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Mohan Bilikallahalli Sannathimmappa [1,*], Rajeev Aravindakshan [2], Vinod Nambiar [3], Walaa Abdelmoeiz Ahmed [1], Layan Salim Al Mazroey [1], Amjad Mohammed Al-Gazali [1], Alrayan Hamood Alhooti [1], Arwa Basim Alhasani [1], Hind Yousuf Abdullah Al Blushi [1] and Elham Said Ahmed AL Risi [4]

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Abstract: Background: Bloodstream infections (BSIs) pose a major health risk to hemodialysis patients, significantly contributing to morbidity and mortality. This study aimed to identify the bacterial pathogens responsible for BSIs in this population, analyze clinical and laboratory profiles, and identify risk factors associated with poor outcomes. **Methods:** This retrospective study was conducted at Sohar Hospital, Oman, analyzing cases from January 2018 to December 2022. Data were obtained from e-health records, focusing on patient demographics, bacterial etiology, antibiotic susceptibility, and clinical outcomes. Statistical analysis included t-tests, Mann-Whitney tests, chi-square, and Fisher's exact tests, with univariate odds ratios calculated for mortality associations using the R package GTSUMMARY. **Results:** Among 1332 hemodialysis patients, 148 (11.1%) developed a BSI, with an average age of 60.43±14.46 years. Infections were more common among females (54%) and those over 60 years. The predominant comorbidities were hypertension (86%) and diabetes mellitus (74%). The main causative agents were coagulase-negative staphylococci (29.7%), *Staphylococcus aureus* (20.3%), *Pseudomonas aeruginosa* (12.2%), and *Klebsiella pneumoniae* (8.8%). Gram-negative bacteria showed high susceptibility (80-100%) to carbapenems and piperacillin-tazobactam, while Gram-positive bacteria exhibited 80-100% susceptibility to amoxicillin-clavulanic acid and universal sensitivity to linezolid and vancomycin. **Conclusions:** BSIs in hemodialysis patients at Sohar Hospital are associated with high morbidity and mortality rates, underscoring the need for prompt empirical antibiotic therapy and targeted treatment adjustments based on culture results. This study highlights critical mortality-associated factors, offering valuable insights for improving patient management and survival outcomes in this vulnerable population.

Keywords: C-reactive protein; end organ dysfunction; hemodialysis; lactate; sepsis; central venous catheter; hemodialysis; multidrug resistance; sepsis; staphylococcus

1. Introduction

Bloodstream infection (BSI) remains a substantial global health risk, playing a significant role in mortality, disability, and healthcare expenses [1]. However, promptly identifying and initiating appropriate and efficient treatment lead to favorable outcomes [2]. According to the Global Burden of Disease Study report, sepsis remains the second most common cause of death worldwide, leading to almost 7.7 million fatalities in 2019 [3]. These data led the World Health Organization (WHO) to declare sepsis a global health priority [4]. The 2016 sepsis definition defines sepsis as a state marked

by the life-threatening malfunctioning of organs, caused by an unregulated reaction of the body to an infection. Sepsis can result from a wide range of bacteria, fungi, and viruses. Approximately 90% of cases can be attributable to bacterial causes [5,6]. Patients with End Stage Renal Disease (ESRD) require hemodialysis (HD) and are at risk of contracting BSI, which can result in consequences such as sepsis, septic shock, multiorgan failure, and death [7]. Bacterial sepsis is the second most common cause of death in patients with HD, behind cardiovascular disease (CVD) [8,9]. The main factors contributing to the substantial risk of BSI and sepsis in patients with end-stage renal disease (ESRD) who undergo hemodialysis are vascular access, the hemodialysis method, and iron overload.

Furthermore, patients undergoing hemodialysis are at an elevated risk of experiencing serious infection and mortality as a result of multiple reasons. These factors comprise infections caused by pathogens that are resistant to multiple drugs, the frequent utilization of invasive procedures or devices in intensive care or critical care units, older age, and the existence of additional comorbid conditions such as diabetes mellitus, chronic kidney disease, malnutrition, anemia, and uremia [8–10]. The selection of vascular access in hemodialysis is also correlated with the occurrence of infection. BSI primarily affects patients who are receiving dialysis through a central venous catheter (CVC), with arteriovenous graft (AFG) and arteriovenous fistula (AVF) being less common [11]. Previous studies have shown a significantly higher infection rate in patients who get dialysis using a CVC compared to those who use AVG or AVF [8,11,12]. Despite the fact that AVF has a lower likelihood of infection and death, most patients in the United States initiate hemodialysis with a CVC or AVG [10]. In Oman, the primary approach to dialysis is the utilization of CVCs, rather than AVFs and AVGs [8].

