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Research Article

TO STUDY THE PROFILE OF BACTERIAL INFECTIONS IN END-STAGE RENAL DISEASE PATIENTS ON MAINTENANCE HEMODIALYSIS

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ABSTRACT

Objectives: The aims and objectives of the study are to characterize bacterial infections in end-stage renal disease (ESRD) patients on maintenance hemodialysis.

Methods: This forward-looking study was carried out over the course of 1 year in the Microbiology Department. Data were collected in pre-structured proforma, which included demographic details, risk factors, investigations, laboratory parameters, follow-up, and outcomes. Samples were collected on the basis of clinical suspicion and processed according to standard protocols. Identification and antimicrobial-susceptibility of bacterial isolates were done by BACTEC and VITEK I/D system.

Results: A total of 673 cases were enrolled, out of which 166 had bacterial infections. There was an overall male preponderance (68%), and the most common age group was 61–70 years (30.1%). A total of 225 infections were observed in 203 episodes. Most common infection was urinary tract infection (54.3%). The majority of the isolates were Gram-negative bacteria (77.3%), out of which *Klebsiella pneumoniae* (36.3%) was most common. Gram-negative isolates demonstrated highest susceptibility to amikacin, gentamicin, and cefoperazone+sulbactum.

Conclusion: Infections in ESRD patients on maintenance hemodialysis are prevalent and significantly impact morbidity and mortality. Identifying infection profiles can aid in targeted interventions and improve patient outcomes.

Keywords: Hemodialysis, End-stage renal disease, Automated methods, Gram negative.

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INTRODUCTION

End-stage renal disease (ESRD) refers to a clinical condition marked by a permanent loss of kidney function, requiring long-term dependence on renal replacement therapy. The population undergoing maintenance hemodialysis is witnessing a yearly increase of 9% [1]. A variety of chronic conditions can lead to ESRD, with diabetes mellitus being the leading cause in both developed and developing countries In addition, various glomerular diseases including membranous nephropathy, immunoglobulin A nephropathy, minimal change disease, focal and segmental glomerulosclerosis, as well as tubulointerstitial diseases contribute to its etiology [2]. Dialysis patients are prone to infections due to a combination of factors including advanced age, compromised primary host defence mechanisms, and the presence of co-morbid condition such as malnutrition and diabetes-mellitus [3]. In the United States, diabetes accounts for approximately 30–40% of all cases of ESRD [4]. In these patients, septicemia stands as a significant contributor to both morbidity and mortality [5]. It emerges as common factor, contributing to 75% of fatalities [6]. Hemodialysis is a life-saving renal replacement therapy for ESRD patients. It is essential for failed kidneys those cannot perform their natural detoxifying function. This procedure involves circulating blood outside the body through a dialysis machine, and this machine is equipped with a dialyzer, referred as artificial kidney, which filters waste products, excess fluids and electrolytes from the blood [7]. In recent decades, substantial progress has been made in understanding the pathogenesis of bacterial infections in hemodialysis patients. The three key factors involved are host immunity, bacterial virulence, and the dialysis procedure [8]. Various studies report that Gram-positive bacteria make up 28–65% of the isolates in blood cultures from hemodialysis patients, while 45% of the isolates are Gram-negative bacteria. This bacterial profile is closely linked to elevated mortality rates. The occurrence of septic shock and polymicrobial infections significantly elevates mortality rates within this demographic. Nevertheless, the escalating utilization of antibiotics and frequent interaction with healthcare settings has contributed to a surge in infections caused by multidrug-resistant organisms [9]. The incidence of ESRD stabilized between 2007 and 2011 but saw an increase in 2012 from 357.2 to 372.4 cases/million annually. Data from North America indicate that the rate of bloodstream infections among hemodialysis patients varies from 0.5 to 27.1/100 patients/month, depending on the type of access used. ESRD is a progressive disorder and to prevent death in these patients, timely replacement therapy is necessary. The frequent infections associated with numerous hospitalizations, increased healthcare cost, and metabolic changes and mortality rate are significantly higher in these patients than those without disease [10].

