Original Article

Antibiotic Resistance Pattern of Bacteria causing Urinary Tract Infection in a Tertiary Care Hospital

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Abstract:

Background: *Increasing incidence of antibiotic resistance poses a threat to global health including Bangladesh. For effective management of Urinary Tract Infection (UTI), knowing resistance pattern is utmost needed. Therefore, this study is aimed to assess the temporal changes of antimicrobial resistance patterns of uropathogens in a tertiary care center.* ***Methods:*** *The study design was cross-sectional and was conducted at the Enam Medical College & Hospital, Dhaka. Clinically diagnosed cases of UTI were initially approached and cultured subsequently. Total 54 culture positive cases were finally included. Urine culture and antibiotic sensitivity were studied using Kirby Bauer disc diffusion method in accordance with Clinical Laboratory Standard Institute (CLSI). Informed consent was taken in all cases and data were recorded in a preformed case record form. Data analysis was done by SPSS 23.* ***Results:*** *Mean age of the study population was 48.62±16.25 years with female (65%) predominance. E. coli (61.1%) is the most prevalent bacteria followed by S. aureus (31.5%), S. saprophyticus (5.6%) and Citrobacter (1.9%). Isolated E. coli indicated the highest antibiotic resistance to cefradine (95.5%), cotrimoxazole (80%) and cefixime (60%) and frequently sensitive to imipenem (92%), ceftazidime (91.7%), meropenem (91.3%), gentamycin (84.6%), nitrofurantoin (74.2%), ceftriaxone (72.3%) and netilmicin (71.4%). S. aureus highly resistant to levofloxacin (92.3%), ciprofloxacin (83.3%) and cefixime (75%) and showed high frequency of sensitivity to imipenem (100%), meropenem (100%), nitrofurantoin (93.8%), amoxicillin and clavulanic acid combination (92.3%) and ceftriaxone (85.7%). Overall resistant pattern depicted that 84.8% isolates of E. coli are resistant to more than one drug whereas almost all isolates (100%) of the S. saprophyticus and 88.2% S. aureus have shown multidrug resistance.* ***Conclusion:*** *E. coli was the most common causative organism of UTI in adult with varied percentage of resistance to different drugs. Therefore, antibiotic susceptibility testing should be performed prior to prescribing antibiotics.*

Key words: Urinary Tract Infection, Antibiotic resistance pattern, Antibiotic sensitivity pattern, Uropathogens

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Introduction:

The emergence and rapid dissemination of resistant bacteria has put the efficacy of many vital antibiotics in danger[1]. As a result bacterial infection is once again rising as an ominous threat, many years after the introduction of the first antibiotic. Most of the commonly encountered pathogens have been reported to exhibit substantial levels of resistance to the frequently used antimicrobial agents[2]. Urinary Tract Infection (UTI) is such disease, stumbled across routinely in clinical settings[3]. UTIs are the fourth most common type of healthcare associated infection affecting all age groups[4,5]. Spectrum of UTI includes cystitis, pyelonephritis and urethritis. Usual presentation is scalding pain during urination, increased frequency, urgency, suprapubic pain, loin pain and fever. Asymptomatic case may occur[6,7]. Diagnosis is based on clinical presentation but urinalysis and urine culture confirms the diagnosis. More than 90% of acute UTI in community acquired infection is caused by Escherichia coli and coagulase negative Staphylococci especially Staphylococcus saphrophyticus which is the second most common cause of UTI in young sexually active women and 5% or less by other Enterobacteriaceae and Enterococci[8].

Although the empirical treatment started earlier but, for that, knowledge on current trend of uropathogens according to local epidemiology and their susceptibility to various antibiotics are essential for cost effective and appropriate therapy for UTI as a large number of patient do not respond to conventional antimicrobial agents[9]. Treatment becomes even more challenging in the presence of

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risk factors such as higher age, pregnancy, comorbidity and immunosuppression. Moreover, the causative microorganisms often tend to vary in their susceptibility to antimicrobials from place to place and time to time[10]. Recent studies have indicated likewise, as in community and hospital settings, the etiology of UTIs and the antimicrobial susceptibility of uropathogens have been found to be changing over the years[11]. A study reported significant increased resistance of E. coli to ceftriaxone & co-amoxiclav and reduced resistance to nalidixic acid, mecillinam, cefixime and cefuroxime in 2016 as compared to 2011[12]. Inappropriate, extensive use and irrational prescription of antibiotics has led to the development of multidrug resistance among the pathogens[13].

