcal/mol, N-[5-[(3S,6R,9S)-3-butan-2-yl-6-[(4-methoxyphenyl)methyl]-2,5,8,11-tetraoxo-1,4,7,10-tetrazabicyclo[10.4.0]hexadecan-9-yl]pentyl]-N-hydroxyformamide (Pubchem ID: 10054097) and N-[5-[(3S,6R,9S,12R)-3-[(2R)-butan-2-yl]-6-[(4-methoxyphenyl)methyl]-2,5,8,11-tetraoxo-1,4,7,10-tetrazabicyclo[10.4.0]hexadecan-9-yl]pentyl]-N-hydroxyacetamide (Pubchem ID: 56662146) with binding affinities of -8.0 and -8.0 kcal.mol⁻¹, respectively showed the favorable values between of selected compounds. Also, computational based predicted attributes of the indicated compounds confirmed their potential to may use as efficient medicine.

Conclusion: The ligand 59S interacts with 3CLpro by occupying a hydrophobic canal near His41 and Cys145 via hydrophobic and electrostatic interactions. The use of virtual screening methods can be considered and used as an efficient and effective method to find effective and specific inhibitors of SARS-CoV-2 3CLpro. Such chemical structures with high affinity to SARS-CoV-2 3CLpro and acceptable pharmaceutical properties may inhibit the replication and function of the SARS-CoV-2 virus. The novel compounds also are recommended as a starting ligand for further research with the aim of exploring a solution to treat the ongoing COVID-19 disease.

Keywords; SARS-CoV-2, COVID-19, SARS-CoV-2 3CLpro, Virtual Screening.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-2

Molecular Identification of SARS-CoV2 Omicron Subvariants among COVID-19 Patients in Tehran, Iran

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Abstract

Background and Aim: SARS-CoV2 has displayed several variants with various features. The circulating variant known as Omicron has become the dominant strain since 2020. The different subvariants of were classified from BA.1 to BA.5. Molecular differentiation between subvariants is a useful method for identifying co-circulating strains in epidemiological studies.

Methods: SARS-CoV-2 infection was confirmed using real-time PCR in all patients included in the current study. Sampling of the different lineages of Omicron was conducted from May to August 2022. Differentiation was performed using triple-target real-time PCR for Q493R, L452R, and Δ69-70.

Results: The mean age of 30±8 years and 58 (38.6%) and 92 (61.4%) patients were male and female, respectively. The suggested triple-target real-time PCR detected 117 (78%) of the evaluated samples with clear results and 33 (22%) with no clear conclusion. The majority of samples analyzed were of the Omicron variant lineages BA.5 or BA.4 91 (60.7%).

Conclusion: Considering the high prevalence of the BA.4/5 subvariant (60.7%) among all samples studied, co-circulating variants are important and specific primer sets for each subvariant in epidemiological studies are helpful tools for monitoring future waves of COVID-19. Therefore, the suggested primer sets could be a simple approach to screening sample variants and lineages of Omicron. Despite the lack of resources in certain countries, molecular epidemiology with sequencing can still be conducted on a wide variety of specimens. Screening panels can help prioritize which samples should be sequenced first, allowing us to focus on the most important ones.

Keywords: SARS-CoV2, Omicron variants, L452R, Q493R, Δ69-70.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-3

Prevalence of Occult Hepatitis C Virus Infection (OCI) among Hemodialysis Patients; A Cross-Sectional Study from Lorestan Province, Western Iran

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Abstract

Background and Aim: Patients with chronic kidney disorders, such as hemodialysis, are at a higher risk of infection with hepatitis viruses than the other population due to high nosocomial transmission by the dialysis units. The incidence of occult HCV infection (OCI) among chronic hemodialysis (CHD) remains controversial and the real burden of HCV in this population may be affected by the rate of OCI. This study aimed to evaluate the prevalence of OCI among patients with CHD from Lorestan province, Western Iran.

Methods: In this cross-sectional study, whole blood specimens were collected from 122 subjects with CHD. Subsequently, anti-HCV antibody and HCV-RNA were assessed in serum/peripheral blood mononuclear cells (PBMCs) by using Enzyme-Linked Immunosorbent Assay and Real-Time PCR technique, respectively.

Results: Out of the 122 cases, 61.15% were male and 38.8% were female. Regarding HCV results, out of the 122 studied cases, 4 patients (3.3%) were positive for anti-HCV IgM Ab and 3 patients (2.47%) for anti-HCV IgG Ab in their serum. Moreover, none of the 122 cases were positive for HCV-RNA in serum samples, while in PBMC specimens, two cases (1.6%) tested positive for HCV-RNA, of which one case was anti-HCV Ab positive. Furthermore, the prevalence of OCI was correlated with the history of blood transfusion and serum level of transaminases ($P=0.012$).

Conclusion: The results of the current study suggest that there is a potential risk of occult HCV infection among patients undergoing hemodialysis. Therefore, it is necessary to use appropriate molecular techniques for early diagnosis and treatment of these patients.

Keywords: HCV, OCI, PBMCs, Hemodialysis, ESRD.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-4

Higher Neurological Symptoms and Mortality Rate in Parkinson's Patients following COVID-19: Retrospective Report from Iranian Network for Research in Viral Diseases (INRVD)

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Abstract

Background and Aim: The COVID-19 pandemic, caused by SARS-CoV-2, has presented global health challenges. Understanding its impact, especially on vulnerable groups, is crucial. This study investigates COVID-19's effects on Parkinson's disease (PD) patients with positive and negative for COVID-19.

Methods: Data from 54 patients between March 2020 and March 2021. Among the 54 PD patients included in the study, 27 were positive for COVID-19 disease. Of the 54 subjects analyzed, 38.9% were female, and 61.1% were male.

Results: Comparison of COVID-19 symptoms revealed higher odds of sore throat (OR = 3.6) and breath shortness (OR = 12.6) in the COVID-19 positive group. Following the study, high levels of AST, ALT and CRP are also reported in PD with SARS-CoV-2 infection. This study contributes to the growing understanding of COVID-19's diverse clinical manifestations and its impact on individuals with underlying health conditions like PD. The heightened prevalence of neurological symptoms in PD patients warrants continued exploration. This study revealed that Parkinson's patients who contract COVID-19 exhibit a higher prevalence of neurological symptoms, underscoring the importance of providing comprehensive care to these patients due to the elevated risk of neurological disorders.

Conclusion: While neurological symptoms in Parkinson's patients can result from an underlying neurological disorder or be linked to medication and medical interventions, respiratory symptoms are typically associated with COVID-19. Nevertheless, there remains a potential for these symptoms to exacerbate following a SARS-CoV-2 infection.

Keywords: Parkinson, COVID-19, SARS-CoV-2, Respiratory Infection, Neurologic symptoms).





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PV-5

Therapeutic approaches for HTLV-1-associated adult T-cell leukemia/lymphoma: A comprehensive review

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Abstract

Adult T-cell leukemia/lymphoma (ATLL), an infrequent malignancy resultant from human T-cell lymphotropic virus type I (HTLV-1), exhibits a spectrum of phenotypes, encompassing acute, smoldering, lymphomatous, and chronic variants, each bearing distinct clinical presentations. The preponderant acute manifestation is characterized by hypercalcemia, systemic manifestations, organomegaly, and dermatological eruptions. Conversely, the chronic phenotype is typified by lymphocytosis and/or cutaneous eruptions, while smoldering ATLL assumes an asymptomatic course. Immunocompromise afflicts ATLL patients, heightening their vulnerability to opportunistic infections that frequently intricately intertwine with disease progression. Therefore, an early diagnosis is crucial to manage the disease appropriately. While conventional chemotherapeutic regimens have shown limited success, especially in acute and lymphoma types, recent studies suggest that allogeneic stem cell transplantation might enhance treatment results because it has shown promising outcomes in some patients. Novel therapeutics, such as interferon and monoclonal antibodies, have also shown promise, but more research is needed to confirm their efficacy. Moreover, the identification of biomarkers for ATLL and genetic changes in HTLV-1 infected cells has led to the development of targeted therapies that have shown remarkable success in clinical trials. These targeted therapies have the potential to offer a more personalized approach to the treatment of ATLL. The aim of our review is to elaborate on conventional and novel therapies and the efficiency of mentioned treatments.

Keywords: ATLL, chemotherapy, stem cell transplantation, monoclonal antibodies; targeting surface molecules, clinical features, HTLV-1.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PV-10

Syncytia formation in the pathogenesis of SARS-CoV-2 infection: Lessons from viral infections

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Abstract

Many enveloped viruses, including SARS-CoV-2 responsible for COVID-19, can create multinucleated cells known as syncytia through viral entry-related membrane fusion events. Syncytia formation is believed to aid viral replication by evading host defense responses. These syncytia form when viral spike proteins (S) interact with neighboring cell receptors, causing merged cell collections. The response of the innate immune system, particularly interferon-stimulated genes (ISGs), can modify cell membranes to prevent fusion.

SARS-CoV-2 is rapidly evolving, and mutations in its S protein have been identified. Variants like Alpha, Beta, Gamma, and Delta carry mutations significantly affecting S protein function and syncytia formation. The implications of syncytia in emerging variants are not fully understood. Moreover, S protein variations in SARS-CoV-2 can enhance receptor interactions, fusogenicity, and antibody reactivity. COVID-19 infections result in various clinical symptoms, from mild febrile illness to severe respiratory distress and occasionally fatal lung damage, involving fibrosis, pneumocyte necrosis, and lung infection.

COVID-19 shares similarities with MERS and SARS-CoV in causing lung illnesses, but it notably induces severe lung thrombosis compared to other acute respiratory syndromes.

