Antimicrobial resistance pattern of bacterial isolates causing urinary tract infection

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Abstract

Introduction Urinary tract infection (UTI) is one of the most important cause of mortality and morbidity in the world affecting all age groups. It is estimated that 150 million cases of UTI occur on a global basis per year resulting in more than 4 billion pounds (6 billion dollars) in direct health care expenditure. Resistance to antibiotics is highly prevalent in bacterial isolates all over the world, particularly in developing countries and is an evolving and growing problem in UTI.

Objectives To isolate the bacteria causing UTI and determine their antimicrobial resistance trend in urinary isolates in current situation.

Methods This prospective study was conducted in microbiology section of NPHL, Teku from May to September 2006. During this period, three hundred and fifty two mid-stream urine samples collected were investigated by conventional semi-quantitative culture technique and antibiotic susceptibility test.

Results Altogether 11 different bacteria were isolated among which *Escherichia coli* (48.8%) was the most predominant organism followed by *Klebsiella pneumoniae* (18.8%), *Proteus mirabilis* (7.5%), *Proteus vulgaris* (6.3%), Coagulase-negative Staphylococci (5.0%), *K. oxytoca* (3.8%), *Enterobacter* spp. (3.8%), *Citrobacter freundii* (2.5%), *Acinetobacter* spp. (1.3%), *Alcaligenes* spp. (1.3%) and *Staphylococcus aureus* (1.3%). The rate of infection was high in females (29.8%) than males (15.2%). Multidrug resistance (MDR) isolates accounted for 36 out of total 80 isolates (45.0%).

Conclusion Regular monitoring of emergence of resistance is highly recommended and specific antibiotics should be given only after the laboratory results are available. A regular feedback and antibiogram should be given to the clinicians for effective management of UTI.

Key words Urinary tract infection, Multidrug-resistance.

Introduction

Urinary tract infection is one of the commonest domiciliary and nosocomial bacterial infections, comprising of a variety of clinical conditions caused by microbial invasion of tissue lining the urinary tract which extends from renal cortex to urethral meatus[1]. UTI is a serious health problem affecting millions of people each year. It has been estimated that about six million patients visit out patient departments and about 300,000 are treated in the wards every year for UTI worldwide[2]. It is estimated that 150 million cases of UTI occur on a global basis per year resulting in more than 4 billion pounds (6 billion dollars) in direct health care expenditure[3]. According to the annual report published by Department of Health Services (2002/03), morbidity of UTI in Nepal is 1, 25,058. Geographical distribution of UTI in Mountain, Hill and Terai regions of Nepal are 13, 518, 68,858 and 42,682 respectively[4].

Reporting of antimicrobial susceptibility testing of the urinary tract is usually achieved 48 hours following sampling, and therefore in the majority of community-acquired UTIs (CA-UTIs), the treatment decision is empirical, being influenced by available data reflecting antibiotic resistance[5]. Since the initiation of antimicrobial therapy in CA-UTIs is

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empirical knowledge of the antimicrobial resistance patterns of common uropathogens is essential to provide clinically appropriate and cost effective therapy[6]. In many parts of Nepal, the facilities for urine culture and antimicrobial susceptibility testing are not available thus leading to incorrect diagnosis and management of UTI[7].

Effective management of UTIs in both the inpatient and outpatient settings has been complicated by the fact that many uropathogenic strains have developed resistance to antimicrobials, including Cotrimoxazole, the current first-line treatment for uncomplicated UTIs in the US and many other countries[8]. The current trend of rising Trimethoprim-sulphamethoxazole (TMP/SMX) and beta-lactam resistance rates is problematic. Of more concern, however, are the emerging issues of fluoroquinolone resistance and MDR among community-acquired urinary isolates[9]. MDR was defined as resistance to three or more of the antimicrobial agents evaluated in the study[10]. This study was conducted to observe the current trend of antibiotic resistance of bacteria causing UTI.