For a developing country like Bangladesh, cost-effectiveness and antimicrobial susceptibility are highly considered when prescribing[14] but unfortunately, there is no nationally representative data except few center-based evidences[14,15,16,17,18]. Therefore, to portraits a local resistance patterns aiming to make a local treatment guideline, the study was designed so.

Materials and Methods:

This research was a hospital based cross-sectional study and was conducted at the Enam medical college hospital, Dhaka, Bangladesh from November 2018 to April 2019. Total 54 patients aged ≥18 years, irrespective of gender, culture positive cases and not receiving antibiotic were included in the study. Patients with complicated UTI, known urogenital malformations, pregnant, immunocompromised patients like patients with HIV, on corticosteroids or immunosuppressant therapy, organ transplant recipient were excluded. After inclusion they were described about the purpose and procedure of the study. Clean-catch midstream urine specimens from patients were collected and inoculated on Blood agar and MacConkey agar plates. Subsequently the sample was incubated aerobically at 37°C overnight. Plates showing growth suggestive of significant bacteriuria, with colony count exceeding 10^5 cfu/ml were subjected to standard biochemical tests for identification of the organism. Antimicrobial sensitivity test was performed using Kirby Bauer disc diffusion method as described by the Clinical Laboratory Standard Institute (CLSI)[19]. Interpretation as Sensitive or Resistant was done on the basis of the diameters of zone of inhibition of bacterial growth as recommended by disc manufacturer. The antibiotics used for susceptibility testing were Ceftriaxone, Cefixime, Cefuroxime, Cefradine, Ceftazidime, Amoxicillin-clavulanic acid, Imipenem, Meropenem, Azithromycin, Ciprofloxacin, Gentamicin, Netilmicin, Doxycycline, Nitrofurantoin, Linezolid and Co-trimoxazole. All the subjects were ensured that they are independent of giving any information in the whole interview procedure. They have got no financial benefits from this study other than usual management. Informed written consent was taken from each subject. Ethical measures were followed in accordance to the Helsinki declaration and ethical clearance was taken from the ethical review board of the study place. Complete privacy of the patient during interview and strict confidentiality of the gathered information was maintained throughout the procedure. Following signing consent form, within the time frame, patients were interviewed. Data collection was done by the lead researcher and was recorded in a separate case record form. Data analysis was done by SPSS 23.

Results:

Mean age of 54 patients with UTI was 48.62 ±16.25 (SD) years with range from 18 to 69 years. Majority patients were aged more than 60 years (37%) followed in second by 20.4% patient aged between 31 to 40 years (Figure-1). Most of the patients were female (65%) (Figure-2).

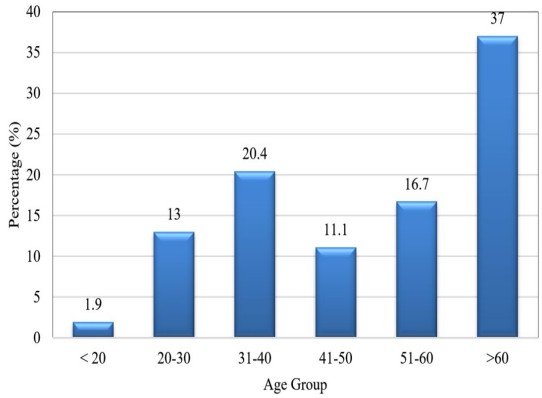

Figure-1: Age distribution of patients (n=54)

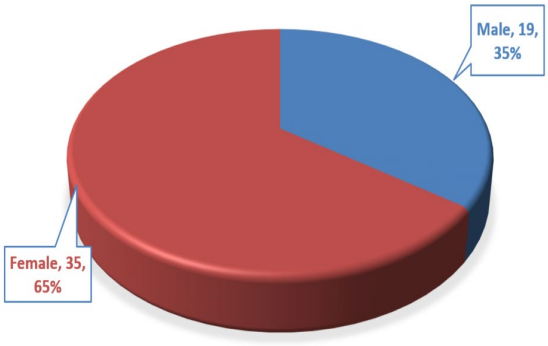

Figure-2: Sex distribution of patients (n=54)

DM was the most common risk factor found among patients accounting for 31.5% cases. Besides, 14.8% cases had indwelling catheter, 7.4% had BEP and 3.7% had neurological problems (Table-I).

Table-I: Distribution of risk factors among patients (n=54)

Risk factors	Frequency	Percentage
Diabetes Mellitus	17	31.5 %
Indwelling catheter	8	14.8 %
Benign enlargement of prostate	4	7.4 %
Neurological problem	2	3.7 %

Multiple response considered.

In this study most common presenting complaint was dysuria (59.3%) followed in decreasing order by increased frequency (27.8%) and urge incontinence (11.1%). Among all 31.5% were asymptomatic (Table-II).

