

Bloodstream infection at hemodialysis facilities in Jeddah: a medical record review

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BACKGROUND: Bloodstream infections (BSI) are a major complication of hemodialysis. The risk of infection among hemodialysis patients is usually associated with the dialysis procedure itself, specifically the means of vascular access.

OBJECTIVES: Estimate the rate of BSI and assess factors possibly associated with BSI.

DESIGN: Analytical retrospective medical record review.

SETTING: Hemodialysis unit in a tertiary care center.

PATIENTS AND METHODS: Adult patients (18-60 years old) who had hemodialysis as first renal replacement therapy in the 20-month period from January 2014 to August 2016 were included in this study. Demographic and clinical characteristics were used in a multivariate logistic regression to assess factors that might be associated with BSI.

MAIN OUTCOME MEASURES: The rate of BSI and associated factors among chronic hemodialysis outpatients.

SAMPLE SIZE AND CHARACTERISTICS: 160 outpatients on hemodialysis, median (IQR) age 47.7 (37.0-56.0) years, males (60.6%).

RESULTS: The rate of BSI was 0.4 per 100 patient-months. Multivariate logistic regression revealed that patients who had central venous catheters had the highest risk for BSI (odds ratio: 10.088; 95% CI= 2.595-39.215; $P=.001$) compared with arteriovenous fistulas. Gram-negative bacteria were isolated in 54.6% of cases, with coagulase-negative *Staphylococcus* the most frequent isolate (18.2%), followed by *Klebsiella pneumoniae* and Enterobacteriaceae (15.2%, each).

CONCLUSIONS: The type of vascular access type is the main risk factor associated with BSI in hemodialysis patients. The arteriovenous fistula, which has a lower infection rate compared to the catheter, is the best available option for hemodialysis patients.

LIMITATIONS: Retrospective, single center and relatively small sample size.

CONFLICT OF INTEREST: None.

There are many complications of dialysis. Some lead to a high morbidity and mortality. In 2016, the annual mortality rate in Saudi hemodialysis patients was 10%.¹ According to the United States Renal Data System registry: "Infection is the second leading cause of death in patients with end-stage renal disease".² The risk of infection among dialysis patients is usually associated with the dialysis procedure itself, specifically the means of vascular access. Hemodialysis patients require a vascular access from which to remove and replace blood; these vascular accesses are a major cause of infections.

Rates of bloodstream infection (BSI) in patients undergoing hemodialysis vary depending on the type of vascular access. According to North American data, the rate of BSI among hemodialysis patients ranges from 0.5 to 27.1 per 100 patient-months.³ The central venous catheter (CVC) is more commonly the source of bacteremia, as opposed to a surgically created arterio-venous fistula, the other often used means of vascular access. The use of a CVC is associated with an up to ten times increased risk of bacteremia.⁴ According to data for 2008-2011 from the United States Centers for Disease Control, an estimated 37 000 BSIs related to central lines occurred among hemodialysis patients.⁵ Gram-positive bacteria, mainly *S aureus*, are most frequently isolated in blood cultures from hemodialysis patients.⁶⁻¹⁰ Other risk factors associated with infection include old age, the severity of illness, long-term hospital stay, repeated antibiotic treatment and specific immune system defects associated with renal dysfunction.¹¹ Infection among hemodialysis patients results in major medical complications, long hospital stays and a high economic burden (cost per infection has been estimated between \$34 508-\$56 0002). Intervention strategies focus on infection prevention, especially with increasing resistance to antimicrobials and the challenges of using newly discovered antibiotics.

The number of patients undergoing dialysis in Saudi Arabia is increasing each year, according to the Saudi Center of Organ Transplantation.¹ A total of 16 315 patients on hemodialysis therapy were recorded in 2016; of these 4150 were new patients. The current study aimed to estimate the rate of BSIs and assess factors associated with BSI among chronic hemodialysis attending outpatient clinics in the National Guard Hospital in Jeddah, Saudi Arabia.

PATIENTS AND METHODS

This retrospective medical record review study was conducted on patients who underwent dialysis between January 2014 and August 2016. Data were col-

lected on demographic characteristics, comorbidities, type of current vascular access, the occurrence of BSI, type of vascular access during BSI, causative microorganisms and resistant profiles of antimicrobials. All adult patients (18-60 years old) who had first hemodialysis for renal replacement therapy in King Abdulaziz Medical City hospital and the affiliated King Abdullah hemodialysis center in Jeddah, Saudi Arabia, between January 2014 and August 2016 were included in the study.

