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ORIGINAL RESEARCH ARTICLE

ANTIBIOTIC SENSITIVITY PATTERN IN URINARY TRACT INFECTION AMONG ADULTS IN CENTRAL PART OF NEPAL

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ABSTRACT

Background: Urinary tract infection (UTI) is characterized by pathological invasion of the urinary tract by microorganisms. Majorities of organisms causing UTI are gram negative bacteria, most common of which is E. coli. Urine culture and sensitivity test is used to isolate the organism and to identify the susceptible drug of choice for appropriate treatment. This hospital-based study was carried out to analyze the spectrum and antibiotic susceptibility of microorganisms causing UTI.

Methods: A retrospective study was done to analyze the results of urine culture and sensitivity test done at Chitwan Medical College Teaching Hospital over a period of two and half years. Standard guideline and protocol were used to collect the urine sample and to perform the test. Data analysis was done using SPSS version 21.0.

Result: Out of 12, 925 urine samples submitted for culture and sensitivity test during the study period, bacterial pathogens were isolated from 3, 173 (24.54%) samples, which was significantly higher among females (28%) than the males (17%). The most common organism isolated on the culture was *E. coli* (68.5%) followed by *Klebsiella* (18.4%). Sensitivity of the uropathogens was seen highest with colistin (79.2%) followed by teicoplanin (64.58%), Aztreonam (63.25%) and Nitrofurantoin (61.16%). Most common antibiotics that showed resistance to the microorganisms in this study were Ampicillin (60.93%), Cotrimoxazole (53.72%), Cefixime (40.57%) and Levofloxacin (32.93%).

Conclusions: This study has found a usual pattern of UTI with higher prevalence among females and *E. coli* being the most common organism. Nitrofurantoin has been found to have a good susceptibility for the treatment of UTI.

INTRODUCTION

Urinary tract infections (UTI), which is characterized by pathological invasion of the urinary tract by microorganisms producing symptoms, are one of the most common bacterial infections in the human body that account for about 25% of all infections.[1] It is more common in the females than in the males with a ratio of 8:1. Around 50–60% of women will experience an episode of UTI in their lifetime.[2] Risk factors for the development of UTI could be divided into the behavioral, urologic and biologic or genetic factors.[3]

UTI is mainly caused by the gram-negative bacteria, most common of which being *Escherichia coli (E. coli)* that account for 65-90% of all UTI[4,5] followed by *Proteus mirabilis, Staphylococcus saprophyticus, Staphylococcus epidermidis* and *Klebsiella pneumonia*.[6] Pseudomonas infections are more common in patients requiring long term catheterization.[7] UTI is diagnosed using a combination of urinary symptoms and urine culture.[8] Urine Routine and microscopy examination, culture, and biochemical assays would confirm the diagnosis of UTI. Around 20% of women who present with the clinical features suggestive of UTI will have a negative urine culture. Although the treatment of UTI is initiated with empirical antibiotic, the definitive choice of the treatment should be guided by the susceptibility patterns to the organism isolated. The type and frequency of pathogens isolated from urinary tract and the antibiotic sensitivity patterns of organisms are dependent upon several factors, most important of which are age and gender of the person, catheterization and hospitalization status, virulence of the isolated organism and previous exposure to antibiotics.[9,10]

The type of the urinary pathogens and their susceptibility to antibiotics may differ in different setups. So, it becomes crucial to acquire an idea about the distribution of these pathogens and their susceptibility to antibiotics in a setting that would help to determine the selection of the precise empirical treatment. This study was conducted in a tertiary level hospital in central part of Nepal to determine the prevalence of UTI, detect common isolates in the urine culture and their *in vitro* sensitivity and resistance patterns to commonly prescribed antibiotics.

METHODS

This retrospective study was conducted at Chitwan Medical College Teaching hospital (CMCTH) after getting ethical

clearance from the Institutional review committee of Chitwan Medical College (CMC-IRC). CMCTH is a 750 bedded tertiary level teaching hospital located at Bharatpur, Chitwan that provides health services to a large number of populations from Chitwan and adjacent districts.

