

# Frequency and antimicrobial resistance pattern of pathogens implicated in urinary tract infection at a hospital in Tehran

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## ABSTRACT

**Purpose:** Urinary tract infection is a common infectious presentation in the community practice. It is also the most common cause of antimicrobial resistance in the society. The aim of this study was to investigate the frequency and antimicrobial resistance pattern of the uropathogens isolated from patients with urinary tract infection.

**Materials and Methods:** This study was conducted on the patients with urinary tract infection at a hospital in Tehran from March 2010 to March 2013. Mid-stream urine samples were collected in sterile disposable containers. Then, specimens were transferred to 5% blood agar and Eosine-Methylene Blue (EMB). Identification of uropathogens was done on the basis of gram reaction, morphology and biochemical features. Antimicrobial susceptibility test was performed according to Clinical and Laboratory Standards Institute (CLSI) guidelines.

**Results:** A total of 8200 urine samples (545 inpatients and 850 outpatients) were collected and 1395 uropathogens were recovered from them. Most of the pathogens were more prevalent in women. Gram-negative bacteria (81.8%) were the main cause of urinary tract infection. *Escherichia coli* (60.5%) was the predominant pathogen associated with urinary tract infection, while *Pseudomonas aeruginosa* (0.3%) had the least occurrence. *Escherichia coli* isolates showed high resistance to Ceftriaxone, Amoxicillin and Ciprofloxacin and high sensitivity to Nitrofurantoin, Amikacin and Gentamicin.

**Conclusion:** Antimicrobial resistance is becoming a big challenge for the public health with significant morbidity and health costs. Therefore it seems that a periodic monitoring of etiologic agents of urinary tract infection and their susceptibility pattern in the community is necessary.

**Keywords:** urinary tract infection; antimicrobial; resistance; frequency; Imam Reza hospital.

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## INTRODUCTION

Urinary tract infection is a common infectious presentation in community practice, having large global socioeconomic impacts. About 150 million people are diagnosed with urinary tract infection per annum worldwide.<sup>1</sup> Urinary tract infection can be asymptomatic

or symptomatic. Its clinical presentations include mild irritation, bacteremia, sepsis or even death.<sup>2</sup> Site of infection may include the urethra, bladder, ureter, renal pelvis or renal parenchyma.<sup>3</sup> Urinary tract infection is classified into complicated and uncomplicated based on its selective treatment.<sup>4</sup>

Etiology of urinary tract infection is influenced by factors like age, diabetes, AIDS, multiple sclerosis, urinary catheterization, etc. Urinary tract infection is more common in women since their urethra is less effective anatomically for prevention of bacterial entry. This may be due to the proximity of the genital and urinary tracts. Pregnancy and sexual activity are other predisposing factors.<sup>6,7</sup>

Bacteria are the major causative organisms and responsible for more than 95% of urinary tract infection cases.<sup>8</sup> Most commonly encountered microorganisms are gram-negative bacteria including *escherichia coli*, *citrobacterspp.*, *enterobacteraerogenes*, *pseudomonas aeruginosa* and *proteus vulgaris* whereas *klebsiellaspp.*, *staphylococcus aureus* and *salmonellaspp.* are rarely found.<sup>9</sup> According to the reports, *escherichia coli* is the most common etiological agent among both outpatients and inpatients, accounting for 75% to 90% of uncomplicated urinary tract infection isolates, while complicated ones show a broader bacterial spectrum as the cause of infection.<sup>10</sup> Increasing multiple antibiotic resistance in bacterial uropathogens is an important and emerging public health challenge. The Infectious Disease Society of America (IDSA) has recommended some microorganisms for new effective therapies. Those microorganisms were called “ESKAPE pathogens” which include *enterococcus faecium*, *staphylococcus aureus*, *klebsiellaspp.*, *acinetobacterspp.*, *pseudomonasspp.* and *enterobacterspp.*<sup>11</sup>

The prevalence of etiologic agents and the pattern of their resistance to antibiotics are changing from place to place and time to time due to the frequent misuse of antibiotics. In most cases, empirical antimicrobial treatment initiates before the results of the laboratory susceptibility tests are seen.<sup>12-14</sup>

For this reason, using susceptibility data provided by regional microbiological laboratories may aid clinicians to select proper and cost-effective antimicrobial treatment; however, these conditions are limited to complicated urinary tract infection as the samples of uncomplicated urinary tract infection are rarely sent to the laboratories. Therefore, it seems that a periodic monitoring of etiologic agents of urinary tract infection and their susceptibility pattern in the community is necessary.<sup>15,16</sup>

This study was conducted to determine the frequency and antimicrobial resistance of uropathogens causing urinary tract infection among the patients admitted to a hospital in Tehran during a three-year period.

