PREVALENCE AND SUSCEPTIBILITY PATTERN OF BACTERIAL UROPATHOGENS AMONG PATIENTS WITH URINARY TRACT INFECTION AT BIRAT MEDICAL COLLEGE TEACHING HOSPITAL OF EASTERN NEPAL

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ABSTRACT

Introduction

Urinary tract infection (UTI) is a frequent condition encountered in clinical settings. Empirical treatment is common. The treatment without urine culture and sensitivity leads to antimicrobial resistance. This is a major global concern.

Objective

The objective of this study was to find the prevalence and susceptibility pattern of Bacterial Uropathogens among patients with Urinary Tract Infection at Birat Medical College and Teaching Hospital of eastern Nepal.

Methodology

A cross-sectional study was conducted among patients with UTI attending Birat Medical College and Teaching Hospital from August 2018 to December 2018. The sample size of the study was 530. Ethical clearance was taken from the Institutional Review Committee of Birat Medical College and Teaching Hospital (Ref: IRC-PA-009/2075-76). Data were entered into Microsoft Excel and analyzed by using SPSS.

Results

The prevalence of bacterial uropathogens among urine culture was 66.04%. The common uropathogens isolated were *E.coli* (66.9%) and Klebsiella spp (15.1%). *E.coli* was highly susceptible to Chloramphenicol (100%) followed by Ceftrixone (82.4%), Cefpodoxime (77.8%) and Amikacin (77.9%); while *Klebsiella* spp were susceptible to nalidixic acid (40%) followed by co-trimoxazole (17.9%).

Conclusion

Almost 2 out of 3 samples had bacterial uropathogens isolated. *E. coli* and *Klebsiella* spp were common. Chloramphenicol and Nalidixic acid were highly susceptible to *E.coli* and *Klebsiella* spp respectively.

KEYWORDS

Prevalence, Nepal, urinary tract infections, teaching hospitals, bacterial Uropathogens

INTRODUCTION

Urinary tract infections (UTI) describe microbial colonization and infection of structures of the urinary tract. UTI is categorized by infection site as pyelonephritis, cystitis, and urethritis, and can be classified as uncomplicated or complicated.[1] UTIs are most prevailing in the community with substantial clinical and financial burdens.[2] Presence of one lakh or more colony forming units (CFU) per ml of urine is defined as significant bacteriuria.[3] This leads criteria has been questioned and bacterial counts of 10^2 or more microorganisms per ml particularly when accompanied by pyuria (more than 10 WBC/mm3) provide impressive evidence of urinary tract infections in symptomatic young women.[4] The Infectious Disease Society of America (IDSA) gave a slightly more relaxed consensus definition requiring 10^5 CFU per ml to diagnose cystitis and pyelonephritis.[3-5] There were studies with different prevalence of UTI in the general population of Nepal. Studies done at Sindhupalchowk district reported UTI prevalence as 36.9%[6] and at a medical college of Kathmandu was 40.4%.[7] A study at Kathmandu Medical College Teaching Hospital found that most common pathogens isolated were E.coli (79.1%) followed by Klebsiella spp (11.7%), Citrobacter spp (8.0%) and Proteus spp (7.0%).[8] In another study, the highest percentage of sensitivity was found with Ofloxacin (63.0%), Ciprofloxacin (62.0%), Nitrofurantoin (49.1%) and Amikacin (40.1%).[9] Patients attending Birat Medical College and Teaching Hospital has an unknown prevalence of UTI with unknown drug susceptibility pattern. Previous studies conducted in surrounding communities of this medical college teaching hospital reported that self-medication was 44.04% with antibiotic being the second most common group for UTI.[10] Due to this, it creates a gap in the treatment of UTI. The clinicians are following empirical treatment without appropriate culture and sensitivity, which may lead to antibiotic resistance. This study was conducted with an objective to find theprevalence and susceptibility pattern of Bacterial Uropathogens among patients with Urinary Tract Infection at Birat Medical College and Teaching Hospital of eastern Nepal.

