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Original Article

Prevalence and Antibiogram of Bacterial Uropathogens from a Tertiary Care Hospital of Eastern Nepal

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Abstract

Background

Urinary tract infection (UTI) is defined as growth of micro-organisms >10^5 CFU/ml in mid-stream urine samples. [1] Globally, urinary tract infection is considered a major public health concern with the second most common bacterial infection affecting individuals of different ages. It is estimated that worldwide 150 million cases of UTI occur per year and bacteria are responsible for about 95% of all the cases with each year. [3, 4] This study was designed to describe the pattern of microorganisms causing UTI and their antibiotic sensitivity.

Materials and Methods

This is a hospital based cross-sectional study conducted in the Department of Microbiology from January 2022 to June 2022 after taking ethical approval from Institutional Review Committee, Nobel Medical College and Teaching Hospital, Biratnagar, Nepal. The patient profiles or records visiting a tertiary care hospital of both sex and every age group who were having symptoms and clinical diagnosis of urinary tract infection were included.

Results

A total of 2247 urine samples were collected, 501(22.29%) of the urine sample yielded significant growth of uropathogenes. The most common bacteria was found to be *Escherichia coli* (*E. coli*) that accounts for 73.05% followed by *Enterococcus species* 11.57%, *Klebsiella pneumoniae* 8.98% Amikacin and nitrofurantoin was found to be the most sensitive antibiotic to gram negative uropathogens.

Conclusion

The prevalence of uropathogenes was found to be higher in our study. Significant bacteriuria was seen in the female than male. The total number of patient with culture positivity was higher in younger age groups with high frequency of antibiotic resistance.

Keywords: *Antibiotic resistance, Female, Urinary tract infection*

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Introduction

Urinary tract infection (UTI) is defined as growth of micro-organisms >10^5 CFU/ml in mid-stream urine samples but significant bacteriuria is lacking in some cases of true UTI especially in symptomatic patient. A smaller number of bacteria (10^2-10^4) may signify infection when urine specimens obtained by suprapubic aspiration or in-and-out catheterization and in samples from a patient with an indwelling catheter [1,2]. Globally, urinary tract infection is considered a major public health concern with the second most common bacterial infection affecting individuals of different ages. It is estimated that worldwide 150 million cases of UTI occur per year and bacteria are responsible for about 95% of all the cases with each year costing about 6 billion dollars of the global economy [3,4]. UTI's are categorized as uncomplicated or complicated and uncomplicated UTI's typically affects individuals who are otherwise healthy and have no structural or neurological urinary tract abnormalities. Complicated UTI's are defined as UTI's associated with factors that compromise the urinary tract or host defense, including urinary obstruction, retention caused by neurological disease, immunosupression disease, renal failure, renal transplant, pregnancy and the presence of foreign bodies such as calculi, Indwelling catheter etc [5].

Extremes of age, female gender, pregnancy, infants, urinary tract abnormalities and dysfunction, catheterized patient with spinal cord injury, renal disease, diabetes mellitus and immune suppressant patient are predisposing factors of UTI [4]. The incidence of uncomplicated UTI in healthy women is 50/1000/year. It is estimated that 50% of women experience at least one episode of UTI at some point in their lifetime and between 20% and 40% have recurrent episodes with approximately 20% of all UTI's in men [2]. The *E. coli* accounts for approximately 85% of community acquired UTI's and 50% of hospital acquired UTI's and the emergence of extended –spectrum-beta-lactamases has threatened the empirical use of cephalospo-rins and ciprofloxacin. Microorganisms use various mechanisms to develop drug resistance by recombination of foreign DNA in bacterial chromosome, horizontal gene transfer and alteration in genetic material [6].

Sensitivity of antibiotics varies in different places and in same place from time to time because of easy availability and non-judicious use of antibiotics that have led to increased resistance of common pathogens against commonly used antibiotics. Thus empirical choice of antibiotics in community acquired UTI is not uniform and probably not justified as well. Choice of antibiotics depends on local guidelines, if available. This study was designed to describe the pattern of uropathogens causing UTI and their antibiotic sensitivity [1].

Materials and Methods

This is a hospital based cross-sectional study conducted in the Department of Microbiology from January 2022 to June 2022 after taking ethical approval from Institutional Review Committee, Nobel Medical College and Teaching Hospital, Biratnagar, Nepal. The study population included was patients of different age groups, who visited Nobel Medical College and Teaching Hospital. The patient profiles or records visiting a tertiary care hospital of both sex and every age group who were having symptoms and clinical diagnosis of urinary tract infection were included while the insufficient information of the patient history including antibiotic usage and patient with a history of recent antibiotic therapy (within the last 72 hours) were excluded from the study population. [4, 3] The sample size was estimated to be 384 by using formula, $n=Z^2 P (1-P)/e^2$, where Z is the confidence level of 95% (1.96); e is the error taken as 5% and P is the expected prevalence from literature [4].