## MATERIALS AND METHODS

This study was conducted on patients with or without

the symptoms of urinary tract infection in Imam Reza Hospital in Tehran during a three-year period from March 2010 to March 2013.

A number of 8200 mid-stream urine samples were collected in sterile disposable tubes. To culture the samples using a calibrated loop method, the specimens were transferred to 5% blood agar and Eosine-Methylene Blue (EMB) culture media (Merck, Germany). Culture plates were incubated at 37°C for 18 to 24 hours. Then, sediments of remaining samples were used for microscopic white blood cell count after centrifugation at 1500 rpm for 10 minutes. Samples with colony count  $\geq 10^5$  CFU/mL plus more than 10 leukocytes per high power field microscopy were considered as positive.

Identification of bacterial pathogens was done on the basis of gram reaction, morphology and biochemical features. All culture media were purchased from Merck, Germany.<sup>17,10</sup> Examination of antimicrobial susceptibility was carried out on Mueller-Hinton agar (Merck, Germany) by Kirby Bauer's disk diffusion technique according to Clinical and Laboratory Standards Institute (CLSI) guidelines.<sup>18,19</sup> Mueller-Hinton agar plates were incubated for 24 hours at 37°C.

The tested antibiotics were Ceftriaxone (30µg), Ciprofloxacin (5µg), Co-trimoxazole (25µg), Nitrofurantoin (30µg), Gentamicin (10µg), Amikacin (10µg), Ceftazidim (30µg), Amoxicillin (10µg), Nalidixic Acid (30µg), and Imipenem (10µg). Antibiotic disks were purchased from Padtanteb Company, Iran. In this test, *escherichia coli* (ATCC® 25922) was used as quality control strain. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 16 software.

## RESULTS

During a three-year period, 8200 urine samples were collected and 1395 uropathogens recovered from urine samples of 545 (39%) inpatients and 850 (61%) outpatients. Most samples (67%) were from women (**Table 1**).

In this study gram-negative bacteria (81.8%) were the main cause of urinary tract infection. *Escherichia coli* (60.5%) was the predominant pathogen associated with urinary tract infection, while *pseudomonas aeruginosa*

**Table 1.** Distribution of patients with respect to gender.

	Outpatients (%)	Inpatients (%)
Women	573 (67.4)	362 (66.4)
Men	277 (32.6)	183 (33.6)
Total	850 (61)	545 (39)

had the least occurrence (0.3%) (Table 2). Most pathogens were more prevalent in women.

Predominant pathogens in women were *klebsiella* spp. (76.7%), *enterobacterspp.* (80.4%) and *escherichia coli* (70.8%), respectively (Figure 1). All bacteria isolated

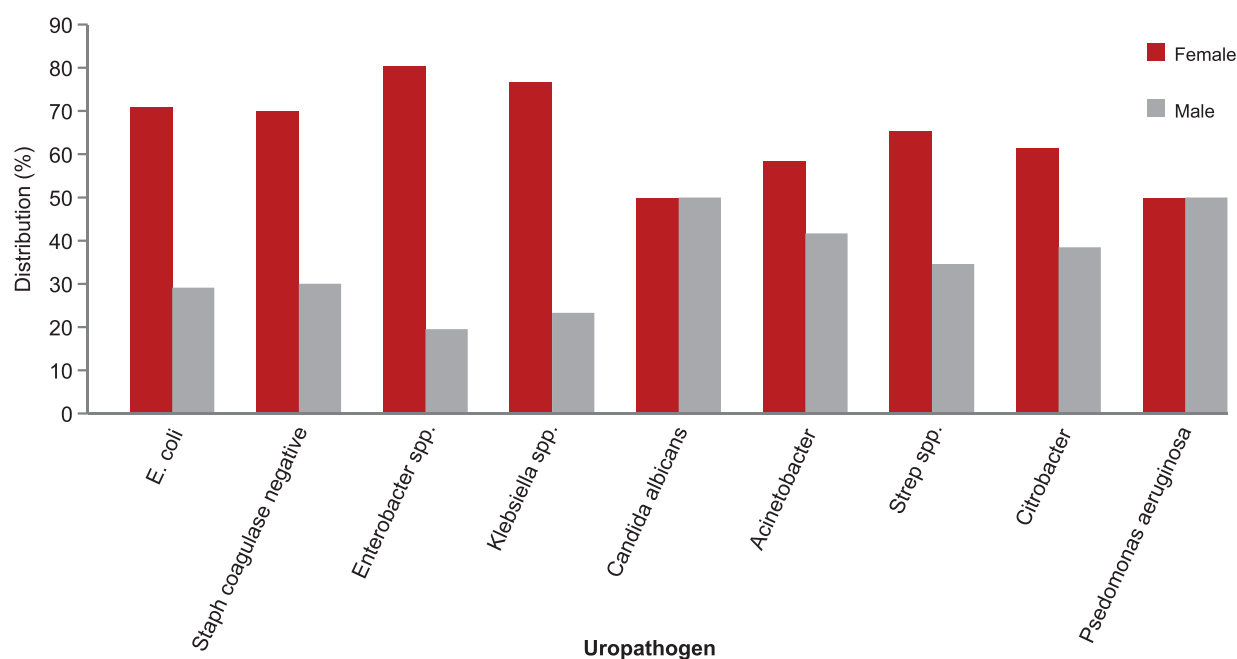
from women were also isolated from men. The gender distribution about *candida albicans* and *pseudomonas aeruginosa* was equal although the number of these isolates was low.

