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# An Epidemiological Study on the Prevalence and Antibiotic Resistance Patterns of Bacteria Isolated from Urinary Tract Infections in Central Iran

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## Abstract

**Background:** Urinary tract infection (UTI) is one of the most common bacterial diseases in outpatients and inpatients worldwide. Treatment of UTI has become challenging due to the emergence of pathogens with increasing resistance to antimicrobial agents.
**Objectives:** The aim of this study was to determine the prevalence and antimicrobial resistance patterns of main bacteria responsible for UTI.
**Methods:** In this study, 326 patients with UTI, referring to Shahid Motahari hospital of Fuladshahr, Iran, were evaluated between March 2015 and February 2016. The isolated bacteria were identified by biochemical tests. Disk diffusion method was applied to determine the antibiotic sensitivity of bacterial agents.
**Results:** In a total of 326 positive urine cultures, 273 (83.74%) and 53 (16.25%) samples belonged to females and males, respectively. The most prevalent isolates were *Escherichia coli* (58.28%), *Klebsiella* spp. (11.65%), *Staphylococcus* spp. (11.65%), *Enterobacter* spp. (7.05%), *Streptococcus* spp. (3.68%), *Enterococcus* spp. (2.45%), *Proteus* spp. (1.22%), *Pseudomonas* spp. (0.61%), and *Citrobacter* spp. (0.61%), respectively. The antimicrobial susceptibility analysis of *E. coli*, as the predominant cause of UTI, revealed the following results: gentamicin (28.6%), ciprofloxacin (48.4%), nitrofurantoin (12.2%), nalidixic acid (63.7%), trimethoprim/sulfamethoxazole (67.9%), cephalothin (60%), cefotaxime (44.8%), imipenem (9.5%), amikacin (66.7%), and ampicillin (85.3%).
**Conclusions:** According to the present survey, *E. coli* isolates were the predominant pathogens in UTIs and were more prevalent in women than men. In the present study, the frequency of UTI pathogens was comparable to that reported in previous studies, showing an increasing resistance pattern to commonly prescribed antibiotics.

*Keywords:* Urinary Tract Infection, Antimicrobial resistance, *E. coli*

## 1. Background

Urinary tract infection (UTI) is considered a serious public health problem. It is the second most common bacterial infection, following respiratory tract infections in the community and hospital settings (1). UTI can be asymptomatic or symptomatic, with a wide range of symptoms ranging from mild irritative voiding to bacteremia. This type of infection can lead to an elevated risk of morbidity and mortality and increased healthcare costs (2-4).

The annual incidence of UTI is nearly 150 - 250 million people worldwide (5-7). According to previous reports, UTI is predominant among women. In fact, it is estimated that half of women will have a UTI during their lifetime (1, 8, 9). Although different microorganisms can cause UTI, *Escherichia coli* accounts for the overwhelming majority of UTI cases (approximately 75% of UTI reports) (10, 11).

Treatment of patients with symptomatic UTI is commonly achieved through administration of antibiotics, which can in turn cause alterations in the gut commensal microbiota and eventually lead to the development of multidrug-resistant microorganisms (5, 10, 11). The preva-

lence of antimicrobial resistance among uropathogens, both in the community and hospital settings, has been increasing worldwide due to different factors, including improper antibiotic use while feeding animals, indiscriminate prescription of antibiotics, and poor infection control strategies (4, 7, 12).

Considering the high recurrence rates and emergence of antibiotic resistance in uropathogens, knowledge about the area-specific prevalence of these pathogens and their antimicrobial resistance patterns is necessary (13). Also, in order to select more appropriate antibiotics and prevent therapeutic failures, it is important to determine uropathogens and their antibacterial susceptibility patterns (11). With this background in mind, in the present study, we aimed to determine the prevalence and antimicrobial susceptibility patterns of uropathogens among patients, referring to Shahid Motahari hospital of Fuladshahr, Iran.

## 2. Methods

### 2.1. Organism Collection and Identification

The present cross sectional study was conducted in Shahid Motahari hospital of Fuladshahr, Iran during March 2015 and February 2016. The study population consisted of all inpatients and outpatients with positive urine cultures. A total of 326 samples with significant bacterial counts ($10^5$ CFU/mL) were recruited during this period.