The collected samples were inoculated using a calibrated wire loop on Cystein Lactose Electrolyte Deficient agar (CLED), blood agar and MacConkey agar for the isolation and identification of microorganisms causing UTI's and incubated overnight at 37°C. Colony counts >10^5 CFU/ml were considered significant.[7] The culture plates with no growth were further incubated for 48 hours. The pure isolated bacterial colonies were identified using standard microbiological techniques, such as Gram staining, colony morphology and biochemical testing. The antibiotic susceptibility testing was carried out on Muller-Hinton agar and blood agar using Kirby Bauer disc diffusion method as per the CLSI guidelines [3]. Interpretation as Sensitive or Resistant was done on the basis of the diameters of zone of inhibition of bacterial growth as recommended by disc manufacturer [2]. The antibiotic discs and concentration (µg) used for both Gram-positive and Gram- negative bacteria were as follows: (HiMedia) penicillin (P 10 U), ampicillin (AMP 10 mcg), cloxacillin (COX 10 mcg), amikacin (AK 30 mcg), ceftriaxone (CTR 30 mcg), cefotaxime (CTX 30 mcg), ceftazidime (CAZ 30mcg),

ciprofloxacin (CIP 5 mcg), levofloxacin (LE 5 mcg, tobramycin (TOB 10 mcg), gentamicin (GEN 10 mcg), nitrofurantoin (NIT 300 mcg), vancomycin (VA 30mcg), linezolid (LZ 30 mcg), teicoplanin (TEI 30 mcg), cotrimoxazole (COT 30 mcg) as per CLSI guidelines [8]. The collected data were entered in Microsoft Exel 2007 and alalysed using SPSS version 20.

Results

A total of 2247 urine samples were collected, 501(22.29%) of the urine sample yielded significant growth of bacteria. The total number of male patient was 884 (39.34%) and female were 1363 (60.65%). Significant bacteriuria was seen in the male and female were 227 (45.3%) and 274 (54.69%) as shown in table 1. The patients were in between the ages of 1 day and 91years with mean age of 46 years. Out of 2247 urine samples, 433 (19.27%) were from the patient age ≤20 years, 780 (34.71%) were from the age between 21-40 years, 623 (27.72%) were from the age between 41- 60 years and 411 (18.29%) were from the age above 60 years which is depicts in table no. 2. The most common bacteria was found to be *E. coli* that accounts for 73.05% (366) followed by *Enterococcus species* 11.57% (58), *Klebsiella pneumoniae* 8.98% (45), *Staphylococcus epidermidis* 5.18% (26), *Pseudomonas aeruginosa* 0.99% (5), *Staphylococcus aureus* 0.19% (1) as shown in table no. 3 The antibiotic susceptibility test of selected antibiotics for *E. coli* shows that amikacin was the most sensitive antibiotic i.e. 93.44% followed by nitrofurantoin 89.89%, gentamicin 88.79% and ciprofloxacin 65.02%. The most resistant antibiotic for *E. coli* was ampicillin which accounts 98.91% followed by ceftazidime 63.37% and cefotaxime 61.48%. The antibiotic susceptibility test of *Klebsiella pneumonia* shows that amikacin to be the most sensitive which accounts for 66.66% followed by nitrofurantoin 64.44% and gentamicin 57.77% and most resistant was ampicillin 100% followed by ceftazidime 77.77%. The antibiotic susceptibility test for *Pseudomonas aeruginosa* shows that amikacin, gentamicin and tobramycin shows 80% sensitive followed by levofloxacin and ciprofloxacin which accounts for 60% of sensitivity and most resistant antibiotic was ceftazidime 60% as shown in table no. 4 The antibiotic susceptibility pattern of *Enterococcus species* shows that linezolid to be the most sensitive antibiotics which accounts for 94.82% of sensitivity followed by vancomycin 86.2% and teicoplanin 72.41% and the most resistance antibiotic was ciprofloxacin (100%) followed by penicillin (94.82%) and gentamicin (60.34%). The most sensitive antibiotic for *Staphylococcus epidermidis* was vancomycin (88.46%) followed by linezolid (84.61%) and teicoplanin (84.61%) and the most resistant was penicillin (100%) followed by ciprofloxacin (84.61%) and gentamicin (30.76%). There was only one *Staphylococcus aureus* isolated where penicillin was only the resistant antibiotic. The antibiotic susceptibility pattern of Gram positive bacteria is depicted in table no. 5

Table 1: Distribution of male and female patient out of total urine samples and positive culture

