ORIGINAL ARTICLE

Antibiotics susceptibility patterns of uropathogenic E. coli with special reference to fluoroquinolones in different age and gender groups

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Abstract

Objectives: To identify frequency of uropathogenic Escherichia coli and its antibiotic susceptibility pattern.

Methods: This cross-sectional study was conducted at Khyber Teaching Hospital, Peshawar, Pakistan, from January 2014 to September 2015, and comprised urine specimens. Biochemical techniques were used to identify Escherichia coli and antibiotic susceptibility was determined by Kirby-Bauer disk diffusion and minimum inhibitory concentration methods. SPSS 23 was used for data analysis.

Results: Of the 787 urine samples, 458(58.2%) grew significant positive growths. Escherichia coli growths were present in 351(76.6%) positive cultures of which 108(30.8%) came from males and 243(69.2%) from female patients. Resistance to fluoroquinolones tested was almost similar ($p>0.05$). Escherichia coli was highly sensitive to imipenem (98.6%), meropenem (97.8%), tazobactum (96.2%), cefoperazone+sulbactam (93.9%) and amikacin(92.5%).

Conclusion: Escherichia coli was a common pathogen causing urinary tract infections and was highly sensitive to imipenem, meropenem, tazobactum, cefoperazone+sulbactam and amikacin.

Keywords: Urinary tract infection, Escherichia coli, Antibiotic sensitivity, Antibiotic resistance, Fluoroquinolones.

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Introduction

Urinary tract infections (UTIs) are amongst the highly prevalent infectious diseases worldwide. They affect approximately 150 million people annually and cause more than 6 billion US dollars healthcare cost to the global economy.[1,2] In general practice uncomplicated UTI are common and account for 25% of all antibiotic prescriptions.[3]

Escherichia coli (E. coli) is the most common causative agent of UTI.[4] Throughout the world, E. coli resistance is increasing both in community and health care settings,[5] causing limited choice of effective antibiotics.[6] Fluoroquinolones (FQs) are commonly prescribed for empirical treatment of UTI.[6] But over-prescription of FQs has led to their increasing resistance worldwide in recent years, particularly in gram-negative bacteria.[7,8] In many parts of the world, Enterobacteriaceae have variable resistance to FQs ranging from more than 50% in community-acquired uncomplicated UTI to up to 98% for strains causing community-acquired complicated UTI. Hospital-acquired UTI are less FQs sensitive than community acquired.[9] FQs-resistant uropathogenic E. coli are responsible for 20% of all hospital-acquired infections.[10]

Selection of antimicrobial drugs for empiric therapy depends upon the susceptibility pattern of organismisolated, current trends in antimicrobial susceptibility and the efficiency of commonly prescribed antibiotics in the given locality. Therefore, knowledge of the organisms involved and their antibiotics susceptibility trends are essential for prescribing appropriate and cost-effective treatments.

The situation is much worse in Pakistan due to the absence of surveillance data, non-evidence based prescriptions, over-the-counter availability and injudicious use of antibiotics, and incomplete courses along with over- and under-dosing of antimicrobials. Knowledge of frequency of causative organisms, current trends in drug resistance, antibiotic options and pharmacoeconomic considerations require regular assessment from time to time for effective therapy.

The current study was planned to provide resistance patterns of uropathogenic E. coli to various antibiotics with special reference to FQs.

Materials and Methods

This cross-sectional study was conducted at Khyber Teaching Hospital (KTH) under supervision of medical B ward in collaboration with the microbiology department, Peshawar, Pakistan, from January 2014 to September 2015, and comprised urine specimens.

Fresh midstream urine specimens were collected through aseptic measures from suspected urinary tract infected

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cases. Patients of any age who came through outpatient or inpatient departments and whose routine urine examination revealed numerous pus cells on microscopy were included. The consecutive sampling was used and one urine sample was collected per patient.

Specimens were cultured on MacConkey agar and blood agar media, using calibrated loop, delivering 0.01ml of the sample and incubated aerobically for 24 hours at 37°C. The plates showing significant growth as per Kass count were processed further.[11] Identification of E. coli was done by 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.

