Incidence, Risk Factors and Outcomes of Catheter Related Bloodstream Infections Among Adult Filipino Hemodialysis Patients: A Retrospective Cohort Study

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Research Article

Keywords: Catheter related Bloodstream Infection, Chronic Kidney Disease, Hemodialysis, Central Venous Catheter, Multidrug resistant organisms

Posted Date: May 12th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2904428/v1

Abstract

Background: Despite efforts to improve the management of catheter-related bloodstream infections (CRBSI) in literature, temporary CVCs continue to be used for maintenance hemodialysis outside of acute care settings, particularly in the Philippines.

Methods: We conducted a retrospective cohort study to investigate the incidence, outcomes, risk factors, and microbiological patterns of CRBSI among adult kidney disease patients undergoing hemodialysis at the Philippine General Hospital, the country's largest tertiary referral center. We included all adult patients who received a CVC for hemodialysis from January 1, 2018 to August 31, 2019, and followed them for six months to observe the occurrence of CRBSI and its outcomes.

Results: Our study documented a CRBSI incidence rate of 6.72 episodes per 1000 catheter days, with a relapse rate of 6.60%, a reinfection rate of 15.74%, and a mortality rate of 6.09%. We identified autoimmune disease, dialysis frequency of > 3x per week, use of CVC for either blood transfusion or IV medications, renal hypoperfusion, drug-induced nephropathy, and hypertensive kidney disease as significant risk factors for CRBSI. Gram-negative bacteria, including *Burkholderia cepacia*, *Enterobacter*, and *Acinetobacter* spp, were the most common organisms causing CRBSI. Multidrug resistant organisms (MDROs) comprised almost half of the isolates (n=89, 44.5%), with Coagulase negative *Staphylococcus* species, having the highest proportion among gram positive organisms and *Acinetobacter* spp. among gram negative isolates.

Conclusion: Our findings emphasize the need for more stringent measures and interventions to prevent the propagation of identified pathogens, such as a review of sterile technique and adequate hygiene practices, continued surveillance, and expedited placement and utilization of long-term access for patients on maintenance hemodialysis. Furthermore, CVC use outside of hemodialysis should be discouraged, and common antibiotic regimens such as piperacillin-tazobactam and fluoroquinolones should be reviewed for their low sensitivity patterns among gram-negative isolates. Addressing these issues can improve outcomes for hemodialysis patients and reduce the burden of CRBSI in our institution.

Background

Dialysis catheters are an important mode of vascular access in patients undergoing hemodialysis.[1] It is estimated that 80% of incident hemodialysis patients depend upon central venous catheters (CVC) as their primary vascular access, with a majority of patients initiating hemodialysis with a non-tunneled CVCs in the developing world [2,3], such is the case in the Philippines where more than 32,000 patients need dialysis services, with over 96% of patients being initiated or maintained on hemodialysis.[4]

It is currently recommended that CVCs be removed or exchanged within twenty-one days; however, this is rarely possible in developing countries due to socioeconomic and logistic constraints.[3] Refusals to accept long-term dialytic prognosis, inability to create a timely vascular access, poor vasculature suitability for fistula or graft creation and maturation failure are some of the reasons for the prevalent use of CVC among the dialysis population.[5]

Unfortunately, CVCs are responsible for half of the infections in hemodialysis patients, with catheter-related bloodstream infections (CRBSI) being the second most common cause of mortality.[1,5-9] CRBSI incidence varies from 0.6 to 6.5 episodes per 1000 catheter-days, depending on definition, local policies for catheter placement and care, and duration of catheterization.[1,5,10,11] *Staphylococcus* spp. is the most common causative organism, however; infections may also be due to other gram positive or gram negative pathogens.[1,12,13] CRBSI can also be complicated by catheter dysfunction and metastatic infections such as endocarditis, osteomyelitis, septic arthritis, and epidural abscess.[10,14] Risk factors for CRBSI include previous catheter-related bacteremia, left-sided internal jugular vein catheters, old age, diabetes mellitus, malnutrition, prolonged use, hypoalbuminemia, and immunosuppression.[10,12,15,16] Another evolving problem is the development of multidrug resistant organisms (MDROs). Risk factors for MDROs include residence in a long-term health facility and recent antibiotic use, both of which are common in patients undergoing hemodialysis.[17]

Despite having CRBSI as a focus of regulation and quality improvement, temporary CVCs are still being maintained outside of acute care settings for use as maintenance hemodialysis in our country. To our knowledge, there is also a noticeable paucity of local publications pertaining to CRBSI specifically among hemodialysis patients. It is the aim of our study to describe CRBSI incidence and outcome rates, identify associated risk factors and present the microbiological patterns of cultures and isolates among our adult kidney disease patients undergoing hemodialysis. This study also serves as a foundation for future quality improvement initiatives and provide a benchmark and performance indicator for our institution.

Methods

Study Population and Recruitment

We conducted a retrospective cohort study which included all adult patients inserted with a CVC for hemodialysis in the University of the Philippines - Philippine General Hospital, the country's largest referral center for tertiary care, from January 1, 2018 to August 31, 2019.

Patients less than 18 years old, incomplete data sets and CVCs placed in another institution were excluded. All included participants were monitored for occurrence of outcomes (CRBSI, relapse, reinfection and mortality) from the date of first CVC placement until the following: use of a long term, non-catheter hemodialysis access (fistula or graft), conversion to peritoneal dialysis or transplant, mortality or up to six months after study inclusion, whichever comes first. Sources of data included medical charts, dialysis unit and microbiological laboratory records. Clinical and demographic data (age, gender, comorbidities, baseline serum creatinine and serum albumin, frequency of dialysis), and catheter information (previous history of catheter insertion, access type, duration of use, use outside of hemodialysis, duration of insertion to diagnosis of CRBSI and isolate identity and sensitivity) were collected. Antibiotics used as initial empiric regimen (for antibiotic naïve patients) and those already on board since CRBSI diagnosis were also recorded.

The most commonly used criteria for the diagnosis of CRBSI among dialytic patients is the Infectious Disease Society of America (IDSA) criteria of 2009. In the IDSA guidance, the mainstay in diagnosing CRBSI are positive blood cultures from the peripheral veins and catheter hub that must all meet the quantitative or differential time to positivity (DTP) criteria.[18] However, implementing the IDSA criteria is controversial due to the difficulty in obtaining a culture from a peripheral vein in HD patients because of an exhausted vascular access and lack of validation for the dialytic population. In a study by Quittnatt et al., a combination of venous catheter hubs and HD circuits were reported to be the most sensitive and accurate way to diagnose CRBSI as compared to peripheral venipunctures.18 With this in mind, we opted to use the 2019 Kidney Disease Outcomes Quality Initiative (KDOQI) CRBSI case definition which incorporates both the Centers for Disease Control (CDC) and IDSA case definitions.[19] In the KDOQI definition, CRBSI is diagnosed if all four criteria are present: 1) presence of clinical manifestations consistent with CRBSI (fever, chills, hypotension), 2) at least one positive blood culture result from a peripheral source (dialysis circuit or vein), 3) the same organism is isolated from the catheter segment and a peripheral source blood sample and 4) no other apparent source of the bloodstream infection. Either a positive semi-quantitative (more than fifteen colony forming units or CFU/catheter segment, hub or tip) or quantitative (more than 102 CFU/catheter segment) culture can be used to define a positive blood culture. If available, the following would be supportive of the diagnosis: simultaneous quantitative cultures of blood samples with a ratio of greater than or equal to 3:1 (catheter hub/tip vs peripheral [dialysis circuit/vein]) and differential period of catheter culture versus peripheral blood culture positivity of two hours.[20]

Sample size

Minimum sample size required was computed using R version 4.0.3. A sample size of at least six hundred and twenty three subjects is needed to achieve 80% power at 5% significance level in a Cox regression of the log hazard ratio to detect a desired hazard ratio of at least 1.57 (the hazard ratio equivalent to Cohen's d=0.35, the threshold for the likelihood of relevance for d).19 The sample size was adjusted for an anticipated event rate of 31% CVC-related blood stream infections among hemodialysis patients with CVC (Agrawal, 2019) [3], and to multiple regression, to adjust for the different clinical variables considered with assumed proportion of 50% as confounders, with covariates anticipated to have an R-squared of 20%.