METHODOLOGY

A cross-sectional study was conducted among patients with UTI attending Birat Medical College and Teaching Hospital from August 2018 to December 2018. All the patients suspicious to have urinary tract infection with the history of pain while micturition, frequency, urgency, lower abdominal pain and fever were subjected to urine culture. Bacterial pathogen isolated with antibiotics sensitivity pattern were taken into account and the findings were correlated. The sample size of the study was 530. Ethical clearance was taken from the Institutional Review Committee of Birat Medical College and Teaching Hospital (Ref: IRC-PA-009/2075-76). Data were entered into Microsoft Excel and analyzed by using SPSS. The statistical significance difference is considered at p <0.05.Midstream and catheter-catch urine samples (information on how to collect proper sample in sterile container aseptically was given prior to the collection) were collected into a sterile wide-mouth container with all aseptic measures from clinically suspected UTI patients of different age and sex attending either outpatient department (OPD) or inpatient department (IPD) of Birat Medical College and Teaching Hospital. There has not been defined the minimum level of bacteriuria demonstrating an infection of the urinary tract in scientific literature or standardized by microbiological laboratories. As many laboratories define 10^5 colony forming units (cfu)/mL urine as the threshold for UTI.[11] The urine samples from UTI cases were Inoculated aseptically on Blood agar and Cystine Lactose Electrolyte deficient agar (CLED) media by using a calibrated wire loop of 28G with an internal diameter of 3.26 mm holding 0.004 ml of urine and incubated overnight at 37°C aerobicallyand observed for growth. A specimen was considered positive for UTI if a single organism was cultured at a concentration of $\geq 10^5$ cfu/mL.[11] Bacterial identification was made using biochemical tests, namely Indole, Citrate, Oxidase, H2S production, lactose fermentation, Urea hydrolysis, gas production, Catalase, Coagulase, and Novobiocin susceptibility test.[12] Mueller-Hinton agar was used for antimicrobial susceptibility testing (AST) following the Kirby–Bauer disc diffusion method.[13] Selection of the most appropriate antimicrobial agent requires knowing the organisms identity gram positive/negative. Against a panel of 11 antibiotics; Amoxicillin (10 mcg), Nitrofurantoin (300 mcg), Cephalexin (30 mcg), Cefuroxime (30 mcg), Cefpodoxime (30 mcg), Ceftrixone (30 mcg), Ciprofloxacin (10 mcg), Gentamicin (10 mcg), Nalidixic acid (30 mcg) and Co-trimoxazole (25 mcg). The antimicrobial agents tested were as per Clinical and Laboratory Standards Institutes (CLSI) and The European Committee on Antimicrobial Susceptibility Testing (EUCAST) rules for each isolate.[12] For the quality control of susceptibility tests Escherichia coli ATCC 25922, E. coli ATCC 35218, Staphylococcus aureus ATCC 29213, Enterococcus faecalis ATCC 29212, E. faecalis ATCC 51299 and Pseudomonas aeruginosa ATCC 27853 strains were used. As per the Clinical Laboratory Standard Institute (CLSI) guidelines susceptibilities were noted as sensitive and resistant based on the diameter of the zone of inhibition.[14] These antimicrobial agents were selected because of the frequent empirical treatment used by the clinicians. Multidrug resistance was defined as resistance to two or more of the antimicrobials tested. Positive results from urine culture and antimicrobial sensitivity test results were reported to the attending physician for subsequent treatment and follow up.

RESULTS

In this study, out of 530 cultured urine samples, 350 were found to be positive for uropathogens. So the prevalence of uropathogens was 66.04%.

