



ORIGINAL RESEARCH

Emergence of antibiotic resistance in bloodstream infections associated with catheters in hemodialysis patients: a prospective observational study

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Abstract

Background: Catheter-related bloodstream infections (CRBSIs) are a significant cause of hospitalization and mortality among hemodialysis patients. Incidence rates and resistance patterns vary widely. Recent studies show a rise in CRBSIs caused by multidrug-resistant organisms (MDROs). This study aims to determine the incidence, microbiological profile, antibiogram and outcomes of CRBSIs in hemodialysis patients at our institution. Methods: This prospective single center observational study included all patients initiating hemodialysis with central venous double-lumen catheters. Results: During the study, 240 catheters were inserted in 240 patients. A total of 48/240 (20%) developed CRBSI with 41/48 (85.4%) having culture-positive probable CRBSI and 07/48 (14.6%) having culture-negative possible CRBSI. Concomitant exit site infection was present in 09/48 (18.8%). The CRBSI incidence rate was 1.46 episodes per 1000 catheter days, based on 48 episodes over 32,782 catheter days. The mean time to CRBSI was 204.6 ± 87.1 days. Grampositive bacteria were cultured in 15 cases (31.3%), Gram-negative bacteria in 26 cases (54.2%), and 7 cases (14.6%) had negative culture. Coagulase negative Staphylococcus Aureus (CoNS) was the most common Gram-positive pathogens isolated, making up 46.7% of the cases. Klebsiella pneumonia, Pseudomonas, and Acinetobacter species were identified as the most prevalent Gram-negative pathogens (n = 06/26 each; 23.1%. Among 8 cultured Gram-negative bacterial species, resistance patterns observed was Ampicillin: 4/4 tested (100.0%), Quinolones: 4/6 tested (66.7%), Clotrimazole: 3/5 tested (60.0%), Carbapenems: 3/6 tested (50.0%), Gentamicin: 2/5 tested (40.0%), Amikacin: 1/3 tested (33.3%), and Piperacillin-Tazobactam: 1/5 tested (20.0%). A total of 39/48 catheters were salvaged. Conclusions: CRBSI remains a significant issue in patients using central venous catheters. The rise of multidrug-resistant Gram-negative infections necessitates stricter measures, including improved hygiene, surveillance and long-term vascular access. Proper cultures should precede empirical antibiotic therapy, and healthcare centers should tailor their antibiotic policies to local susceptibility patterns.

Keywords: Catheter related blood stream infection; Cuffed dialysis catheter; Un-cuffed dialysis catheter; Hemodialysis

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Introduction

Hemodialysis (HD) catheters are crucial for initiating treatment in most patients with end-stage renal disease (ESRD). Central venous catheters (CVCs) used in HD are linked to a significant proportion of infections, with catheter-related bloodstream infections (CRBSIs) being a leading cause of mortality among these patients [1–4]. The incidence of CRBSI ranges from 0.6 to 6.5 episodes per 1000 catheter days, influenced by factors such as the definition used, local catheter placement and care policies, and the duration of catheter use [1, 5–7], highlighting the importance of local epidemiological data for guiding prevention strategies. A recent study has highlighted a notable escalation in the incidence of catheterrelated bloodstream infections (CRBSIs) caused by multidrugresistant organisms (MDROs), with a prevalence of 44.5% [8]. This study addresses the limited regional data on antimicrobial resistance patterns in catheter-related bloodstream infections (CRBSI) among hemodialysis patients, focusing on a tertiary care center in Northern India.

This prospective observational study was conducted at the Department of Nephrology, a tertiary care center in Northern India, over a one-year period from September 2023 to September 2024. All patients initiated on hemodialysis through central venous double-lumen catheters (both cuffed and non-cuffed) were enrolled. Demographic data, clinical variables including age, gender, type of catheter placed (cuffed or non-cuffed), site and date of catheter insertion, and cause of ESRD were collected at the initial visit. Patients who developed symptoms and signs of CRBSI like fever, chills, hypotension, and /or catheter exit site discharge on follow-up, were hospitalized and evaluated using peripheral vein and central venous catheter blood cultures, alongside baseline blood tests. The 2006 National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) Clinical Practice Guidelines for Vascular Access classification were followed for classifying culture-positive probable CRBSI and culture-negative possible CRBSI. All patients received empirical intravenous antibiotics targeting both Gram-positive (including Methicillin resistant Staphylococcus Aureus MRSA) and Gram-negative organisms, reflecting global guidelines for CRBSI management. Empirical Gram-positive cover was given by vancomycin or teicoplanin depending on physician discretion and empirical Gram-negative cover was given by piperacillin tazobactam or meropenem A 2D Echocardiography was done to rule out infective endocarditis when clinically indicated.