Data Analysis

The clinical, catheter, and demographic profile of the adult kidney disease patients undergoing hemodialysis in Philippine General Hospital were summarized by descriptive statistics. Numerical variables were presented as median and interquartile range, because of non-normal distribution, as assessed by Shapiro-Wilk test of normality. Categorical variables were presented as absolute or relative frequencies. The patients were grouped into with or without CRBSI and compared the different clinical, catheter, and demographic characteristics using Mann-Whitney U test for the numerical variables, and chi-square or Fisher exact test of homogeneity for the categorical variables, as appropriate.

The incidence of CRBSI among adult kidney disease patients undergoing hemodialysis was presented as number of events per 1,000 patient-catheter days. The time-at-risk utilized was the time, in days, from catheter insertion, to the day of noting CRBSI (day of blood extraction of the culture positive blood specimen) for those who had the event, i.e., CRBSI, while for those who did not have the event, it was the time, in days, from catheter insertion, to the day of catheter removal. The incidence of CRBSI was calculated for the first CRBSI episode only; subsequent catheter insertions in the same patient were recorded as either reinfection or relapse. Reinfection (recurrence of the infection in the same patient with a different microorganism), relapse (recurrence of the infection in the same patient due to the same organism) and mortality rates were expressed in percent. Catheter-specific rates were presented as CRBSI events per 1000 patient-catheter days for each catheter type.

Survival analysis was done, using Cox proportional hazards regression, to determine the association of the different clinical, catheter, and demographic characteristics of the patients with developing CRBSI. The time-to-event used was as described above. Initial univariable regression was performed to screen for probable risk factors, and those with p-value < 0.20 were included in the multivariable analysis. Factors with p-value < 0.05 in the multivariable regression were considered significant risk factors for CRBSI.

Results

Clinical Demographics

A total of eight hundred and thirty-two patients were screened at the start of the study. Ninety-five patients were excluded due to CVC insertion outside of our institution. A total of seven hundred seven patients were included in the final analysis. One hundred ninety-seven patients were classified with CRBSI while five hundred ten participants were classified as without CRBSI. (Figure 1). Table 1 presents the demographics of the study population. The median age of participants was roughly the same (with CRBSI 54 years old vs without CRBSI 53 years old) with males comprising the majority in both groups (with CRBSI n = 119, 60.41% vs without CRBSI n = 282, 55.29%).

Hypertension was the most common comorbidity found in both groups (with CRBSI n = 118, 59.9% and without CRBSI n = 201, 39.41%). This was followed by diabetes mellitus (n = 68, 34.52%) and cardiac disease (n = 36, 18.27%) in those with CRBSI and without comorbidities (n= 151, 29.61%) and diabetes mellitus among those without CRBSI.

The majority utilized a right sided (with CRBSI n = 190, 96.45%; without CRBSI n = 505, 99.02%), non tunneled (with CRBSI n = 192, 97.46%; without CRBSI n = 503, 98.63%), internal jugular access (with CRBSI n = 173, 87.82%; without CRBSI n = 490, 96.08%). Most of the participants were also on a hemodialysis frequency of less than or equal to three times per week (with CRBSI n = 137, 69.54%; without CRBSI n = 451, 88.43%). Patients with CRBSI also had more previous CVC inserted (with CRBSI n = 20, 10.15%; without CRBSI n = 3, 0.59%) and more frequent use of the CVC outside of hemodialysis, with intravenous medications being the most commonly infused substance through the CVC (n = 103, 52.28%).

Hypertensive kidney disease (with CRBSI n = 101, 51.27%; without CRBSI n = 112, 21.96%), sepsis associated nephropathy (with CRBSI n = 81, 41.12%; without CRBSI n = 142, 27.84%), and diabetes kidney disease (with CRBSI n = 63, 31.98%; without CRBSI n = 116, 22.75%) were the most common etiologies of renal failure in both groups.

Table 1. Baseline Characteristics of Patients

Patient Characteristics	With CRBSI	Without CRBSI	P value
	n = 197	*n = 510*	
Age	54 (20)	53 (22)	0.959
Sex			0.219
Male	119 (60.41%)	282 (55.29%)	
Female	78 (39.59%)	228 (44.71%)	
Comorbidities			
Hypertension	118 (59.90%)	201 (39.41%)	<0.001*
Diabetes Mellitus	68 (34.52%)	126 (24.71%)	0.009*
Cardiac Disease	36 (18.27%)	48 (9.41%)	0.001*
Neurologic Disease	19 (9.64%)	32 (6.27%)	0.120*
Malignancy	22 (11.17%)	79 (15.49%)	0.141*
Autoimmune Disease	13 (6.60%)	15 (2.94%)	0.025*
No comorbidity	26 (13.20%)	151 (29.61%)	<0.001*
Laboratory Data			
Baseline Creatinine (mg/dL)	8.02 (5.55)	2.675 (3.97)	0.312
Serum Albumin (g/dL)	3.0 (0.90)	3.2 (0.90)	0.014*
Hemodialysis Data			
Prior central venous catheterization	20 (10.15%)	3 (0.59%)	<0.001*
Catheter type			0.330
Non-tunneled	192 (97.46%)	503 (98.63%)	
Tunneled	5 (2.54%)	7 (1.37%)	
Access Site			
Internal jugular	173 (87.82%)	490 (96.08%)	<0.001*
Subclavian	5 (2.54%)	7 (1.37%)	0.330
Femoral	19 (9.64%)	13 (2.55%)	<0.001*
Access Laterality			0.018*
Left	7 (3.55%)	5 (0.98%)	
Right	190 (96.45%)	505 (99.02%)	
Dialysis frequency (per week)			<0.001*
>3x/week	60 (30.46%)	59 (11.57%)	
≤3x/week	137 (69.54%)	451 (88.43%)	
Use outside HD			
Blood transfusion	32 (16.24%)	9 (1.76%)	<0.001*
Intravenous medications	103 (52.28%)	32 (6.27%)	<0.001*
Total parenteral nutrition	3 (1.52%)	6 (1.18%)	0.715
Etiology of Kidney Disease			
Sepsis	81 (41.12%)	142 (27.84%)	0.001*
Renal Hypoperfusion	31 (15.74%)	80 (15.69%)	0.987
Tubulo-interstitial Nephritis	10 (5.08%)	74 (14.51%)	0.001*
Drug Induced Nephropathy	30 (15.23%)	50 (9.80%)	0.041*
Obstructive Uropathy	22 (11.17%)	81 (15.88%)	0.111*
Diabetic kidney disease	63 (31.98%)	116 (22.75%)	0.011*
Hypertensive kidney disease	101 (51.27%)	112 (21.96%)	<0.001*

Glomerulonephritis	41 (20.81%)	95 (18.63%)	0.509
Cardio-renal syndrome	33 (16.75%)	44 (8.63%)	0.002*
Polycystic Kidney Disease	1 (0.51%)	11 (2.16%)	0.128*