The main clinical features displayed by sepsis patients comprise hypotension, body temperature exceeding 38.3ºC or falling below 36ºC, tachycardia, tachypnea, indications of inadequate tissue perfusion (such as alterations in mental status, restlessness, and oliguria), and signs of vital organ dysfunction. The laboratory abnormalities observed in sepsis patients can be attributed to the root cause of sepsis, inadequate blood flow to tissues, or dysfunction of organs due to sepsis. The condition can present with leukocytosis or leucopenia, arterial hypoxemia, hyperglycemia without diabetes, increased levels of C-reactive protein (CRP) and creatinine, abnormalities in blood clotting, low platelet count, high levels of bilirubin, low sodium levels, high potassium levels (suggestive of adrenal insufficiency), high lactate levels, elevated inflammatory cytokines, increased serum procalcitonin (PCT), and other indicators [13]. Serum PCT and lactate levels have the potential to serve as diagnostic indicators for sepsis and predictors of death in sepsis patients, surpassing other conventional markers of sepsis [14,15].

Sepsis can arise from a wide range of bacterial infections. Nevertheless, the occurrence of pathogenic bacteria and their vulnerability to antimicrobial medications differ according on the geographic region. *Coagulase-negative Staphylococcus (CONS)* and *Staphylococcus aureus* are the most common gram-positive bacteria linked to BSI. While *Escherichia coli, Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*, are the common gram-negative bacteria associated with BSI in HD patients [7]. A prior investigation conducted in Palestine revealed that over 80% of BSIs in hemodialysis patients were attributed to gram-positive microorganisms, with *CONS* being the predominant pathogen. The study identified *E. coli* and *Stenotrophomonas maltophilia* as the predominant gram-negative pathogens [16]. Another study found that 32.2% of hemodialysis patients experienced bloodstream infections (BSI), with *CONS* being the primary cause, followed by *S. aureus* and *E. coli*. Patients infected with multidrug-resistant (MDR) pathogens and those who required intensive care admission and mechanical ventilation had a higher mortality rate [17]. There is notable variation in the frequency of sepsis occurrence and fatality rates among sepsis patients in hospitals across various geographic regions [18,19]. Therefore, it is crucial to prioritize sepsis monitoring and increase physicians' understanding of the specific factors in the local environment that contribute to bacterial sepsis and the trends in antibiotic resistance. Furthermore, it is imperative to improve infection control measures and advocate for responsible use of antibiotics in order to successfully reduce the impact of sepsis and the resulting death rate in hemodialysis patients [20]. This study aims to analyze the clinical and laboratory characteristics of hemodialysis patients diagnosed with BSI, including sepsis and septic

shock at a secondary-care hospital in Oman from January 2018 to December 2022. The study will also focus on the bacterial causes of BSI and antibiotic resistance patterns, as well as the outcomes of BSI in the study subjects.

The significance of conducting the study lies in its emphasis on the prevalence, bacterial aetiology, and consequences of bloodstream infections in haemodialysis patients in Oman, an area with little prior research on the subject. The study is unique as it examines local epidemiological patterns, which may differ greatly from worldwide trends due to regional variances in bacterial resistance and health care practices. The study fills gaps in the current understanding of sepsis and its management in the Omani context, providing critical insights into local infection rates and resistance patterns. The findings can help lead the creation of personalised infection control strategies and antibiotic stewardship programs, with the ultimate objective of improving patients' outcomes and lowering mortality rates in haemodialysis patients. The study contributes valuable data that can inform local healthcare strategies, enhance infection control practices, and guide the development of targeted antibiotic stewardship programs. These insights can improve patient management and outcomes address the urgent need for region-specific infection control measures and providing foundation for the future research in similar settings.

2. Materials and Methods

A single-center retrospective study was conducted at Sohar Hospital, a secondary-care hospital situated in North Batinah region of Oman. Retrospective study design was chosen to capitalize on existing data and swiftly examine trends over s substantial time period. The strategy is both cost-effective and time-efficient, allowing for complete analysis without the need for further data collecting. It allows for the assessment of clinical outcomes, bacterial profiles, and antibiotic resisting patterns in a large haemodialysis patient population. Additionally, a retrospective analysis is ideal for investigating historical trends and outcomes, providing useful insights into local infection patterns and assisting in the creation of targeted infection control methods.

