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Prevalence of antibiotic resistant UTI in immunocompromised patients

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Abstract

Background: Urinary tract infections (UTIs) are amongst the most common bacterial infections, affecting about 150 million individuals per year.Urinary tract infection (UTI) is one of the most common diseases in human societies which occur in women more than men. Women of all ages are more likely to experience such an infection than men, while half of them may be affected by a uropathogen once in their lives, and 25-30% may develop recurrent UTIs not associated with any functional or anatomical abnormality. The aim of this study was to explore the prevalence of antibiotic resistance of urinary tract infections in immunocompromised patients. **Material & Methods:** This was a retrospective observational study and was conducted in the Department of Medicine of Dhaka Central International Medical College and Hospital, and National Institute of Kidney Diseases & Urology, Dhaka, Bangladesh during the period from June, 2021 to June, 2022. We included 70 immunocompromised patients with UTI. **Results:** In our study we found 44% patients were aged between 18-30 years old and 83% of our patients were female. Among all respondents, 58 patients were culture positive. We found 38% & 62% and 33% & 67% had history of upper & lower UTI in female and male patients respectively, 29% & 36% and 17% & 25% had urethritis & cystitis in female and male patients respectively. We found culture positive patients with E. coli (41%), Klebsiella spp.(19%), Enterobacter spp.(16%) and 12% with Pseudomonas spp in our study. We found amoxicillin showed resistance to E. coli (58.3%), Staphylococcus (75%), & Klebsiella (36.4%) and amikacin showed resistance mostly to E. coli(50%), Klebsiella (54.5%) & Pseudomonas (42.9%). **Conclusion:** In our study, we found the most common MDR pathogen among patients with UTI in our institution was E. coli & Staphylococcus. We discovered that being above 40 years old, having DM, CKD and previously received antibiotic medication inappropriately were risk factors for the development of MDR infection. Given the high prevalence of multidrug resistant uropathogens among immunocompromised patients, the growth in Penicillin resistance is alarming. We discovered the significant incidence of MDR bacterial strains, adherence to currently suggested empiric therapy is extremely challenging and is linked with high failure rates.

Keywords:- Urinary tract infections, Uropathogen, Immuncompromised.

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INTRODUCTION

Urinary tract infections (UTIs) are amongst the most common bacterial infections, affecting about 150 million individuals per year.[1] Urinary tract infection (UTI) is one of the most common diseases which occur in women more than men.[2,3,4] Women of all ages are more likely to experience such an infection than men, while half of them may be affected by a uropathogen once in their lives , and 25-30% may develop recurrent UTIs not associated with any functional or anatomical abnormality.[5,6] Since UTIs can lead to life-threatening infections such as septicaemia, they are considered as a significant cause of morbidity especially in elderly patients.[1,7] The infection may be restricted to lower urinary tract or can expand to upper urinary tract resulting to several clinical manifestations from asymptomatic bacteriuria, to urethritis, cystitis, ureteritis, epididymitis, prostatitis and pyelonephritis.[8] Taking into consideration several host factors that predispose to the infection, UTIs can be classified as uncomplicated or complicated. Risk factors related to uncomplicated UTIs include age, female gender, a prior UTI, sexual activity, vaginal infection, while complicated UTIs are commonly related to pregnancy, immunosuppression due to urinary tract carcinoma, diabetes, CKD, long term steroid therapy or immunosuppressive agents, renal failure or transplantation.[9,10]

The UTI occurrence depends on several factors provide the presence of bacteria (more than 105 /ml) in urine.[4] These bacteria cause UTI and if not treated, the infection will spread and cause serious damage to the patient.[4,11,12] UTI treatment with antibiotics is carried out usually before receiving microbiology test results. This therapy, without rational drug prescription occasionally leads to antibiotic resistance and treatment failure.[4,13] Discovery of antibiotics was one of the greatest advances of modern medicine, but the availability and increased use of antibiotics gradually lead to microbial resistance to them.[14] Antimicrobial resistance is increasing around the world, especially in developing countries.[15] According to the World Health Organization in 2014, antimicrobial resistance is increasingly a global threat for public health and all countries have focused on this problem which is a serious threat to modern medicine.[16] The first important factor in increasing microbial resistance is improper use of antibiotics.[17,18] The other is incorrect and unreasonable antibiotics prescription. Considering time, the appropriate dose and manner of administration are the most important aspects of rational drug prescription.[18,19] Studies have shown that 30%–60% of the prescribing and usages of antibiotics have been improper. Many hospitals have turned their supervision on the use of certain antimicrobial agents to change this worrying trend in Iran and all over the world.[20,21] Although UTI is a common disease, it is treated easily if antibiotics are used reasonably. Identification of bacteria that cause UTI and analysis of antibiotic susceptibility pattern of them is effective in the treatment.[3,22] Current data indicate a rising incidence of multidrug-resistant (MDR) strains of urinary pathogens worldwide.[23,24,25] Infections caused by MDR pathogens have become a therapeutic challenge for clinicians and a threat for immunocompromised patients. Few antibiotics