BSI is defined according to the National Healthcare Safety Networks Dialysis Event Surveillance Manual as any positive blood culture.¹² Blood cultures were processed in accordance with standardized protocols in the hospital laboratory. We considered BSI as a separate hemodialysis event when there was 21 days or more between positive blood cultures, even if the organisms were different. One of the following four suspected sources of a positive blood culture is required to indicate BSI:¹²

- Vascular access: if there is a local access infection (pus, redness, swelling or pain at the access site), or a positive culture from the vascular access showing the same organism found in the blood.
- A source other than vascular access: if (1) a culture from another site shows the same organism found in the culture from the bloodstream (e.g., infected wound, urine), or (2) there is clinical evidence of an infection at another site that was not sampled for culture.
- Contamination: if the isolated organism is a common commensal and it is isolated from only one of several blood cultures, the infection is more likely to be contamination and the source is thought to be nosocomial, i.e., a physician and health care provider.
- Uncertain: if there is not enough evidence to decide among the three previous categories.

Data are presented using frequencies and percentages for categorical variables, and mean and standard deviation (SD) for continuous variables other than age and duration of hemodialysis, which are presented as median and interquartile range since these variables were not normally distributed. The outcome was the presence or absence of BSI. Associations between BSI were tested using the chi-square test for categorical variables and the t test or nonparametric equivalent for continuous variables. Multiple logistic regression analysis was conducted to determine the independent variables that were associated with the presence of BSI and presented as odds ratios with 95% confidence intervals. To evaluate the fit of the multivari-

ate logistic regression model on our data we applied Hosmer-Lemeshow goodness-of-fit test. The Hosmer-Lemeshow statistic indicates a poor fit if the *P* value is less than .05. IBM SPSS version 24.0 for Windows was used for statistical analysis. Level of significance was a *P* value $\leq .05$.

RESULTS

During the study period, there were 167 outpatients with end-stage renal disease on hemodialysis. Seven patients (4.2%) were excluded as one was pregnant and 6 had previous treatment with peritoneal dialysis. The final study population included 160 patients, including 42 (26.3%) from the hemodialysis unit at King Abdulaziz Medical City and 118 (73.8%) from King Abdullah hemodialysis center who met the inclusion criteria. Demographic characteristics and co-morbidities are presented in **Table 1** and the age and sex distribution of the population are shown in **Figure 1**. The

most common means of vascular access was arteriovenous fistula (AVF) in 90 patients (56.3%). One patient had arteriovenous graft (AVG) and the rest of the patients (*n*= 69, 43.1%) had CVCs (**Table 1**).

The rate of BSI in our study population was 0.4 per 100 patient-months (13.1% over two years and 8 months). Six cases were identified in the hemodialysis unit at King Abdulaziz Medical City and 15 cases at the King Abdullah hemodialysis center. Patients with BSIs had been on hemodialysis for the median (IQR) duration 725 (604, 897) days vs. 325 (232, 774) days for patients without BSIs (*P*=.007) (**Table 1**). BSIs varied according to the type of vascular access, only three episodes of BSI in patients with AVFs (3.6%), compared to 18 episodes (24%) in patients with CVC and none in patients with AVG (*P*=.0002). Contamination was reported in 8 episodes (24.2%) and two other episodes were classified as unknown.

Multivariate logistic regression revealed that there

Table 1. Demographic and clinical characteristics of the study population.

	All patients (<i>n</i> =160)	Patients with bloodstream infection (<i>n</i> =21)	Patients without bloodstream infection (<i>n</i> =139)	<i>P</i> (with vs without BSI)
Age (y), median (IQR)	48 (37, 56)	49 (40, 56)	47 (36, 56)	.3613 ^a
Gender				
Male	97 (60.6)	10 (10.3)	52 (82.5)	.285
Female	63 (39.4)	11 (17.5)	87 (89.7)	
Comorbidities	151 (94.4)	21 (100.0)	130 (93.5)	
Hypertension	140 (87.5)	21 (100.0)	119 (85.6)	.078
Diabetes mellitus	76 (47.5)	13 (61.9)	63 (45.3)	.236
Heart diseases	42 (26.3)	8 (38.1)	34 (24.5)	.290
Dyslipidemia	18 (11.3)	3 (24.3)	15 (10.8)	.709
Organ transplantation	19 (11.9)	0	19 (13.7)	.0797
Serological tests				
Hepatitis C virus positive	20 (12.5)	0	20 (14.4)	.0778
Hepatitis B virus positive	4 (2.5)	2 (9.5)	2 (1.4)	.0839
Duration of hemodialysis (median, IQR), days	435.5 (236.5, 801.8)	725 (604, 897)	325 (232, 774)	.007 ^a
Vascular access				
Arteriovenous fistula	90 (56.3)	3 (14.3)	81 (58.3)	.0002
Arteriovenous graft	1 (0.6)	0	1 (0.7)	
Central venous catheter	69 (43.1)	18 (85.7)	57 (41.0)	