On the other hand, the study was approved by the Ethical and Review committee of the Ministry of Health, Oman as well as from the College of Medicine and Health Sciences (COMHS), National University of Science and Technology (NU) wide under **approval number MOH/CSR/23/27627**. The study included all hemodialysis patients diagnosed with BSI, including sepsis and septic shock at Sohar hospital from January 2018 to December 2023 were included. The pertinent data of study subjects such as demographic characteristics, bacterial profile and antibiotic susceptibility pattern, clinic-laboratory characteristics, underlying risk factors including comorbidities, treatment and outcomes was retrieved from the hospital's electronic health records.

Sample size calculation: The sample size was calculated using www.raosoft.com/samplesize.html**. Assuming 150 hemodialysis patients who have developed BSI and applying 95% confidence interval and 5% margin error, the minimum sample size was calculated as 109. The sample size was chosen to maintain a balance between statistical power and practicalities, providing for accurate representation of the population while accounting for potential data variability. With the current sample size, the study efficiently detects significance changes and trends providing valuable insights into the epidemiology, bacterial profiles, and consequences of BSI in the specific patient group. The method is critical for creating evidence-based infection control and treatment plans.**

Inclusion criteria: All hemodialysis patients who have developed BSI including sepsis, and septic shock, confirmed by positive blood culture as per the Clinical Laboratory Standards Institute (CLSI) criteria during January 2018 to December 2023 were included in the study [**23**].

Exclusion criteria: The study excluded hemodialysis patients who had not developed bloodstream infections (BSI) or had negative blood culture reports, as well as those with incomplete data. Furthermore, the study excluded the isolation of bacteria from blood samples in cases where potential contamination was taken into account.

Bacterial identification and antibiotics susceptibility testing: Blood samples received at the Sohar microbiology laboratory were cultured in BACT/Alert procured from Biomerieux company

(https://www.biomerieux.com/us/en.html)   as per standard Clinical Laboratory Standards Institute (CLSI) criteria [**23**]. Pathogen identification up to the species was performed by convention identification method or VITEK II automated microbiological system as per CLSI criteria [**23**]. Antibiotic susceptibility testing of the isolated pathogen was performed by conventional method by using Mueller Hinton agar plate or VITEK II automated microbiological system. Broth microdilution method was performed for vancomycin and colistin antibiotic susceptibility testing. Disc diffusion method for antibiotic susceptibility testing for antibiotics amikacin, cefotaxime, ceftazidime, ampicillin, cefuroxime, amoxicillin-clavulanic acid, ciprofloxacin, gentamicin, imipenem, meropenem, tigecycline, trimethoprim-sulfamethoxazole, tetracycline, chloramphenicol was performed as per CLSI guidelines [**23**]. Results were interpreted as sensitive, resistant, and intermediate as per the standard CLSI guidelines [**23**].

Statistical analysis: Data were entered into spreadsheet files and analyzed using the R package GTSUMMARY. Means, standard deviations for continuous variables, and frequencies, percentages for categorical variables were calculated. Independent t-tests (and Mann Whitney Test wherever appropriate) for continuous variables and chi-square or Fisher's exact tests for categorical variables to compare characteristics between groups were used. Univariate odds ratios with 95% confidence intervals (CIs) for each characteristic to assess the association with mortality was also calculated. Statistical significance of each characteristic was considered with a p value <0.05. Infinite odds ratio was handled appropriately by considering it as a strong indicator of mortality.

Case definitions:

- Bacteremia was defined as the presence of a positive pathogen (except contamination) in blood culture [21,22].
- **Systemic inflammatory response syndrome**: Systemic inflammatory response syndrome (SIRS) is a widespread inflammatory response to a variety of severe clinical insults. This syndrome is clinically recognized by the presence of two or more of the following: Temperature >38 °C or <36 °C, Heart rate >90 beats/min, Respiratory rate >20 breaths/min or PaCO2 <32 mmHg, WBC >12,000 cells/mm3, <4000 cells/mm3, or >10 percent immature (band) forms [21,22].
- **Sepsis**: Sepsis is the systemic response to infection. Thus, in sepsis, the clinical signs describing SIRS are present together with definitive evidence of infection [21,22].
- **Severe sepsis**: Sepsis is considered severe when it is associated with organ dysfunction, hypoperfusion, or hypotension. The manifestations of hypoperfusion may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status [21,22].
- **Septic shock**: Septic shock is sepsis with hypotension despite adequate fluid resuscitation. It includes perfusion abnormalities such as lactic acidosis, oliguria, or an acute alteration in mental status. Patients receiving inotropic or vasopressor agents may not be hypotensive at the time that perfusion abnormalities are measured [21,22].

3. Results

Out of 1332 patients who received hemodialysis from 2018 to 2022, 148 (11.1%) developed BSI, and were included in the study.

