

**Assessment of humoral immunity in workers occupationally exposed to low levels of ionizing radiation**Mehrangiz. Rajaii Oskouii<sup>1</sup>, Soheila. Refahi<sup>2,3</sup>, Masoud. Pourissa<sup>4</sup>, Yaser Tabarraei<sup>5\*</sup><sup>1</sup>Department of Immunology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.<sup>2</sup>Department of Medical Physics and Engineering, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran.<sup>3</sup>Department of Medical Physics, Faculty of Medicine, Ardebil University of Medical Sciences, Ardebil, Iran.<sup>4</sup>Neurosciences research Center, Tabriz University of Medical Sciences, Tabriz, Iran.<sup>5\*</sup>Department of Biostatistics, Faculty of Health, Sabzevar University of Medical Sciences, Sabzevar, Iran.\*Corresponding Author: [yasertabarraie@yahoo.com](mailto:yasertabarraie@yahoo.com)

**Abstract:** The aim of this study was investigating the effect of low levels of ionizing radiation on immunoglobulin, complement levels in radiology workers occupationally exposed to ionizing radiation. **Materials and Methods:** The present study was conducted in the Department of immunology, college of medicine, Tabriz University of medical sciences, Iran. during the year of 2006-2007. Blood samples were taken from 45 radiology staff and from 35 subjects who had never been exposed to radiation. Samples were analyzed for immunoglobulin, complement levels. **Results:** Serum total IgA, IgM, c3, c4 levels were as significantly lower in the radiology workers exposed to ionizing radiation compared to the controls ( $p < 0.05$ ). A significant difference was observed in IgA, IgM levels and age in radiology workers ( $p < 0.05$ ). A statistical significant difference between IgA, IgM and c3 and working period was found in this study. **Conclusion:** The present study suggests that exposure to low levels of ionizing radiation causes decreased IgA, IgM, c3, c4 levels in radiology workers. Further studies are needed for determining the appropriateness of periodic check-ups of immune functions for detecting early changes in the immune system. [Mehrangiz. Rajaii Oskouii, Soheila. Refahi, Masoud. Pourissa, Yaser Tabarraei. **Assessment of humoral immunity in workers occupationally exposed to low levels of ionizing radiation.** *Life Sci J* 2013;10(5s):58-62] (ISSN:1097-8135). <http://www.lifesciencesite.com>. 10

**Keywords:** Immunology, X- ray, Occupational radiation exposure**Introduction**

It is well established that ionizing radiation has negative biologic effects on living organisms depending on dose of radiation and duration of exposure (1). The single largest contributor of man-made radiation is the medical profession. The effects of ionizing radiation on a given population are generally divided into two categories, acute and chronic. The acute effects are considered to be those which happen in the immediate post irradiation periods, i.e. from the time of radiation exposure up to 6 months to a year post exposure. Acute effects are generally the result of long radiation exposure delivered to the whole body, or at least a major part of it, in average short time, on the other hand the chronic effects of radiation results from relatively low exposure levels delivered over long periods of time. Therefore long – time effects of low doses seems to be the main risk factor and that might results from occupational exposure (2). There are some difficulties in radiation studies in attempting to investigate effects due to radiation, particularly at the very low exposure levels. Thus, any association of a particular biologic effect with an exposure to ionizing radiation must have with it a degree of uncertainty. Another problem that we encounter in the study of low – level radiation effects is the latent period, for

example effects of low dose irradiation on genetic abnormalities, immune system functions and immune system cells (T & B cells) (2, 3). Individuals working in radiology-related occupation are among persons exposed to long-term levels of ionizing radiation that have been shown to have immunocompromising effects due to occupation (4). Health consequences of the Chernobyl accident with regard to ionizing radiation have been well studied in subjects living in Russia and neighboring countries. There are limited numbers of studies investigating the effect of long - term, low dose ionizing radiation exposure on the immune status of radiology workers. Therefore, the objective of our study was investigating the effect of low levels of ionizing radiation on immunoglobulin, complement levels in radiology workers occupationally exposed to ionizing radiation.

