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Original Research Article

# A Hospital Based Prospective Assessment of Sepsis and its Markers in Renal Failure Patients on Hemodialysis

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**Conflict of interest: Nil**

**Abstract**

**Aim:** To study the presence of bacteremia, markers of sepsis and Inflammation in renal failure patients on hemodialysis.

**Methodology:** The present study was conducted at Department of Medicine, Darbhanga Medical College and Hospital, Darbhanga, Bihar, India for the period of 1 year. Total of 50 patients of both sexes who were diagnosed as case of renal failure which include both acute kidney injury (AKI) and CKD on basis of clinical history, examination, biochemical markers and were advised for hemodialysis were included in the study. Patients of renal failure with newly inserted hemodialysis catheter subclavian venous catheter, internal jugular venous catheter or femoral catheter who developed systemic signs and symptom of sepsis e.g. fever, chills and rigor, tachycardia, tachypnea, hypotension, confusion, disorientation, and agitation after hemodialysis catheter insertion and hemodialysis and patients with local swelling, redness, pain or pus discharge at the site of hemodialysis catheter were included in the study.

After recruiting patient for study, clinical history and relevant blood and radiological investigation were performed. After 72 hours of the insertion of catheter, subcultures were done from Hartley‘s broth onto blood agar (BA) and MacConkey medium after overnight incubation at $37^0$C and also on the 2nd, 4th and 7th days and were then discarded, if negative. Sample that yielded pure bacterial growth of ≥105 cfu/ml was regarded as significant bacteriuria. Counts between 104 and 105 cfu/ml repeated while counts ≤104 cfu/ml considered as negative.

**Results:** Among 50 patients of renal failure on hemodialysis, the mean age in our study was 43.86±13.52 years with 36 male patients. Out of 50 patients, 9 (18%) had positive blood and catheter tip culture and 41 (82%) of patients had negative blood and catheter tip culture. 7 (14%) patients had urinary tract infection, 9 (18%) patients diagnosed as catheter related blood stream infection (CRBIS) and 2 (4%) patients had pneumonia. 5 (55.6%) patients' blood culture was positive for S. aureus, and E. coli found in blood culture 2 (22.2%) patient, Acinectobacter in 1 (11.1%) patient and Candida in 1 (11.1%) patient. Among 9 patients of renal failure on hemodialysis with sepsis, 2 (22.2%) patients had internal jugular line for hemodialysis, 1 (11.1%) had subclavian line and 6 (66.7%) had femoral line for hemodialysis. Catheter duration of 7-14 days was found in 1 (11.1%), 2 (22.2%) patients had central line between 14–21 days, and 6 (66.7%) patients had central line >21 days.

**Conclusion:** Use of vascular access to deliver haemodialysis therapy in renal failure patients has increased due to which they are prone to infections because of risk factors like advanced age, male sex, diabetes, anemia, hypoalbuminemia, hyperphosphatemia and prolonged duration of hemodialysis. Gram positive cocci (S. aureus) is the commonest cause of sepsis. Sepsis was most common in patients with prolonged duration of dialysis (>21 days).

**Keywords:** Haemodialysis, peritoneum, renal diseases.



## Introduction

Sepsis is a serious medical condition and is caused by a dysregulated host response to infection. Despite advances in antibiotic therapy and life support, the fatality rate of patients with sepsis has remained at least 25% and is increasing in incidence [1]. The recognition of sepsis dates back to 2000 years, when Hippocrates claimed that sepsis was the process by which flesh rots and wounds fester [2]. After the rapid development of microbiology in the modern era, the understanding of sepsis gradually matured and medical researchers began to realize that sepsis is caused by microbial infection [3]. Sepsis is a life-threatening systemic inflammatory response to an infection that might result in organ injury, shock, or death [4, 5]. In the United States, sepsis ranks as the 10th leading cause of death, and it accounts for 10% of all ICU admissions [6, 7].

