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Bacteriology of Urinary Tract Infection of Chronic Renal Failure Patients Undergoing for Hemodialysis

Abstract

Introduction: Urinary tract infections (UTIs) are the second most common bacterial infectious diseases in human, and they occur in all age group, and usually require urgent treatment. Usually asymptomatic UTI is most common among Hemodialysis (HD) patients with Chronic Renal Failure (CRF) due to their disturbed defense mechanism. Clinically, UTI is defined as the presence of bacteria undergoing multiplication in urine more than 105 colony forming unit (CFU) or organism/ml in the clean catch midstream urine [1,2].

Objectives: To examine the prevalence of urinary tract infection in CRF patients undergoing for hemodialysis and to evaluate the emerging pattern of MDR isolates.

Methods: A cross-sectional study was designed in CRF patients on HD in the National Kidney Center of Nepal from June 2013 to November 2013. Clean-catch midstream urine samples were collected from study patients and inoculated in Blood agar and MacConkey agar and incubated aerobically at 37 °C for 18-24 hours. Macroscopic and microscopic observations were done and conventional biochemical tests were done to identify the isolated organisms. The isolated organisms were tested for antimicrobial susceptibility by using modified Kirby Bauer technique.

Results: In total, 150 urine cultures from CRF patients undergoing for hemodialysis were evaluated. Gram-negative organisms were isolated in 33(84.6%) of 39 cases with *Escherichia coli* 13(33.3%), *Proteus vulgaris* 7(17.9%), *Klebsiella oxytoca* and *Pseudomonas aeruginosa* 3(7.7%), *Proteus mirabilis* and *Enterobacter aerogenes* 2(5.1%) and *Klebsiella pneumoniae, Providencia alcalifacience* and *Morgnella morganii* 1(2.6%). In case of Gram positive, *Staphylococcus saprophyticus* 6(15.4%), was the only one organism isolated. In antibiotic sensitivity patterns of the isolated organisms, Gram-negative microorganisms were found to be most effective towards imipeneme and gentamicin whereas Gram-positive microorganisms were most effective against imipeneme and oxacillin. Out of the total isolates 23 isolates were found to be multidrug resistant.

Conclusion: In CRF patients on HD, asymptomatic urinary tract infection was detected significantly. *E. coli* was found to be predominant organisms and resistant towards most of the studied antibiotics.

Keywords: Urinary Tract Infection; Chronic Renal Failure; Antibiotic Sensitivity; Cons; Hemodialysis

Research Article

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Introduction

Urinary tract infection is the most common bacterial infection in humans. It can be either symptomatic or asymptomatic. Symptomatic infection is associated with a wide spectrum of morbidity, from mild irritative voiding symptoms to bacteremia, sepsis and occasionally death. Asymptomatic urinary infection is the isolation of bacteria from urine in quantitative counts consistent with infection, but without localizing genitourinary signs or symptoms, and with no systemic symptoms attributable to the infection [3]. UTI is considered to be uncomplicated when it occurs in patients with urinary tracts that are normal from both a structural and functional perspective [4]. Chronic kidney disease (CKD) is a common problem among males compared to females due to stress, alcoholism, hypertension and diabetes mellitus. Due to urinary stagnation, alkalization of urine and absence of flushing action, the presence of urinary tract infection (UTI) in CKD of males is higher compared to normal males [5]. Surveillance of urinary pathogens in a hospital is important for monitoring the spectrum of micro- organisms that infect the urinary drainage system and types of organisms associated with a particular clinical discipline. An early and accurate etiological diagnosis is not always easy, especially since the disease may start with minimal or non-specific symptoms. Delayed treatment until clinical recognition of signs and symptoms entails risk of preventable mortality, notwithstanding the fact that presumptive

antibiotic therapy may result in Correspondence over-treatment. The uncertainty surrounding the clinical approach to treatment of bacteriuria can be minimized by periodic epidemiological surveys of etiological agents and their antibiotic sensitivity patterns leading to recognition of the most frequently-encountered pathogens in a particular patient setting. This study was undertaken to identify the bacterial pathogens from midstream urine samples, to determine the prevalence of asymptomatic bacteriuria among CRF patients undergoing for hemodialysis.

Methods

An analysis was done on urine culture of 150 CRF patients under hemodialysis from June 2013 to November 3013 at the National Kidney Center, Banasthali, and Kathmandu. Exclusive criteria were the HD patients who were HIV and Hepatitis C infected.

