Original Article

Urinary tract pathogens and their antibiotic susceptibility patterns in different age and gender groups at a tertiary care hospital of Peshawar, Pakistan

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Objective: To investigate frequency of various urinary tract infections (UTI) pathogens and their antibiotic susceptibility in patients of different age and gender groups at a tertiary care hospital in Peshawar.

Methodology: This descriptive cross-sectional study was carried out at Khyber Teaching Hospital, Peshawar from January 2014 to September 2015. Total of 787 urine cultures were performed using conventional microbiological techniques. Biochemical techniques were used to identify the organisms and antibiotic sensitivity was determined by Kirby-Bauer and Minimum Inhibitory Concentration methods

Results: Out of 787 samples cultured, 458 (58.2%) were positive and were included in study. Age ranged from 1 year to 111 years (mean 41.7). 314 (68.6%) were female and 144 (31.4%) male. UTI was commoner in female (68.6%) than male (31.4%). E. coli was the most common pathogen and accounted for 76.6% of all growths. Up to age 10 years Enterobacter spp., (25%) and between age 41-50 years Morganella spp., (8.3%) were second common pathogens in females. In rest of all age groups Citrobacter spp., were second common pathogens accounting for 10.5% of all positive cultures. Morganella spp., (5.0%), Pseudomonas spp., (3.5%), Enterobacter spp., (1.3%), Klebsiella spp., (1.1%), Staphylococcus aureus (0.9%), Proteus spp., (0.7%) and Streptococcus faecalis (0.4%) were present in less than 13% cases. E. coli was sensitive to Imipenem (98.6%), Meropenem (97.8%), Tazobactam (96.2%), Cefoperazone+sulbactam (93.9%) and Amikacin (92.5%) and was resistant to Nalidixic acid (91.7%) and Ampicillin (90.8%). Citrobacter spp., had sensitivity to Amikacin (93.8%), Meropenem (93.8%) and Imipenem (93.0%) and was absolutely resistant to Ampicillin (100%)

Conclusion: Common uropathogens were E. coli and Citrobacter spp. All gram-negative uropathogens were sensitive to Imipenem, Meropenem, Tazobactam, Cefoperazone+ sulbactam and Amikacin. There was high resistance to Penicillin, Cephalosporin, and Fluoroquinolones. (Rawal Med J 201;42:181-187)

Keywords: Urinary tract infection, UTI, Escherichia coli, antibiotic resistance.

INTRODUCTION

Urinary Tract Infection (UTI) is a common infection worldwide. Except for infants and old age, it commonly affects females.[1] The annual incidence of UTI in females is about 12% and it is estimated that by end of 32 years 50% of all females have at least one UTI episode[2] while 50-80% of females experience UTI at least once or twice in their lives. About 20-30% of women who have had one episode of UTI will have recurrent episodes.[1] UTI are leading cause of gram-negative bacteremia in patients of all ages and are associated with a high risk of morbidity and mortality, especially in the elderly, and account for significant health care costs.[3]

The most common pathogen identified in the adult population is Escherichia coli.[3] Other gram-negative bacteria including Klebsiella spp., Enterobacter spp., Pseudomonas aeruginosa and Proteus spp., and gram-positive organisms including Staphylococci and Streptococci account for 5 to 15% of all the cases of UTI.[4] The resistance

of uropathogens to antibiotics is on the rise and is linked to significantly worse clinical outcomes.[5] Choice of antibiotics depends upon the type of organism isolated and its antibiotic susceptibility pattern. Therefore, knowledge of antimicrobial resistance trends among isolates of uropathogens is essential to provide clinically appropriate and cost effective therapy.

In Pakistan, the situation is worse and will deteriorate further due to quackery, self-medication, and poverty, lack of hospital antibiotic policy and prescriptions of antibiotics by general physicians without isolation and sensitivity for pathogens. With the constantly shifting trends in drug resistance, antibiotic options and pharmacoeconomic considerations, knowledge of the frequency of causative organisms and their susceptibility patterns require re-appraisal from time to time for effective treatment. This clinical laboratory based study analyzes uropathogens and their current trends in drug susceptibility in gender specified age groups.

