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Original Article

A 3-Year Study Of Demographic Characteristics Of Patients With Urinary Tract Infection, Microbial Etiology, And Susceptibility Of Isolated Bacteria To Antibiotics In Shaheed Mostafa Khomeini Hospital

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ABSTRACT

Background and Objectives: **This study was designed as a retrospective study on urine samples during three years in Shaheed Mostafa Khomeini Hospital to determine demographic characteristics of patients with urinary tract infection (UTI), microbial etiology, and susceptibility of isolated bacteria to antibiotics.**

Materials and Methods: **All urines fulfilling the criteria for significant bacteriuria (>10^4 colony-forming units/ml of urine) were included in the study. Isolation and identification of bacteria was performed by standard method and susceptibility testing was determined by disk diffusion method according to NCCLS guideline. A total of 909 patients with urinary tract infection were enrolled in this study.**

Results: **Mean age of the patients was 53.2 years. In addition, females were affected more often than males (female/male sex ratio was 2.22). Meanwhile, considering all strains, 79.5% were Gram-negative bacilli and 67.7% were Enterobacteriaceae. Furthermore, E.coli and Klebsiella spp represented the most common Gram-negative and Enterococci and S. aureus represented the most frequent Gram-positive isolates. The four most frequently isolated bacteria were E. coli (52.1%), Enterococci (10.5%), klebsiella spp. (10.3%), and pseudomonas spp. (9.4%). In addition, E. coli was significantly more common in females (56.6%) than in males (42.2%) and in outpatients (57.4%) than in inpatients (47.4%). The proportion of pseudomonas spp. was significantly higher in males (17.7%) than in females (5.6%). Enterococci were significantly more common in inpatients (12.5%) than in outpatients (8.4%). Altogether, the rate of susceptibility of all UTI pathogens was very low to ampicillin (6.9%) and high to cefotaxime (83.6%) and ciprofloxacin (78.2%). Urinary pathogens isolated from female patients and outpatients were more susceptible to most of examined antibiotics than those isolated from males and inpatients.**

Conclusion: **It was found out that degrees for antibiotic resistance of urinary pathogens are alarming and show the necessity of keeping up the monitoring of antibiotics susceptibility in UTI isolates and restricting antibiotic consumption in our population.**

Keywords: **Urinary tract infections, Demographic characteristics, Microbial etiology, Susceptibility**

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Introduction

Urinary tract infections (UTI) are amongst the most common infections, with an estimated annual global incidence of at least 250 million (1). It also account for a large proportion of antibiotic consumption (2). Most cases of UTI are initially treated empirically (3). For optimizing the treatment and finding updated recommendations for UTI treatment, physicians should know the etiology of UTI and the susceptibility pattern of UTI pathogens in their population (4). The etiology of UTI and the antimicrobial susceptibility of urinary pathogens have been changing over the years (5). In fact, uropathogens have shown a slow but steady increase in resistance to several antibiotics, for example, E. coli and other Enterobacteriaceae have become less susceptible to ampicillin, co-trimoxazole and in some geographical areas, to fluoroquinolones (6). Therefore, this study was performed to determine demographic characteristics of patients with UTI, microbial etiology, and susceptibility of isolated bacteria to commonly used antibiotics during 3 years at Shaheed Mostafa Khomeini Hospital.

Materials and Methods

This study was designed as retrospective and its population consisted of patients with UTI being treated in inpatient section or outpatient clinic of the hospital from 1 January 2001 until 31 December 2003. Demographic data such as age, sex, and type of admission (outpatient or inpatient) were obtained. In addition, UTI was defined as the growth of a single pathogen of $>10^4$ colony forming units/ ml and presence of pyuria in properly collected urine specimen. Identification of isolated bacteria was carried out by standard methods (7).