Table 1 represents baseline characteristics of the study subjects. The age of the study subjects ranged from 20 to 95 years, with a mean age of 60.43±14.46. Bacteria were more frequently isolated from females (54%) and in people aged > 60 years (57%). Most of the study subjects had hypertension (128, 86%) and diabetes mellitus (110, 74%) as the predominant comorbidities, followed by cardiovascular diseases (88, 59%), pulmonary diseases, including asthma and chronic obstructive pulmonary disease (51, 34.5%), Chronic neurological disorders (35, 24%), and chronic kidney diseases (32, 22%).   Previous antibiotic therapy within 3 months (127, 86%), surgical interventions (89, 60%), and mechanical ventilation (38, 26%) were the major risk factors observed in our study subjects. Concerning a type of BSI, majority of patients were diagnosed with sepsis (62, 42%), followed by bacteremia (45, 30%) and septic shock (41, 28%). Out of 148 study subjects, 74 (50%) died of BSI and its complications.

Table 1. Baseline characteristics of study subjects.

Characteristic	Number (n) & percentage (%)
Gender	
Male	68 (46%)
Female	80 (54%)
Age (years)	
Mean ± SD.	60.43±14.46
Minimum age	20
Maximum age	95
<60	63 (43%)
>60	85 (57%)
Type of specimen	
Blood culture	122 (82%)
Catheter tip	26 (18%)
Comorbidities	
Diabetes mellitus	110 (74%)
Chronic kidney disease	32 (22%)
Hypertension	128 (86%)
Cardiovascular disease	88 (59%)
Respiratory disease (asthma & COPD)	51 (34.5%)
CNS disorders	35 (24%)
Category of BSI	
Bacteremia	45 (30%)
Sepsis	62 (42%)
Septic shock	41 (28%)
Risk factors	
Mechanical ventilation	38 (26%)
Surgical interventions	89 (60%)
Invasive radiological investigations	9 (6.1%)
Blood transfusion	8 (5.4%)
Previous antibiotic therapy	127 (86%)
Length of hospital stay.	
<1 week	70 (47%)
>1 week	78 (53%)
Outcome of infection	
Death	74 (50%)
Recovery	74 (50%)

Table 2 displays the bacterial agents associated with BSI. *CONS* (44, 29.7%) and *S. aureus*, including *MRSA* (30, 20.3%) were the predominant pathogens, followed by *P. aeruginosa* (18, 12.2%), *K. pneumoniae* (13, 8.8%), and others (≤ 5% each). Amongst, 16.9% (n=25) were multidrug-resistant pathogens.

Table 2. Etiological agents of bloodstream infection.

Etiological agent	Number (n) and percentage (%)		
	MDR	Non-MDR	Total
Gram-negative bacteria (GNB)			
Escherichia coli	4 (16%)	2 (1.6%)	6 (4.1%)
Klebsiella pneumoniae	7 (28%)	6 (4.9%)	13 (8.8%)
Enterobacter spp.	1 (4%)	8 (6.5%)	9 (6.1%)
Other Enterobacteriaceae	0	4 (3.3%)	4 (2.7%)
Pseudomonas aeruginosa	1(4%)	17 (13.8%)	18 (12.2%)
Acinetobacter baumannii	3 (12%)	5 (4.1%)	8 (5.4%)
Stenotrophomonas maltophilia	0	2 (1.6%)	2 (1.4%)
Gram-positive cocci (GPC)			
Staphylococcus aureus	9 (36%) *	21 (17.1%)	30(20.3%)

Coagulase negative staphylococci (CONS)	0	44 (35.8%)	44 (29.7%)
Enterococcus spp.	0	8 (6.5%)	8 (5.4%)
Streptococcus spp.	0	6 (4.9%)	6 (4.1%)
Total	25 (16.9%)	123 (83.1%)	148 (100%)

*Methicillin-resistant *S. aureus* (MRSA).

Table 3 displays the antibiotic susceptibility pattern of gram-negative bacteria, while **Table 4** shows the antibiotic susceptibility pattern of gram-positive bacteria. Enterobacteriaceae have exhibited high susceptibility (80-100%) to amikacin, imipenem, meropenem, and piperacillin-tazobactam. Conversely, no strain has demonstrated resistance to colistin and tigecycline. All members of the Enterobacteriaceae family have exhibited low susceptibility to beta-lactam antibiotics, including cephalosporins, with a range of 0-70%. Within the category of nonfermenters, *P. aeruginosa* has exhibited high susceptibility to all the antibiotics that were tested, ranging from 77% to 100%. On the other hand, *A. baumannii* has displayed a low susceptibility to all the antibiotics that were tested, with a range of 50% to 70%. Nevertheless, all strains of *A. baumannii* exhibited susceptibility to colistin and tigecycline. *S. maltophilia* has exhibited high susceptibility (100%) to cotrimoxazole, but no susceptibility (0%) to amikacin, ceftazidime, carbapenems, and piperacillin-tazobactam. However, the quantity of *S. maltophilia* is insufficient to accurately interpret the susceptibility pattern. Amoxicillin-clavulanic acid (Augmentin) and Linezolid have demonstrated high efficacy (80-100%) against all gram-positive bacteria, whereas no strains have exhibited resistance to vancomycin. The susceptibility of gram-positive bacteria to other tested antibiotics exhibited variability, as indicated in Table 4.

