Research Article

Community Acquired Urinary Tract Infections' Etiological Organisms and Antibiotics Susceptibility Patterns

Hossein Keyhan,[1,*] Sepideh Sedighi,[2] Behruz Mashayekhi,[2] Mehrnoush Fathi,[3] and Majeed Mokhtari[4]

[1]Assistant Professor of Urology, Islamic Azad University, Tehran Medical Branch, Bouali Hospital
[2]Medical Doctor, Islamic Azad University, Tehran Medical Branch, Bouali Hospital
[3]Infectious Disease Specialist, Islamic Azad University, Tehran Medical Branch, Bouali Hospital
[4]Lab Manager, Bouali Hospital

*Corresponding author: Hossein Keyhan, Assistant Professor of Urology, Islamic Azad University, Tehran Medical Branch, Bouali Hospital. E-mail: h.keyhan@hotmail.com

Abstract

Objectives: This study aimed at estimating the prevalence of bacterial strains isolated from patients with community acquired urinary tract infections (UTIs) and comparing the antibiotic susceptibility patterns among different genders.

Methods: This prospective study was conducted between June 2011 and August 2012 in Iran, Tehran, on patients referred with symptomatic UTI. Midstream samples were taken and sent to the laboratory. The bacterial resistance was determined in patients with proven UTI by the Kirby Bauer's disc diffusion method. Data were stratified by age and gender.

Results: A total of 762 individuals were included in this prospective study, from which 573 (75.1%) were female and 189 (24.9%) were male patients. The most prevalent pathogen in different age, gender, inpatient and outpatient groups was *Escherichia coli*. The *E. coli* isolates were significantly higher in females compared to males (P = 0.03). High prevalence of resistance was observed against nalidixic acid (77.9%) in male patients, while amoxicillin (74%) was the most resistant antibiotic in females. However, the highest sensitivity was observed against imipenem in both male and female groups (97.9% and 97.2%, respectively) with no significant difference among them (P > 0.05).

Conclusions: To date, this is the first study to determine the distribution and antibiotic susceptibility patterns in patients with UTI in Iran. This study showed that *E. coli* was the leading bacterial pathogen of community acquired UTIs in Iran, Tehran. An increasing resistance to first line antibiotics for UTI pathogens was also indicated, which emphases the need to improve empiric treatment.

Keywords: Lower Urinary Tract Symptoms, Drug Resistance

1. Background

Urinary tract infection (UTI), as the second most common infectious disease, affects about 150 million people per year with a high global economy cost (1). It could affect both lower and upper urinary tracts with different symptoms, including fever, dysuria, urgency, frequency, and intermittent suprapubic tenderness (2).

A steady antimicrobial resistance to frequently applied antibiotics, such as ampicillin and trimethoprim, has been reported in the field of UTIs as a result of extensive use of antimicrobial agents (3, 4). Considering the concerns about infection with possible resistant organisms, UTI is usually treated with broad-spectrum antibiotics, such as fluoroquinolone, as the first line antibiotic for empiric therapy (5, 6). High bacteriological and clinical cure rates and low resistance rates of fluoroquinolone to most usual uropathogens is the main reason for its application when the patient is suspected to be affected with a resistant organism (7, 8). However, resistance to fluoroquinolones has also been reported in some countries (9). National and international surveillance programs are necessary to observe antimicrobial resistance and combat this growing problem (10).

In spite of a major worldwide problem regarding the development of antibiotic resistance, no extensive study has been conducted in order to determine the resistance pattern of community-acquired UTI pathogens in Iran. Herein, the researchers compared the distribution, antibiotic susceptibility, and drug resistance patterns of uropathogens isolated from male and female patients with community acquired UTI.

2. Methods

After institutional review board approval and obtaining informed consent from patients referred to the Bouali

hospital, Tehran, between June 2011 and August 2012, patients with symptomatic UTI and positive urine culture (growth of pathogens) were included in this prospective study. Patients with negative urine culture, sterile bacteriuria, and a history of antibiotic administration during the last one week were excluded from the study. The study was explained to the patients and informed consent was obtained from each participant. Every single individual was notified regarding the application of their urine culture for research purposes. If they did not agree, the data was not included in the study. Demographic data, regarding age, gender and inpatient/outpatient group, were collected by forms completed by the laboratory.