METHODOLOGY

This descriptive cross-sectional study was conducted at Khyber Teaching Hospital (KTH) under the supervision of medical B ward in collaboration with microbiology department KTH from January 2014 to September 2015._Ethical approval was taken from hospital ethical committee and total of 787 patients were included in the study. One fresh midstream urine specimen was collected per patient, through aseptic measures, from suspected urinary tract infected cases. Patients included were of any age, from outpatient or inpatient departments, with urinary symptoms (fever with vomiting, urinary frequency, burning micturition, flank pain) and >10 pus cells on urine microscopy were considered to have UTI.

The specimens were processed immediately in the laboratory for physical and chemical examination and microscopy for cells. Specimen were cultured on MacConkey agar and blood agar media. The plates showing significant growth as per Kass count[6] were processed further. Identification of isolates was done by a standard method depending on observation of colony characteristics, gram-stain as well as using biochemical tests for further identification. Specimens which grew more than one type of colonies and the specimens whose age or sex record were not available were excluded. Lactobacilli and coagulase-negative Staphylococci were considered as contaminants and were also excluded from the study.

Susceptibility to antimicrobial agents was determined both by Disc Diffusion method of Kirby-Bauer and Minimum Inhibitory Concentration (MIC) method on Muller-Hinton agar as described by the Clinical Laboratory Standard Institute (CLSI) (CLSI, 2014).[7] The antibiotics used for antibiogram determination of the collected strains were: ampicillin ticarcillin, co-amoxiclav, tazobactam, ceftriaxone, cefixime, cefotaxime cefoperazone, ceftazidime, cefepime cefoperazone-sulbactam norfloxacin, ciprofloxacin, ofloxacin, enoxacin, moxifloxacin, sparfloxacin, nalidixic acid, meropenem, imipenem, aztreonam, pipemedic acid, sulphamethoxazole + trimethoprim, gentamicin and amikacin. Statistical analysis was done using SPSS v. 23.

RESULTS

Out of 787 urine samples 458 (58.2%) samples grew significant positive growths. Samples contributed by male and female patients were 144 (31.4%) and 314 (68.6%), respectively with the male to female ratio of 1:2.2. Samples collected from admitted patients were 290 while 168 cases came from OPD.

Table 1. Age and gender distribution.

Age Groups	Male n=144	%	Female n=314	%
0-10	5	3.5	8	2.5
11-20	24	16.7	48	15.3
21-30	27	18.8	46	14.6
31-40	20	13.9	45	14.3
41-50	20	13.9	60	19.1
51-60	21	14.6	62	19.7
61-70	13	9.0	24	7.6
71-80	11	7.6	20	6.4
>80	3	2.1	1	0.3

Table 2. Micro-organism growth in culture media.

Gram staining	Micro-organisms	Male n=144	Female n=314	n= 458 n (%)
		n (%)	n (%)	
Gram negative	Escherichia coli	108 (75)	243 (69.2)	351 (76.6)
	Citobacter	20 (13.9)	28 (58.3)	48 (10.5)
	Morganella	4 (2.8)	19 (82.6)	23 (5.0)
	Pseudomonas	6 (4.2)	10 (62.5)	16 (3.5)
	Enterobacter	1 (0.7)	5 (83.3)	6 (1.3)
	Klebsiella	2 (1.4)	3 (60)	5 (1.1)
	Proteus	2 (1.4)	1 (33.3)	3 (0.7)
Gram positive	Staphylococcus aureus	1 (0.7)	3 (75)	4 (0.9)
	Streptococcus faecalis	0 (0.0)	2 (100)	2 (0.4)

The minimum age was 1 year and the maximum was 111 years with mean age of 41.7 years. Below 11 and above 60 years UTI appeared to be more common in male (3.5% and 18.7%) than female (2.5% and 14.3%), respectively (Table 1). The ratio between gram negative and gram positive organisms was 75.3:1. E. coli was the most common pathogen in both genders (male 75% and female 69.2%) and accounted for 76.6% of all the growths, followed by Citrobacter spp., (male 13.9% and female 58.3%) accounting for 10.5% of all positive cultures. While Morganella spp., (5.0%), Pseudomonas spp., (3.5%), Enterobacter spp., (1.3%), Klebsiella spp., (1.1%), Staphylococcus aureus (0.9%), Proteus spp., (0.7%) and Streptococcus faecalis (0.4%) were present in less than 13% cases (Table 2).