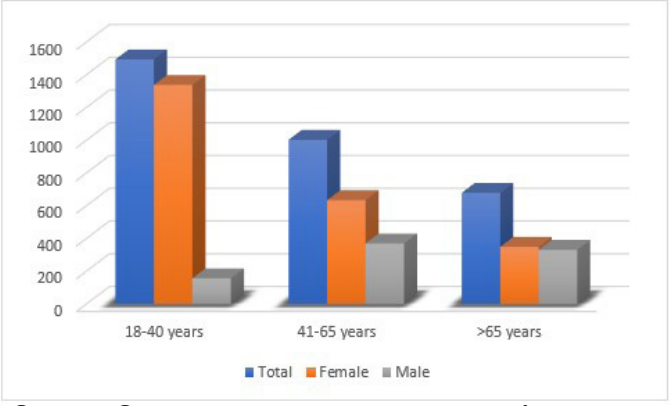
Only the adult patients aged more than 18 years who underwent urine tests over the period of two and a half years between January 2017 and June 2019 were included in the study. Standard self-designed pro-forma was used to collect the demographic information and clinical characteristics of both inpatients and outpatients. As per the protocol of the laboratory department of our Institute, the patients were instructed to collect clean catch mid-stream urine in a sterile leak proof universal bottle and were subjected to be cultured within 30 minutes of collection. The samples were plated out on MacConkey and blood agar media and incubated aerobically overnight at 37^0 C. Samples that showed pure growth of isolate in a count of $\geq 10^5$ colony-forming units (CFU) per ml of urine after overnight incubation were considered to indicate significant bacteriuria. Isolated organisms were identified with the use of standard biochemical tests. Identified uropathogens were subjected for antibiotic susceptibility testing with the use of the Kirby–Bauer disc diffusion technique on muler Hilton agar following standard procedures recommended by the Clinical and Laboratory Standards Institute (CLSI).[11] After incubation and diameter measurements, the sensitivity of the organisms was categorized into either of the three categories as sensitive, partially-sensitive and resistant to certain antibiotic.

A protocol has been developed at the microbiology laboratory of CMCTH to choose the antibiotics to be tested for the sensitivity to microorganisms, which are reviewed periodically every two years taking consideration of the susceptibility results. After incubation and diameter measurements, depending upon the sensitivity of the organisms was categorized into either of the three categories as sensitive, partially-sensitive and resistant to certain antibiotic[12]

Data were entered and analyzed by using Statistical Package for Social Sciences software version 21.0 (SPSS Inc, Chicago, IL). Descriptive statistics were used to summarize the findings. Discrete variables were expressed as percentages and Pearson Chi-square test was employed to test the existence of association between discrete variables. Variables with a p value < 0.05 were considered statistically significant.

RESULTS

Out of 12, 925 urine samples submitted for culture and sensitivity test during the study period, bacterial pathogens were isolated from 3, 173 (24.5%) samples. The overall prevalence of UTI was significantly higher among females than the males (23.1% versus 6.2%; P= 0.01). Among the patients with positive urine cultures, females (73.13%) outnumbered males (26.87%) with female to male ratio of 2.7:1. Mean age of the patient was 57.21 years and majority (47.05%) of the patients were in the age group of 18 to 40 years (Figure 1).



positive urine cultures

The most common organism isolated on the culture was E. coli (68.5%) followed by Klebsiella (18.4%). Other organisms responsible for the infection were *Candida* (3.5%), *Pseudomonas* (3.2%), *Acinetobacter* (2.8%), E*nterobacter spp.* (1.4%), *Proteus* (1%), *Citrobacter* (0.9%) and *Staphylococcus aureus* (0.4%).