Statistical methods

Continuous variables were reported as mean \pm standard deviation (SD), while categorical variables were expressed as percentages (proportions). Chi-square tests assessed associations between categorical variables. Mann-Whitney U tests compared non-normally distributed continuous variables. All analyses were performed using IBM SPSS Statistics for Windows (version 25, Armonk, NY, USA).

Results

A total of 240 catheters (in 240 patients) were inserted during the study period, cuffed and non-cuffed dialysis catheters accounted for 195/240 (81.3%) and 45/240 (18.8%) respectively. Men and women accounted for 141 (58.8%) and 99 (41.3%) respectively. Hypertension and diabetes mellitus were the most common comorbidities, present in 212 (88.3%) and 189 (78.8% respectively). The mean age was 52.5 \pm 15.7 years. Most patients were in the 30 to 60-year age group, followed by 60 to 90 years, accounting for 142/240 (59.2%) and 75/240 (31.3%). A total of 48/240 (20%) developed CRBSI with 41/48 (85.4%) having culture-positive probable CRBSI and 07/48 (14.6%) having culture-negative possible CRBSI, as defined by the 2006 NKF-KDOQI criteria. Intradialytic chills followed by fever were the most common presenting complaints present in 91.7% (44/48) and, 89.5% (43/48) patients respectively Mean Age of CRBSI vs. Non-CRBSI Patients was 51.6 \pm 15.6 and 56.1 \pm 15.8 years respectively; p-value 0.15. Out of 48 cases of CRBSI, men and women accounted for 23 (48%) and 25 (52%) cases respectively; p-value 0.09. A total of 41/48 (85.4%) episodes occurred in patients with cuffed dialysis catheters and 07/48 (14.6%) in non-cuffed dialysis catheters; p-value 0.536. The mean catheter days were 177.5 \pm 94.9 days. The median catheter days for un-cuffed and cuffed dialysis lines were

28 days and 210 days respectively p-value < 0.001. The mean and median time to CRBSI were 204.6 \pm 87.1 days and 231.5 days respectively. The incidence rate for un-cuffed and cuffed dialysis lines was 4.31 and 1.32 episodes per thousand catheter days. Concomitant exit site infection was present in 09/48 (18.8%). The overall CRBSI incidence was 1.46 episodes per 1000 catheter days (48 cases/32,782 catheter days \times 1000). When stratified by classification, culture-positive probable CRBSIs (n = 41) occurred at a rate of 1.25 per 1000 catheter days, while culture-negative possible CRBSIs (n = 7) had a lower incidence of 0.213 per 1000 catheter days. Hypertension and diabetes were the most common comorbidity present in 45/48 (93.8%) and 40/48 (83.3%) of CRBSI patients respectively. Grampositive organisms were isolated in 15/48 cases (31.3%), while Gram-negative bacteria accounted for 26/48 cases (54.2%), and 7/48 cases (14.6%) had negative cultures. Coagulase-negative Staphylococcus aureus (CoNS) was the most common Gram-positive pathogen isolated (07/15; 46.7%), all were methicillin-resistant. Among the remaining Gram-positive isolates, methicillin-sensitive Staphylococcusaureus (MSSA), methicillin resistant Staphylococcus aureus (MRSA), and Enterococcus species were identified. Klebsiella pneumonia, Pseudomonas, and Acinetobacter were the most common among Gram-negative organisms grown (n = 6 each; 23.1%), followed by Escherichia coli, Pantoea agglomerans, Stenotrophomonas Maltophillia and Serratia Marcescens. Among 8 cultured Gram-negative bacterial species, resistance patterns observed was Ampicillin: 4/4 tested (100.0%), Quinolones: 4/6 tested (66.7%), Cotrimoxazole: 3/5 tested (60.0%), Carbapenems: 3/6 tested (50.0%), Gentamicin: 2/5 tested (40.0%), Amikacin: 1/5 tested (20%), and Piperacillin-Tazobactam: 1/5 tested (20.0%). Most Gram-positive isolates demonstrated susceptibility to the empirically administered antibiotics, while a predominant proportion of Gram-negative organisms were identified as extended-spectrum betalactamase (ESBL)-producing strains. The CRBSI group had a mean age of 56.1 \pm 15.8 years, while the non-CRBSI group averaged 51.6 \pm 15.6 years; *p*-value 0.150. In 60 to 90-year age group, 17/75 (22.7%) developed CRBSI followed by 29/142 (20.4%) in 30 to 60-year age group. Men and women accounted for 23/48 (47.9%) and 25/48 (52.1%) of CRBSI cases respectively; p-value 0.08. Leukocytosis (>11,000 cells/mm³) was present in 44/48 (91.7%) patients and 3/48 (6.3%) had normal total leucocyte count.