The isolates were identified and characterized, based on the standard microbiological tests. For urine culture, midstream urine samples were collected. The samples were inoculated within 1 hour of sampling on blood agar and MacConkey agar. Depending on the microorganism type, the plates were incubated in both aerobic and anaerobic conditions at 37°C for 24 - 48 hours. Standard microbiological tests were conducted, depending on the type of isolated bacteria (Gram-positive or Gram-negative) from various isolates. In order to identify Gram-negative bacteria, triple sugar iron (TSI) test, as well as indole, citrate, urea, lysine decarboxylase, oxidase, and motility tests, was performed. On the other hand, for Gram-positive bacteria, catalase, coagulase, novobiocin, optochin disk, CAMP, and esculin agar tests were carried out.

### 2.2. Antimicrobial Susceptibility Patterns

Antibiotic susceptibility patterns of the isolates were tested on Mueller-Hinton agar through disk diffusion method, according to the guidelines by the clinical and laboratory standards institute (CLSI) (14). The following antibiotics were evaluated in the study: ampicillin (10 $\mu$g), cephalothin (30 $\mu$g), ciprofloxacin (5 $\mu$g), tetracycline (30 $\mu$g), nalidixic acid (30 $\mu$g), nitrofurantoin (300 $\mu$g), gentamicin (10 $\mu$g), trimethoprim/sulfamethoxazole (25 $\mu$g), cefotaxime (5 $\mu$g), imipenem (10 $\mu$g), amikacin (30 $\mu$g), oxacillin (1 $\mu$g), ofloxacin (5 $\mu$g), clindamycin (2 $\mu$g), erythromycin (15 $\mu$g), and vancomycin (30 $\mu$g) (HiMedia, India). In order to classify the samples as resistant or susceptible, the inhibition zone diameter (mm) of each antimicrobial disc was measured. Also, *E. coli* (ATCC25922) was used as the control strain.

### 2.3. Statistical Analysis

Data were analyzed using WHONET version 5.6, downloaded from the World health organization (WHO) website.

## 3. Results

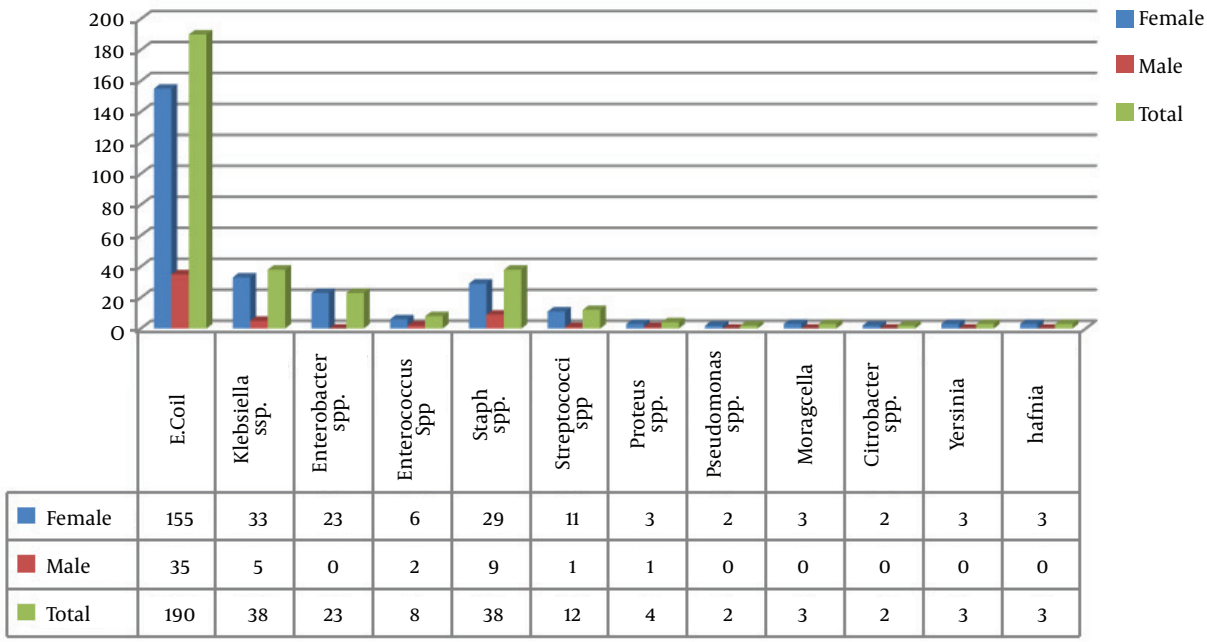
A total of 326 patients were evaluated in the present study, including 273 (83.74%) females and 53 (16.25%) males. The frequency of isolated bacteria according to sex is presented in Figure 1. In both male and female subjects, *E. coli* (n = 190, 58.28%) was the most commonly isolated microorganism, followed by *Klebsiella* spp. (n = 38, 11.65%), *Staphylococcus* spp. (n = 38, 11.65%), *Enterobacter* spp. (n = 23, 7.05%), *Streptococcus* spp. (n = 12, 3.68%), *Enterococcus* spp. (n = 8, 2.45%), *Proteus* spp. (n = 4, 1.22%), *Pseudomonas* spp. (n = 2, 0.61%), and *Citrobacter* spp. (n = 2, 0.61%), respectively.