Table 3. Antibiotic susceptibility report of Gram-negative bacteria (GNB).

Antibiotic sensitivity report	GNB: Enterobacteriaceae				GNB: Nonfermenters		
ANTIBIOTICS	*K. pneumoniae (%)*	*E. coli (%)*	*Enterobacter spp. (%)*	*Other Enterobacteriaceae (%)*	*P. aeruginosa (%)*	*A. baumannii (%)*	*S. maltophilia (%)*
Amikacin	**81.8**	**100**	**100**	**100**	88.2	62.5	0
Ampicillin	0	20	0	25	---	---	---
Augmentin	50	33.3	0	50	---	---	---
Cefotaxime	66.7	40	62.5	50	---	---	---
Cefuroxime	50	33.3	0	33.3	---	---	---
Ciprofloxacin	75	33.3	88.9	100	88.9	62.5	
Colistin	**100**	**100**	**100**	---	**100**	**100**	**100**
Cotrimoxazole	41.7	50	88.9	75	---	71.4	100
ceftriaxone	40	33.3	66.7	66.7	---	---	---
Ceftazidime	40	33.3	71.4	50	83.3	50	0
Gentamicin	72.7	50	88.9	100	77.8	62.5	50
Imipenem	**90**	**100**	**100**	**100**	88.2	62.5	0
Meropenem	**90.9**	**100**	**100**	**100**	88.2	62.5	0
Piperacillin-tazobactam	**91.7**	**100**	**87.5**	**100**	100	62.5	0
Tigecycline	**100**	**100**	**100**	---	---	**100**	---

Table 4. Antibiotic susceptibility report of Gram-positive cocci (GPC).

ANTIBIOTICS	*S. aureus (%)*	*MRSA (%)*	*CONS (%)*	*Enterococcus spp. (%)*	*Streptococcus spp. (%)*
Ampicillin	100	---	---	71.4	100
Augmentin	93.3	---	100	83.3	100
Cephalexin	85.7	---	100	0	---

Cefuroxime	---	---	---	---	100
Ciprofloxacin	90	66.7	54.8	20	100
Clindamycin	90	100	73.7	0	60
Cloxacillin	100	0	27.6	---	---
Cotrimoxazole	94.7	---	70	0	100
Erythromycin	75	100	29.3	50	100
Gentamicin	100	77.8	41.5	---	---
Linezolid	100	100	100	100	100
Penicillin G	5	---	6.9	50	100
Vancomycin	100	100	100	100	100

Table 5 presents the results of a univariate regression analysis that examines the risk factors associated with the outcome of infection. There was a strong correlation (p value <0.05) between patient mortality and factors including septic shock, mechanical ventilation, cardiovascular, neurological, and respiratory comorbidities, longer hospital stays, elevated levels of C-reactive protein, serum lactate, neutrophil count, and serum bilirubin. Additionally, patients with decreased platelet count, lower serum creatinine levels, and those who experienced end organ dysfunction were also more likely to die.

Table 5. Univariate regression analysis of the risk factors for outcome of infection.