Materials and Methods

During May to September 2006, a total of 352 mid-stream urine samples from patients suspected of UTI were collected and processed according to the standard laboratory methods. These samples were cultured on MacConkey agar and Blood agar plates and incubated at 37^0C for 24 hours. The isolated bacteria were identified by Gram staining and biochemical tests. Bacterial colonies more than 10^5 CFU/ml of urine were considered as significant. The isolates were then subjected to antibiotic susceptibility test on Mueller Hinton agar using different antibiotic discs by Kirby-Bauer's disc diffusion method. The drugs used were Ampicillin (Amp), Ceftriazone (CRO), Ciprofloxacin (Cip), Cloxacillin (Ob), Cotrimoxazole (Co), Erythromycin (E), Gentamicin (G), Nitrofurantoin (Nf), Norfloxacin (Nx), Ofloxacin (Ofx) and Oxacillin (Ox). Data were statistically analysed using Chi-square test.

Result

Of the total 352 patients suspected of UTI, 171 males and 181 females were included in this study and 22.7% (80/352) showed significant bacteriuria (Figure 1).

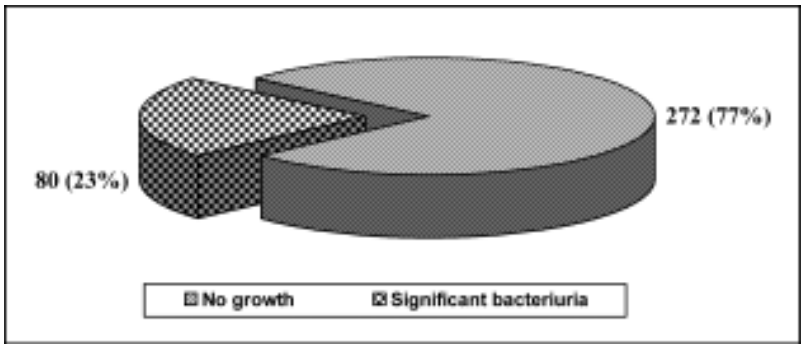

Figure 1: Pattern of urine culture result

As shown in figure 2, *Escherichia coli* (48.8%) was the predominant bacterial isolate causing UTI followed by *Klebsiella pneumoniae* (18.8%), *Proteus mirabilis* (7.5%) and so on.

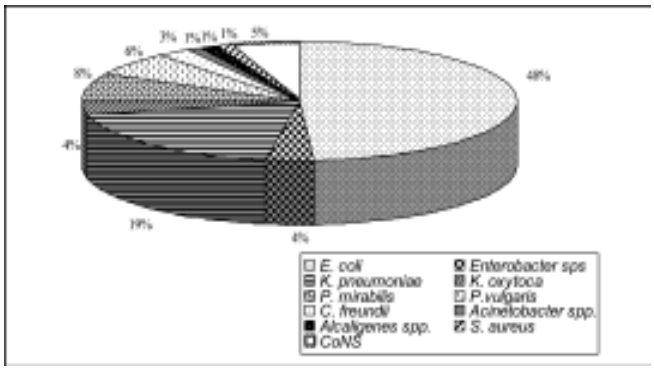

Figure 2: Percentage distribution of bacterial isolates from urine culture

Higher rate of infection was found in female patients 29.8 percent (54/181) compared to male patients 15.2 percent (26/171) as shown in figure 3.