Total	2247 (100%)	501 (100%)
Male	884 (39.34%)	227 (45.3%)
Female	1363 (60.65%)	274(54.69%)

Table 2: Distribution of total number of urine samples and positive culture according to age

Age in years	Total numbers of patients	Number of positive samples
=20	433 (19.27%)	109 (21.75%)
21-40	780 (34.71%)	161 (32.13%)
41-60	623 (27.72%)	136 (27.14%)
>60	411 (18.29%)	95 (18.96%)
Total	2247 (100%)	501 (100%)

Table no 3: Distribution of uropathogenes out of total culture positive cases

Uropathogenes	Total number	Total percentages
Escherichia coli	366	73.05%
Enterococcus species	58	11.57%
Klebsiella pneumonia	45	8.98%
Saphylococcus epidermidis	26	5.18%
Pseudomonas aeruginosa	5	0.99%
Staphylococcus aureus	1	0.19%
Total	501	100%

Table 4: Antibiotic susceptibility pattern of Gram Negative Uropathogens

	Escherichia coli (n=366)		*Klebsiella pneumoniae* (n=45)		*Pseudomonas aeruginosa* (n=5)	
	S	R	S	R	S	R
Ampicillin	4 (1.09%)	362 (98.9%)	0 (0%)	45 (100%)	NT	NT
Gentamicin	325 (88.79%)	41 (11.21%)	26 (57.77%)	19 (42.22)	4 (80%)	1 (20%)
Cefotaxime	141 (38.52%)	225 (61.48%)	19 (42.22%)	26 (57.77%)	NT	NT
Ceftazidime	133 (36.33%)	233 (63.67%)	10 (22.22%)	35 (77.7%)	2 (40%)	3 (60%)
Amikacin	342 (93.44%)	24 (6.56%)	30 (66.66%)	15 (33.33%)	4 (80%)	1 (20%)
Levofloxacin	200 (54.64%)	166 (45.36%)	18 (40%)	27 (60%)	3 (60%)	2 (40%)
Ciprofloxacin	238 (65.02%)	128 (34.98%)	24 (48.88%)	21 (46.66%)	3 (60%)	2 (40%)
Nitrofurantoin	329 (89.89%)	37 (10.11%)	29 (64.44%)	16 (35.55%)	NT	NT
Tobramycin	NT	NT	NT	NT	4 (80%)	1 (20%)

NT= Not Tested

Table 5: Antibiotic susceptibility pattern of Gram Positive Uropathogens

	Enterococcus species (n=58)		*Staphylococcus epidermidis* (n=26)		*Staphylococcu aureus* (n=1)	
	S	R	S	R	S	R
Penicillin	3 (5.17%)	55 (94.82%)	0 (0%)	26 (100%)	0 (0%)	1 (100%)
Gentamicin	23 (34.65%)	35 (60.34%)	18 (69.23%)	8 (30.76%)	1 (100%)	0 (100%)
Vancomycin	50 (86.20%)	8 (13.79%)	23 (88.46%)	3 (11.53%)	1 (100%)	0 (0%)
Ceftriaxone	28 (48.27%)	30 (51.72%)	20 (76.92%)	6 (11.53%)	1 (100%)	0 (0%)
Linezolid	55 (94.82%)	3 (5.17%)	22 (84.61%)	4 (15.38%)	1 (100%)	0 (0%)
Teicoplanin	42 (72.41%)	16 (27.58%)	NT	NT	NT	NT
Ciprofloxacin	0 (0%)	58 (100%)	4 (15.38%)	22 (84.61%)	1 (100%)	0 (0%)
Nitrofurantoin	38 (65.51%)	20 (34.48%)	22 (84.61%)	4 (15.38%)	1 (100%)	0 (0%)
Cotrimoxazole	NT	NT	NT	NT	1 (100%)	0 (0%)
Cloxacillin	NT	NT	NT	NT	1 (100%)	0 (0%)

NT=Not Tested

Discussion

Antibiotics remain the mainstay for treating bacterial infections, but increasing and changing resistance pattern of bacteria against antibiotics are prime barrier against infection [1]. Due to ongoing emergence of multi drug resistance uropathogens the empirical treatment has become difficult and unpredictable as local variation exist among them in different geographical settings [7]. In the present study we have evaluated the bacterial pathogens causing UTI and their antibiotic susceptibility pattern.