Characteristic	Alive (N = 74)	Death (N = 74)	OR	p-value
Bacteremia	40 (54%)	5 (6.8%)	0.06 (0.02, 0.16)	**<0.001**
Sepsis	33 (45%)	28 (38%)	0.76 (0.39, 1.46)	0.4
Septic shock	0 (0%)	41 (55%)	Infinite	**<0.001**
DM with ESRD	50 (68%)	60 (81%)	2 (0.47, 10.1)	0.2
Hypertension	61 (82%)	67 (91%)	2.2 (0.41, 16.2)	0.4
Cardiovascular disease	39 (53%)	59 (80%)	3.03 (0.56, 22.6)	0.4
Pulmonary diseases (COPD, asthma, and others)	20 (27%)	32 (43%)	2.06 (1.04, 4.14)	0.2
Chronic kidney disease	19 (26%)	24 (32%)	2.01 (0.86, 4.78)	0.2
Chronic neurological disease	9 (12%)	26 (35%)	3.91 (1.73, 9.54)	**0.001**
Length of hospital stay (average no. of days of hospital stay)	6 (3, 12)	9 (5, 17)		**0.012**
< 1 week	72 (97%)	69 (93%)	0.38 (0.05, 1.84)	0.3
>1 week	2 (2.7%)	5 (6.8%)	2.61 (0.54, 18.6)	0.3
Mechanical ventilation	6 (8.1%)	32 (43%)	8.63 (3.54, 24.5)	**<0.001**
Surgical intervention	41 (55%)	48 (65%)	1.49 (0.77, 2.90)	0.2
Previous antibiotic therapy	61 (82%)	66 (89%)	1.76 (0.69, 4.72)	0.2
MDRO infection	8 (11%)	16 (22%)	2.28 (0.93, 5.98)	0.079
Non-MDRO infection	66 (89%)	58 (78%)	0.44 (0.17, 1.08)	0.079
C-reactive protein level (average level in mg/dL)	41 (12, 83)	75 (39, 158)	1.01 (1.00, 1.02)	**0.003**
Serum creatinine level (average level in µmol/L)	545 (442, 777)	471 (362, 641)	1 (1.00, 1.00)	**0.031**
Serum lactate level (average level in mmol/L)	1.5 (1.1, 2.5)	2.1 (1.7, 5.5)	1.05 (0.93, 1.24)	**0.053**
Neutrophil count (average level per microliter (µL) of blood)	4 (3, 7)	7 (4, 15)	1.19 (1.10, 1.31)	**<0.001**
Lymphocyte count (average level per microliter (µL) of blood)	1.32 (1.00, 1.83)	1.28 (0.79, 1.86)	0.98	0.3

Neutrophil lymphocyte cell ratio (NLCR) – average level	3 (2, 5)	6 (2, 11)	1 (0.98, 1.03)	0.06
Platelet level (average level in microliter (µL)	246 (191, 325)	200 (119, 287)	1 (0.99, 1.00)	**0.012**
Coagulation abnormality	1.10 (1.06, 1.23)	1.57 (1.22, 1.94)	79.9 (5.29, 3,698)	**<0.001**
Serum potassium level (average level in mEq/L)	4.89 (4.28, 5.46)	4.82 (4.01, 5.41)	0.91 (0.66, 1.24)	0.3
Serum sodium level (average level in mEq/L)	135.5 (131.8, 137.1)	134.1 (131.8, 138.5)	0.99 (0.94, 1.02)	0.9
Serum bilirubin level (average level in mg/dL)	5 (4, 9)	10 (8, 13)	1.09 (1.01, 1.23)	**0.009**
Type of hemodialysis procedure				
Central venous catheterization (CVC)	29 (35.4%)	30 (40.4%)		0.074
Arterio-venous graft (AVG)	9 (12%)	8 (11%)		0.8
Arterio-Venous fistula (AVF)	38 (51%)	43 (58%)		0.4
End organ dysfunction	6 (8.1%)	40 (54%)		**<0.001**

Hypothesis:

Table 6. Table of Hypothesis.

Hypothesis	Accepted/Rejected	Evidence from Previous Literature
H1: Patients with end-stage renal disease (ESRD) have a higher risk of mortality from sepsis compared to non-ESRD patients.	Accepted	Bou Chebl et al. (2021) and Himali et al. (2023) show increased mortality risk in ESRD patients due to sepsis. Sakr et al. (2018) provides global data supporting higher mortality in ICU patients, including those with ESRD.
H2: The presence of a central venous catheter is associated with an increased incidence of sepsis in hemodialysis patients.	Accepted	Suzuki et al. (2016) and Fisher et al. (2020) indicate that central venous catheters are a significant risk factor for sepsis in hemodialysis patients. Rteil et al. (2020) supports this with data on infection risks related to vascular access.
H3: Procalcitonin is a reliable marker for early diagnosis and management of sepsis in hemodialysis patients.	Accepted	Vijayan et al. (2017) support the use of procalcitonin as a diagnostic marker for sepsis. Evidence from multiple studies highlights its utility in early detection and treatment decisions.
H4: Antimicrobial de-escalation improves outcomes in sepsis patients undergoing hemodialysis.	Rejected	Tanzarella et al. (2024) and Ippolito & Cortegiani (2023) discuss antimicrobial stewardship but do not provide clear evidence that de-escalation improves outcomes specifically for hemodialysis patients.
H5: Patients with multidrug-resistant bacterial infections have worse outcomes compared to those with non-resistant infections.	Accepted	Zilberman-Itskovich et al. (2022) and Corona et al. (2023) report that multidrug-resistant infections are associated with increased mortality and poorer outcomes. Evidence from Sakr et al. (2018) supports the impact of resistance on patient outcomes.

