Prescription pattern of antibiotics in urinary tract infection based on antimicrobial susceptibility test at a tertiary care hospital

Laxmi Shrestha[1*], Shristi Adhikari[2], Anjan Palikhey[1], Buddhi Raj Pokhrel[3], Amit Shrivastava[1], Bishal Joshi[4], Chandrajeet Kumar Yadav[2]

[1]Department of Pharmacology, Universal College of Medical Sciences, Rupandehi, Bhairahawa, Nepal, [2]Department of Pharmacy, Universal College of Medical Sciences, Rupandehi, Bhairahawa, Nepal, [3]Department of Biochemistry, Universal College of Medical Sciences, Rupandehi, Bhairahawa, Nepal, [4]Department of Physiology, Universal College of Medical Sciences, Rupandehi, Bhairahawa, Nepal

ABSTRACT

Introduction: Urinary tract infection is a common bacterial infection associated with significant morbidity, mortality, and financial burden. This study aimed to identify the causative bacteria, assess their antimicrobial susceptibility patterns and evaluate empirical and definitive antibiotic therapy for urinary tract infection. **Methods:** A hospital-based cross-sectional study was conducted at the outpatient medicine department at a teaching hospital in Nepal from February 15 to July 14, 2022. Two hundred participants with positive urine cultures and antimicrobial susceptibility testing were included. The microorganism causing urinary tract infection and prescription pattern of antibiotics pre-and post-AST report were analyzed. **Results:** The majority of isolated pathogens were gram-negative bacteria (73%), with Escherichia coli being the most common (53.5%), followed by Staphylococcus aureus among gram-positive bacteria (14.5%). Female patients had a higher incidence of urinary tract infection (59.5%) than males (40.5%). The age group above 60 years had the highest occurrence (34%). Antibiotic susceptibility testing revealed that Escherechia coli exhibited higher sensitivity to nitrofurantoin, amikacin, and meropenem, while resistance was observed against ampicillin, cefixime, and norfloxacin. Empirical antibiotics were commonly prescribed, with levofloxacin and ceftriaxone being the most frequent choices. After antibiotic susceptibility testing, nitrofurantoin and levofloxacin were frequently prescribed. **Conclusions:** This study provides valuable insights into the etiology of urinary tract infection and antibiotic susceptibility patterns, aiding in selecting appropriate antimicrobial therapy based on local resistance patterns.

Keywords: AST, empirical, gram negative, gram positive, UTI.

***Correspondence:**
Dr. Laxmi Shrestha
Department of Pharmacology
Universal College of Medical Sciences, Bhairahawa, Rupandehi, Nepal
Email: drshresthalaxmi@gmail.com

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INTRODUCTION

Urinary tract infection (UTI) is the most common bacterial infection with a high morbidity, and mortality affecting all age groups, with higher prevalence with increasing age and in females.[1] It is usually classified by the infection site, symptomatic or asymptomatic and may be complicated and uncomplicated.[2,3] The common pathogen causing UTIs is mainly gram-negative microorganisms like Escherichia coli (E. coli), Klebsiella pneumonia (Kleb. spp.), etc. And gram-positive microorganisms like Staphylococcus aureus (S. aureus), Enterococcus species.[4,5]

UTI is one of the most common diseases among the Nepalese population.[6] Broad-spectrum antibiotics are generally used for empirical treatment of UTI.[4] Use of empirical therapy have increases the incidence of drug resistance among uropathogens necessitating antibiotic susceptibility tests (AST), a scenario that needs to be promptly addressed in Nepal.[7,8]

The aim of this study was to find the prescription pattern of

antibiotics in UTI based on AST at a tertiary care hospital.

METHODS

A cross-sectional study was conducted at the outpatient medicine department at Universal College of Medical Sciences and Teaching Hospital, Bhairahawa, Ranigaun, over the period of February 15 to July 14, 2022. Ethical approval for the study was obtained from Institutional Review Committee of the institute (Ref No. UCMS/IRC/029/22). A total of 200 urine samples of clinically diagnosed UTI patients between 16 to 80 years of either sex were sent for urine culture and AST to the department of microbiology. Patients with complicated and recurrent UTIs and prolonged antibiotic therapy were excluded. Both verbal and written consent was taken from the patients.