**Material and Methods**

The investigation was carried out in 80 subjects divided in two groups: the first (study group) consisted of 45 radiology staff ( 27 males, 18 females aged 25-60 years, range,  $40.6 \pm 9.45$  years), and the second (control group) consisted of 35 subjects (17 males, 18 females aged 28-60 years, range  $42.22 \pm 8.1$  years) who had never been exposed to radiation. This study was conducted within the Department of immunology of faculty of medicine, Tabriz

University of medical sciences, Iran, between March 2006 and March 2007. Details of occupational and medical history were obtained from a questionnaire form completed by each subject. Subjects who had gross anemia, known history of diabetes mellitus, cardiopulmonary disease, acute or chronic infection, autoimmune disease, malignancy, and current or previous tobacco were excluded from the study. Length of working period in radiology staff varied from 3 to 30 years (average length  $15.17 \pm 7.2$  years) with daily at least 25 (average  $37.44 \pm 10.48$ ) exposures. With respect to sex and working period the following subgroups were then selected-the subgroup of women-18 subjects aged from 25 to 41 years (mean= $32.94 \pm 4.91$  years) and one of men-27 subjects aged from 31-60 years (mean= $45.7 \pm 8.24$  years), the subgroup of radiology staff that had > 10 years working period- 33 subjects and subgroup of 12 subjects working period <10 years.

Blood samples were collected from the antecubital vein (before breakfast, between 7:00 and 9:00 h) of radiology staff and persons qualified for the control group with the purpose of obtaining immunology markers. Serum of blood samples was obtained by centrifuging at 5000 rpm for 10 min. Assessment of immunoglobulins (IgG, IgM, IgA, C<sub>3</sub>, and C<sub>4</sub>) carried out using SRID (Single Radial Immunodiffusion) technique with the ready for use plate of Germany Behringer Company product. In this procedure preformed mixture of gel and antihuman globulin (C<sub>3</sub>, C<sub>4</sub> and heavy chain of immunoglobulins) were distributed into the plates with 12 wells. We put on 5  $\mu$ l of serum samples in wells of plates with Hamilton syringe then after 72 h measured the diameters of formed immune complex circle around the wells. There is a direct relationship between serum concentrations of immunoglobulins and diameters of formed immune complex circles.

This study had been approved by the local bioethics commission and all persons were informed about the aims and scope of the study and gave their informed consent prior to their inclusion in the investigation. All statistics were performed in SPSS version 11.5 software. The obtained results were compared on the following manner: (A) between total group of radiology staff (45 persons) and control group (35 persons); (B) between the subgroup of females (18 workers) and males (27 workers) in study group and subgroup of females (18 subjects) and one of males (17 subjects) in control group; (C) between the subgroup of workers for >10 years (33 Subjects) and the subgroup of persons working <10 years (12 subjects).

Parameters among control and study groups and testing effect of gender were compared using Mann-Whitney U test. Student t test was used for

comparing parameters between subjects occupationally exposed to ionizing irradiation for < or > 10 years. Pearson correlation test was performed for analyzing correlation among parameters. A level of  $p < 0.05$  was considered significant.

### Results

The demographic characteristics of groups were illustrated in Table 1. Distribution of C<sub>3</sub>, C<sub>4</sub>, and total Ig levels for study and control groups are presented in Table 2. Levels of mean serum total IgA, IgM, C<sub>3</sub>, and C<sub>4</sub> were significantly lower in study group than in control group using Mann-Whitney U test. The C<sub>3</sub>, C<sub>4</sub>, and total Ig levels of men and females subgroups are showed in Table 3. When levels of antibodies were compared with regard to gender of subjects, levels of mean serum IgA, IgM, and C<sub>3</sub> of females were significantly higher than males for study group, whereas level of antibody IgM, male:  $2.45 \pm 0.65$  vs. female:  $1.98 \pm 0.53$  was significantly lower for females than males subjects for control group.

In the study group, there was significant correlation between age and IgA and IgM levels, respectively ( $r$ : -0.348, -0.547,  $p$ : 0.019,  $p$ : 0.000), whereas in control group, there was significant correlation between age and IgM level ( $r$ : 0.354,  $p$ : 0.037).

Levels of total Ig and C<sub>3</sub> and C<sub>4</sub> with regard to working period were demonstrated in Table 4. When comparison was made between subjects in the study group with regard to working period, levels of immunoglobulin IgA, IgM, and C<sub>3</sub> were significantly lower for subgroups of radiology staff >10 years working period than <10 years working period. In study group, we found a positive statistically significant correlation between IgA, IgM, and C<sub>3</sub> and working period, respectively ( $r$ : 0.535, 0.663, 0.398) respectively.

