
Distribution of bacterial species and evaluation of their antimicrobial susceptibility support a general approach that urinary tract infections are considered complicated in men

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Abstract: Background: Urinary tract infections (UTIs) in men are considered complicated, however few studies support this view. We compared the differences in the causative microorganism and their antimicrobial resistance between male and female patients presenting with an UTI. Methods: We evaluated the all microorganism isolated from the urine samples of patients which were admitted to outpatient clinics of our hospital during 2006 – 2011, which diagnosed with uncomplicated community acquired UTI. Results: Totally 8730 bacterial strains were isolated. Of these strains 5168 (59.2%) were isolated in women, whereas 3562 (40.8%) were isolated in men. *Escherichia coli* was the most frequently isolated microorganism (64.4%), followed by other enterobacteriaceae (15.1%) and enterococci (17.8%). However, the frequency of *E. coli* in men was significantly lower than in women, and frequency of other enterobacteriaceae and frequency of enterococci were higher than in women (49.4% versus 74.7%, 21.2% versus 10.8%, 24.7% versus 12.9%, respectively, $p=0.001$). The distribution of microorganism was evaluated according to age groups, similar results were observed in all age groups. In addition, *E. coli*, the most common strains for both sex. *E. coli* strains isolated in men were significantly less sensitive to ampicillin, ampicillin/sulbactam, cefuroxime, ceftriaxone, trimethoprim-sulphamethoxazole, gentamicin, ciprofloxacin, nitrofurantoin and fosfomycin than in women ($p<0.05$). Conclusion: The distribution of bacterial species isolated from urine culture of UTI is different in men. Even though *E. coli* is the most common strains in men as in women. In addition *E. coli* strains isolated in men were more resistant to antibiotics.

Keywords: Urinary Tract Infection, *E. coli*, Antimicrobial Resistance, Community Acquired

1. Introduction

As known urinary tract infection (UTI) is less observed in men than women and most studies on the treatment of acute UTI in outpatients have been performed in women, usually premenopausal women. Although rates are lower in young men, the incidence of UTI's dramatically increases with age; one-third of all 80-year-old men will have had an episode of bacteriuria [1, 2]. UTIs are classified according to type of UTI complication level as complicated or uncomplicated UTI [3]. Generally, UTI in a man of any age

is considered complicated because they result from an anatomic or functional anomaly, but there is a group classified as uncomplicated UTI in young men [2].

Uncomplicated UTIs in females are managed effectively and safely by empirical antibiotic therapy without requiring a urine culture, but the diagnosis and therapy of uncomplicated UTI in men is still difficult. Although cystitis and pyelonephritis are common diagnoses in the both sexes and it was reported that the antibiotic resistance among males was higher than females [4-8]. Therefore, in male UTI's, urine culture and targeted antibiotic therapy has been advocated before a treatment decision is made

[5,6]. In presented study, we aimed to determine the male gender, as underlying risk factors, affects or not the distribution of microbial species in community acquired UTI (CAUTI). In addition, by evaluating the antimicrobial resistance of the most frequently isolated strains, we investigated whether male gender is a risk factor for more resistant strains and is a complicating factor about the selection of empirical antimicrobial therapy in CAUTI.

2. Materials and Methods

The growth in urine cultures of patients with UTI had admitted to outpatient clinics of Cumhuriyet University Training and Research Hospital between January 2006 and December 2011 were evaluated. Patients who had been hospitalized for more than 72 h before the time of the diagnosis of UTI or who had been discharged from an acute care hospital within 10 days before the time of the diagnosis of UTI and patient used any catheterization procedures for neurogenic bladder were excluded, and growth in urine cultures of these patient were not included in this study. In addition, the fungi, mixed cultures and multiple specimens from a given patient in 3 months period (in which case only the first sample per patient was used) were excluded.

In pediatric group, positive urine culture was defined as the growth of $\geq 10^5$, $\geq 10^4$ and any colony-forming unit [CFU]/mL of a single uropathogen for specimens obtained by clean-catch midstream, catheterization, and suprapubic methods, respectively. In adults, midstream urine sample was obtained from patients and isolates from urine cultures that yielded $\geq 10^5$ CFU/mL underwent susceptibility testing. The susceptibility of each isolated pathogen to ampicillin,

ampicillin/sulbactam, trimethoprim-sulphamethoxazole (TMP-SMX), nitrofurantoin, fosfomycin, cefuroxime, gentamicin, ciprofloxacin, piperacilin-tazobactam and imipenem was determined by Phonex 100 antimicrobial susceptibility testing using the Clinical and Laboratory Standards Institute (CLSI) criteria [9].