This introduction effectively sets the stage for a study on infections in ESRD patients undergoing hemodialysis by highlighting the growing prevalence of ESRD and its significant health burden. It brings novelty by integrating contemporary insights into the rising incidence of ESRD, advancements in dialysis procedures, and the increasing prevalence of multidrug-resistant infections. The mention of specific bacterial profiles (Gram-positive and Gram-negative) and their link to mortality rates provides a focused and modern perspective.

Therefore, this study was designed to examine the incidence and profile of various infections in patients with ESRD undergoing maintenance hemodialysis.

METHODS

This prospective study was approved by institutional ethical committee vide letter number: DMCH/P/2022/988–9. Patients who underwent

dialysis over a 1-year period (October 2022–September 2023) were enrolled and followed for an additional 6 months. A total of 673 patients were enrolled from the outpatient department of Nephrology. The study involved adult patients (aged 18 years and older) with ESRD who were receiving regular maintenance hemodialysis. Exclusion criteria included pregnant women, prior kidney transplant patients, and patients with acute kidney injury. Data were collected using a pre-structured proforma, capturing demographic details, risk factors (old age, comorbidities, malnutrition, and immune-compromised state), and the dates of catheter insertion and removal. Various samples were collected and sent to the microbiology laboratory for processing according to standard protocols. Direct microscopy was performed based on clinical suspicion. Blood and body fluid specimens were processed in BACTEC 9240/BacT/Alert systems and incubated for up to 7 days. Smears were prepared from positive blood culture bottles and sub-cultured on solid media. Identification and antibiotic sensitivity testing of the isolates were conducted using the VITEK 2 system. Further infections were characterized and correlated with the clinical profile of patients.

Statistical analysis

Data were presented as ranges, means±standard deviations, frequencies (number of cases), and relative frequencies (%), as applicable. All statistical analyses will be conducted using the Statistical Package for the Social Sciences, specifically version 21 for Microsoft Windows.

RESULTS

Out of 673 enrolled patients, 166 were observed with bacterial infections. Majority of these patients were male 112 (67.5%) and the most affected age group was 61–70 years. These patients were presented with fever 162 (97.6%) and cough 119 (71.6%). Hypertension 96 (57.6%) and diabetes 92 (55.4%) were prevalent co-morbidity factor among these patients. Anemia 141 (84.9%) and hypotension 105 (63.2%) were observed a major risk factor contributing to infections. Maximum number of patients had albumin level within 3.5–3.9 g/dL. A significant proportion of patients diagnosed with bacterial infections was within the first 3 months of starting dialysis. Majority of patients were undergoing dialysis twice a week 57 (34.3%). The majority of patients had vascular access through arteriovenous fistula, while bloodstream infections were predominantly observed in those with temporary catheterization. In 166 patients, 135 (66.5%) had a single episode of infection, while 31 had 68 (33.5%) multiple episodes. Thus, total of 203 episodes were observed in 166 patients.

In 203 episodes of infection, the maximum number of episodes (57.6%) occurred in the 1st month of follow-up. Out of 203 episodes, single-site infections accounted for 182 (89.6%), while 21 (10.4%) were multi-site. Thus, in total of 225 infections, 120 (53.4%) infections were acquired in the community, and 105 (46.6%) were nosocomial. The most frequently observed infection was urinary tract infection (UTI), with 99 cases (54.3%), followed by respiratory tract infections, which accounted for 32 cases (17.6%). Bloodstream infections were mostly observed in patients with tunneled catheter vascular access (10.8%) (Fig. 1).

