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Prevalance of Sepsis in Chronic Hemodialysis Patients and its Management

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ABSTRACT

Background: Sepsis is a major cause of morbidity and mortality in patients undergoing maintenance hemodialysis due to repeated vascular access, impaired immune function, and frequent healthcare exposure. Understanding the prevalence, microbial spectrum, and antibiotic sensitivity patterns of sepsis in this population is essential for improving infection control and treatment outcomes. Objectives of this study are to determine the frequency of sepsis in patients undergoing chronic hemodialysis and to identify the common causative organisms along with their antibiotic sensitivity patterns. **Methods:** This descriptive cross-sectional study was conducted in the Department of Nephrology at Pakistan Institute of Medical Sciences (PIMS) from May to December 2024. Non-probability consecutive sampling technique was employed to select 165 patients who were aged 18 to 65 years who were on maintenance hemodialysis. Sepsis was diagnosed using Sequential Organ Failure Assessment (SOFA) criteria in the presence of infection along with Systemic Inflammatory Response Syndrome (SIRS), qSOFA score, and serum lactate levels. Microbiological analysis of blood cultures was done on periphery veins and central veins catheters. Standard microbiological identification was done, and testing of antibiotic susceptibility was done as per the Clinical and Laboratory Standards Institute (CLSI) 2022 guidelines. The SPSS version 25 was used to analyze the data. **Results:** Among 165 hemodialysis patients, the mean age was 41.55 ± 13.63 years. Sepsis was identified in 46 patients, yielding a prevalence of 27.9%. Staphylococcus species were the most frequently isolated organisms (52.2%), followed by gram-negative bacteria (30.4%) and Streptococcus species (17.4%). Imipenem (63.0%) and vancomycin (54.3%) showed the highest antibiotic sensitivity, whereas cephazolin (10.9%) and ceftriaxone (13.0%) showed low sensitivity. Methicillin resistance was observed in 65.2% of isolates. A significant association was found between CKD Stage 5 and sepsis ($p = 0.038$).**Conclusion:** Sepsis is a frequent complication in patients receiving maintenance hemodialysis, mostly with gram-positive pathogens. The high level of antimicrobial resistance underlines the role of the prevention of infections and local antibiogram to implement the most effective empirical treatment.

INTRODUCTION

Hemodialysis is the standard method of treatment for patients diagnosed with end-stage renal disease (ESRD). Approximately 90% of those requiring dialysis undergo hemodialysis [1]. The mortality rate for sepsis among patients with end-stage renal disease (ESRD) was 49.04% during their hospitalization, compared to 31.78% for patients without ESRD. Septic patients with end-stage renal disease (ESRD) had 1.44 times higher likelihood of mortality during their hospitalization compared to septic patients without ESRD [2].

Sepsis is a prominent factor contributing to hospitalization and mortality rates in those undergoing hemodialysis. Risk factors for sepsis in haemodialysis patients include a past infection with methicillin-resistant Staphylococcus aureus (MRSA), hypoalbuminemia, diabetes mellitus, anaemia, malnutrition, or bacteremia. Among haemodialysis patients with bloodstream infections (BSIs), gram-positive bacteria, such as Staphylococcus aureus and coagulase-negative staphylococci, are the most frequently detected [3,4].

Due to the high colonisation pressure that allows for "patient-to-patient transmission" of MDROs and the high selective pressure that allows for "emergence of resistance" among the patient's own non-MDRO susceptible strains, MDRO infections are relatively common among dialysis patients [5,6]. Individuals with sepsis in hemodialysis patients had a three-fold higher likelihood of mortality compared to individuals without sepsis.

Patients who meet at least two of the following clinical criteria, known as quick SOFA (qSOFA), are likely to experience negative consequences commonly associated with sepsis: a respiratory rate of 22/min or higher, altered mental state, or a systolic blood pressure of 100 mm Hg or below. Achieving a SOFA score of 2 or above indicates a mortality risk of around 10% in a broad community of patients in a hospital setting who are believed to have an infection [7].