Data are number of isolates (percentage) unless noted otherwise. ^aWilcoxon rank sum test with continuity correction, categorical variables by Pearson chi-squared test with Yates' continuity correction or Fisher's Exact test as appropriate.

was a highly significant overall effect of type of vascular access on the occurrence of BSI ($P=.001$) (**Table 2**). The highest risk for BSI was in patients who had CVCs (OR=10.088, 95% CI=2.595-39.215; $P=.001$). No statistically significant association was reported between BSI and other studied variables.

Among the 21 patients who had BSIs, 29 episodes of infection were recorded. Some patients had repeated episodes, 2 (9.5%) had two episodes, and 3 (14.3%) had three episodes. Thirty-three isolates were reported as single microbial isolates in 26 episodes (89.65%) and as polymicrobial isolates in 3 episodes (10.3%). The most prevalent microorganisms isolated from blood cultures were gram-negative bacteria 18 (54.6%), followed by gram-positive bacteria 15 (45.5%). Among the gram-negative bacteria, non-fermenters were isolated in 38.9% of cases (*Acinetobacter baumannii*, 9%; *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia*, 6% each), followed by 15.2% each for *Klebsiella pneumoniae* and the *Enterobacteriaceae* family (*Serratia marcescens*, *Enterobacter cloacae*, 6% each), and *Escherichia coli*, 3%). Of the gram-positive bacteria, coagulase-negative *Staphylococcus* (a common skin contaminant) and *S aureus* were isolated in 18.2% of blood cultures each. In *S aureus*, 50% were methicillin-resistant *S aureus* (MRSA). Other common skin contaminants were found in 9% of isolates (*Corynebacterium spp.*, 6%) and alpha-hemolytic *Streptococcus*, 3%). Among all microorganisms isolated, coagulase-negative *Staphylococcus* and *S aureus* were the more common isolates in blood cultures (18.2% each), followed by *Klebsiella pneumoniae* (15.2%) (**Table 3**).

Most *Klebsiella pneumoniae* (60%) and

Staphylococcus aureus (83.3%) cases were identified in patients with CVC. Simultaneously, all cases with common skin contaminants (*Corynebacterium spp.*, coagulase-negative *Staphylococcus*, and alpha-hemolytic *Streptococcus*) and other gram-negative cases were identified in patients with CVC (**Table 4**).

Vancomycin was used in 55.2% of BSI cases, followed by ceftazidime (48.3%), and gentamicin (13.8%). Antimicrobial susceptibility showed that 12 out of the 33 isolated bacteria (36.4%) were multiply resistant, 33.3% to ampicillin (45.5% of which were *Klebsiella pneumoniae*), 21.2% to amoxicillin, 18.2% to cefazolin, 15.2% to oxacillin, and 12.1% were resistant to trimethoprim.

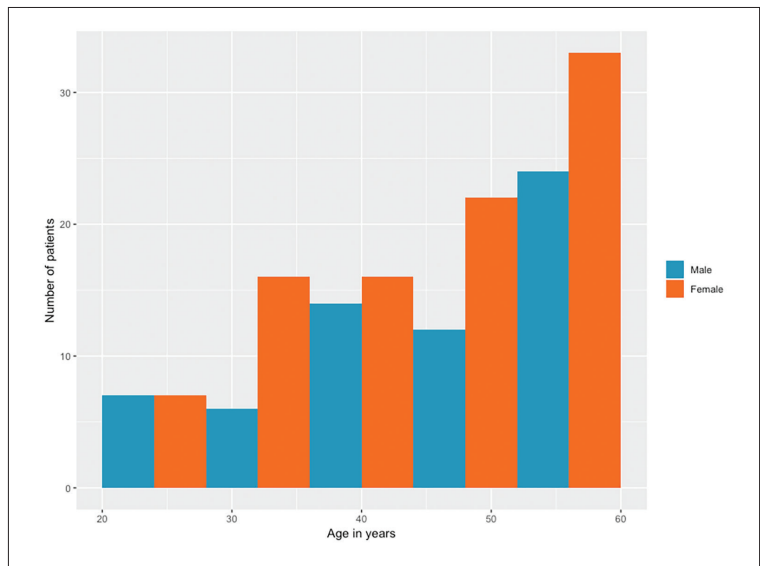


Figure 1. Age and sex distribution of the study population (n=160).