Common pathogens in male until 10 years of age were E. coli (40%) and Citrobacter spp., (40%), while in female there were E. coli (37.5%) and Enterobacter spp., (25%). E. coli remained common in all age and gender groups. Between 41-50 years Morganella spp., (8.3%) was second common pathogen after E. coli in females. Above 80 years only E. coli was present. In remaining of age and gender groups Citrobacter spp., was second common growth (Table 3).

E. coli was highly sensitive to Imipenem (98.6%) followed by Meropenem (97.8%), Tazobactam (96.2%), Cefoperazone+sulbactam (93.9%) and Amikacin (92.5%). Among cephalosporin resistance pattern was: Cefepime (43.3%), Ceftazidime (45.8%), Cefoperazone (69.2%), Cefotaxime (72.6%), Cefixime (76.1%) and Ceftriaxone (78.0%). Resistance to fluoroquinolones tested was almost similar Highest resistance was found against Nalidixic acid (91.7%) and Ampicillin (90.8%) and significant resistance were also found against sulphamethoxazole + trimethoprim (Co-Trimoxazole) (67.2%) (Table 4). Citrobacter spp., had similar sensitivity to Amikacin (93.8%), Meropenem (93.8%) and Imipenem (93.0%) and was absolutely resistant to Ampicillin (100%).

DISCUSSION

UTI is a common clinical problem in both the community and healthcare-associated settings and is responsible for significant morbidity and mortality.[8] Its prevalence varies according to gender and age,[9] being more common in female during reproductive age. They account for 25% of all antibiotic prescriptions in general practice.[10] In our study, UTI was found to be more prevalent in female with the male to female ratio of 1:2.18, which is almost same as the study by Ahmad et al.[11]

In majority patients, UTI was found to be due to E. coli, followed by Citrobacter spp**,** Morganella spp, Pseudomonas spp, Enterobacter spp, Klebsiella spp, Staphylococcus aureus, Proteus spp and Streptococcus faecalis. Malik et al also reported E. coli and Citrobacter freundii (8.08%) to be the most frequent organisms involved in UTI**.**[12] But the prevalence of other organisms were different in the said study. Abdullah et al[13] reported E. coli, Klebsiella pneumoniae, Staphylococcus aureus, Pseudomonas aeruginosa, Enterobacter spp, Enterococcus faecalis, Proteus mirabilis, Streptococcus agalactiae and Salmonella spp. Kashef et al reported E. coli, Proteus spp, and Klebsiella spp from Iran[14] while Chowdhury et al reported E. coli, Klebsiella spp, Proteus spp, Pseudomonas spp, Enterobacter spp, Citrobacter spp and Morganella morganelli causing UTI.[15] The difference in pathogens so reported may be due to several population attributes, sample size and hygienic conditions of the patients but more importantly it reflects the changing spectrum of microbiome involved in UTI.

Table 3. Micro-organism growths in gender specified age groups.