*Escherichia coli* isolates, the predominant cause of urinary tract infection, showed high resistance to Ceftriaxone, Amoxicillin and Ciprofloxacin and high sensitivity to Nitrofurantoin, Amikacin and Gentamicin (Table 3). *Staphylococcus coagulase negative* was found to be susceptible against Nitrofurantoin, Ceftazidime, Ciprofloxacin and Meropenem.

*Klebsiella* isolates showed high susceptibility against Imipenem (95%) followed by Nitrofurantoin and Gentamicin. They were resistant to Amoxicillin, Ciprofloxacin and Amikacin. *Acinetobacter* isolates were highly resistant to all of the commonly used antibiotics in this study. *Pseudomonas aeruginosa*, which

**Table 2.** Frequency of uropathogen isolated from urine specimens.

Isolated bacteria	No (%)
<i>Escherichiacoli</i>	844 (60.5)
<i>Staphylococcuscoagulase negative</i>	223 (16)
<i>Enterobacter spp.</i>	164 (11.8)
<i>Klebsiella spp.</i>	73 (5.2)
<i>Strep spp.</i>	26 (1.9)
<i>Acinetobacter</i>	24 (1.7)
<i>Candida albicans</i>	24 (1.7)
<i>Citrobacter</i>	13 (0.9)
<i>Pseudomonas aeruginosa</i>	4 (0.3)
Total	1395



**Figure 1.** Distribution of uropathogens based on gender.

**Table 3.** Prevalence and antimicrobial resistance to uropathogens

	Imipenem	Meropenem	Nitrofurantoin	Gentamicin	Amikacin	Ciprofloxacin	Ceftazidime	Ceftriaxone	Amoxicillin	Co-trimoxazole	Nalidixic acid
<i>Escherichiacoli</i>	12.22	29	5.5	9.4	8.8	20	15	20.3	20.1	15.3	17
<i>Staphylococcuscoagulase negative</i>	32	18	7.7	29	25.6	15.6	14.3	31.3	33	24.9	32.6
<i>Enterobacterspp.</i>	31	29	42	37.7	30.5	44	36.6	32	35	39.8	24
<i>Klebsiellaspp.</i>	5	21	9	15	24.6	26.8	22	17	28.8	17	22
<i>Acinetobacter</i>	57	46	87	66	88	46	71.4	88	75	83.3	77
<i>Pseudomonas aeruginosa</i>	23.3	47	97	25	31	33.3	52	66.6	78	66	55

has a high resistance worldwide, had 97% resistance to Nitrofurantoin, 78% to Amoxicillin, 66.6% to Ceftriaxone and 66% to Co-trimoxazole. The best activity against *pseudomonas* (23.3% susceptibility) was attained with Imipenem.

## DISCUSSION

Urinary tract infection is a common medical disease in medical practice with significant morbidity and health costs in all ages.<sup>20</sup> Published studies show a geographical variation in etiology of urinary tract infection. Moreover, the international resistance surveillance studies have demonstrated an increasing resistance pattern against commonly used community antibiotics.<sup>21,22</sup> Therefore regional studies analyzing etiology of urinary tract infection and their antimicrobial susceptibility are currently of great value to guide clinicians in its empirical treatment. IDSA recommends that the first-line empirical therapy should be modified in cases with resistance rate of 10-20%.<sup>23</sup>

In accordance with previous reports, the prevalence of urinary tract infection was 17% by urine culture in the present study.<sup>24,25</sup> The prevalence of urinary tract infection was higher in women (67%) than in men (33%) which is in line with another study (Table 1).<sup>26</sup> The uropathogens profile in our study was similar to other studies and the frequency of gram-negative urinary tract infection was more than gram-positive bacteria.<sup>27</sup>