End-Stage Renal Disease (ESRD), defined as an irreversible decline in a person's kidney function, which is severe enough to be fatal in the absence of dialysis or transplantation, is a frequent comorbid factor in approximately 1 in 25 Emergency Department (ED) septic shock patients [8]. Moreover, an international surveillance investigation of hospitalised adults with septic shock identified 7.7% of patients to be on chronic dialysis [9]. Sepsis and bacterial infections are very common in ESRD patients and following cardiovascular disease; sepsis is the second leading cause of death in patients with ESRD [7, 10-12].

Gram-negative bacteria were previously the most common cause of sepsis, in the last decade, gram-positive bacteria, most commonly staphylococci cause more than 50% of cases of sepsis [13]. The type of vascular access in use also plays an important role in the subsequent development of bloodstream infections. Central venous catheters significantly increase the risk of bacteremia in hemodialysis patients. Those with temporary catheters had been shown to have a 50% higher risk of septicemia than patients with a native fistula.

Catheter-related bloodstream infection (CRBSI also called catheter-related sepsis) is defined as the presence of bacteraemia originating from a central intravenous catheter. It is one of the most frequent and lethal complications of central venous catheterization. Almost all HD catheters had biofilm formation on their surfaces and this serves as a good reservoir for microorganisms. The gold standard is the combination of a positive blood culture with the same organism isolated from the catheter [14]. The present study was conducted to study the presence of bacteremia, markers of sepsis and Inflammation in renal failure patients on hemodialysis.

## Materials and Methods

The present study was conducted at Department of Medicine, Darbhanga Medical College and Hospital, Darbhanga, Bihar, India for the period of 1 year. Total of 50 patients of both sexes who were

diagnosed as case of renal failure which include both acute kidney injury (AKI) and CKD on basis of clinical history, examination, biochemical markers and were advised for hemodialysis were included in the study.

The criteria used for AKI in the study was risk, injury, failure, loss of kidney function, and end-stage kidney disease (RIFLE) criteria [15]. The kidney disease outcomes quality initiative (KDOQI) defines CKD as either kidney damage or a decreased glomerular filtration rate (GFR) of less than 60 ml/min/1.73 $m^2$ for 3 or more months [16]. Criteria for the systemic inflammatory response syndrome, adapted from the American college of chest physicians/society of critical care medicine consensus conference [17].

Patients of renal failure with newly inserted hemodialysis catheter subclavian venous catheter, internal jugular venous catheter or femoral catheter who developed systemic signs and symptom of sepsis e.g. fever, chills and rigor, tachycardia, tachypnea, hypotension, confusion, disorientation, and agitation after hemodialysis catheter insertion and hemodialysis and patients with local swelling, redness, pain or pus discharge at the site of hemodialysis catheter were included in the study. Those patients who had renal failure due to septicemia or post-operative renal failure, had history of hemodialysis in past, had known source of infection e.g. diabetic foot, pyelonephritis, bedsore, or had A-V fistula were excluded from study.

After recruiting patient for study, clinical history and relevant blood and radiological investigation (hemoglobin, total leucocyte count (TLC), differential leucocyte count (DLC), and platelet count), renal function test (RFT) (serum creatinine, blood urea, and serum electrolyte), serum phosphorus, C-reactive protein, liver function test (LFT) (serum bilirubin, serum total protein, serum albumin, alkaline phosphatase), thyroid function test - TFT (T3, T4, and thyroid stimulating hormone-TSH), urine routine and microscopy, urine culture and sensitivity, blood culture, central line catheter tip culture sensitivity, chest X-ray (CXR) P/A view, ultrasonography (USG) abdomen and kidney, ureter and bladder (KUB) were performed. Leukocyte count and blood culture were done prior to catheter insertion and a single sample was collected from the peripheral vein before insertion of the catheter to rule out any existing bacteremia. If positive, the patient was excluded from the study.

