Original Article

Bacterial Pathogens responsible for Urinary Tract Infection Among Patients Attending a Tertiary Hospital in Eastern Nepal

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ABSTRACT

Introduction: UTI has been more complicated to treat because of the appearance of the pathogen with increasing resistance to antimicrobial agents. It is useful to obtain the local sensitivity pattern in the hospital setting to guide empirical prescription.

Methods: This is a prospective hospital-based study to identify the organisms causing UTI and their antibiotic susceptibility. A total of 400 urine samples were collected from the patients attending general OPD of BPKIHS, Dharan, Nepal, having the symptoms of UTI using the purposive sampling technique. We analyzed the midstream, clean catch of the urine and cultured to analyze the bacterial presence. Antibiotics susceptibility was tested using the Kirby-Bauer Disk Diffusion method. The findings were analyzed for the presence of bacteria in different age and sex groups along with their response to different antibiotics commonly used in Nepal.

Results: Out of 400 culture samples, 163 (40.7%) showed bacterial growth. *Escherichia coli* was the most common bacteria (68.7%), followed by Klebsiella spp. (7.4%). Female urine samples showed more bacterial growth compared to males (2.79:1). UTI was common among the young population of the age group (20-29 years). Most of the isolated bacteria were sensitive to Nitrofurantoin (89.7%).

Conclusion: UTI commonly occurs both in males and males of all age groups. However, females are more vulnerable to infection. Among many, *E. coli* is the most prevalent pathogen causing the disease, which is more susceptible to nitrofurantoin. Similarly, this antibiotic is sensitive to the majority of bacteria. Therefore, nitrofurantoin may be the first choice of drug for the population in the Eastern part of Nepal suffering from UTI. Since this study was carried out among a small sample size in one tertiary care hospital, we recommend a bigger study covering a larger population, to further validate the result.

Keywords: Urinary tract infection (UTI), Bacterial pathogen, Antibiotics, Antibiotic susceptibility

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Introduction

Urinary tract infection (UTI) is a common and recurrent medical condition both in males and females due to the bacterial infection in different parts of the urinary tract causing inflammation; often called acute cystitis or pyelonephritis. It often happens with bacteria entering the urinary tract from the skin or rectum via the urethra. UTI is associated with hygiene behaviors and the availability of sanitary infrastructure,[1] therefore people with poor personal hygiene are more vulnerable to the disease. Apart from water, sanitation, and hygiene (WASH) related factors, elderly people and those living with non-communicable diseases like diabetes and hypertension, which are on the rise, are also prone to infection owing to their immunocompromised state.[2, 3]

Traditional management of UTI is based upon the principle that pathogens and their susceptibility to antibiotics are highly predictable since *Escherichia coli* and *Staphylococcus saprophyticus* account for more than 90% of the cultured isolates.[4] Therefore, antibiotic treatment often initiates before the laboratory results of urine culture are available, increasing the risk of their misuse. Several studies have highlighted the risk of antibiotic resistance in UTI pathogens further aggravating the problem.[5-8]

Furthermore, drug response against bacteria varies significantly with the population and the geography. [5] So, knowledge of the etiological agents and their antimicrobial resistance patterns in specific geographical locations and the population helps to choose the appropriate antimicrobial treatment. There are some studies carried out in Kathmandu highlighting the UTI causing bacteria, and their antimicrobial susceptibility and drug resistance.[6-8] However, no such studies were carried out in eastern Nepal. This study is focused on exploring the bacterial pathogens associated with UTI, their sensitivity, and resistance pattern against different antibiotics among the patient's groups of different age and sex categories visiting OPD of BP Koirala Institute of Health Science, Dharan.