Table 1: General characteristics of the study participants having positive culture for uropathogens (n = 350)

Variables	Frequency (n)	Percentage (%)
Sex		
Male	107	30.6
Female	243	69.4
Age group (in Years)		
0-14	16	4.6
15-24	85	24.3
25-39	89	25.4
40-59	95	27.1
60-74	45	12.9
≥75	20	5.7

As in table 1, the majority of the participants (69.4%) were female, 27.1% in the age categories of 40-59 years. The male to female ratio was 1:2.3.

Table 2: Uropathogens isolated from urine samples (n=350)

Uropathogens	Frequency (n)	Percentage (%)
Escherichia coli	234	66.9
Klebsiella pneumoniae	53	15.1
Staphylococcus aureus	*29*	*8.3*
Enterococcus faecalis	10	2.9
Proteus mirabilis	9	2.6
Staphylococcus saprophyticus	7	2.0
Pseudomonas aeruginosa	6	1.7
Acinetobacter baumannii	2	0.5

The most common uropathogens isolated were *Escherichia coli (*66.9%) followed by *Klebsiella pneumoniae* (15.1%) (Table 2).

Table 3: Age distribution of different uropathogens isolated from urine samples (n=350)

Age (Year)	E.coli	Klebsiella spp	Pseudomonas spp	Proteus spp	Enterococcus spp.	Acinetobacter spp	S. aureus	S. saprophyticus	Total
0-14	7(43.8%)	6(37.5%)	1(6.2%)	0	0	1(6.2%)	1(6.2%)	0	16 (100%)
15-24	54(63.5%)	15(17.6%)	1(1.2%)	3(3.5%)	3(3.5%)	0	7(8.2%)	2(2.4%)	85(100%)
25-39	66(74.2%)	11(12.4%)	1(1.1%)	0	3(3.4%)	0	6(6.7%)	2(2.2%)	89(100%)
40-59	72(75.8%)	8(8.4%)	1(1.1%)	3(3.2%)	1(1.1%)	0	10(10.5%)	0	95(100%)
60-74	24(53.3%)	12(26.7%)	0	3(6.7%)	1(2.2%)	1(2.2%)	2(4.4%)	2(4.4%)	45(100%)
≥75	11(55%)	1(5%)	2(10%)	0	2(10%)	0	3(15%)	1(5%)	20(100%)
Total	234(66.9%)	53(15.1%)	6(1.7%)	9(2.6%)	10(2.9%)	2(0.6%)	2(8.3%)	7(2%)	350(100%)

Table 3 shows, the highest prevalence of *E.coli* was observed in the age group 40-59 years followed by 25-39 years. Similarly, the highest prevalence was observed for *Klebsiella pneumoniae* at 0-14 years, *Pseudomonas aeruginosa* at ≥75 years, Proteus spp at 60-74 years, *Enterococcus spp* at ≥75 years, *Acinetobacter spp* at 0-14 years, S. aureus at 40-59 years and *S. saprophyticus* at 60-74 years.

Table 4: Antibiotics and bacteria sensitivity pattern of uropathogens from urine samples (n=350)