Table 2 demonstrates the multivariable analysis of risk factors for CRBSI. The presence of autoimmune disease (adjusted HR 2.71, 95% CI 1.41, 5.20, p=0.003), dialysis frequency of more than three times per week (adjusted HR 2.45, 95% CI 1.71, 3.49, p<0.001), use of CVC for either blood transfusion (adjusted HR 1.63, 95% CI 1.04, 2.55, p=0.032) or IV medications (adjusted HR 3.49, 95% CI 2.47, 4.93, p<0.001), renal hypoperfusion (adjusted HR 1.63, 95% CI 1.05, 2.53, p=0.028), drug induced nephropathy (adjusted HR 2.50, 95% CI 1.60, 3.93, p<0.001) and hypertensive kidney disease (adjusted HR 2.22, 95% CI 1.32, 3.73, p=0.003) were all significantly associated with CRBSI development. Every 1 mg/dL increase in baseline serum creatinine also increased the hazard of developing CRBSI by 3%. On the other hand, a right sided access placement was associated with a reduced risk for CRBSI (adjusted HR 0.25, 95% CI 0.11, 0.55, p=0.001) together with serum albumin, which also decreased the hazard of developing CRBSI by 24% for every 1 g/dL increase.

Figure 2 illustrates the Kaplan-Meier infection free survival curve of developing CRBSI among patients undergoing hemodialysis using a CVC with a median infection free survival time of 90 days (95% CI 81, 111).

Table 2. Factors Associated with Catheter related Blood Stream Infections

Factors	Univariable			Multivariable		
	HR	*95% CI*	*P value*	*Adj. HR*	*95% CI*	*P value*
Age	1.00	0.99, 1.01	0.394			
Female Sex	0.73	0.55, 0.98	0.038	0.85	0.61, 1.19	0.351
Comorbidities						
Hypertension	1.29	0.96, 1.72	0.092	0.86	0.52, 1.41	0.545
Diabetes Mellitus	0.97	0.71, 1.31	0.823			
Cardiac Disease	1.35	0.93, 1.95	0.113	0.98	0.66, 1.46	0.919
Neurologic Disease	1.62	1.01, 2.61	0.046	0.94	0.56, 1.58	0.818
Cancer	1.02	0.65, 1.60	0.922			
Autoimmune Disease	2.18	1.24, 3.83	0.007	2.71	1.41, 5.20	0.003*
Laboratory Data						
Baseline Creatinine (mg/dL)	1.03	1.00, 1.06	0.090	1.03	1.01, 1.06	0.015*
Serum Albumin (g/dL)	0.67	0.53, 0.85	0.001	0.72	0.56, 0.92	0.009*
Hemodialysis Data						
Prior central venous catheterization	1.33	0.78, 2.24	0.293			
Tunneled catheter	0.20	0.06, 0.64	0.007	0.50	0.15, 1.63	0.249
Right-sided access	0.29	0.13, 0.61	0.001	0.25	0.11, 0.55	0.001*
Dialysis >3x/week	4.65	3.39, 6.39	<0.001	2.45	1.71, 3.49	<0.001*
Use outside HD						
Blood transfusion	3.81	2.56, 5.66	<0.001	1.63	1.04, 2.55	0.032*
IV medications	6.83	5.10, 9.15	<0.001	3.49	2.47, 4.93	<0.001*
Total parenteral nutrition (TPN)	1.80	0.57, 5.63	0.316			
Etiology of Kidney Disease						
Sepsis	3.18	2.35, 4.31	<0.001	*		
Renal Hypoperfusion	2.11	1.41, 3.17	0.001	1.63	1.05, 2.53	0.028*
Tubulo-interstitial Nephritis	1.17	0.61, 2.25	0.639			
Drug Induced Nephropathy	3.55	2.34, 5.37	<0.001	2.50	1.60, 3.93	<0.001*
Obstructive Uropathy	0.84	0.53, 1.31	0.431			
Diabetic kidney disease	0.90	0.65, 1.23	0.495			
Hypertensive kidney disease	1.64	1.22, 2.20	0.001	2.22	1.32, 3.73	0.003*
Glomerulonephritis	0.89	0.63, 1.25	0.498			
Cardio-renal syndrome	1.27	0.87, 1.86	0.216			
Polycystic Kidney Disease	0.29	0.04, 2.07	0.217			

Incidence rates and Outcomes of CRBSI

One hundred ninety-seven episodes of CRBSI were recorded during the observation period (Table 3). A total of forty-one patients experienced multiple CRBSI events, ten of whom experienced a relapse while thirty-one had a reinfection episode. The median duration of catheter placement among patients with CRBSI was 21 days.

Overall, the CRBSI incidence rate was documented at 6.72 episodes per 1000 catheter days with a relapse rate of 6.60 %, reinfection rate of 15.74 % and a mortality rate of 6.09 %. CRBSI were found to be most frequent with a left sided placement (21.88 episodes per 1000 catheter days), non-tunneled catheter type (6.91 episodes per 1000 catheter days) and a femoral location (15.04 CRBSI per 1000 catheter days).

Table 3. Outcomes of Catheter related Blood Stream Infections

Outcome Measure	Value
Overall CRBSI Incidence rate	6.72 CRBSI per 1000 person-catheter days
Relapse rate	n = 10, 5.07 %
Reinfection rate	n = 31, 15.74 %
Mortality rate	n = 12, 6.09 %
Catheter Specific CRBSI Rates	
Location	
Internal Jugular catheter	6.5 CRBSI per 1000 person-catheter days
Subclavian catheter	3.52 CRBSI per 1000 person-catheter days
Femoral catheter	15.04 CRBSI per 1000 person-catheter days
Type	
Tunneled catheter	3.52 CRBSI per 1000 person-catheter days
Non-Tunneled catheter	6.91 CRBSI per 1000 person-catheter days
Laterality	
Right sided placement	6.56 CRBSI per 1000 person-catheter days
Left sided placement	21.88 CRBSI per 1000 person-catheter days

CRBSI Microbiological isolates

Table 4 presents the microbiological profiles of the isolates in the study. A total of two hundred organisms were isolated with the majority of infections being monomicrobial (n = 187, 94.92 %). The most common organism causing CRBSI were gram negative bacteria (n = 104, 52 %) with *Burkholderia cepacia* (n = 26, 13 %), *Enterobacter* spp (n = 26, 13 %) and *Acinetobacter* (n = 22, 11 %) comprising the most common isolates. Among gram positive organisms, Coagulase negative *staphylococci* (CONS) (n = 69, 34.5 %) and *Staphylococcus aureus* (n = 26, 13 %) predominated. Fungal species were also noted, comprising around 2% of the total isolates.