Catheter salvage was achieved in 39 of 48 cases (81.3%). Concurrent exit-site infections requiring catheter removal occurred in 9 patients (18.8%) with CRBSI. No mortality was reported during the study period. The results are summarized in Tables 1,2,3,4,5,6.

Discussion

In resource-limited settings, low socioeconomic status, limited health literacy, and inadequate reimbursement systems contribute to delayed medical care and late referrals for arteriovenous fistula (AVF) creation, often leading to emergent dialysis initiation via central venous catheters (CVCs). This is reflected by the historical data

Emergence of antibiotic resistance in bloodstream

Table 1. Baseline characteristics of CRBSI group.					
Parameter	Minimum	Maximum	Mean \pm SD		
Hemoglobin (g/dL)	4.90	11.30	8.0 ± 1.5		
WBC/µL	2.30	28.00	14.8 ± 4.5		
Neutrophils (%)	65.20	98.00	84.8 ± 7.2		
Creatinine (mg/dL)	4.73	13.09	8.12 ± 1.96		
Urea (mg/dL)	79.00	299.00	176.83 ± 50.14		
Uric acid (mg/dL)	2.68	12.00	7.11 ± 2.15		
Albumin (g/dL)	1.57	3.90	2.71 ± 0.55		
No. of catheter days	25.00	319.00	204.6 ± 87.1		
Empiric therapy (d)	1.00	3.00	1.65 ± 0.67		
Culture positivity (d)	0.00	3.00	1.02 ± 1.01		

SD: standard deviation; WBC: White blood cells.

Table 2. Comparison between CRBSI and Non-CRBSI group.

Characteristics	No CRBSI	CRBSI	<i>p</i> -value
Percentage of events	192/240 (80%)	48/240 (20%)	
Age mean \pm SD in years	56.1 ± 15.8	51.6 ± 15.6	0.150
Gender (M/F)	118/74	23/25	0.088
DM (Yes/No)	149/43	40/08	0.385
HTN (Yes/No)	167/25	45/03	0.191
Type of catheter (Cuffed/un-cuffed)	154/38	41/7	0.408

M/F: Male/Female; DM: Diabetes mellitus; HTN: Hypertension; SD: standard deviation; CRBSI: Catheter-related bloodstream infections.

Table 3. Incidence of CRBSI per 1000 catheter days.						
Variable	Catheters	Catheter days	Incidence rate (per 1000 catheter days)			
Total	240	32,782				
No CRBSI	192 (80%)	23,083				
CRBSI						
Total	48/240 (20%)	9699	1.46			
Probable	41 (85.41%)	8705	1.25			
Possible	7 (14.58%)	994	0.21			

CRBSI: Catheter related blood stream infection.

Table 4. Microbiological spectrum of CRBSI.

Gram positive	Frequency (%)	Gram negative	Frequency (%)
CoNS	07 (46.7)	Pseudomonas	06 (23.1)
MRSA	04 (26.7)	Acinetobacter	06 (23.1)
MSSA	03 (20)	Klebsiella pneumoniae	06 (23.1)
Enterococcus	01 (6.7)	E. Coli	02 (7.7)
		Pantoea agglomerans	02 (7.7)
		Stenotrophomonas maltophilia	02 (7.7)
		Serratia marcescens	01 (3.84)
		Enterobacter cloacae	01 (3.84)
Total	15/48 (31.3%)	Total	26/48 (54.2%)

CoNS: Coagulase negative staphylococcus aureus; MRSA: Methicillin resistant Staphylococcus aureus; MSSA: Methicillin sensitive staphylococcus aureus; E. Coli: Escherichia Coli.