Drugs	Antibiotic susceptibility pattern	E.coli	Klebsiella	Pseudomonas	Proteus	Enterococcus	Acenetobacter	S. aureus	S. saprophyticus	Total
Ampicillin	S	1(10%)	1(10%)	0	0	0	0	7(70%)	1(10%)	10(100%)
	R	5(50%)	0	0	0	1(10%)	0	4(40%)	0	10(100%)
Nalidixic Acid	S	5(50%)	4(40%)	1(10%)	0	0	0	0	0	10(100%)
	R	9(90%)	0	0	0	0	0	1(10%)	0	10(100%)
Amikacin	S	53(77.9%)	8(11.8%)	1(1.5%)	1(1.5%)	NA	1(1.5%)	2(2.9%)	1(1.5%)	68(100%)
	R	4(57.1%)	1(14.3%)	0	0		1(14.3%)	0	0	7(100%)
Cotrimoxazole	S	36(64.3%)	10(17.9%)	0	1(1.8%)	1(1.8%)	0	8(14.3%)	0	56(100%)
	R	50(80.6%)	3(4.8%)	0(0.0%)	1(1.6%)	3(4.8%)	2(3.2%)	29(4.8%)	0	62(100%)
Vancomycin	S	2(7.4%)	0	0	0	2(7.4%)	0	21 (77.8%)	NA	27(100%)
	R	0	0	0	0	0	0	0		1(100%)
Cefpodoxime	S	7 (77.8%)	0	0	0	1(11.1%)	1(11.1%)	0	0	9(100%)
	R	12(92.3%)	1(7.7%)	0	0	0	0	0	0	13(100%)
Nitrofurantoin	S	216(72.7%)	43(14.5%)	NA	NA	6(2%)	0	16(5.4%)	6(2%)	297(100%)
	R	5(38.5%)	2(15.4%)			2(15.4%)	2(15.4%)	0	0	13(100%)
Chloramphenicol	S	3(100%)	0	0	0	0	0	0	0	3(100)%
	R	1(33.3%)	2(33.3%)	0	0	0	0		1(33.3%)	4(100%)
Ceftriaxone	S	42(82.4%)	2(3.9%)	0	4(7.8%)	2(3.9%)	1(2%)	0	0	51(100%)
	R	42(85.7%)	5(10.2%)	0	1(2%)	0	1(2%)	0	0	49(100%)
Ciprofloxacin	S	80(67.8%)	20(16.9%)	2(1.7%)	3(2.5%)	2(1.7%)	1(0.8%)	8(6.8%)	2(1.7%)	118(100%)
	R	77(68.5%)	10(9%)	1(0.9%)	3(2.7%)	7(6.3%)	0	10(9%)	4(3.6%)	112(100%)
Ofloxacin	S	79(64.8%)	24(19.7%)	4(3.3%)	3(2.5%)	1(0.8%)	0	9(7.4%)	2(1.6%)	122(100%)
	R	80(66.1%)	13(10.7%)	2(1.7%)	3(2.5%)	5(4.1%)	1(0.8%)	12(9.9%)	5(4.1%)	121(100%)
Levofloxacin	S	27(52.9%)	13(25.5%)	3(5.9%)	0	1(2%)	0	6(11.8%)	1(2%)	51(100%)
	R	12(48%)	3(12%)	1(4%)	0	3(12%)	0	4(16%)	2(8%)	25(100%)
Gentamicin	S	15(33.3%)	5(11.1%)	1(2.2%)	0	NA	0	16(35.6%)	2(4.4%)	45(100%)
	R	2(28.6%)	0	1(14.3%)	0		0	3(42.9%)	1(14.3%)	7(100%)
Total		234(66.9%)	53(15.1%)	6(1.7%)	9(2.6%)	10(2.9%)	2(0.6%)	29(8.3%)	7(2%)	350(100%)

Table 4 shows *E. coli* were most sensitive (100.0%) to Chloramphenicol followed by Ceftrixone (82.4%), Amikacin (77.9%), Cefpodoxime (77.8%) and Nitrofurantoin (72.4%). Moreover, *E.coli* was resistant to Nalidixic acid (90%). *Klebsiella spp* was most susceptible to Nalidixic acid (40%) while resistant to Chloramphenicol (33.3%).