Because of the high risk of sepsis in hemodialysis patients, the antibiotic resistance, the specific challenges in identifying and managing sepsis in these patients and influence of sepsis on death rates worldwide, it is necessary to conduct research on sepsis in this population. The findings of the research may guide the development of more effective diagnostic techniques, individual treatment strategies, and eventually improved patient outcomes in high-risk population.

MATERIAL AND METHODS

The study was a descriptive cross-sectional study carried out in the Department of Nephrology at the Pakistan Institute of Medical Sciences (PIMS) from 1st May 2024 to 1st December 2024 after getting approval from CPSP. The target group included adult patients who were on maintenance hemodialysis in the nephrology department at the time of the study. The WHO sample size calculator was used to determine the sample size of 165 patients using non-probability consecutive sampling technique and sample size was calculated keeping confidence interval as 955 whereas margin of error was 7% and expected prevalence of sepsis kept as 29.8% [19]. The study included patients aged between 18 and 65 years who were taking maintenance hemodialysis, both males, and females. The patients awaiting renal transplantation, patients with autoimmune syndromes like systemic lupus erythematosus (SLE), patients at the terminal stage of malignancy, and the patients with terminal illnesses or with chronic conditions that severely weaken the immune system were not included in the study.

Operationally defined variables used in this research were maintenance hemodialysis which was defined as hemodialysis done at least two times in a week with a minimum of six months. The SOFA criteria were used to define sepsis in the presence of infection and the Systemic Inflammatory Response Syndrome (SIRS). SIRS was deemed when the following criteria were met: body temperature had to be either above 38 C and below 36 C, heart rate had to be above 90 beats per minute, respiratory rate had to be above 20 breaths per minute and arterial PaCO 2 had to be less than 32 mmHg, or greater than 12 × 10 3/ uL, or greater than 4 × 10 3/ uL or greater than 10%. Moreover, an increase of two or more points in the SOFA score was a diagnostic instrument of sepsis. Sepsis evaluation also included qSOFA scoring, which is where a qSOFA score 2 or above or serum lactate level above 2 mmol/L favors the diagnosis.

In the case of microbiological assessment, the blood culture samples were collected at the peripheral vein and available central venous catheters when available. Using the collected samples, suitable media was used to culture them in order to enable the growth of organisms. Isolated organisms were characterized using the conventional microbiological methodologies such as gram staining. Following the isolation of the organism in blood cultures, susceptibility analysis was performed using the Clinical and Laboratory Standards Institute (CLSI) 2022 guidelines on some selected antibiotics whose zone of inhibition breakpoints were available.

All data collected were analyzed and inputted by use of Statistical Package of Social Sciences (SPSS) version 25. The quantifiable variables such as age, period of disease, period of dialysis, SOFA score, qSOFA score, CRP level, hematology parameters, white blood cell count, temperature, heart rate, respiratory rate, and BMI were given as mean and standard deviation. The qualitative variables like gender, marital status, residential location, comorbid conditions and the stage of chronic kidney disease were expressed in the form of frequencies and percentages. Frequencies and percentages were also used in reporting the prevalence of sepsis, types of septic organisms, and patterns of antibiotic resistance. The possible effect modifiers such as age, gender, marital status, BMI, comorbidities, and years of dialysis were regulated by the stratification. To establish the relationship between these variables and the outcome variable (sepsis), post-stratification chi-square was used. The p-value of 0.05 was taken to be statistically significant.

