Original Article

Predictors for multidrug-resistant organisms (MDROs) carriage in haemodialysis patients

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Abstract

Introduction: Infections in haemodialysis (HD) patients are an important cause of morbidity, hospitalization, and mortality. Patients undergoing HD are more prone to develop bacterial infections by multidrug-resistant organisms (MDROs). **Objectives:** This study is aimed to detect MDROs colonization in HD patients and its associated risk factors and outcome. **Methodology:** A total of 62 nasal swabs and 124 rectal swabs were collected from 62 patients coming to the haemodialysis unit from of March to May 2021 and were further screened for MRSA, VRE and CRE. **Results:** Out of 62 patients, 22.59% showed the presence of methicillin-resistant staphylococcus aureus (MRSA) while VRE was present in four patients (4/62). CRE was found as 24.2% (15/62). Duration of dialysis was found as a significant risk factor-associated MRSA carriage, Whereas Charlson index and drug and medication were found as significant risk factor for VRE carriage. **Discussion & Conclusion:** HD patients are particularly vulnerable to life threatening infections. Therefore, continuous epidemiological surveillance for these MDROs, including genotypic analysis and implementation of adequate decolonization strategies, is crucial and will reduce the possibility of autoinfection as well as disrupt transmission of multi-resistant isolates to others.

Keywords: Haemodialysis, MDRO, risk factor

Introduction

Infections in haemodialysis (HD) patients represent the second most common cause of morbidity, hospitalization and mortality after cardiovascular diseases.[1] Patients undergoing HD are more prone to develop bacterial infections. Among the bacterial infections, infections due to methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE) and carbapenem-resistant Enterobacteriaceae (CRE) are the most common infections among HD patients that may lead to serious infections including bacteraemia, infective endocarditis and toxic shock syndrome (TSS).[2] Compared to the general population, HD patients are more susceptible for colonization as well as infection because of repeated hospitalization, frequent and long-term use of antibiotics, exposure to invasive procedures, weakened immune system and regular contact with other colonized patients.[3-6]

Multidrug-resistant organisms (MDROs) can colonize in different sites of body such as nasal, axilla and rectum.[7] A number of factors unique to the dialysis population may contribute significantly to these rapidly rising rates. The proximity of patients in a haemodialysis unit during extended periods provides an optimal setting for cross-transmission of these MDR pathogens between them. Furthermore, dialysis patients are predisposed to colonization as a result of co-morbid conditions, frequent antibiotic exposure, numerous hospitalizations and type of vascular access.[8-11]

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MDROs have now become a serious menace inside the hospital. Invasive infections due to these multidrug-resistant pathogens are associated with high mortality rate.[12] Optimal screening of these MDROs and implementation of infection control practices that are currently recommended have the potential to substantially reduce transmission of infection with MDROs. This study is aimed to detect MDROs colonization in HD patients and its associated risk factors and outcome.

Materials and Methods

A prospective hospital-based pilot study was conducted in the Department of Nephrology and Department of Microbiology of AIIMS Bhubaneswar. All patients admitted to the HD unit from March to May 2021 were included in the study as a part of infection control programme. Swab samples were obtained from two different sites including nasal and rectum from all patients attending HD unit. Patients' clinical data including gender, age any co-morbid conditions, previous hospitalization in the past one year, antibiotic exposure in preceding 90 days, length of duration of dialysis, type of vascular access, duration of renal failure <3/>3 months were recorded before sample collection. The study was approved from institutional ethics committee (Ref no.-IEC/AIIMS/BBSR/STS/2020-21/01).

Identification of MRSA from nasal swab

Nasal swabs after collection were placed in enrichment broth (trypticase soy broth) and vortexed for 10 seconds. 10 µl from this broth was inoculated on commercially available Hi media sheep blood agar and oxacillin resistance screening agar base (Hi media 1454) containing 2 µg/ml oxacillin. Colonies of suspected *Staphylococcus spp* were further subjected to gram staining and coagulase test. Antibiotic susceptibility was done on Mueller–Hinton agar with cefoxitin 30 µg disc. Isolates having zone diameter ≤21 mm or growing in oxacillin resistance screening agar were confirmed as MRSA following CLSI 2021[13] guidelines.