Out of 225 infections, 208 (92.4%) were monomicrobial, and 17 (7.6%) were polymicrobial. Hence, total of 242 isolates were obtained. The majority of isolates were Gram-negative 187 (77.3%), with *Klebsiella pneumoniae* 68 (36.3%) and *Escherichia coli* 60 (32%) being the most predominant. Among Gram-positive isolates, Coagulase-negative staphylococci 21 (38.1%) and *Enterococcus* spp. 25 (34.5%) were most common (Table 1).

In UTIs, Gram-negative isolates showed maximum susceptibility to fosfomycin (86.5%) and nitrofurantoin (64.6%), with the lowest susceptibility to ciprofloxacin (18.2%) and ceftriaxone (19.2%). In respiratory tract infections, high susceptibility was observed to colistin (85.7%) and cefoperazone-sulbactam (59.5%), while low susceptibility was noted to ciprofloxacin (16.6%) and cefuroxime (23.8%) (Figs. 2 and 3). Multidrug resistance was observed in 200 (82.6%) isolates, whereas 180 (74.3%) were extensively drug resistant. Among 166 patients, 21 (12.6%) expired, while 145 (87.3%) patients were survived.

In comparison of patient with infections 166 and without infection 507, we observed that the mean age of patients with infection (57.41 years) was significantly higher than that of patients without infection (54.86 years), with a p=0.01. Diabetes mellitus was more prevalent in patients with infection (81.3%) than in those without (67%), with a p=0.001. Hypotension and fluid overload were notably more prevalent in patients with infections (63.2% and 60.8%, respectively) compared

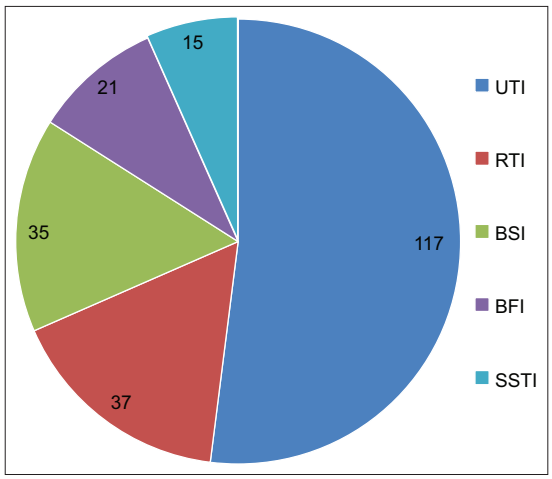

Fig. 1: Distribution of bacterial infections (n=225)

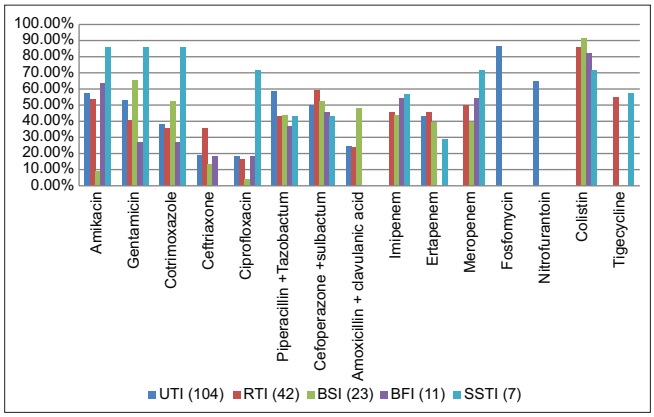

Fig. 2: Antibiotic susceptibility profile of Gram-negative isolates (n=187)

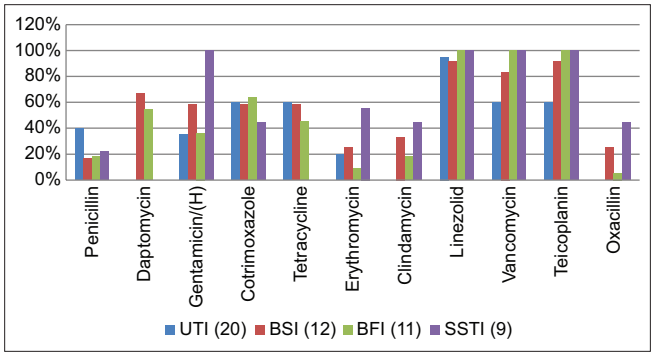

Fig. 3: Antibiotic susceptibility profile of Gram-positive isolates (n=55)