4. Discussion

This retrospective study is the first investigation conducted in Oman that systematically assesses BSI in patients undergoing hemodialysis. Additionally, it aims to analyze the risk factors associated with mortality in these study subjects. Hemodialysis patients have a greater susceptibility to infections compared to the general population. In a longitudinal study spanning 7 years, Powe et al. discovered that 11.7% of hemodialysis patients experienced at least one episode of BSI [24]. In line with this discovery, 11.1% of the participants in our study were found to have microbiologically confirmed BSI. Deceased infected patients were significantly older in our study with an overall mean age of 60.43±14.46 which aligns with the findings of a similar study conducted by Can O et al. [25]. Infection-related complications remain the primary causes of heightened morbidity and mortality among HD patients. There are several potential factors that could contribute to this, including weakened immune system, existing health conditions, medical procedures, and the strength of the pathogen [17]. In this study, it was observed that the majority of the subjects had one or more comorbidities. The most prevalent comorbidities were hypertension and diabetes mellitus, followed by cardiovascular, pulmonary, neurological, and chronic renal disorders. Furthermore, a significant number of patients were found to have been exposed to risk factors such as mechanical ventilation, invasive surgical or radiological procedures, blood transfusion, and previous antibiotic therapy. Abbasi et al. conducted a study that identified several significant risk factors for nosocomial BSI among hemodialysis patients. These risk factors include diabetes, a history of blood transfusion, longer duration of hemodialysis, longer hospital stays, and multiple catheter sites [26].

The type of vascular access can impact the occurrence of infectious complications. A study conducted by Krzanowski M et al revealed a significant incidence of central venous catheter (CVC) infections, which were found to be associated with a higher mortality rate when compared to patients who had arteriovenous fistula (AVF) [27]. According to a study conducted by Locham et al., CVC (31.2%) and AVG (30.6%) procedures were found to have a higher incidence of sepsis cases compared to AVF (22.9%) [11]. Furthermore, patients with AVF had better survival rate and low hospitalization in a study by Kim et al. [28]. Contrastingly, we did not find any significant difference in the relationship between the type of hemodialysis procedure and mortality. Patients with severe sepsis and septic shock face a considerably greater likelihood of death [29]. In line with these findings, all patients with septic shock, and nearly half of the patients with sepsis in our study did not survive, while most of the patients with bacteremia survived.

There is a lack of information on the microbiology of infections in hemodialysis patients from Middle Eastern countries. Nevertheless, a study conducted in Lebanon revealed that the predominant pathogens linked to BSI in hemodialysis patients were coagulase-negative staphylococci (CONS), followed by S. aureus and E. coli [17]. We also found preponderance of CONS and S. aureus as the most common pathogens of BSI. Among gram-negatives, our study found P. aeruginosa as the most prevalent pathogen, followed by K. pneumoniae, A. baumannii, and E. coli. In contrast, a study conducted by Schamroth Pravda et al. revealed that K. pneumoniae was the most prevalent pathogen, with S. aureus, CONS, E. coli, and P. aeruginosa [30].

The prevalence of infection in HD patients, causative agent, and their antibiotic susceptibility pattern widely varies geographically, contingent upon the specific hospital environment, infection control measures, and policies regarding antibiotic prescriptions. Hence, it is imperative to regularly monitor infection rates, etiology, antibiotic resistance patterns, and antibiotic prescribing guidelines in local healthcare establishments. The worldwide escalation in infection caused by multidrug-resistant organisms has become a grave concern. The indiscriminate utilization of antibiotics, lack of compliance with antibiotic stewardship, and inadequate implementation of infection control measures are considered significant factors that contribute to the increase in multidrug-resistant pathogens. The current study found a relatively low overall prevalence (16.9%) of multidrug-resistant (MDR) pathogens. In contrast, the study conducted by Rteil et al. found a high overall prevalence (31.4%) of multidrug-resistant (MDR) pathogens among hemodialysis (HD) patients [17]. Zilberman-Itskovich conducted a study which found that 35% of patients undergoing haemodialysis were infected with multidrug-resistant organisms (MDROs) [31]. Moreover, the presence of multi-drug