Age Groups	Gender	E. coli n=351	Citrobacter n=48	Morganella n=23	Pseudomonas n=16	Enterobacter n=6	Klebsiella n=5	Staph aureus n=4	Proteus n=3	Strep fecalis n=2	Total 458
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
0-10	**M**	2 (40)	2 (40)	-	-	1 (20)	-	-	-	-	5
	F	3 (37.5)	1 (12.5)	1 (12.5)	1 (12.5)	2 (25)	-	-	-	-	8
11-20	**M**	21 (87.5)	2 (8.3)	-	1 (4.2)	-	-	-	-	-	24
	F	34 (70.8)	7 (14.6)	4 (8.3)	3 (6.3)	-	-	-	-	-	48
21-30	**M**	20 (74.1)	3 (11.1)	-	2 (7.4)	-	-	1 (3.7)	1 (3.7)	-	27
	F	32 (69.6)	7 (15.2)	3 (6.5)	1 (2.1)	-	1 (2.1)	-	1 (2.1)	1 (2.1)	46
31-40	**M**	13 (65.0)	4 (20.0)	1 (5.0)	2 (10.0)	-	-	-	-	-	20
	F	35 (77.8)	3 (6.7)	1 (2.2)	1 (2.2)	2 (4.4)	2 (4.4)	1 (2.2)	-	-	45
41-50	**M**	17 (85.0)	2 (10.0)	1 (5.0)	-	-	-	-	-	-	20
	F	50 (83.3)	2 (3.3)	5 (8.3)	1 (1.7)	-	-	1 (1.7)	-	1 (1.7)	60
51-60	**M**	11 (52.4)	5 (23.8)	2 (9.5)	1 (4.8)	-	1 (4.8)	-	1 (4.8)	-	21
	F	47 (75.8)	7 (11.3)	3 (4.8)	3 (4.8)	1 (1.6)	-	1 (1.6)	-	-	62
61-70	**M**	13 (100)	-	-	-	-	-	-	-	-	13
	F	22 (91.7)	1 (4.2)	1 (4.2)	-	-	-	-	-	-	24
71-80	**M**	8 (72.7)	2 (18.2)	-	-	-	1 (9.1)	-	-	-	11
	F	19 (95)	-	1 (5.0)	-	-	-	-	-	-	20
>80	**M**	3 (100)	-	-	-	-	-	-	-	-	3
	F	1 (100)	-	-	-	-	-	-	-	-	1

Table 4. Antibiotics susceptibility for uropathogens.

Organisms	E. Coli		Citrobacter		Morganella		Pseudomonas		Enterobacter		Klebsiella		Staph aureus		Proteus		Streptococcus fecalis	
Antibiotics	**S[1](%)**	**R[2](%)**	**S(%)**	**R(%)**	**S(%)**	**R(%)**	**S (%)**	**R (%)**	**S (%)**	**R (%)**	**S (%)**	**R (%)**	**S (%)**	**R (%)**	**S (%)**	**R (%)**	**S (%)**	**R (%)**
Imipenem	98.6	1.4	93.0	7.0	94.1	5.9	58.3	41.7	100	0.0	100	0.0	100	0.0	100	0.0	0.0	100
Meropenem	97.8	2.2	93.8	6.3	100	0.0	61.5	38.5	100	0.0	100	0.0	100	0.0	100	0.0	-	-
Tazobactum	96.2	3.8	83.9	16.1	94.1	5.9	66.7	33.3	75.0	25.0	100	0.0	-	-	100	0.0	0.0	100
Cefoperazonesulbactam	93.9	6.1	89.1	10.9	100	0.0	64.3	35.7	100	0.0	100	0.0	66.7	33.3	100	0.0	-	-
Amikacin	92.5	7.5	93.8	6.3	91.3	8.7	75.0	25.0	83.3	16.7	100	0.0	50.0	50.0	100	0.0	-	-
Gentamicin	69.1	30.9	65.0	35.0	83.3	16.7	50.0	50.0	50.0	50.0	66.7	33.3	-	-	100	0.0	-	-
Cefepime	56.7	43.3	57.1	42.9	88.2	11.8	63.6	36.4	50.0	50.0	80.0	20.0			50.0	50.0	-	-
Ceftazidime	54.2	45.8	51.7	48.3	76.5	23.5	50.0	50.0	100	0.0	80.0	20.0	-	-	100	0.0	-	-
Co-Amoxiclav	50.2	49.8	45.9	54.1	78.9	21.1	26.7	73.3	33.3	66.7	75.0	25.0	66.7	33.3	100	0.0	0.0	100
Ticarcillin	42.7	57.3	45.5	54.5	0.0	100	25.0	75.0	0.0	100	-	-	0.0	100	100	0.0	-	-
Aztreonam	40.8	59.2	40.5	59.5	52.6	47.4	53.8	46.2	50.0	50.0	60.0	40.0	0.0	100	100	0.0	-	-
Co-Trimoxazole	32.8	67.2	15.8	84.2	0.0	100	12.5	87.5	0.0	100	-	-	-	-	100	0.0	0.0	100
Cefoperazone	30.8	69.2	32.4	67.6	41.2	58.8	50.0	50.0	50.0	50.0	33.3	66.7	50.0	50.0	100	0.0	-	-
Cefotaxime	27.4	72.6	28.1	71.9	44.4	55.6	26.7	73.3	33.3	66.7	100	0.0	75.0	25.0	66.7	33.3	-	-
Moxifloxacin	25.6	74.4	37.8	62.2	52.9	47.1	30.8	69.2	40.0	60.0	50.0	50.0	0.0	100	50.0	50.0	-	-
Cefixime	23.9	76.1	11.4	88.6	33.3	66.7	9.1	90.9	0.0	100	60.0	40.0	0.0	100	100	0.0	-	-
Ceftriaxone	22.0	78.0	17.2	82.8	33.3	66.7	8.3	91.7	0.0	100	100	0.0	-	-	100	0.0	0.0	100
Ciprofloxacin	20.7	79.3	38.3	61.7	47.8	52.2	46.7	53.3	40.0	60.0	40.0	60.0	0.0	100	100	0.0	0.0	100
Sparfloxacin	19.9	80.1	41.5	58.5	54.5	45.5	54.5	45.5	50.0	50.0	60.0	40.0	0.0	100	100	0.0	-	-
Ofloxacin	19.7	80.3	36.4	63.6	52.2	47.8	63.6	36.4	50.0	50.0	40.0	60.0	0.0	100	100	0.0	-	-
Norfloxacin	19.1	80.9	33.3	66.7	58.8	41.2	33.3	66.7	100	0.0	50.0	50.0	-	-	100	0.0	0.0	100
Enoxacin	18.2	81.8	42.4	57.6	55.6	44.4	40.0	60.0	50.0	50.0	50.0	50.0	0.0	100	100	0.0	-	-
Pipemedic Acid	13.8	86.2	29.6	70.4	47.1	52.9	0.0	100	0.0	100	80.0	20.0	-	-	100	0.0	-	-
Ampicillin	9.2	90.8	0.0	100	0.0	100	0.0	100	0.0	100	-	-	-	-	-	-	-	-
Nalidaxic acid	8.3	91.7	30.8	69.2	50.0	50.0	0.0	100	33.3	66.7	-	-	-	-	-	-	-	-