In conclusion, the presence of multinucleated syncytial cells in the lung tissues of COVID-19 patients has been observed through various histological analyses. Although the full impact of syncytia on the disease remains incompletely understood, recent research has provided insights into their role in SARS-CoV-2 infection and the underlying mechanisms of their formation. Syncytia play a crucial role in viral spread and immune evasion, allowing the viruses to move between the cells. However, rapid collapse of syncytia can restrict viral replication and trigger an inflammatory immune response. The SARS-CoV-2 syncytium is to likely contribute to the pathogenicity of the virus. Importantly, syncytia are also susceptible to the antiviral response of the innate immune system, with certain interferon-stimulated genes capable of modifying the cell membranes to prevent fusion. The S protein of SARS-CoV-2 has undergone numerous mutations, particularly in the Alpha, Beta, Gamma, and Delta variants, significantly impacting the function of spike protein and syncytia formation. However, the precise effects of syncytia on the pathophysiology of emerging variants are not fully known yet. In conclusion, further research is required to gain a comprehensive understanding of the role of syncytia in COVID-19 pathogenesis and their implications in the context of emerging variants. Exploring the interactions between syncytia formation, viral evolution, and the immune response can provide valuable insights for developing effective antiviral strategies and therapeutics against COVID-19 and future viral infections. As the pandemic continues to evolve, ongoing investigation in this area remains critical to combat the virus effectively.

Keywords: SARS-CoV-2, Syncytia, Spike protein, Pathogenesis, Fusion.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-11

A Predictive Model of Clinical Signs and Symptoms to predict SARS-CoV-2 infection based on the first four-month surveillance data in Iran-Mazandaran

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Abstract

Background and Aim: In evidence-based medicine, the description of clinical signs and symptoms is an appropriate tool for primary diagnosis. The COVID-19 diagnosis was critical during the epidemic. Based on routinely surveillance system data such as fever& chills, cough, breathing difficulty, prostration or weakness, myalgia, irritability or confusion, sore throat, coryza, diarrhea, nausea or vomiting, headache, chest pain, abdominal pain, arthralgia, anorexia for symptoms and body temperatures>37.8, exudate pharyngeal, conjunctivitis, dyspnoea or tachypnea and some other clinical signs were collected. We aimed to develop a model to predict COVID-19 infection in suspected hospitalized patients reported in the surveillance system in North Iran.

Methods: The data of this cross-sectional study collected from hospitalized patients in which its catchment setting was the health centers and outpatient clinics for SARS-CoV2, in Mazandran province in north Iran between February 20 and June 20, 2020. The chi-square test was performed to compare clinical symptoms and signs and other related variables in confirmed covid-19 and negative covid-19. Also, two models were established based on clinical symptoms and signs and other related variables by multivariate logistic regression. The diagnostic performance of developed models was compared by receiver operating characteristic curve.

Results: Among 7,784 hospitalized patients tested for COVID-19 and included in the analyses, 2,233 (28, 7%) had RT-PCR confirmed COVID-19. Multivariate logistic regression analysis showed that Fever& chills (OR= 2.06; 95% CI: 1.83, 2.31), cough (OR= 2.23; 95% CI: 2.01, 2.49), breathing difficulty (OR= 1.59; 95% CI: 1.43, 1.78), Headache (OR= 1.29; 95% CI:1.08, 1.54) for symptoms and body temperature >37.8 (OR=1.15; 95% CI: 1.01, 1.33) for signs were informative in predictive Model of all clinical signs and Symptoms to identify COVID-19-positive patients. In this model, values of area under curve (AUC) in the training and testing groups were 0.6810 and 0.6980, respectively.

Conclusion: This predictive model showed the symptoms were more informative than signs for identification of COVID-19-positive cases. Also, the clinical signs and symptoms included in surveillance system forms in Iran at the first 6 months from beginning of COVID-19 epidemic could not collect valid information.

Keywords: COVID-19; clinical characteristics, syndromic patterns, Diagnostic Evaluation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-12

Association of lipid profile with the severity of COVID-19

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Abstract

Background And Aim: COVID-19 is a highly infectious disease that has affected millions of people worldwide. Pro-inflammatory cytokines in COVID-19 infection led to changes in lipid metabolism as well as changes in lipid profile. This study aims to investigate the correlation between lipid profile and COVID-19 severity in patients referred to the Teaching Hospital of Mazandaran University of Medical Sciences, IRAN, during April-May and July-August 2020.

Methods: This study was conducted on 140 patients with COVID-19 based on their clinical symptoms, imaging results, and laboratory findings. Based on CDC criteria, patients were categorized as severe and non-severe groups. Blood samples (5-7 ml) were collected from patients after 12 hours of fasting. Serum lipids levels were measured using TG-PA, cholesterol-PA, HDL-C-PA, and LDL-C-PA kits.

Results: Out of 140 COVID-19 patients, 33.57% had severe and 66.43% had non-severe disease. Patients with severe disease had a significantly lower mean LDL serum level compared to those with non-severe involvement (56.39 ± 3.62 vs. 70.10 ± 3.74) (P value=0.023). There was a significant negative correlation between HDL serum level and CRP and ESR ($P=0.0001$ and $r=-0.482$) and ($P=0.01$ and $r=-0.258$) respectively. Additionally, there was a significant correlation between cholesterol level and CRP as well as TG and ESR ($P=0.016$ and $P=0.02$) respectively.

Conclusion: The present study highlights the potential of lipid profiling as a cost-effective and accessible marker to assess COVID-19 severity and prognosis.

Keywords: Lipid profile, Severity, Outcome, COVID-19.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-13

KI and WU Polyomavirus DNA in the CSF of Children with Suspected Meningitis and Encephalitis

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Abstract

Background and Aim: KI and WU polyomaviruses were described by PCR detection of virus sequences in the respiratory tract samples from patients, mainly children, with respiratory disease. However, they have not yet been linked to a specific primary illness.

Methods: A groups of specimens from patients with suspected meningitis or encephalitis were examined for the presence of KI and WU polyomavirus. PCR was utilized to screen KI and WU DNA sequences from 200 cerebrospinal fluid (CSF).

Results: Of the 200 samples analyzed, 2 (1 %) were positive for KI and WU viruses (1 KI positive; 1 WU positive). Infection mainly occurred in two groups of patients; KI Polyomavirus was identified in 1 (0.5 %) CSF samples from children aged 7 years-14 years who were immunocompetent. WUV DNA was also detected in 1 (0.5%) CSF samples taken from patients aged 40-70 years who were severely immunosuppressed from HIV. Both groups had upper or lower respiratory tract infection. Co-infections with other viruses were not found in KI and WU polyomavirus positive samples.

Conclusion: These results suggest that KI and WU viruses may be associated with neurological diseases either in immunocompetent or immunocompromised patients. Detection of KIV and WUV DNAs in the CSF of the patients suspected to have either meningitis or encephalitis suggests that these viruses may have an etiological role.

Keywords: Human polyomavirus; KI; WU; PCR; Neurological Disorders.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-14

Molecular characterization of human astrovirus infection in children less than 5 years of age with acute gastroenteritis in Tehran, Iran, 2021-2022: Co-infection with rotavirus

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Abstract

Background and Aim: Human astroviruses (HAstVs) are important causative pathogens of acute gastroenteritis (AGE) in children under 5 years of age worldwide, along with group A rotavirus (RVA), norovirus (NoV), and enteric adenovirus (EAdV). The objective of the present study was both detect HAstV and its co-infections and investigate genetic analysis of circulating HAstV and co-infected virus in hospitalized children under 5 years of age with AGE in Iran.

Methods: Accordingly, a sum of 200 stool specimens were screened by PCR for HAstV during 2021–2022.

Results: The HAstV was found in 0.5% of 200 specimens (n=1) while was co-infected with RVA. The genetic and phylogenetic analysis indicated HAstV1 genotype from Iran, which clustered with viruses from lineage 1b, and in so far as we are aware, the detection of this lineage in Iran has not been previously reported. Furthermore, the detected RVA strain from Iran belonged to G1-lineage II/P[8]-lineage III, which has been reported previously in Iran as the most common strain. The further genetic analysis of RVA VP6 and NSP4 demonstrated an atypical genotype pattern G1P[8]-I1-E2, as a mono reassortant of a Wa like genogroup, which appeared to be reassorted with the NSP4 gene of E2 genotype of the G2P[4] DS-1 genogroup.

Conclusion: Although clinical outcomes of the AGE-causing viruses' co-infection is not yet entirely clear, it seems that future studies will be helpful to merge clinical and epidemiological data of co-infecting viruses for a more accurate medical and clinical relevance in symptomatic children.

Keywords: Human astrovirus; Rotavirus; Co-infection, Acute gastroenteritis.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-15

Evaluation of the relationship between inflammatory markers of covid-19 and clinical disease characteristics

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Abstract

Background and Aim: The COVID-19 disease is caused by a new strain of coronaviruses belonging to the group β . It spreads through asymptomatic respiratory infections and leads to symptoms ranging from moderate to severe, similar to acute respiratory syndrome, SARS (severe acute respiratory syndrome), and MERS (Middle East Respiratory Syndrome). Coronavirus can cause respiratory illnesses, including sinusitis, laryngitis, pharyngitis, nasopharyngitis, and laryngotracheitis. These conditions affect the respiratory system and can cause coughing, sore throat, and difficulty breathing. The objective of the article is to explore the correlation between COVID-19 and inflammatory markers.

Methods: Our study involved 800 patients who were admitted to Ghaem Hospital and tested positive for COVID-19 using the RT-PCR test. The patients were sampled using sterile swabs and experienced symptoms such as runny nose, sore throat, fever, and chest pain during the sampling process. Diagnostic tests were carried out using kits that utilized colorimetric optical absorption and immunoturbidimetric techniques to measure CRP, LDH, and D-Dimer levels, respectively.

Results: Our study investigated the connection between clinical symptoms and inflammatory factors, such as CRP, LDH, and D-Dimer. We found that there is a significant relationship between survival and inflammatory factors such as CRP ($p=0.009$), LDH ($p\leq 0.001$) and D-dimer ($p\leq 0.001$) among the patients. Additionally, we observed a significant relationship between LDH reduction and symptoms of weakness ($p=0.003$).

