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Original Article

Spectrum and Antibiotic Resistance Pattern of Bacteria Causing Urinary Tract Infections (UTI) in a Tertiary Care Hospital

Sadia Afroz[1], Zakir Hossain Habib[2], Syed Muhammad Baqui Billah[3], Hasina Akhter[4], Hosne Jahan[5], Rafia Parveen[6]

ABSTRACT

Background: Urinary tract infection (UTI) is one of the most common bacterial infections encountered by clinicians particularly in developing countries. Current knowledge on antimicrobial resistance pattern is essential for appropriate therapy. The aim of the present study was to identify the causative organisms for UTI and to determine the antibiotic susceptibility pattern of organisms causing UTI.

Method: This cross sectional study was carried out in the department of Microbiology, Sir Salimullah Medical College, Dhaka, from a period of January 2014 to December 2014.

Results: Out of 2136 clinical sample of urine, 430 (20.1%) showed significant bacterial growth. *Escherichia coli* was the commonest urinary pathogen (76.3%), followed by *Pseudomonas* spp. (7.9%), *Proteus* spp. (7.2%), *Klebsiella* spp., *Citrobacter* spp. (1.9% each) and *Staphylococcus aureus* (1.6%). Isolated uropathogens showed highest resistance for Amoxycillin (86%-97%) and Cefradin (71%-100%), resistance rate for other commonly used antimicrobial agents was high; Cefixime (52%-85%), Ceftriaxone (50%-71%), Ciprofloxacin (50%-88%), Cotrimoxazole (50%-75%), Gentamicin (57%-75%) and Nitrofurantoin (43%-100%), while uropathogens were least resistant to Imipenem (0%-15%) and Amikacin (0%-29%).

Conclusion: Due to high degree of resistance to commonly used antimicrobials to treat UTI, routine monitoring and evaluation studies should be conducted to update physicians' knowledge about most effective antibiotics for treatment of UTI.

Keywords: UTI; Antimicrobial resistance; Uropathogens

Introduction

Urinary tract infection (UTI) remains one of the most common bacterial infections encountered in clinical practice world wide.[1] It is considered a major public health problem in terms of morbidity and financial cost. There is an estimated 150 million urinary tract infections per year worldwide which cost global economy more than 6 billion US dollars.[2]

UTIs are described as bacteruria with urinary symptoms.[3] They are categorized clinically as uncomplicated or complicated UTI. The term complicated infection refers that the urinary tract is somehow obstructed or is abnormal. Uncomplicated infections are more common and refer to infections within a normal, unobstructed tract.[4] UTI affect patients of all age groups and both sexes, but neonates, young female, and older men are more susceptible to UT.I[5] The incidence of UTI is higher in women than men.

1. Associate Professor, Department of Microbiology, Satkhira Medical College, Satkhira;
2. Principal Scientific Officer, Department of Microbiology, Institute of Epidemiology, Disease Control & Research (IEDCR), Mohakhali, Dhaka;
3. Assistant Professor, Department of Epidemiology, Sulaiman Al Rajhi Medical University, Al Bukairiyah, KSA; \
4. Assistant Professor, Department of Microbiology, Bangladesh Dental College;
5. Assistant Professor, Department of Microbiology, Shaheed Suhrawardi Medical College; 6Associate Professor, Department of Radiology & Imageing, Delta Medical College.

Correspondence to: Dr. Sadia Afroz, Associate Professor, Department of Microbiology, Satkhira Medical College, Satkhira (Mobile: 01715686131; e-mail: afrozsadia@yahoo.com)

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About 40%-50% of women will suffer at least one clinical episode at some point in their life time.[6] The increased risk of UTI in women is due to a variety of factors, which makes female urethra less effective in preventing the bacterial entry to urinary tract.[7]

The spectrum of bacteria causing UTI is large and diverse. However, the most commonly encountered microorganisms are Gram negative bacteria like, *Escherichia coli*, *Proteus* spp., *Pseudomonas aeruginosa*, *Klebsiella* spp., *Enterobacter aerogenes* and others. UTI may also be caused by Gram positive bacteria, particularly *Enterococcus* spp., *Staphylococci* and *Streptococcus agalactiae*.[8]

Generally the antimicrobial treatment of UTI cases are started empirically before the laboratory results of urine culture are available, which has lead to frequent misuse of antibiotics. Such uncontrolled and widespread use of antibiotics has contributed to the emergence of resistant uropathogens.[9,10] In recent years increasing multidrug resistance in bacteria causing UTI has become a major problem worldwide. Pattern of antibiotic resistance of uropathogens changes from time to time and from place to place.[11] Since most UTIs are treated empirically, the criteria for selection of proper antibiotic should be determined on the basis of most likely pathogen and its expected susceptibility pattern in a given geographical area. Thus periodic evaluation of causative agents of UTI and their susceptibility pattern in a given locality is needed for effective treatment and to prevent emergence of resistant strains.[12]

This study therefore was carried out to determine the bacterial aetiologic agents of UTI and to evaluate their susceptibility pattern to commonly used antimicrobial agents, among patients with complaints of UTI attending in a tertiary care hospital of Dhaka city.