Based on the findings, *E. coli* showed greater sensitivity to imipenem (85.7%), nitrofurantoin (74.5%), and gentamicin (66.7%) and higher resistance to ampicillin (85.3%), trimethoprim/sulfamethoxazole (67.9%), and nalidixic acid (63.7%) (Figure 2). In total, 268 (82.2%) and 58 (17.79%) Gram-negative bacilli and Gram-positive cocci were isolated from the positive cultures, respectively.

The susceptibility of the isolated bacteria to antimicrobials showed significant differences. Based on the antibiotic susceptibility test results (Table 1), all the bacteria isolated from UTIs showed the highest level of resistance to ampicillin and cefotaxime. The Gram-negative bacilli, isolated from UTIs, were sensitive to gentamicin (69.6%) and nitrofurantoin (67.3%), while Gram-positive cocci were sensitive to nitrofurantoin (86.5%) and ciprofloxacin (62.5%). In the present study, most of the isolated bacteria were resistant to ampicillin (79.5%) (Table 1).

## 4. Discussion

UTIs are common bacterial infections, which result in considerable economic and public health burdens. Approximately 3.5 billion dollars are annually spent on these infections in the United States alone. Despite the progress




| | E.Coil | Klebsiella ssp. | Enterobacter spp. | Enterococcus Spp | Staph spp. | Streptococci spp | Proteus spp. | Pseudomonas spp. | Moragcella | Citrobacter spp. | Yersinia | hafnia |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Female | 155 | 33 | 23 | 6 | 29 | 11 | 3 | 2 | 3 | 2 | 3 | 3 |
| Male | 35 | 5 | 0 | 2 | 9 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| Total | 190 | 38 | 23 | 8 | 38 | 12 | 4 | 2 | 3 | 2 | 3 | 3 |