Conclusion: It is crucial to investigate the inflammatory factors CRP, LDH, and D-Dimer in patients who have tested positive for Covid. The presence of a significant relationship between these factors highlights their importance. Additionally, these inflammatory factors are significantly associated with certain symptoms caused by respiratory diseases.

Keywords: COVID-19, D-Dimer, LDH, CRP.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-16

Assessing the clinical manifestations of SARS-CoV-2 infection in pregnant women admitted to Ghaem Hospital, Mashhad, Iran

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Abstract

Background and Aim: Due to physiological changes in various biosystems, a pregnant woman is susceptible to severe infection and its subsequent complications. Many studies have proven that during the Covid-19 epidemic, pregnant individuals were more susceptible to severe infection compared to other members of society. Also, the occurrence of complications such as premature birth, oligohydroamnios, abortion, and caesarean section have been significantly associated with covid. Therefore, examining the initial manifestations of patients, the course of the disease and its consequences in pregnant women can affect the health of mothers and their babies during the Covid-19 pandemic.

Methods: In this cross-sectional study, in order to detect SARS-CoV-2 infection in pregnant mothers, Real time PCR test was used. The study population included all pregnant women admitted to Ghaem Hospital from September 2019 to August 2019, who had symptoms of Covid-19 and positive RT-PCR test. Other patient information such as demographic characteristics, initial manifestations and clinical tests were collected through patient files and the electronic patient information registration system.

Results: A total of 95 pregnant mothers with an average age of 32 years and with a positive RT-PCR test for SARS-CoV-2 infection were included in the study. Forty-eight patients (50.52%) had mild symptoms, 24 patients (25.26%) had moderate symptoms and 23 patients (24.21%) had severe symptoms. There was no significant relationship between the severity of patients' symptoms and their age. Sixty percent of patients had no underlying disease, 34.7% reported one underlying disease and 5.2% reported more than one underlying disease. Among the admitted population, 34 individuals were admitted to ICU due to respiratory distress. Examining the symptoms of the patients at the time of visit showed that the majority of the patients (89.9%) were symptomatic while 10 patients (10.1%) were asymptomatic. Eighty-six (86.9%) patients had more than two symptoms. Among the symptoms of the patients, cough and shortness of breath ranked first with 71 cases (61.6%) and fever and chills ranked second with 37 cases (37.8%). Also, the relationship between the viral load and the symptoms of the patients was assessed and no significant relationship was found between these two indicators.

Conclusion: Our study showed that the most common symptoms at the first visit were cough and shortness of breath, followed by fever and chills. On the other hand, there was no correlation between the severity of the disease and the type of symptoms of the patients. Therefore, it is not possible to predict the clinical condition of patients based on initial symptoms. Also, none of the laboratory factors, even the inflammatory and hematological factors, were related to the severity of the disease. Therefore, using laboratory parameters alone to predict the clinical condition of pregnant mothers with covid-19 is not effective. On the other hand, the viral load was not related to the symptoms of the patients. Having or not having an underlying disease does not make a difference in the severity of the disease in pregnant mothers.

Keywords: COVID-19; pregnant; symptoms; clinical manifestations.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-17

Investigation of anti-Hepatitis A and anti-Hepatitis E antibodies in the northwest of Iran during 2018-2019: A retrospective study

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Abstract

Background and Aim: Hepatitis A virus (HAV) and Hepatitis E virus (HEV) are small, non-enveloped RNA viruses with similar characteristics. Both are common viral infections around the world that are transmitted by the fecal-oral route. Recently, the epidemiology of these infections has changed due to the lifestyle changes of people in society. Unfortunately, there is no published information about the sero-epidemiology of these infections in the northwest of Iran. The aim of this study is to investigate the prevalence of HAV and HEV antibodies in the northwest of Iran.

Methods: A cross-sectional study was conducted using 700 serum samples from individuals who visited Ardabil Gastroenterology and Liver Research Center, both from urban and rural areas. The population was divided into seven age groups from 1 to 69 years. there were 352 (50.3%) men and 348 (49.7%) women, with an average age of 34.40 ± 19.74 . Ethical consent was obtained from the subjects. A blood sample was taken from the patients for the serological examination of total Hepatitis E and A antibodies and a questionnaire was also completed. The samples were tested using enzyme-linked immunosorbent assay (ELISA). The data obtained in this study were analyzed using descriptive statistics methods, Pearson chi-square test, independent T-test, and Mann-Whitney U test in SPSS version 24.

Results: The serological results of the study showed that 19.30% of subjects (135 people) have positive serology in terms of Hepatitis E antibody. Additionally, 401 (60.30%) participants were found to be HAV-positive, while 5 (0.75%) were in borderline status. Furthermore, the study also found that there is no significant difference between the prevalence of the infections and the gender of the studied subjects. Comparing the age groups and the rate of infections, it was shown that with increasing age, the rate of positivity and prevalence of Hepatitis E and A antibodies among people increased significantly.

Conclusion: The results of our study showed that there is no significant difference between genders of population. However, it was observed that the rate of these infections significantly increased with the age of individuals. it is better for the population of this area to be vaccinated and receive health education to protect against these infections.

Keywords: Hepatitis A; Hepatitis E; Seroepidemiology; Antibody.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-18

Isolation and characterization of Human rotavirus strain from fecal specimen of children under five years of age for attenuated vaccine development

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Abstract

Background and Aim: Human rotaviruses are the main cause of diarrhea in children under five years of age. In this study, we isolated and characterization of Human rotavirus strain from fecal specimen of children under five years of age for vaccine development. For this purpose, 48 RVA strains were detected during the 2021–2022 seasons. G9 genotype was found as the most common G genotype and P[8] genotype, followed by P[4] genotype in terms of frequency, the most common circulating genotypes. The two combinations of G9P[4] and G9P[8] RVA strains were predominant. However, several other combinations of RVA also were detected. Based on the distribution of I and E genotypes (46 strains) with respect to G and P, the most common strains were G9P[4]-I2-E2 (19.5%), G9P[4]-I2-E1 (6.5%), G9P[4]-I1-E1 (4.3%), G9P[8]-I1-E1 (19.5%), and G9P[8]-I2-E2 (10.9%), which were followed by several other combinations of G and P RVA strains with different pattern of I-E genotypes and also emerging, rare and uncommon strains. The present study described the continued circulation of G9 strains with the emergence of uncommon G9P[4] and G9P[8] reassortants with three and two different I-E genotypes, respectively, which have not been reported previously in Iran. RVA isolation was carried out on MA104 cells after inoculates were treated with different concentrations of trypsin. All rotaviruses isolated from stool samples in this study were human strains, and the results of their isolation in MA-104 cell culture could only be traced up to passage 7. This study showed that three genotypes G1P[8]-I1-E1, G9P[4]-I2-E1, and GntP[8]-I1-E1 could be isolated for 7 consecutive passages for proliferation in MA-104 cells. Also, HT-29 and Caco2 cell lines were found to be ineffective for human rotavirus replication.

Our findings indicated that predominant circulating RVA strains in Iran have been different from RVA strains present in both RVA vaccines. Given that, the introduction of RVA vaccines into national vaccination programs in Iran that is considered as a high priority by Health Ministry, needs to be scrutinized regarding the increase in the number of G9P [4] and G9P [8] strains versus a decrease in G1P[8] strains in Iran.

Methods: The present study was conducted to monitor the genotypes of circulating species A rotavirus (RVA) in Iran and investigate genetic linkages between specific RVA VP7, VP4, VP6, and NSP4 segments. RVA isolation was carried out on MA104, HT-29 and Caco2 cells.





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Results: For this purpose, 48 RVA strains were detected during the 2021–2022 seasons. G9 genotype was found as the most common G genotype and P[8] genotype, followed by P[4] genotype in terms of frequency, the most common circulating genotypes. The two combinations of G9P[4] and G9P[8] RVA strains were predominant. The most common strains based on I and E genotypes with respect to G and P were G9P[4]-I2-E2 (19.5%), G9P[4]-I2-E1 (6.5%), G9P[4]-I1-E1 (4.3%), G9P[8]-I1-E1 (19.5%), and G9P[8]-I2-E2 (10.9%). This study described the circulation of G9 strains with the emergence of uncommon G9P[4] and G9P[8] reassortants, which have not been reported previously in Iran. RVA isolation was carried out on MA104 cells. This study showed that three genotypes G1P[8]-I1-E1, G9P[4]-I2-E1, and GntP[8]-I1-E1 could be isolated for 7 consecutive passages for proliferation in MA-104 cells. Also, HT-29 and Caco2 cell lines were found to be ineffective for human rotavirus replication.

Conclusion: Our findings indicated that predominant circulating RVA strains in Iran have been different from RVA strains present in both RVA vaccines. Given that, the introduction of RVA vaccines into national vaccination programs in Iran that is considered as a high priority by Health Ministry, needs to be scrutinized regarding the increase in the number of G9P[4] and G9P[8] strains versus a decrease in G1P[8] strains in Iran.

Keywords: rotavirus, genotype, vaccine.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-21

RSV virus, a neglected infection, during the outbreak of corona and influenza infection

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Abstract

Background and Aim: During the pandemic Covid-19 special care is important for the possible reappearance of other respiratory viruses. Since respiratory viruses are largely indistinguishable in terms of clinical symptoms, it is necessary to use molecular diagnostic method. The purpose of this study is to investigate the frequency of common respiratory viruses such as coronavirus, influenza and RSV in different age groups.

Methods: To access the purpose of study infection to common respiratory viruses in the method Multiplex Real Time PCR extracted during a year and using them and data collected using statistical software SPSS is analyzed.