Materials and Methodology

A cross-sectional study was carried out from September 2014 – August 2015 among the patients visiting the general outpatient's department (OPD) of BP Koirala Institute of Health Sciences (BPKIHS) Dharan, with the complaints resembling those of urinary tract infection (UTI). We adopted convenient sampling techniques to register patients for the study. All the patients irrespective of age and sex offering written consent of being part of the study and having the signs and symptoms of UTI, further confirmed through routine microscopic examination, were included. Socio-demographic information of the participant were collected using structured questionnaire. Significant bacteriuria was confirmed after urine RE/ME report. The samples that showed more than 5 pus cells per high power field were taken as significant bacteriuria. The patients who were reported to have other illnesses together with UTI, through clinical checkups were excluded from the study. The sample size was determined using the formula,

Sample size (n) = z2pq/l2 (z=1.96, at 95% confidence interval, p=20, q=80(100-p), l= 20% of p i.e., 80% of power. [9] The laboratory staffs team of BPKISH was trained to counsel the patients to clean the periurethral area with soap and water in the toilet and collect midstream urine specimen in two sterile containers. They were followed up to reconfirm the periurethral cleaning, however, we could not verify further due to practical difficulties. The urine specimen was transported to the microbiology laboratory in BPKIHS within 2 hours and processed for culture and sensitivity tests.

Urine culture was performed by using calibrated loop direct streak method [10] using a nichrome

loop delivering 0.001ml of urine specimen. Urine was inoculated in Cysteine Lactose Electrolyte Deficient (CLED) agar medium and incubated at 37 ˚C for 24 hours. Colonies formed in the plate were counted. Colonies forming unit was estimated by multiplying the number of colonies formed by 1000. Bacterial growth was examined and processed for identification. Antimicrobial susceptibility testing was performed by using Kirby-Bauer Disk Diffusion method. [11] Mixed growths of three or four types of organism was taken as contamination and requested for a repeat urine specimen. In case of absence of growth, the specimen was reported as sterile after 24 hours.

The anonymized data recorded by the microbiology laboratory was received for further analysis. Data analysis was done with SPSS (statistical package for social sciences) version 20.0. Descriptive analysis was performed to explore the percentage of positive diagnosis among different age and sex groups and resistance and sensitivity patterns against different antibiotics. Ethical clearance was received from the Ethical Review Board, BPKIHS. (Ref no: 70/071/072-IRC) Code No.: IRC/296/014

RESULT

Out of 400 urine cultures, (231) 57.8% were Negative culture result, (163) 40.7% cultures showed bacterial growth, with (6) 1.5% showing the signs of contamination, which were excluded from our statistical analysis. The female to male ratio among the positive culture was 2.8:1. Gram-negative bacteria were the major cause of UTI in both sexes, with a negative to positive ratio among females
and male 9.9:1 and 9.7:1 respectively. Nine different organisms were isolated from urine culture. *Escherichia coli,* a gram-negative bacterium, was the most prevalent pathogen with its presence in 68.7% (n=163) of the positive samples, and *Pseudomonas* sp., a gram-negative bacterium, with its frequency of 0.6% (n=163) was the least. *Enterococcus sp*. was the most prevalent pathogen among gram-positive UTI-causing bacteria with the frequency of 4.9% and *Actinobacter sp.* the least. (Table 2) Age group 20-29 years had highest numbers of UTI with 33.3% of the positive cases with least frequent among <20 years old age group. (Table 3)

The highest frequency of isolated organisms showed sensitivity towards nitrofurantoin (89.7%) while ampicillin the least (6.3%). (Table 4) Similarly, 93.8% (n=163) of bacterial isolates showed resistance towards ampicillin. Ceftriaxone showed the least resistance with 61.4% of the total isolates. (Table 5)

Both gram-positive and negative showed similar responses towards nitrofurantoin with the highest sensitivity of 90.2% and 85.7% respectively. Nalidixic acid showed the least response against gram-positive bacteria with 21.9% sensitivity, similarly, ceftazidime showed the least response against gram-negative bacteria. *Escherichia coli* one of the most frequent pathogenic causes of UTI followed by *Enterococcus sp, Citrobacter sp.*, showed the highest sensitivity towards nitrofurantoin. Similarly, *Staphylococcus aureus* and *Klebsiella sp.* showed the highest sensitivity to norfloxacin. *Enterobacter sp.* and *Actinobacter sp.* were most sensitive to gentamycin. *Escherichia coli* was least sensitive to ampicillin, *Klebsiella sp, Enterobacter sp.*, and *Citrobacter sp.* to cefotaxime. *Enterococcus sp.* and *Staphylococcus aureus* showed the least response to ceftazidime. Nitrofurantoin is effective against most of the pathogens, but is seen least sensitive to *Actinobacter sp*. similarly, norfloxacin being effective against most of the bacteria was found less sensitive against *Enterococcus sp.* Table: 6.0