Clean-catch midstream urine samples were collected from study patients and inoculated in Blood agar and MacConkey agar and incubated aerobically at 37 °C for 18-24 hours Macroscopic (turbidity, odor and color) and microscopic (WBC and RBC) were done only after inoculation. The most accurate method to detect pyruria is examining an unspun urine sample; the finding of ≥10 leukocytes per high-powered field is considered abnormal [6]. Identification of the isolates was done by using standard microbiological techniques which involve the morphological appearance of the colonies, Gram's staining reactions, and biochemical properties like catalase production test, oxidase test and coagulase production test by tube method, indole production test, methyl red test, Voges-Proskauer (VP) test, citrate utilization test, triple sugar iron (TSI) agar test and urea hydrolysis test [7]. The antibiotic susceptibility pattern of all the strains was determined by using modified Kirby Bauer disc diffusion method. The computer data were studied using the statistical software SPSS version 17. The chi-square test was used to calculate probabilities and determine significance. A p-value of less than or equal to 0.05 was considered to be statistically significant ($p<0.05$).

Results

Out of 150 urine samples of CRF patients, 39 (26%) were showed culture positive result, whereas 111(74%) showed culture negative result (Table1).

Table 1: Growth pattern of Bacteria.

Growth	No. of Samples	Percentage of Samples (%)
Culture positive	39	26
Culture negative	111	74
Total	150	100

Among 150 urine samples 19(12.7%) showed pyuria (>10WBC/HPF) and among these 12(30.8%) gave culture positivity. 131(87.3%) of the total urine samples showed no pyuria (<10WBC/HPF) but among these 27(69.2%) gave positive culture results. The significant growth of organism and pyuria was found to be statistically significant ($p<0.05$) (Table 2).

The highest frequency of culture positive patient fell into 61-70 years. Among 150 samples, 39 positive cases consist of 76.9% (30/39) male and 23.1% (9/39) female. Among the female population, higher rate of culture positivity was observed in 61-70 years age group 33.3%. Though there is no statistical significant relation (Table 3).

Both Gram negative as well as Gram positive organisms was found to be responsible for urinary tract infection. Among Gram negative isolates *E. coli* (33.3%) was found to be most predominant organisms followed by *Proteus spp.,* (17.9%) and among Gram positive only one type of organism was isolated i.e *S. saprophyticus* (15.4%) (Table 4).

Among generally used antibiotics for UTI Gram negative isolates showed 100% sensitivity towards Imipeneme followed by Gentamicin (87.9%), Cotrimoxazole (78.8%) and Chloramphenicol (66.7%). The least effective antibiotics for Gram negative were found to be Amoxycillin (Table 5).

Table 2: Association of pyuria with significant growth.

Pus Cell (>10WBC/HPF)	Significant Growth n (%)	No Growth n (%)	Total N (%)	P-value
Present	12 (63.2)	7 (36.8)	19 (12.7)	
Absent	27 (20.6)	104 (79.4)	131 (87.3)	P=0.000
Total	39(26%)	111(74%)	150	

Table 3: Significant bacteriuria in different sex and age group.

Age Group	Number of Males	Culture Positivity n (%)	Number of Females	Culture Positivity n (%)	Total N (%)	Culture Positivity n (%)
21-30	25	9 (30)	8	1 (11.1)	33 (19.3)	10 (23.1)
31-40	14	1 (3.3)	5	1 (11.1)	19(12.7)	2 (5.1)
41-50	18	5 (16.7)	12	2 (22.2)	30 (20)	7 (17.9)
51-60	19	5 (16.7)	8	1 (11.1)	27 (18)	6 (15.4)
61-70	19	6 (20.7)	8	3 (33.3)	27 (18)	9 (23.1)
Above 71	9	4 (13.3)	5	1 (11.1)	14(8)	5 (12.8)
Total	104	30 (76.9)	46	9 (23.1)	150(100)	39 (100)

Table 4: Bacterial isolates.

Isolated Organisms	Frequency	%
Gram Negative Bacteria		
Escherichia coli	13	33.3
Proteus vulgaris	7	17.9
Proteus mirabilis	2	5.1
Klebsiella oxytoca	3	7.7
Klebsiella pneumoniae	1	2.6
Pseudomonas aeruginosa	3	7.7
Enterobacter aerogenes	2	5.1
Providencia alcalifaciens	1	2.6
Morganella morganii	1	2.6
Gram Positive Bacteria		
Staphylococcus saprophyticus	6	15.4
Total	39	100

Table 5: Antibiotic susceptibility pattern of Gram-negative bacterial isolates.

