Original Article

Antimicrobial Susceptibility Patterns of Community-acquired Urinary Tract Infection

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Abstract:

Urinary tract infection (UTI) is one of the most common bacterial infections encountered by clinicians in developing countries. Area-specific monitoring studies aimed to find out the type of pathogens responsible for UTI and their resistance patterns may help the clinician to choose the correct empirical treatment. Therefore, the aim of this study was to determine the type and antibiotic resistance pattern of the urinary pathogens isolated from patients attending in a diagnostic centre from June 2008 to June 2010.

A diagnostic centre based cross sectional study was conducted. Urine samples were collected using the mid-stream "clean catch" method from 2244 clinically-suspected cases of UTI and tested bacteriologically using standard procedures. Antimicrobial susceptibility test was performed for isolated pathogens using Kirby-Bauer disk diffusion method according to clinical and laboratory standards institute guidelines.

Of the total 2244 mid-stream urine samples collected from suspected cases of UTI, only 161 (7.2%) were positive for pathogen. Mean age± SD was 42.4±24.57 in male and 39.67±18.67 in female. Male was 27.3% and female was 72.7% among all culture sensitive patients. The most common pathogens isolated were Escherichia coli (67.7%), others were Enterobacter (21.1%), Klebsiella pneumoniae (5.0%) and Pseudomonas (3.7%). E. coli and Klebsiella pneumoniae showed the highest percentage of resistance to Ampicillin (97.7%) then to Ciprofloxacin (63.1%) and Co-trimoxazole (58.1%). However, E. coli and K. pneumoniae were susceptible to Furadantin (90.6%) and Pivmecillinam (86.9%).

This study finding showed that E. coli isolates were the predominant pathogens and the presence of bacterial isolates with very high resistance to the commonly prescribed drugs that in turn leaves the clinicians with very few alternative options of drugs for the treatment of UTIs. Drug resistance among bacterial pathogens is an evolving process, routine surveillance and monitoring studies should be conducted to provide physicians knowledge on the updated and most effective empirical treatment of UTIs.

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Introduction:

Development of resistance to antimicrobial agents is an increasing problem world-wide[1]. Misuse of antibiotics may lead to antimicrobial resistance to E.coli and other bacteria causing UTI. Frequent UTI was defined as three or more UTIs during the preceding 3 months. Complicated UTI was diagnosed if the patient suffered from other active diseases in the urinary tract, e.g. tumors, stones and uncorrected congenital malformations, or frequent or recent use of a urinary catheter[2,3]. Upper UTI was diagnosed if clinical signs of pyelonephritis (fever and loin pain or tenderness with bimanual palpation) were present. Uncomplicated lower UTI was defined as significant UTI without the above-mentioned histories or infections in outpatient and emergency department setting. Lower (symptomatic and asymptomatic) uncomplicated UTI in women occurs sporadically, considered to reflect the bacterial ecology in a normal population [4,5].

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The prevalence of UTI varies according to sex and age [6]. It has been usually observed that UTI most commonly occurs in females and up to one-third of all women experience a UTI at some point during their lifetimes [7].

Materials & Methods:

The study was performed on 2244 suspected patients of UTI, who was investigated for Urine C/S attending in a renowned diagnostic centre, Dhaka from June 2008 to June 2010. A total of 2244 clean catch midstream urine samples were collected in a wide mouth sterile container from the study subjects who have not received antimicrobials within the previous 15 days. Then the bacterial uropathogens were isolated and tested for antimicrobial drug resistance pattern. Isolation of uropathogens was performed by a surface streak procedure on both blood and MacConkey agar (Oxoid Ltd. Bashingstore Hampaire, UK) using calibrated loops for semi quantitative method and incubated aerobically at 37 ^{0}C for 24 hours, and those cultures which becomes negative at the end of 24 hrs incubations were further incubated for 48 hours. A specimen was considered positive for UTI if a single organism was cultured at a concentration of 10^5 cfu/ml. Antimicrobial susceptibility of isolates was tested for all 21 bacterial uropathogens by the disk diffusion according to Clinical Laboratory Standards Institute (CLSI) guide lines. Data were entered and analyzed using SPSS version 12.0.1 windows.

Results:

A total of 2244 urine samples were analyzed for isolation and identification of bacterial isolates. Most of the cases were female 1435(63.9%) (Table I) Of these, 161 (7.2%) samples had significant bacteriuria and the remaining 2083 (92.8%) samples were either non-significant bacteriuria or had a very low bacterial count or were sterile urine (Table-II). Among the all culture positive patients, 117 (72.7 %) were female (Table-III). In this study there was a wide range of age variation. Age range is 0.2-96 years in male and 1.50-80 years in female. The mean age of male and female patients was 42.34±24.57 years and 39.67±18.67 years, respectively (Table-IV).