Table 1: Distribution of organisms in patients with bacterial infection (n=242)

Organism	UTI (n=125)	RTI (n=44)	BSI (n=35)	BFI (n=22)	SSTI (n=16)	Total (n=242)
Gram negative (n=187)	n (%)					
Klebsiella pneumoniae	37 (29.6)	19 (43.1)	8 (22.8)	1 (4.5)	3 (18.7)	68 (36.3)
Escherichia coli	43 (34.4)	6 (13.6)	5 (14.2)	3 (13.6)	3 (18.7)	60 (32)
Pseudomonas aeruginosa	14 (11.2)	7 (15.9)	3 (8.5)	3 (13.6)	-	27 (14.4)
Acinetobacter baumannii	2 (1.6)	9 (20.4)	1 (2.8)	3 (13.6)	-	15 (8)
Burkholderia cepacia	-	-	3 (8.5)	-	-	3 (1.6)
Proteus mirabilis	3 (2.4)	-	-	-	-	3 (1.6)
Enterobacter cloacae	1 (0.8)	-	1 (2.8)	-	-	2 (1)
Enterobacter aerogenes	1 (0.8)	1 (2.3)	-	-	-	2 (1)
Enterobacter gallinarum	1 (0.8)	-	-	-	-	1 (0.5)
Achromobacter xylosoxidans	-	-	2 (5.7)	-	-	2 (1)
Morganella morganii	-	-	-	-	1 (6.2)	1 (0.5)
Sphingomonas paucimobilis	-	-	-	1 (4.5)	-	1 (0.5)
Serratia liquefaciens	1 (0.8)	-	-	-	-	1 (0.5)
Citrobacter koseri	1 (0.8)	-	-	-	-	1 (0.5)
Gram Positive (n=55)						
Enterococcus faecium	14 (11.2)	1 (2.3)	1 (2.8)	2 (9)	1 (6.2)	19 (34.5)
Enterococcus faecalis	2 (1.6)	-	2 (5.75)	1 (4.5)	1 (6.2)	6 (10.9)
Staphylococcus aureus	1 (0.8)	-	3 (8.5)	2 (9)	3 (18.7)	9 (16.3)
Coagulase-negative staphylococci	4 (3.2)	1 (2.3)	6 (17.1)	6 (27.2)	4 (25)	21 (38.1)

UTI: Urinary tract infection, RTI: Respiratory tract infection, BSI: Bacterial bloodstream infection, BFI: Bacterial and fungal infection, SSTI: skin and soft-tissue infection

to those without infections (42.4% and 37.2%, respectively), both with a p=0.001. Duration of dialysis showed significant differences between the two groups, with patients with infections having higher proportions in the 0–3-month and 6–12-month category (p=0.014). Mortality rates were significantly elevated in patients with infections (12.6%) compared to those without infections (5.3%), yielding a p=0.002 (Table 2).

DISCUSSION

A total of 673 cases were enrolled and monitored over a 6-month period. The majority of the patients were male (68%), compared to females (32%), consistent with the findings of Dalgaard *et al*. (62.8%) [10], but in contrast with a study conducted in Taiwan (males = 43.4%, females = 56.6%) [3]. The majority of patients were in the age group of 61–70 years (30.1%), followed by those aged 51–60 years (26.4%), consistent with findings from a study conducted in the United States [11].