Detection of VRE

Detection of VRE was carried out both from nasal and rectal swabs as per standard protocol. *Enterococci spp* growing on blood and MacConkey agar from nasal and rectal swabs respectively were further subjected for vancomycin disc screening test by 10 µg disc. Those isolates having zone diameter ≤14 mm were considered as VRE.

Isolation and identification of CRE from rectal swab

The rectal swabs for screening of CRE were processed as per CDC criteria. Swabs were first inoculated in trypticase soy broth containing ertapenem disc (10 µg) and further subcultured on MacConkey agar after overnight incubation. The colonies on MacConkey agar plate were further identified using standard protocol. Carbapenem susceptibility testing of the Enterobacteriaceae isolates was performed by Kirby-Bauer disc diffusion method using ertapenem (10 µg), meropenem (10 µg) and doripenem (10 µg) discs and was interpreted as per CLSI[13] guidelines. Isolates showing positive disc screening test, i.e. zone diameter ≤18 mm, were confirmed as CRE.

All patients were regularly followed up in outpatient dialysis clinic. Patients were followed up till the removal of the catheter or 90 days. Peripheral blood and catheter tip cultures were obtained in patients with episode of fever, and other relevant cultures were also obtained if required.

The results were entered in the EXCEL sheet, and data was analysed by SPSS software. Univariable analysis of risk factors was done by using Chi-square test to identify the risk factors for MDROs colonization. Statistically significant risk factors for MDROs colonization in the study group were considered where *P* value was < 0.05.

Results

A total of 62 nasal swabs and 124 rectal swabs were collected from 62 patients attending haemodialysis unit from of March to May 2021. Out of the 62 patients, 44 were males and 18 were females. Majority of the patients were adults (55) followed by elderly (5) and adolescent (2) age group. Out of the 62 nasal swabs, all 62 samples showed growth of *Staphylococcus spp*. on the blood agar. Out of 62 *Staphylococcus spp*. 35 (56.45%) were *coagulase-negative staphylococci* (CoNS) and 27 (43.55%) were coagulase-positive, i.e. *Staphylococcus aureus*. Out of 27 samples which showed growth of *Staphylococcus aureus*, 14 (22.59%) showed the presence of MRSA and 13 (20.97%) showed growth of methicillin-sensitive *Staphylococcus aureus* (MSSA) [Figure 1]. All the patients from whom MRSA was isolated were followed up for 3 months after the sample collection. Out of the 14 patients who had MRSA, seven of them had fever which subsided either on antipyretics or antibiotics, one of them expired and six of them had no complaints. In our study, duration of dialysis was found to be a significant risk factor associated with MRSA carriage [Table 1].

Out of the 62 rectal swabs, 42 (67.7%) samples showed no growth and 20 (32.3%) samples showed growth. Four (6.45%)

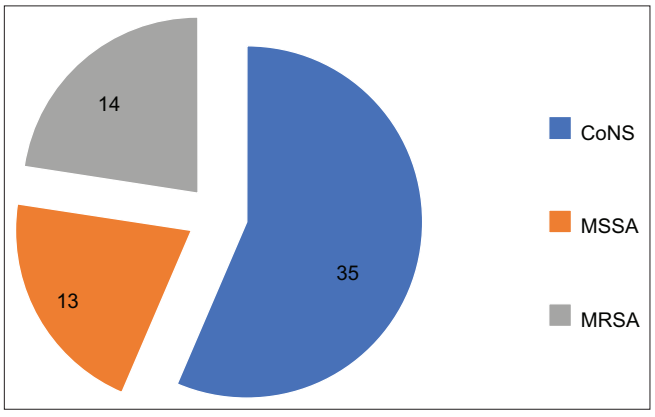

Figure 1: Pie chart showing number of CoNS, MSSA and MRSA isolated from 62 nasal swab

Table 1: Risk factor analysis in patients from whom MRSA was isolated from nasal swab