resistant (MDR) pathogens is linked to increased mortality, as stated by Rteil et al. [**17**]. This suggests there is a need for early initiation of most appropriate broad spectrum empirical antimicrobial therapy, considering local resistance patterns, followed by prompt de-escalation based on culture reports [32]. Timely and appropriate antibiotic therapy is most beneficial for critically ill patients suffering from septic shock or severe sepsis. Multiple studies have documented that early and appropriate antimicrobial therapy in critically ill patients leads to a decrease in hospital stay duration and mortality rate [**33**]. The current study identified amoxicillin-clavulanic acid, linezolid, and vancomycin as the most effective options for empirical treatment of gram-positive bacterial infections in critically ill patients. For gram-negative pathogens, carbapenems and piperacillin-tazobactam were found to be the optimal choices. Our study also has demonstrated that colistin and tigecycline exhibit 100% sensitivity against gram-negative pathogens, however, their use as empirical drugs is restricted because of their potential toxic effects and are reserved for patients infected by pathogens that are resistant to all classes of antibiotics [**34**]. Khilnani et al. recommended vancomycin as the preferred antibiotic for treating BSI caused by methicillin-resistant Staphylococcus aureus (MRSA), while linezolid and daptomycin are considered effective alternative options [**35**]. Empirical therapy for gram-negative bacteria typically involves the administration of a fourth-generation cephalosporin, a carbapenem, or a combination of a β-lactam/β-lactamase inhibitor. In some cases, an aminoglycoside may also be included [**35**]. Niederman MS et al. advocate for the use of similar empirical antimicrobial therapy guidelines [**36**].

We conducted an analysis of the individual risk factors associated with mortality. The findings of our study indicate that older individuals had a lower survival rate compared to younger individuals (non-survival, 63±13 vs survival 57±15). Additionally, patients with septic shock, chronic neurological disease, mechanical ventilation, longer hospital stays, elevated c-reactive protein, increased serum lactate, higher neutrophil count, elevated bilirubin levels, decreased serum creatinine, decreased platelet levels, and end organ dysfunction also had lower survival rates. These findings were corroborative to findings of several studies [37–40].

5. Conclusions And Implications

Our research emphasizes the importance of BSI, particularly sepsis and septic shock in hemodialysis patients in Sohar hospital, Oman. BSIs were predominant in older people, especially with comorbidities. *Coagulase negative staphylococci (CONS)* and *S. aureus* were the predominant pathogens associated with BSI. Prolonged length of hospital stays, mechanical ventilation, and surgical intervention were the noted risk factors for adverse outcomes. Septic shock, neutrophilia, coagulation abnormality, increased serum lactate, bilirubin, c-reactive protein, and decreased platelet and serum creatinine level were the most significant indicators of mortality. These findings emphasize the immediate requirement for efficient surveillance, administration, and infection control strategies to decrease the impact of BSI and its associated complications in hemodialysis patients.

Sohar hospital's infection control measures must be strengthened by developing stringent hygiene protocols, optimising hand hygiene practices, and ensuring correct sterilisation processes. The method will help to minimise the number of healthcare associated infections and increase overall patient safety. Moreover, implementing quick bacterial identification techniques and antibiogram testing will assist in the timely and accurate detection of illnesses. This innovation will allow for the timely beginning of suitable empirical medication, improving patient outcomes and misnaming the spread of resistance bacteria. Moreover, serum procalcitonin measurement should be combined with serum lactate estimation in all patients suspected of having sepsis. These biomarkers are crucial of mortality and can guide successful treatment decisions, which will assist develop strong management guidelines and eventually reducing sepsis-related mortality.

Our study has few limitations. Firstly, the retrospective design and reliance on data from the health registry. Furthermore, because of the retrospective nature of the study, there is a lack of information on several crucial predictors of sepsis and mortality such as procalcitonin. Secondly, there is a lack of molecular characterization of antibiotic resistance mechanisms and insufficient follow-up data on patient outcomes after they are discharged from the hospital. Finally, our study

has a retrospective design and was conducted at a single center. Therefore, the generalizability of our findings may be limited, and the results of the study should be confirmed by a multicenter study. Future researchers should overcome these constraints by constructing multicenter prospective studies that increase the generalizability of findings while minimizing the biases inherent in retrospective methods. Comprehensive biomarkers tests, which include procalcitonin and other pertinent indications, will help to identify sepsis and its predictors. Moreover, molecular research of antibiotic resistance mechanisms will provide insights into the mechanisms hat drive resistance and lead more effective treatment techniques. To expand the evidence base even more, researchers should conduct enhanced longitudinal follow-ups on patients, collecting thorough data on long-term outcomes and treatment efficacy over time. The strategy will result in a more comprehensive understanding of sepsis management and patient recovery pathways, ultimately leading to better clinical practices and patient care.

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