Table 4. Microbiological characteristics of Catheter Related Bloodstream Infections

Culture Parameters	n (%)
Monomicrobial	187 (94.92)
Polymicrobial	10 (5.08)
Total Organisms Isolated	200
Total multidrug resistant organisms isolated	89 (44.5)
Gram Positive Bacteria (n = 96)	
Coagulase negative *Staphylococcus* spp.	
• Methicillin Resistant *Staphylococcus epidermidis*	34 (17)
• Staphylococcus hominis	16 (8)
• Staphylococcus hemolyticus	13 (6.5)
• Methicillin Sensitive *Staphylococcus epidermidis*	5 (2.5)
• Staphylococcus lugdunensis	1 (0.5)
Methicillin Sensitive *Staphylococcus aureus*	16 (8)
Methicillin Resistant *Staphylococcus aureus*	10 (5)
Streptococcus pyogenes	1 (0.5)
Gram Negative Bacteria (n=104)	
Burkholderia cepacia	26 (13)
Enterobacter	
• Klebsiella pneumoniae	12 (6)
• Escherichia coli	11 (5.5)
• Serratia marcescens	1 (0.5)
• Enterobacter cloacae	1 (0.5)
• Providencia stuartii	1 (0.5)
Acinetobacter spp.	
• Acinetobacter baumanii	18 (9)
• Acinetobacter lwolffi	3 (1.5)
• Acinetobacter junii	1 (0.5)
Pseudomonas spp.	
• Pseudomonas aeruginosa	7 (3.5)
• Pseudomonas stutzeri	1 (0.5)
Stenotrophomonas maltophilia	5 (2.5)
Achromobacter spp.	5 (2.5)
Elizabethkingia spp.	3 (1.5)
Ralstonia spp.	3 (1.5)
Enterococcus faecium	3 (1.5)
Eikinella spp	2 (1)
Chrysobacterium spp.	1 (0.5)
Fungi (n=4)	
Candida spp	4 (2)

CRBSI Antimicrobial Susceptibility Patterns

Table 5 illustrates the different antibiotics utilized in our institution during the study period with their respective frequency of use. Vancomycin (n = 70, 33.02 %), meropenem (n = 43, 20.28 %) and piperacillin tazobactam (n = 24, 11.32 %) were the most common options for initial, empiric therapy.

Table 6 demonstrates the antibiotic susceptibility profiles for gram-positive organisms. Most isolates were found to be sensitive to vancomycin (n = 96, 100%), linezolid (n = 95, 98.6%) and tetracycline (n = 87, 87.37%), while being least sensitive to erythromycin (n = 40, 42.11%) and oxacillin (n = 24, 47.06%). Multidrug resistant organisms comprised 39.58% (n = 38) of gram-positive isolates, mostly documented among CONS species (n = 35, 92.11%), with *S. hemolyticus* (n = 10, 76.92%) and *S. hominis* (n = 12, 75%) having the highest proportion of MDRO organisms.

Antibiotic susceptibility profiles of gram-negative organisms are shown in Table 7. Among antibiotics that were tested with at least 50 isolates, gram-negative organisms were found to be most sensitive to meropenem (n = 72, 75.79%), imipinem (n = 48, 71.64%), colistin (n = 47, 71.21%) and minocycline (n = 38, 70.37%) and poorly sensitive to gentamycin (n = 32, 47.06%), levofloxacin (n = 40, 45.98%) and piperacillin-tazobactam (n = 36, 55.38%). MDROs comprised almost half (n = 51, 49.04%) of the isolates, the majority of which were *Acinetobacter* spp. MDROs (n = 15, 29.41%).

All fungal isolates were pansensitive to all antifungal agents (Table 8).

Table 5. Initial antibiotics and frequency

Antibiotic Usage	n (%)
Vancomycin	70 (33.02)
Meropenem	43 (20.28)
Piperacillin-Tazobactam	24 (11.32)
Polymixins	19 (8.96)
Oxacillin	11 (5.19)
Ceftazidime	8 (3.77)
Levofloxacin	7 (3.30)
Trimethoprim-sulfamethoxazole	5 (2.36)
Ceftriaxone	4 (1.89)
Ciprofloxacin	4 (1.89)
Cefazolin	4 (1.89)
Others	13 (6.13)

Table 6. Antibiotic susceptibility profile of Gram-positive organisms

	Coagulase negative *Staphylococcus* spp					*Staphylococcus aureus*		Group A *Streptococcus*	Total n = 96 (%)
	MRSE n = 34 (%)	SHO n = 16 (%)	SHL n = 13 (%)	MSSE n = 5 (%)	SLU n = 1	MSSA n = 16 (%)	MRSA n = 10 (%)	SPY n =1 (%)	
VA	34 (100)	16 (100)	13 (100)	5 (100)	1 (100)	16 (100)	10 (100)	1 (100)	96 (100)
OX	-	3 (18.75)	1 (7.69)	4 (80)	1 (100)	15 (93.75)	-	-	24 (47.06) [1]
SXT	24 (70.59)	9 (56.25)	5 (38.46)	4 (80)	1 (100)	14 (87.5)	8 (80)	-	65 (68.42) [2]
LVX	29 (85.29)	14 (87.5)	2 (15.38)	4 (80)	1 (100)	16 (100)	10 (100)	-	76 (80) [2]
CIP	29 (85.29)	14 (87.5)	1 (7.69)	4 (80)	1 (100)	16 (100)	8 (80)	-	73 (76.84) [2]
LZD	33 (97.06)	16 (100)	13 (100)	5 (100)	1 (100)	16 (100)	10 (100)	1 (100)	95 (98.96)
G	29 (85.29)	15 (93.75)	2 (15.38)	4 (80)	-	16 (100)	10 (100)	-	76 (80.85) [3]
MXF	28 (82.35)	10 (62.5)	3 (23.08)	4 (80)	1 (100)	11 (68.75)	7 (70)	-	64 (67.37) [2]
E	12 (35.29)	2 (12.5)	1 (7.69)	1 (20)	1 (100)	15 (93.75)	8 (80)	-	40 (42.11) [2]
TE	29 (85.29)	12 (75)	12 (92.3)	5 (100)	-	16 (100)	8 (80)	1 (100)	83 (87.37) [2]
CD	29 (85.29)	14 (87.5)	2 (15.38)	4 (80)	1 (100)	16 (100)	10 (100)	1 (100)	77 (80.21)
CRO	-	-	-	-	-	-	-	1 (100)	1 (100) [4]
FEP	-	-	-	-	-	-	-	1 (100)	1 (100) [4]
PEN	-	-	-	-	1 (100)	-	-	1 (100)	1 (100) [5]
AMP	-	-	-	-	-	-	-	1 (100)	1 (100) [4]
MDR	12 (35.29)	12 (75)	10 (76.92)	1 (20)	0	1 (6.25)	2 (20)	0	38 (39.58)

Abbreviations: MRSE, methicillin resistant *Staphylococcus epidermidis*; SHO, *Staphylococcus hominis*; SHL, *Staphylococcus hemolyticus*; MSSE, methicillin sensitive *Staphylococcus epidermidis*; SLU, *Staphylococcus lugdunensis*; MSSA, methicillin sensitive *Staphylococcus aureus*; MRSA, methicillin resistant *Staphylococcus aureus*; SPY, *Streptococcus pyogenes*; VA, vancomycin; OX, oxacillin, SXT, Trimethoprim/Sulfamethoxazole; LVX, Levofloxacin; CIP, ciprofloxacin; LZD, linezolid; G, gentamycin; MXF, moxifloxacin; E, erythromycin; TE, tetracycline; CD, clindamycin; CRO, ceftriaxone; FEP, cefepime; PEN, penicillin G; AMP, ampicillin; MDR, multidrug resistant organism

Note: [1] Calculated in relation to 51 isolates, [2] Calculated in relation to 95 isolates, [3] Calculated in relation to 94 isolates, [4] Calculated In relation to 1 isolate, [5] Calculated in relation to 2 isolates

