

ANTIMICROBIALS RESISTANCE TREND OF BACTERIAL UROPATHOGENS IN PATIENTS ATTENDING IN TERTIARY CARE HOSPITALS IN BANGLADESH

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Abstract

Background: Urinary tract infection (UTI) has now become the most common infectious disease, mostly in developing regions, indicating healthcare and economic constraints. Antimicrobial resistance (AMR) is a condition in which microorganisms use varied resistance mechanisms, including horizontal gene transfer (for example, plasmids and bacteriophages), genetic recombination, and mutations.

Methods: This study is a retrospective cross-sectional study that was conducted at Mitford Hospital and Dhaka Medical College Hospital. The study was conducted from January 2021 to January 2022. The total sample size for this study was 500.

Result: The proportion of uropathogenic species of isolates (from total UTI patients; 250) showed *E. coli* 94(37.6%) and followed by *K. pneumoniae* 28(11.2%), *CONS* 11(4.4%), *S. aureus* 23(9.2%), *Proteus spp.* 4(1.6%), *Citrobacter Spp.* 18(7.2%), *Salmonella Spp.* 1(0.4%), *GNR* 27(10.8%), *Enterobacter Spp.* 9(3.6%), *Streptococcus spp.* 6(2.4%), *Klebsiella Spp.* 8(3.2%), *Pseudomonas Spp.* 1(0.4%), *Providencia spp.* 1(0.4%), *K. ozaenae* 10(4%), *Shigella Spp.* 2(0.8%), *Enterococcus Spp.* 5(2%), *Serratia spp.* 1(0.4%) and *M. morgani* 1(0.4%). Gram-positive isolates presented a high resistance to tetracycline 14(93.3%) and penicillin 13(86.7%). Antimicrobial agents most effective against Gram-positive uropathogens were vancomycin and nitrofurantoin. *Staphylococcus aureus* was the most common isolate of Gram-positive isolates. It was highly resistant to tetracycline 32(100%) and trimethoprim-sulfamethoxazole 26(81.3%). In addition, 9(28.1%) of *S. aureus* were resistant to ceftiofur.

Conclusion: UTI is the most spreading bacterial infection globally. The increase in antimicrobial resistance is associated with UTI, which is a serious threat and has become a global health emergency.

Keywords: Antimicrobials Resistance, Bacterial Uropathogens, Urinary tract infection (UTI)

DOI: <https://doi.org/10.3329/jdmc.v31i1.65463>

J Dhaka Med Coll. 2022; 31(1) : 23-28

Introduction

Urinary tract infection (UTI) has now become the most common infectious disease, mostly in developing regions, indicating healthcare and economic constraints.¹ Urinary tract infection can also be defined as pyelonephritis (kidney infection) or cystitis (bladder infection). This infection's common clinical signs and symptoms are dysuria, frequency, urgency, suprapubic

tenderness, fever, chills, nausea, and vomiting.^{2,3} Studies have found the most common bacterial causes of UTI like *Escherichia coli* (*E. coli*), *Klebsiella pneumoniae* (*K. pneumoniae*), *Citrobacter* species, *Enterobacter* species, *Pseudomonas aeruginosa* (*P. aeruginosa*), and *Staphylococcus* species. Still, only *Escherichia coli* causes 80% of UTIs.⁴⁻⁶ Also, the mechanism of pathogenesis of UTI

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Received: 16-01-2022

Revision: 11-02-2022

Accepted: 30-03-2022

includes adhesion to the host cell epithelium, invasion, and immune evasion via cell wall lipopolysaccharide, capsule, and fimbriae.⁷ The prevalence of this infection is mainly seen in females, influenced by biological factors like the short urethra, anal-genital proximity, and use of spermicides.⁸ However, UTI can also cause increased resistance to antimicrobial agents, including multidrug resistance (MDR), with substantial medical and increased treatment costs.^{9,10}

Antimicrobial resistance (AMR) is a condition in which microorganisms use varied resistance mechanisms, including horizontal gene transfer (for example, plasmids and bacteriophages), genetic recombination, and mutations.¹¹ AMR has now become a global public health concern.^{12,13} AMR's direct and indirect impact is seen in many underdeveloped and developing countries, influenced by several factors like low surveillance capacity and systematic data collection.^{14,15} The Asia-Pacific region (APAC) is a high-risk hotspot for spreading AMR¹⁵. Moreover, self-medication without visiting the doctor, empirical therapy, and misuse and overuse of antimicrobials also add to the existing problem and cause prolonged illness, disability, increased health care costs, and even death.¹⁶⁻¹⁸ As rising antimicrobial resistance prevails worldwide, current studies on the AMR trend of uropathogens are vital to cope with this problem[19]. Hence, this study aimed to assess the prevalence of AMR and AMR trend of bacterial uropathogens among the patients attending a tertiary care hospital in Bangladesh.

Objective of the study

This study aims to assess the proportion of AMR and AMR trend of bacterial uropathogens among the patients attending a tertiary care hospital in Bangladesh.