Materials and Methods

This cross sectional study was carried out in the department of Microbiology, Sir Salimullah Medical College, Dhaka from January 2014 to December 2014. Urine samples were collected from patients of various clinical wards and outpatient departments of Sir Salimullah Medical College & Mitford Hospital. Suspected UTI patients of both sexes and all ages were included in the study.

The clean catch, mid stream urine was collected into a sterile container by standard procedure.[13] Semi quantitative culture by calibrated wire loop was done on Blood agar and MacConkey agar media and then incubated, aerobically at 37^0C for 24 hours and extended to 48 hours in culture negative cases. The bacterial isolates were identified by observing colony morphology, Gram staining characteristics and relevant biochemical tests.[14] Culture results were interpreted according to standard criteria and growth of ed10^5 colony forming units/ml was considered as significant bacteruria.[15]

Antimicrobial susceptibility test of isolates was carried out by the Kirby Bauer disc diffusion technique using Mueller Hinton agar media.[16] Bacterial suspension adjusted to 0.5 McFarland standard was swabbed on Mueller Hinton agar and was allowed to soak for 2 to 5 minutes. Antibiotic discs were placed on the surface of the media and pressed gently. The inoculated plates were incubated at 37^0C for 24 hours, then the inhibition zones were measured and interpretations were made for each bacterial isolates following interpretative criteria recommended by the Clinical Laboratory Standard Institute(CLSI) .[17] Intermediate readings were few and therefore considered as sensitive for the purpose of assessing the data.

The following antibiotic discs from Oxoid Ltd. UK, were used; Amoxycillin (10µg), Cefradin (30µg), Ceftriaxone (30µg), Cefixime (5µg), Ciprofloxacin (5µg), Cotrimoxazole (25µg), Gentamicin (10µg), Amikacin (30µg), Nitrofurantoin (300µg) and Imipenem (10µg). Data were analyzed with SPSS version 20 statistical software by the Chi square test and Student's t test for paired samples. Level of significance was set at the $p<0.05$ level.

Results

Out of 2136 sample of urine, 430 (20.1%) showed significant growth of bacteria (*Table 1*). Age and sex distribution of culture positive cases has been shown in *Fig. 1*. Majority 228 (53.0%) were in the age group 20 to 29 years. Female were predominant than male in younger age group up to 50 years of age, but male

Table 1. *Distribution of urine sample by growth character (n=2136)*

Growth character	Number	Percentage
Significant growth	430	20.1
Insignificant or no growth	1706	79.9
Total	2136	100

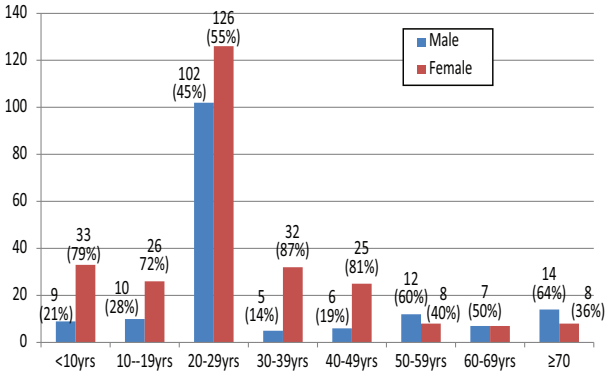

Figure 1. *Age and sex distribution of urine culture positive patients (n= 430)*

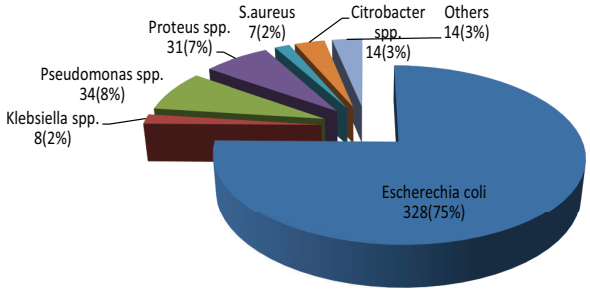

Figure 2. *Distribution of bacteria isolated from urine (n=430); Others in the chart represents, Enterobacter spp. Enterococcus spp. Acinetobacter spp. & Coagulase negative Staphylococci*

predominated in age groups of more than 50 years. Overall infection rate in female (56.0%) was more than in male (44.0%). The most frequently isolated bacteria was *Escherichia coli* 328 (76.3%), followed by *Pseudomonas* spp. (7.9%), *Proteus* spp. (7.2%), *Klebsiella* spp., *Citrobacter* spp. (1.9% each) and 1.6% were *Staphylococcus aureus* (*Fig. 2*).