RESULTS

A total of 165 patients receiving maintenance hemodialysis were included in the study. The mean age of the patients was 41.55 (SD13.63) years with an average duration of the disease being 8.51 (SD4.12) years. The average length of dialysis was 36.35 (SD14.75) months. The mean values of the two parameters, the SOFA and the qSOFA scores, were 5.02 ±3.01 and 1.65 ±1.09 respectively. Inflammatory markers revealed elevated mean CRP levels (105.85 ±57.03 mg/L) and mean WBC count of 12.31 ±4.39×10^3 /uL. Detail analysis on quantitative variables is presented in table 1. Females were 52.7% of the study population. Most patients were aged between 41 - 65 years (56.4%) and 75.8% were on dialysis for more than 24 months. Stage 4 CKD was found in 52.1% of the patients. The most common comorbidity was CVA (60%), followed by diabetes mellitus (52.1%) and ischemic heart disease (50.9%). Detailed analysis of qualitative variables is shown in table 1.

Out of 165 maintenance hemodialysis patients, an overall 46 (27.9%) patients were diagnosed with sepsis and 72.1% did not meet sepsis criteria (table 3). Among septic patients, Staphylococcus species were the most commonly isolated organisms (52.2%), followed by gram-negative bacteria (30.4%) and Streptococcus species (17.4%) See table 4. Imipenem showed the highest rate of sensitivity (63.0%) followed by vancomycin (54.3%). Low sensitivity was present for cephazolin (10.9%), ceftriaxone (13.0%) and beta-lactam combinations (19.6%). Methicillin resistance was found for 65.2% of isolates. Detailed sensitivity and resistivity analysis of different antibiotics is shown in table 5. Sepsis was more common in females (63.0%) than in males (37.0%), but this difference was not significantly different (p = 0.099). A statistically significant correlation was found between

CKD stage and sepsis (p = 0.038). Patients with Stage 5 CKD had a greater proportion of sepsis (60.9%) than did patients with Stage 4 CKD (39.1%). Disease duration (>7 years) and COPD were found to have borderline relationships with sepsis (p = 0.075 and p = 0.053, respectively). No statistically significant associations were found between sepsis and age group, marital status, BMI, dialysis duration, hypertension, diabetes mellitus, ischemic heart disease, cerebrovascular accident, smoking status, thyroid disease, PCOD or other comorbidities (p > 0.05). Detailed stratification analysis can be seen in table 6.

Table 1

Mean ± SD values for various Quantitative Variables among all study subjects (n = 165)

Variable	Minimum	Maximum	Mean ± SD
Age (years)	18	65	41.55 ± 13.63
Duration of Disease (years)	1.2	15.0	8.51 ± 4.12
Duration of Dialysis (months)	6	59	36.35 ± 14.75
SOFA Score	0	10	5.02 ± 3.01
qSOFA Score	0	3	1.65 ± 1.09
CRP (mg/L)	6.1	199.6	105.85 ± 57.03
Hematocrit (%)	25.4	44.9	34.83 ± 5.69
WBC ($\times 10^3/\mu L$)	3.7	19.6	12.31 ± 4.39
Temperature (°C)	36.0	40.0	37.90 ± 1.18
Heart Rate (beats/min)	61	140	102.00 ± 22.28
Respiratory Rate (breaths/min)	14	30	21.99 ± 4.88
BMI (kg/m^2)	18	35	26.57 ± 5.08

Table 2

Qualitative Variables (n = 165)

Variable	Category	Frequency (n)	Percentage (%)
Gender	Female	87	52.7
	Male	78	47.3
Age Group	18–40 years	72	43.6
	41–65 years	93	56.4
Marital Status	Married	83	50.3
	Unmarried	82	49.7
Location	Rural	85	51.5
	Urban	80	48.5
BMI Group	Normal	68	41.2
	Overweight	48	29.1
	Obese	49	29.7
Disease Duration Group	1–7 years	68	41.2
	>7 years	97	58.8
Dialysis Duration	6–24 months	40	24.2
	>24 months	125	75.8
CKD Stage	Stage 4	86	52.1
	Stage 5	79	47.9
COMORBID			
HTN	Yes	75	45.5
	No	90	54.5
DM	Yes	86	52.1
	No	79	47.9
IHD	Yes	84	50.9
	No	81	49.1
COPD	Yes	81	49.1
	No	84	50.9
CVA	Yes	99	60.0
	No	66	40.0
Smoking	Yes	73	44.2
	No	92	55.8
PCOD	Yes	40	24.2
	No	125	75.8
Thyroid Disease	Yes	69	41.8
	No	96	58.2
Other Comorbidities	Yes	77	46.7
	No	88	53.3