Results: The results showed that nationality and employment were effective in these diseases, but gender had no effect. Out of 500 examined cases, 95.8% were identified as Coronavirus, 3% as Influenza and 1.2% as RSV.

Conclusion: As expected during the Covid pandemic, the most common respiratory virus is the Coronavirus. But this does not mean the complete elimination of other respiratory viruses.

Keyword: RSV, Covid-19, influenza, outbreak.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Virology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PV-22

Endocan, a promising biomarker for COVID-19

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Abstract

Background and Aim: COVID-19 disease causes mild to serious infection with lung complications, thrombosis, and other complications that potentially lead to fatal outcomes. Also, since the beginning of the covid-19 pandemic, several biomarkers have been proposed to evaluate the diagnosis and prognosis of the disease, and endocan (endothelial cell damage) as a potential diagnostic and prognostic biomarker can be effective in the diagnosis of covid-19, and we review it in this study.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, Google Scholar, and Embase from 2016 to 2023 by using the keywords Covid-19, endocan, biomarkers, 53 articles related to inclusion criteria were extracted and then analyzed.

Results: The results indicated that various inflammatory biomarkers are involved in covid-19 disease, such as C-reactive protein (CRP), albumin, cytokines, and erythrocyte sedimentation rate (ESR). Currently, there are emerging biomarkers such as endocan, serum amyloid A, pentraxin 3, dimethylarginine that can be evaluated in diagnosis and potential prognosis in this disease.

Conclusion: Endocan can be a new diagnostic and prognostic biomarker for covid-19. Also, more studies with a larger sample size are necessary to evaluate the role of endocan.

Keywords: COVID-19, endocan, biomarkers.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-23

Investigating the relationship between blood factors and viral load in patients with COVID-19

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Abstract

Background and Aim: A number of COVID-19 sufferers, under certain conditions, experience fatal complications due to SARS-CoV-2 infection, which coincides with a number of clinical and laboratory factors. Therefore, in this study, we decided to investigate the relationship between hematological factors and severe symptoms and hospitalization in the ICU. The relationship between these factors and the load of virus was also investigated.

Methods: Hematological factors including WBC, RBC, PLT, Hct, Hb, PMN, Lymph, PT, and PTT were measured according to standard laboratory guidelines. RT-PCR was used to assess the viral load. Samples with CT \leq 35 was considered positive. The hematologic indices and the viral load were compared in patients hospitalized in ICU and not hospitalized in ICU, as well as in patients with severe and non-severe complications. Also, the relationship between hematological factors and different cyclic threshold (CT) values was assessed.

Results: A total of 2667 patients were included in the study, of which 55.9% were men and 44.1% were women. The average age of the participants in the study was 61.17 \pm 15.17 years and 36.4% of the patients were admitted to the ICU. The results of the study showed that none of the hematological factors were related to the severity of Covid-19 symptoms ($p>0.05$). On the other hand, leukocytosis, anemia, thrombocytopenia, neutrophilia, and lymphopenia were directly related to hospitalization in the intensive care unit ($p<0.05$). No correlation was found between viral load and hospitalization in the intensive care unit ($p=0.72$). Viral load was significantly associated with lymphopenia, thrombocytopenia, neutrophilia and increased red blood cell parameters (RBC, Hb, and Hct) ($p\leq 0.001$).

Conclusion: The viral load of SARS-CoV-2 is significantly related to a number of hematologic indices. Both the hematologic indices and the viral load can be used for the better management of COVID infected individuals.

Keywords: Virus load; RT-PCR; Covid-19; Blood factors.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-27

Interleukin-6 Polymorphism and Serum Interleukin-6 Levels: Predictive Factors for COVID-19 Severity

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Abstract

Background and Aim: In patients with COVID-19, the leading cause of mortality in its acute manifestation is acute respiratory distress syndrome (ARDS). This complication arises primarily due to an exaggerated immune response known as cytokine storm. Among the numerous cytokines involved in this response, interleukin-6 (IL6) holds particular significance. The present study aims to investigate the serum concentration of IL6 as well as the IL6 polymorphism, specifically the 174G/C single nucleotide polymorphism (SNP) that known as rs1800795 in COVID-19 patients, while also exploring the potential correlation between this genetic polymorphism and the severity of the disease.

Methods: The study included a total of 224 participants, consisting of 174 patients who tested positive for COVID-19 and were hospitalized, and 50 individuals who tested positive for COVID-19 but were not hospitalized. Two blood samples were collected from each participant: one sample was collected in a clotted state to assess the levels of IL6 in the serum, while the other sample was collected using ethylenediaminetetraacetic acid (EDTA) as an anticoagulant for nucleic acid extraction. The quantification of IL6 serum levels was accomplished using the enzyme-linked immune sorbent assay (ELISA) technique. Simultaneously, the IL6 polymorphism (174G/C SNP or rs1800795), was investigated utilizing the amplification refractory mutation system PCR (ARMS-PCR) method. The ARMS-PCR procedure involved the utilization of two distinct sets of primers, specifically designed for performing PCR to identify the genotypes associated with the targeted polymorphism. Subsequently, agarose gel electrophoresis was performed on the PCR products to visualize and analyze the outcomes. Finally, appropriate statistical tests and software were employed to analyze the obtained data.

Results: The results of the IL6 assay indicate that patients with a mild form of the disease exhibited low levels of IL6, whereas those with a severe form of the disease had high levels of IL6. Three genotypes resulting from a polymorphism at position 174 (-174G/C SNP, rs1800795) of the IL6 gene were identified. Analysis of the data obtained from these polymorphism variants revealed a significant difference in the frequency of CC and GG genotypes between the mild and severe disease groups. However, no such difference was observed for the CG genotype. Additionally, a significant association was found between an increase in IL6 serum levels and the presence of the GG genotype. Conversely, individuals with the CC genotype displayed lower levels of IL6 in their serum. However, this relationship was not observed in individuals with the CG genotype.

Conclusion: The analysis of our data revealed a significant association between elevated levels of IL6 in the serum and the severity of COVID-19. Furthermore, we observed a correlation between the frequency of single nucleotide polymorphism variants -174G/C (rs1800795) of the IL6 gene and the severity of the disease in different patient groups. Specifically, individuals with the CC genotype demonstrated a more favorable prognosis, as they were less likely to progress to the severe form of the disease and experience the inflammatory phase. Conversely, patients with the GG genotype had a higher probability of experiencing a worse prognosis, characterized by a greater likelihood of developing severe symptoms and entering the inflammatory phase. These findings suggest that the presence of the IL6 gene variant -174G/C has the potential to serve as a predictive marker for disease outcome in patients with COVID-19.

Keywords: COVID-19; Interleukin-6; IL6 polymorphism; Cytokine storm; Severity.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-28

Environmental surveillance of Astrovirus in surface water samples of Mazandaran province, Iran

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Abstract

Background and Aim: In both well-off and developing countries, human enteric viruses constitute a prominent factor in acute waterborne illnesses. A virus's ability to spread depends not just on its relationship with the host, but also on how it interacts with the surrounding environment. Human astroviruses (HAstVs) have been well-established etiological agents of viral acute gastroenteritis with a global distribution since their initial detection in the stool samples of children with diarrhea in 1975. Although cases of adult gastroenteritis have been reported, they are mostly thought to be the third most prevalent cause of viral gastroenteritis in children, after rotavirus and norovirus. Our study aimed to investigate the presence of Astroviruses in the surface water of Mazandaran province.

Methods: 78 samples from 3 rivers in Mazandaran province were gathered for a year (from July 2022 to May 2023). Four-liter sterilized plastic carboys were used to collect samples, which were then delivered to the lab at 4°C. The polyethylene precipitation procedure was used to further concentrate the viruses after filtration and elution. Viral RNA was extracted, cDNA was synthesized and real-time PCR was performed to detect Astroviruses in samples.

Results: The Astrovirus genome was detected in 8 of the 78 samples, making up 10.2% of the river samples positive for the virus. For positive samples, Ct values ranging from 16.45 to 36.58 were observed. The virus frequency in river samples seems to be increasing in the cold seasons of the year.

Conclusion: It is essential to take action to monitor the quality of water sources since enteric viruses can spread throughout contaminated water sources and lead to acute gastroenteritis outbreaks. In addition, diarrheal diseases might have a significant adverse influence on public health, along with a negative economic impact on society. Acute gastroenteritis in children is commonly caused by the human astrovirus (HAstV), which can lead to outbreaks of diarrhea and infrequent hospitalizations. To establish specific preventative measures, in addition to environmental monitoring, it may be helpful to have a deeper comprehension of the molecular epidemiology and characteristics of HAstV strains.

Keywords: Astrovirus, water samples, viral gastroenteritis.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-29

Molecular Detection of Human Norovirus in Hospital Wastewater Samples

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Abstract

Background and Aim: Acute gastroenteritis (AGE) poses a significant global threat, especially impacting children under 5 years old in developing countries, as emphasized by the World Health Organization (WHO). Enteric viruses, including Human Norovirus (HNoVs) from the Caliciviridae family, transmitted predominantly through the fecal-oral route are recognized as a leading viral pathogen causing AGE due to its low infectious dosage (18 particles) and prolonged viral shedding (28 days) estimated about 212,000 deaths per year in under-5 children. Genogroups GI and GII of NoV are prevalent in human infections, with GII being the most common worldwide. Virus identification is not routinely performed in Iranian hospitals and medical diagnostic laboratories, resulting in limited studies available on detection and HNoV epidemiology. Wastewater system monitoring can be one of the practical alternatives for studying the epidemiology of viral infection among the population. Viral concentrations and monitoring of wastewater can reflect the correspondingly variable number of infected patients. This study aims to detect HNoV and assess the efficiency of virus removal in both influents and effluents of hospital wastewater treatment plants (HWTP) in 5 hospitals located in Tehran, Iran.