The antimicrobial susceptibility of bacteria was determined by disk diffusion method using antibiotic-containing disks (Padtan Teb Co., Iran) on Mueller-Hinton agar plate (Merck, Germany) according to guidelines of the NCCLS (8). Susceptibility was tested for ampicillin, carbenicillin, cephalexin, cefazoline, cefixime, ceftazidime, cefotaxime, ceftriaxone, tetracycline, doxycycline, amikacin, gentamicin, kanamycin, ciprofloxacine, oflaxacin, nalidixic acid, nitroforantoin, and co-trimonazole for Gram-negative and to penicillin, ampicillin, oxacillin, vancomycin, cephalexin, cefotaxime, tetracycline, amikacin, gentamicin, kanamycin, ciprofloxacine, nitroforantoin, co-trimoxazole, erythromycin, and clindamycin for Gram-positive bacteria.

Statistical analysis was performed using SPSS software (version 10) and Pearson's χ^2 as well as fisher's exact tests, ANOVA, and the Mann-Whitney U tests were applied. A p value less than 0.05 was considered as statistically significant.

Results

A total of 909 non-duplicate bacteria were collected from 627 women (69%) and 282 men (31%) with UTI during the study period. It was found out that females are affected more often than males (female/ male sex ratio was 2.22). In addition, mean age of patients was 53.2 years (53 for females and 53.6 for males). The frequency of pathogens causing UTI is listed in Table 1. Of all studied strains, 79.5% were Gram-negative bacilli and 67.7% were Enterobacteriaceae. The four most frequently isolated bacteria were E. coli (52.1%), Enterococci (10.5%), Klebsiella spp. (10.3%), and pseudomonas spp. (9.4%). Meanwhile, distribution pattern of isolated bacteria was not significantly different between the years of the study, for example, E. coli was identified in 49.1, 51.6, and 54.5% of cases in years 2001, 2002, and 2003 respectively. Furthermore, in patients with UTI due to four most frequently isolated bacteria had the same mean age (52.9, 53.6, 51.1, and 54

Table 1. Distribution of isolated bacteria from UTI

Bacteria	No. of isolates (%)
E. coli	474 (52.1)
Enterococci	96 (10.5)
Klebsiella spp.	94 (10.3)
Pseudomonas spp.	85 (9.4)
S. aureus	48 (5.3)
Enterobacter spp.	36 (4.0)
Acinetobacter spp.	23 (2.5)
Other Streptococci	14 (1.6)
Coagulase negative Staphylococci	14 (1.6)
Streptococcus agalactiae	13 (1.4)
Proteus spp.	12 (1.3)
Total	909 (100)

years for E. coli, Enterococci, Klebsiella spp. and pseudomonas spp. respectively). Meanwhile, distribution of four most frequently isolated bacteria from male and female cases is shown in Table 2. Predominant pathogen in urine samples of both male and female patients was E. coli that significantly occurred more frequently in urines from female (56.6%) than male (42.2%) cases. In addition, the proportion of pseudomonas spp. was significantly higher in males (17.7%) than in females (5.6%). Bacterial etiology in urines from inpatients and outpatients with UTI were similar (Table 3). Predominant pathogen in urine samples of both inpatients and outpatients was E. coli that significantly occurred more frequently in urines from outpatients (57.4%) than from inpatients (47.4%). The proportion of Enterococci was significantly higher in inpatients (12.5%) than in outpatients (8.4%).

Table 2. Distribution of isolated bacteria from male and female cases

Bacteria	No. of isolated bacteria (%)	
	female	male
E. coli	355 (56.6)	119 (42.2)*
Enterococci	59 (9.4)	37 (13.1)
Klebsiella spp.	64 (10.2)	30 (10.6)
Pseudomonas spp.	35 (5.6)	50 (17.7)*
Others	114 (18.2)	46 (16.3)
Total	627 (100)	282 (100)

* A statistically significant difference

Table 3. Distribution of isolated bacteria from inpatients and outpatients

Bacteria	No. (%) of isolated bacteria from	
	outpatients	inpatients
E. coli	247 (57.4)	227 (47.4) *
Enterococci	36 (8.4)	60 (12.5) *
Klebsiella spp.	47 (10.9)	47 (9.8)
Pseudomonas spp.	32 (7.4)	53 (11.1)
Others	68 (15.8)	92 (19.2)
Total	430 (100)	479 (100)

* A statistically significant difference

On the other hand, the rate of susceptibility to antimicrobial agents is summarized in Tables 4 and 5 for Gram-negative and Gram-positive isolated