Midstream urine specimens of all patients were sent to the clinical microbiology laboratory for further evaluations and the distribution and antibiotic susceptibility patterns were determined. The commonly applied antibiotics for urinary tract infection with a high sensitivity were selected. The disk diffusion technique was applied to determine antimicrobial susceptibility, as described by the national committee for clinical laboratory standards (11). Briefly, to detect antimicrobial activity in the urine sample, a sensitive indicator organism was inoculated on a filter paper disk and positioned on agar growth medium.

The SPSS software (v.17, SPSS, Chicago, IL, USA) was applied for statistical analysis. All data were expressed as mean $\pm$ Standard Deviation (SD). To evaluate significant differences among different groups and to determine whether there are any statistically significant differences between the means of independents, one-way analysis of variance (ANOVA) was performed. A P value of < 0.05 was considered statistically significant. The normality and homogeneity was also checked.

3. Results

All patients, who were referred to the Bouali hospital, Tehran, between June 2011 and August 2012 and met the inclusion criteria, were included. From 762 included patients, 573 (75.1%) were female and 189 (24.9%) were male patients. The majority of patients were outpatients in both male and female groups (64% and 71.9%, respectively). Patients aged between 36 and 65 years old had the highest frequency in the female group (34.2%), while the frequency of symptomatic UTI was higher in patients older than 65 years old in the male population (48.1%).

Prevalence of uropathogens revealed that E. coli was the most common infection in both male and female populations (inpatients and outpatients) in different age groups with a higher prevalence in females (62.7% vs. 41.3%). *Staphylococcus aureus* (coagulase positive) was the

second most common uropathogen in females both in outpatient and inpatients groups (40% and 16%, respectively). However, the second most common uropathogen in the male population was found to be Klebsiella, both in outpatient and inpatients groups (16% and 14%, respectively). Table 1 shows the prevalence of 12 uropathogens in males and females. The difference between antibiotic susceptibility of the *Enterobacteriaceae* family in patients aged ≤ 65 years and those aged > 65 years was not statistically significant (P = 0.71).

The highest prevalence of resistance was observed against nalidixic acid (77.9%) and amoxicillin (74%) in male and female population, respectively. Amoxicillin and nalidixic acid were found to be the second most resistant antibiotics against uropathogens in the male and female population, respectively. Additionally, the highest sensitivity was observed against imipenem in both male and female groups (97.9% and 97.2%, respectively). Nevertheless, no significant difference was detected in different groups (P value > 0.05). Table 2 shows the antibiotic resistance of male and female populations.

Nalidixic acid resistance was higher in the male population (77.9%) as compared with females (62.4%). However, statistical analysis was not significantly different (P value = 0.12). Amoxicillin resistance was similar in female and male groups (74%). Similar results were obtained in regards of co-amoxiclav resistance in male and females (20.7% vs. 15.1%), without any significant difference. Statistical analysis revealed no significant difference in resistance to aztreonam between males and females (45.7% and 37.2%, respectively). Cefepime resistance was also similar between the 2 groups without any statistically significant difference (33.6% vs. 29.9%). Bacterial resistance to ciprofloxacin was higher in the male group (52%) as compared with females (40.1%) without any significant difference (P value = 0.08). Clindamycin resistance was also higher in the male population (61.2%) compared with females (49.5%). However, the statistical analysis was not significantly different (P value = 0.1). Statistical analysis revealed similar results in regards of cotrimoxazole resistance in males and females (54.7% vs. 55.7%) Bacterial resistance to gentamycin was higher in the male group (39.1%) as compared with females (30.3%), without any significant difference (P value = 0.07). The rate of bacterial resistance to nitrofurantoin was also similar in males and females without any statistically significant difference (15.1% and 12.5%, respectively).

The rate of uropathogens resistance to imipenem was also similar in male and female groups with lower resistance rate as compared to other analyzed antibiotics (2.1% and 2.1%, respectively).