Table 7. Antibiotic susceptibility profile of gram-negative organisms

	BCE	*Acinetobacter* spp			*Enterobacter* spp					*Pseudomonas* spp		ACH	SMA	ELK	RLS	El
	n = 26	ABA	ALW	AJU	KPN	ECO	SER	ECL	PRO	PAE	PST	n = 5	n = 5	n = 3	n = 3	n
		n = 18	n = 3	n = 1	n = 12	n = 11	n = 1	n = 1	n = 1	n = 7	n = 1					
MEM	26 (100)	5 (27.78)	1 (33.33)	-	12 (100)	11 (100)	1 (100)	1 (100)	1 (100)	7 (100)	1 (100)	3 (60)	-	0	3 (100)	-
TZP	-	4 (22.22)	-	-	9 (75)	10 (90.91)	-	1 (100)	1 (100)	5 (71.43)	1 (100)	2 (40)	-	0	3 (100)	-
COL	-	18 (100)	1 (33.33)	1 (100)	10 (83.33)	10 (90.91)	-	-	-	3 (42.86)	1 (100)	3 (60)	-	0	0	-
CAZ	26 (100)	4 (22.22)	1 (33.33)	-	7 (58.33)	10 (90.91)	-	-	1 (100)	7 (100)	1 (100)	3 (60)	-	0	0	-
SXT	16 (61.54)	5 (27.78)	1 (33.33)	-	7 (58.33)	5 (45.45)	1 (100)	1 (100)	-	-	1 (100)	5 (100)	5 (100)	-	3 (100)	-
MI	15 (57.69)	14 (77.78)	2 (66.67)	1 (100)	-	-	-	1 (100)	-	-	-	-	5 (100)	-	-	-
CZ	-	-	-	-	7 (58.33)	8 (72.72)	-	-	-	-	-	-	-	-	-	-
SAM	-	6 (33.33)	3 (100)	1 (100)	3 (25)	9 (81.82)	-	1 (100)	1 (100)	-	-	-	-	-	-	-
AMC	-	-	-	-	7 (58.33)	7 (63.64)	-	-	-	-	-	-	-	-	-	-
CXM	-	-	-	–	6 (50)	9 (81.82)	-	-	-	-	-	-	-	-	-	-
FOX	-	-	-	-	9 (75)	9 (81.82)	-	-	1 (100)	-	-	-	-	-	-	-
CRO	-	-	2 (66.67)	-	7 (58.33)	9 (81.82)	1 (100)	1 (100)	-	-	1 (100)	-	-	0	3 (100)	-
FEP	-	5 (27.78)	1 (33.33)		8 (66.67)	10 (90.91)	1 (100)	1 (100)	-	7 (100)	1 (100)	5 (100)		0	3 (100)	-
ETP	-	-	-	-	12 (100)	11 (100)	1 (100)	1 (100)	-	-	-	-	-	3 (100)	-	-
IPM	-	5 (27.78)	3 (100)	-	12 (100)	10 (90.91)	-	1 (100)	-	7 (100)	1 (100)	5 (100)	-	0	3 (100)	-
AN	-	0	1 (33.33)	-	12 (100)	11 (100)	1 (100)	1 (100)	-	7 (100)	1 (100)	5 (100)	-	0	0	-
LVX	7 (26.92)	3 (16.67)	1 (33.33)	-	12 (100)	5 (45.45)	-	1 (100)	1 (100)	5 (71.43)	-	-	5 (100)	-	-	0
CIP	-	4 (22.22)	1 (33.33)	-	11 (91.67)	4 (36.36)	1 (100)	1 (100)	1 (100)	7 (100)	1 (100)	5 (100)	-	-	3 (100)	0
G	-	5 (27.78)	1 (33.33)	-	7 (58.33)	7 (63.64)	1 (100)	1 (100)	–	5 (71.43)	1 (100)	3 (60)	-	0	0	-
G120	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2

																(6
MXF	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
LZD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3
VA	-	-	-	-	-	-	-	-	-	-	-	-		-	-	1 (3
AMP	-	-	-	-	-	-	-	-	1 (100)	-	-	-	-	-	-	0
PEN	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
S300	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
TE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
MDR	10 (38.46)	14 (77.78)	1 (33.33)	0	6 (50)	5 (45.45)	0	0	0	2 (28.57)	0	2 (40)	0	3 (100)	3 (100)	2 (6

Abbreviations: BCE, *Burkholderia cepacia*; ABA, *Acinetobacter baumanii*; ALW, *Acinetobacter lwolfii*; AJU, *Acinetobacter junii*; KPN, *Klebsiella pneumoniae*; ECO, *Escherichia coli*; SER, *Serratia marcescens*; ECL, *Enterobacter cloacae*; PRO, *Providencia stuartii*; PAE, *Pseudomonas aeruginosa*; PST, *Pseudomonas stutzeri*; ACH, *Achromobacter* spp; SMA, *Stenotrophomonas maltophilia*; ELK, *Elizabethkingia* spp; RLS, *Ralstonia* spp.; EFM, *Enterococcus faecium*; EIK, *Eikinella* spp; CHR, *Chrysobacterium* spp; MEM, meropenem; TZP, piperacillin-tazobactam; COL, colistin; CAZ, ceftazidime; SXT, Trimethoprim /Sulfamethoxazole; MI, minocycline; CZ, cefazolin; SAM, ampicillin/sulbactam; AMC, amoxicillin/clavulanic acid; CXR, cefuroxime; FOX, cefoxitin; CRO, ceftriaxone; FEP, cefepime; ETP, ertapenem; IPM, imipenem; AN, amikacin; LVX, levofloxacin; CIP, ciprofloxacin; G, gentamycin; G120, high gentamycin; MXF, moxifloxacin; LZD, linezolid; VA, vancomycin; AMP, ampicillin, PEN, penicillin G; S300, streptomycin; TE, tetracycline; MDR, multidrug resistant organism

Note:

[1] Calculated in relation to 95 isolates, [2] Calculated in relation to 65 isolates, [3] Calculated in relation to 66 isolates, [4] Calculated in relation to 93 isolates, [5] Calculated in relation to 89 isolates

[6] Calculated in relation to 54 isolates, [7] Calculated in relation to 23 isolates, [8] Calculated in relation to 47 isolates, [9] Calculated in relation to 24 isolates, [10] Calculated in relation to 38 isolates,

[11] Calculated in relation to 68 isolates, [12] Calculated in relation to 28 isolates, [13] Calculated in relation to 67 isolates, [14] Calculated in relation to 87 isolates, [15] Calculated in relation to 69 isolates

[16] Calculated in relation to 3 isolates, [17] Calculated in relation to 4 isolates

Table 8. Antibiotic susceptibility profile of fungal organisms

	CAL	CFA	CGL	CTR
	n = 1 (%)	n = 1 (%)	n = 1 (%)	n = 1 (%)
Fluconazole	1 (100)	1 (100)	1 (100)	1 (100)
Caspofungin	1 (100)	1 (100)	1 (100)	1 (100)
Voriconazole	1 (100)	1 (100)	1 (100)	1 (100)
Micafungin	1 (100)	1 (100)	1 (100)	1 (100)
Amphotericin B	1 (100)	1 (100)	1 (100)	1 (100)
Flucytosine	1 (100)	1 (100)	1 (100)	1 (100)

Abbreviations: CAL, *Candida albicans*; CFA, *Candida famata*; CGL, *Candida glabrata*; CTR, *Candida tropicalis*

Discussion

CVCs provide a reliable access for prompt treatment in those with urgent indications to initiate hemodialysis.[10] With its ease of use and minimal preparation, the majority of patients, especially in developing nations, continue to start, and at times, maintain dialysis through CVC.[3] However, prolonged use of these catheters has been shown by several studies to promote complications such as CRBSI. Our goal was to identify the incidence and risk factors and describe outcome measures and microbial patterns of susceptibility among our hemodialysis patients utilizing a central venous catheter among Filipino Hemodialysis patients in our institution.