Methods: In total, 30 influent and treated effluent samples were collected from wastewater treatment plants of 5 hospitals located in Tehran, Iran during 2023 for 3 months (September to November). Firstly, an adsorption-elution concentration method was tested followed by RNA extraction. Afterward, probe based reverse transcription-real time polymerase chain reaction (RT-PCR) was used to detection of NoV.

Results: Totally, NoV was detected in 50% of samples, comprising 80% in influent and 20% in effluent systems, indicating 33.3% NoV removal inefficiency in wastewater treatment plants (HWTPs). The prevalent genogroup was GI (66.7%), with GII accounting for 33.3% of cases.

Conclusion: The findings revealed a potential route for viral transmission, high survival rates of viruses in the wastewater treatment processes, also the relative inefficiency of wastewater treatment plants in eliminating HNoV. Furthermore, the prevalent genogroup observed was GI, this finding is in contrast to the global pattern where GII is typically the most common genogroup of NoV infections. This contradiction raises important questions about the local epidemiology and circulation of NoV genogroup in Tehran, Iran.

Keywords: Norovirus; Molecular epidemiology; Wastewater-based epidemiology.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-30

Detection of JC and BK polyomaviruses in swimming pool water

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Abstract

Background and Aim: Research on viral contamination in swimming pools is of global significance. As swimming pools are increasingly used for therapeutic purposes in addition to recreational activities and are frequented by individuals of various age groups, the risk of contamination is always present. This study aimed to detect polyomaviruses, which serve as important markers for viral contamination in public pool waters.

Methods: Multiple samples were collected from ten randomly selected pools in Tehran during the summer, from June 2023 to September 2023. The samples were concentrated using an electronegative filtration method. Probe-based real-time PCR technique was employed to detect JC and BK polyomaviruses. Additionally, the presence of fecal bacteria, fecal coliforms, and E. coli was investigated using the most probable number (MPN) technique.

Results: Out of 30 samples obtained, 26.6% tested positive for bacteria, while 53.3% were positive for polyomaviruses. Environmental factors such as chlorine levels, sample temperature, and pH were evaluated on-site during each sampling time, and the results were consistent with the findings. Chlorine levels, temperature, pH, nitrate, and total dissolved solids were found to significantly impact water quality from a microbial perspective.

Conclusion: Our findings indicate a gradual increase in water pollution as the summer progressed, likely attributed to an increased number of pool users and inadequate adherence to necessary hygiene practices and timely replacement of pool water.

Keywords: swimming pool; norovirus; gastrointestinal infections; Environmental indices; quality of water.

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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PV-31

MS2 bacteriophage applications as an appropriate model virus in molecular and environmental virology research

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Abstract

Background and Aim: MS2 Bacteriophage is a small, icosahedral, nonenveloped, positive-sense, single-stranded RNA (ssRNA) virus that infects Escherichia coli bacteria. It has served as a model system for understanding the fundamental principles of RNA biology, molecular virology, and protein-RNA interactions. MS2 has a simple genome consisting of approximately 3,500 nucleotides, encoding for four proteins: maturation protein, coat protein, replicase, and lysis protein. Its simplicity and ease of manipulation have made it a popular model in modeling science. This study highlights the importance of bacteriophage MS2 as an appropriate model for inactivation studies and discusses its applications in molecular and environmental virology.

Methods: To conduct this research, we studied 31 articles on PubMed and google scholar regarding “MS2 Bacteriophage applications”.

Results: While the use of MS2 bacteriophage as a model virus in molecular and environmental sciences, has yielded significant insights, there remain limitations and challenges. The behavior of MS2 does not always perfectly mimic that of all human enteric viruses, and thus, it may not be a perfect model in all contexts. Moreover, the detection and quantification of MS2 in different samples can be challenging due to issues such as sample matrix interference. Future work should focus on improving the detection methods for MS2, and on studying the behavior of MS2 under a broader range of conditions. Additionally, the development of more sophisticated models that incorporate the behavior of MS2 could provide more accurate predictions of viruses.

Conclusion: The MS2 bacteriophage has proven to be a valuable tool in molecular and environmental virology research. Its use in Environmental monitoring and food microbiology, drug delivery and nanotechnology, molecular biology, and genetic Engineering has led to important insights into the behaviour of viruses. Despite some limitations, the future of MS2 in science as a model looks promising, with potential for improvements in detection methods and techniques.

Keywords: Bacteriophage MS2, Molecular Biology, Virology, Environmental Virology, Nanotechnology, Drug delivery.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-32

Survey of otoacoustic emission screening test and Auditory Brain Response test in new born in a referral hospital in Tehran, Iran

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Abstract

Background and Aim: Most neonates are screened for hearing loss a few first after birthdays, and the most of the hospitals use a 2-stage protocol in which all infants are screened first with otoacoustic emissions (OAEs) and ABR. This study evaluated how many infants who failed the OAE and passed or failed the ABR.

Methods: In our cross-sectional study, all infants born during one year (between March 2019 and April 2020) at Mahdijeh Gynecology Hospital were enrolled in this study. 2-stage protocol in which all infants are screened first with OAEs. In this protocol, no additional testing is done for those passing the OAE, but infants failing the OAE are screened with ABR.

Results: 859 newborns enrolled in this study 58.3% showed abnormal OAE and referred to check the ABR. The ABR of them were normal at one year of age.

Conclusion: In our study, the prevalence of OAE failed in 58.3%. We commend that hearing screening tests (OAE) be performed for all neonates and if impaired, in addition to auditory follow up, the infant should also be evaluated for inborn some viruses which related to hearing loss like CMV.

Keywords: newborns, hearing loss screening, OAE, ABR.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Virology

Presentation Type: Poster

Abstract Type: Systematic Review/Meta-Analysis

Code of Abstract: PV-33

Prevalence of Norovirus in Patients with acute gastroenteritis in Iran: A Systematic Review and Meta-analysis

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Abstract

Background and Aim: Norovirus is the common etiologic agent of acute gastroenteritis. This study aimed to provide a systematic review and meta-analysis of norovirus prevalence in Iranian patients with gastroenteritis.

Methods: A literature search was done in PubMed, Embase, and Google Scholar databases in 2022. The keywords were “Norovirus,” “Gastroenteritis,” “Prevalence,” and “Iran”. The information, including sampling size, the number of norovirus-positive subjects, and the norovirus genogroups were extracted from articles.

Results: Fifteen articles, involving a total of 4421 patients, were included in the analysis. The pooled prevalence of norovirus was estimated at 8% (95% CI: 6% - 11%). The pooled prevalence of norovirus GI and GII genogroups was 2% (95% CI: 1% - 4%) and 12% (95% CI: 8% - 16%), respectively.

Conclusion: To manage norovirus-related gastroenteritis, monitoring patients with acute gastroenteritis is essential.

Keywords: Norovirus, Gastroenteritis, Prevalence, Iran.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PV-34

Virome

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Abstract

Background and Aim: Virome encompasses a diverse range of viruses, including bacteriophages, and is ubiquitous in all environments. Insights into food cycling and the primary origin of genes have been obtained through the study of the virome. Marine sediment from seawater in the 2000s was found to contain viromes, resulting in soil contamination among individuals of all ages, including children under seven years old. Viruses affect their human hosts in various ways. Human cells are susceptible to viral invasion. When referring to a human virome, we are describing an assemblage of viruses that invade the human body and have the capability to infect both human cells and other microbes, notably bacteria (bacteriophages). In the context of the human virome, the constituents are eukaryotic RNA viruses, eukaryotic DNA viruses, endogenous retroviruses, and bacteriophages.

Methods: In 2023 we reviewed various articles. Search was performed from June to August in the PubMed database and Google Scholar using the following terms “virome, human virome and components of the virome.

Results: A total collection of viruses that can colonizing in the human body by replicating in the cells is called the human virome. The human virome can infect both human cells and also the other components of the microbiome such as bacteria (by bacteriophages). The structural composition of the virome can be influenced by factors such as age, diet and the presence of other microbial factors. Viruses, despite their abundance, continue to be a mystery as their separation and classification pose significant challenges. The human virome has been detected in 9 out of the 31 organs of the human body using NGS and qPCR techniques. Detecting and also destroying the invading bacteria before causing serious damage is one of the benefits of the human virome.

Conclusion: Because of the unstable and rapidly evolving characteristics, the full exploration of the human virome is still pending. Understanding the virome is of great significance given its impact on nine organs; included in the list of organs are the liver, brain, skin, hair, kidneys, heart, lungs, large intestine, and blood.

Keywords: Virome; Human Virome; viruses.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-35

Prevalence and Subtype of BK virus among Hemodialysis patients in Qom province

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Abstract

Background and Aim: BK virus is one of the members of the Polyomaviridae family, which has become a big challenge for the transplant community due to nephropathy in kidney transplant patients. BK virus is divided into four genotypes based on the sequence changes of the VP1 genomic region, and genotype I is the most prevalent in the human population. The aim of this study was determined BK virus subtypes in hemodialysis patients and also renal transplant patients in Qom province.

Methods: 146 urine samples from hemodialysis patients were collected. The DNA was extracted and investigated using polymerase chain reaction (PCR). The SPSS 23 software was used for data analysis.

Results: Our patients included 91 (63%) men and 55(37%) women. The age of patients between 19 to 94 years. Among the 146 samples, 8 (5.5%) of them were positive for BK virus. All samples were subtype I.

Conclusion: The results of our study showed that prevalence of BK virus was low in hemodialysis patients in Qom province and sub-type I was prevalent in this province.

Keywords: Hemodialysis, BK virus, Urine, Qom.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-36

Antigen Inactivation and Conservation of SARS CoV-2 Virus by Gamma Irradiation

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Abstract

Background and Aim: *Coronaviruses* are enveloped RNA viruses that are widely distributed among humans, other mammals, and birds. The *SARS-CoV-2* virus is the causative agent of the emerging respiratory zoonosis disease. One of the most important requirements for the control of emerging and re-emerging zoonosis is the development of vaccines within a short time. The most recent example is the inactivated whole virus vaccine against *SARS-CoV-2*, which is still in use. Recently, use of ionizing radiation to inactivate pathogens has been developed for the rapid production of effective vaccines. In this study, Gamma radiation used to inactivate SARS CoV-2 virus and antigen conservation was analyzed.