Among 673 patients, 166 patients with bacterial infections, 67.5% were male and 32.5% were female, contrasting with a study in Birmingham where females were predominant (56.6%) [12]. The most affected age group was 61–70 years (36.9%), similar to findings by Steven [13]. Fever (97.6%) was the most common symptom associated with bacterial infections a finding supported by Jessica *et al.* [14]. Hypertension (57.8%) was the most prevalent comorbidity, consistent with a study by Dayana *et al*. [9]. Anemia was the most prevalent risk factor among patients with bacterial infections, which aligns with the findings of a study by Shu Hong *et al*. [15].

In 166 patients, 203 episodes were recorded, with a rate of 5.7 episodes per 1000 dialysis days, similar to findings from a study in Hawaii [13]. Out of 203 infection episodes, 225 bacterial infections were observed, with UTIs (54.3%) being the most common, whereas respiratory tract infections (32.7%) were reported by Ali *et al*. [16]. Among 242 isolates, Gram-negative bacteria accounted for 77.3% and Gram-positive bacteria accounted for 22.3%, similar to findings by Peter *et al*. [17].

The predominant Gram-negative isolates were *K. pneumoniae* (36.3%) and *E. coli* (32%), contrasting with a study in Ghana and Tamil Nadu where *Acinetobacter baumannii* (17.6%) and *E. coli* (68.8%) were most predominant [17,18]. The most predominant Gram-positive organism was *Enterococcus faecium* (34.5%), followed by *Enterococcus faecalis* (10.9%), differing from a tertiary hospital study where CoNS (20.6%) and *Staphylococcus aureus* (14.7%) were most common [17].

The predominant isolates in central line-associated bloodstream infections were *K. pneumoniae* (22.8%) and CoNS (17.1%), contrasting with a study in Uttar Pradesh where CoNS (61.9%) and *A. baumannii* (11.9%) were reported. Another study by Berman *et al*. found CoNS followed by *S. aureus* as the most common pathogens in bloodstream infections among patients on hemodialysis [13]. Gram-negative isolates showed maximum sensitivity to colistin (91.3%), and CoNS to linezolid (100%), similar to findings by Abhilash *et al*. [19]. In this study, 82% of isolates were multi-drug resistant, consistent with findings by Edoh *et al*. (MDR=73.9%) [20]. Methicillin-resistant *Staphylococcus aureus* (MRSA) was found in 33.3% of cases and MR-CoNS in 35%, differing from a study by Edmond *et al*. where MRSA was 29.3% and MR-CoNS was 80% [21]. This highlights the importance of initiating broad-spectrum empirical antimicrobial therapy, followed by de-escalation once culture results are available. Vancomycin-resistant enterococci (VRE) was found in 11% of cases, similar to a study by Smout *et al*. (VRE=12.4%) [22].

The majority of infections were community acquired (53.3%) compared to hospital-acquired (46.6%). Gram-negative isolates were predominant in community-acquired infections (50.8%), similar to findings from St. Francis Renal Institute, where 82% of infections were community acquired, predominantly caused by Gram-negative isolates (55%) [13]. In this study, advanced age (61–70 years) was a significant risk factor for mortality (p=0.01), consistent with findings by Rojas *et al*. In addition, bloodstream infections were the most frequent complication in patients with temporary catheters, aligning with results from a study by Sarnak *et al*. [23].

In comparison of patient with infections 166 and without infection 507, we observed that the mean age of patients with infection (57.41 years) was significantly higher than that of patients without infection (54.86 years), with a p=0.01 indicating high significance, which is similar to study done at Massachussets [23]. Diabetes mellitus was more prevalent in patients with infection (81.3%) than in those without (67%), with a p=0.001. This is consistent with other studies by peter puplampu showing higher rates of diabetes among infected hemodialysis patients [17]. Patients with infections experienced significantly higher rates of hypotension (63.2%) and fluid overload (60.8%) compared to those without infections (42.4% and 37.2%, respectively), with both differences showing a p=0.001. These findings are supported by research highlighting these conditions as common co-morbidities in infected patients. Duration of dialysis showed significant differences between the two groups, with patients with infections having higher proportions in the 0–3-month and 6–12-month categories