Using the 2019 KDOQI CRBSI definition, we found an overall CRBSI incidence rate of 6.72 CRBSI episodes per 1000 catheter days, which is higher compared to developed nations [10, 11, 14, 21, 22]but lower than those documented in other developing countries.[5,11,23-27] In general, incidence rates more than two episodes per 1000 catheter days indicate room for improvement.[14] There are several factors that may account for this observation. Frequent use of the dialysis access outside of hemodialysis (n = 103, 52.28%), extensive use of non tunneled catheters (n = 192, 97.46%) and prolonged duration of placement (median duration = 21 days) are all risk factors in our cohort that have been documented to promote CRBSI formation.[1,10,11,28] Our incidence may have also been affected by our study criteria used for the diagnosis of CRBSI. Previous studies have already demonstrated an inter-criteria variability between the IDSA and Center for Disease Control (CDC) definitions among the hemodialysis population.[3,9,22] While there have been no direct comparisons made between the KDOQI, CDC and IDSA criteria, we suspect the KDOQI criteria may also produce variable incidence reporting compared to the other two.

We also identified variable CRBSI rates depending on specific catheter characteristics. Left sided (21.88 episodes per 1000 catheter days), non-tunneled (6.91 episodes per 1000 catheter days), and femoral (15.04 CRBSI per 1000 catheter days) access provided the highest infection rates among our study cohort, consistent with existing literature supporting increased CRBSI rates with these types of features.[10,11,26,29-33]

Our multivariable analysis also affirms previous findings that an immunocompromised state, frequent hemodialysis schedules, manipulation of the CVC outside of hemodialysis and elevated creatinine levels are all associated with increased risk of CRBSI.[6,7,11,28,34]Conversely, we also found that a right sided CVC placement and elevated serum albumin levels decreased the risk of developing CRBSI, both of which were also consistent with published studies.[10,31] We attempted to identify infusion related risk factors that may influence formation of CRBSI. Studies allude to the increased risk of CRBSI with infusion of blood products, intravenous medications and parenteral nutrition via catheter access.[35-37]We found both blood products and IV medication infusion, but not parenteral nutrition use, were significant risk factors for CRBSI development. This finding of non significance with TPN use is likely from an underpowered sample of patients utilizing TPN in both CRBSI and non CRBSI groups (n = 9). Renal disease arising from hypoperfusion, hypertension and drug induced nephrotoxicity were also considered as risk factors CRBSI development by our study. It is postulated that the paucity of regulatory T cells and their dysfunction in a variety of cardiovascular diseases such as hypertension predisposes these patients to infection such as CRBSI.[5] On the other hand, renal hypoperfusion and drug induced nephrotoxicity are likely a reflection of the rate of CVC use in our cohort as these patients are more likely to utilize their catheters in either resuscitation or administration of medications or blood products.

Gram positive bacteria have always been the predominant isolates in CRBSI among the hemodialysis population.[5,9,10,13,14,38] However, an evolving microbial epidemiology of CRBSI is now being observed globally; increasing rates of gram-negative organisms are being reported in literature.[3,12,39,40]Consistent with these findings, our study found a higher proportion of gram negative (n = 104, 52%) compared to gram positive (n = 96, 48%) organisms. *Enterobacter* spp. and CONS formed the majority of all gram-negative and gram-positive growth respectively, findings also echoed in several studies.[12,13,41,42] However, together with *Enterobacter* spp., *B. cepacia* and *Acinetobacter spp.* comprised a surprising majority of gram-negative isolates. We suspect that these isolates may be indicative of nosocomial transmission from health care providers and possible poor compliance to sterile protocols in accessing the CVC.

Multidrug resistant organisms comprised an alarming proportion of isolates (n = 89, 44.5%) with coagulase negative *staphylococcus* species and *Acinetobacter* species encompassing the most common MDROs in our cohort. Consequently, we also found concerning resistance to aminoglycosides, fluoroquinolones and piperacillin tazobactam by gram negative isolates. It is possible that our increased use of strong antibiotic therapy such as carbapenems and glycopeptides (Table 5), and prolonged catheter duration, have contributed to the increased risk for gram negative infections and proliferation of MDROs.[43-47] Our results also reflect the need to review our some of our empiric antibiotic regimen such as piperacillin tazobactam and levofloxacin which demonstrated low sensitivity patterns among our gram-negative isolates (Table 7).

A fifth of our CRBSI cohort experienced disease recurrence (n = 41, 20.81 %) with mostly a different organism (reinfection rate = 15.74% vs relapse rate = 5.08%), a finding comparable to the experience of Shahar et al. and Mokrzycki et al. who noted recurrence rates of 9 - 31% in their HD cohorts.[8, 48] We also documented a mortality rate of 6.09 %, at par with previously reported attributable mortality to CRBSI, ranging from 4-18%.[2,11,14,48] Factors contributory to this include a high incidence rate leading into a high event rate, presence of MDROs and comorbidities in the population (41% of CRBSI with sepsis).

Strength and Limitations

To our knowledge, this is the first local study to identify CRBSI rates, risk factors and outcomes and provide a sensitivity analysis of microbial growth utilizing the 2019 KDOQI CRBSI criteria.

The study has several limitations. First, the retrospective nature of our study increases the risk for confounders. Second, we did not include exit site infection rates, which itself may be a risk factor for CRBSI. Third, hygiene practices by the hospital staff were not accounted for by the study, leaving the possibility of poor compliance to standard hygiene an unknown risk factor. Surrogates for hygiene such as educational background and financial status may be utilized and considered in future studies. Lastly, catheter tip positioning has been recently documented as a significant risk factor for CRBSI. In a study by Engstrom et al, although CVC infection were higher for left sided approaches, no significant difference in CRBSI rates were observed for left compared with right-sided approaches when CVC tips were placed in the mid to deep right atrium, emphasizing proper catheter placement and confirmatory imaging.[29]

Conclusions

This study highlights the incidence and catheter-specific rates of central line-associated bloodstream infections (CRBSIs) in our hemodialysis cohort and identifies modifiable risk factors that impact our rates. Our findings suggest that there is a concerning predominance of gram-negative and multidrug-resistant organisms among bacterial isolates, which emphasizes the need for more stringent measures and interventions, including a review of sterile technique and adequate hygiene practices, continued surveillance, and expedited placement and utilization of long-term access for patients on maintenance hemodialysis.

Moreover, CVC use outside of hemodialysis should be discouraged. We also observed low sensitivity patterns among gram-negative isolates for commonly used antibiotics such as piperacillin-tazobactam and fluoroquinolones, highlighting the importance of balancing antimicrobial stewardship and adequate coverage when selecting antibiotic regimens. By addressing these issues, we can prevent further propagation of identified pathogens and improve outcomes for our hemodialysis patients.

Abbreviations

CRBSI – Catheter Related Bloodstream Infection

CVC – Central Venous Catheter

MDRO – Multidrug Resistant Organism

DTP – Differential Time to Positivity

IDSA - Infectious Disease Society of America

KDOQI - Kidney Disease Outcomes Quality Initiative

CFU – Colony Forming Units

CONS – Coagulase Negative Staphylococcus

CDC - Center for Disease Control

TPN – Total Parenteral Nutrition

Declarations

Ethics approval and consent to participate: The study was approved by the University of the Philippines Manila Research Ethics Board (UPM-REB, code 2021-153-01). All methods described in this manuscript were carried out in accordance with relevant guidelines and regulations, including the Declaration of Helsinki for research involving human participants, human material, or human data. The waiver for informed consent was also granted by the University of the Philippines Manila Research Ethics Board as our retrospective study involved the use of pre-existing data that were analyzed anonymously.

Consent for publication: Not applicable. This manuscript does not contain any identifying images or information

Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

Funding: The study was self-funded by the authors and no external funding was obtained.

Authors' contributions: Renz Michael Pasilan and Isabelle Dominique Tomacruz-Amante designed the study, collected and analyzed the data, and wrote the manuscript. Coralie Therese Dimacali contributed to the study design, data collection, and manuscript preparation.

