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Prevalence and Antimicrobial Susceptibility Patterns of Uropathogens among Patients Referring to Valieasr Laboratory in Najafabad, Isfahan, Iran

Forouzan Moinzadeh Zahra arabi and Amir banazadehi

Islamic Azad University Najaf Abad Branch, Najaf Abad, Isfahan, Iran

Abstract: Urinary tract infection is one of the most prevalent infections. Microorganisms causing UTI vary in their susceptibility to antimicrobials and the empirical choice of antimicrobial treatment is generally guided by susceptibility data provided by regional microbiological laboratories. This study was designed to determine the prevalence and antimicrobial susceptibility patterns of uropathogens among patients referring to Valieasr laboratory in Najafabad, Isfahan, Iran from 2009 to 2012. This study was aiming at isolation of bacteria causing UTI from urine of patients at the Valieasr laboratory of Najafabad..Antimicrobial resistance testing was performed by the standard disc diffusion technique in accordance with the recommendation of the clinical and laboratory standards institute. 187 uropathogens were isolated from 2201 patients. *Escherichia coli* (*E. coli*) was the most common isolate (55%) followed by Enterobacter (13.3%) and S. Aureus (11.76%). Susceptibility of E. coli to Nitrofurantoin was 85.7%, Gentamicin 82.5%, Cefotaxime 81.9% and ciprofloxacin 78%. High resistance rate was observed among E. coli against ampicillin (100%). The sensitivity rates of Enterobacter isolates for ciprofloxacin, gentamicin and cefotaxime were 75, 76.4 and 77.7%, respectively. S.Aureus strains were sensitive to gentamicin (84.2%), nitrofurantoin (75%) and ciprofloxacin (60%). It can be concluded that in our study E. coli was the most common isolated uropathogen. Entrobacterspp, Staphylococcus aureus and streptococcus were reported in second to forth degree of prevalence. Because of increasing resistance to FQ, FQ should be restricted for UTI. Nitrofurantoin should be used for first line empirical treatment in UTI instead of FQ.TMP-SMX

Key words: Urinary Tract Infection · Microbial Sensitivity Tests · Antibiotics

INTRODUCTION

Urinary tract infection (UTI) is one of the most prevalent infections. UTI is classified into uncomplicated and complicated infections with respect to choices for treatment [1].

Among patients referred to physicians, Escherichia coli (*E. coli*) is the most common etiological agent, approximately isolated form 75 to 90% of uncomplicated patients [2, 3], while complicated ones show a broader bacterial spectrum as the cause of infection [1].

In comparison with men, UTI is reported more in women. It could be due to the proximity of genital tract and urethra/anus, as earlier suggested by Audu and Kudi[4] and anatomical predisposition or urothelial mucosa adherence to Muco polysaccharide lining or other host factors [5].

Microorganisms causing UTI vary in their susceptibility to antimicrobials from place to place and time to time [6]. The empirical choice of antimicrobial treatment is generally guided by susceptibility data provided by regional microbiological laboratories, however, since samples of uncomplicated UTIs are rarely sent for culture, these data are mainly found in complicated UTIs [7, 8].

Etiology of UTI is influenced by factors like age, diabetes, urinary catheterization and other ones. The spectrum of bacteria which causes complicated UTI is much broader than uncomplicated ones. Resistances to antimicrobial agents have undergone dramatic variations and consequently the empirical treatment of UTI needs constant updating of the antibiotic sensitivity of the main uropathogens of that area. To correctly explicate the global data on sensitivity, the type of UTI (uncomplicated

Corresponding Author: Forouzan, M. oinzadeh, Islamic Azad University, Najaf Abad Branch, Najaf Abad.Isfahan, Iran.

versus complicated), gender, age and previous antibiotic therapy in each patient must be taken into attention. Resistance in uncomplicated UTI has clinical significance, which relies on whether the infection is cystitis or pyelonephritis [9].

Multidrug resistance of bacterial uropathogens has been determined as an important public health problem. Some microorganisms have been identified for urgent new effective therapies by The Infectious Diseases Society of America (IDSA). They were called "ESKAPE pathogens", a key word that stands for *Enterococcus faecium*, *Staphylococcus aureus*, Klebsiella spp., Acinetobacter spp., Pseudomonas spp. and Enterobacter spp. Morbidity and mortality would be increased if they did not covered by suitable antibiotics [9].

The aim of this study was determination of prevalence and antimicrobial susceptibility patterns of uropathogens among patients referred to Valieasr laboratory in Najafabad, Isfahan, Iran during a three-year period from 2009 to 2012.

MATERIAL AND METHODS

This study was done during June 2009 to February 2012 in Valieasr laboratory that is located in the central part of Najafabad, Isfahan, Iran.

The study population consisted of patients with positive community acquired urine culture with a colony count of more than10^5 CFU/ml.

The symptomatic UTI was identified with dysuria, frequency, urgency and supra Pubic tenderness with no fever [9].