Table 1: Distribution of uropathogens isolated on urine samples by sex of the patients

Organism	Female (n=2322)	Male (n=851)	Total (3173)
E. coli	1645 (70.8%)	528 (62.0%)	2173 (68.5%)
Klebsiella	438 (18.9%)	147 (17.3%)	585 (18.4%)
Candida	72 (3.1%)	38 (4.5%)	110 (3.5%)
Pseudomonas	32 (1.4%)	69 (8.1%)	101 (3.2%)
Acinetobacter	60 (2.6%)	29 (3.4%)	89 (2.8%)
Enterobacter	26 (1.1%)	17 (2%)	43 (1.4%)
Proteus	21 (0.9%)	12 (1.4%)	33 (1%)
Citrobacter	18 (0.8%)	9 (1.1%)	27 (0.9%)
Staph. aureus	10 (0.4%)	2 (0.2%)	12 (0.4%)

We also analyzed the distribution of organisms that were categorized into 3 groups- E. coli, Klebsiella and all others by male and female sex that shows that two major organisms (E. coli and Klebsiella) were dominantly present in females whereas males were affected by multitude of other organisms too (Table 2).

Table 2: Categories of isolated uropathogens by sex

Organism	Female	Male	Grand Total	p-value
E. coli	1645 (70.8%)	528 (62.0%)	2173 (68.5%)	0.000
Klebsiella	438 (18.9%)	147 (17.3%)	585 (18.4%)	
All Other	239 (10.3%)	176 (20.7%)	415 (13.1%)	
Grand Total	2322	851	3173	

Most of the isolated pathogens were susceptible to

nitrofurantoin, aminoglycosides, teicoplanin, colistin, piperacillin/tazobactam, meropenem and aztreonam. Sensitivity of the uropathogens was seen highest with colistin (79.2%) followed by teicoplanin (64.5%), Aztreonam (63.2%) and Nitrofurantoin (61.1%). Antibiotics with least sensitivity were Ampicillin (13.9%), Cefixime (14.3%), Ceftriaxone (17%) and Cotrimoxazole (17.5%). Details of antibiotic sensitivity pattern is shown on Figure 2.

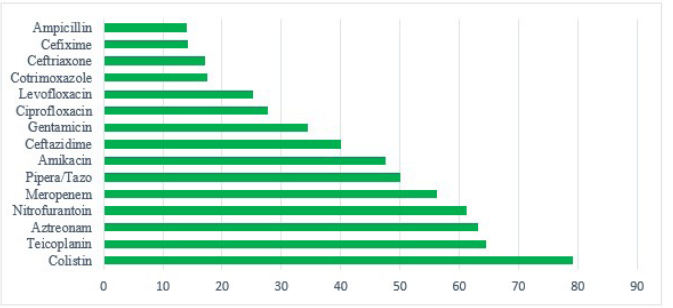
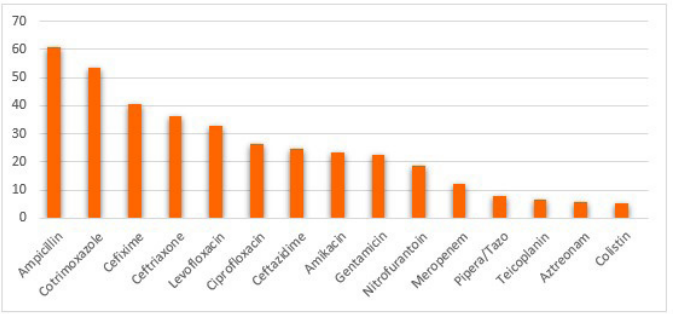


Figure 2: Antibiotic sensitivity pattern of pathogenic microorganisms

Most common antibiotics that showed resistance to the microorganisms in this study were Ampicillin (60.93%), Cotrimoxazole (53.72%), Cefixime (40.57%) and Levofloxacin (32.93%). Least resistance was found with colistin (5.17%), aztreonam (5.93%), Teicoplanin (6.61%) and piperacillin tazobactam (8.08%). Details of resistance pattern of different antibiotics is shown on Figure 3.



Analysis of the sensitivity and resistance pattern of the uropathogens with individual drugs was also done. Nitrofurantoin and colistin were effective against over 80% of the strains of E. coli, Klebsiella spp. and Pseudomonas. Higher frequencies of resistance of most of the uro-pathogens were seen with ampicillin, cefixime, ceftriaxone, cotrimoxazole, and quinolones. Table 2 and 3 show the details of sensitivity and resistance of organisms on urine culture.