Table 3

Prevalence of sepsis among hemodialysis patients (n = 165)

Sepsis Status	Frequency (n)	Percentage (%)
No	119	72.1
Yes	46	27.9
Total	165	100.0

Table 4

Distribution of Organisms in Septic Patients (n = 46)

Organism Isolated	Frequency (n)	Percentage (%)
Staphylococcus	24	52.2
Gram-negative bacteria	14	30.4
Streptococcus	8	17.4
Total	46	100.0

Table 5

Antibiotic Sensitivity Pattern among Septic Patients (n = 46)

Antibiotic	Sensitive n (%)	Resistant n (%)
Methicillin	16 (34.8%)	30 (65.2%)
Piperacillin/Tazobactam	9 (19.6%)	37 (80.4%)
Ampicillin/Sulbactam	9 (19.6%)	37 (80.4%)
Cephazolin	5 (10.9%)	41 (89.1%)
Ceftriaxone	6 (13.0%)	40 (87.0%)
Levofloxacin	12 (26.1%)	34 (73.9%)
Imipenem	29 (63.0%)	17 (37.0%)
Meropenem	15 (32.6%)	31 (67.4%)
Vancomycin	25 (54.3%)	21 (45.7%)
Co-trimoxazole	13 (28.3%)	33 (71.7%)

Table 6

Stratification analysis for various Demographic and Clinical Variables (n = 165)

Variable	Category	Sepsis No n (%)	Sepsis Yes n (%)	Total (n)	p-value
Gender	Female	58 (48.7%)	29 (63.0%)	87	0.099
	Male	61 (51.3%)	17 (37.0%)	78	
Age Group	18–40	49 (41.2%)	23 (50.0%)	72	0.305
	41–65	70 (58.8%)	23 (50.0%)	93	
Marital Status	Married	57 (47.9%)	26 (56.5%)	83	0.321
	Unmarried	62 (52.1%)	20 (43.5%)	82	
BMI Group	Normal	53 (44.5%)	15 (32.6%)	68	0.373
	Overweight	33 (27.7%)	15 (32.6%)	48	
	Obese	33 (27.7%)	16 (34.8%)	49	
Location	Rural	60 (50.4%)	25 (54.3%)	85	0.651
	Urban	59 (49.6%)	21 (45.7%)	80	
Disease Duration	**>7 years**	75 (63.0%)	22 (47.8%)	97	0.075
	1–7 years	44 (37.0%)	24 (52.2%)	68	
Dialysis Duration	**>24 months**	90 (75.6%)	35 (76.1%)	125	0.951
	6–24 months	29 (24.4%)	11 (23.9%)	40	
CKD Stage	**Stage 4**	68 (57.1%)	18 (39.1%)	86	**0.038***
	Stage 5	51 (42.9%)	28 (60.9%)	79	
COMORBID					

HTN	**No**	64 (53.8%)	26 (56.5%)	90	0.751
	Yes	55 (46.2%)	20 (43.5%)	75	
DM	**No**	54 (45.4%)	25 (54.3%)	79	0.301
	Yes	65 (54.6%)	21 (45.7%)	86	
IHD	**No**	54 (45.4%)	27 (58.7%)	81	0.125
	Yes	65 (54.6%)	19 (41.3%)	84	
COPD	**No**	55 (46.2%)	29 (63.0%)	84	0.053
	Yes	64 (53.8%)	17 (37.0%)	81	
CVA	**No**	49 (41.2%)	17 (37.0%)	66	0.620
	Yes	70 (58.8%)	29 (63.0%)	99	
Smoking	**No**	67 (56.3%)	25 (54.3%)	92	0.821
	Yes	52 (43.7%)	21 (45.7%)	73	
Thyroid Disease	**No**	66 (55.5%)	30 (65.2%)	96	0.255
	Yes	53 (44.5%)	16 (34.8%)	69	
Other Comorbidities	**No**	64 (53.8%)	24 (52.2%)	88	0.853
	Yes	55 (46.2%)	22 (47.8%)	77	
PCOD (n=87 females)	**No**	34 (58.6%)	13 (44.8%)	47	0.224
	Yes	24 (41.4%)	16 (55.2%)	40	