Totally, the most common bacterium isolated from the urine specimens was *escherichia coli*, followed by *staphylococcus coagulase negative*, *enterobacterspp.*, *klebsiella spp.* and *streptococcus* (Table 2). This is in agreement with the results of previous studies in which *escherichia coli* was the main pathogen isolated from patients with urinary tract infection.<sup>28,29</sup> These bacteria were the principal uropathogens in our study in spite of a variation in distribution of these etiological agents between different studies. For example, *klebsiellaspp.* was the 4<sup>th</sup> common isolated bacterium in our study (5.2%) while it was the first or second urinary tract infection agent among the most published literatures.<sup>31,32</sup> In addition, *staphylococcus coagulase negative* was the most common cause of urinary tract infection in gram-positive bacteria.<sup>33</sup>

In our study, resistance of *escherichia coli* to Co-trimoxazole (15.3%) was nearly the same as studies in USA (18.6 %) and Europe (14.1%).<sup>34,35</sup> Moreover, the resistance rate against this antibiotic in other countries like Senegal (55%), Spain, (33%), Taiwan (56%), and India (75%) is comparable with Iranian isolates (Table 3).<sup>36,37</sup> In

this study the overall Co-trimoxazole resistance was high (41.05%). Still IDSA guidelines consider Co-trimoxazole for empirical treatment of urinary tract infection.<sup>23</sup>

In the present study, Nitrofurantoin had a low resistance rate to *escherichia coli* and *klebsiella* isolates (5.5% and 9.0%, respectively) which is comparable to another studies' results (0–5.4%).<sup>38</sup> Indian *escherichia coli* and *klebsiella* isolates are highly resistant against Nitrofurantoin (80% and 76% resistant, respectively).<sup>39</sup>

Generally, the isolated bacteria showed the highest and least resistance to Amoxicillin (44.98%) and Imipenem (26.75%), which is in agreement with a previous study in Baghdad. The 10% resistance against Imipenem raises a concern about the effectiveness of carbapenems that were nearly 100% effective against resistant gram-negative bacteria. However, some uropathogens have now developed effective ways to deal with Carbapenems.<sup>40</sup>

Resistance rate of *acinetobacter* isolates to the tested antibiotics was 46% to 88%. Our results were in agreement with a study by Demir and Buyukguclu, in which *acinetobacter* isolates were highly resistant to all of the commonly used antibiotics.<sup>41</sup> However, unlike this study, Khan and colleagues reported the highest susceptibility of Imipenem, Amikacin and Ciprofloxacin against *acinetobacter* (100%).<sup>39</sup>

In a report from 48 European hospitals during years 2002–2004, only 73.1% of *acinetobacter* isolates were susceptible to Meropenem and 69.8% were susceptible to Imipenem. Susceptibility to other antibiotics was also very low, with 32.4%, 34.0% and 47.6% being susceptible to Ceftazidime, Ciprofloxacin and Gentamicin, respectively.<sup>41</sup> According to Howard and colleagues, up-regulation of the *acinetobacter*'s innate resistance mechanisms coupled with the acquisition of foreign determinants have an important role in becoming a multidrug-resistant pathogen.<sup>42</sup>

Fungal etiology, particularly *candida pp.* are encountered in about 10% of urinary tract infections. As in most published studies of candiduria, the prevalence of candida was low in our study.<sup>43</sup> Manikandan and Amsath reported 3.4% prevalence for candiduria in critically ill patients with women being predominant.<sup>44</sup> In this study in accordance with previous reports, *candida albicans* was the most frequently isolated species in candiduria.<sup>43,45</sup>

Our findings demonstrate in accordance with other regional reports that urine culture and sensitivity test are essential for diagnosis of urinary tract infection, since the clinical presentation plays a minor role in confirming diagnosis in urinary tract infection. *Escherichia coli* is still the most prevalent pathogen causing urinary tract



infection in the community.

Thus, antimicrobial susceptibility/resistance pattern should be determined and a special antimicrobial treatment protocol should be planned based on susceptibility data provided by regional microbiological laboratories because of the different spectra of pathogens and the susceptibility patterns.

## CONCLUSION

High resistance rate to all antibiotics tested in this study can be explained as uncontrolled consumption of many antibiotics in our region. This shows that a strong policy is needed to avoid over sale of drugs. Also, periodical studies at local and regional levels should be done in this regard.

It is an important issue to implement a strict antibiotics prescription policy in Iran. Studies such as ours may aid clinicians to select a proper and cost effective antimicrobial treatment. Therefore an alternate supervision of etiologic agents of urinary tract infection and their susceptibility/resistance pattern in the community is necessary.

## CONFLICT OF INTEREST

None declared.

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