Table 1: Summary of the sample distribution and result

Culture results			Gram staining in positive cultures		Sex distribution among positive cultures	
Positive	Negative	Contamination	Positive	Negative	Male	Female
163	231	6	16	147	43	120

Table 2: Prevalence of pathogens in the culture sample

Isolated Organisms	Frequency	Percentage (%)
Escherichia coli	112	68.7
Klebsiella sp.	12	7.4
Citrobacter sp.	9	5.5
Enterococcus sp.	8	4.9
Staphylococs aureus	*7*	4.3
Enterobacter sp.	*6*	3.7
Acinetobacter sp.	5	3.1
Proteus sp.	3	1.8
Pseudomonas sp.	1	0.6

Table 3: Age distribution of urine cultured patients (n=163)

Age interval	<20 yrs	20-29 yrs	30-39 yrs	40-49 yrs	>50 yrs
Percentage	7.8%	33.3%	19.5%	9.5%	30%

Table 4: Percentage sensitivity of different antibiotics against bacteria

NIT	GEN	LEX	AMK	CIP	NOR	CRO	CTX	CAZ	NAL	AMP
89.7%	83.8%	66.7%	66.4%	51.1%	50.5%	38.6%	29.2%	26.8%	19.7%	6.3%

NIT= Nitrofurantoin, GEN= Gentamicin, AMK=Amikacin, LEX= Cephalexin, CIP =Ciprofloxacin, NOR= Norfloxacin
CRO = Ceftriaxone, AMP= Ampicillin, CTX=cefotaxime, CAZ=Ceftazidime, NAL= Nalidixic acid, OFX= Ofloxacin

Table 5: Percentage of sample resistance of different bacteria against antibiotics

AMP	NAL	CAZ	CTX	CRO	NOR	CIP	AMK	LEX
93.8%	80.3%	73.2%	70.8%	61.4%	49.5%	48.9%	33.6%	33.3%

Table 6: Antibiotic sensitivity of different microorganisms

	Antibiotics										
Pathogen	NIT	NOR	GEN	CIP	AMP	CAZ	AMK	CTX	CRO	NAL	OFX
Enterococcus sp.	87.50%	50%	50%	33.3%	33.3%	20%	20%				
Staphylococcus aureus	83.3%	100%	100%			66.7%	100%	85.7%			
E. coli	98.1%	44.8%	87.5%	47.2%	4.3%	26.8%	70.7%	27.4%	15.2%	17%	
Klebsiella sp.	70%	75%	66.7%	66.7%	33.3%	33.3%	42.9%	28.6%	28.6%	51.7%	
Citrobacter sp.	66.7%	66.7%	66.7%	60%			66.6%	20%	33.3%		100%
Enterobacter sp.	60%	25%	100%	33.3%		25%	66.7%	25%	66.7%	50%	
Actinobacter sp.	20%	50%	75%	60%		25%	50%		66.7%		

DISCUSSION

The antibiotic sensitivity pattern of bacteria keeps changing depending upon prescription practice and users' behaviors towards antibiotics. This is true for developing countries like Nepal where antibiotics are prescribed irrationally not only by the medical practitioners but also purchased directly from the pharmacists.[12, 13] Therefore, to decrease the resistance of urinary pathogens against antibiotics, periodic evaluation of sensitivity patterns is essential for rational and appropriate use of antibiotics. Our study explored the prevalence of UTI among patients from different age and sex groups and the sensitivity of the UTI-causing pathogens towards the commonly practiced antibiotics in Nepal.

The prevalence of isolated microorganisms in our study was 40.7%, which was higher in comparison to those reported from Kathmandu. For example, a study conducted by Chaudhari et al reported 20% [9], and that by Raza et al. reported 19.7% prevalence. [14] The prevalence of microorganisms in the collected sample is defined by the clinical screening of the patients before collecting the sample for culture, geographical location, and sanitary behavior of the people. Kathmandu and its surrounding districts have relatively good sanitation infrastructures. It is relatively better in the Sunsari district as well, where BPKIHS is located as well; however, those in *Madhesh Pradesh*, it is still poor. [15] BPKISH receives patients from the districts having poor sanitation infrastructures including *Madhesh*, which probably is the reason for the higher prevalence of UTI among the patients visiting BPKIHS.