1. SENSITIVE. 2. RESISTANT

Antimicrobial resistance is a growing problem and cause of great concern throughout the world.[16] The pattern of resistance of the micro-organisms causing UTI vary from place to place and from time to time. Knowledge of local antibiotic susceptibility is of utmost importance for prescribing appropriate treatment. In our study, E. coli was found to be highly sensitive to Imipenem , Meropenem, Tazobactam, Cefoperazone+sulbactam and Amikacin and highest resistance were present against Nalidixic acid and Ampicillin. E. coli had low sensitivity level for commonly prescribed antimicrobials including cephalosporin and fluoroquinolones. This antibiotic susceptibility pattern is quite similar with the studies by Mehr et al[17] and Deepthy et al.[18]

Citrobacter spp., was second most common uropathogens identified being sensitive to Amikacin, Meropenem, Imipenem and Cefoperazone+sulbactam and resistant to Co-Trimoxazole and Ampicillin. Susceptibility pattern was almost similar to a study by Bawankar et al.[19]

The major limitation of the study is that it did not distinguish complicated, uncomplicated or recurrent UTI cases, the distribution of organisms in the community acquired UTI and nosocomial UTI. As a result, the prevalence of microorganisms and their resistance patterns in the mentioned cases could not be ascertained.

CONCLUSION

E. coli was the predominant pathogen causing UTIs in our population followed by Citrobacter spp. The majority of the isolates of E. coli, Citrobacter spp., and other gram-negative enterobacteria causing UTI were sensitive to Imipenem, Meropenem, Tazobactam, Cefoperazone+sulbactam and Amikacin. Resistance to Penicillin, Cephalosporin and Fluoroquinolones were high among gram-negative uropathogens. Routine monitoring studies should be conducted in different parts of the country to provide surveillance data along with antibiogram for empirical treatment of UTIs and for the preparation of antibiotic policy for UTI.

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