Table 5. Antibiogram of Gram-positive of gamsins.							
Antibiotics	CoNS (N = 7)	MRSA (N = 4)	MSSA (N = 3)	Enterococcus $(N = 1)$			
Vancomycin	S	S	S	R			
Linezolid	S	S	S	S			
Teicoplanin	S	S	S	R			
Ciprofloxacin	S	R	S	ND			
Clindamycin	S	S	S	ND			
Tigecycline	S	S	S	ND			
All beta lactams	R	R	S	R			
Gentamicin	S	S	R	ND			
Erythromycin	R	R	R	ND			

Table 5 Antibiogram of Cram positive organisms

S: Sensitive; R: Resistant; ND: Not done; CoNS: Coagulase negative staphylococcus aureus; MRSA: Methicillin resistant Staphylococcus aureus; MSSA: Methicillin sensitive staphylococcus aureus.

Table 0. Antibiogram of Gram-negative organisms.								
Antibiotics	PM	KP	E. Coli	AB	PA	SM	SMA	EC
	(N = 6)	(N = 6)	(N = 2)	(N = 6)	(N = 2)	(N = 2)	(N = 1)	(N = 1)
Amikacin	ND	S	S	S	S	ND	ND	R
Gentamicin	R	ND	ND	S	S	ND	S	R
Ampicillin	R	R	R	ND	ND	ND	ND	R
Ceftriaxone	ND	ND	S	S	ND	ND	ND	ND
Cefepime	S	S	ND	S	S	ND	S	R
Piperacillin-tazobactam	S	S	ND	S	S	ND	ND	R
Cefaperazone-sulbactam	S	S	S	S	ND	ND	ND	R
Imipenem/meropenem	R	S	ND	R	S	ND	S	R
Colistin	S	ND	ND	ND	ND	ND	R	S
Cotrimoxazole	R	ND	ND	R	S	S	ND	R
Ciprofloxacin/Levofloxacin	R	R	S	R	ND	S	ND	R
Tigecycline	ND	S						

Table 6. Antibiogram of Gram-negative organisms.

PM: Pseudomonas species; KP: Klebsiella Pneumoniae; AB: Acinetobacter Baumanii; PA: Pantoea Agglomerans; SM: Stenotrophomonas Maltophillia; SMA: Serratia Marcescens; EC: Enterobacter Cloacae; S: Sensitive; R: Resistant; ND: Not done; E. Coli: Escherichia Coli.

where non-cuffed dialysis catheters accounted for about 80 to 100% of all central venous hemodialysis catheters in developing nations [9-11]. In our study cuffed tunneled double-lumen catheters accounted for 81.3% of all central venous hemodialysis catheters. These results are favorable reflecting a trend towards more use of tunneled cuffed double-lumen HD catheters. Non-tunneled catheters exhibit a 2-3 times higher CRBSI incidence compared to tunneled catheters, as demonstrated by multiple studies [12, 13] and Cuffed double-lumen hemodialysis catheters (e.g., PermCath) serve as effective intermediate-term vascular access while awaiting arteriovenous fistula (AVF) creation and maturation. A total of 48/240 (20%) patients developed CRBSI during the study period. Our results are better than Shingarev R et al. [14] where 54% had a CRBSI by six months of a newly placed tunneled hemodialysis catheter. This reflects improvement in aseptic technique and better catheter care over the years. However, the study by Shingarev R et al. [14] included more

