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Asymptomatic Bacteriuria, their Related Risk Factors and Antibiotic Susceptibility Pattern of Isolates Among Hemodialysis Patients

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ABSTRACT

Background: Asymptomatic bacteriuria in hemodialysis patients is a common problem due to their decreased immunity and renal function which often leads to development of urinary tract infection and other complications. However, there are no adequate guidelines that recommend the routine screening and management of such patients in most of the developing countries including Nepal resulting in antibiotic misuse. This study was done to find the magnitude of asymptomatic bacteriuria among hemodialysis patients along with their antibiotic susceptibility and related risk factors.

Methods: A descriptive cross-sectional study was conducted on hemodialysis patients from July 2023 to January 2024. Midstream clean catch technique was used for urine collection. Urine specimens were processed for identification of uropathogens and their antibiotic susceptibility test by Kirby Bauer disk diffusion method following standard guidelines. Statistical analysis was done by Excel 2016 and SPSS 26, the point estimate was calculated at a 95% confidence interval.

Results: The overall prevalence of asymptomatic bacteriuria was 27%. *Escherichia coli* (43.47%) was the most frequent isolate. Imipenem and Amikacin were the most sensitive antibiotics among Gram negative isolates while Ceftriaxone and Nitrofurantoin were the most resistant antibiotics. *Pseudomonas aeruginosa* was the major multidrug resistant pathogen. Hypertension and Diabetes Mellitus were commonly associated risk factors for asymptomatic bacteriuria in hemodialysis patients.

Conclusions: This study demonstrates high prevalence of asymptomatic bacteriuria among hemodialysis patients. Routine screening of asymptomatic bacteriuria aids in early detection and management of complications along with optimization of antibiotic use.

Keywords: Antimicrobial susceptibility; asymptomatic bacteriuria; hemodialysis.

INTRODUCTION

Asymptomatic bacteriuria (ASB) is defined as the presence of bacteria (≥10^5) in a mid-stream urine specimen without any signs and symptoms of urinary tract infections (UTI). [1,2] Patients undergoing hemodialysis are more prone to develop asymptomatic bacteriuria due to their depleted immune status, bladder stasis and frequent hospitalization.[3] Bacteriuria in hemodialysis patients is thought to be a potential reservoir for infections and readily progresses to urinary tract infection (UTI) and perinephric abscess.[4] The Infectious Diseases Society of America (IDSA) recommends the treatment of ASB only in limited conditions such as pregnancy and prior invasive urologic procedures.[5] However, a study by Asghar et al suggested the routine screening of ASB and the impact of early detection and treatment is related to lower rates of complications and hospital readmission.[6]

Although the current guidelines do not recommend the medical treatment for ASB in hemodialysis patients but injudicious use of antibiotics in such cases seem to be overwhelming, promoting the risks of antimicrobial resistance.[7] Therefore, this study was conducted to assess the magnitude of ASB in hemodialysis patients, their bacteriological culture and antibiotic susceptibility

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profile along with the identification of the related risk factors.

METHODS

A descriptive cross-sectional study was carried out among 85 hemodialysis patients attending hemodialysis unit in a tertiary care centre from July 2023 to January 2024. Ethical clearance was obtained from Institutional Review Committee (Ref no 27/080/081-S).Convenient sampling method was used to collect the specimen and 85 samples were included in the study.

Patients of all ages and gender admitted in hemodialysis unit were included in the study. Also, those patients exhibiting classical clinical features of UTI were excluded from the study. An informed written consent was taken from all the patient prior urine sample collection.

Following proper instructions, mid-stream urine sample was collected in a wide mouth screw capped sterile container. Samples were transported within two hours and were proceeded without delay.

First of all, 1µL of urine specimen was inoculated on blood agar and Mac Conkey agar (HiMedia, India) by semi-quantitative method using sterile standardized loop and incubated aerobically at 37°C for 24 hours. ASB was considered significant when there was presence of at least 10^5 CFU/ml in culture from midstream urine. Identification of isolates was done considering their colony characteristics, Gram staining morphology and biochemical properties. All identified bacterial isolates were subjected to antibiotic susceptibility testing following Kirby Bauer disk diffusion method on Mueller Hinton agar (HiMedia, India)). The susceptibility of organisms to the following antimicrobial agents was tested using following antibiotics (HiMedia, India): amikacin, ceftazidime, cotrimoxazole, imipenem, norfloxacin, piperacillin-tazobactam, doxycycline, cefazolin, cefoxitin and nitrofurantoin. The results were interpreted as per Clinical and Laboratory Standards Institute guidelines (CLSI).[8] Multidrug resistance (MDR) is defined as an acquired resistance to three or more categories of antimicrobials.[9]

Data entry and analysis were done in Microsoft Excel 2016 and IBM SPSS Statistics version 26.0. The point estimate was calculated at a 95% confidence interval.