### Conclusion

The effects of low level exposure to ionizing radiation are of concern to a large number of people, including workers occupationally exposed to radiation. Medical radiation workers are employees of hospitals, clinics and private offices where radiation is used in the process of delivering health care to human (5). It is very important to estimated doses from individuals occupationally exposed to ionizing radiation in order to carry out radioprotection procedures and restrict the hazards to human health (6), but the extent of the health hazards is difficult to assess. Therefore, the development of procedures that can be used to precisely identify health hazards in exposed populations is important to establish effective programmes for disease prevention (7).

**Table 1.** Demographic characteristics of groups

|                         | Study group (n=45) | Control group (n=35) |
|-------------------------|--------------------|----------------------|
| Age (years)             | 40.6 ± 9.45        | 42.22 ± 8.1          |
| Gender (M/F)            | 27/18              | 17/18                |
| >10-year working period | 33                 | -                    |
| <10-year working period | 12                 | -                    |

**Table2.** C<sub>3</sub>, C<sub>4</sub>, and total Ig levels among groups

| Group                   | IgA (g/L)   | IgM (g/L)   | IgG (g/L)     | C <sub>3</sub> (g/L) | C <sub>4</sub> (g/L) |
|-------------------------|-------------|-------------|---------------|----------------------|----------------------|
| Study group             | 2.15 ± 0.81 | 1.70 ± 0.80 | 12.73 ± 15.28 | 0.98 ± 0.30          | 0.29 ± 0.11          |
| Control group           | 2.63 ± 0.45 | 2.20 ± 0.63 | 12.03 ± 2.81  | 1.20 ± 0.10          | 0.32 ± 0.06          |
| P (Mann-Whitney U test) | 0.001       | 0.001       | 0.009         | 0.000                | 0.009                |

**Table 3.** C<sub>3</sub>, C<sub>4</sub>, and total Ig levels of men and females subgroups

|                      | Study group   |              | P (Mann-Whitney U test) | Control group |              | P (Mann-Whitney U test) |
|----------------------|---------------|--------------|-------------------------|---------------|--------------|-------------------------|
|                      | Male          | Female       |                         | Male          | Female       |                         |
| IgA (g/L)            | 1.8 ± 0.73    | 2.66 ± 0.65  | 0.001                   | 2.49 ± 0.50   | 2.77 ± 0.38  | 0.134                   |
| IgM (g/L)            | 1.34 ± 0.61   | 2.24 ± 0.76  | 0.000                   | 2.45 ± 0.65   | 1.98 ± 0.53  | 0.016                   |
| IgG (g/L)            | 12.84 ± 19.79 | 12.58 ± 2.44 | 0.000                   | 11.62 ± 2.29  | 12.41 ± 3.24 | 0.108                   |
| C <sub>3</sub> (g/L) | 0.92 ± 0.32   | 1.06 ± 0.25  | 0.005                   | 1.21 ± 0.10   | 1.19 ± 0.09  | 0.555                   |
| C <sub>4</sub> (g/L) | 0.27 ± 0.12   | 0.30 ± 0.10  | 0.1                     | 0.31 ± 0.06   | 0.34 ± 0.06  | 0.246                   |

**Table4.** Levels of total Ig and C<sub>3</sub> and C<sub>4</sub> with regard to working period

|                      | >10 year working period | <10 year working period | P(Student t test) |
|----------------------|-------------------------|-------------------------|-------------------|
| IgA (g/L)            | 1.88 ± 0.70             | 2.86 ± 0.67             | 0.000             |
| IgM (g/L)            | 1.38 ± 0.57             | 2.58 ± 0.69             | 0.000             |
| IgG (g/L)            | 12.47 ± 17.86           | 13.45 ± 2.34            | 0.853             |
| C <sub>3</sub> (g/L) | 0.90 ± 0.32             | 1.18 ± 0.11             | 0.007             |
| C <sub>4</sub> (g/L) | 0.27 ± 0.11             | 0.34 ± 0.11             | 0.075             |