Table-II: Distribution of presenting complaints among patients (n=54)

Presenting complaints	Frequency	Percentage
Dysuria	32	59.3 %
Increased frequency	15	27.8 %
Urge incontinence	6	11.1 %
Asymptomatic	17	31.5 %

Multiple response considered.

The most common bacteria isolated was E. coli (61.1%) followed in decreasing order by S. aureus (31.5%), S. saprophyticus (5.6%) and Citrobacter (1.8%) (Table-IV).

Table-III: Antibiotic resistance pattern of isolated bacteria (n=54)

Bacteria	*S. aureus*			*E. coli*			*S. Saprophyticus*			*Citrobacter*		
Antibiotics	**Number tested**	**Number resistant**	**Percentage (%)**	**Number tested**	**Number resistant**	**Percentage (%)**	**Number tested**	**Number resistant**	**Percentage (%)**	**Number tested**	**Number resistant**	**Percentage (%)**
Beta lactams												
Amoxicillin + Clavulanic acid	13	1	7.7	24	9	37.5	2	1	50			
Cefradine	11	8	72.7	22	21	95.5	1	0	0			
Cefuroxime	11	8	72.7	27	16	59.3	3	1	33.3			
Ceftriaxone	14	2	14.3	30	8	26.7	2	0	0			
Ceftazidime	11	5	45.5	24	2	8.3	2	1	50			
Cefixime	12	9	75.0	25	15	60.0	1	1	100			
Imipenem	12	0	0	25	2	8.0	2	0	0			
Meropenem	15	0	0	23	2	8.7	1	0	0			
Aztreonam				20	9	45.0						
Aminoglycosides												
Gentamicin				26	4	15.4	2	1	50	1	0	0
Netilmicin				21	6	28.6	1	0	100			
Nitrofuran												
Nitrofurantoin	16	1	6.2	31	8	25.8	3	0	0			
Oxazolidinone												
Linezolid	10	4	40	3	0	0	1	1	100			
Macrolide												
Azithromycin	16	8	50	25	14	56.0	2	1	50			
Fluoroquinolones												
Ciprofloxacin	12	10	83.3	31	18	58.1	2	0	0			
Levofloxacin	13	12	92.3	2	50							
Tetracycline												
Doxycycline	9	3	33.3	22	13	59.1	1	0	0			
Sulfonamide												
Cotrimoxazole	14	6	42.9	25	20	80	3	3	100	1	0	0

Table-IV: Distribution of bacteria isolated from culture (n=54)

Bacteria	Frequency	Percentage
Escherichia coli	33	61.1 %
Staphylococcus aureus	17	31.5 %
Staphylococcus saprophyticus	3	5.6 %
Citrobacter	1	1.8 %

Table-III enlists the antibiotic resistance pattern of isolated bacteria. E. coli was frequently resistant to cefradine (95.5%), cotrimoxazole (80%), cefixime (60%), cefuroxime (59.3%), doxycycline (59.1%), ciprofloxacin (58.1%) and azithromycin (56%) and was frequently sensitive to imipenem (92%), ceftazidime (91.7%), meropenem (91.3%), gentamycin (84.6%), nitrofurantoin (74.2%), ceftriaxone (72.3%) and netilmicin (71.4%). S. aureus showed high frequency of resistance to levofloxacin (92.3%), ciprofloxacin (83.3%), cefixime (75%), cefuroxime (72.7%) and cefradine (72.7%) and showed high frequency of sensitivity to imipenem (100%), meropenem (100%), nitrofurantoin (93.8%), amoxicillin and clavulanic acid combination (92.3%) and ceftriaxone (85.7%).

Table-V: Proportion of isolates, resistant to more than two drugs

Bacteria	Frequency	Percentage
Staphylococcus saprophyticus	3	100 %
Staphylococcus aureus	15	88.2 %
Escherichia coli	28	84.8 %

Table-V shows 100, 88.2 and 84.8% isolates of S. saprophyticus, S. aureus, and E. coli were resistant to more than two drugs respectively.

Discussion:

Urinary Tract Infection (UTI) is one of the most common diseases encountered in general practice both in outpatient and inpatient now a days[17]. This leads to the widespread use of various antimicrobial agents for the treatment worldwide[18]. That eventually leads to development of antimicrobial resistance which is progressively increasing[19]. The aim of this study was to determine the current pattern of uropathogens in both groups of patient with their frequency and antimicrobial resistance.