DISCUSSION

Urinary tract infection (UTI) is a common problem encountered in the hospital. Antimicrobial resistance to various classes of antibiotics to uropathogens continues to be a major health problem in different parts of the world.[15] Increasing drug resistance is a great concern to common bacterial infections including UTI. Antimicrobial agents like Amoxicillin, Cotrimoxazole, Nalidixic acid, Cephradine, Ciprofloxacin, and Azithromycin are commonly used to treat many gram-positive and gram-negative infections such as UTI in many developing and underdeveloped countries. Study conducted at surrounding communities of this medical college teaching hospital reported 44.04% prevalence of self medication and antibiotic was the second most common cause of UTI.[10] This finding further suggests the growing need of urine culture for prevention of UTI. This study found 66.04% prevalence of uropathogens. In a study from eastern Nepal, the prevalence was found to be 43.98% where 91.98% were unimicrobial.[16] In a study from India, It was found to be 59.67 % where 94.41 % unimicrobial and 5.59 % polymicrobial.[17] Other studies also reported similar prevalence.[18,19] In a study from Duwakot, Bhaktapur, It was found that the prevalence of uropathogens was 13.8%.[8] In a study from Nepalgunj reported that the prevalence of uropathogens were 27.05%.[9] It is documented that UTI is more common in females than in males which is also reflected in this study. Similar findings were reported by a recent study done by Deshpande et el.[18] *Escherichia coli* (*E. coli*) is the major aetiological agent of UTI, which accounts for up to 90% of cases.[20] In this study, the most common uropathogens was *E. coli* (66.9%). Other studies reported similar findings.[20, 23] This study found *Klebsiella spp* was the second most common uropathogens (15.1%). In contrast to this study, other studies reported second most common uropathogens was *Staphylococcus aureus*.[22,24] A study from Duwakot, Bhaktapur, it was found that the most common pathogenic microorganism isolated was *E.coli* (79.1%) followed by *Klebsiella spp* (11.7%), *Citrobacter spp* (3.34%) and *Proteus spp* (2.92%).[8] In a study from Nepalgunj reported that the most common pathogenic microorganism isolated was *E.coli* (73.65%) and *Klebsiella spp* (19.9%).[9]

Resistance to antimicrobial agents has been noted since the first use of these agents and is increasing globally.[25] This study revealed that commonly used antimicrobial agent are resistant to certain uropathogens. *E. coli* (66.9%) and *K. pneumoniae* (15.1%) were resistant to Amoxicillin and Ampicillin is of great importance and implies that these antibiotics cannot be used as empirical therapy for urinary tract infection, particularly in the study area. Similar study from Duwakot, Bhaktapur found that maximum sensitivity with the antibiotics Ofloxacin and Ciprofloxacin. The isolated microorganism demonstrated resistance with Nalidixic Acid and Co-Trimoxazole.[8] In a study from Nepalgunj reported that the maximum sensitivity was with Nitrofurantoin and Amikacin.[9]

On the other hand very low levels of resistance were detected to antibiotics such as Ceftrixone, Nitrofurantoin and Gentamicin. Similar findings were reported in the studies elsewhere.[22,23,26-28] Low resistance was observed for these drugs because they are not easily accessible and relatively expensive in price compared to others. It was suggested that, In Nepal transformation of paramedics healthcare practices into policies and public health advocacy at the era of sustainable development goals is the need of time.[29] As Antibiotic resistance is a growing concern in Nepal and the paramedics are the major prescribers of this. We need to train them for better result. The pharmacovigilance center needs to be established to control growing antibiotic resistance.[30]

CONCLUSION

Every 2 out of 3 urine samples were positive for uropathogens with more predominance in females and adult age group. *E. coli* and *Klebsiella* spp were common. Chloramphenicol and Nalidixic acid were highly susceptible to *E.coli* and *Klebsiella* spp respectively.

RECOMMENDATIONS

The isolation of bacterial uropathogens with a higher resistance to commonly used antimicrobials challenges the clinicians for very few options to choose a drug for empirical treatment of UTIs. Therefore, it is important to urge physicians and other health workers in the field on the need of re-evaluation of empirical treatment of UTI. This will reduce unnecessary antibiotic use.

LIMITATION OF THE STUDY

The study is a hospital-based study and may not truly reflect population level status. Antimicrobial susceptibility testing against pathogenic bacteria in the laboratory is an invitro activity and may not always reflect in vivo activity. There may be some observational errors, especially with the error due to parallax in measuring the inhibition zone diameter.

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CONFLICT OF INTEREST

FINANCIAL DISCLOSURE

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