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are available to treat infections caused by these pathogens, and those that can be prescribed are mostly for parenteral administration and carry a higher risk of adverse effects. Moreover, infections caused by MDR rods are often associated with worse outcomes.[26,27,28] In this study we aimed to investigate the bacteria associated with UTI cases and their antibiotic susceptibility pattern in tertiary care hospitals.

Objective of the study

The main objective of the study was to explore the prevalence of antibiotic resistance of urinary tract infections in immunocompromised patients in a tertiary care hospital.

MATERIAL AND METHODS

This was a retrospective observational study and conducted in the Department of Medicine of Dhaka Central International Medical College and Hospital and National Institute of Kidney Diseases & Urology, Dhaka, Bangladesh during the period from June, 2021 to June,2022. We included 70 immunocompromised patients with UTI. Among all patients 58 patients were culture positive and 12 patients were culture negative.

These are the following criteria to be eligible for the enrollment as our study participants: a) Patients aged >18 years old; b) Patients with urinary tract infection; c) Patients with previous transplantation; d) Patients undergoing treatment with immunosuppressive agents; e) Patients with DM & CKD were included in our study And a) Patients with known allergy to study drugs; b) Patients with previous surgical complication; c) Patients with urinary tract stone were excluded from our study.

Clean-catch midstream or catheter-catch urine was collected into a sterile wide mouth container/test tube with all aseptic measures and was screened for microscopic demonstration of pus cells in male ≥ 5/ HPF and female ≥ 10/ HPF (high power field) in a centrifuged deposit before considering culture.[29] Diagnosis of UTI was established on the basis of urine R/E, urine C/S and USG of our patients.

Antimicrobial susceptibility testing (AST): Mueller-Hinton agar and Kirby-Bauer disk diffusion method,[30] were used for AST against a panel of 20 commercial antibiotic disks (Oxoid, UK): amoxicillin(30µg), amikacin (30µg), azithromycin (15µg), aztreonam (30µg),colistin(≤2 µg/ml), cefixime (5µg), cefepime (30µg), ceftazidime (30µg), ceftriaxone (30µg), ciprofloxacin (10µg), cotrimoxazole (25µg), doxycycline (30µg), gentamicin (30µg), imipenem (10µg), levofloxacin (5µg), meropenem (10µg), netilmicin (30µg), nitrofurantoin (300µg), piperacillin/ tazobactam (≤16 µg/ml) and polymyxin B (≤2 µg/ml). Isolates were labeled as 'sensitive' and 'resistant' according to the guidelines of Clinical Laboratory Standard Institute (CLSI). Escherichia coli ATCC 25922 and Staphylococcus aureus ATCC 25923 were used as control strains for AST.[31]

Statistical Analysis: We collected demographic, laboratory, and clinical data, including potential risk factors (such as the recent use of antibiotics, DM and comorbidities). All data were recorded systematically in preformed data collection form and quantitative data was expressed as mean & standard deviation and qualitative data was expressed as frequency distribution & percentage. Statistical analysis was performed by using SPSS 23 (Statistical

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Package for Social Sciences) for windows version 10. Probability value <0.05 was considered as level of significance. Ethical Review Committee of Dhaka Central International Medical College and Hospital, Dhaka, Bangladesh approved the study.