**Statistically significant at p ≤ 0.05*

DISCUSSION

Sepsis is one of the primary causes of morbidity and mortality in patients undergoing maintenance hemodialysis. The current research paper appraised the prevalence, microbiological spectrum, and patterns of antimicrobial susceptibility of sepsis in chronic hemodialysis patients. The prevalence of sepsis was about 28% and gram-positive bacteria (mainly *Staphylococcus* species) then gram-negative and *Streptococcus*. The statistically significant correlation was found between the advanced CKD stage (Stage 5) and sepsis occurrence, which highlights the susceptibility of patients with more serious renal dysfunction. The result of our investigation aligns with that of published literature that has shown a disproportionately high rate of sepsis among dialysis patients. A cohort study carried out in a large population in the United States the authors Sarnak et al. found that infection-related hospitalization and mortality rates among hemodialysis patients were markedly higher than the general population [8]. In the same manner, Dalrymple et al. demonstrated that sepsis hospitalization was significantly higher among dialysis patients, especially those ones who had catheter-based vascular access [9]. The statistics of the United States Renal Data System (USRDS) regularly show that infection is the second most frequent cause of mortality among dialysis patients [10]. Chan et al. observed high incidences of bacteremia in hemodialysis patients in a Canadian cohort, especially when the latter had central venous catheters [11]. Similarly, Kato et al. of Japan found that mortality attributed to infection was much greater among patients with high CKD stages, and it was associated with impaired immune response and the immune dysregulation due to uremia [12].

Various regional and local studies also endorsed the findings of our study. In a multicenter study conducted in India, Jha et al. found infection to be a major complication among ESRD patients under dialysis, especially in facilities with resources constraints [13]. In a Karachi based study, Rashid S et al. established that bloodstream infections caused by catheters were mainly due to Staphylococcus aureus with a high level of antimicrobial resistance. Their report indicated that the catheter-related bloodstream infections were registered in 21 people (17.5%). CoNS at 5.9 percent was the most prevalent followed by Vancomycin-resistant Enterococcus (VRE) at 4.2 percent. There was an insignificant correlation found between catheter-related bloodstream infection and the age groups, gender, comorbidities, length of catheter inserts and haemodialysis, catheter infection site, and haemodialysis causes ($p > 0.05$) [14]. The study by Sonia et al. also revealed high levels of MRSA in dialysis patients in Pakistan. The most common bacterial infection (48.5%) in patients under haemodialysis ESRD was blood stream tunnel infection. Infective endocarditis was found to be present in 28.1 per cent of the patients, tunnel infection in 25.1% of patients and exit site infection in 23.4of the study subjects [15]. A similar study in other countries suggested a large share of hospital admission to dialysis-dependent CKD patients because of infections. The statistical analysis of the variables, as demonstrated by univariate statistics, showed a strongly correlated relationship between infection-related hospitalisations and diabetes (P=0.02) and lower concentrations of haemoglobin (P<0.0001), creatinine (P=0.045), albumin (P=0.01), and higher weight gain between dialysis sessions (P=0.01). The significant risk variables of infection-related hospitalisation in the multivariate Cox regression analysis only included haemoglobin concentration (P=0.001, RR=0.96), interdialytic weight gain (P=0.002, RR=1.38), and creatinine level (P=0.02, RR=0.99). The relative risk of infection-related hospitalisation was found to be 4.4 times greater when the haemoglobin level was less than 100 g/L (P<0.001) and when the increment of interdialytic weight was more than 4% of body weight (P=0.008). [16] Our microbiological profile is reflective of the South Asia close-by neighboring centers as gram-positives have always dominated the dialysis-related microbiological profile [17].

