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Original Article

Pattern of bacterial bloodstream infections in hemodialysis patients

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Abstract

Introduction: Bloodstream infection (BSI) is a major contributor to morbidity and mortality in hemodialysis patients. Our objective was to identify pathogens causing BSI, its incidence, and associated risk factors.

Methodology: Retrospective positive blood culture data were analyzed from five hemodialysis centers (January 2019 until December 2023) across Saudi Arabia.

Results: There were 437 bacteremia episodes in 432 patients, with 405 central line and 367 peripheral samples. The BSI rate was 0.67 per 100 patient months. 375 (85.8%) patients had a Central Venous Catheter (CVC), 27 (6.17%) had an arteriovenous fistula (AVF), 5 (1.14%) had an arteriovenous graft (AVG), and 30 (6.9%) had dual access. The central line-associated bloodstream infection (CLABSI) rate was 1.41 per 100 patient months. Gram-positive organisms in the central line blood culture were 169 (44%), and Gram-negative were 200 (51.81%); 16 (4%) cases were polymicrobial, and there was one case of fungi. In peripheral blood cultures, 158 (48.9%) were Gram-positive and 150 (46.4%) were Gram-negative. The most common pathogens were *Staphylococcus aureus, MRSA, and Staphylococcus epidermidis* in Gram-positive organisms, and *Enterobacter cloacae, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa* in Gram-negative organisms. Three cases of fungal infection occurred during the study period. Two-thirds of patients (68%) required hospital treatment, and in 54% of the cases, there was loss of vascular access. Mortality due to sepsis within 4 weeks occurred in five patients.

Conclusions: The risk of BSI in hemodialysis patients is high. Gram-negative pathogens contribute to half of the events. In Saudi Arabia, Gram-negative pathogen incidence is significant, and measures are required to curtail it.

Key words: hemodialysis; bacteremia; bloodstream infection; central line-associated bloodstream infection; central venous catheter; CLABSI.

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Introduction

The infection rate is higher in hemodialysis patients compared to the general population [1,2]. Bloodstream infections can lead to hospitalization and are a major cause of morbidity and mortality in hemodialysis patients [3,4]. Infection is the second-leading cause of mortality reported in studies across the globe [5,6]. Hemodialysis patients have a higher rate of bacteremia due to multiple factors, including reduced immunity, comorbidities, and the use of central venous catheters [7]. Measures have been taken to reduce the use of central venous catheters, but a significant number of patients still start renal replacement therapy with dialysis catheters. This predisposes them to increased bacterial infection and may lead to hospitalization. Our aim is to identify patterns of pathogens across hemodialysis satellite units in Saudi Arabia under the Ministry of National Guard Health Affairs. This will help us better manage our patients and take drastic measures to reduce the burden of bloodstream infections.

Methodology

A retrospective (five-year) observational study was conducted at outpatient hemodialysis centers under the Ministry of National Guards. The centers included Jeddah, Makkah, Medina, North Riyadh, and South Riyadh (distribution of patients shown in Figure 1). The study aimed to determine the prevalence of bacteremia in hemodialysis patients. The primary objectives of this

research study were to identify the incidence of bloodstream infections in hemodialysis patients, analyze the causative microorganisms, and evaluate their impact on patient outcomes.

The data collected includes demographics, comorbidities, dialysis vintage, vascular access, laboratory results (including peripheral and central blood cultures), treatment at the hemodialysis center or hospital, and clinical outcomes such as hospitalization, catheter loss, and mortality. Patients were closely monitored from the time of bacteremia diagnosis to assess overall mortality within 30 days (4 weeks).

The study was conducted on hemodialysis patients regularly enrolled in outpatient satellite centers between January 2019 and December 2023 who were 15 years of age and older. Tourist patients and patients with temporary hemodialysis catheters were excluded from the study. Contaminated blood cultures were also excluded. Patient confidentiality was maintained through written consent. Patient data was recorded on an Excel sheet from the electronic record using the Best Care system and kept anonymous in the hospital's computer system, with access restricted to the principal investigator and co-investigators to maintain confidentiality.