Table 4. Susceptibility of Gram-negative isolated bacteria to antibiotics

	Percent of isolates susceptible of :					
Antibiotics	E.coli	Klebsiella spp	Enterobacter spp	Proteus spp	Pseudomonas spp	Acinetobacter spp
Ampicillin	2	0	ND	12.5	0	0
Carbenicillin	33.9	25.6	13.6	ND	18.9	ND
Cephalexin	28.9	46.3	13.3	33.3	ND	ND
Cefazoline	22.1	ND	ND	ND	ND	ND
Cefixime	30.4	39.5	ND	ND	ND	ND
Ceftazidime	71.2	79.3	50	ND	36	ND
Cefotaxime	89	ND	ND	ND	ND	ND
Ceftriaxone	72.7	66.7	ND	ND	3.3	ND
Tetracycline	22.4	33.8	30	ND	18.6	23.5
Doxycycline	12.3	7.7	33.3	ND	10.3	ND
Amikacin	64.7	53.7	39.1	77.8	39.4	14.3
Gentamicin	47	34.4	21.9	50	24.7	14.3
Kanamycin	18	29.6	40	ND	2.3	ND
Ciprofloxacine	79.5	92.3	80	88.9	50	46.7
Ofloxacin	85.7	94.4	ND	ND	34.6	ND
Nalidixic acid	61	57	54.5	58.3	ND	20
Nitroforantoin	40.8	10.1	27.3	0	1.3	4.8
Co-trimoxazole	29.8	18.9	13.3	25	1.4	9.1

ND = not determined

Table 5. Susceptibility of Gram-positive isolated bacteria to antibiotics

Antibiotics	Percent of isolates susceptible to:				
	S. aureus	Coagulase negative strep.	Enterococci	Strep agalactiae	Other strep
Penicillin	10.3	60	9.9	100	50
Ampicillin	5.9	11.1	27.8	100	58.3
Oxacillin	11.5	ND	ND	ND	ND
Vancomycin	100	100	71.8	100	100
Cephalexin	65.8	92.8	27.7	100	100
Cefotaxime	43.8	ND	43.3	ND	ND
Tetracycline	54.5	54.5	37.3	10	33.3
Amikacin	58.3	90.9	11.3	63.6	60
Gentamicin	51.4	83.3	16.7	30.8	46.2
Kanamycin	23.8	ND	5.6	ND	ND
Ciprofloxacine	74.4	84.6	57.9	90.9	100
Nitroforantoin	95	76.9	64.6	100	100
Co-trimoxazole	20.5	42.8	25.6	7.7	35.7
Erythromycin	46.3	53.8	34.1	76.9	100
Clindamycin	66.7	50	23.8	90.9	90

ND= not determined

bacteria respectively. In Gram-negative bacilli, the rate of susceptibility to ampicillin was very low and to ofloxacin was higher than others. Vancomycin, nitroforantoin and ciprofloxacine were more effective against Gram-positive bacteria. In contrast, penicillin and ampicillin had low effect against Gram-positive isolates other than Streptococcus agalactiae. Altogether, the rate of susceptibility of all UTI pathogens was very low to ampicillin (6.9%) and high to cefotaxime (83.6%) and ciprofloxacin (78.2%). Meanwhile, uropathogens isolated from female patients tends to be come susceptible to most of examined antibiotics than those isolated from males (Table 6) and this difference was statistically significant for some of the antibiotics including ampicillin, cephalexin, cefixime, amikacin, ciprofloxacin, and nitrofurantoin. In addition, antibiotic susceptibility of isolated bacteria from inpatients was lower than outpatients (Table 7) which was statistically significant for cephalexin, cefixime, cefotaxime, gentamicin, ciprofloxacin, nalidixic acid, and nitrofurantoin.