**Figure 1.** Frequency and Type of Pathogens Isolated from UTI Samples in Males and Females

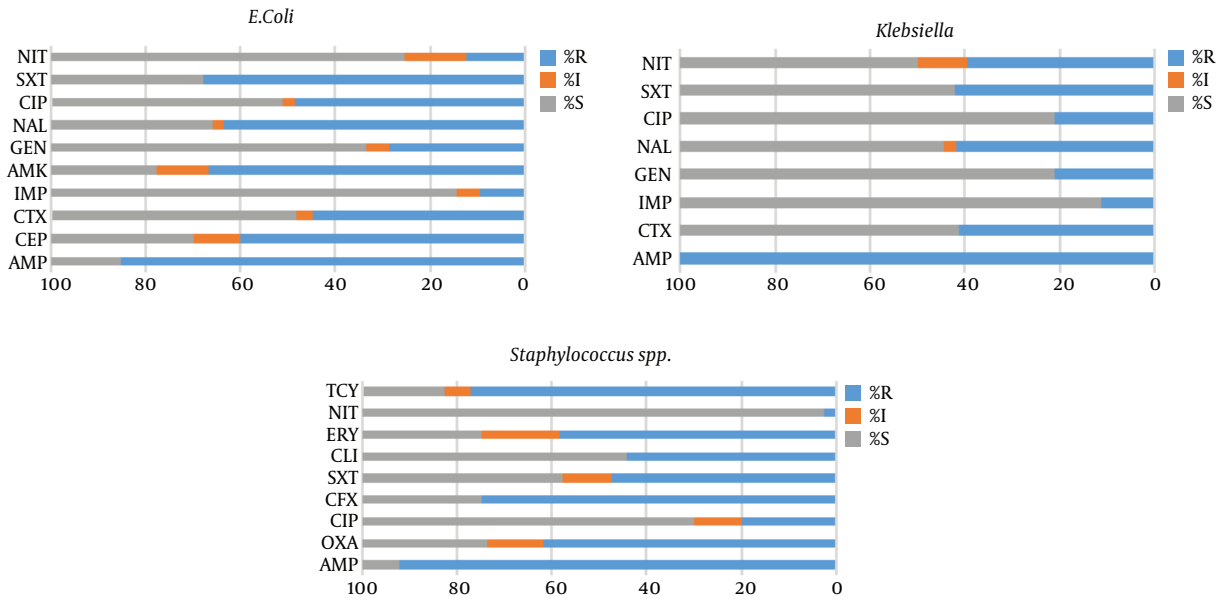



**Figure 2.** Susceptibility of Microorganisms to Each Antimicrobial Agent

in antimicrobial therapies, UTI remains the leading cause of mortality (1, 11, 15). The shorter period of antibiotic therapy, as well as drug administration regardless of the antimicrobial susceptibility patterns, results in the emergence of resistant strains.

Antibiotic resistance patterns vary in different regions. In order to apply a suitable treatment strategy in each region, awareness of dominant pathogens and their sensi-

**Table 1.** Antimicrobial Resistance Profile of Bacterial Agents Isolated from UTIs

| Organism | Resistance Rate, % | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TMP-SXT | GEN | NIT | CIP | AMP | CEP | NA | TCY | CLI | VAN | OXA | OFL | IMP |
| *E. coli* (n = 190) | 128 (67.3) | 50 (26.3) | 25 (13.0) | 95 (50) | 157 (82.3) | 78 (41.0) | 121 (63.6) | NA | NA | NA | NA | NA | 18 (9.5) |
| *Klebsiella* spp. (n = 38) | 16 (42.1) | 8 (21.0) | 18 (47.3) | 9 (23.6) | 38 (100) | 17 (44.7) | 15 (39.4) | NA | NA | NA | NA | NA | 4 (11) |
| *Staphylococcus* spp. (n = 38) | 18 (47.3) | NA | 2 (5.2) | NA | 25 (65.7) | 16 (42.1) | NA | 24 (63.1) | 18 (47.3) | 4 (10.5) | 25 (65.7) | 28 (73.6) | NA |
| *Enterobacter* spp. (n = 23) | 13 (56.5) | 8 (34.7) | 8 (34.7) | 8 (34.7) | 17 (73.9) | 7 (30.4) | 7 (30.4) | NA | NA | NA | NA | NA | NA |
| *Streptococcus* spp. (n = 12) | 3 (25) | NA | 5 (41.6) | 4 (33.3) | 6 (41.6) | NA | NA | 6 (50) | 9 (75) | 0 (0) | NA | NA | NA |
| *Enterococcus* spp. (n = 8) | 5 (62.5) | NA | NA | NA | 4 (50 | NA | NA | 8 (100) | 8 (100) | 2 (25) | NA | 8 (100) | NA |
| *Proteus* spp. (n = 4) | 1 (25 | 1 (25) | 2 (50) | 0 (0) | 4 (100) | 1 (25) | 1 (25) | NA | NA | NA | NA | NA | 1 (25) |
| *Yersinia* spp. (n = 3) | 0 (0) | 0 (0) | 0 (0) | 1 (33.3) | NA | 2 (66.6) | 2 (66.6) | NA | NA | NA | NA | NA | NA |
| *Hafnia* spp. (n = 3) | 0 (0) | 0 (0) | 1 (33.3) | 0 (0) | 2 (66.6) | 1 (33.3) | NA | NA | NA | NA | NA | NA | NA |
| *Moraxella* spp. (n = 3) | 0 (0) | 0 (0) | 0 (0) | 1 (33.3) | 2 (66.6) | 0 (0) | 1 (33.3) | NA | NA | NA | NA | NA | NA |
| *Pseudomonas aeruginosa* (n = 2) | 1 (50) | 0 (0) | 0 (0) | NA | 2 (100) | NA | 2 (100) | 0 (0) | 1 (50) | NA | NA | NA | NA |
| *Citrobacter* spp. (n = 2) | 2 (100) | 0 (0) | 2 (100) | 1 (50) | 2 (100) | 1 (50) | 1 (50) | NA | NA | NA | NA | NA | NA |

Abbreviations: AMP, ampicillin; CEP, cephalothin; CIP, ciprofloxacin; GEN, gentamicin; CLI, clindamycin; IMP, imipenem; NA, nalidixic acid; NA, not applicable; NIT, nitrofurantoin; OFL, ofloxacin; OXA, oxacillin; TCY, tetracycline; TMP-SXT, trimethoprim/sulfamethoxazole; VAN, vancomycin.

tivity to common antibiotics is essential (13). The present study was performed with the aim of surveying the prevalence of antibiotic resistance patterns of bacterial agents, isolated from patients with UTI-positive cultures at a hospital in Fuladshahr, Iran.