Table 2. Multiple logistic regression showing factors associated with the occurrence of bloodstream infection.

Factor	B	S.E.	P value	Odds ratio	95% C.I. for OR	
					Lower	Upper
Age (y)	0.022	0.029	.45	1.022	0.966	1.082
Female gender	0.679	0.527	.198	1.971	0.702	5.535
Diabetes mellitus	0.300	0.662	.65	1.350	0.369	4.940
Heart disease	-0.640	0.630	.31	0.528	0.153	1.813
Dyslipidemia	0.563	0.777	.469	1.756	0.383	8.054
Hepatitis B	-1.632	1.137	.151	0.195	0.021	1.814
Duration on HD (days)	0.000	0.000	.567	1.000	1.000	1.000
Central venous catheter	2.311	0.693	.001	10.088	2.595	39.215

HD: hemodialysis. -2 Log likelihood: 100.452, Cox and Snell R square: .139, Nagelkerke R square: .257; Hosmer and Lemeshow test: χ^2 10.622, df 8, $P=.224$; Omnibus test of model coefficients: χ^2 23.950, df=9, $P=.004$

DISCUSSION

The rate of BSI in the current study was 0.4 per 100 patient-months (i.e. 13.13% over two years and 8 months) in two hemodialysis centers. Since the number of patients undergoing hemodialysis in Saudi Arabia continues to grow,¹ the rate of BSI will rise as well. To the best of our knowledge, only a few studies have been conducted in Saudi Arabia to estimate the rate of BSI in hemodialysis patients. In a prospective study in Al Qassim, involving 57 patients undergoing hemodialysis via temporary catheters, 19.3% developed catheter-related infection.¹³ Another another prospective study in the eastern region of Saudi Arabia, 40.6% had of

209 hemodialysis patients had septicemia.¹⁴ Such variations in BSI rates are possible because of differences in the characteristics of patients and vascular access management protocols that are applied at different hemodialysis units.

Type of vascular access is a known risk factor for BSI among hemodialysis patients. Several studies have found that rates of BSI in patients undergoing hemodialysis appear to vary depending on the type of vascular access.⁶⁻¹⁰ In our study, all patients had tunneled (long-duration) CVC and findings showed that the use of CVC was the independent risk factor for the occurrence of BSI among hemodialysis patients compared to AVF. Multivariate logistic regression confirmed that use of CVC was associated with a 10-fold increased risk of developing BSI among hemodialysis patients. This finding is consistent with those of Fram et al who reported an 11.2-fold increase the chance of developing BSIs with the use of CVC compared to AVF (OR: 11.2, 95% CI: 5.17–24.29; $P < .001$).¹⁰ In another study, the absence of fistula was a risk factor for developing BSI (OR: 2.933; $P = .047$).⁷

Use of AVF is thought to be the most appropriate vascular access, with a lower risk of complications including infection.¹⁵ Our findings emphasize the importance of reducing the use of catheters in hemodialysis patients as much as possible and using a fistula instead. However, the use of a fistula has some limitations and is not always possible especially in elderly and diabetic patients.¹⁶ Use of AVF in the current study was higher (56.3%) compared to catheters (43.1%) as in the study by Karkar et al who found a significant increase in the use of AVF and a reduction in CVC implantation associated with a decrease in infection rates.¹⁷

Regarding isolated microorganisms, previous studies have reported a high prevalence of gram-positive organisms in patients undergoing hemodialysis treatment, mainly *S aureus*.^{6-10,16} However, we observed that gram-negative organisms were the predominant organisms (54.6%). *Klebsiella pneumoniae* was the most frequently isolated (15.2%), and they were 100% resistant to ampicillin. Gram-positive organisms represented 45.5% of the isolated organisms from blood cultures and coagulase-negative *Staphylococcus* and *S aureus* were the most frequent (18.2% each). Half of the *S aureus* were methicillin resistant and all were isolated from blood cultures of patients with CVCs. McCann et al found that BSI with MRSA in dialysis patients was 100 times more frequent than in the general patient population, and was more frequent among hemodialysis patients dialyzed via CVCs (68.9%) than the

Table 3. Causative microorganisms isolated from blood culture.