However, antibiotic resistance was different in male

Table 1. Distribution of Uropathogens in Males and Females

Variables	Male		Female		P Value
	No.	%	No.	%	
Escherichia coli	78	41.3	359	62.7	0.03
Klebsiella	30	15.9	46	8	0.02
Pseudomonas aeruginosa	10	5.3	10	1.7	0.001
Proteus	7	3.7	11	1.9	0.02
Enterococcus	15	7.9	30	5.2	0.07
Staphylococcus aureus (Collagenase +)	16	8.5	48	8.4	0.5
Streptococcus	2	1.1	10	1.7	0.5
Staphylococcus (Collagenase -)	2	1.1	25	4.4	0.01
Enterobacter	1	0.5	12	2.1	0.02
MRSA	2	1.1	18	3.1	0.04
Citrobacter freundii	7	3.7	2	0.3	0.001
MRSE	13	6.9	1	0.2	0.0001
Acinetobacter baumannii	1	0.5	1	0.2	0.06

Table 2. Antibiotic Sensitivity in Different Gender

Variables	Male		Female		P Value
	No.	%	No.	%	
Amoxicillin	15	31.3	53	27	0.2
Co-Amoxiclav	43	55.8	164	58	0.4
Aztreonam	27	46.6	161	60	0.08
Cefepime	49	62.8	198	72.5	0.07
Ceftriaxone	44	56.4	57	70.4	0.07
Ciprofloxacin	56	49.1	241	64.8	0.08
Clindamycin	17	53.1	40	48.8	0.1
Cotrimoxazole	41	45.6	150	46.6	0.9
Gentamycin	62	58.8	212	58.4	0.07
Imipenem	25	96.2	84	96.6	0.9
Kanamycin	15	55.6	75	62.5	0.8
Nalidixic acid	10	16.9	74	37.6	0.12
Nitrofurantoin	73	73.7	304	82.6	0.6
Ofloxacin	11	39.3	67	71.3	0.03

and female populations regarding the age distribution. Comparing the groups according to age, the elderly group (aged > 65) was more resistant to amoxicillin in the female population (76.5%) as compared with patients aged 6 to 15 years old in the male population (100%). Additionally, same results were obtained for male patients aged 6 to 15 years old for co-amoxiclav resistance (50%), as compared with fe-males aged 1 to 5 years old (30%). Aztreonam resistance was higher in the female population aged 1 to 5 years old (55.5%) as compared with males aged 6 to 15 years old (100%). Resistance to cefepime was higher in the elderly population of females (60%) as compared with patients aged 1 > years old in the male group (47.1%).

4. Discussion

This study revealed the distribution and antibiotic resistance pattern of uropathogens isolated from patients with symptomatic UTI at Bouali hospital, Tehran. Urinary samples were obtained from a wide range of patients with different ages, in which the pediatric population was also included. The majority of specimens were obtained from adult patients (67.1%) with the main population being the female group (75.19%). This could be because of the fact that adult females are expected to have a higher prevalence of UTI than males as a result of anatomic and physical factors (12, 13).

The principal problem in treatment of UTI, as an important infection, is antibiotic resistance, which is increasing over the years with variant resistance rates from country to country (14). Isolates from Latin American, Asian-Pacific, and European countries have the lowest susceptibility rates to all antimicrobial agents.

The results of the current study showed that *E. coli* was the predominant pathogen isolated from patients with symptomatic UTI. This finding was in accordance with previous studies with the same results (15, 16). However, in the current study *Klebsiella pneumonia* was the second common encountered uropathogen in patients with community-acquired UTI with a higher incidence in the female population. This finding was in contrast with previously published studies, in which *Klebsiella pneumonia* was rarely found in patients with UTI (13, 17). Considering the fact that these isolates are resistant against first generation cephalosporin and a wide range of antibiotics (18), it is crucial to find a fundamental antibiotic prescription policy in countries with the same bacterial distribution.

The isolates of the current study were mostly resistant to amoxicillin and nalidixic acid (75.7% and 70.7%, respectively). However, Indian isolates showed highest resistance against ampicillin and co-trimoxazole (16). Additionally, the resistance against co-trimoxazole was 39.1% for isolates from the USA (19), while this rate was 56.05% in the present study. Moreover, co-trimoxazole resistance was 14.1% in a study conducted in Europe, which shows the difference in antimicrobial resistance considering the findings of the current study (20). However, rate of resistance against co-trimoxazole in this study was more similar to countries like Senegal (55%), Taiwan (56%), Spain (33%), and Israel (26%) (21-24).

In another study, common isolates were highly resistant (70% - 80%) against nitrofurantoin (16). Whereas, resistance was significantly lower in the present study (15.06%). The results of the present study were in accordance with the low resistance rate of this drug (0% - 5.4%) in the major part of the world, despite its application for many years

(25). The wide application of nitrofurantoin over the past decade may be the cause of its low resistance in this area (26, 27).