Patients who had symptoms for more than 7 days, signs of pyelonephritis, three or more episodes of UTI in the past year, positive upper UTI, indwelling or recent Foley catheter, current pregnancy, antibiotic use during three months, patients who were hospitalized for any reason during past three months and patients with diabetes mellitus or immunodeficiency were excluded from this study [10].

2201 midstream urine samples were collected in sterile urine containers from suspected UTI cases. For infants sterile urine bags were used.

Samples were inoculated onto blood agar and Eosin Methylene Blue agar plates and were investigated after over night incubation at 37°C. For this study significant bacteriuria was defined as culture of a single bacterial species from the urine sample at concentration of more than 10^5CFU/ml associated with microscope finding of more than 10 white blood cells in each high power field [11]. All culture media were obtained from Merck, Germany.

Bacterial counts less than 10^5 CFU/ml were considered as negative samples. Pathogens were identified according to Gram reaction, morphology and biochemical features [2].

The antimicrobial susceptibility of each isolated pathogen was determined by disc diffusion method according to Bauer-Kriby *et al.* [12]. Mueller-Hinton agar plates were incubated for 24 hrs at 37°C after inoculation with microorganisms and placement of the disks and the diameters of the inhibition zones were measured.

The antibiotics used included Ciprofloxacin (CP), Trimethoprim-sulfamethoxazole (SXT), Gentamicin (GM), Ampicillin (AM), Nitrofurantoin (FM), Nalidixic acid (NA), Ceftizoxime (CT), Cephalexin (CN), Norfloxacin (NOR), Cefotaxime (Ctx), Imipenem (Ipm), Cefixime (Cfm) and Erythromycin (E) (Padtaneb company,Iran.). The results were interpreted according to standard procedures by the Clinical and Laboratory Standards Institute (CLSI, formerly the national committee for clinical laboratory) [13].

All data and information have been secured according to ethical committee and just used by their ID. All steps of our work were observed and approved by ethical committee of Isfahan, university.

The data from the study were analyzed by SPSS vs.18 (PASW) and presented with 95% confident intervals (CI).

RESULTS

A total of 2201 patients with clinical symptoms of UTI were investigated in this study and 86% of them were female and 14% were male. 187(8.49%) of cases had positive urine culture and 2014 (91.5%) ones did not have significant bacteriuria or bacterial count of their urine samples were very low.

Table 1: Frequency of occurrence of community-acquired uropathogens

Organisms	No. of isolates (%)
E. coli	*103(55.1%)*
Entrobacter spp.	*25(13.36%)*
Staphylococcus aureus	*22(11.76%)*
Streptococcus spp.	*11(5.88%)*
Coagulase-Negative staphylococci[1]	*10(5.3%)*
Proteus spp.	*7(3.7%)*
Klebsiella spp.	*3(1.6%)*
Enterococcus spp.	*3(1.6%)*
Pseudomonas spp.	*2(1.06%)*
serashia	*1(0.53%)*

[1] includes *S. saprophyticus* (6) and *S. epidermidis* (4)

Table 2: Antimicrobial susceptibility of community-acquired uropathogens (Note that intermediate categories were not mentioned)

	E.coli (103)		*Enterobacter spp. (25)*		*S. aureus (22)*		*Streptococcus spp.(11)*		*CoNs (10)*		*Proteus spp.(7)*		*Klebsiella spp.(3)*		*Enterococcus spp.(3)*		*Pseudomonas spp.(2)*	
	#T [1]	%S[2]	#T	%S	#T	%S	#T	%S	#T	%S	#T	%S	#T	%S	#T	%S	#T	%S
Ciprofloxacin	103	78	25	75	22	60	11	33.6	10	60	6	25	3	100	2	50	2	0
Norfloxacin	90	76.6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Nalidixic acid	103	56.4	22	50	16	0	-	-	-	-	-	-	2	0	3	0	-	-
Gentamicin	90	82.5	25	76.4	22	84.2	11	14.2	10	88.8	7	85.7	3	66.6	3	100	2	0
Nitrofurantoin	101	85.7	24	30	18	75	9	60	-	-	6	16.6	-	-	3	100	-	-
Cephalexin	98	44.9	19	35.7	18	66.6	10	75	10	50	6	50	3	100	2	50	1	0
Trimethoprim-Sulfamethoxazole	103	50.5	25	59	22	25	11	11.1	10	28.5	7	20	2	0	3	33.3	2	0
Erythromycin	-	-	-	-	16	35.7	11	25	-	-	-	-	-	-	2	0	-	-
Ampicillin	103	0	20	15.3	18	0	-	-	-	-	-	-	-	-	2	0	-	-
Tetracycline	83	41.9	21	58.3	20	15.3	11	12.5	10	12.5	6	16.6	2	100	-	-	2	0
Cefotaxime	103	81.9	-	-	-	-	9	40	8	50	6	66.6	-	-	1	0	2	0
Cefixime	103	75.6	25	44.4	-	-	-	-	10	10	5	40	2	50	2	50	-	-
Imipenem and Ceftizoxime	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	100

1) Number of isolates tested against each antimicrobial agent

2) Percent of isolates susceptible to antimicrobial agent

Ten types of microorganisms were isolated from positive urine cultures. The most common isolates were *E. coli* (55%), followed by Entrobacter (13.36%), *S.* Aureus (11.76%) and Streptococcus (5.88%) (Table 1).