The overall frequency and rank order of community-acquired uropathogens is shown in Table V. The most common pathogens isolated were Escherichia coli (67.7%), others were Enterobacter (21.1%), Klebsiella pneumoniae (5.0%) and Pseudomonas (3.7%), Coagulase negative Staphylococcus (CNS) (1.9%). E.coli is most common in female (76.1%), whereas only 23.9% man had C/S positive for E. coli, Pseudomonas was present only in man, Klebsiella was responsible in 10% man & 90% woman. S.typhi was present in woman (Table-VI). Majority of culture positives were middle aged (Figure-1).

E. coli were mostly susceptible to Imipenum (100%), Furadantin (90.6%), followed by Pivmecillinam (86.9%). E. coli had the highest resistance rate to Ampicillin and Nalidixic acid (97.1% and 78.4%, respectively). Importantly, only 38.2% of E. coli isolates were susceptible to Trimethoprim-Sulfamethoxazole. Enterobacter was highly sensitive to Imipenum (100%), Ceftriaxone (87%), followed by Pivmecillinam (87.9%), Furadantin (84.4%) & highly resistant to Piperacillin (66.75%), Ampicillin (63%). *Klebsiella* spp. had the highest sensitivity to Imipenum (100%) followed by Pivmecillinam (75%) and highest resistance to Ampicillin, Ceftazidime, Piperacillin (100%). and Ciprofloxacin (62.5%). *Pseudomonas*, which has a high resistance rate worldwide, was 100% resistant to Ampicillin, Nalidixic acid and Nitrofurantoin. The best activity against *Pseudomonas* Imipenum (83%) followed by Piperacillin (66.7%). CNS was highly (100%) sensitive to Cephalexin, Nitrofurantoin, Gentamycin, Ciprofloxacin, Aztreonam & resistant (100%) to Nalidixic acid. (Table-VII).

Table-I

Gender distribution of all respondents

	Frequency	Percent
Male	809	36.1
Female	1435	63.9
Total	2244	100.0

Table-II

Distribution of growth

	Frequency	Percent
Present	161	7.2
Absent	2083	92.8
Total	2244	100.0

Table-III

Gender distribution of all culture sensitive patients

	Frequency	Percent
Male	44	27.3
Female	117	72.7
Total	161	100.0

Table-IV

Age distribution of all culture sensitive patients.

Statistics	Male	Female
Mean ±SD	42.34±24.57	39.67±18.67
(95% CI)	(34.87-49.81)	(36.26-43.09)
Range of age	0.2-96	1.50-80
Median	45.5	40

Table-V

Distribution of yielded growth

	Frequency	Percent
E. coli	109	67.7
Enterobacter	34	21.1
Klebsiella	8	5.0
Pseudomonus	6	3.7
CNS	3	1.9
S. typhi	1	.6
Total	161	100.0

Table-VI

Growth pattern of different organism in male and female.

Growth	Gender		Total No (%)
	Male	Female	
E. coli	26 (23.9)	83 (76.1)	109 (100%)
Enterobacter	10 (29.4)	24 (70.6)	34 (100%)
Klebsiella	1 (12.5)	7 (87.5)	8 (100%)
Pseudomonus	6 (100)	0 (00)	6 (100%)
CNS	1 (33.3)	2 (66.7)	3 (100%)
S. typhi	0 (00)	1 (100)	1 (100%)