Materials and methodology

This study is a retrospective cross-sectional study that was conducted at Mitford Hospital and Dhaka Medical College Hospital. The study was conducted from January 2021 to January

2022. The total sample size for this study was 500. Among the 500 study patients, 250 were from Mitford Hospital, and 250 were from Dhaka Medical College Hospital.

Inclusion criteria

- We included patients with accurate demographic and clinical information, like age and sex.
- The included patients must have The urine culture result, including antimicrobial susceptibility test (AST) and results for significant bacteriuria (10⁵ CFU/ml).
- The patients consented to participate in the study.

Exclusion criteria

- We excluded the Patients with improper information on the variables like age, sex, urine culture results, and AST results of cultures with insignificant bacteriuria.

The patients were selected in this study by reviewing the hospital's nominal UTI register. We correctly recorded all the information in the hospital course. Then the positive samples were processed at the laboratories of the concerned hospitals and sub-culturing on a specific medium such as MacConkey agar, chocolate agar, mannitol salt agar, and blood agar plates. Gram staining of bacterial colonies was also tested. We did the Conventional biochemical tests, including catalase, oxidase, Indole, Voges Proskauer, Methyl red, Citrate, Triple Sugar Iron Agar, Klingler Iron Agar, Bile Esculin Agar, 6% NaCl, Motility test, and DNase test. The expert clinicians of the concerned laboratories did these cultures. The most commonly prescribed antibiotics for those patients were Ceftriaxone (30 mg), Cefotaxime (30 mg), Amikacin (30 mg), Gentamicin (10 mg), Nitrofurantoin (300 mg), Ciprofloxacin (5 mg), Tobramycin (10 mg) Trimethoprim. Trimethoprim-sulphame-thoxazole (25 mg) was tested using Kirby – Bauer's disc diffusion method.

Result

Table I
Age Distribution of the Respondents

Age Distribution	Positive		Negative	
	N	Percentage (%)	N	Percentage (%)
<18	66	26.4	103	41.2
>18	184	73.6	147	58.8

Table I show the age distribution of the respondents. Among the 500 patients, 250 patients showed positive UTI, where 66(26.4%) were <18 years and 184(73.6%) were >18 years. On the other hand, 103(41.2%) of the negative UTI patients were <18 years and 147(58.8%) were >18 years.

Table II
Gender Distribution of the Respondents

Gender Distribution	Positive		Negative	
	N	Percentage (%)	N	Percentage (%)
Male	115	46	112	44.8
Female	135	54	138	55.2

Table II shows the gender distribution of the respondents. Among the positive UTI patients, 135(54%) were female and 115(46%) were male. Among the negative UTI patients, 138(55.2%) were female, and 112(44.8%) were male.

Table III
The proportion of Uropathogenic Species of isolates (from total UTI patients; 250)

Species of isolates (from total UTI patients; 250)	N	Percentage (%)
E. coli	94	37.6
K. pneumoniae	28	11.2
CONS	11	4.4
S.aureus	23	9.2
Prouteus Spp.	4	1.6
Citrobacter Spp.	18	7.2
Salmonella Spp.	1	0.4
GNR	27	10.8
Enterobacter Spp.	9	3.6
Streptococcus Spp.	6	2.4
Klebsiella Spp.	8	3.2
Pseudomonas Spp.	1	0.4
Providencia Spp.	1	0.4
K.ozaenae	10	4.0
Shigella Spp.	2	0.8
Enterococcus Spp.	5	2.0
Serratia Spp.	1	0.4
M.morgani	1	0.4

Table IV
The Proportion of Resistant Gram-positive Isolates among UTI Patients

Antibiotics	CONS		S. aureus		Streptococcus spp		Enterococcus spp	
	N	(%)	N	(%)	N	(%)	N	(%)
AMP	0	0.0	0	0.0	1	16.7	3	50.0
PEN	13	86.7	16	50.0	2	33.3	1	16.7
CIP	11	73.3	23	71.9	2	33.3	6	100.0
GEN	9	60.0	8	25.0	2	33.3	1	16.7
NIT	5	33.3	1	3.1	1	16.7	4	66.7
NOR	6	40.0	17	53.1	1	16.7	3	50.0
TET	14	93.3	32	100.0	4	66.7	3	50.0
CAF	2	13.3	5	15.6	0	0.0	1	16.7
FOX	1	6.7	9	28.1	1	16.7	1	16.7
SXT	1	6.7	26	81.3	6	100.0	5	83.3
CRO	5	33.3	5	15.6	2	33.3	1	16.7
VAN	0	0.0	0	0.0	1	16.7	1	16.7

Key: AMP-ampicillin, PEN- penicillin, AMC-amoxicillin-clavulanic acid, CIP- ciprofloxacin, GEN-gentamycin, NIT- nitrofurantoin, NOR- norfloxacin, TET-tetracycline, TOB- tobramycin, FOX- cefoxitin, CRO- ceftriaxone, VAN-vancomycin, NA- nalidixic acid, OXA-oxacillin.