RESULTS

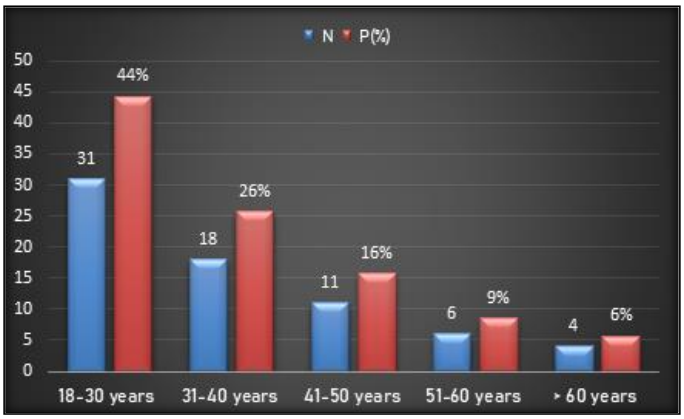

Figure 1: Age distribution of our study subjects

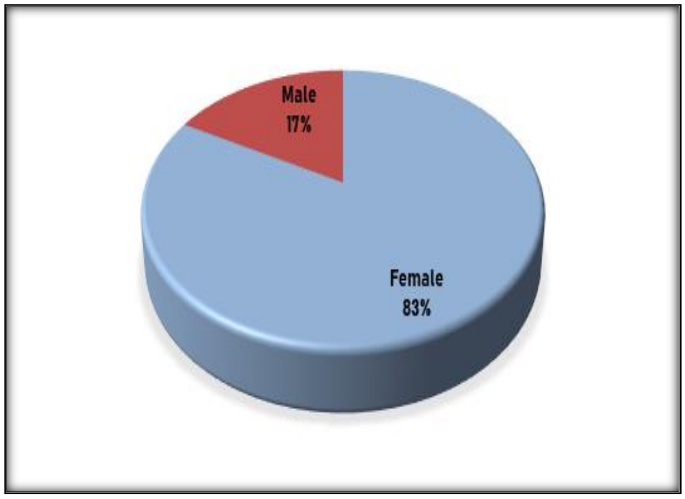

Figure 2: Gender distribution of our study respondents

Table 1: Baseline characteristic of our study respondents.

Baseline characteristic	Resistant UTI(n=58)		Non-resistant UTI (n=12)		P-value
	N	P(%)	N	P(%)	
Age (years)					
18–30	28	48.28	3	25.00	
31-40	12	20.69	6	50.00	
41-50	9	15.52	2	16.67	
51-60	5	8.62	1	8.33	
>60	4	6.90	0	0.00	
Mean ±SD (years)	31.58 ± 9.32				0.011
Sex					
Male	7	12.07	5	41.67	
Female	51	87.93	7	58.33	
Immunocompromised					
Pregnant	6	10.34	2	16.67	0.142
DM	34	58.62	3	25.00	
CKD	36	62.07	1	8.33	
Steroid therapy	14	24.14	2	16.67	
Transplant	7	12.07	1	8.33	

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Table 2: Distribution of our study subjects based on clinical manifestations.

Clinical manifestations	**Female(N=58)**		**Male(N=12)**		**P-value**
	N	**P(%)**	**N**	**P(%)**	
Upper UTI	22	37.93	4	33.33	0.412
Lower UTI	36	62.07	8	66.67	
Urethritis	17	29.31	2	16.67	
Cystitis	21	36.21	3	25	
Pyelonephritis	20	34.48	2	16.67	
Prostatitis	-	-	3	25	
Epididymitis	-	-	2	16.67	
S. creatinine					
<1.2 mg/dl	24	41.38	4	33.33	0.000
>1.2 mg/dl	34	58.62	8	66.67	
Mean ± SD(mg/dl)	1.78±0.86				

Table 3: Distribution of our study subjects based on isolated microorganism.

Uropathogens	**N**	**P(%)**	**P-value**
Escherichia coli(ESBL)	24	41.38	0.014
Staphylococcus aureus	4	6.90	
Enterobacter spp	9	15.52	
Pseudomonas spp	7	12.07	
Klebsiella spp(ESBL)	11	18.97	
Acinetobacter spp.	3	5.17	

Table 4: Distribution of our study respondents based on the antimicrobial resistance of uropathogens