Susceptibility to antimicrobial agents was determined both by disk diffusion method of Kirby-Bauer and minimum inhibitory concentration (MIC) method on Muller-Hinton agar as described by the Clinical Laboratory Standard Institute (CLSI) 2014.[12] Antibiotics used for antibiogram determination of the collected strains among FQ were: norfloxacin, ciprofloxacin, ofloxacin, enoxacin, moxifloxacin, and sparfloxacin and nalidixic acid. Other antibiotics tested were: imipenem, meropenem, tazobactum, amikacin, cefoperazone sulbactam, gentamicin, cefepime, ceftazidime, co-amoxiclav, ticarcillin, aztreonam, cefoperazone, co-trimoxazole, cefotaxime, cefixime, ceftriaxone, pipemidic acid and ampicillin.

SPSS 23 was used for data analysis. The subjects were divided into four age groups and comparison among the groups was made using chi-square test. P<0.05 was considered significant.

Results

Of the 787 urine samples, 458(58.2%) grew significant positive growths. E. coli growths were present in 351(76.6%) positive cultures and included 108(30.8%) male and 243(69.2%) female patients with male-to-female ratio of 1:2.2. Samples collected from admitted patients were 232(66.1%) while 119(33.9%) cases came from the outpatient department. The overall mean age was 43.1±20 years (range: 1-111 years). Mean age of male subjects was 41±22.1 years and of female subjects was 44±18.9years. The subjects were divided into four groups: 30(8.55%) children (aged1-15 years), 106(30.2%) young adults (aged16-35 years), 116(33%) middle-aged adults (aged 36-55 years), and 99(28.2%) older adults (aged above 55 years).

E. coli had similar frequency among males and females in

Table-1: E. coli antibiotic sensitivity and resistance.

Antibiotics		Male	Female	Total
Imipenem	S[1] %	97.6	99.0	98.6
	R[2] %	2.4	1.0	1.4
Meropenem	S %	98.0	97.7	97.8
	R %	2.0	2.3	2.2
Tazobactum	S %	96.0	96.3	96.2
	R %	4.0	3.7	3.8
Amikacin	S %	88.8	94.1	92.5
	R %	11.2	5.9	7.5
Cefoperazone sulbactam	S %	92.3	94.6	93.9
	R %	7.7	5.4	6.1
Gentamicin	S %	70.5	68.4	69.1
	R %	29.5	31.6	30.9
Cefepime	S %	53.0	58.5	56.7
	R %	47.0	41.5	43.3
Ceftazidime	S %	58.2	52.2	54.2
	R %	41.8	47.8	45.8
Co-Amoxiclav	S %	44.2	52.9	50.2
	R %	55.8	47.1	49.8
Ticarcillin	S %	19.0	50.8	42.7
	R %	81.0	49.2	57.3
Aztreonam	S %	39.3	41.3	40.8
	R %	60.7	58.7	59.2
Cefoperazone	S %	27.7	32.1	30.8
	R %	72.3	67.9	69.2
Co-Trimoxazole	S %	40.5	29.1	32.8
	R %	59.5	70.9	67.2
Cefotaxime	S %	22.1	30.1	27.4
	R %	77.9	69.9	72.6
Moxifloxacin	S %	21.8	27.4	25.6
	R %	78.2	72.6	74.4
Cefixime	S %	16.7	27.4	23.9
	R %	83.3	72.6	76.1
Ceftriaxone	S %	19.7	23.0	22.0
	R %	80.3	77.0	78.0
Ciprofloxacin	S %	20.6	20.8	20.7
	R %	79.4	79.2	79.3
Sparfloxacin	S %	20.7	19.5	19.3
	R %	79.3	80.5	80.1
Ofloxacin	S %	20.4	19.3	19.7
	R %	79.6	80.7	80.3
Norfloxacin	S %	17.7	19.7	19.1
	R %	82.3	80.3	80.9
Enoxacin	S %	21.5	16.6	18.2
	R %	78.5	83.4	81.8
Pipemidic Acid	S %	14.7	13.5	13.8
	R %	85.3	86.5	86.2
Ampicillin	S %	13.3	7.4	9.2
	R %	86.7	92.6	90.8
Nalidaxic acid	S %	7.4	8.8	8.3
	R %	92.6	91.2	91.7

S: Sensitivity
R: Resistance.