Antibiotics Used	Antibiotic Susceptibility Pattern		Total N
	Sensitive n (%)	Resistant n (%)	
Amoxycillin	4 (12.1)	29 (87.9)	33
Ceftriazone	15 (45.5)	18 (54.5)	33
Cephalexin	13 (39.4)	20 (60.6)	33
Chloramphenicol	22 (66.7)	11 (33.3)	33
Ciprofloxain	18 (54.5)	15 (45.5)	33
Cotrimoxazole	26 (78.8)	7 (21.2)	33
Gentamicin	29 (87.9)	4 (12.1)	33
Imipeneme	33 (100)	0	33
Nitrofurantoin	19 (57.6)	14 (42.4)	33
Norfloxacin	18 (54.5)	15 (45.5)	33

The antibiotics Imipeneme (100%), Oxacillin (83.3%) and Gentamicin (66.7%) were found to be most effective, whereas Erythromycin and Amoxycillin were found to be least effective drug against Gram positive isolates (Table 6).

Among 39 isolates 23 isolates were MDR isolates as they showed resistant towards more than two groups of antibiotics. MDR was observed in both groups of isolates that were Gram negative 19 as well as Gram positive 4. MDR was found most commonly in *E. coli* (Table 7) [8].

Table 6: Antibiotic susceptibility pattern of Gram-positive bacterial isolates.

Antibiotics used	Antibiotic Susceptibility Pattern		Total
	Sensitive n (%)	Resistant n (%)	N
Amoxycilline	**0**	6 (100)	6
Ceftriaxone	2 (33.3)	4 (66.7)	6
Chloramphenicol	3 (50)	3 (50)	6
Ciprofloxacin	2 (33.3)	4 (66.7)	6
Cotrimoxazole	3 (50)	3 (50)	6
Erythromycin	0	6 (100)	6
Gentamicin	4 (66.7)	2 (33.3)	6
Imipeneme	6 (100)	0	6
Nitrofurantoin	2 (33.3)	4 (66.7)	6
Norfloxacin	2 (33.3)	4 (66.7)	6
Oxacillin	5 (83.3)	1 (16.7)	6

Table 7: Distribution of MDR isolates among total isolates.

Isolated Organism	Number of MDR isolates n (%)	Total N (%)
Escherichia coli	6 (26)	23 (59)
Proteus vulgaris	4 (17)	
Proteus mirabilis	1 (4.4)	
Klebsiella oxytoca	2 (8.7)	
Klebsiella pneumoniae	0	
Pseudomonas aeruginosa	3 (13)	
Enterobacter aerogenes	2 (8.7)	
Providencia alcalifaciens	1 (4.4)	
Morganella morganii	0	
Gram negative MDR isolates	**19 (82.6)**	
Staphylococcus saprophyticus	4 (17.4)	
Gram positive MDR isolates	**4 (17.4)**	

Discussion

The present study was carried out in National Kidney Center, Banasthali**,** among CRF patients under hemodialysis of age 20-90 years. Out of 150 urine samples processed, 39(26%) were found to be culture positive, whereas 111(74%) were found to be culture negative. The prevalence of bacteriuria among male was found to be 69.3% and female was found to be 30.7%. The incidence of bacteriuria was highest i.e. 33.3% in the age group of 61-70 years. Chronic kidney disease (CKD) is common among the elderly people with increased rate of infections among which UTI is most [9]. Though there is no statistical correlation between the growth of organisms and age group of the patients. The study did not find the similarity with the recent study conducted in western Nepal by workers Jaiswal et al. [10] reporting a 30% culture positivity rate. A study, which was done in Iran in 2011 showed the isolation rate to be 35.5% [11]. A similar study, which was done in Baghdad showed a higher positive growth rate of 62% [12]. The reason behind obtaining such result in this study may be due to the fact that the patients are undergoing for various treatments, due to slow growing organisms or due to those organisms that were not able to grow on the routine media we used. A similar study carried out by Dhakal et al. [13] showed growth positivity of 25.16%, which is very much similar to our study. Significant pyuria was observed in 19(12.7%) of the total sample among which 12(30.8%) showed culture positivity.