Risk factors	MRSA positive (*n*=14)	MRSA negative (*n*=48)	*P* (Univariate analysis)
Age			
>64 yrs. (*n*=5)	1/14	4/48	0.679002.
<64 yrs. (*n*=57)	13/14	44/48	
Gender			
Male (*n*=44)	9/14	35/48	0.770734
Female (*n*=18)	5/14	13/48	
History of co-morbidities (*n*=42)	8/14	34/48	0.522631.
Charlson index (*n*=62)			
0-3	10/14	33/48	0.890124
≥4	4/14	15/48	
Family history of chronic illness (*n*=4)	2/14	2/48	0.4460605
Drug or medication history (*n*=42)	9/14	33/48	0.991638
Antibiotic use in last 3 months (*n*=19)	6/14	1348	0.425448.
Duration of dialysis			
>1 month (*n*=42)	5/14	37/48	0.009636
<1 month (*n*=20)	9/14	11/48	
Type of vascular access			
AV Fistula (*n*=33)	5/14	28/48	0.234807
Central venous catheter (*n*=29)	9/14	20/48	
Duration of renal failure			
>3 months (*n*=44)	9/14	35/48	0.770734
<3 months (*n*=18)	5/14	13/48	

showed the presence of VRE and 16 (25.8%) samples were susceptible to vancomycin [Figure 2]. The prevalence of VRE is maximum in adults, which is 7.27%. All four samples identified as VRE were collected from adults, and all of them were from IPD patients. Out of the 62 nasal swabs inoculated in blood agar no sample showed growth of *Enterococcus. spp.* All the patients from whom VRE was isolated were followed up for 3 months after sample collection. Out of four patients who had VRE, two of them had fever which subsided on taking antibiotics and two of them had no complaints. Charlson index and drug or medication history was found as a significant risk factor for VRE carriage [Table 2].

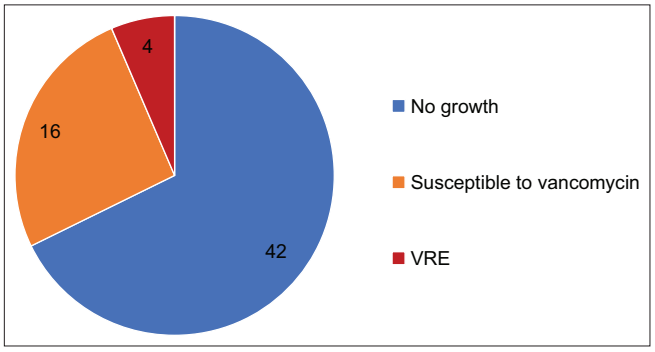

Figure 2: Distribution of 62 total samples into no growth, susceptible to vancomycin and VRE

Out of the 62 rectal samples, CRE was found in 15 (24.2%), no growth was seen in 26 (41.9%) and 21 (33.88%) samples showed growth which was susceptible to carbapenems [Figure 3]. CRE was found to be more prevalent among adult population, which is 25.45%. Prevalence of CRE was not found to be associated with any of the risk factors [Table 3]. All the patients from whom CRE were isolated were followed up for 3 months after sample collection. Out of the 15 patients who had CRE, five of them had fever which subsided on taking either antibiotics or antipyretics, three of them expired and seven of them had no complaints.

Discussion

Infections in haemodialysis patients is a matter of significant public health concern. The unique ability of long-lasting colonization of MDR pathogens make them difficult to eradicate which poses a persistent threat to patients on haemodialysis (HD). Colonization plays a key role in development of not only community-acquired infections but also infections at dialysis units.[1]

MRSA as a nosocomial pathogen, it is involved in a diverse array of lifethreatening diseases such as bacteraemia, skin and soft tissue infections, pneumonia, endocarditis, osteomyelitis, and toxinmediated syndromes with significant morbidity and mortality.[14] The prevalence of staphylococcal infections is largely dependent on nasal and hand colonization and a critical proportion of these infections are of endogenous source (from hospital and dialysis vicinity).