Antimicrobial agent	**Uropathogens n(%)**					
	Escherichia coli (n=24)	**Staphylococcus aureus (n=4)**	**Enterobacter spp. (n= 9)**	**Pseudomonas spp. (n= 7)**	**Klebsiella spp.(n= 11)**	**Citrobacter spp. (n=3)**
Amoxicillin	14(58.3%)	3(75%)	3(33.3%)	4(57.1%)	4(36.4%)	2(66.7%)
Amikacin	12(50%)	2(50%)	2(22.2%)	3(42.9%)	6(54.5%)	1(33.3%)
Azithromycin	11(45.8%)	3(75%)	4(44.4%)	4(57.1%)	3(27.3%)	1(33.3%)
Aztreonam	8(33.3%)	2(50%)	1(11.1%)	3(42.9%)	8(72.7%)	1(33.3%)
Ciprofloxacin	11(45.8%)	1(25%)	2(22.2%)	2(28.6%)	2(18.2%)	1(33.3%)
Colistin	9(37.5%)	1(25%)	4(44.4%)	1(14.3%)	1(9.1%)	0
Ceftazidime	5(20.8%)	1(25%)	4(44.4%)	0	7(63.6%)	0
Cefixime	4(16.7%)	3(75%)	0	0	1(9.1%)	0
Ceftriaxone	12(50%)	2(50%)	0	2(28.6%)	4(36.4%)	0

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Cefepime	5(20.8%)	2(50%)	0	0	3(27.3%)	0
Cotrimoxazole	9(37.5%)	0	0	0	1(9.1%)	0
Doxycycline	11(45.8%)	1(25%)	2(22.2%)	2(28.6%)	2(18.2%)	1(33.3%)
Gentamicin	4(16.7%)	1(25%)	0	1(14.3%)	4(36.4%)	0
Imipenem	3(12.5%)	0	0	1(14.3%)	5(45.5%)	1(33.3%)
Meropenem	4(16.7%)	1(25%)	0	0	6(54.5%)	0
Levofloxacin	5(20.8%)	1(25%)	0	2(28.6%)	5(45.5%)	1(33.3%)
Netilmicin	4(16.7%)	0	0	1(14.3%)	1(9.1%)	0
Nitrofurantoin	6(25%)	0	0	0	2(18.2%)	0
Piperacillin/ Tazobactam	5(20.8%)	1(25%)	1(11.1%)	2(28.6%)	4(36.4%)	2(66.7%)
Polymyxin B	6(25%)	3(75%)	2(22.2%)	3(42.9%)	2(18.2%)	1(33.3%)

In [Figure 1] we showed the age distribution of our study respondents. Majority (44%) of our patients were aged between 18-30 years old, followed by 26% & 16% were aged between 31-40 & 41-50 years old respectively. The least prevalence 9% & 6% was found among 51-60 years & more than 60 years old respectively.

In [Figure 2] we showed the gender distribution. We found majority of our patients were female (83%) compared to male (17%).

[Table 1] showed the baseline characteristic of our study respondents. Among all patients, 58 patients were culture positive. Majority (48%) of our positive patients belonged to 18-30 years group and most of them (88%) were female. Among all our patients who showed resistance,10% were pregnant and found DM (59%), CKD (62%), Transplant was done in 12% patients and 24% patients had a history of taking steroid therapy.

In [Table 2] we summarized the clinical manifestations of our patients. Among all respondents, 38% & 62% and 33% & 67% had history of upper & lower UTI in female and male patients respectively, 29% & 36% and 17% & 25% had urethritis & cystitis in female and male patients respectively. Prostatitis & epididymitis was found 25% & 17% only in male patients respectively. The mean of s. creatinine was 1.78±0.86 mg/dl.

In [Table 3] we distributed our study patients based on isolated uropathogens. Most of our patients (41%) were found culture positive with E. coli, 19 % with Klebsiella spp., 16% with Enterobacter spp. and 12% with Pseudomonas spp.

In [Table 4] we showed our study distribution based on the antimicrobial resistance. The antimicrobial agents of our study showed mainly resistance to E. coli & Staphylococcus. We found amoxicillin showed resistance to E. coli (58.3%), Staphylococcus (75%), Klebsiella (36.4%) and amikacin showed resistance mostly to E. coli(50%), Klebsiella (54.5%) & Pseudomonas (42.9%).