RESULTS

A total of 85 participants were enrolled in this study. Among the participants, 23 (27%) were seen to have ASB. Preponderance of males (56.5%) was seen for asymptomatic bacteriuria and more commonly seen in the age group of 51-70. Of all participants with ASB, related risk factors were noted of which chronic kidney disease patients with hypertension and diabetes mellitus were most likely risk factors to develop ASB. (Table 1) Those participants undergoing hemodialysis for more than five years were more prone to develop ASB.

Table 1. Risk factors of asymptomatic bacteriuria in hemodialysis patients.

Risk factors	Categories	Number of growth (N=23)
Age in years (Number of patients)	20-50 (24)	9
	51-70 (41)	11
	>70 (20)	3
Sex (Number of patients)	Male (45)	13
	Female (40)	10
Hypertension	Yes	17
	No	6
Diabetes Mellitus	Yes	21
	No	2
Alcoholism	Yes	9
	No	14
Duration of hemodialysis	<5years	5
	>5years	18
Frequency of hemodialysis	1 time/week	3
	>1time/week	20

Overall, 23 (27%) urine specimens were culture positive for both Gram positive as well as Gram negative bacteria. Out of 23 bacterial isolates, *E.coli* (45%) was the most frequently isolated pathogen followed by *Pseudomonas aeruginosa* (21.7%). Distribution of bacterial isolates among positive samples is described in Figure 1.

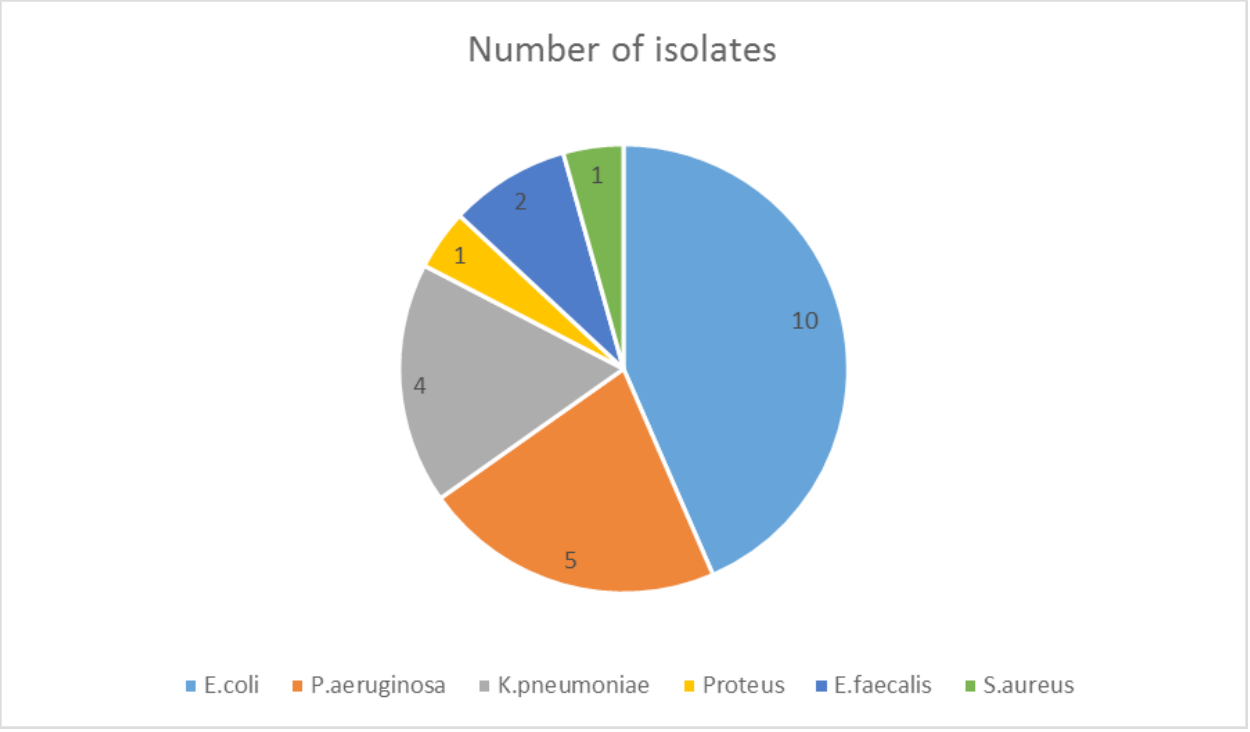

Figure 1. Distribution of bacterial isolates among positive samples.

On antibiotic susceptibility testing, Gram negative isolates were highly susceptible to Imipenem (86%) and Amikacin (80%), while Doxycycline and Ceftriaxone were highly resistant. Amongst Gram positive isolates, Amikacin and Nitrofurantoin were 100% sensitive, whereas Co-trimoxazole and Norfloxacin were the most resistant antibiotics. Eleven out of 20 Gram negative isolates were found to be multidrug resistant. (Table 2)

Table 2. Number (%) of common urinary pathogens sensitive (S) to antimicrobial agents.