Following the implementation of our study protocol, we excluded 32 patients due to contaminated samples from the initial pool of 482, and 13 duplicate samples were excluded. Four hundred and thirty-seven positive bacteremia cases were identified in 432 patients. Bloodstream infection (BSI) and central line bloodstream infection (CLABSI) rates were calculated for every year. Episodes of bacteremia were recorded yearly, and the denominator was the patient's number recorded at each facility on the first two working days of the month. Patients with positive blood cultures were reviewed using a non-probability consecutive sampling technique. Data collection involved categorical variables such as center name, comorbidities, dialysis vintage, and vascular access type, as well as means and standard deviations for numerical variables such as age, height, and weight. For data analysis, SPSS Statistics for Windows, version 20.0, was used to conduct a comprehensive analysis of the data. Descriptive statistics, univariate and multivariate analysis, and chi-square tests/Fisher's exact tests, as appropriate, were performed to identify risk factors associated with bacteremia and determine its effect on patient outcomes.

Figure 1. Patients' distribution in five Hemodialysis Centers.

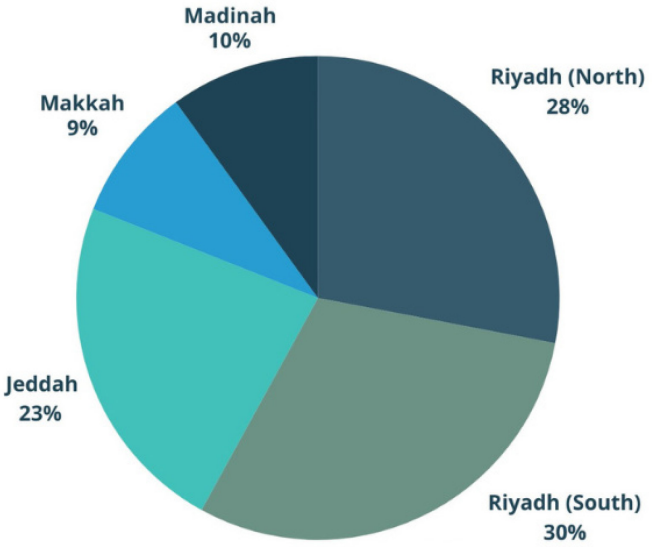
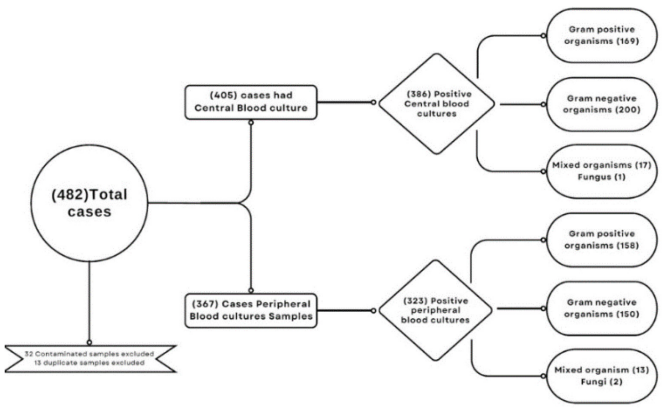


Figure 2. Study Flow diagram.



Results

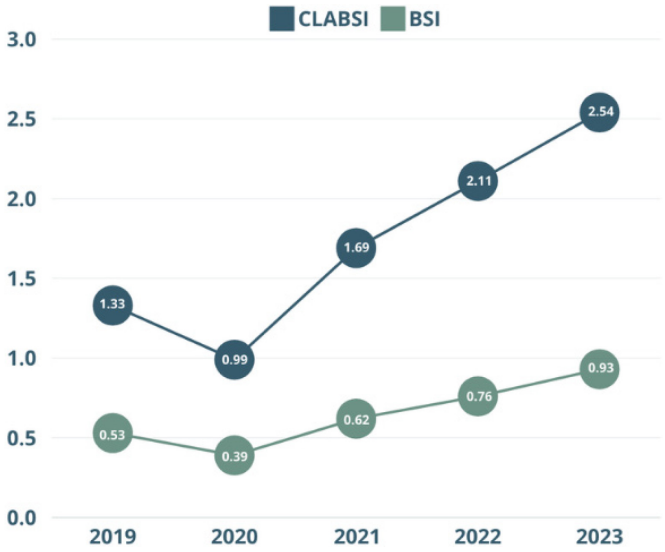
A total of 482 cases were recorded during the study period (2019-2023) in five dialysis units. Thirty-two samples were reported as contaminated by the laboratory, and we found 13 patients had duplicate blood cultures taken within 21 days. The remaining 437 episodes of bacteremia were recorded in 432 patients. Out of these, 405 cases were of central line blood cultures and 367 cases of peripheral blood cultures. Paired samples (central and peripheral blood culture) were taken in 335 cases (Figure 2). The study sample consisted of 267 male patients (61.1%) and 170 females (38.9%). Two-thirds of the patients were in the 46-70 age group. Patients were divided into four BMI (body mass index) groups, and we have not noticed any statistically significant predominance of positive blood cultures in any specific group. Positive blood cultures were more common with central venous catheters. Patient demographic data, including age, gender, BMI, comorbidities, and type of vascular access, for those with positive blood cultures, are detailed in Table 1.