Total 54 cases were taken for the study. All of them had microbial growth in urine culture and sensitivity reports. Mean age of these 54 cases was 48.62±16.25 years with a range of 18 to 69 years. This is nearly similar to the findings reported by Moue and her colleague[20]. They found a mean age of 46.24 years among their patients. Age distribution of patients suffering from UTI differed from study to study depending on the inclusion criteria. The present study only included adult patients. Otherwise, UTI can occur in all age groups. UTI is frequent in young sexually active women and men[21,22], decreases during middle age but rises in older adult[23-25]. The present study found a similar pattern in terms of age distribution. Most of the patients were aged above 60 years (37%) followed by an age group of 31-40 years (20.4%).

In this study 65% patients were female and 35% were male. This is similar to findings of many other studies[14,18,20,26,27]. This is explainable as women are more prone to UTI because of close proximity of the urethral meatus to the anus, shorter urethra, sexual intercourse, incontinence and bad toilet[28].

The most common risk factor identified was DM, followed in decreasing order by indwelling catheter, Benign Enlargement of Prostate (BEP) and neurological problem. In a review, Storme *et al.* showed that urological conditions predisposing to infections include pathological alterations to urothelium, neurogenic bladder and catheterization. Pathological changes to urothelium are related to DM, neurogenic bladder and urinary retention due to benign enlargement of prostate[28,29].

The pattern of uropathogens isolated in this study is in agreement with other studies[17,18,20,26,30,31] except no isolates of Klebsiella was found.

A great concern is increasing drug resistance to common bacterial infections including UTI. Antimicrobial agents like cefradine, cefixime, cefuroxime, nalidixic acid, ciprofloxacin, levofloxacin and azithromycin are still used to treat UTI in many underdeveloped and developing countries including Bangladesh. All these agents were found to have unacceptable range of resistance to uropathogens isolated in this study. Antibiotics with acceptable range of sensitivity were amoxicillin and clavulanic acid combination, nitrofurantoin, gentamicin in the lower cost range and ceftriaxone, imipenem and meropenem in the upper cost range. This finding is alarming in regards to the choice of effective therapeutic options in the treatment of UTI and obviously a great concern to treating physicians.

Ciprofloxacin was once considered to be the drug of choice for uncomplicated and complicated UTI but due to lack of rational use, it lost its efficacy not only in UTI but to other common infections too. Similar picture is also noted in case of 1st, 2nd and 3rd generation cephalosporins. Even the broad-spectrum antibiotics like ceftriaxone, imipenem and meropenem have started to show resistance to both

gram positive and gram negative organisms as is evident from this and other studies[17,30,32]. In a systematic review of antibiotic resistance pattern Ahmed et al. showed that the most common uropathogen E. coli shows high resistance to almost all drugs except amikacin, gentamicin, nitrofurantoin and imipenem which is similar to the findings of this study[31]. In concordance with other studies[17,31] S. aureus was also found to be highly resistant to cefuroxime and ciprofloxacin.

Nitrofurantoin was found to be reasonably high efficacious agent among all antimicrobials used to almost against all uropathogens in the current setting and similar results were also reported from other studies[14,17,32]. In the context of gradually decreasing sensitivity of other low-cost oral antimicrobials for UTI the higher sensitivity of nitrofurantoin is good news for developing countries like Bangladesh. Though moderate to high susceptibility was also noted for gentamicin, amikacin and ceftriaxone for most of the uropathogens but their uses are limited due to parenteral route and patient's noncompliance. Also, use of imipenem and meropenem is not possible in every patient due to high cost and route of administration.

All these findings indicate that number of efficacious antimicrobial options available for use in UTI are decreasing. This should warrant the authorities to take appropriate measures to decrease emergence of more antibiotic resistance.

Conclusion:

The study highlights that E. coli contributes to the majority of the urinary tract infections diagnosed in our center. In addition, the current drug sensitivity pattern signifies the need for conducting antibiotic sensitivity test in each patient with UTI. The current study also signifies the need of implementing strategies of rational prescribing to combat against antibiotic resistance. Nitrofurantoin, with good activity against a high percentage of the cultured organisms causing UTI, rationalizes its use for empirical treatment of UTI.

Limitation of the study:

- Small sample size.
- The study was conducted in a single center, therefore, it cannot be inferred to general population.
- Evaluation of antibiotic resistance pattern among the patients with complicated UTI and patients with immunocompromised state was beyond the scope of the study.

Ethical consideration:

The researchers were duly concerned about the ethical issues related to the study. Formal ethical clearance was taken from relevant site before commencing the study. Confidentiality was maintained properly and these data were not used other than the study.

Conflict of Interest:

The authors declare that there is no conflict of interests regarding the publication of this paper.

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