Chi-square value=18, df=5, p value=.003

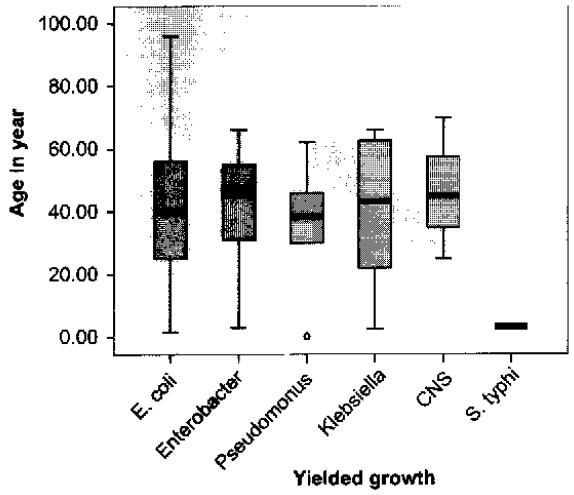

Fig.-1: *Growth of microbes in different age*

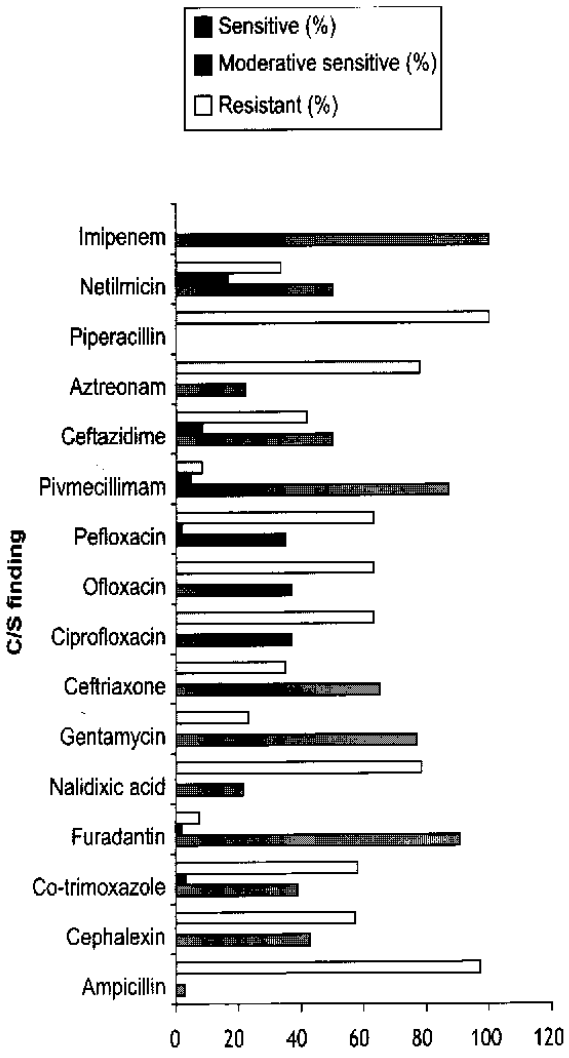

Fig.-2: *Sensitivity results of E.coli*

Table-VII

Antibiotic sensitivity and resistance pattern of isolated organisms

	E. Coli			Enterobacter			Pseudomonus			Klebsiala			CNS		
	S (%)	MR(%)	R (%)	S (%)	MR (%)	R (%)	S (%)	MR (%)	R (%))	S (%)	MR (%)	R (%)	S (%)	MR (%)	R (%)
Ampicillin	2.9	0.0	97.1	38.7	0.0	61.3	0.0	0.0	100.0	0.0	0.0	100.0	66.7	0.0	33.3
Cephalexin	42.7	0.0	57.3	77.4	0.0	22.6	0.0	0.0	100.0	37.5	0.0	62.5	100.0	0.0	0.0
Cotrimoxazole	38.7	3.2	58.1	38.7	3.2	58.1	0.0	0.0	100.0	50.0	0.0	50.0	66.7	0.0	33.3
Furadantin	90.6	1.9	7.5	84.4	0.0	15.6	0.0	0.0	100.0	50.0	25.0	25.0	100.0	0.0	0.0
Nalidixic acid	21.6	0.0	78.4	29.0	0.0	71.0	0.0	0.0	100.0	37.5	0.0	62.5	0.0	0.0	100.0
Gentamycin	76.9	0.0	23.1	83.9	0.0	16.1	33.3	0.0	66.7	62.5	0.0	37.5	100.0	0.0	0.0
Ceftriaxone	65.0	0.0	35.0	87.1	0.0	12.9	33.3	16.7	50.0	37.5	0.0	62.5	100.0	0.0	0.0
Ciprofloxacin	36.9	0.0	63.1	67.7	3.2	29.0	33.3	0.0	66.7	37.5	0.0	62.5	100.0	0.0	0.0
Ofloxacin	36.9	0.0	63.1	67.7	3.2	29.0	33.3	0.0	66.7	37.5	0.0	62.5	100.0	0.0	0.0
Pefloxacin	35.0	1.9	63.1	54.8	12.9	32.3	16.7	16.7	66.7	37.5	0.0	62.5	100.0	0.0	0.0
Pivmecillimam	86.9	4.7	8.4	87.9	0.0	12.1	.0	0.0	100	75.0	25.0	0.0	33.3	0.0	66.7
Ceftazidime	50.0	8.3	41.7	50.0	0.0	50.0	50.0	16.7	33.3	0.0	0.0	100.0	-	-	-
Aztreonam	22.2	0.0	77.8	33.3	0.0	66.7	50.0	0.0	50.0	0.0	0.0	100.0	100.0	0.0	0.0
Piperacillin	0.0	0.0	100.0	33.3	0.0	66.7	66.7	16.7	16.7	0.0	0.0	100.0			
Netilmicin	50.0	16.7	33.3	80.0	0.0	20.0	33.3	33.3	33.3	25.0	25.0	50.0			
Imipenum	100.0	0.0	0.0	100.	0.0	0.0	83.3	16.7	0.0	100.0	0.0	0.0			

Discussion:

A total of 2244 urine specimens were collected from patients suspected of having UTI, out of which 161 (7.2%) had significant bacterial growth. The frequency is close to the incidence reported by Ahmed and Avasarala (12.7%) [8], but is higher than the community based study of Singh MM et al. (4.2%) [9]. Bashar et al. and Rahman et al. reported higher frequency of UTI i.e., 27% and 24.14% respectively in hospital or clinic based study [10,11].