Methods: The isolated *SARS-CoV-2* virus from tracheal swabs of an infected man was multiplied on Vero cells (NCBI under accession number: MW709393), and the supernatant of the infected cell suspension was taken as virus stock. The 20% trehalose was added to the first part, and the second contained no trehalose. The first and second virus stocks were used for irradiation with a Cobalt-60 irradiator, Gamma cell 220, at a dose rate of 0.93 Gy/s and an activity of 3985 Ci to inactivate *SARS-CoV-2* virus genomic RNA. Viral titration of all irradiated and un-irradiated samples was performed using the TCID₅₀ method. The infectivity of the irradiated, inactivated *SARS-CoV-2* virus was determined after inoculation of Vero cell monolayers, and then sub-cultured in four blind cultures on fresh Vero cells for evaluation safety test. The antigenic properties of irradiated and native virus samples were tested using the ELISA assay for S (spike) protein.

Results: Using 50% endpoint titers of irradiated and un-irradiated SARS CoV-2 virus samples, a dose-response curve were generated and used to calculate the D₁₀ value. Based on the dose-survival curve, the D₁₀ value was set at 1.7 kGy. Based on the D₁₀ value, the initial titer (10^{5.93}/ml), and according to the safety test the minimum dose required for complete inactivation was calculated approximately 14 kGy. *SARS CoV-2* virus samples irradiated 14 kGy gamma rays were used to evaluate the antigenicity of the spike protein (S1 subunit). The results of the indirect ELISA assay to evaluate the antigenic properties of the spike protein subunit S1 of *SARS-CoV-2* virus show that the gamma-irradiated virus samples have no significant difference in antigenic properties compared with the non-irradiated virus (P < 0.05). However, the optical density of the irradiated and non-irradiated virus samples plus 20% trehalose is higher than that of the samples without trehalose. It may be that the disaccharide plays an important role in maintaining the properties of proteins.

Conclusion: The gamma irradiated inactivated SARS CoV-2 viruses are a safe candidate antigen to immunize animal against Covid-19 with conserved antigenic characteristics. Also, the disaccharide Trehalose plays an important role in maintaining the properties of proteins.

Keywords: SARS CoV-2 virus, Gamma Irradiation, Antigen conservation.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-37

Investigating the relationship between the level of IgM and IgG antibodies and the clinical symptoms of hospitalized patients with SARS-CoV-2 infection

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Abstract

Background and Aim: COVID-19 is caused by a new strain of coronavirus called SARS-CoV-2. This virus is mainly transmitted through respiratory infections and can cause mild to severe respiratory diseases, resulting in pandemics worldwide. A better understanding of this emerging disease can help us in better prevention and treatment of symptoms. Evaluation of serological responses plays a vital role in this regard. However, due to a lack of information in this field, a study was conducted to investigate the relationship between clinical symptoms and anti-SARS-CoV-2 IgM and IgG levels.

Methods: Our study was conducted in Khorasan Razavi province, Mashhad, between 2021 and 2022. We conducted the study on patients admitted to Ghaem Hospital, who were tested positive for Real Time Polymerase chain reaction (RT-PCR). We took samples for RT-PCR from the pharynx and nose of patients with sterile Dacron swabs. The most common symptoms observed were dyspnea (34.3%), fever (14.3%), vomiting (4.8%), and cough (3.8%), respectively. We selected 81 patients and checked the onset of symptoms and the IgG and IgM antibody titers against SARS-CoV-2 using the Pishtaz Teb ELISA kit after five days.

Results: The most common symptom was dyspnea (34.3%), followed by fever (14.3%), vomiting (4.8%) and cough (3.8%). The disease was classified as severe in 48.1% of the study population. There was a significant relationship between the severity of the disease and the type of symptoms ($p < 0.0001$). However, no significant relationship was observed between the level of IgM/IgG antibodies and the severity of disease at the beginning of infection ($p = 0.37$).

Conclusion: It is important to conduct serial testing on patients infected with SARS-COV-2 on different days and for a longer period to fully understand the process of seroconversion after exposure to the virus. In conclusion, the severity of SARS-CoV-2 infection cannot be predicted by IgM/IgG antibody testing alone.

Keywords: antibody responses; COVID-19, IgM/IgG antibody assay, SARS-CoV-2.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-38

Investigation of frequency of human papillomavirus types in breast cancer samples among women in Ardabil province

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Abstract

Background and Aim: Breast cancer is the third cause of death among women worldwide. Identified risk factors encompass age, genetic mutations (like BRCA, P53), hormonal influences, lifestyle, and possibly viral infections, including human papillomavirus (HPV). Given the debate on HPV's cancer causation role and breast cancer's high prevalence, a study was initiated in Ardabil province to investigate HPV prevalence in breast cancer cases.

Methods: Our study examined 176 tissue samples, divided into two groups, which were neoplastic and healthy groups, gathered from cancerous & fibroadenoma patients. To ensure the accuracy of our results, we only included samples with sufficient tumoral tissue, no necrosis, and no bleeding. We began by gathering data on the age range of the patients and conducting clinical and pathological studies to determine the grade of malignancy and location of the cancer. For this study, we utilized fresh-frozen samples stored in portable nitrogen tanks at minus 70 degrees Celsius until analysis. We used a DNA extraction kit to extract DNA from the samples and then amplified each piece using the conventional PCR method with primers designed for HPV's L1 gene. For more accuracy, we did real-time PCR.

Results: All biopsy samples of breast cancer patients tested by PCR methods did not show positivity for HPV DNA sequences in conventional PCR. Further testing of these samples by real-time PCR also failed to detect HPV DNA sequences.

Conclusion: The absence of HPV DNA in the collected tumor tissue of breast cancer patients by employing the highly sensitive real-time PCR does not support the etiological role of oncogenic HPV in the pathogenesis of breast cancer in Ardabil women.

Keywords: Breast Cancer, Human Papillomavirus, HPV, Malignant Neoplasm.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-39

Mucosal Immune response on Intranasal Vaccinated chicken by Gamma Irradiated Avian Influenza Virus Subtype H9N2

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Abstract

Background and Aim: The poultry breeding industry in Iran is a vital revenue-generating sector, fulfilling an annual demand of over 2.5 million tons of chicken meat and playing a significant role in the country's protein consumption. Globally, it ranks seventh. Despite widespread vaccination efforts, H9N2 avian influenza strains persist in various Iranian provinces. This study aimed to immunize broiler chickens using irradiated H9N2 avian influenza vaccines via inhalation method.

Methods: The research involves assessing mucosal immune responses and analyzing neutralizing antibody titration via ELISA and HI techniques. The H9N2 virus subtype was inactivated using gamma radiation for immunization trials. Chickens were vaccinated in four treatment groups: a pre-immune group, negative controls with PBS through inhalation, an inactive vaccine irradiated with gamma radiation, an irradiated vaccine with disaccharide Trehalose through inhalation. Serum was analyzed to determine neutralizing antibody titers against hemagglutinin antigen using the hemagglutinin inhibition test. The nasal cavity and Bronchoalveolar (BAL) fluids were collected two weeks after the booster vaccination (on 38 day) to evaluate IgA by ELISA test. The nasal cavity and Bronchoalveolar (BAL) fluids were collected and used for mucosal Antibody-IgA by ELISA assay using Goat Anti- Chicken IgA Secondary Antibody- HRP (Invitrogen).

Results: The results indicated significant increases in neutralizing antibody titers in vaccinated chickens compared to negative and pre-immune controls, particularly with the inhalation method of the irradiated trehalose sugar vaccine ($P < 0.05$). The data for IgA assay showed that there is significant increasing of sIgA (secretary IgA) in Irradiated vaccine plus Trehalose by intranasal route of administration (Irr.vacT.IN) compared to NC ($P < 0.05$). This study highlights the importance of mucosal immunity, particularly the high levels of IgA antibodies in the respiratory mucosa, for disease prevention. Inhalation vaccination appears to be more effective than traditional injection methods in enhancing immunity against influenza in chickens.

Conclusion: One of reason for increasing IFN- γ , antibody titration and splenic lymphocyte proliferation in the Irradiated vaccine plus Trehalose (IN) group is that Trehalose not only is as a protectant for viral protein during irradiation and freezing of the viral stock at -70 ° C, but also it increases viscosity of the vaccine solution. Therefore, when a drop of vaccine is applied on the bird's nose, the bird shakes its head and it spills a portion, however, the vaccine solution with Trehalose doesn't spill as much because of more viscous solution.

Keywords: Avian Influenza Virus, Vaccine, Gamma Radiation, Mucosal Immune Response.



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The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PV-40

Screening for Viral Infections: A Comprehensive Overview

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Abstract

Screening for viral infections plays a pivotal role in public health interventions, disease control, and individual healthcare management. This article provides a comprehensive overview of the principles, strategies, and considerations involved in screening for viral infections. Various screening methods, including serological assays, nucleic acid amplification techniques such as polymerase chain reaction (PCR), rapid antigen tests, and next-generation sequencing (NGS), are discussed in detail. The benefits and limitations of each screening method are explored, with a focus on sensitivity, specificity, turnaround time, and cost-effectiveness. Key considerations for screening program design, including target population selection, timing, frequency, and criteria for positivity, are highlighted. The importance of adequate sample collection, handling, and storage protocols is emphasized to maintain the integrity and reliability of screening results. The impact of screening on early detection, timely interventions, and disease prevention is examined, together with the potential challenges of over diagnosis, false-positive results, and the psychological impact on individuals. The role of public health authorities, healthcare professionals, and laboratory services in the implementation and coordination of screening programs is discussed. Finally, the evolving landscape of viral infections, emerging technologies, and future directions in screening approaches are considered. By understanding the principles and intricacies of screening for viral infections, healthcare practitioners and policymakers can make informed decisions to effectively combat the spread of viral diseases and protect public health.