Results of antibiotic susceptibility of the isolates were shown in table 2. *E. coli* sensitivity to antibiotics varied from 41.9% for tetracycline to 85.7% for Nitrofurantoin. Ampicillin was reported as the most resistant antibiotic for *E. coli* (100%).

Entrobacter spp. showed the highest sensitivity to Gentamicin (76.4%) and the highest resistance to Ampicillin (84.7%).

S. aureus had the highest sensitivity to Gentamicin (84.2%) and the highest resistance to Ampicillin (100%) and Nalidixic Acid (100%).

Pseudomonas spp. included only 1% of the isolates and was susceptible to Imipenem (100%) and 100% resistant to many antibiotics.

DISCUSSION

This study provides valuable data to comparison and monitor status of antimicrobial resistance among uropathogens to improve efficient empirical treatment. All around the world increasing antimicrobial resistance has been documented [10, 14-20].

Main international guidelines recommend empirical therapy in UTI [1, 21]. The efficacy of such empirical therapy depends on periodic assessment of antimicrobial resistance profile. Although the spectrum of bacteria isolated from patients with UTI around the world has remained largely unchanged in which *Escherichia coli* is most prevalent microorganism, there have been significant changes in the resistance patterns of uropathogens over the past few decades and antibiotic resistance has become a major problem in UTI [10].

In the present study, *E. coli* was the most common isolated uropathogen. Enterobacter spp., *Staphylococcus aureus* and streptococcus were reported in second to forth degree of prevalence in our investigation. The prevalence of bacterial species isolates is similar to those described in several pervious studies [5, 17, 22-26].

The frequency of UTI is greater in female as compared to male just like our study which showed that female in outpatients were more affected than males [4, 10, 17].

Nitrofurantoin, Gentamicin and Ciprofloxacin had minimum antimicrobialresistance rate in our investigation. Pervious Iranian studies report similar results [14, 18, 19].

An important resistance to Trimethoprim-Sulfamethoxazole was reported in our study that is similar to other studies in Iran and worldwide. It indicated the emergence of high levels of Trimethoprim-Sulfamethoxazole resistance in a significant percentage of community-acquired *E. coli* UTI isolates [15, 16, 26, 27].

E. coli showed resistance to the Fluoroquinolones that used in our study (Ciprofloxacin and Norfloxacin).This finding is similar to studies conducted in Spain and Europe and other Iranian studies [20,30]. Gobermado *et al*. [30] showed reducing susceptibility of *E. coli* isolated from patients with UTI to TMP-SMX (26%) and Fluoroquinolones (16%) in Spain. This reducing susceptibility might be due to using antibiotics without restriction.

In several studies it has been shown that the prescribing habits of the physicians are the driving factor for the antibiotic resistance [31-33]. Goettsche *et al*. [32] reported that the resistance against FQ is strongly associated with a high number of prescriptions for this group of antibiotics.

This finding may be related to the empirical treatment of UTI with FQ for first line antibiotic in Iran and around the world. McEwen *et al*. [35] found that 37% of physicians actually prescribe TMP-SMX, closely followed by FQ (32%) and average duration of antibiotic therapy is 8.6 days in the United States. Because of these problems, empiric use of FQ should be restricted and foundation the strategies against increasing resistance of pathogens to these antibiotics should be done.

Nitrofurantoin represented better activity against *E. coli* isolates, but this drug would not be recommended for serious upper urinary tract infections or for those cases with systemic involvement [36].

In this study, Ampicillin resistance rate was more than 90%. The beta (β)-lactam Antibiotics such as Ampicillin has other problems beside resistance [14].

The other reason is that β-lactams are relatively ineffective in clearing Gram-negative rods from the vaginal and colonic mucosa, thus possibly predisposing to recurrences when used to treat UTI [21, 36]. According to pervious studies high rate of resistance to Ampicillin was reported in several countries such as Senegal(77%), Spain (65%), Taiwan (80%), India (88%) and Iran (88%) [14, 37-40].

Limitation: The data of our retrospective study were collected from general laboratory of Najaf Abad, Iran. It was restricted to patients who could pay for medical costs and also all of patient samples did not have enough uropathogens for antimicrobial susceptibility test because most patients were initially treated empirically for their UTI.

Because of increasing the resistance of FQ, prescription of FQ should be restricted for UTI. Nitrofurantoin should be used for first line empirical treatment in UTI instead of FQ, TMP-SMX.

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