The immune systems of the atomic-bomb (A-bomb) survivors were damaged proportionately to irradiation levels at the time of the bombing over 60 years ago. Although the survivor's immune system repaired and regenerated as the hematopoietic system has recovered, significant residual injury persists, as manifested by abnormalities in lymphoid cell composition and function (8). There are limited studies in the literature investigating effects of ionizing radiation exposure on humoral immunity. Lakovlev et al found that natural and specific immunoglobulin production were decreased (9). The results of present study illustrated that mean serum c<sub>3</sub>, c<sub>4</sub>, IgA and IgM levels of radiology workers were significantly lower than those of control group subjects. Similar study in Turkey showed that levels of serum total IgG, IgA, IgM, c<sub>3</sub> and c<sub>4</sub> were determined as significantly lower in workers exposed to ionizing radiation compared with controls. Thus it can be postulated that risk of infections by extracellular agents increase in subjects exposed to long-term low dose of ionizing radiation (10).

Another study by Serhatlioglu et al showed that total immunoglobulins (IgA, IgG, IgM), c<sub>3</sub>, c<sub>4</sub> levels were lower in radiology workers exposed to long-term ionizing radiation (11). In study group our results is in consistent with above reports except IgG level that were significantly higher in radiology workers when compared with control group. In this study, the number of female subjects was lower than for males; perhaps, by making subject ratio equal, differences of IgG would be lower or higher. Levels of immunoglobulins may vary by gender and race (12-15). Generally, human subjects throughout the world show differences, though small, in serum immunoglobulin levels, this is due, presumably, to environmental, nutritional, health, and ethnic variations (16, 17).

Data analysis showed a significant difference between the male and female subjects. In study group results for c<sub>4</sub> level was similar in both sexes, but for IgG levels, it has been observed that, in males, the IgG level significantly is higher than in females.

Kardar et al in their study measured local reference ranges of immunoglobulins in Iranian healthy adult blood donor volunteers. They showed the means of IgM in females were higher than for males (18). Other investigations showed that results for IgA and IgG levels are similar in both sexes, but IgM levels in females is higher than male subjects (19, 20) and some studies found a relationship between number of X chromosomes and IgM concentration(21). Also it was reported that immune response is regulated by sex hormones (22, 23). However, this hypothesis was not proved by other studies (24, 25)

In control group a variation on IgM level was significantly observed, being lower in female than in males. This data is not connected with above works.

When we considered working period of radiology workers, our results is consistent with observations from Ahmet et al in the IgG and c4 levels (10).

There is no established threshold for initiation of biologic changes as a consequence of exposure to low level of irradiation. Since the radiology workers are vulnerable to side effects of radiation being exposed in addition to avoiding radiation as much as possible, we think that periodic checks of immune response levels in them could be of importance for early detection of immune deficiencies. Additionally, we recommended that X-ray workers should regularly use appropriate personal protective equipments at their work site. These measures may assist in the process of reducing the radiation dose received by individuals to prevent the hazards of X-ray radiations.