Acknowledgments: We thank Emilio Villanueva III M.D. for his contributions to the statistical analysis of the study.

References

1. Salem, H. Y., Ahmed, M., Gulzar, K., Alalawi, F., & Alhadari, A. (2021). Hemodialysis catheter-related infections: incidence, microbiology and outcome 5 years of Dubai hospital experience. *European Journal of Clinical Medicine*, *2*(3), 111-115
2. Farrington CA, Allon M. Complications of Hemodialysis Catheter Bloodstream Infections: Impact of Infecting Organism. *Am J Nephrol*. 2019;50(2):126-132.
3. Agrawal V, Valson AT, Mohapatra A, et al. Fast and furious: a retrospective study of catheter-associated bloodstream infections with internal jugular nontunneled hemodialysis catheters at a tropical center. Clin Kidney J. 2019;12(5):737-744.
4. Tang SCW, Yu X, Chen HC, et al. Dialysis Care and Dialysis Funding in Asia. *Am J Kidney Dis*. 2020;75(5):772-781
5. Masoodi, Ibrahim & Alharth, Fahad & Irshad, Summaiya & Mastan, Abdul & Alzaidi, Ahmed & Sirwal, Irshad. (2019). Hemodialysis catheter-related infections: Results of a tertiary care center study in Saudi Arabia. International Journal of Medical Science and Public Health
6. Chang, C., Fan, P., Kuo, G. et al. Infection in Advanced Chronic Kidney Disease and Subsequent Adverse Outcomes after Dialysis Initiation: A Nationwide Cohort Study. Sci Rep 10, 2938 (2020)
7. James MT, Laupland KB, Tonelli M, et al. Risk of bloodstream infection in patients with chronic kidney disease not treated with dialysis. Arch Intern Med. 2008;168(21):2333-2339

8. Lata C, Girard L, Parkins M, James MT. Catheter-related bloodstream infection in end-stage kidney disease: a Canadian narrative review. Can J Kidney Health Dis. 2016;3:24. Published 2016 May 5.
9. Shahar, S., Mustafar, R., Kamaruzaman, L., Periyasamy, P., Pau, K. B., & Ramli, R. (2021). Catheter-Related Bloodstream Infections and Catheter Colonization among Haemodialysis Patients: Prevalence, Risk Factors, and Outcomes. *International Journal of Nephrology*, *2021*, 1–9
10. Demirci R, Sahtiyancı B, Bakan A, Akyuz O. The predictors of catheter-related bloodstream infections in patients undergoing hemodialysis: A single center experience [published online ahead of print, 2021 Jun 17]. *J Vasc Access*. 2021;1129729821998836
11. Tarpatzi A, Avlamis A, Papaparaskevas J, Daikos GL, Stefanou I, Katsandri A, Vasilakopoulou A, Chatzigeorgiou KS, Petrikkos GL. Incidence and risk factors for central vascular catheter-related bloodstream infections in a tertiary care hospital. New Microbiol. 2012 Oct;35(4):429-37
12. Alhazmi, S. M., Noor, S. O., Alshamrani, M. M., & Farahat, F. M. (2019). Bloodstream infection at hemodialysis facilities in Jeddah: a medical record review. *Annals of Saudi Medicine*, *39*(4), 258–264
13. Abd El-Hamid El-Kady R, Waggas D, AkL A. Microbial Repercussion on Hemodialysis Catheter-Related Bloodstream Infection Outcome: A 2-Year Retrospective Study. *Infect Drug Resist*. 2021;14:4067-4075
14. Martín-Peña A, Luque Márquez R, Guerrero MJ, Espinosa N, Blanco Y, Ibeas J, Ríos-Villegas MJ, Cisneros JM; Spanish Network for Research in Infectious Diseases. Tunneled hemodialysis catheter-related bloodstream infections: a prospective multicenter cohort study from Spain. J Vasc Access. 2012 Apr-Jun;13(2):239-45
15. Kallen AJ. Identifying and classifying bloodstream infections among hemodialysis patients. Semin Dial. 2013;26(4):407-415
16. Nguyen DB, Shugart A, Lines C, et al. National Healthcare Safety Network (NHSN) Dialysis Event Surveillance Report for 2014. Clin J Am Soc Nephrol. 2017;12(7):1139-1146.
17. Pop-Vicas A, Strom J, Stanley K, D'Agata EM. Multidrug-resistant gram-negative bacteria among patients who require chronic hemodialysis. Clin J Am Soc Nephrol. 2008;3(3):752-758.
18. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, Raad II, Rijnders BJ, Sherertz RJ, Warren DK. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2009 Jul 1;49(1):1-45.
19. Quittnat Pelletier F, Joarder M, Poutanen SM, Lok CE. Evaluating Approaches for the Diagnosis of Hemodialysis Catheter-Related Bloodstream Infections. *Clin J Am Soc Nephrol*. 2016;11(5):847-854
20. Lok CE, Huber TS, Lee T, et al. KDOQI Clinical Practice Guideline for Vascular Access: 2019 Update [published correction appears in Am J Kidney Dis. 2021 Apr;77(4):551]. *Am J Kidney Dis*. 2020;75(4 Suppl 2):S1-S164
21. Shah, S., Singhal, T., Naik, R., & Thakkar, P. (2020). Incidence and Etiology of Hemodialysis Catheter Related Blood Stream Infections at a Tertiary Care Hospital in Mumbai: A 5 Year Review. Indian journal of nephrology, 30(2), 132–133
22. Thompson S, Wiebe N, Klarenbach S, et al. Catheter-related blood stream infections in hemodialysis patients: a prospective cohort study. BMC Nephrol. 2017;18(1):357. Published 2017 Dec 8
23. Wang, K., Wang, P., Liang, X., Lu, X., & Liu, Z. (2015). Epidemiology of haemodialysis catheter complications: a survey of 865 dialysis patients from 14 haemodialysis centres in Henan province in China. *BMJ Open*, *5*(11), e007136
24. Sedhain, Arun & Sapkota, Abja & Mahotra, Narayan. (2019). Hemodialysis Catheter-Related Infection in a Teaching Hospital of Central Nepal. Journal of Institute of Medicine Nepal. 41. 11-16. 10.3126/jiom.v41i2.26541.
25. Nuradeen, B. E., Omer, S. A., & Sharif, D. A. (2018). Catheter-related bloodstream infection among hemodialysis patients: incidence and microbiological profile. *Journal of Sulaimani Medical College*, *8*(4), 223–235
26. Caylan, R., Yilmaz, G., Sözen, E. E., Aydin, K., & Köksal, I. (2010). Incidence and risk factors for bloodstream infections stemming from temporary hemodialysis catheters. *Turk J Med Sci*, *40*(6), 835–841
27. Viswanath, M. V., Rao K, V. P., Rao K, V., & Kolla, P. K. (2021). Clinical profile of hemodialysis catheter related bloodstream infections. *European Journal of Molecular & Clinical Medicine*, *08*(2), 919–933.
28. Grothe, C., Belasco, A. G. D. S., Bittencourt, A. R. D. C., Vianna, L. A. C., Sesso, R. D. C. C., & Barbosa, D. A. (2010). Incidence of bloodstream infection among patients on hemodialysis by central venous catheter. *Revista Latino-Americana de Enfermagem*, *18*(1), 73–80.
29. Engstrom BI, Horvath JJ, Stewart JK, et al. Tunneled internal jugular hemodialysis catheters: impact of laterality and tip position on catheter dysfunction and infection rates. J Vasc Interv Radiol. 2013;24(9):1295-1302
30. Shingarev R, Barker-Finkel J, Allon M. Natural history of tunneled dialysis catheters placed for hemodialysis initiation. J Vasc Interv Radiol. 2013;24(9):1289-1294.
31. Fysaraki M, Samonis G, Valachis A, et al. Incidence, clinical, microbiological features and outcome of bloodstream infections in patients undergoing hemodialysis. Int J Med Sci. 2013;10(12):1632-1638
32. Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. Mayo Clin Proc. 2006;81(9):1159-1171
33. de Jesus-Silva SG, Oliveira JDS, Ramos KTF, et al. Analysis of infection rates and duration of short and long-term hemodialysis catheters in a teaching hospital. J Vasc Bras. 2020;19:e20190142
34. Ishigami J, Grams ME, Chang AR, Carrero JJ, Coresh J, Matsushita K. CKD and Risk for Hospitalization With Infection: The Atherosclerosis Risk in Communities (ARIC) Study. Am J Kidney Dis. 2017;69(6):752-761