A purposive sampling technique was used for patient selection. The required sample size was calculated using Cochrane's formula: sample size (n) = z^2PQ/d^2, where z = 1.96; P = proportion of study population estimated to have UTI from previous study = 13.8% [9]; Q = 100 - P; d = allowable error = 5%. The calculated minimum sample size was 182.79 ~ 183. Finally, a total of 200 participants were taken into the study. The participants were interviewed face to face regarding socio-demographic and clinical details like age, gender, and data regarding uropathogens, antibiotic pattern, and antimicrobial susceptibility tests were recorded in case proforma from the patient's AST report. Data were entered into Microsoft Excel (MS, 2010) and analyzed using a statistical package for social science (SPSS) version 20.0. UTI-causing microorganisms were depicted in the bar diagram. Sex and age-wise distribution of pathogens, AST pattern, and pre-and post-AST treatment pattern were represented in tabulated form.

RESULTS

Among 200 samples, 73% of isolated bacterial pathogens were gram-negative, and 27% were gram-positive. E. coli was the most predominant bacterial species (53.5%) causing UTI, followed by S. aureus (14.5%), Kleb. spp. (11%). (Figure1)

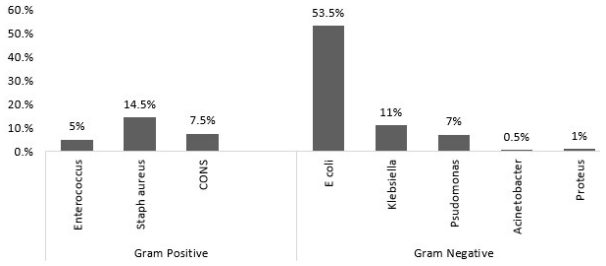

Figure 1: Gram positive and gram negative organisms causing UTI

The incidence of UTI in female patients (59.5%) was higher than in males (40.5%). UTI was highest in the age group above 60 years (34%) and lowest in 16 to 30 years (20.5%). The major microorganisms among gram-negative and gram-positive bacteria were E. coli (53.5%) and S. aureus (14.5%) respectively. E. coli and S. aureus were the most frequently isolated pathogen in both sexes. E.coli was highest in females (60.5%) compared to male (43.2%) patients among gram-negative microorganisms. The age group and sex-wise distribution of gram-positive and gram-negative organisms are shown in Table 1.

Table 1: Age and sex-wise distribution of UTI causing pathogens

	Gram Negative (n =146)					Gram Positive (n = 54)			Total
	E coli (n=107)	Kleb. Spp (n=22)	Pseudo. Aer. (n=14)	Acineto (n=1)	Proteus spp. (n=2)	Entero. spp (n=10)	S. aureus (n=29)	CONS (n=15)	
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	
Age group									
16-30	22 (53.7%)	7 (17.07%)	3 (7.31%)	1 (2.43%)	1 (2.43%)	1 (2.43%)	5 (12.2%)	1 (2.43%)	41
31-45	19 (41.33%)	6 (13.05%)	2 (4.34%)	-	-	4 (8.71%)	9 (19.56%)	6 (13.04%)	46
46-60	23 (51.1%)	2(4.4%)	3 (6.7%)	-	-	3 (6.7%)	9 (20%)	5 (11.1%)	45
>60	43 (63.2%)	7 (10.3%)	6(8.8%)	-	1 (1.5%)	2(3%)	6 (8.8%)	3 (4.4%)	68
Sex									
Male	35 (43.2%)	10 (12.35%)	10 (12.35%)	1(1.23%)	-	5 (6.17%)	12 (14.82%)	8 (9.88%)	81
Female	72 (60.5%)	12 (10.08%)	4 (3.36%)	-	2 (1.68%)	5 (4.20%)	17 (14.28%)	7 (5.9%)	119

Abbreviations: E. coli: Escheresia coli; Kleb: Klebsiella; Entero: Enterococcus; Pseudo. Aer.: Pseudomonas Aeruginosa; Acenito: Acenitobacter; Staph: Staphylococcus; CONS: Coagulase negative staphylococcus aureus; Spp –Species; Row Percentages are used