Table-2: Fluoroquinolones susceptibility patterns in different age and gender groups.

Antibiogram		Children (1-15 years)			Young adults (16-35 years)			Middle aged adults (36-55 years)			Older adults (>55 years)		
		Male	Female	P	Male	Female	p	Male	Female	p	Male	Female	p
Ciprofloxacin	S1 (%)	55.6	25.0	0.739	15.8	29.5	0.014	11.5	19.3	0.002	24.1	14.9	0.467
	R2 (%)	44.4	75.0	0.007	84.2	70.5	0.204	88.5	80.7	<0.05	75.9	85.1	<0.05
Ofloxacin	S (%)	55.6	16.7	0.479	18.9	28.8	0.088	8.7	16.0	0.007	20.8	15.8	0.285
	R (%)	44.4	83.3	0.011	81.1	71.2	0.392	91.3	84.0	<0.05	79.1	84.2	0.0003
Norfloxacin	S (%)	0.0	20.0	-	18.7	31.1	0.073	9.5	16.4	0.007	26.1	14.5	0.592
	R (%)	100.0	80.0	0.131	81.3	68.9	0.507	90.5	83.6	<0.05	73.9	85.5	0.0001
Enoxacin	S (%)	50.0	20.0	0.705	15.6	26.3	0.196	15.0	10.6	0.205	26.3	15.9	0.563
	R (%)	50.0	80.0	0.045	84.4	73.7	0.507	85.0	89.4	<0.001	73.7	84.1	0.001
Sparfloxacin	S (%)	55.6	16.7	0.479	13.9	30.6	0.025	15.0	16.9	0.020	22.7	14.0	0.405
	R (%)	44.4	83.3	0.011	86.1	69.4	0.710	85.0	83.1	<0.05	77.3	86.0	<0.05
Moxifloxacin	S (%)	83.3	29.4	1	16.1	38.6	0.010	14.3	22.4	0.012	20.0	22.4	0.070
	R (%)	16.7	70.6	0.002	83.9	61.4	0.890	85.7	77.6	0.0006	80.0	77.6	0.002
Nalidixic acid	S (%)	20.0	8.3	1	0.0	14.3	-	0.0	4.8	-	26.1	8	1
	R (%)	80.0	91.7	0.070	100.0	85.7	0.841	100.0	95.2	0.001	73.9	85.5	0.165

S: Sensitivity
R: Resistance.

both children (i.e. 9(8.3%) and 21(8.6%), respectively) and older adults group (i. e. 31(28.7%) and 68(28%), respectively). E. coli was common among males in young adults 42(38.9%) than females 64(26.3%) while in middle-aged group it was more common among females 90(37%) than males 26(24.1%).

E. coli was highly sensitive to imipenem (98.6%), meropenem (97.8%), tazobactum (96.2%), cefoperazone+sulbactam (93.9%) and amikacin (92.5%). Among cephalosporin,the resistance pattern was: cefepime (43.3%), ceftazideme (45.8%), cefoperazone (69.2%), cefotoxime (72.6%), cefixime (76.1%) and ceftriaxone (78.0%). The highest resistance was found against nalidixic acid (91.7%) and ampicillin (90.8%) and significant resistance was also found against sulphamethoxazole + trimethoprim (co-trimoxazole) (67.2%).

Overall resistance to FQs tested was almost similar: moxifloxacin (74.4%) ciprofloxacin (79.3%), sparfloxacin (80.1%), ofloxacin (80.3%), norfloxacin (80.9%) and enoxacin (81.8%) with greater resistance to nalidixic acid (91.7%).

Antibiogram tested had almost similar sensitivity and resistance patterns both among males and females except for resistance to ticarcillin which was higher among males than females (87(81%) and 120(49.2%), respectively). Lower resistance in males was present for co-trimoxazole than females (64[59.5%] and 172[70.9%], respectively). Amikacin had higher resistance among males than females (12[11.2%] and 14[5.9%], respectively).