Keywords: Diagnostics, Pathogen discovery, PCR, Serology, Surveillance, Virus.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-41

Development of Covid-19 neutralizing antibody detection test using a truncated recombinant ACE2 protein

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Abstract

Background and Aim: Covid-19 is the third most common viral disease of the coronavirus family in the 21st century. The interaction of the ACE2 receptor and receptor binding domain (RBD) of the S protein plays a major role in the entry of the SARS-CoV-2 virus into host cells. The validity of a vaccine is assessed by evaluating the cellular and humoral immune responses (neutralizing antibodies) for each of the COVID-19 vaccines. Our long-term goal is to design and produce a truncated recombinant human ACE2 protein and use it to construct a coronavirus-neutralizing antibody detection kit by mimicking viral infection (ACE2-S-protein interaction).

Methods: The sequence was designed for expression in a eukaryotic host into the pcDNA3.1 vector. The synthesized genes were transfected to HEK293 cells for protein expression. The protein expression efficiency was confirmed by SDS-PAGE gel and Western blotting. The binding of the recombinant ACE2 protein with the COVID-19 virus was evaluated through an ELISA test with an anti-His tag antibody.

Results: In summary, we present an efficient expression system for preparing a functional recombinant ACE2 using the pcDNA3.1 expression system and the HEK293 cell.

Conclusion: The recombinant ACE2 produced in the present study can be used as starting material in developing diagnostic kits and screening potential vaccines.

Keywords: ACE2, neutralizing antibody, SARS-CoV-2, spike protein, vaccine.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-42

Investigation of SARS-CoV-2 Mutations in the Envelope Protein and Their Impact on Conformational Characteristics

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Abstract

Background and Aim: Since December 2019, COVID-19 disease caused by severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2) has spread rapidly around the world. The dramatic increase in the number of COVID-19 cases worldwide leads to the emergence of various mutations, which act as the main obstacle to the control and treatment of the disease. The envelope (E) protein, which is a structural protein of the virus, is less studied than other viral structural proteins. This study aimed to determine the prevalence of E protein mutations and how they influence the structure, stability, antigenicity, and Its binding affinity to PALS1 protein.

Methods: A total of 120 SARS-CoV-2 positive samples were selected from the central laboratory of Tabriz province. After genome extraction and confirmation of positivity by Real-Time PCR using a special kit for variant detection, the variants of the samples were determined. cDNA was synthesized from the RNA extracted from the samples. Using a special software, specific primer for the envelope (E) protein was designed. Afterward, the standard PCR was performed, followed by the visualization of bands by gel electrophoresis. Furthermore, to identify the E gene mutations, direct sequencing of the E genes was also done. Bioinformatics techniques were used to investigate the possible effects of changed antigenic and 3D characteristics of amino acid substitutions. Also, the immunogenicity of wild-type and mutant E was investigated utilizing a ClusPro docking server and the IEDB online platform.

Results: After alignment into the sequence of patient samples with the reference sequence, a total of 10 mutations were found (Same sense and Missense mutations). Of these, only two mutations caused amino acid substitutions and the rest caused silent mutations. The non-synonymous mutations in the E protein were at amino acids 68 and 73, with substitutions of phenylalanine to serine at position 68 (S68F) and phenylalanine to leucine at position 73 (L73F). The L73F and S68F mutants belonged to the alpha and Delta variants, respectively. The amino acid position of 73 in the E protein is in a motif called DLLV. These mutations alter the structure of E protein and are important for its interaction with the host PALS-1.

Conclusion: Our findings in the present study suggest that the stability of the E protein sequence was conserved over time and demonstrated that S68F and L73F mutations had a stabilizing effect on the structure of the E protein and did not change its antigenic properties. Additionally, the results of molecular docking studies showed that both S68F and L73F substitutions could notably enhance the binding affinity of the E protein's C-terminal motif to PALS1. This study could be beneficial in improving the management of COVID-19 and the development of future vaccines and drugs.

Keywords: SARS-CoV-2, COVID-19, Mutation, Envelope protein.





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Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Systematic review/Meta analysis

Code of Abstract: PV-43

The use of artificial intelligence in the diagnosis of cardiovascular diseases in cancer patients: A systematic review study

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Abstract

Background and Aim: One of the important developments in the field of improving the diagnosis and treatment of cardiovascular diseases is the use of artificial intelligence for accurate and time-consuming diagnosis. Cancer patients are at risk of developing cardiovascular diseases, which can have very vague and challenging symptoms. The use of artificial intelligence, including deep learning algorithms and discrete artificial intelligence, can be used in the effective diagnosis of cardiovascular diseases in cancer patients with the help of information related to cancer disease and aggregated cardiovascular symptoms. The purpose of this study is to investigate the use of artificial intelligence in the diagnosis of cardiovascular diseases in cancer patients.

Methods: This study is a systematic review study that was conducted in 2023 by using the keywords of artificial intelligence, diagnosis, cardiovascular diseases, cancer it was done in reliable databases including PubMed, Scopus, Cochrane, Web of Science and Google scholar search engine without time limit. To ensure the completeness of the search results, the sources of the articles were checked and after removing the duplicate titles from the endnote software and checking the titles and abstracts, the related articles were checked using JBi tools, after checking the quality of the articles, the findings in the checklist the target was entered.

Results: 3290 articles were reviewed and finally 31 related articles showed that due to the large number of cancer patients who suffer from cardiovascular diseases at the same time and the number of unclear symptoms, the need for an accurate and fast method to diagnose these diseases is felt. Artificial intelligence is able to increase the potential of rapid and accurate diagnosis of cardiovascular diseases in cancer patients with the help of deep learning algorithms. Artificial intelligence methods, such as deep neural networks, can diagnose patients with cardiovascular diseases based on accurate prediction and aggregation of relevant information, and improve treatment based on this diagnosis. For this purpose, there is a need for databases of cancer patients that have information about their cardiovascular symptoms, even if they do not have cardiovascular disease.

Conclusion: As a result, the use of artificial intelligence in the diagnosis of cardiovascular diseases in cancer patients can lead to significant results in improving the diagnosis and treatment of patients. In addition to increasing the accuracy of diagnosis, these methods can also reduce the time and cost of treatment. In general, the use of artificial intelligence in the diagnosis of cardiovascular diseases in cancer patients is recommended as a powerful tool in diagnostic medicine.

Keywords: artificial intelligence, diagnosis, cardiovascular diseases, cancer.



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The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-44

Using Bacteriophages in New Ways to Treat Wounds: A Promising Strategy

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Abstract

Background and Aim: Wound infections are a significant healthcare issue causing slow healing, increased morbidity, and high costs. Bacteriophages, viruses that attack and destroy specific bacteria, are becoming popular as a non-toxic substitute for antibiotics. They are effective against various diseases, including those resistant to antibiotics, and can be applied to wounds using various delivery techniques. Research has shown that phages can selectively target harmful bacteria, such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli*. Bacteriophages offer numerous benefits in wound care, including high specificity, breaking through biofilms, and the potential for lowering inflammation and speeding up healing. They can modulate immunological responses by releasing growth factors and anti-inflammatory cytokines from the host. Bacteriophages are a desirable treatment alternative due to their dual function of stimulating wound healing and eradicating germs. Further research is needed to create standard operating procedures, assess long-term safety, and solve regulatory issues. In this study, we had a look at how bacteriophages heal various types of wounds using fewer antibiotics.

Methods: Using bacteriophage-based therapeutics to heal wounds was the goal of this investigation. An extensive literature examination was done to gather pertinent papers, clinical trials, and case studies. Using the terms "bacteriophages," "wound treatment," "infection control," and "wound healing," the search technique used resources including PubMed, MEDLINE, and Google Scholar.

Results: According to the review's findings, bacteriophage treatment effectively treats various infected wound types. Bacteriophages can selectively target and eradicate particular germs while sparing healthy host cells and microorganisms. Studies have shown that bacteriophage-based treatments effectively treat burn infections, diabetic foot ulcers, and chronic wounds. Bacteriophages have also shown the ability to overcome antibiotic resistance, providing a workable substitute for traditional antibiotic therapies.

Conclusion: Bacteria offer benefits in wound therapy, such as high bacterial specificity, biofilm piercing, and tissue damage reduction. However, further engineering modifications are needed to enhance their therapeutic effectiveness. Addressing issues like manufacturing and delivery methods, clinical data scarcity, and regulatory considerations is crucial. Further studies and clinical trials are needed to confirm the security, effectiveness, and long-term effects of bacteriophage-based therapy for wound management.

Keywords: Bacteriophage, wound, wound treatment, virus, pathogenic agents.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-45

Assessing the prevalence of SARS-CoV-2 infection in infants born to mothers with COVID-19 in Mashhad, Iran

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Abstract

Background and Aim: The new corona virus called SARS-CoV-2 is a life-threatening respiratory disease that has caused enormous public health problems worldwide. According to the official statistics reported in the epidemic of infectious diseases, pregnant mothers and their fetuses are among the high-risk population. In addition, during epidemics of infectious diseases, special attention should be paid to newborn infants, because infected infants may be asymptomatic or exhibit mild or severe symptoms. This study was conducted to assess the rate of SARS-COV-2 infection in infants born to infected mothers with the virus.

Methods: This study was conducted retrospectively on data collected from September 2019 to October 2021 in Ghaem Hospital, Mashhad, Iran. Infants born to mothers infected with SARS-CoV-2 based on the results of the RT-PCR test were selected and tested if they were infected. Information related to the demographic characteristic of the infants as well as the data on symptoms were collected from the records in the Health Information System (HIS). Data were analyzed using SPSS statistical software, version 26.