Gram-negative	18 (54.5)
<i>Klebsiella pneumoniae</i>	5 (15.2)
<i>Acinetobacter baumannii</i>	3 (9.1)
<i>Pseudomonas aeruginosa</i>	2 (6.1)
<i>Stenotrophomonas maltophilia</i>	2 (6.1)
<i>Serratia marcescens</i>	2 (6.1)
<i>Enterobacter cloacae</i>	2 (6.1)
<i>Escherichia coli</i>	1 (3.0)
<i>Achromobacter xylosoxidans</i>	1 (3.0)
Gram-positive	15 (45.5)
Coagulase-negative staphylococci	6 (18.2)
<i>Staphylococcus aureus</i>	3 (9.1)
Methicillin-resistant <i>S aureus</i>	3 (9.1)
<i>Corynebacterium spp</i>	2 (6.1)
Alpha-haemolytic <i>Streptococcus</i>	1 (3.0)

Data are number of isolates (percentage).

Table 4. Microorganisms isolated from blood culture by type of vascular access.

	Catheter-associated BSI	Fistula-associated BSI
<i>Klebsiella pneumoniae</i>	3 (60)	2 (40)
<i>Staphylococcus aureus</i>	5 (83.3)	1 (16.7)
Common skin contaminants	9 (100)	0 (0)
Other gram-negative	11 (84.62)	0 (0)

Data are number of isolates (percentage). Common skin contaminants: *Corynebacterium sp.*, coagulase-negative *Staphylococcus* and alpha-hemolytic *Streptococcus*. BSI: bloodstream infection

dialysis patient population.¹⁸ Consistent with previous findings,^{3,7,19} our study showed that common skin contaminants were the most frequently reported microorganisms among hemodialysis patients with catheters.

In our study, non-fermenters were represented in 38.9% of isolates distributed as follows: 3 isolates of *Acinetobacter baumannii* (9%), 2 isolates for each of *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia* (6%). BSIs caused by non-fermenting gram-negative rods, such as *Acinetobacter baumannii*, *Stenotrophomonas maltophilia* and *Pseudomonas aeruginosa* were highly resistant to antibiotics. Also, they can cause outbreaks of nosocomial infection, and often associated with high mortality rates.⁸

Infections in hemodialysis patients are often caused by resistant microorganisms, due to the frequent need for antimicrobial therapy and frequent hospitalizations.⁷ Antimicrobial susceptibility in this study showed that more than a third of isolated bacteria were multiply resistant. According to the United States Centers for Disease Control, the rational use of antibiotics is an important measure for controlling the spread of multiply resistant microorganisms.¹² Fram et al found that prior antimicrobial use was associated with a higher occurrence of BSI (OR: 2.53; $P=.013$).¹⁰ The proportion of microorganisms resistant to ampicillin in our study was remarkably high, reflecting the problem of irrational use of antibiotics in this community. Healthcare providers should be aware of the resistant profiles in their units and restrict the use of antibiotics with high resistance rates. No vancomycin resistance has been reported and vancomycin was the

first-line therapy used in 55.2% of cases, followed by ceftazidime (48.3%) which had no resistant isolates.

This study had some limitations related to its retrospective nature and relatively small sample size. The current study showed a distinct possibility for hospital-acquired infection since there were more gram-negative organisms with high resistance, which highlights the importance of specifying the source of infection in recording data in episodes of infection. Also, although the study was done in two separate centers, it involved a single hospital in one geographic area, and thus represents a single center experience. Multiple geographic locations and other centers in the country may present a more comprehensive view, and better define the species distribution and resistance patterns of pathogens causing BSIs in hemodialysis facilities.

In conclusion, type of vascular access represents the main risk factor associated with BSI in patients undergoing hemodialysis. Vascular access has a strong influence on the clinical outcomes of hemodialysis treatment. The fistula is the best available option for hemodialysis patients, with a much lower infection rate compared to the catheter. A longitudinal study with comparison of multiple units representing different healthcare sectors would improve our knowledge on risk factors and practices associated with BSIs among hemodialysis patients in Saudi Arabia.

Ethical considerations

Ethical approval was taken from King Abdullah International Medical Research Center (KAIMRC) at the National Guard Hospital in Jeddah.

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