Table 1. Demographic Data & Vascular access type.

Characteristics	N = 437	%
Age (years) (n = 430)		
15-20	8	1.9
21-45	75	17.4
46-70	269	62.6
> 71	78	18.1
Gender		
Male	267	61.1
Female	170	38.9
BMI (n = 436)		
< 18	13	3.0
18-25	164	37.6
25-30	109	25.0
> 30	150	34.4
DM		
No	172	39.4
Yes	265	60.6
HTN		
No	49	11.2
Yes	388	88.8
IHD		
No	357	81.7
Yes	80	18.3
Vascular Access Type		
Dual	30	6.9
CVC	375	85.8
AVF	27	6.17
AVG	5	1.14

Variables (type of organisms, exit site infection, other focus of infection, hospital treatment, loss of vascular access and mortality) were compared in four sets of age groups (15-20 years, 21-45 years, 46-70 years, and > 71 years of age). The chi-square test & Fisher's exact test were applied. Tunnel infection and the same organism in paired blood culture were found statistically significant ($p = 0.041$ and $p = 0.028$, respectively) in the younger age group of 15-20. In other age groups, variables were not statistically significant.

Figure 3. Five-year BSI and CLABSI Rate.



During the 5 years of study, bloodstream infection (BSI) was 0.67 per 100 patient-months, and the CLABSI rate was 1.55 per 100 patient-months. Figure 3 shows the yearly pattern of BSI and CLABSI rates.

Central blood cultures from 386 cases identified 169 Gram-positive and 200 Gram-negative organisms. Mixed organisms in 16 cases and 1 case of fungi were also noted. Among Gram-positive cocci, *Staphylococcus aureus (methicillin-susceptible Staphylococcus aureus, MSSA)* was the most common organism, followed by *MRSA (methicillin-resistant Staphylococcus aureus)* and *Staphylococcus*

Table 2. Bacterial organisms' classification in Central and Peripheral Blood samples.

	Central	n	%		Peripheral	n	%
Gram Positive cocci total		**165**		**Gram Positive cocci total**		**150**	
1	*Staphylococcus aureus*	82	21.2	1	*Staphylococcus aureus*	69	21.4
2	*Staphylococcus epidermidis*	24	6.2	2	*Staphylococcus epidermidis*	22	6.8
3	*MRSA*	26	6.7	3	*MRSA*	24	7.4
4	*Enterococcus faecalis*	18	4.7	4	*Enterococcus faecalis*	17	5.3
5	other	15	3.9	5	other	18	5.6
Gram Positive bacilli total		**4**		**Gram Positive bacilli total**		**8**	
1	*Corynebacterium*	3	0.8	1	*Corynebacterium*	5	1.5
2	*Bacillus cereus*	1	0.3	2	*Bacillus cereus*	2	0.6
3	other	0	0.0	3	other	1	0.3
Gram Negative bacilli total		**199**		**Gram Negative bacilli total**		**149**	
1	*Enterobacter cloacae*	46	11.9	1	*Enterobacter cloacae*	37	11.5
2	*Klebsiella pneumoniae*	42	10.9	2	*Klebsiella pneumoniae*	32	9.9
3	*Pseudomonas aeruginosa*	28	7.3	3	*Pseudomonas aeruginosa*	20	6.2
4	*Serratia marcescens*	21	5.4	4	*Serratia marcescens*	20	6.2
5	*Escherichia coli*	16	4.1	5	*Escherichia coli*	10	3.1
6	*Stenotrophomonas maltophilia*	11	2.8	6	*Stenotrophomonas maltophilia*	7	2.2
7	other	35	9.1	7	other	23	7.1
Gram Negative coccobacilli total		**1**		**Gram Negative coccobacilli total**		**1**	
1	Unclassified coccobacilli	1	0.3	1	Unclassified coccobacilli	1	0.3
Other organisms		**17**		**Other organisms**		**15**	
1	Mixed organisms	16	4.1	1	Mixed organisms	13	4.0
2	fungus	1	0.3	2	fungus	2	0.6
Total		**386**		**Total**		**323**	