Additionally, uropathogens had the lowest resistance rate against imipenem and amikacin in the study of Akram et al. (16), which was in accordance with the findings of the current study. The researchers found that the highest sensitivity was observed against imipenem in both the male and female population (97.9% and 97.2%, respectively) without any statistically significant difference.

The high resistance rate of uropathogens against a wide spectrum of cephalosporins may be explained as uncontrolled consumption of these antibiotics during the past decades in Iran and other countries (16, 26, 27). This prospective study may guide clinicians and authorities in management of patients with UTI and formulating antibiotic prescription policies. However, this study had some limitations. The researchers only determined the most common uropathogens and antibiotic susceptibility in these patients, and susceptibility to each uropathogen was not evaluated separately. Considering the fact that the sample was collected from a single hospital in Tehran, the results may still not be comprehensive enough to draw firm conclusions regarding the prevalence of uropathogens among the Iranian population. More studies are required to understand the exact magnitude of the problem in Iran.

4.1. Conclusion

Antibiotic resistance is a significant dilemma for public health, threatening both hospitalized individuals as well as patients with chronic diseases. The results of the current study revealed that imipenem and nitrofurantoin are the first 2 sensitive antibiotics against uropathogens both in male and female population. Therefore, strict antibiotics prescription policy should be formulated by policy makers in Iran.

References

1. Gonzalez CM, Schaeffer AJ. Treatment of urinary tract infection: what's old, what's new, and what works. *World J Urol.* 1999;**17**(6):372–82. doi: 10.1007/s003450050163. [PubMed: 10654368].
2. Nicolle LE. Urinary tract infection. *Intensive Care Med.* 2012:2359–64. doi: 10.1016/b978-1-4160-3362-2.00056-7.
3. Winstanley TG, Limb DI, Eggington R, Hancock F. A 10 year survey of the antimicrobial susceptibility of urinary tract isolates in the UK: the Microbe Base project. *J Antimicrob Chemother.* 1997;**40**(4):591–4. doi: 10.1093/jac/40.4.591.
4. Trienekens T. The antibiotic susceptibility patterns of uropathogens isolated from general practice patients in southern Netherlands. *J Antimicrob Chemother.* 1994;**33**(5):1064–6. doi: 10.1093/jac/33.5.1064.
5. Schaeffer AJ. The expanding role of fluoroquinolones. *Am J Med.* 2002;**113**(1):45–54. doi: 10.1016/s0002-9343(02)01059-8.

6. Biswas D, Gupta P, Prasad R, Singh V, Arya M, Kumar A. Choice of antibiotic for empirical therapy of acute cystitis in a setting of high antimicrobial resistance. *Indian J Med Sci.* 2006;**60**(2):53. doi: 10.4103/0019-5359.19913.

7. Goldstein FW. Antibiotic susceptibility of bacterial strains isolated from patients with community-acquired urinary tract infections in France. *Eur J Clin Microbiol.* 2000;**19**(2):112–7. doi: 10.1007/s100960050440.

8. Tankhiwale SS, Jalgaonkar SV, Ahamad S, Hassani U. Evaluation of extended spectrum beta lactamase in urinary isolates. *Indian J Med Res.* 2004;**120**(6):553–6. [PubMed: 15654142].

9. Aguiar JM, Chacon J, Canton R, Baquero F. The emergence of highly fluoroquinolone-resistant Escherichia coli in community-acquired urinary tract infections. *J Antimicrob Chemother.* 1992;**29**(3):349–50. doi: 10.1093/jac/29.3.349. [PubMed: 1592705].

10. Wise R, Hart T, Cars O, Streulens M, Helmuth R, Huovinen P, et al. Antimicrobial resistance. Is a major threat to public health. *BMJ.* 1998;**317**(7159):609–10. doi: 10.1136/bmj.317.7159.609. [PubMed: 9727981].

11. National Committee for Clinical Laboratory Standards . Methods for disk susceptibility tests for bacteria that grow aerobically. Wayne NCf-CLSte; .

12. Khan AU, Musharraf A. Plasmid-mediated multiple antibiotic resistance in Proteus mirabilis isolated from patients with urinary tract infection. *Med Sci Monit.* 2004;**10**(11):CR598–602. [PubMed: 15507850].

13. Kumar MS, Lakshmi V, Rajagopalan R. Occurrence of extended spectrum beta-lactamases among Enterobacteriaceae spp. isolated at a tertiary care institute. *Indian J Med Microbiol.* 2006;**24**(3):208–11. [PubMed: 16912442].