In our study majority of growth positive cases were in the age group of 21-50 years, followed by children up to 10 years. This results are more or less consistent with other studies[12,13]. The prevalence of UTI (growth positive cases) was recorded higher in women than in men. Women had 72.7% of urine culture positivity, whereas the men had only 27.3%. Similar observations were also recorded by Astal et al[14] and Khalifa et al [15]. Bacteriological studies usually reveal the involvement of gram negative enteric organisms that commonly cause urinary tract infections, such as *E. coli*, the *Klebsiella* species, and the *Proteus* species[16]. The most common organism implicated in UTIs (80-85%) is *E. coli*[17]. Similarly, gram negative bacilli was the major isolate in our study, Escherichia coli 67.7%, Enterobacter (21.1%), Klebsiella (5%), & *Pseudomonas sp* only 3.7% . Other investigators (Basar et al. and Saber et al. also reported higher association of *E. coli* (66.67% and 77.8% cases respectively) in UTI patients [18,19]. The study conducted in 2014 in Lahore; Pakistan shows the prevalence of UTI with the highest prevalence of *E-coli* (80%) followed by *Staphylococcus aureus* (9.4%), *Proteus species* (5.4%) and Pseudomonas species (5.2%). In most of the studies *Escherichia coli* was the prevalent organism in UTI[20]. According to a Turkish study[21], *E. coli* isolates were highly resistant to Ampicillin (97.1%) and higher resistance rates to Ampicillin have been reported in other countries including Senegal (77%), Spain (65%), Taiwan (80%), and India (88%) [22,23]. In our study, the Ampicillin resistance rate was 88%. The β-lactam antibiotics such as Ampicillin have relatively poor action in treating symptomatic cystitis. One hypothesis is that it is rapidly excreted and the duration of significant drug concentration in the urine is short. 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 [24,25].

The pattern of antimicrobial resistance of the micro-organisms causing UTI infections vary in their susceptibility to antimicrobials from place to place and from time to time. In this study *E. coli* was observed to be sensitive to almost all the antibiotics tested, though to varying degrees. *E. coli* was found to be most sensitive to Imipenem (100%), Furadatin (90.6%), Gentamycin (76.9), and resistant to most commonly used drugs like Piperacillin (100%), Ampicillin (97.1%), Aztreonam (77.8%), Ciprofloxacin, Ofloxacin, Pefloxacin were

(63.1%), Cephalexin (57.3), Nalidixic acid (78.4). Antibiotic abuse and practicing incomplete antibiotic regimen has considerably promoted the dissemination of multidrug resistant bacteria. Our study showed that *E. coli* had lower resistance for less commonly used drugs like pivmecillinam and nitrofurantoin & most sensitive imipenum. This finding is supported by the study of Sharmin et al. which reported a good sensitivity for Imipenem, Ceftazidime and Amikacin against UTI-isolates of *E. coli* in Bangladesh [26]. The antibiotic susceptibility patterns of *Pseudomonas sp* were also variable. This study also showed that *E. coli* and *Pseudomonas sp* both of them are nearly 70% resistant to Ciprofloxacin. This finding suggests the use of drugs that are less commonly prescribed by practitioners for arresting the pathogens in UTI patients may be beneficial.

Moreover, most of the UTI strains were highly resistance to nalidixic acid and Sulfamethoxazole. Drug resistance is one of nature's never ending process by which the organisms develop tolerance to new environmental condition. It may be due to a pre-existing factor in the organisms or result from the acquired factor(s). Rella and Hass (1982) first reported that a nalidixic acid resistant *P. aeruginosa* of UTI showed resistance to β-lactam antibiotics[26]. The findings of this study coincide with the findings of Shittu and Mandere (1999) that *S. aureus* strains were highly resistant to naladixic acid[27]. All the isolates in this study showed resistance to at least 5 different antibiotics, which emphasize the need for judicious use of antibiotics. Indiscriminate and irrational use of antibiotics among general population has favored the emergence of resistance strains.

Conclusion:

UTI among female is more prevalent and the most predominant uropathogen was *E coli*. Most effective antimicrobial agents for *E coli* are imipenem, pivmecillinam, amikacin and furadantin. It is resistant to most commonly used oral drugs like ampicillin, nalidixic acid, cotrimoxazole and ciprofloxacin.

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