Antimicrobial susceptibility pattern showed that, *E.coli* were highly resistant to Amoxycillin (95.1%), Cefradin (89.9%) followed by Cefixime (75.9%), Ciprofloxacin (67.9%) and Ceftriaxone (66.8%). About 48% *E.coli* isolates were resistant to Nitrofurantoin. All (100%) *Klebsiella* spp. were resistant to Cefradin and Nitrofurantoin, while resistance was lower for Gentamicin, Cefixime and Ciprofloxacin (62.5% each), Cotrimoxazole and Ceftriaxone (50% each). *Pseudomnas* spp. were highly resistant to Amoxycillin 1%), Cefradin (94.1%) and Cefixime (82.3%). istance to Ciprofloxacin was 52.9%. *Proteus* spp. wed high degree of resistance to Nitrofurantoin 1%) and Cefradin (77.4%), moderately resistant Ciprofloxacin, Cotrimoxazole and Gentamicin 5% each), resistance was lower for Cefixime .6%). *S. aureus* were mostly resistant to Amoxycillin (85.7%), Cefradin, Ceftriaxone (71.4% each); while 42.9% *S. aureus* were resistant to Nitrofurantoin. Uropathogens were highly sensitive to Imipenem (93%-100%) and Amikacin (71%-100%) (*Table 2*).

Table 2. *Antimicrobial resistance pattern of bacterial isolates from urine culture (n=430)*

Antibiotic	Number (%) of isolates resistant to						
	E. coli (n=328)	*Klebsiella* spp. (n=8)	*Pseudomonas* spp. (n=34)	*Proteus* spp. n=31)	*S.aureus* (n=7)	*Citrobacter* spp. (n=8)	Others (n=14)
Amoxycillin	312 (95.1)	7 (88.5)	33 (97.1)	29 (93.5)	6 (85.7)	7 (87.5)	13 (92.9)
Cefradin	295 (89.9)	8 (100)	32 (94.1)	24 (77.4)	5 (71.4)	7 (87.5)	10 (71.4)
Cefixime	249 (75.9)	5 (62.5)	28 (82.3)	16 (51.6)	4 (57.1)	5 (62.5)	11 (84.6)
Ceftriaxone	219 (66.8)	4 (50)	22 (64.7)	17 (54.8)	5 (71.4)	4 (50.0)	9 (64.3)
Ciprofloxacin	223 (67.9)	5 (62.5)	18 (52.9)	20 (64.5)	4 (57.1)	7 (87.5)	7 (50)
Cotrimoxazole	212 (64.6)	4 (50.0)	24 (70.6)	20 (64.5)	1 (14.3)	6 (75)	10 (71.4)
Gentamicin	210 (64.1)	5 (62.5)	24 (70.6)	20 (64.5)	4 (57.1)	6 (75)	10 (71.4)
Amikacin	55 (16.8)	2 (25)	10 (29.4)	7 (22.6)	0 (0)	1 (12.5)	3 (21.4)
Nitrofurantoin	157 (47.9)	5 (100)	24 (70.6)	27 (87.1)	3 (42.9)	5 (62.5)	9 (64.3)
Imipenem	49 (14.9)	1 (12.5)	6 (17.6)	5 (16.1)	0 (0)	1 (12.5)	1 (7.1)

*Figures within parentheses indicate percentage

Discussion

UTI is one of the common causes for seeking medical attention in the community. Effective management of patients suffering from bacterial UTIs largely depends on identification of the causative organism and selection of proper antibiotic for the organism in question.[18] Effective treatment of UTIs is a good example of cooperation between the clinician and the microbiologist. In the present study 430 (20.1%) urine specimen showed significant bacterial growth. Similar rate of isolation of uropathogen was reported by Ekweozor et al (22%).[19] But this rate is lower than that of other studies.[20,21] Rest of the samples (79.9%) showed insignificant bacteriuria or no growth. This might be due to prior antibiotic therapy before submitting the urine sample, incomplete dose of antibiotic and clinical conditions like non gonococcal urethritis or other conditions that mimic UTI.