Table 6. Antibiotic susceptibility of bacteria isolated from male and female patients with UTI

Bacteria	Susceptibility rate of isolates from	
	female	male
Ampicillin	8.4	6.2 *
Vancomycin	64.9	60.7
Cephalexin	36	22 *
Cefixime	24.7	22.6 *
Cefotaxime	74.1	65.7
Tetracycline	27	27.1
Amikacin	56.6	46.8 *
Gentamicin	39.8	38
Ciprofloxcin	79.1	67.0 *
Nalidixic acid	54.1	48.8
Nitrofurantoin	47.8	35.9 *
Co-trimoxazole	22.8	26.5

* A statistically significant difference

Table 7. Antibiotic susceptibility rates in bacteria isolated from outpatients and inpatients with UTI

Bacteria	Susceptibility rate of isolates from	
	outpatients	inpatients
Ampicillin	8.7	6.8
Vancomycin	64.1	63.2
Cephalexin	34.7	29.1 *
Cefixime	30.3	19.2 *
Cefotaxime	82	51.8 *
Tetracycline	26	28
Amikacin	54.3	53
Gentamicin	43.5	35.2 *
Ciprofloxcin	77.9	73.1 *
Nalidixic acid	57.6	47.3 *
Nitrofurantoin	46.2	42.3 *
Co-trimoxazole	27.3	20.8

* A statistically significant difference

Discussion

In the present study, an evaluation was conducted on species distribution and antibiotic susceptibility of UTI isolates in Tehran. The most frequent uropathogen was E. coli that comprised 52.1% of all isolates in this study. Although a similar frequency for isolates of E.coli has been obtained in studies performed in Latin America (52%) (3) and Norway (56.7%) (2), but a different frequency for isolates of E. coli has been reported in studies performed in Dakar (38.6%) (9), South Croatia (62.62%) (4), Great Britain (65.1%) (10), and USA (68 and 69% as obtained from two studies) (11, 12). However, in all studied areas, E. coli had been the most common pathogen in UTI. According to the demographic data of this study, females were affected more often than males. The question of an underlying urinary pathology of infection in females as compared to male cases was beyond the scope of this study. In addition, the failure rate in female patients with UTI is expected to be greater than in males (13), but isolated bacteria from females in this study tend to be more sensitive to most of the examined antibiotics and this difference was statistically significant for some of them. The same result was obtained in a similar study in Dakar (9). This means that empiric treatment with some of the antibiotics (i.e. ampicillin) is more effective in female than in male cases. The reason for this disparity is not clear. Men may treat themselves empirically, wait a long time before going to clinics, and thus have more resistant bacteria than women in the studied population.

It was also found out that Enterococci caused a significantly higher proportion of infections in inpatients than in outpatients, while E. coli was more common in outpatients than in inpatients. This finding correlates with previous studies in Norway (2). In this respect, Enterococci are often multi-resistant and there may be selection for the multi-resistant phenotypes in hospitals, where there is a higher consumption of antibiotics. In fact, in the present study, resistance was higher in isolated bacteria from inpatients than outpatients, which this difference was statistically significant for some of the antibiotics. In addition, the most frequent uropathogen in this study was E. coli, which over than 70% of them was resistant to ampicillin, cefalexin, cefazoline, co-trimonazole, kanamycin, doxycycline, and tetracycline. High frequency resistance to these antibiotics was also reported among E. coli isolates in other studies (2, 3, 9, 14). In contrast, the resistance rate to ceftazidime, cefotaxime, ceftriaxone, ciprofloxacine, and ofloxacin was low in our study which has also been reported in other studies (9, 3). Recommended therapy for UTI is co-trimoxazole, but when rates of resistance to this drug in UTI isolates in population exceeds 10-20%, it is ignored as a first line drug for empirical therapy (4). In the present study, the resistance rate to this antibiotic was 68.4% in 2003, which is much higher than USA and industrial countries, where resistance rate was reported as 29% (4). Therefore, it appears that co-trimoxazole is inadequate in at least two third of cases of urinary tract infections in our population. In this study, the susceptibility rate for UTI isolates to antibiotics was lower than other studies (2-4, 13, 15, 16).

Conclusion

Taken together, it is concluded that degree of antibiotic resistance for uropathogens is alarming and this certainly warrants the necessity of keeping up the monitoring of antibiotics susceptibility in UTI isolates and restricting antibiotic consumption in our population.

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