DISCUSSION

This study has evaluated the spectrum of UTI, types of bacterial uropathogens and their susceptibility to antimicrobial agents among patients attending a tertiary hospital in central Nepal. Overall prevalence of UTI in this study was found to be 13.5% with higher prevalence among females (23.1%) than in the males (6.2%). The prevalence of UTIs in the current study is similar to the finding by Pradhan et al[13] but is lower than the studies by Mwaka et al (10%),[14] Tibyangye et al (22%)[15] and Odoki et al (32%)[16] from Uganda; and Khatiwada et al from Nepal.[17] The possible explanation for the variation in the prevalence in these studies could be the differences in the types of the populations studied.

The prevalence of UTI among females in this study was significantly higher than the males. Nearly 160 million individuals are affected by UTI each year[18] and almost half of the women experience recurrence of UTIs.[19] Studies have shown that UTIs in women are very common; therefore, one in five adult women experience UTI in her life.[20,21] Such sex-related vulnerability could be ascribed to the structural and physiological peculiarity of the female lower urinary tract. Structural characteristics of the female urinary tract that make them susceptible for the infections are the shorter urethra22 and the proximity of the urethral opening to the entrance of vagina and anal opening, which houses large numbers of microbes.[23] Other possible factors for increased vulnerability of UTI in females are the defects in urothelial lining,[24] and thinner detrusor muscle.[25] Physiologic factors that increase the probability of UTI are the hormonal factors, reticuloendothelial system and the microbiome of the lower urinary tract (LUT).[26]

Mean age of the patient in this study was 57.21 years with most of the patients (47.05%) being in the age group of 18 to 40 years. Although the prevalence of bacteriuria has a higher frequency among the very young and a gradual increase with age,[27] symptomatic infection has the highest frequency among women aged 15–29 years.[28]

Although several different species can cause UTI, most infections in all populations are caused by the Gram negative, facultative anerobic, uropathogenic *E. coli* (UPEC). E. coli causes 80% of UTI among otherwise healthy women, aged between 18 and 39 years.[29] In this study, *E. coli* was the most common organism isolated in the culture of the urine sample (68.5%) followed by klebsiella (18.4%), which is in congruence with other studies.[13,30-33] This study also showed a lower prevalence of Gram-positive pathogens (0.4%). Contrary to our findings, few other studies have demonstrated a higher proportion of these pathogens ranging up to 26%.[34, 35]

This study revealed the highest sensitivity of the uropathogens to colistin, teicoplanin, aztreonam and nitrofurantoin. Upon analysis of the sensitivity of drugs with individual uropathogens, E. coli and klebsiella had the highest sensitivity to nitrofurantoin, colistin, teicoplanain and amikacin. In a multicentric study done in various European countries, nitrofurantoin was found to be sensitive in >90% of the strains.36 Raza S et al had found that ciprofloxacin was the most sensitive antibiotic in UTI.[37]

The four most resistant antibiotic in this study were ampicillin (60.9%), cotrimoxazole (53.7%), cefixime (40.5%) and ceftriaxone (36.1%). Ampicillin resistance among uropathogens ranges from 33% to 80%and resistance to trimethoprim ranges from 9% to 61%in different parts of the world.[38-41] Infectious

Table 3: Percentage of antibiotic sensitivity and resistance to different pathogens