35. Erbay A, Ergönül O, Stoddard GJ, Samore MH. Recurrent catheter-related bloodstream infections: Risk factors and outcome. *Int J Infect Dis*. 2006;10(5):396-400
36. Chin BS, Han SH, Lee HS, et al. Risk factors for recurrent catheter-related infections after catheter-related bloodstream infections. *Int J Infect Dis*. 2010;14(1):e16-e21
37. Fonseca G, Burgermaster M, Larson E, Seres DS. The Relationship Between Parenteral Nutrition and Central Line-Associated Bloodstream Infections: 2009-2014. *JPEN J Parenter Enteral Nutr*. 2018;42(1):171-175
38. Rojas-Moreno CA, Spiegel D, Yalamanchili V, Kuo E, Quinones H, Sreeramoju PV, Luby JP. Catheter-Related Bloodstream Infections in Patients on Emergent Hemodialysis. Infect Control Hosp Epidemiol. 2016 Mar;37(3):301-5
39. Gupta, S., Mallya, S. P., Bhat, A., & Baliga, S. (2016). Microbiology of Non-Tunnelled Catheter-Related Infections. *Journal of clinical and diagnostic research : JCDR*, *10*(7), DC24–DC28
40. Braun E, Hussein K, Geffen Y, Rabino G, Bar-Lavie Y, Paul M. Predominance of Gram-negative bacilli among patients with catheter-related bloodstream infections. *Clin Microbiol Infect*. 2014;20(10):O627-O629
41. Mohamed H, Ali A, Browne LD, et al. Determinants and outcomes of access-related blood-stream infections among Irish haemodialysis patients; a cohort study. *BMC Nephrol*. 2019;20(1):68
42. Hadian, B., Zafarmohtashami, A., & Razani, M. (2020). Catheter-related blood stream infections in hemodialysis patients. *Journal of Renal Injury Prevention*, *9*(4), e34.
43. Lendak D, Puerta-Alcalde P, Moreno-García E, et al. Changing epidemiology of catheter-related bloodstream infections in neutropenic oncohematological patients. PLoS One. 2021;16(4):e0251010. Published 2021 Apr 30
44. Cheng S, Xu S, Guo J, et al. Risk Factors of Central Venous Catheter-Related Bloodstream Infection for Continuous Renal Replacement Therapy in Kidney Intensive Care Unit Patients. Blood Purif. 2019;48(2):175-182
45. Marcos M, Soriano A, Iñurrieta A, et al. Changing epidemiology of central venous catheter-related bloodstream infections: increasing prevalence of Gram-negative pathogens. J Antimicrob Chemother. 2011;66(9):2119-2125
46. Hajjej Z, Nasri M, Sellami W, Gharsallah H, Labben I, Ferjani M. Incidence, risk factors and microbiology of central vascular catheter-related bloodstream infection in an intensive care unit. J Infect Chemother. 2014;20(3):163-168
47. Calò F, Retamar P, Martínez Pérez-Crespo PM, et al. Catheter-related bloodstream infections: predictive factors for Gram-negative bacteria aetiology and 30 day mortality in a multicentre prospective cohort. J Antimicrob Chemother. 2020;75(10):3056-3061
48. Mokrzycki MH, Schröppel B, Gersdorff GV, Rush H, Zdunek MP, Feingold R. Tunneled-cuffed catheter associated infections in hemodialysis patients who are seropositive for the human immunodeficiency virus. *J Am Soc Nephrol*. 2000;11(11):2122-2127

Figures

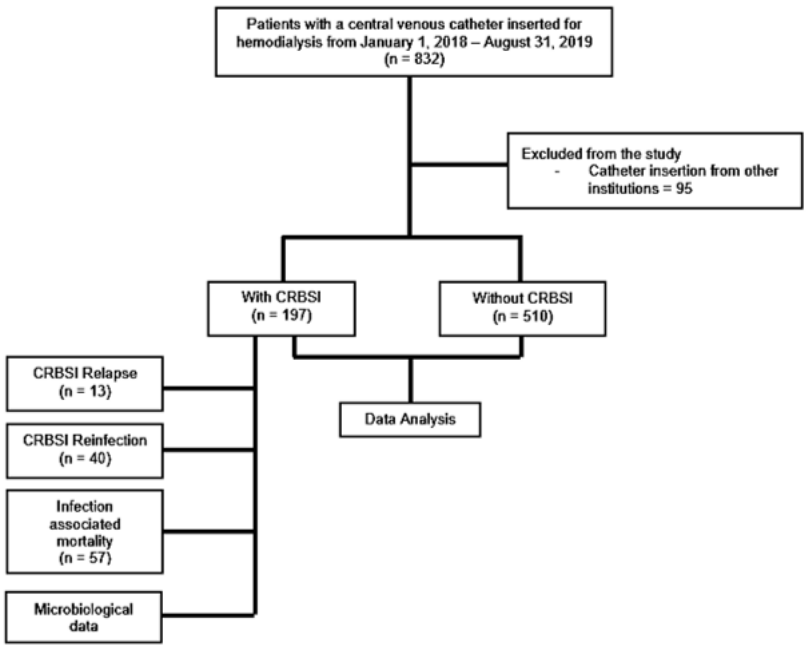

Figure 1

Flow diagram of the study

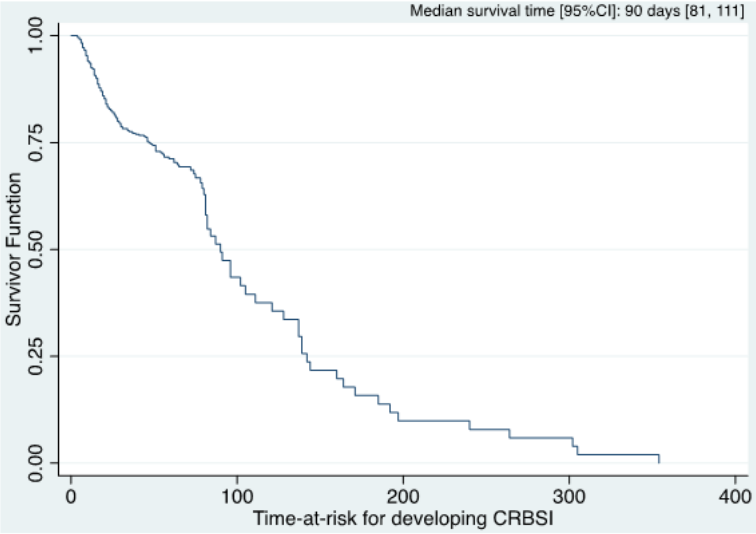

Figure 2

Survival curve of developing CRBSI among the adult kidney disease patients undergoing hemodialysis