The antibiotic susceptibility pattern of gram negative and gram positive bacterial isolates are shown in table 2 and 3, respectively. Among the performed antibiotic susceptibility test for E. coli, the higher proportion of test organism were sensitive to nitrofurantoin 89(83.2%), amikacin 88(82.24%), meropenem 65(60.7%), amoxicillin and clavulanic acid 56(52.3%), gentamicin 53(49.5%). Similarly, significant percentage of test organisms showed resistance to ampicillin 76(71.03%), cefixime 65(60.74%), norfloxacin 65(60.74%), cotrimoxazole 61(57%), and ceftriaxone 58(54.2%). Kleb. spp. was the second commonly isolated causative organism of UTI, which showed resistant to ampicillin (68.1%), cefixime (59.1%), cotrimoxazole and ceftriaxone (45.5%), norfloxacin (36.3%), nitrofurantoin (31.8%). In Pseudo. Aer., nitrofurantoin (64.2%), and norfloxacin (42.8%) were resistant. The remaining antibiotics tested were moderately resistant. AST pattern of gram positive micro-organisms second-line antibiotics used in the management of UTI in the present study,

amikacin and meropenem were moderately sensitive. In case of Proteus species, most of the antibiotics tested were moderately sensitive. However, levofloxacin and vancomycin were not tested in these organisms. (Table 3)

The major etiological gram-positive organism causing UTI was S. aureus. Among the performed antibiotic susceptibility test, the organisms were sensitive to nitrofurantoin (86.2%), vancomycin (72.4%), cotrimoxazole (68.9%), and amikacin (65.5%). Similarly, the test organisms showed resistance to cefixime (65.5%), ceftriaxone (58.6%), and norfloxacin (44.8%). However, meropenem and piperacillin + tazobactam were not tested in these organisms.

Table 2: AST pattern of Gram negative microorganisms

Antibiotics	Escheresia coli (n=107)			Klebsiella Pneumoniae (n=22)			Pseudomonas Aeruginosa (n=14)		
	S n(%)	R n(%)	NT n(%)	S n(%)	R n(%)	NT n(%)	S n(%)	R n(%)	NT n(%)
Cotrimoxazole	36 (33.64%)	61 (57.01%)	10 (9.35%)	11 (50%)	10 (45.45%)	1(4.55%)	2 (14.29%)	1 (7.14%)	11 (78.57%)
Amoxicillin + Clavulanic acid	56 (52.34%)	9 (8.41%)	42 (39.25%)	10 (45.45%)	5 (22.73%)	7 (31.82%)	-	1 (7.14%)	13 (92.86%)
Ampicillin	5 (4.67%)	76 (71.03%)	26 (24.30%)	-	15 (68.19%)	7 (31.81%)	1 (7.14%)	2 (14.28%)	11 (78.57%)
Cefixime	14 (13.1%)	65 (60.74%)	28 (26.16%)	5 (22.73%)	13 (59.09%)	4 (18.18%)	-	-	14(100%)
Nitrofurantoin	89 (83.18%)	8 (7.47%)	10 (9.35%)	14 (63.64%)	7 (31.81%)	1 (4.55%)	3 (21.43%)	9 (64.29%)	2 (14.28%)
Gentamycin	53 (49.53%)	10 (9.35%)	44 (41.12%)	14 (63.64%)	2(9.09%)	6 (27.27%)	2 (14.28%)	-	12 (85.72%)
Norfloxacin	36 (33.64%)	65 (60.75%)	6 (5.61%)	11 (50%)	8 (36.36%)	3 (13.64%)	3 (21.43%)	6 (42.86%)	5 (35.71%)
Ceftriaxone	28 (26.17%)	58 (54.20%)	21 (19.63%)	8 (36.36%)	10 (45.45%)	4 (18.18%)	1 (7.14%)	-	13 (92.86%)
Amikacin	88 (82.24%)	7 (6.54%)	12 (11.22%)	17 (77.27%)	1 (4.55%)	4 (18.18%)	9 (64.29%)	2 (14.28%)	3 (21.43%)
Meropenem	65 (60.75%)	4 (3.74%)	38 (35.51%)	13 (59.09%)	2 (9.09%)	7 (31.81%)	9 (64.29%)	1 (7.14%)	4 (28.57%)
Piperacillin + Tazobactam	2 (1.87%)	1 (0.93%)	104 (97.20%)	7 (31.81%)	-	15 (68.18%)	7 (50%)	2 (14.28%)	5 (35.72%)
Levofloxacin	11 (10.28%)	-	96 (89.72%)	-	1 (4.55%)	21 (95.45%)	5 (35.72%)	3 (21.43%)	6 (42.86%)
Vancomycin	6 (5.61%)	-	101 (94.39%)	1 (4.55%)	-	21 (95.45%)	1 (7.14%)	-	13 (92.86%)