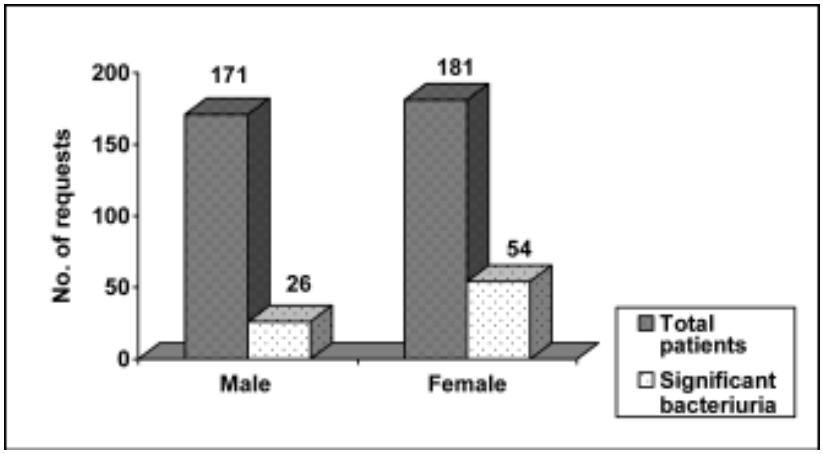

Figure 3: Pattern of urine culture results in male and female patients

The antibiotic susceptibility profile studied showed that most of urinary bacterial isolates were resistant to almost all the common antibiotics tested. Among the common antibiotics tested against all Gram negative bacteria, the most effective antibiotic was found to be Gentamicin (80.0%) followed by Ceftriaxone (76.0%). Most of the Gram negative bacteria i.e.71 (94.7%) was resistant to Ampicillin. Among the 5 Gram positive bacteria, 100 percent of the isolates were susceptible to Nitrofurantoin. Oxacillin and Cloxacillin (60%) were found to be the least effective. The percentage resistance and susceptibility of gram-negative isolates to each antibiotic tested was as shown in table 1.

Table 1: Antibiotic susceptibility pattern of gram-negative bacterial isolates causing UTI

Isolates tested	Amp		CRO		Cip		Co		G		Nf		Nx		Ofx	
	% R	% S	% R	% S	% R	% S	% R	% S	% R	% S	% R	% S	% R	% S	% R	% S
E. coli (N=39)	97.4	2.6	20.5	79.5	30.8	69.2	46.2	53.9	18.0	82.1	10.3	89.7	53.9	46.2	33.3	66.7
Klebsiella pneumoniae (N=15)	86.7	13.3	26.7	73.3	26.7	73.3	40.0	60.0	20.0	80.0	26.7	73.3	33.3	66.7	26.7	73.3
Klebsiella oxytoca (N=3)	100.0	0	33.3	66.7	66.7	33.3	66.7	33.3	33.3	66.7	0	100	100.0	0	66.7	33.3
Proteus mirabilis (N=6)	100.0	0	16.7	83.3	0	100.0	33.3	66.7	0	100.0	0	100	0	100.0	0	100
Proteus vulgaris (N=5)	80.0	20	20	80	20	80	40	60	20	80	20	80	20	80	0	100
Enterobacter spp.(N=3)	100.0	0	0	100	33.3	66.7	33.3	66.7	0	100	33.3	66.7	33.3	66.7	33.3	66.7
Citrobacter freundii (N=2)	100	0	0	100	50	50	50	50	0	100	50	50	50	50	50	50
Acinetobacter spp.(N=1)	100	0	100	0	100	0	100	0	100	0	100	0	100	0	100	0
Alcaligenes spp.(N=1)	100	0	0	100	0	100	0	100	0	100	100	0	0	100	0	100

Note: R=Registance, S=Susceptibility, Amp=Ampicillin, Cro=Cedriazone, Cip=Ciprofloxacin, Co=Cotrinoxazole, G=Gentamicin, Nf=Nitrofurantoin, Nx=Norflaxacin, Ofx=Ofloxacin

Most of the bacteria isolated were found to be resistant to three or more drugs (45.0%) and were considered MDR. Among the MDR strains, 51.3 % (20/39) of *E. coli* and 33.3 % (5/15) of *K. pneumoniae* were found to be MDR (Table 2).