A total of 2247 urine samples were examined in which 501(22.29%) showed significant bacteriuria, that shows the prevalence of uropathogenes in our study is 22.49%. Out of total samples collected 884 (39.34%) were male and 1363 (60. 65%) were female where significant bacteriuria was seen in the male and female were 227 (45.3%) and 274 (54.69%) respectively which was in accordance other findings [4, 9]. The incidence of UTI is high among the female than male due proximity of the urethral meatus to the anus, shorter and wider urethra, sexual intercourse, incontinence, and less acidic pH of vaginal surface and poor hygienic conditions. In contrast to these observations, study done by Mallikarjuns et al reported UTI's in males (59%) is more than in females (41%) [10]. Among the sample analyzed, 416 (83%) were gram-negative bacteria and 85(17%) were gram-positive bacteria which was a similar finding done by various studies [9,11]. In our study, the total number of patient and culture positivity were higher in age group between 21-40 years of age i.e. 780 (34.71%) and 161 (32.13%) respectively followed by age group between 41-60 years of age, this was in agreement with other studies [12, 13]. Females of the reproductive age group (18-49 years) constituted 56.37% of the total patients with UTI. However, elderly (50-90years) males had a higher incidence of UTI [2]. About uropathogens, *E coli* were the commonest organism causing UTI in our study which was consistent with local as well as international reports. The study demonstrates that *E. coli* remains the leading bacteria being responsible for 73.05% of UTI. This is in consistence with findings of other studies in which *E. coli* was the most frequently reported isolate from patients with UTIs [1, 2, 3, 4]. *Enterobacteriaceae* have several factors responsible for their attachment to the uroepithelium. These gram negative aerobic bacteria colonize the urogenital mucosa with adhesion, pilli, fimbriae and P1-blood group phenotype receptor [2]. Overall bacteriological spectrum was almost similar to other recent studies, but the antibiotic resistant pattern is somewhat different. Increasing resistance to common antimicrobials like cephalosporins, cotrimoxa-zole and quinolones are becoming evident, but amikacin and nitrofurantoin remain sensitive to almost all types of gram negative uropathogens. Similar reports were published in recent literatures from various places. Thus empirical use of antibiotics for UTI is becoming difficult and unwise [1]. *E. coli*, the predominant etiological organism of UTI in study showed moderately sensitive to ciprofloxacin (65%), levofloxacin (54.6%) and gentamicin (88%); highly sensitive to amikacin (93.4%) and nitrofurantoin (89.9%) as similar pattern was seen in other studies [13]. However, rest of other antibiotics tested was highly resistant. In different parts of the world, resistance of *E. coli* to penicillin group of antibiotics have been on higher side and is increasing day by day, but there are only few reports which indicates 100% resistance to penicillin. Resistance to other beta lactam antibiotics including cefotaxime (61.4%), ceftazidime (63.6%) was also very high rendering many of these inefficient for empirical prescription of these antibiotics to treat UTIs. [6] *Klebsiella species*, the second isolated causative agent of UTI in the study, showed absolutely resistance to ampicillin (100%); highly resistance to ceftazidime (77.7%) and rest of others were moderately resistance. The findings of this study coincide with other [14]. Amikacin was the most sensitive antibiotic among studied antibiotics which was in contrast with other findings [4]. In case of *Pseudomonas aeruginosa* isolates, amikacin, gentamicin and tobramycin were moderately sensitive and ceftazidime were highly resistance. The findings of this study coincide with other [8]. In the case of gram positive bacteria, linezolid and vancomycin were highly sensitive but penicillin seems to be highly resistance; the rest of other antibiotics were moderately sensitive.

Cotrimoxazole and cloxacillin were not tested for *Enterococcus species* and teicoplanin were not tested for *Staphylococcus epidermidis* and *Staphylococcus aureus*. Penicillin and ciprofloxacin was found to be highly resistance towards *Enterococcus species* and *Staphylo-cccus epidermidis* whereas Linezolid and vancomycin were highly sensitive. The findings of this study coincide with other [8]. In case of *Staphylocccus aureus* except penicillin all antibiotics were sensitive and this may be due to isolation of only one of it. The main limitation of the present study was our lacking of clinical information as on categorization of UTI patients whether complicated or uncomplicated and further, distribution of patients based on the sources of infection like catheter-associated, community acquired or nosocomial are also not mentioned.

Conclusion

The prevalence of uropathogenes in our study was higher with female predominance. Gram-negative bacteria were found to be more common Uropathogens and positivity was higher in younger age groups. *E. coli* was the most common etiological agent and remains highly susceptible to amikacin and nitrofurantoin. Increasing resistance to common antimicrobials like cephalosporins, cotrimoxazole and quinolons but amikacin and nitrofurantoin remain sensitive to most of gram negative uropathogens. In the case of gram positive bacteria, linezolid and vancomycin were highly sensitive but penicillin seems to be highly resistance.

Recommendation

Drug resistance among bacterial pathogens is an evolving process, regular surveillance and monitoring is necessary to provide us knowledge on the updated and crucial for the better management of the patients.

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Conflict of interest: None

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