In the present study, in a total of 326 patients, 273 (83.74%) and 53 (16.25%) cases were female and male, respectively. In accordance with previous studies, prevalence of UTI was higher among females than males (3, 6, 7). This difference in the prevalence could be due to several factors, including anatomic differences and shorter path to the urethra and vagina, which causes pathogenic bacteria to have an easier passage to the bladder (5, 6, 16).

In the present study, the most common uropathogen was *E. coli* (n = 190, 58.28%), followed by *Klebsiella* spp. (n = 38, 11.65%) and *Staphylococcus* spp. (n = 38, 11.65%). Similar observations have been reported in a previous study (11). Furthermore, in a study by Tajbakhsh et al. *E. coli* was identified as the predominant cause of UTIs (51.70%), followed by *Klebsiella pneumoniae* (16.32%) (7). Also, Farajnia et al. demonstrated that *E. coli* was the most commonly isolated pathogen in both genders (17).

*Klebsiella* spp., as the second most common uropathogen in the present study, showed a high degree of sensitivity to imipenem, gentamicin, and ciprofloxacin. In a study by Shanthi and Kayathri, *Citrobacter* spp. were the second most frequently isolated bacterial agents (14%) (18). In general, host-related factors and various environmental conditions and practices, such as health and educational programs and socioeconomic standards of sanitation in each country, can lead to similarities and differences in the type and distribution of uropathogens (1).

Knowledge of antibiotic resistance patterns in *E. coli*, as the predominant causative agent of UTI, is of great importance in selecting an empirical antimicrobial therapy (19, 20). According to Figure 2 the highest antibiotic resistance of *E. coli* isolates was reported in drugs, such as ampicillin (82.63%) and trimethoprim/sulfamethoxazole (67.9%), which have been used for a long time. The present results are similar to previous studies conducted in Iran (13, 21). The most effective antibiotics against *E. coli* were imipenem, nitrofurantoin, and gentamicin. Sensitivity to these antibiotics was reported to be 85.7%, 73.1%, and 68.4%, respectively (Figure 2).

Imipenem is a carbapenem antibiotic, which is highly stable against lactamase hydrolysis. This agent is considered the drug of choice against *E. coli*, *P. aeruginosa*, *Acinetobacter* spp., *Klebsiella* spp., and *Enterobacter* spp. Although carbapenem resistance is currently rare among these microorganisms, its widespread use has led to increased resistance in recent years (22, 23). Although *E. coli* exhibits high sensitivity to nitrofurantoin, this antibiotic is not suggested for cases with serious upper urinary tract infections or systemic involvement (10).

In the present study, sensitivity of *E. coli* to gentamicin and nitrofurantoin was less than that reported in other surveys performed in Iran and other parts of the world (10). In this regard, in a previous study by Ghorbani et al. *E. coli* was more susceptible to ciprofloxacin, amikacin, and nitrofurantoin (11). Comparison of the present findings with previous research showed that the prevalence of gentamicin and cephalothin resistance in *E. coli* isolates was much lower in our study, compared to the research by Khoshbakht et al. in Shiraz, Iran (5).

Furthermore, according to our previous study, conducted during April 2013 and October 2014 in Hamadan,

Iran, *E. coli* was the most frequent isolate (n = 425, 54.9%), followed by *Klebsiella* spp. (n = 79, 10.2%). In this study, the most susceptible antibiotics for the most prevalent pathogens included nitrofurantoin (n = 24, 5.6%) and amikacin (n = 42, 9.9%). Also, *E. coli* showed the highest antibiotic resistance against trimethoprim/sulfamethoxazole (n = 278, 65.4%) and nalidixic acid (n = 235, 55.2%) (24).

### 4.1. Conclusions

Based on the findings, Gram-negative bacteria were more often involved in UTIs than Gram-positive bacteria in the hospital setting. *E. coli* was the predominant cause of UTI, while imipenem, nitrofurantoin, and gentamicin were the most effective antibiotics. Considering the antimicrobial susceptibility patterns, in order to reduce the incidence of UTIs, appropriate use of antibiotics is proposed. Considering the constant variations in the isolates, UTI causative pathogens, and antibiotic susceptibility patterns, identification of antimicrobial resistance profiles is suggested in different populations every year.

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## Footnote

**Conflicts of Interest:** The authors declare no conflicts of interest regarding the publication of this paper.

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