Table 2: Resistance pattern and distribution of MDR bacterial isolates

Organisms	Total no. of isolates	Sensitive to all	Resistant to 1 drug	2 drugs	MDR Strains 3 drugs	%
E. coli	39	1	8	10	20	51.3
K.pneumoniae	15	3	4	3	5	33.3
K. oxytoca	3	0	0	0	3	100.0
Proteus mirabilis	6	0	5	0	1	16.7
Proteus vulgaris	5	1	1	1	2	40.0
Enterobacter spp.	3	0	1	1	1	33.3
Citrobacter freundii	2	0	0	1	1	50.0
Acinetobacer spp.	1	0	0	0	1	100.0
Alcaligenes spp.	1	0	0	1	0	
S. aureus	1	0	0	1	0	
CoNS	4	0	2	0	2	50.0
Total	**80**	**5**	**21**	**18**	**36**	**45.0**

Discussion

This study revealed the pattern of UTI prevalent according to sex, organism affecting and the antimicrobials used. In this study, overall 22.7 percent of MSU samples from patients visiting NPHL with suspected cases of UTI showed significant bacteriuria. The low growth positive rate observed in this study might be due to inclusion of kidney transplant patients and others for routine check up only and also due to self medication.

In present study, the rate of growth positivity was found to be 29.8 percent (54/181) in females and 15.2 percent (26/171) in males. This higher growth positivity seen in females was found to be statistically significant ($p<0.05$) and may be attributed to their anatomical structure (short urethra and proximity to anal orifice) leading to easy access for coliform bacilli. This was in agreement with the findings of other investigators from Nepal[11,12,13,14] and elsewhere[15].

In this study, 93.8 percent (75/80) Gram negative bacteria were isolated which was higher than Gram positive bacteria 6.3 percent (5/80). The most prevalent organism found was *E. coli* (48%), which was in agreement with other studies conducted both in Nepal[7,11,12,16,17] and elsewhere[15,18,19].

In this study, gentamicin (80%) was found to be the most effective antibiotic against Gram negative bacteria followed by Ceftriaxone with a susceptibility of 76 percent. In a similar study by Jha and Bapat[14] at Sukhraraj Tropical Hospital, 92.5 percent of urinary isolates were susceptible to Gentamicin. On the other hand, Ampicillin was found to be the least effective drug against Gram negative bacteria (94.7% resistant). Similarly, 97.4 percent of *E. coli* and 86.7 percent of *K. pneumoniae* were found to be resistant to Ampicillin in this study. Resistant to Ampicillin was also observed by various other researchers[7,16,17,20]. In this study, Nitrofurantoin was the choice of drug for *E. coli* followed by Ceftriaxone, Gentamicin and others. Among Gram positive isolates, the most effective drug was found to be Nitrofurantoin (100%) ≥ followed by Ampicillin, Ceftriaxone, Cotrimoxazole, Ciprofloxacin and Erythromycin with the susceptibility of 80 percent for all five drugs.

As evident from table 2, MDR isolates accounted for 36 out of the 80 isolates (45%). In a study done by Tuladhar et al [21] at TUTH, MDR bacterial strains were detected in 35.2 percent cases.

Higher resistance rates to all antibiotics tested except Gentamicin and Nitrofurantoin may be explained due to high and uncontrolled consumption of these antibiotics during the past decade. These antibiotics were prescribed not only for UTI, but also for infections in other body sites. Previous reports have indicated that the high resistance of uropathogenic bacteria to antimicrobial agents in developing countries[22] is often due to self-medication, the suboptimal quality of antimicrobial drugs, and poor community and patient hygiene[23]. Second, inappropriate use of antimicrobial agents is widespread as many people can easily buy antibiotics from pharmacy stores and patent medicine stores, with or without prescriptions. This widespread and inappropriate use of antibiotics is recognized as a significant contributing factor to the spread of bacterial resistance and the development

of resistance to antimicrobial agents[24]. Third, there is evidence that for most bacteria, increased usage of a particular antimicrobial agent correlates with increased levels of bacterial resistance to that agent[25].

Conclusion

Inappropriate use of antimicrobial agents should be avoided. Regular monitoring of emergence of resistance is highly recommended and specific antibiotics should be given only after the laboratory results are available. A regular feedback and antibiogram should be given to the clinicians for effective management of UTI.

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