*S: Sensitive; R: Resistant; NT: Not Tested

Table 3: AST pattern of Gram positive microorganisms

Antibiotics	Enterococcus Spp (n=10)			S. aureus (n=29)			CONS (n=15)		
	S	R	NT	S	R	NT	S	R	NT
n(%) of First line Antibiotics									
Cotrimoxazole	6 (60%)	0 (0)	4 (40%)	20 (68.97%)	8 (27.59%)	1 (3.44%)	8 (53.33%)	3 (20%)	4 (26.67%)
Amoxicillin+ Clavulanic acid	1 (10%)	3 (30)	6 (60%)	5 (17.24%)	3 (10.35%)	21 (72.41%)	8 (53.33%)	1 (6.67%)	6 (40%)
Ampicillin	-	2 (20)	8 (80%)	-	1 (3.44%)	28 (96.55%)	-	2 (13.33%)	13 (86.67%)
Cefixime	1 (10%)	3 (30%)	6 (60%)	2 (6.90%)	19 (65.52%)	8 (27.58%)	1 (6.67%)	10 (66.66%)	4 (26.67%)
Nitrofurantoin	6 (60%)	4 (40%)	-	25 (86.21%)	1 (3.44%)	3 (10.34%)	11 (73.33%)	4 (26.67%)	0(0%)
Gentamycin	3 (30%)	-	7 (70%)	11 (37.93%)	8 (27.59%)	10 (34.48%)	10 (6.66%)	-	5 (33.33%)
Norfloxacin	1(10)	7(70%)	2 (20%)	12 (41.38%)	13 (44.83%)	4 (13.79%)	4 (26.67%)	8 (53.33%)	3 (20%)
Ceftriaxone	1(10)	4 (40%)	5 (50%)	5 (17.24%)	17 (58.62%)	7 (24.14%)	4(26.67%)	2 (13.33%)	9 (60%)
Amikacin	3(30)	4 (40%)	3 (30%)	19 (65.52%)	4 (13.79%)	12 (80%)	12 (80%)	-	3 (20%)
Meropenem	1(10)	1 (10%)	8 (80%)	-	-	-	-	-	15 (100%)
Piperacillin + Tazobactam	-	-	10 (100%)	-	-	29 (100%)	-	-	15 (100%)
Levofloxacin	2 (20%)	8 (80%)	-	1 (3.45%)	-	28 (96.55%)	-	-	15 (100%)
Vancomycin	8 (80%)	-	2 (20%)	21 (72.41%)	-	8 (27.59%)	11 (73.33%)	-	4 (26.67%)

*S: Sensitive; R: Resistant; NT: Not Tested

Table 4 shows the prescription of antibiotics before and after the antibiotic susceptibility test (AST). The antibiotics like ceftriaxone, levofloxacin, nitrofurantoin, norfloxacin, and cefixime were prescribed before the antibiotic susceptibility test as empirical therapy. Similarly, nitrofurantoin, levofloxacin, amikacin, cefixime, norfloxacin, and ceftriaxone were prescribed after an antibiotic susceptibility test (AST). Likewise, piperacillin tazobactam, meropenem, gentamicin, and cotrimoxazole were the antibiotic most commonly prescribed only after an antibiotic susceptibility test (AST). Empirical antibiotics were used in all UTI cases. Among them, the most commonly prescribed antibiotics were levofloxacin (23%) and ceftriaxone (23%), followed by nitrofurantoin (19%). Nitrofurantoin was frequently prescribed antibiotic after antibiotic susceptibility test (AST), followed by levofloxacin (14%), and amikacin (13.5%).

Table 4: Prescription pattern of antibiotics pre-and post AST

Antibiotic group	Antibiotics	Empirical (before AST)	After AST
n(%) of Antibiotics prescribed before and after AST			
Cephalosporins	Ceftriaxone	46(23%)	11(5.5%)
	Cefixime	28(14%)	15(7.5%)
	Cefazolin	4(2%)	1(0.5%)
Penicillins	Ampicillin	3(1.5%)	1(0.5%)
Aminoglycosides	Amikacin	3(1.5%)	27(13.5%)
Fluoroquinolones	Levofloxacin	46(23%)	28(14%)
	Norfloxacin	27(13.5%)	13(6.5%)
	Ofloxacin	5(2.5%)	1(0.5%)
Nitrofuran derivative	Nitrofurantoin	38(19%)	74(37%)
n(%) of Antibiotics prescribed only after AST			
Cephalosporins	Cefodoxime	-	1(0.5%)
	Cefotaxime	-	1(0.5%)
	Cefuroxime	-	1(0.5%)
Penicillins	Amoxycillin	-	1(0.5%)
	Piperacillin + Tazobactam	-	6(3%)
	Meropenem	-	6(3%)
Glycopeptides	Vancomycin	-	3(1.5%)
Polypeptides	Polymyxin B	-	2(1%)