Results: The studied population included 142 newborns to mothers with a positive RT-PCR covid test. The average age of infants at the time of sampling was $26.01 \pm 22/63$ days, among which the covid test was positive for 47 (33.1%) infants and negative in 95 (66.9%) infants. In total, 89 infants recovered and were discharged from the hospital, 36 infants were discharged by personal consent, 9 infants were transferred to another treatment center, and 11 infants died. Patients were divided into severe, moderate and mild categories based on clinical symptoms. The only variable that had a statistically significant difference between the PCR positive and PCR negative groups was the severity of the disease ($p=0.004$). Comparison of cycle threshold of N and RdRp genes was higher in patients with diarrhea and this difference was statistically significant ($p<0.05$). Also, the average ct in both genes was lower in patients with weakness and this difference was statistically significant ($p<0.05$).

Conclusion: Our study showed that in total, the corona test was positive for one third of babies born to mothers with covid-19 disease. We recommend that pregnant mothers, as a high-risk group, should be under higher care in this field, and the health care of the newborn should be done with greater precision, and these cares require more attention in babies with more severe symptoms.

Keywords: SARS-CoV-2; Covid-19; newborn; viral load; RT-PCR test.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Case Report

Code of Abstract: PV-46

Herpes Simplex Virus encephalitis in a child diagnosed with Bruton agammaglobulinemia; A Case report

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Abstract

Background and Aim: Primary B cell immunodeficiency can result from disruption or alteration of B cell development resulting in reduced or absent immunoglobulin production. In addition to X-linked agammaglobulinemia (XLA) and Bruton agammaglobulinemia, which account for about 85% of cases, other genetic forms of agammaglobulinemia have been discovered. As a result of Bruton agammaglobulinemia, individuals are more susceptible to encapsulated pyogenic bacteria. In this study, we presented a child diagnosed with Bruton agammaglobulinemia and HSV encephalitis.

Case presentation: A 5-year-old boy with fever and a generalized tonic-clonic seizure was referred to our emergency department. A status seizure occurred during his hospitalization. CSF Polymerase Chain Reaction (PCR) detected Herpes Simplex Virus Type 1 (HSV-1) DNA. After treatment, the neurological symptoms were presented as motor developmental disorder and cognitive disorder. His parents mentioned recurrent respiratory tract infectious from his childhood. The PCR tests for Covid-19 and influenza were negative. The immunological analysis showed low serum levels of immunoglobulins. The level of CD19 was reduced in flow cytometry analysis. The diagnosis of Bruton agammaglobulinemia was confirmed.

Conclusion: As of now, HSV infectious may also reported in children with Bruton agammaglobulinemia. Early detection of HSV leads to the prevention of complications and improvment the outcomes in children with Bruton agammaglobulinemia.

Keywords: Bruton agammaglobulinemia, children, Herpes Simplex Virus.





The 15th International Congress of Medical Laboratory & Clinic



Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024

Section: Virology

Presentation Type: Poster

Abstract Type: Review

Code of Abstract: PV-47

Investigating asexual transmission of HPV and the effectiveness of vaccination on prevalence and infection rates: A State-of-the-art review

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Abstract

Background and aim: Human papilloma viruses (HPVs) are a family of nonenveloped double-stranded DNA viruses with over 200 identified types. HPV is the most prevalent sexually transmitted disease globally, and high-risk strains are responsible for approximately 5% of all cancer cases worldwide. This includes cervical, anal, vaginal, vulvar, and oropharyngeal cancers, with an estimated 570,000 women and 60,000 men developing HPV-related cancers annually. The purpose of this study is to examine the routes of asexual transmission of HPV and evaluate the effectiveness of vaccination in reducing its prevalence and infection rates.

Methods: A comprehensive review of databases was conducted to ensure the accuracy and validity of the information presented in this study. An attempt has been made to include all relevant research on the prevalence and transmission routes of HPV.

Results: The primary route of HPV transmission is through skin-to-skin or skin-to-mucous contact, including sexual and non-sexual routes such as fomites, fingers, and mouth-to-skin contact. Mother-to-child transmission is also possible, with evidence of HPV transmission through amniotic fluid, placenta, and contact with the mother's genital mucosa during birth. While transmission through water has not been definitively proven, HPV DNA has been detected in aquatic environments. Contaminated medical equipment has been found to contain HPV particles even after standard disinfection, and procedures such as loop electrosurgical excision procedure (LEEP) and carbon dioxide (CO₂) lasers can release HPV particles into the air, posing a risk to those working in these environments. The implementation of comprehensive vaccination programs has been shown to decrease high-grade cervical abnormalities and prevent new cases of genital warts. Overall, this evidence highlights the effectiveness of HPV vaccination in reducing the prevalence and infection rates of HPV-related diseases.

Conclusion: The HPV vaccination program is a cost-effective long-term healthcare measure that helps prevent unnecessary medical expenses and societal damage. Studies have shown that vaccinating both sexes before sexual activity begins is safe and effective in reducing the incidence of HPV-related cancers and other diseases. Further research is needed to explore non-sexual routes of HPV transmission and improve hygiene practices to reduce HPV transmission in medical settings.

Keywords: HPV vaccination, HPV transmission routes, human papillomavirus.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Virology

Presentation Type: Poster

Abstract Type: Systematic review/Meta analysis

Code of Abstract: PV-48

Cofactors in HPV

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Abstract

Background and Aim: Human papillomavirus (HPV) is a common sexually transmitted infection that can cause a range of diseases, including cervical cancer, genital warts, and other cancers of the anus, penis, vagina, and oropharynx. While HPV infection is the primary cause of these diseases, various cofactors have been shown to increase the risk of HPV persistence and progression to cancer.

Method: in this systematic review, we tried to gather data were collected by searching keywords such as: HPV, cofactor, risk factor, prevalence in scientific articles in web of science, Google scholar, PubMed, and etc.

Result: One of the most well-known cofactors for HPV-related diseases is smoking. Smoking has been shown to increase the risk of cervical cancer in women infected with HPV, as well as other HPV-related cancers. This is thought to be due to the carcinogenic chemicals in tobacco smoke that damage DNA and weaken the immune system, making it harder for the body to fight off HPV infection. Immunosuppression is another cofactor that can increase the risk of HPV persistence and progression to cancer. People with weakened immune systems, such as those with HIV/AIDS or who have undergone organ transplants, are more susceptible to HPV-related diseases. This is because the immune system plays a critical role in controlling HPV infection and preventing the development of cancer. Hormonal contraceptives have also been implicated as a cofactor for HPV-related diseases. Some studies have suggested that women who use hormonal contraceptives for an extended period may have an increased risk of cervical cancer, although the evidence is not conclusive. It is thought that hormonal contraceptives may alter the immune system's response to HPV infection, making it more difficult for the body to clear the virus. Other cofactors for HPV-related diseases include fungal and bacterial infections, such as candidiasis and bacterial vaginosis, as well as other high-risk types of HPV. These cofactors can interact with each other in complex ways, making it difficult to fully understand their individual contributions to HPV-related diseases.

Conclusion: Overall, understanding the role of cofactors in HPV-related diseases is critical for developing effective prevention and treatment strategies. Further research is needed to fully understand the interactions between these cofactors and their impact on HPV infection and disease progression.

Keywords: HPV; cofactors; Sexually transmitted infections.





The 15th International Congress of Medical Laboratory & Clinic

Venue:
Tehran University of Medical Sciences, Tehran, Iran.
January 25-28, 2024



Section: Virology

Presentation Type: Poster

Abstract Type: Original Research

Code of Abstract: PV-49

Comparison of laboratory results between positive and negative COVID-19 cardiovascular patients hospitalized in Ghaem hospital, Mashhad, Iran

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Abstract

Background and Aim: Patients with COVID-19 infection have different manifestations and their prognosis is influenced by various factors. One of the common underlying diseases in hospitalized patients following COVID-19 was the simultaneous suffering from cardiovascular diseases. The main purpose of this research is to determine the differences in laboratory results in cardiovascular patients following COVID-19 infection.

Methods: This study was conducted retrospectively on the available information of all patients who were admitted to Ghaem hospital due to COVID-19 infection in the period of 2020-2021 and had symptoms and signs of cardiovascular diseases. Also, patients with any of the cardiovascular disorders such as ischemic heart disease, high blood pressure, heart failure and arrhythmias were included in this study. Demographic information of patients such as age, sex, family history, duration of illness, existence of other underlying diseases, symptoms of illness, results of laboratory tests and radiological findings were extracted from their files. In addition, the level of liver enzymes, lactate dehydrogenase (LDH), C- reactive protein (CRP) and troponin (as predictors of tissue damage and inflammation) were analyzed. Subsequently, the laboratory findings of negative covid-19 cardiovascular patients (as the control group) were evaluated and compared with the case group.

Results: In this study, a total of 400 patients were assessed (200 people in case group and 200 people in control group). The mean age of the case and control groups were 65.65 ± 14.25 and 64.16 ± 15.69 years ($P=0.32$), respectively. The level of creatine phosphokinase (CPK) in the case group was significantly higher than the control group ($P<0.001$). Also, the level of alkaline phosphatase (ALP) in the case group was 400 ± 561 and in the control group was 239 ± 225 units per liter ($P<0.001$). In addition, there was no considerable differences between two groups in the level of CRP, LDH, Troponin I, aspartate aminotransferase (AST) and alanine transaminase (ALT).

Conclusion: Analyzing the results of the study indicates that the level of CPK and ALP in hospitalized cardiovascular patients following COVID-19 infection was remarkably higher than the COVID-19 negative group. Various factors increase in inflammatory conditions in the body. However, identifying factors at the time of prognostic evaluation can be helpful in the management of COVID-19 patients with various underlying diseases.

Keywords: COVID-19, cardiovascular diseases, laboratory findings.