Drugs		*E. coli* (2173)	*Klebsiella* (585)	*Pseudomonas* (101)	*Acinetobacter* (89)	*Enterobacter* (43)	*Proteus* (33)	*Citrobacter* (27)	*S. aureus* (12)
Nitrofurantoin	S (%)	88.9	79.6	72.5	46.1	44.6	77.4	66.3	11.9
	R (%)	3.2	12.9	19.5	31.7	22.8	11.7	5.3	36.8
Amikacin	S (%)	78.5	67.4	34.8	36.9	58.9	58.3	41.9	11.7
	R (%)	14.5	16.3	23.1	24.5	11.9	23.9	25.3	46.7
Gentamicin	S (%)	38.9	34.8	33.7	29.6	35.8	39.5	56.9	34.6
	R (%)	11.6	27.2	13.6	32.1	27.6	21.7	34.8	14.8
Ciprofloxacin	S (%)	21.8	15.7	43.6	27.8	47.9	12.4	36.7	14.6
	R (%)	20.1	21.2	36.3	12.3	21.6	32.5	42.1	24.5
Levofloxacin	S (%)	21.5	14.5	31.6	25.6	42.1	15.3	25.7	34.6
	R (%)	17.3	27.5	36.1	32.1	38.9	45.5	36.2	29.9
Cotrimoxazole	S (%)	31.6	15.2	9.6	13.8	16.9	11.9	26.1	12.5
	R (%)	17.5	63.1	59.7	36.4	56.3	59.2	57.3	79.2
Ampicillin	S (%)	9.2	4.3	14.6	24.2	17.4	5.6	21.4	14.8
	R (%)	57.5	93.2	39.4	57.9	62.1	54.6	71.5	44.9
Ceftriaxone	S (%)	15.8	19.4	11.8	14.8	19.5	12.6	33.7	12.5
	R (%)	21.6	15.9	54.8	76.3	16.2	26.5	52.1	25.5
Ceftazidime	S (%)	46.8	39.5	58.2	43.2	37.5	38.3	21.8	35.3
	R (%)	10.5	25.1	11.6	12.4	20.9	33.2	46.7	39.5
Cefixime	S (%)	14.7	12.5	12.8	16.7	11.6	14.1	14.8	17.3
	R (%)	50.1	37.7	48.9	37.8	57.7	37.3	34.7	45.8
Pipera/Tazo	S (%)	57.9	42.9	57.8	73.2	42.9	39.7	67.2	38.9
	R (%)	13.5	5.6	18.3	5.5	4.7	6.9	3.5	6.1
Meropenem	S (%)	64.7	54.6	62.4	57.3	53.6	39.4	68.9	50.4
	R (%)	20.6	16.9	6.7	5.7	17.8	12.6	6.3	11.4
Colistin	S (%)	82.5	83.1	89.4	78.4	75.3	78.4	72.1	76.4
	R (%)	7.4	4.5	3.1	5.2	4.3	5.6	2.9	8.4
Teicoplanin	S (%)	77.8	55.3	75.8	67.8	67.9	57.4	56.3	58.4
	R (%)	11.9	7.3	11.5	2.9	5.3	5.1	4.1	4.8
Aztreonam	S (%)	41.3	56.7	74.3	57.4	56.8	78.1	67.9	73.5
	R (%)	12.8	9.2	5.6	3.6	5.2	4.3	2.9	3.9

Disease Society of America (IDSA) guidelines consider nitrofurantoin and cotrimoxazole for empiric treatment of UTI.[42] This guideline in relation to nitrofurantoin might be appropriate in our setup, as we have found that more than 60% of the isolates were sensitive to nitrofurantoin with less than 20% resistance. However, use of cotrimoxazole as a first line therapy in UTI might not be applicable in our setup as the sensitivity to it has been found to be only 17.5% with a higher percentage of resistance (53.25%). Although fluoroquinolones like ciprofloxacin and levofloxacin, which are quite commonly used to treat UTI for a long duration, most of the organisms causing UTI have been found to be resistant in a variable percentage in this study, which is consistent with few other studies.[43, 44] Higher resistance rates to this group of antibiotic in our study may be explained by high and uncontrolled consumption of these antibiotics.

Relatively newer antibiotics like colistin, teicoplanin and aztreonam were found to have relatively better effectiveness with less resistance in this study. However, as these drugs can be used only by the parenteral route, they cannot be routinely used in outpatient basis. They need to be reserved for critically ill patients with multi-drug resistant infections. The dose of colistin needs modification in patients with renal impairment. Findings of the study would be useful to choose the empirical antibiotic for the treatment of UTI in our setup. However, due to the retrospective design of the study, all the required clinical details of the patients that would be helpful to analyze the risk factors for UTI, clinical course including outcomes of the disease could not be arranged.

CONCLUSION

The present study reveals a familiar pattern with respect to the species of uropathogens involved in UTIs, and it showed considerable bacterial resistance to common empirically prescribed antibiotics. The work suggests that nitrofurantoin has relatively better susceptibility to uropathogens that can be chosen for the empirical treatment of UTI.

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CONFLICT OF INTEREST

None

FINANCIAL DISCLOSURE

None

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