Our study reported a higher prevalence of UTI among females compared to those among males. This result was consistent with the study from Nepal [1] and other countries.[16, 17] Ascending nature of the bacteria and short anatomy of the urethra in females make them easier to colonize the bladder making females more vulnerable to UTI.[18] Analysis of the occurrence of UTI among different age groups revealed a higher prevalence among the sexually active age groups (33.3%) followed by the elderly population (30%); this finding is consistent with those found in Kathmandu.[19] We did not explore the relationships between sexual behavior and the prevalence of UTI; however, the higher prevalence of UTI among the women in the sexually active group hints at the higher transmission of the pathogens due to sexual activity, which is reported to facilitate the entry of bacteria present in the periurethral region into the urinary bladder causing UTI. [20, 21]

The immune response of the body decreases with the aging with the possible emergency of multiple comorbidities like bladder outflow obstruction and diabetes this cause increases the incidences of UTI among the elderly population of both sexes [3], which probably is the cause of higher incidence of UTI among elderly in our case. *E. coli* was the most prevalent pathogen occurring in 68.7% of the cultured samples, followed by *Klebsiella sp* occurring in 7.4% of the cultured samples. A similar finding was reported by the studies conducted in Nepal.[19, 22] In some cases, *Proteus sp*. was also found as the predominant pathogen [13].

E. coli is one of the most common microorganisms present in the rectal area. The proximity of the rectal region offers easy access of the pathogen to the urinary tract and causes the infection. The pathogen colonizes the urethral meatus and perineum before ascending to the bladder and is well adapted to invade the urinary tract. It adheres to P fimbriae (pyelonephritis-associated pili) and produces alpha and beta hemolysins. This ability of *Escherichia coli* enables the organism to infect both sexes all over the world. Furthermore, *E. coli* is adapted to the higher adherence to the uroepithelial cells of younger women as compared to the elderly, whereas the elderly male has higher adherence

and therefore higher prevalence of UTI. [23] Therefore, this nature and adaptability of *E. coli*, one of the most common UTI-causing pathogens, maybe the reason behind the high prevalence of UTI among young and sexually active populations and the elderly.

Our study on antibiotic sensitivity and resistance patterns of the isolated bacteria showed maximum isolates to be sensitive to nitrofurantoin (89.9%). This result is in conformity with a similar study carried out in Kathmandu [19], whereas some studies suggested the highest sensitivity to amikacin (86%) [13]. Norfloxacin (75%) was most sensitive against *Klebsiella* followed by nitrofurantoin (70%), and ciprofloxacin (66.7%). Isolates were most resistant to ampicillin (93.8%) and nalidixic acid (80.3%); a similar pattern of resistance towards ampicillin was found in research conducted in other parts of Nepal as well.[24, 25] Knowledge about local microbiological patterns is essential for rationalizing both prophylaxis and treatment regimens. A review of the antibiotic policy for treating urinary tract infections enables the precise prescription of the antibiotics so that unnecessary exposure of the patients towards antibiotics and hence the resistance to antibiotics is prevented. With this result, nitrofurantoin should be considered as the drug of choice for acute, non-complicated UTI particularly in view that it continues to show low resistance. Low resistance to vancomycin and nitrofurantoin may be explained by irrational and uncontrolled use of other antibiotics during the past decades.

Conclusion

UTI commonly occurs both in males and males of all age groups. However, females and the elderly are more vulnerable to infection. Among many, *E. coli* is the most prevalent pathogen causing the disease, which is more susceptible to nitrofurantoin. Similarly, this antibiotic is sensitive to the majority of bacteria. Therefore, nitrofurantoin may be the first choice of drug for the population in the Eastern part of Nepal suffering from UTI. Since this study was carried out among a small sample size in one tertiary care hospital, we recommend a bigger study covering a larger population, to further validate the result.

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