DISCUSSION

UTI is a frequent complication after kidney transplantation and often leads to recurrence.[32] In recent years, antimicrobial resistance has become a major public health problem

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worldwide, and several studies have reported an increasing incidence of infections by MDR organisms in both immunocompetent and immunocompromised hosts. Some studies have reported a high frequency of infection caused by MDR organisms in solid organ recipients, ranging from 6.5% to 56%.[23,24,25,27]

In our study we found majority (44%) of our patients were aged between 18-30 years old, followed by 26% & 16% were aged between 31-40 & 41-50 years old respectively. [Figure 1] Martin et al found the age of the patients was from 8 months to 95 years and the mean of the study participants was 33.09 ± 23.7 years.[33] Islam et al. found 81% patients were aged above 18 years old.[34]

In this study we found majority of our patients were female (83%) compared to male (17%). [Figure 2]

Martin et al. found that among study participants 65.9% were majorly female.[33] Islam et al. found that 73% were females which correlates to our findings.[34] Among all patients, 58(83%) patients were culture positive. Islam et al found 71% of study respondents tested positive being defined as case of UTI. Their finding is similar to our study.[34] Chandrika Dasgupta et al. found that 42.8% tested as positive out of 1255 clinically suspected UTI patients.[35] Most of our patients were immunocompromised associated with Pregnancy (10%), DM (59%), CKD (62%) and Transplantation (12%). [Table 1] Chandrika Dasgupta et al found DM (18.4%), IHD (4.1%) among patients associated with UTI infection.[35] In this study, we found 38% & 62% and 33% & 67% had history of upper & lower UTI in female and male patients respectively, 29% & 36% and 17% & 25% had urethritis & cystitis in female and male patients respectively. Prostatitis & epididymitis was found 25% & 17% only in male patients respectively. [Table 2] Chandrika Dasgupta et al found dysuria (79%), frequency (53.5%), fever (33.7%), supra-pubic pain (26.5%), were noted with fever and supra-pubic pain had significant association with UTI.[35] Comparable prevalence rate of MDR uropathogens to commonly prescribed antimicrobials have also been reported by some recent studies.[36,37] It has been reported previously that in 80% of acute and recurrent UTI cases in women, E. coli is involved as the primary organism, followed by S. saprophyticus (10% - 15%). Other less common uropathogens with the potential to cause UTI include Klebsiella, Enterobacter, Serratia, Proteus, Pseudomonas, and Enterococcus.[38] In our study antimicrobial agents showed mainly resistance to E. coli & Staphylococcus. [Table 4] Chandrika Dasgupta et al. found MDR ranged from 3.7 to 88.1% and isolates were found to be moderate to highly resistant (28.6 to 92.9%) to commonly used antibiotics like ciprofloxacin, cotrimoxazole, azithromycin, nalidixic acid, cephalosporin and aztreonam.[35] A similar study from Alighar, India reported that 42% of uropathogens were ESBL-producing, while another study from Pakistan showed that 66% of uropathogens were ESBL-producing.[39] Studies from India and Pakistan reported the occurrence of MDR E. coli as 43% and 59%, respectively.[40,41,42] Islam et al. found that 74% of E. coli isolates were MDR and 69% of isolates were resistant to third-generation cephalosporins, which is higher than the prevalence of MDR E. coli (58%) reported earlier from Bangladesh.[34,43]

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Limitations of The Study

Our study was a double centre study. We did not generalize the results to the entire country because of our limited resources and short study period. We couldn't state the precise clinical classification of UTI patients. We also didn't classify MDR uropathogens according to their genotypic or phenotypic characteristics. After evaluating once those patients we did not follow-up them for a long term and have not known other possible interference that may happen in the long term with these patients.

CONCLUSIONS

In our study, we found the most common MDR pathogen among patients with UTI in our institution was E. coli & Staphylococcus. We discovered that being above 40 years old, having DM, CKD and previously received antibiotic medication inappropriately, immunosuppresive agents were risk factors for the development of MDR infection. Given the high prevalence of multidrug resistant uropathogens among hospitalized patients, the growth in Penicillin resistance is alarming. We discovered that because of the significant incidence of MDR bacterial strains, adherence to currently suggested empiric therapy is extremely challenging and is linked with high failure rates. Hospitals should develop an antibiotic stewardship program to combat antimicrobial resistance.

So further study with a prospective and longitudinal study design including larger sample size needs to be done to select appropriate empiric antimicrobial therapy taking into the account local patterns of resistance.

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