This study showed that rate of UTI is higher in female (56%) than in male (44%), and patients in age group 20-29 years constituted highest (53.0%) proportion of UTI cases. This is consistent with reports of other studies.[22,23,24] It has been reported that adult women have a higher prevalence of UTI principally due to anatomical and physiological factors, such as shorter urethra, close proximity of urethral meatus to the anus, sexual intercourse, pregnancy, incontinence and unhygienic toilet practice.[25] Among males, increased rate of UTI was observed in elderly patients of age group above 50 years in the present study, which is in agreement with other studies.[26,27] This is probably because with advancing age, the incidence of UTI increases in men due to prostatic enlargement with subsequent obstruction or instrumentation and neurogenic bladder.[28]

Escherichia coli (76.3%) was the most prevalent bacteria isolated from positive urine samples. This findings is in agreement with reports from other studies.[20,21,22] Following *E. coli*, *Pseudomonas* spp. (7.9%) was found second most common bacterial isolate, which correlates with other studies too.[29,30] In contrary to our findings, some studies reported *Klebsiella* spp. as second common isolate.[20,31] The pattern of isolation of urinay pathogen in the present study is consistent with reports of studies published elsewhere recently.[20,21,31] Higher incidence of Gram negative rods related to enterobacteriaceae in UTI have several factors responsible for their attachment to the urothelium. These Gram negative aerobic bacteria colonize the urogenital mucosa with adhesion, pilli, fimbriae and P1-blood group phenotype receptor, and play role in precipitating UTI.[32]

Increasing resistance to antimicrobial agent is a world-wide problem. Our study also revealed a high rate of resistance to commonly prescribed antibiotics. Uropathogens were mostly resistant to Amoxycilin (86%-97%), which is consistent with other studies.[21,23,33] Widespraed and nonjudicial use of this antibiotic without sensitivity testing and abuse of this drug by self medication to treat all kind of infection due to its low cost may have promoted development of resistance to this antibiotic. Considering Cephalosporin group, organisms were highly resistant to Cefradin (71%-100%), which is in agreement with Sharmin *et al.* who found 60-100% isolates resistant to Cefradin.[34] Similarly resistance to third generation Cephalosporins like Cefixime and Ceftriaxone was high (50%-85%). This finding is consistent with other studies.[21,23] This might be an indication that many of the isolated organisms were ESBL producers, that was not separated in the present study due to limitations or it might be due to the fact that, the 3rd generation Cephalosporins have been used for long period, so due to indiscriminate and overuse of these drugs over time organisms have developed resistance against them.

In this study isolated organisms showed high level of resistance to commonly used antibiotics namely Ciprofloxacin, Cotrimoxazole and Gentamicin. Almost similar susceptibility pattern was also reported by other investigators.[20,21,31] This increased resistance might be due to very extensive use of these antibiotics in clinical practice. A large majority of patients were found prescribed by these drugs on their first contact with physician. All the *Klebsiella* spp. (100%) isolated in the present study were resistant to Nitrofurantoin. High resistance rate (48%-87%) was observed for other enterics also. Almost similar high resistance pattern was reported in Iran and Nigeria.[35,36] But in contrary to our findings, other studies have reported that greater percentage of UTI isolates were sensitive to this antibiotic.[21,23,33] Nitrofurantoin was considered drug of choice for UTI, as it was found to be reasonably high efficacious agent among all antimicrobials used against uropathogens. Increased resistance to Nitrofurantoin is a threat for treatment of UTI and is a major concern.

The most effective antibiotics found in our study were Imipenem and Amikacin. Uropathogens were least resistant (0%-29%) to these antimicrobial agents. This observation has been supported by other studies.[21,37] This may be due to the fact that these antibiotics are less commonly prescribed for empirical treatment of UTIs and they are used only in hospitalized patients according to sensitivity reports. Sensitivity pattern of uropathogens is changing drastically. They are gaining resistance to commonly used antimicrobials at an alarming rate, as revealed in this study. Clinicians should look for recent trends of sensitivity pattern, specially of that locality when choosing a treatment regimen for treating UTI.

Conclusion

From the present study it may be concluded that, Gram negative bacteria are the common organisms isolated from UTI patient and *Escherichia coli* was the most frequent causative agent. Higher prevalence of UTI was seen in female than male. Urinary pathogens showed increased resistance to commonly used antibiotics. So, antibiotic treatment should be limited to symptomatic UTIs and initiated after antimicrobial susceptibility testing. As drug resistance among pathogen is an evolving process, routine surveillance and monitoring should be conducted to establish reliable information about susceptibility pattern of uropathogens and an effective antibiotic policy should be formulated to ensure optimal therapy for patients with UTI.

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