## REFERENCES

1. Brant WE, Helms CA (1999) *Fundamental of diagnostic radiology*. 1nd ed. New York: Lippincott, Williams & Wilkins.
2. Fang SP, Tago F, Tanaka T, Simura N, Muto Y, Goto R, Kojima S(2005) Repeated irradiations with gamma-rays at a Dose of 0.5 Gy may exacerbate asthma. *J Radiat Res (Tokyo)*. 46(2):151-6.
3. Rozgaj R, Kasuba V, Sentija K, Prlić I(1999) Radiation-induced chromosomal aberrations and haematological alterations in hospital workers. *Occup Med (Lond)*. 49(6):353-60.
4. Hande MP4, Azizova TV, Burak LE, Khokhryakov VF, Geard CR, Brenner DJ(2005) Complex chromosome aberrations persist in individuals many years after occupational exposure to densely ionizing radiation: an mFISH study. *Genes Chromosomes Cancer*. 44(1):1-9.
5. Garaj-Vrhovac V, Kopjar N (2003) The alkaline Comet assay as biomarker in assessment of DNA damage in medical personnel occupationally exposed to ionizing radiation. *Mutagenesis*. 18(3):265-71.
6. Ramalho AT, Costa ML, Oliveira MS (1998) Conventional radiation-biological dosimetry using frequencies of unstable chromosome aberrations. *Mutat Res*. 3;404(1-2):97-100.
7. Au WW, McConnell MA, Wilkinson GS, Ramanujam VM, Alcock N (1998) Population monitoring: experience with residents exposed to uranium mining/milling waste. *Mutat Res*. 20; 405(2):237-45.
8. Kusunoki Y, Hayashi T (2008) Long-lasting alterations of the immune system by ionizing radiation exposure: implications for disease development among atomic bomb survivors. *Int J Radiat Biol*. 84(1):1-14. Review.
9. Iakovlev NI9, Fedorova MV, Zhilenko MI, Aleksandrova AV, Rebrova TV (1991) The immune status of nonpregnant and pregnant women living constantly under ionizing radiation exposure conditions. *Akush Ginekol (Mosk)*. (11):42-5.
10. Godekmerdan A, Ozden M, Ayar A, Gursu MF, Ozan AT, Serhatlioglu S (2004) Diminished cellular and humoral immunity in workers occupationally exposed to low levels of ionizing radiation. *Arch Med Res*. 35(4):324-8.
11. Serhatlioglu S, Oğur E, Ozan AT, Gursu F, Gödekmerdan A, Ayar A (2004) [Biochemical and immunological effects of ionizing radiation in radiology staff members]. *Tani Girişim Radyol*. 10(2):97-102. Turkish.
12. Van Rijswijk AW, Van Niekerk CH, Taljaard JJ (1985) Plasma immunoglobulin levels in newborn infants of different race groups in the Western Cape. *S Afr Med J*. 21; 68(13):925-6.
13. Siegel M, Lee SL, Ginsberg V, Schultz F, Wong W (1965) Racial differences in serum gamma globulin levels: comparative data for Negroes, Puerto Ricans, and other Caucasians. *J Lab Clin Med*. 66(5):715-20.
14. Grundbacher FJ, Massie FS (1985) Levels of immunoglobulin G, M, A, and E at various ages in allergic and nonallergic black and white individuals. *J Allergy Clin Immunol*. 75(6):651-8.
15. Hesselting PB, Cooper RC, Girdle-Brown B (1986) Serum immunoglobulin and complement values in onyalai. Comparison with black, San and white inhabitants of Kavango, SWA/Namibia. *S Afr Med J*. 16; 70(4):203-5.
16. Allansmith M, McClellan B, Butterworth M (1969) The influence of heredity and

- environment on human immunoglobulin levels. *J Immunol.* 102(6):1504-10.
17. Kohler PF, Rivera VJ, Eckert ED, Bouchard TJ Jr, Heston LL (1985) Genetic regulation of immunoglobulin and specific antibody levels in twins reared apart. *J Clin Invest.* 75(3):883-8.
  18. Kardar GA, Shams SH, Pourpak Z, Moin M (2003) Normal value of immunoglobulins IgA, IgG, and IgM in Iranian healthy adults, measured by nephelometry. *J Immunoassay Immunochem.* 24(4):359-67.
  19. Hatagima A19, Cabello PH, Krieger H (1999) Causal analysis of the variability of IgA, IgG, and IgM immunoglobulin levels. *Hum Biol.* 71(2):219-29.
  20. Kacprzak-Bergman I20. (1994) Sexual dimorphism of heritability of immunoglobulin levels. *Ann Hum Biol.* 21(6):563-9.
  21. Grundbacher F(1972) Human X chromosome carries quantitative genes for immunoglobulin M. *Science.* 176(32):311-2.
  22. Sthoeger ZM, Chiorazzi N, Lahita RG (1988) Regulation of the immune response by sex hormones. I. In vitro effects of estradiol and testosterone on pokeweed mitogen-induced human B cell differentiation. *J Immunol.* 1; 141(1):91-8.
  23. Kenny JF23, Pangburn PC, Trail G (1976) Effect of estradiol on immune competence: in vivo and in vitro studies. *Infect Immun.* 13(2):448-56.
  24. Escobar V, Bixler D (1979) Analysis of intrafamilial correlations, serum levels of IGM and the human X-chromosome. *Hum Hered.* 29(5):306-9.
  25. McGue M, Borecki IB, Gerrard JW, Rao DC (1990) Sex-linked determinants for IgM? *Hum Hered.* 40(4):231-4.

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