In our study, 22.59% showed the presence of MRSA and 20.97% showed growth of methicillin-sensitive *Staphylococcus aureus* (MSSA). Similar results were observed in studies done by Elzorkany *et al.*[15] In our study, the rate of MRSA colonization among dialysis patients was higher in

Table 2: Risk factor analysis of patients from whom VRE was isolated from rectal swab

Risk factors	VRE positive (*n*=4)	VRE negative (*n*=58)	*P* (Univariate analysis)
Age			
>64 yrs (*n*=5)	0/4	5/58	----------
≤64 yrs (*n*=57)	4/4	53/58	
Gender			
Male (*n*=44)	1/4	43/58	0.127349
Female (*n*=18)	3/4	15/58	
History of co-morbidities (*n*=42)	3/4	39/58	0.816634
Charlson index			
0-3	3/4	1/58	<0.00001.
≥4	1/4	57/58	
Family history of chronic illness (*n*=04)	0/4	4/58	----------
Drug or medication history (*n*=42)	4/4	38/58	----------
Antibiotic use in last 3 months (*n*=19)	3/4	16/58	0.153065.
Duration of dialysis			
>1 month (*n*=42)	0/4	42/58	----------
<1 month (*n*=20)	4/4	16/58	
Type of vascular access			
AV Fistula (*n*=33)	1/4	32/58	0.514582
Central venous catheter (*n*=29)	3/4	26/58	
Duration of renal failure			
>3 months (*n*=44)	2/4	42/58	0.69968
<3 months (*n*=18)	2/4	16/58	

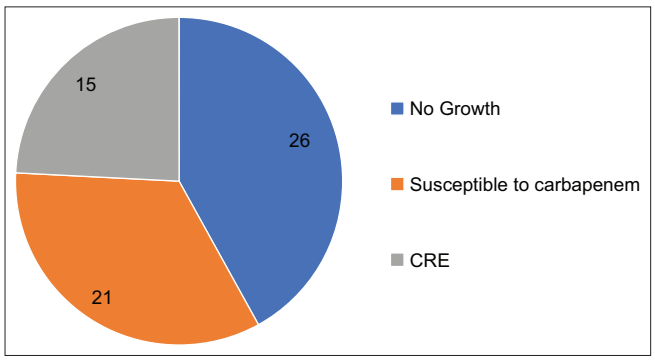

Figure 3: Pie chart showing number of samples showing no growth, susceptible to carbapenem, CRE

comparison with the study done by Schmid H *et al.*[16] where the prevalence was 11.7%. The higher carriage frequencies may be due to HD patients are continuously exposed to invasive procedures, repeated hospitalization, heavy pressure of antibiotic usage, and maintain contact with other colonized patients and health care professionals. It is important to identify the nasal carriage risk factors in dialysis patients so that the clinicians would be careful with this patient group. In this study, the maximum prevalence of MRSA was found in IPD patients which is 71.4%.

Lu PL *et al.*[17] have indicated that age is the most important factor for the *S. aureus* colonization. Duran *et al.*[18] on the other hand has not identified age and gender as risk factors. Majority of patients in our study were adults among which the MRSA prevalence was found in 23.6% followed by 20% in elderly. Our study does not confirm age and gender as a risk factor.

Duration of dialysis was found significantly associated MRSA colonization in our study. However in a study done by Celik G *et al.*[19] found that diabetes mellitus, chronic lung diseases, impaired general state of health and infection history are statistically related to MRSA carriage. Wide-spectrum antibiotics, if taken, have been identified as independent risk factors for MRSA colonization and infection.[20] Lu PL *et al.* and Leman R *et al.*[17,20] have indicated that hospitalization in the past year and antibiotic use are risk factors for MRSA carriage in HD patients. However, in our study there is no statistically significant correlation with these two parameters.