epidermidis. In Gram-negative bacteria, the most common pathogen identified was *Enterobacter cloacae*, followed by *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. The pattern of peripheral blood cultures was almost similar to that of central blood cultures. The classification of the organism is shown in Table 2.

Vascular access is categorized into three categories (central venous catheter, arteriovenous fistula, and dual access). Positive blood culture patients in these groups were evaluated for exit site infection, tunnel infection, other focus of infection, treatment in dialysis center or hospital, outcome of vascular access, and mortality. Patients with CVC required more hospital treatment and had a significantly higher rate of vascular access loss ($p < 0.001$). Mortality was observed in five patients in a 4-week follow-up as per study design, but it was not statistically significant. In the case of AVF access, the probability of other foci of infection was notably high and statistically significant ($p < 0.001$). Table 3.

Discussion

Hemodialysis patients with central venous catheters have bacteremia episodes ten times more frequent than those with AV fistulas or AV grafts [8,9]. The mortality rate is also higher for patients with central venous catheters compared to those with AVF or AVG [10,11]. International guidelines recommend AVF as the preferred choice of vascular access in hemodialysis patients, but dependency on CVC still exists. Catheter-related bacteremia has significant clinical consequences, including morbidity and mortality from conditions such as osteomyelitis, endocarditis, septic arthritis, and epidural abscess [12]. Risk factors for catheter-related bloodstream infection (CRBSI) include prolonged catheter use, diabetes mellitus, recent surgery, iron overload, immunosuppression, and hypoalbuminemia [13–15]. Local risk factors such as poor hygiene, occlusive dressings, moisture around the exit site, and *Staphylococcus aureus* colonization (skin and nose) have also been well-established [16].

Gram-positive organisms are responsible for catheter-related infections (40–80%) in most studies. A retrospective analysis of a prospective vascular access database from a large academic dialysis center found that nearly 80% of BSIs were caused by Gram-positive pathogens [12]. Loo *et al.* report from a large tertiary care hospital that there is a predominance of Gram-positive pathogens as a cause of infection in dialysis patients [17]. A 6-year record from Greece showed that 65% of cases of catheter-related bloodstream infection (CRBSI) were caused by Gram-positive pathogens [18]. Similarly, a 14-year observational study from Spain found that Gram-positive organisms were predominant, accounting for 84.5% of cases, while Gram-negative organisms were responsible for only 15.5% [19].

On the contrary, high rates of Gram-negative infections have been reported in various studies, and the reason is probably multifactorial. This could be due to increased preventive strategies for Gram-positive organisms and less defined strategies to prevent Gram-negative BSIs. Balkhy *et al.* conducted a prospective study from 2008 to 2016 in hospitals under the Ministry

Table 3. Variables comparison in different vascular access.