Table III shows the proportion of uropathogenic species of isolates (from total UTI patients; 250). *E. coli* 94(37.6%) and followed by *K. pneumoniae* 28(11.2%), CONS 11(4.4%), *S. aureus* 23(9.2%), *Proteus Spp.* 4(1.6%), *Citrobacter Spp.* 18(7.2%), *Salmonella Spp.* 1(0.4%), GNR 27(10.8%), *Enterobacter Spp.* 9(3.6%), *Streptococcus spp.* 6(2.4%), *Klebsiella Spp.* 8(3.2%), *Pseudomonas Spp.* 1(0.4%), *Providencia spp.* 1(0.4%), *K. ozaenae* 10(4%), *Shigella Spp.* 2(0.8%), *Enterococcus Spp.* 5(2%), *Serratia spp.* 1(0.4%) and *M. morgani* 1(0.4%).

Table IV shows the proportion of resistant Gram-positive isolates among the UTI patients. Gram-positive isolates presented a high resistance to tetracycline 14(93.3%) and penicillin 13(86.7%). Antimicrobial agents most effective against Gram-positive uropathogens were vancomycin and nitrofurantoin. *Staphylococcus aureus* was the most common isolate of Gram-positive isolates. It was highly resistant to tetracycline 32(100%) and trimethoprim-sulfamethoxazole 26(81.3%). In addition, 9(28.1%) of *S. aureus* were resistant to cefoxitin.

Discussion

Human health is at great risk due to antimicrobial-resistant infections worldwide. WHO launched the Global Antimicrobial Resistance Surveillance System (GLASS) program to raise awareness about AMR through surveillance and research. The main targets of GLASS are the chief etiologic agents of UTI and common resistant bacteria such as *Escherichia coli*, *K. pneumoniae*, and *S. aureus*.²⁰ Epidemiological studies in this field can help select effective antimicrobial agents for treatment, prevention, and control actions.²¹ Among the 500 patients, 250 showed positive UTIs, where 26.4% were <18 years and 73.6% were >18 years. On the other hand, 41.2% of the negative UTI patients were <18 years and 58.8% were >18 years [Table I]. A study conducted in Addis Ababa found that participants' most affected age group was from 21–30 years.²² Another study also showed an increased infection rate in elderly participants, similar to the present study.²³ Hence, age-related weakened immunity, changes in vaginal hormonal secretion, or other comorbidities can cause the elderly to acquire UTIs.²⁴ Among the

positive UTI patients, 135(54%) were female, and 115(46%) were male. Among the negative UTI patients, 138(55.2%) were female, and 112(44.8%) were male [Table II]. Nahar et al., in their study, found the female participants were 65.02% and the males 34.98%.²⁵ Regarding the proportion of bacterial isolates in this study, *E. coli* was 37.6%, followed by *K. pneumoniae* 11.2%, *CONS* 4.4%, *S. aureus* 9.2%, *Proteus Spp.* 1.6%, *Citrobacter spp.* 7.2%, *Salmonella Spp.* 0.4%, *GNR* 10.8%, *Enterobacter Spp.* 3.6%, *Streptococcus spp.* 2.4%, *Klebsiella Spp.* 3.2%, *Pseudomonas Spp.* 0.4%, *Providencia spp.* 0.4%, *K. ozaenae* 4%, *Shigella Spp.* 0.8%, *Enterococcus Spp.* 2%, *Serratia spp.* 0.4% and *M. morgani* 0.4% [Table III]. Some studies reported similar findings: Gondar[23], Bahir Dar[26], Hawassa.²⁷ Addis Ababa, Ethiopia[28], and India[29]. Gram-positive isolates presented a high resistance to tetracycline 93.3% and penicillin 86.7%. Antimicrobial agents most effective against Gram-positive uropathogens were vancomycin and nitrofurantoin. *Staphylococcus aureus* was the most common isolate of Gram-positive isolates. It was highly resistant to tetracycline at 100% and trimethoprim-sulfamethoxazole at 81.3%. In addition, 28.1% of *S. aureus* were resistant to cefoxitin [Table IV]. This finding is much higher than the resistance rate of 34.6% reported in a study conducted in Iran.²¹ Studies reported that uropathogens are highly resistant to some antibiotics like ampicillin, amoxicillin-clavulanate, and trimethoprim-sulfamethoxazole.^{30,31} The recommendations from national guidelines for antimicrobial use in different countries could have resulted in varying resistance among countries.³² Considering the existing resistance from the result of this study, it is suggested that healthcare providers encourage them to use effective antibiotics selectively. Communities worldwide would understand the severity of antibiotic resistance and design comprehensive policies by aggregating reports from diverse geographic locations.

Conclusion

UTI is the most spreading bacterial infection globally. The increase in antimicrobial resistance is associated with UTI, a severe threat

that has become a global health emergency. Also, antibiotic-resistant bacteria are rising and contributing to increased morbidity and mortality rates. This situation also leads to more extended hospital stays. The emergence of antibiotic resistance in bacteria from the urinary tract is associated with significant adverse outcomes. Hence, it is required to take steps regarding this matter. However, the treatment procedure's effectiveness depends on proper and timely diagnosis. But the actual cause most of the time remains unknown due to a lack of diagnostics or timely visits to the doctor's chamber. The patients should be made aware so that they become motivated to visit the doctor when needed and stop self-medication practice, and this may help reduce the resistance rate to some extent.

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