14. Gales AC, Jones RN, Turnidge J, Rennie R, Ramphal R. Characterization of Pseudomonas aeruginosa isolates: occurrence rates, antimicrobial susceptibility patterns, and molecular typing in the global SENTRY Antimicrobial Surveillance Program, 1997-1999. *Clin Infect Dis.* 2001;**32 Suppl 2**:S146–55. doi: 10.1086/320186. [PubMed: 11320454].

15. Philippon A, Arlet G, Lagrange P. Escherichia coli : fréquence de résistance et évolution à divers antibiotiques urinaires dont la fosfomycine en milieu hospitalier (11 816 souches, 1991–1995). *Med Mal Infect.* 1996;**26**(5):539–41. doi: 10.1016/s0399-077x(96)80239-3.

16. Akram M, Shahid M, Khan AU. Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in J N M C Hospital Aligarh, India. *Ann Clin Microbiol Antimicrob.* 2007;**6**:4. doi: 10.1186/1476-0711-6-4. [PubMed: 17378940].

17. Kunin CM. Urinary tract infections in females. *Clin Infect Dis.* 1994;**18**(1):1–10. doi: 10.1093/clinids/18.1.1. [PubMed: 8054415] quiz 11-2.

18. Al Benwan K, Al Sweih N, Rotimi VO. Etiology and antibiotic susceptibility patterns of community- and hospital-acquired urinary tract infections in a general hospital in Kuwait. *Med Princ Pract.* 2010;**19**(6):440–6. doi: 10.1159/000320301. [PubMed: 20881410].

19. Vromen M, van der Ven AJ, Knols A, Stobberingh EE. Antimicrobial resistance patterns in urinary isolates from nursing home residents. Fifteen years of data reviewed. *J Antimicrob Chemother.* 1999;**44**(1):113–6. doi: 10.1093/jac/44.1.113. [PubMed: 10459818].

20. Kahlmeter G. Prevalence and antimicrobial susceptibility of pathogens in uncomplicated cystitis in Europe. The ECO.SENS study. *Int J Antimicrob Agents.* 2003;**22 Suppl 2**:49–52. doi: 10.1016/S0924-8579(03)00229-2. [PubMed: 14527771].

21. Colodner R, Keness Y, Chazan B, Raz R. Antimicrobial susceptibility of community-acquired uropathogens in northern Israel. *Int J Antimicrob Agents.* 2001;**18**(2):189–92. doi: 10.1016/S0924-8579(01)00368-5. [PubMed: 11516944].

22. Dromigny JA, Nabeth P, Perrier Gros Claude JD. Distribution and susceptibility of bacterial urinary tract infections in Dakar, Senegal. *Int J Antimicrob Agents.* 2002;**20**(5):339–47. doi: 10.1016/S0924-8579(02)00196-6. [PubMed: 12431869].

23. Daza R, Gutierrez J, Piedrola G. Antibiotic susceptibility of bacterial strains isolated from patients with community-acquired urinary tract infections. *Int J Antimicrob Agents.* 2001;**18**(3):211–5. doi: 10.1016/S0924-8579(01)00389-2. [PubMed: 11673032].

24. Lau SM, Peng MY, Chang FY. Resistance rates to commonly used antimicrobials among pathogens of both bacteremic and non-bacteremic community-acquired urinary tract infection. *J Microbiol Immunol Infect.* 2004;**37**(3):185–91. [PubMed: 15221039].

25. Honderlick P, Cahen P, Gravisse J, Vignon D. [Uncomplicated urinary tract infections, what about fosfomycin and nitrofurantoin in 2006?]. *Pathol Biol (Paris).* 2006;**54**(8-9):462–6. doi: 10.1016/j.patbio.2006.07.016. [PubMed: 17027182].

26. Hillier SL, Magee JT, Howard AJ, Palmer SR. How strong is the evidence that antibiotic use is a risk factor for antibiotic-resistant, community-acquired urinary tract infection? *J Antimicrob Chemother.* 2002;**50**(2):241–7. doi: 10.1093/jac/dkf121. [PubMed: 12161405].

27. Svetlansky I, Liskova A, Foltan V, Langsadl L, Krcmery V. Increased consumption of fluoroquinolones is not associated with resistance in Escherichia coli and Staphylococcus aureus in the community. *J Antimicrob Chemother.* 2001;**48**(3):457–8. doi: 10.1093/jac/48.3.457. [PubMed: 11533023].