Statistical Package for the Social Sciences (SPSS) version 14 for Windows (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Proportions for categorical variables were compared using the Chi-square test.

A p value of <0.05 was considered significant.

3. Results

A total of 8716 strains were isolated in urine culture of patients with UTI. The subjects comprised 5154 (59.1%) females and 3562 (40.9%) males, for an overall female-to-male ratio is 1.45. Rates of female-to-male according to age groups are 2532 (57.1%) females, 1901 (42.9%) males in <18 age group; 1606 (81.7%) females, 358 (18.3%) males in 18-50 age group; 1016 (43.8%) females, 1303 (56.2%) male in >50 age group.

Expected in, *E. coli* was the most common organism and responsible for 64.5% of UTIs, followed by enterococci (%17.7), non- *E. coli* enterobacteriaceae (15.0 %), and others (2.8%). When analyzed distribution of pathogens for gender, we found that *E. coli* ratio in female urine cultures are greater than male urine cultures, enterococci and other strains ratio greater in male urine cultures and the differences are statistically significant totally and also in all age groups (Table I).

Table I. The percentage distribution of the uropathogens isolated from patients with community acquired urinary tract infection according to age group and gender.

Uropathogen	Frequency (%) of isolated strains											
	< 18 y (n=4433)			18-50 y (n=1964)			> 50 y (n=2319)			Total (N=8716)		
	F	M	p	F	M	p	F	M	p	F	M	p
Escherichiacoli	72.0	40.2		76.7	61.5		79.0	59.6		74.9	49.4	
Other Enterobacteriaceae species	11.1	31.0	0.001	12.6	12.0	0.001	7.2	9.4	0.001	10.8	21.2	0.001
Enterococci	16.1	28.8		9.6	15.4		10.3	21.3		12.9	24.7	
Other	0.8	0		1.2	11.2		3.4	9.7		1.4	4.7	

Commonly used antibiotics (i.e., amoxicillin-clavulanic acid, cefuroxime, ceftriaxone, TMP-SMX, ciprofloxacin and gentamicin) for treatment of UTIs at outpatient setting were examined for antimicrobial susceptibility. *E. coli* strains isolated in urine culture of male patients with UTI had higher resistance than women and statistically significant differences were observed in all tested antibiotics (Table II). We also showed that there was higher resistance in *E. coli* isolates isolated in male patients in all age groups to all tested antibiotics except ciprofloxacin,

nitrofurantoin and fosfomycin. Ciprofloxacin resistance of *E. coli* isolates was higher in male patients in 18-50 years age and over 50 years age ($p=0.001$ and $p=0.001$, respectively), but it was similar in both sexes under 18 years age ($p=0.98$). The resistance rate of *E. coli* to nitrofurantoin and fosfomycin were the lowest among the all tested antibiotics in both genders and it was observed that there were very small differences about resistance rate between age groups and gender (Table 2).

Table.2. The comparison of resistance rates among *Escherichia coli* isolates between age groups and gender.

	Resistance rate (%) of <i>Escherichia coli</i> isolates											
	< 18 y (n=2588)			18 – 50 y (n=1451)			> 50 y (n=1584)			Total (N=5623)		
	M	F	p	M	F	p	M	F	p	M	F	p
Ampicillin	74.0	61.9	0.001	61.8	47.9	0.001	74.0	56.3	0.001	70.5	57.3	0.001
Ampicillin/sulbactam	56.5	43.1	0.001	48.0	32.2	0.001	60.0	39.4	0.001	54.8	39.2	0.001
Cefuroxime	38.0	25.9	0.001	37.7	19.6	0.001	48.5	28.3	0.001	38.8	23.7	0.001
Ceftriaxone	31.0	23.5	0.001	30.0	17.8	0.001	41.3	22.9	0.001	33.3	20.8	0.001
Co-trimoxazole	55.2	50.1	0.018	45.5	35.4	0.005	53.7	42.1	0.001	47.9	42.9	0.001
Gentamicin	18.5	15.0	0.034	20.0	11.9	0.002	27.4	16.2	0.001	19.6	15.3	0.001
Ciprofloxacin	16.1	16.2	0.98	45.0	23.2	0.001	64.4	44.2	0.001	31.2	23.5	0.001
Nitrofurantoin	2.2	0.3	0.001	3.6	1.1	0.008	4.2	2.7	0.13	3.1	1.2	0.001
Fosfomycin	1.0	0.3	0.076	0	0	-	2.0	0.2	0.001	1.3	0.2	0.001

4. Discussion

The bacterial spectrum, antibiotic resistance patterns and the activity of the antibiotic at the site of infection are critical for an effective therapy [4]. In addition, rising antimicrobial resistance against microorganism which commonly isolated and constitute the main objective of empirical therapy complicates the selection of the empirical therapy [10]. In this study, we observed statistically significant differences between females and males patients about bacterial spectrums and resistance rate of *E. coli* strains, *E. coli* is the most frequently isolated strains in both gender and all age groups in our study, to antibiotics which are commonly used in UTI in outpatient setting.