Antibiotics	Gram negative isolates				Gram positive isolates	
	E.coli	*K.pneumoniae*	*P.mirabilis*	*P.aeruginosa*	*S.aureus*	*E.faecalis*
Amikacin	8(80%)	2 (50%)	1(100%)	3(60%)	1(100%)	2(100%)
Cotrimoxazole	7(70%)	1(25%)	0	IR	1(100%)	1(50%)
Ceftriaxone	7(70%)	0	0	-	-	-
Ceftazidime	6(60%)	2(50%)	0	1(20%)	-	-
Imipenem	10(100%)	3(75%)	1(100%)	4(80%)	-	1(50%)
Norfloxacin	5(50%)	2 (50%)	0	1(20%)	1(100%)	1(50%)
Nitrofurantoin	5(50%)	2 (50%)	IR	-	1(100%)	2(100%)
Doxycycline	5(50%)	1(25%)	0	-	1(100%)	-
Piperacillin-tazobactam	8(80%)	2 (50%)	1(100%)	1(20%)	-	1(50%)
Linezolid	-	-	-	-	1(100%)	1(50%)
Cefazolin	-	-	-	-	1(100%)	-
Cefoxitin	-	-	-	-	1(100%)	-

*IR: intrinsic resistance, - : not tested

DISCUSSION

Hemodialysis is the mainstay therapeutic modality for the management of chronic kidney diseases. However, patients receiving hemodialysis are prone to develop ASB due to their compromised renal function and prolonged hospital stay with frequent interventions. The overall frequency of ASB in hemodialysis patients in this study was 27%. Similar result was seen in a study conducted by Chaudhary et al.[10] On the contrary, Alaiman L et al. reported a lower prevalence ASB in hemodialysis patients.[11] The present finding was lower than those reported by Young et al.[12]

The prevalence of both ASB and UTI are more profound in females due to their short urethra which reduces the distance for bacterial ingress and its proximity to reproductive organs.[13] ASB was higher in males in our study. This finding might be due to the recruitment of a higher number of male participants in the study. The present finding was discordant with the results of Asghar et al. which showed higher ASB rates in females.[6]

In the current study, ASB was more frequently observed in those hemodialysis patients having one or more risk factors such as diabetes mellitus. Diabetes mellitus is one of the most commonly known etiology for renal insults as it leads to an alteration of glucose metabolism that affects the immune system exacerbating susceptibility to develop ASB.[14] Diabetes mellitus as the most notorious risk factor for asymptomatic bacteriuria had been demonstrated by Matthiopoulou et al.[15] The longer duration of hemodialysis also play a key role in development of ASB as shown by our study finding. This might be due to frequent and prolong exposure of patients in the hospital and their depleted immune status.

E.coli was the most frequently isolated pathogen in this study. This finding coincides with various other reports which defines *E.coli* as the significant contributor of ASB.[16,17] *Pseudomonas aeruginosa* was the second most common organism isolated in our study. The frequency of *Pseudomonas* infections has increased dramatically in hospital admitted patients with indwelling devices.[17]

All 23 isolates were subjected to antibiotic susceptibility testing against various antibiotics. Imipenem (86%) and Amikacin (80%) were found to be highly sensitive antibiotics among gram negative isolates. High sensitivity of imipenem against uropathogens was seen in the study by Almutawif et al.[18] A study conducted by Firissa et al exhibited showed that urinary tract pathogens were highly susceptible to amikacin.[19] These identified gram negative isolates were highly resistant against nitrofurantoin and norfloxacin. Various studies have reported the increasing resistance of nitrofurantoin and norfloxacin.[19,20] However, the gram positive isolates were 100% sensitive towards nitrofurantoin. Higher coverage of nitrofurantoin were seen in the previous studies conducted by Bhargava et al.[21] *Enterococcus faecalis*, a notorious pathogen seemed to exhibit high resistance towards imipenem(50%) in the present study. This finding differed from the study conducted by Kraszewska et al, which demonstrated 100% sensitivity towards imipenem.[22] *Pseudomonas* spp. isolated exhibited high resistance to most of the antibiotics and was seen to be the most drug resistant among the isolates. This result synchronized with the study findings of Khan et al. and Asamanew et al.[23,24] The resistance to different antimicrobial agents among various microbial species pose a serious threat to human health all over the world at a terrifying rate and mandates a quest for alternative therapeutic approaches. It also reiterates the optimal use of antibiotics to overcome the burden of MDR especially in the cases of ASB, which are often over treated.

CONCLUSIONS

The overall magnitude of ASB in hemodialysis patients was very high and E.coli was the most frequently identified isolate. The current study revealed the increased MDR pattern among isolates. Usually treatment of asymptomatic bacteriuria is not recommended but it connotes higher risks of symptomatic UTI. Thus, improving the diagnosis of asymptomatic bacteriuria and optimizing the management of asymptomatic bacteriuria are needed in order to minimize antimicrobial resistance.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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