than 450 participants and all the patients had cuffed dialysis catheters as against our study which included both cuffed and non cuffed dialysis catheters. In our study 41/48 (85.4%) had culture-positive probable CRBSI and 07/48 (14.6%) had culture-negative possible CRBSI. Our culture positivity rate is better than the study done by Sethi et al. [15] where the culture positivity rate was only 62.2%. The improvement in culture positivity rates reflects early recognition of symptoms and appropriate collection of septic screens before empirical antibiotic exposure. All patients with culture-negative CRBSI in our cohort had received IV antibiotics in the community before the collection of septic screens which was the most likely reason for negative cultures. Intradialytic chills followed by fever were the most common presenting complaints present in 91.7% (44/48) and, 89.5% (43/48) of our patients respectively. The most common age group involved in our study was 60-90 years which is similar to a study reported by Tao et al. [16] and Murea et al. [17]. This phenomenon may stem from factors such as immune-senescence, atypical clinical presentations in older adults, and delays in diagnosis. Cuffed catheters showed numerically higher CRBSI rates but the difference was not statistically significant (p-value 0.536). This looks contrary to the expected. The likely reason for such a discrepancy in our study is the under-representation of patients with non-cuffed dialysis catheters and significantly fewer at-risk catheter days in non-cuffed dialysis catheters. This underscores the need for larger studies and risk-stratified protocols to clarify this association. The median catheter days for un-cuffed and cuffed dialysis lines were 28 days and 210 days respectively (*p*-value < 0.001). The historical incidence of CRBSIs associated with hemodialysis catheters falls within the range of 3-6 per 1000 catheter-days [18]. Studies report widely differing CRBSI rates, from 0.4 to 1.27 cases per 1000 catheter-days [19-21]. The CRBSI incidence rate in our cohort is 1.46 episodes/1000 catheter days (48/32,782 \times 1000) compared to an incidence of 1.30 episodes/1000 catheter days by Mark A. Little et al. [22]. The high incidence rate can be decreased by implementation of standard catheter insertion and catheter care protocol. The median time to CRBSI in our cohort was 136.5 days, higher as compared to 24.5 days reported by Agrawal et al. [23]. The main reason for this discrepancy could be partly due to better infection control practices in our center and the fact that study of Agrawal et al. [23] is done in patients on non-tunneled catheters which are at higher risk of infection and have less longevity. While most of the centers in the world encounter predominantly Gram-positive CRBSIs [14, 24, 25], Gram-negative organisms accounted for the majority of catheter-associated bloodstream infections (CRBSIs) in our study. Similar results have been reported from many other Indian studies [9, 26]. Given the fecal origin of most Gram-negative pathogens, we hypothesize that suboptimal hygiene practices contribute to the high incidence of Gramnegative CRBSIs. The other reason for increased incidence of Gram negative CRBSI could be due to indiscriminate use of broad-spectrum antibiotics. Staphylococcus aureus emerged as the most frequently isolated pathogen in the study cohort. The most prevalent Gram-negative pathogens isolated included Klebsiella pneumoniae, Acinetobacter and Pseudomonas spp. While Western literature spp. frequently associates percutaneously inserted catheters with Staphylococcus-aureus and Enterobacteriaceae-related CRBSIs, this study observed a Gram-negative predominance alongside notable Gram-positive contributions.

Among Gram-positive isolates, coagulase-negative staphylococci (CoNS) were predominant, with all exhibiting methicillin resistance. Additional Gram-positive pathogens included methicillin-sensitive Staphylococcus-aureus (MSSA), methicillin resistant Staphylococcus-aureus (MRSA), and Enterococcus species.

A majority of Gram-negative isolates demonstrated extended-spectrum beta-lactamase (ESBL) production, aligning with global trends of rising ESBL prevalence in Gram-negative infections.

The variations in microbiological profiles and antibiotic susceptibility patterns underscore the necessity for individual centers to analyze their local pathogen distribution and integrate these findings into empirical antibiotic selection protocols.

Our study has certain limitations. It is a single-center study with a limited sample size, a larger multicenter study needs to be done to reproduce the results.

Conclusions

CRBSI remains a major clinical challenge in patients receiving hemodialysis via central venous catheters, compounded by the growing prevalence of multi-drug resistant Gram-negative infections. This evolving resistance landscape necessitates enhanced preventive strategies, including rigorous sterile protocols, improved hygiene, ongoing surveillance, and accelerated transition to long-term vascular access (*e.g.*, AV fistulas). Appropriate cultures should be taken before starting empirical antimicrobial therapy and every center should frame its antibiotic policy based on regional antibiotic susceptibility patterns.

Abbreviations

CRBSI, Catheter related blood stream infection; ESRD, End stage renal disease; ESBL, Extended spectrum beta-lactamase; NKF KDOQI, National kidney foundation-kidney disease outcomes quality initiative; MDROs, multidrug-resistant organisms; CoNS, Coagulase-negative Staphylococcus aureus; HD, Hemodialysis; CVCs, Central venous catheters; MRSA, methicillin resistant *Staphylococcus aureus*; SD, standard deviation; AVF, arteriovenous fistula; MSSA, methicillin-sensitive *Staphylococcus-aureus*; TLC, Total leucocyte count; WBC, White blood cells.

Availability of data and materials

The data presented in this study are available on reasonable request from the corresponding author.

Author contributions

MB, DM, RY, MP, IW and Muzafar W—contributed to the design and development of the study; contributed data analysis and interpretation. DM, RY, MP, AF, Muzamil W and IK—contributed to data collection; participated in the writing of the manuscript. MB, IW and Muzafar W—participated in the critical review. All authors contributed to editorial changes in the manuscript; provided approval for the final manuscript.

Ethics approval and consent to participate

The study is approved by Institutional Ethics Committee SKIMS under no: SIMS131/IEC-SKIMS/2023-369. The consent has been taken from all participants of the study.

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Conflict of interest

The authors declare no conflict of interest.

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