Out of 131(87.3%) cases of insignificant pyuria, 27(69.2%) showed culture positive while remaining 104 (93.7%) showed culture negative results. In general, as the number of pus cells/HPF increases, the chance of getting culture positive results will also be higher [14]. But in our study the culture positive cases for UTI is higher among insignificant pyuric case than significant pyuric cases. Similarly Eisinger and colleagues assessed the prevalence of pyuria and UTI in patients with chronic kidney disease. They observed only 1 of 9 patients with a positive pyuria who had a positive culture. They concluded that pyuria was not a suitable marker for detection of UTI [15]. Recently Vij et al. [16] concluded that the number of urinary white blood cells (WBC) is a useful marker of urinary tract infection in patients without renal insufficiency as it is unclear what urinalysis data are normal in hemodialysis (HD) patients because the number of urinary WBC was closely related to the urinary volume in HD patients.

In the present study, it was found the high prevalence of significant bacteriuria in male as compared to female. This may be due to the inclusion of higher no of male patients suffering from chronic renal failure in our study. The study done by Ghimire et al. [17] on the prevalence of UTI among kidney transplant patients visiting NPHL included 73.0% males and 27.0% females and significant bacteriuria was seen only in 30 cases (15.0%). This fact is supported by the study done by Biswas et al. [18].

In this study among the positive urine culture, Gram negative bacteria were found to be more responsible for causing bacteriuria 84.6% (33/39) than Gram positive bacteria which was 15.4% (6/39). Similar finding was also reported by Obi et al. [19]; Karki et al. [20]; Manandhar et al. [21]; Sherstha et al. [22] and Tuladhar et al. [23] in their study and they also isolated Gram negative organisms as the predominant organisms. Altogether 10 different bacterial isolates were found in this study. Among the isolates, *E. coli* (33.3%) was found to be the most predominant organisms followed by *Proteus vulgaris* (17.9%), *Staphylococcus aureus* (15.4%), *Klebsiella oxytoca* (7.7%), *Pseudomonas aeruginosa* (7.7%), *Enterobacter aerogens* (5.1%), *Proteus mirabilis* (5.1%), *Klebsiella pneumonia* (2.6%), *Providentia alcalifacience* (2.6%) and *Morgnella morgani* (2.6%).

In this study Gram negative bacterial isolates showed more sensitivity towards Imipeneme (100%), Gentamicin (87.9%), Cotrimoxazole (78.9%) and Chloramphenicol (66.7%). The least effective antibiotics for Gram negative were found to be Amoxycillin. Such was also reported by FalahS et al, [12]. Only one type of Gram positive cocci has been isolated that is *Staphylococcus saprophyticus* which is more sensitive towards Imipeneme (100%), Oxacillin (83.3%) and Gentamicin (66.7%) whereas Erythromycin and Amoxycillin were found to be the less sensitive drugs against Gram positive organism.

Infections caused by MDR strains often lead to death [24]. Among 39 isolates 23(59%) were multi drug resistant isolates as they showed resistant towards more than two groups of antibiotics. MDR was observed in both groups of isolates that is Gram negative 82.6% (19/23) as well as Gram positive 17.4% (4/23). MDR of *E. coli* was analyzed and 6 out of 13 isolates were found MDR. Among the MDR *E. coli* isolates, 13 were resistant to Amoxycillin, 8 were resistant to Cephalexin and Norfloxacin whereas 6 were resistant to Nitrofurantoin. But the present study does not correlate with the study done by Kurutepe et al. [25], where 100.0% of MDR *E. coli* isolates were resistant to ampicillin whereas 80.6%, 74.1% and 33.3% of them were resistant to ciprofloxacin, gentamicin and nitrofurantoin respectively. In present study the resistivity capacity of Nitrofurantoin against *E. coli* has become higher, this may be due to the continual use of broad spectrum antibiotic therapy during hemodialysis period. This may have been due to the fact that this antibiotic has been widely used in treating UTI. During hemodialysis several types of complications occur and to control those various antibiotics are used and which increases the resistivity of various organisms.

Conclusion

Asymptomatic UTI is most common in CRF patients so continuous urine culture need to be required during hemodialysis in order to control the threat of asymptomatic UTI which may be chronic if not treated in time. This finding showed *E. coli* is most predominant uropathogen as well as MDR isolate too. Imipeneme was found to be the most effective antibiotic against Gram negative and Gram positive bacteria. The result of our study also emphasizes the need for continuous evaluation of local antibiotic sensitivity patterns of pathogen for the formulation of a rational antibiotic policy. Studies such as this should provide a useful information base to guide practice and policies on rational use of antibiotics.

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