Aminoglycosides	Gentamicin	-	5(2.5%)
Tetracyclines	Doxycycline	-	1(0.5%)
Sulfonamides	Cotrimoxazole	-	2(1%)

DISCUSSION

Effective management of UTI requires proper identification of microorganisms causing the disease and selection of effective antibiotics for that microorganism. The present study showed the antibiotic susceptibility pattern of various bacterial species isolated from patients with UTI and the prescription pattern of antibiotics for managing UTI.

A total of 200 patients with UTI were included in the study. Among them, 73% were gram-negative, and 27% were gram-positive microorganisms. E. coli was the predominant etiological agent (53.5%), followed by S. aureus (14.5%). These findings are similar to various studies.[10-12] However, in the study conducted by Khatiwada et al., the second common isolate was Klebsiella.[13]

In the present study, the prevalence of UTI in female patients (59.5%) was higher compared to male patients (40.5%). UTI prevalence was higher in the age group above 60 years (34%). These findings are similar to other studies.[13-16] The higher incidence of UTI in females was likely due to anatomical and hormonal variations in females, and benign prostate enlargement and neurogenic bladder may be the cause among male patients. Age-related changes in the urinary tract and comorbidities in older individuals could contribute to higher UTI prevalence.[17,18]

The present study revealed the prevalence of resistance to the commonly prescribed antibiotics. The gram-negative organisms E. coli and Kleb. pneumoniae were resistant to ampicillin, cefixime, and cotrimoxazole and were ineffective in treating the patients with UTIs. In contrast, nitrofurantoin (83.2%), amikacin (82.24%), and meropenem (60.7%) were the most susceptible drug for gram-negative microorganisms. These antibiotic susceptibility tests were consistent with prior studies.[19-21] This highlights the importance of conducting antibiotic susceptibility tests before prescribing treatment to ensure the appropriate choices of antibiotics.

The prescription patterns of antibiotics before and after conducting the AST were analyzed. Among antibiotics used, nitrofurantoin was the most commonly prescribed drug, followed by levofloxacin in both empirical and after AST. Empirical antibiotics, such as ceftriaxone, levofloxacin, nitrofurantoin, norfloxacin, and cefixime, were commonly prescribed before AST. After AST, nitrofurantoin, levofloxacin, amikacin, cefixime, norfloxacin, and ceftriaxone were frequently prescribed. This suggests that AST results influenced the choice of antibiotics, leading to more targeted and effective treatment for UTIs. The prescription pattern of antibiotics varies depending on the individual choice made by the physician and microbial resistance pattern. Thus the selection of antibiotics depends on the prevailing resistance pattern within a specific local setting and may even vary within the same location over time.

Our study had few limitations. The study did not evaluate the susceptibility of these organisms to meropenem and piperacillin tazobactam, suggesting a gap in knowledge regarding their effectiveness on UTI. Further studies with larger sample size covering wide array of microorganisms for AST are recommended.

CONCLUSIONS

E.coli and S. aureus were the predominant pathogens involved in UTI. The resistance to the commonly used antibiotics like cefixime, norfloxacin and ceftriaxone is a serious problem that should be identified, through AST to guide appropriate treatment decisions. These findings can help healthcare providers make informed choices regarding empirical and targeted antibiotic therapies for managing UTIs.

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AUTHORS CONTRIBUTION

LS did concept designing, literature search, clinical studies, data acquisition and analysis, statistical analysis, manuscript preparation, editing and review; SA did concept designing, literature search, clinical studies, data acquisition and manuscript review; AP defined intellectual content, manuscript editing and review; BRP defined intellectual content, literature search, data analysis, statistical analysis, and manuscript review; AS defined intellectual content, and manuscript editing; BJ and CKY did manuscript editing and review.

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