Table 2: Comparison of various factors in patients with infection (n=166) and without infection (n=507)

Factors	With infection (%)	Without infections (%)	p-value	Significance
Age (mean)	57.41±12.5	54.86±14.2	0.01	HS
Sex (M/F)	112/54	347/160	0.89	NS
Comorbidity				
Hypertension	120 (72.2)	406 (80)	0.01	HS
Diabetes mellitus	135 (81.3)	340 (67)	0.001	HS
Cardiovascular disease	33 (19.8)	85 (16.7)	0.036	HS
Risk factors				
Anemia (Mean Hb-8.29 g/dL)	141 (84.9)	426 (84)	0.874	NS
Hypotension	105 (63.2)	215 (42.4)	0.001	HS
Fluid overload	101 (60.8)	189 (37.2)	0.001	HS
Albumin values (g/dL)	(n=140)	(n=264)		
<2.5	28 (20)	39 (7.69)		
2.5–3	35 (25)	63 (12.4)	0.137	NS
3–3.4	40 (28.5)	64 (12.6)		
3.5–3.9	30 (21.5)	68 (13.4)		
>4	7 (5)	30 (5.9)		
Duration of dialysis				
0–3 month	56 (33.7)	138 (27.2)	0.014	HS
3–6 months	12 (7.2)	51 (10.5)		
6–12 months	36 (21.7)	63 (12.4)		
1–2 years	23 (13.9)	83 (16.1)		
2–3 years	23 (13.9)	105 (20.2)		
3–4 years	12 (7.2)	57 (11.7)		
>4 years	4 (2.4)	10 (1.9)		
Frequency of dialysis				
Once weekly	39 (23.5)	115 (22.6)	0.457	NS
Twice weekly	57 (34.3)	160 (31.5)		
Thrice	53 (31.9)	155 (30.6)		
Irregular	17 (10.3)	77 (15.3)		
Vascular access				
Arteriovenous fistula	60 (36.1)	210 (41.4)	0.44	NS
Non -tunneled	56 (33.7)	150 (29.6)		
Tunneled catheter	50 (30.2)	147 (29)		
Outcomes				
Transplanted	1 (0.6)	5 (0.9)	0.002	HS
Shifted outside	72 (45.3)	267 (52.6)		
Deaths	21 (12.6)	27 (5.3)		

(p=0.014). This reflects the increased vulnerability of patients early in their dialysis treatment. The mortality rate was significantly greater in patients with infections (12.6%) compared to those without (5.3%), with a p=0.002. This is in line with studies showing that infections significantly impact the survival rates of hemodialysis patients [24].

A total of 48 patients (7.1%) experienced mortality, while 625 patients (92.8%) survived, which is lower than the mortality rate reported by Muhammad *et al*. [25].

CONCLUSION

This study underscores the substantial impact of infections on patients with ESRD undergoing maintenance hemodialysis. Our findings indicate that these patients are at a heightened risk of various infections due to multiple factors. The high prevalence of multidrug-resistant organisms underscores the necessity for stringent infection control practices and targeted antibiotic stewardship. Moreover, patient education on the importance of infection prevention and timely reporting of symptoms is crucial.

A multidisciplinary approach is essential to mitigate the risk of infections in this vulnerable population. Further research is needed to implement more effective strategies to prevent and manage infections in these patients for improving patient's outcome and quality of life.

AUTHOR'S CONTRIBUTION

Dr. Sejshi: Data acquisition, data analysis, manuscript preparation, manuscript editing, and review. Dr. Veenu Gupta: Concept design, data analysis, manuscript editing, and review. Dr. Vikas Makkar: Data analysis, manuscript editing and review. Dr. Manisha Aggarwal: Data analysis, manuscript editing, and review.

CONFLICT OF INTEREST STATEMENT

None.

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None.

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