In this study out of the 14 who had MRSA, seven of them had fever which subsided either on antipyretics or antibiotics and one of them expired. Prior or concurrent MRSA colonization was the strongest risk factor for the development of post-discharge invasive MRSA infections. Patients can carry MRSA in their nares for >1 year, with one study estimating the half-life of MRSA colonization to be 40 months.[21]

Out of the 62 rectal swabs, 16 samples were sensitive to vancomycin and four samples showed the presence of vancomycin-resistant *Enterococcus* (VRE). All four samples identified as VRE were collected from adults and all of them were from IPD. VRE prevalence in haemodialysis patients ranges from 1.0% to 13.8% among centres.[22,23]

The increased risk of acquiring VRE in chronic haemodialysis (HD) patients is due to several factors including extensive contacts with the healthcare system, close proximity to other VRE patients, multiple co-morbid conditions.[24] In our study, use of antibiotics/medication was found strongly associated with the

Table 3: Risk factor analysis of CRE patients

Risk factors	CRE positive (*n*=15)	CRE negative (*n*=47)	*P* (Univariate analysis)
Age			
>64 yrs.	0/15	5/47	----------
<64 yrs	15/15	42/47	
Gender			
Male	9/15	35/47	0.454361
Female	6/15	12/47	
History of co-morbidities (*n*=42)	7/15	35/47	0.091357
Charlson index			
0-3	11/15	32/47	0.950363
≥4	4/15	15/47	
Family history of chronic illness (*n*=4)	1/15	3/47	0.572333
Drug or medication history (*n*=42)	9/15	33/47	0.674841
Antibiotic use in last 3 months (*n*=19)	6/15	13/47	0.561239
Duration of dialysis			
>1 month (*n*=42)	8/15	34/47	0.291929
<1 month (*n*=20)	7/15	13/47	
Type of vascular access			
AV Fistula	7/15	26/47	0.773664
CVC	8/15	21/47	
Duration of renal failure			
>3 months (*n*=44)	8/15	36/47	0 0.161067
<3 months	7/15	11/47	

prevalence of VRE. Previous studies have demonstrated an increased risk of VRE colonization with male gender, increased age, concomitant critical illnesses, severe underlying diseases and immunosuppression, receipt of antibiotics, use of vancomycin, injection drug use and hospitalization.[25,26] However, the present study only found association of antibiotic consumption and Charlson index with VRE colonization.

Because spontaneous mutations that would result in vancomycin resistance have not been described in enterococci, this increase is attributable to patient-to-patient transmission. The primary risk factors for infections caused by VRE are increasing severity of illness and receipt of antimicrobial agents, particularly vancomycin. However, the present study only found association of antibiotic consumption with VRE colonization. Dialysis patients have a prominent role in the epidemic of VRE and frequently are recognized as sources of outbreaks, of note is that the first reports of isolation of VRE and vancomycin-resistant *Staphylococcus aureus* involved dialysis patients.[27]

There is limited information about rectal colonization for CRE in haemodialysis patients. In the present study**,** out of the 62 rectal samples, prevalence of CRE was 24.2%. Majority of the prevalence of CRE was seen in adults which is 25.45%. CRE carriage was not found to be associated with any risk factors in our study. Similar findings were observed in the study done by Pop Vicas A *et al.*[28]

The prevalence of antimicrobial-resistant microorganisms in various healthcare settings has increased dramatically in the last decade.[29] Certain groups of pathogens, in which the frequency of resistance, has risen rapidly in recent years pose a particular threat to severely ill patients.

Antimicrobial use and control policies have been useful in limiting inappropriate use of antimicrobials in hospitals and may be useful in outpatient dialysis centres as well. Because of the important role of ESRD patients in the epidemic of vancomycin resistance, physicians providing care for dialysis patients have an important responsibility to use antimicrobials judiciously and to carefully follow other practice guidelines that could limit the further spread of vancomycin resistance.

In conclusion, *S. aur*eus nasal carriage must be screened on regular intervals in elderly, diabetic, immune-suppressed patients suffering from chronic diseases, such as HD patients. Nasal *S. aureus* carriage follow-up and treatment is a process that will protect patients from more severe clinical pictures.

HD patients are particularly vulnerable to lifethreatening infections. Therefore, continuous epidemiological surveillance for these MDROs, including genotypic analysis and implementation of adequate decolonization strategies, is crucial and will reduce the possibility of autoinfection as well as disrupt transmission of multiresistant isolates to others.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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