Generally it was believed that the causative organism of UTIs differed between male and female patients, but more recent data has shown that the primary causative pathogen is *E. coli* in both sexes, which accounts for 64.5-90% of UTIs [11-13]. Our study is compatible with the literature with these findings, however the rate of *E. coli* is lower in our study group, it was found as 64.5%, than reported previous studies [14]. Female to male ratio is 1.45 in our study and was lower than other studies (3.42-3.82) reported previously [10, 12, 15]. We thought that this situation is due to rate of patients over the age of 50 and under the age of 18 are more than the other studies. Otherwise, uncomplicated cystitis in women is commonly treated by empirically without culturing, and we think that this condition may explain the lower rate of *E. coli* in our study population.

Most antimicrobial susceptibility surveillance studies of urinary isolates focus on nosocomial patients [16]. However, antibiotic resistance has become an important consideration in the treatment of community-acquired UTIs and complicating factor in urinary tract infections [7]. McGregor at al. [13] reported that statistically significant differences between males and females in the age-specific resistance of *E. coli* to ampicillin, amoxicillin-clavulanate, ciprofloxacin, and nitrofurantoin. Urinary *E. coli* isolates from male patients had increased antibiotic resistance than

isolates from female patients. Linhares et al. [12] demonstrated that urinary isolates of *E. coli* were significantly more resistant to fluoroquinolones, penicillins, nitrofurantoin, and first and second generation cephalosporins among men compared to women with 10-year study of community UTI in Portuguese. CANWARD and NAUTICA studies also showed that outpatient UTIs reported greater antibiotic resistance to ciprofloxacin, levofloxacin, and TMP-SMX among all urinary *E. coli* isolates from U.S. and Canadian male patients [15-17]. The findings of our study are similar to the literatures and several explanations for differences about susceptibility rate of *E. coli* strains between both genders in our study can be given. Relatively short term treatment was used cystitis in women and that may not influence much resistance. The male patients with UTI have generally additional risk factors and more frequently exposed to antibiotics, with a consequent higher risk of selection resistance species. In addition, ciprofloxacin resistance are lower in under 18 years age than other age groups in our study, it is generally not recommended as treatment choice for persons less than 18 years of age because the drug cause cartilage damage, and that supports also the known epidemiological association between antimicrobial use and resistance.

In an American study designed by Lutter et al. Performed during 1997-2001, the resistance rates of all isolates ranged from 48% to ampicillin, 17% to TMP/SMX and 7% to nitrofurantoin in paediatric age group [18]. In Taiwan, Tseng et al. reported 77.4% resistance to ampicillin, 44.6% to TMP/SMX, 27.2% to cephalotin, and 8.4% to nitrofurantoin, with growing resistance rates to ampicillin, TMP/SMX, and cephalosporins in the first generation during the 14-year study period [19]. In accordance with the above-mentioned studies, in under 18 age group our results showed a similarly high resistance rate to ampicillin (71-61,9% male-female), and high resistance to ampicillin/sulbactam (56,5-43,1% male-female). The resistance of all uropathogens to nitrofurantoin remained low, while the resistance of *E. coli* to nitrofurantoin was even lower (2.2-0.3% male-female). In the paediatric age

group which require long-term antibiotic prophylaxis particular attention should be in this situation.

In conclusion, the distribution of bacterial species isolated from urine culture of UTI is different in men. Even though *E. coli* is the most common strains in men as in women, other enterobacteriaceae and enterococci constitutes nearly half of the cases. In addition *E. coli* strains isolated in men with UTI were more resistant to commonly used antibiotics for CAUTIs in outpatient setting than women. Therefore, we think that determination of the causative microorganism of UTI and knowing their antimicrobial susceptibility according to risk factors such as age, gender and others will provide the most significant contribution for improvement of rational empirical therapy for UTIs. Ongoing surveillance studies investigating etiologic agents and more importantly investigating antimicrobial susceptibility of etiologic agent constitute the main goal of empirical therapy at the local, national and international levels are needed to achieve favorable therapeutic outcomes.

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