Female children had more resistance than males against moxifloxacin (p=0.002), ciprofloxacin (p=0.007), ofloxacin (p=0.011), sparfloxacin (p=0.011) and enoxacin (p=0.045). Norfloxacin had more resistance among male than female children (100% and 80%, respectively) but this resistance was not significant (p=0.131) (Table-1).

In young adults, better sensitivity was found among females than males for moxifloxacin (p=0.010), ciprofloxacin (p=0.014) and sparfloxacin (p=0.025). All tested FQs had higher, although statistically insignificant, resistance among males than females.

In the middle-aged group, males had significant resistance to all tested FQs than females (p<0.05), while sensitivity was significantly better (p<0.05) for FQs among females than males except for enoxacin and nalidixic acid.

In the old age group, significant resistance was found among females than males (p<0.05) against all tested FQs except for nalidixicacid (Table-2).

Discussion

UTI is a common clinical problem in both the community and health care-associated settings and is responsible for significant morbidity and mortality.[13] Its prevalence varies according to gender and age,[14] being more common in females during reproductive age while males are predominantly affected in extreme ages.[15]

Rising antimicrobials resistance is related with worse outcomes.[16] In our study, only 0.8% E. coli strains were sensitive to all tested antibiotics. Pattern of antimicrobial resistance of micro-organisms vary in both time and space. Local surveillance data is essential for prescribing appropriate treatment. In our study, E. coli was found to be highly sensitive to imipenem (98.6%), meropenem (97.8%), tazobactum (96.2%), cefoperazone + sulbactam (93.9%) and amikacin (92.5%) and highest resistance was found against nalidixic acid (91.7%) and ampicillin (90.8%). This antibiotic susceptibility pattern is almost similar to studies reported by Ullah F. et al.,[13] and Deepthy BJ et al.[17]

In gender groups comparison, most of the antimicrobials had similar resistance among males and females except for ticarcillin (81% and 49.2%), co-trimoxazole (59.5% and 70.9%) and amikacin (11.2% and 5.9%), respectively. A study conducted by Bashir MF et al.[18] found similar resistance for co-amoxiclav and tazobactum among females compared to our study, but other antibiotics comparisons among males and females were different from our study.

FQs are recommended as initial empirical therapy for uncomplicated UTI in areas where resistance to co-trimoxazole exceeds 20% and that to FQ is less than 10%.[19] E. coli had similar resistance to tested FQs: moxifloxacin (74.4%) ciprofloxacin (79.3%), sparfloxacin (80.1%), ofloxacin (80.3%), norfloxacin (80.9%) and enoxacin (81.8%). The highest resistance was found against nalidixic acid (91.7%). Reported resistance to ciprofloxacin andofloxacin was 62% and to enoxacin was 61%, in astudy.[13] Ali I. et al. reported resistance as: ciprofloxacin (60.8%), sparfloxacin (60.1%), and norfloxacin (58.7%).[20] Ciprofloxacin resistance was 73.04% in a study by Mandal J. et al.[21] Another study identified 79% of ciprofloxacin-resistant E. coli isolates in subjects aged 35 years and 21% in those aged below 35 years.[13]

During the reproductive age, UTI commonly affects females, but in children and older people their prevalence is higher among males.[15] In our study, FQs resistance was higher among female in children and older adults groups, but in young and middle-aged adults, FQs resistance was higher among male subjects. In middle-aged adults, female had significant sensitivity to FQs comparing to male. However, further studies are needed for better understanding of prevalence of FQs susceptibility in various age and gender groups.

The current study had a number of limitations, including the lack of patient-level data on the antimicrobial use.Moreover, complicated, uncomplicated or recurrent UTI cases were not distinguished. As a result, resistance patterns in the mentioned cases could not be ascertained.

Conclusion

E. coli was the common pathogen-causing UTI in our study and had good sensitivity to imipenem, meropenem, tazobactum, cefoperazone+sulbactam and amikacin. Overall FQs resistance was similar in both gender groups. However, higher resistance was present among females in extreme aged groups and in young and middle-aged groups resistance was much higher among males. Regular monitoring for prevalence of microorganisms and their resistance patterns and further clinical studies are required to develop local guidelines for effective therapies of the conditions that warrant antimicrobial treatments.

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