	Vascular Access						*p*
	Dual		CVC		Fistula		
	n = 30	%	n = 375	%	n = 27	%	
Exit Site Infection							
No	26	6.8	335	87.0	24	6.2	0.834†
Yes	4	8.5	40	85.1	3	6.4	
Tunnel infection							
No	23	7.5	261	85.6	21	6.9	0.501*
Yes	7	5.5	114	89.8	6	4.7	
Other Focus of infection							
No	29	7.5	349	90.4	8	2.1	< 0.001†
Yes	1	2.2	26	56.5	19	41.3	
Centre Treatment							
No	16	7.5	185	86.9	12	5.6	0.798*
Yes	14	6.4	190	86.8	15	6.8	
Hospital Treatment							
No	12	8.5	114	80.9	15	10.6	0.018*
Yes	18	6.2	261	89.7	12	4.1	
Loss of vascular access							
No	15	7.6	158	79.8	25	12.6	< 0.001*
Yes	15	6.4	217	92.7	2	.9	
Mortality within 4 weeks							
No	30	7.0	370	86.7	27	6.3	> 0.99†
Yes	0	0.0	5	100	0	0.0	

*Chi-squared test; †Fisher's exact test.

of National Guard, showing Gram-negative pathogens (59.1%), Gram-positive pathogens (27.5%), and fungi (13.5%) as causative organisms in catheter-related bloodstream infection (CRBSI) [20]. In 2019, a university hospital in Jeddah published a record review of BSIs in hemodialysis (HD) patients, revealing that 54.6% of Gram-negative pathogens were causative pathogens [21]. Data from the NHS Greater Glasgow & Clyde and NHS Forth Valley hemodialysis populations showed that central venous catheters (CVC) and diabetic foot ulcers are risk factors for Gram-negative pathogens and emphasized the importance of vascular access planning [22].

Contaminated water and other fluids are recognized to be associated with healthcare-associated infections. A Gram-negative outbreak at a hemodialysis center in Maryland was investigated, and the result was found to be incompetent ports [23]. Another outbreak was reported due to contamination during the reprocessing of the dialyzer [24]. Additionally, fifty-eight cases of Gram-negative bloodstream infection were reported due to wall boxes, which were identified as an undescribed source of infection [25].

It seems that the incidence of BSI and CLABSI varies from region to region and from one medical facility to another. These divergent rates can be attributed to different geographical locations, climate, infection control practices, and adherence to hand hygiene measures. Our BSI rates are comparable to the published data. We observed a decline in infections in 2020, which may be attributed to the COVID-19 pandemic. This decline could be due to enhanced focus on hand hygiene practice by both staff and patients.

Our study highlights a significant issue regarding bloodstream infections among hemodialysis patients, particularly those with central venous catheters. Gram-negative and Gram-positive microorganisms are responsible for the vast majority of BSI episodes. We have reviewed the antibiogram of the last 5 years. Our most common isolates (*Enterobacter cloacae, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa*) are sensitive to carbapenems, aminoglycosides, and cefepime (4th-generation cephalosporins). Overall, Gram-negative bacteria were resistant to penicillin and first-generation and second-generation cephalosporins; third-generation cephalosporins showed partial resistance among isolates.

Conclusions

In our study, we aimed to determine the prevalence of Gram-negative and Gram-positive BSIs among our hemodialysis patients. Our findings revealed that Gram-negative pathogens accounted for half of these events. In other studies, conducted in Saudi Arabia, the incidence of Gram-negative pathogens is significantly high.

Our study has some limitations, as it focused on hemodialysis patients confined to satellite centers. Infection rates may vary in acute hospital settings, where patients are more critically ill. We focused on the basic spectrum of pathogens and some known associated factors. Microbial pathogen sensitivity and the need to look for metastatic infection were not the targets of our study. Our research highlighted a basic spectrum of pathogens and some known associated risk factors, but we did not delve into the complexities of microbial pathogen sensitivity or investigate the potential for metastatic infections. Metastatic infections such as infective endocarditis, osteomyelitis, septic arthritis, and discitis are well-known morbidities secondary to catheter-related bacteremia. In this project, we are not directly assessing these conditions, as our patient cohort belongs to various tertiary care hospital settings. It was not possible to obtain long-term data regarding metastatic complications in the majority of cases.

The data from our 5-year study will assist in planning empirical antibiotic therapy. We aim to implement strict hand hygiene practices and infection control measures to significantly reduce the incidence of Gram-negative bacteremia episodes. Further research on metastatic infections and microbial sensitivity patterns is suggested for future studies. Additionally, we propose using a taurolidine-citrate lock to reduce Gram-negative bacteremia, as supported by published studies [26].

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Conflict of interest

No conflict of interest is declared.

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