The sepsis-associated deaths constituted 19.7% of all deaths in the world ranging from 18-22 % as reported by global burden of disease study [18]. A research involving 870,571 hemodialysis patients, 259,686 (29.8%) of the patients had sepsis. Septic cases were higher with Hemodialysis catheter -HC (31.2%) and arteriovenous graft -AVG (30.62) in comparison to arteriovenous fistula -AVF (22.9%). The rate of incidence was 12.66 sepsis episodes per 100 personal years. The commonest microbes in HD related sepsis were streptococcus (13%), gram-negative (25%), and staphylococcus (56%). The prevalence of Staphylococcus was higher in AVF (51.2%), and in HC (56.7%) [19]. In comparative research sepsis occurred more frequently in the patients who received

maintenance haemodialysis (145.4 per 1,000 persons) compared to the general population (3.5 per 1,000) [20]. It was found that at a tertiary care hospital in Peshawar, 144/176 cultures reflected antibiotic resistance/sensitivity pattern; whereas, amikacin, gentamicin, imipenem and meropenem were most susceptible antibiotics [21].

The fact that Staphylococcus species are dominant in our cohort is biologically plausible and is consistent with previous evidence that multiple manipulations of vascular access and biofilm formation put dialysis patients at risk of gram-positive bloodstream infections [22]. The relationship between CKD Stage 5 and sepsis is most likely to be due to deep immune dysfunction in a severe renal failure, such as weak neutrophil chemotaxis, complement failure, and cellular immunity abnormalities [23]. We also obtained high susceptibility rates to carbapenems and glycopeptides, which are in line with other previous regional antibiogram reports which have indicated lower effectiveness of commonly used beta-lactams in dialysis populations because of antimicrobial resistance pressures [5,24,25]. These similarities support the external validity of our results.

Clinically, our findings indicate that improved preventive measures against infection in hemodialysis units are highly needed. It is recommended to focus on reducing the number of catheters, arteriovenous fistula formation, aseptic measures, and regular surveillance cultures where necessary. The outcome of antimicrobial resistance as observed in this study also confirms that the use of evidence-based empirical therapy through local antibiogram instead of standardized therapy is also needed. By detecting high-risk patients early, especially when in more advanced stages of CKD, it is possible that inhibitory measures can be applied specifically and preventive interventions put in place, which might help minimize the morbidity and mortality associated with infections. There are some limitations that should be considered. To begin with, the single-center design can restrict the applicability to the larger populations with various practices of infection control or microbial ecology. Second, the study is cross-sectional and cannot be used to establish causality of the risk factors and the incidence of sepsis. Third, the stratification by the type of vascular access was not completely available in detail, which can have an impact on the evaluation of infection risk. Lastly, molecular characterization of resistant organisms was out of the scope of the present research and would give important insight to prospective analyses.

CONCLUSION

The issue of sepsis is also a major clinical problem in patients receiving maintenance hemodialysis. The current research has shown that approximately one-third of hemodialysis patients developed sepsis, and Staphylococcus species became the most frequent causative organisms. Analysis of the antibiotic susceptibility showed a relatively high sensitivity towards carbapenems and glycopeptides, with less prevalence of commonly used beta-lactam antibiotics indicating a significant level of resistance. The high correlation between high CKD stage and sepsis also indicates the high susceptibility of the patients with severe renal dysfunction. The implications of these findings are the need to adhere to excellent standards of infection control, close observation of the vascular access sites, and wise administration of antibiotics as informed by local antibiograms. This high-risk population has a high likelihood of experiencing infection-related morbidity and mortality, which can be minimized by early diagnosis and antimicrobial treatment. Additional multicentric and prospective research is suggested to gain a better insight into the dynamics of infections and preventive and therapeutic effective approaches to sepsis in the hemodialysis patients.

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