Secondly, after 72 hours of the insertion, two 5 ml samples of blood were collected, one from the peripheral vein and the other from the catheters; the latter being collected after at least 12 hours of hemodialysis. In the laboratory, subcultures were done from Hartley‘s broth onto blood agar (BA) and MacConkey medium after overnight incubation at $37^0$C and also on the 2nd, 4th and 7th days and were then discarded, if negative [18]. Aseptically collected mid-stream urine sample in sterile bottle containing boric acid was transported to microbiology laboratory. Bacterial culture was performed by streaking 0.002 ml of mid-stream collected urine with a standard calibrated loop on MacConkey agar and 5% sheep blood agar plates which was incubated at 37ºC for 24 hours, under aerobic conditions and the colonies was counted by a colony counter. Sample that yielded pure bacterial growth of ≥105 cfu/ml was regarded as significant bacteriuria. Counts between 104 and 105 cfu/ml repeated while counts ≤104 cfu/ml considered as negative [19].

Catheter tip was collected only from patients who had their catheters removed on completion of their HD sessions or in case they showed any signs of infection. It was cultured by Maki’s standard semi quantitative method on blood agar and

then put in trypticase soy broth (TSB). A colony count of ≥15 was considered significant for cultures done by Maki's method [18]. If the same organisms grew from both peripheral and central venous catheter (CVC) blood cultures confirmation was done by the pour-plate quantitative method [20]. Association and correlation assessment were done by statistical package for the social sciences (SPSS).

## Results

Among 50 patients of renal failure on hemodialysis, the mean age in our study was 43.86±13.52 years with 36 male patients. Out of 50 patients, 9 (18%) had positive blood and catheter tip culture and 41 (82%) of patients had negative blood and catheter tip culture. Out of 9 patients with sepsis, 3 (33.3%) were in the age group between 15–25 years, 2 (22.2%) were in the age group between 26–45 years, 1 (11.1%) were in the age group 36–45 years and 3 (33.3%) were above 45 years of age. All 9 (100%) patients had episode of fever with chills and rigor, 4 (44.4%) patients had redness and pain at hemodialysis catheter site, 3 patients (33.3%) were confused, disoriented or comatose and 2 patients (22.2%) had hypotension. 7 (14%) patients had urinary tract infection, 9 (18%) patients diagnosed as catheter related blood stream infection (CRBIS) and 2 (4%) patients had pneumonia.

Among 9 patients of renal failure with sepsis, none had TLC less than 4.8/cumm (leucopenia), 2 (22.2%) patients had count between 4.8–10.8/cumm and 7 (77.8%) patients had TLC more than 10.8/cumm. 5 (55.6%) patients' blood culture was positive for S. aureus, and E. coli found in blood culture 2 (22.2%) patient, Acinectobacter in 1 (11.1%) patient and Candida in 1 (11.1%) patient. Among 9 patients of renal failure on hemodialysis with sepsis, 2 (22.2%) patients had internal jugular line for hemodialysis, 1 (11.1%) had subclavian line and 6 (66.7%) had femoral line for hemodialysis. Catheter duration of 7-14 days was found in 1 (11.1%), 2 (22.2%) patients had central line between 14–21 days, and 6 (66.7%) patients had central line >21 days.

Out of 9 patients of renal failure on hemodialysis with sepsis, none had serum phosphate level less than 3.5 mg/dl, 3 (33.3%) had serum phosphorus level between 3.5–5.5 mg/dl and 6 (66.7%) patients had serum phosphorus level >5.5 mg/dl. Albumin level less than 3.4 gm/dl was found in 6 patients (66.7%), 3 (33.3%) had serum albumin level more than 3.4 gm/dl.

**Table 1: Patients with positive blood/catheter tip culture among 50 patients of renal failure patients on hemodialysis.**

| Parameter | Renal failure patients on hemodialysis with symptoms of sepsis | |
|---|---|---|
| | N | % |
| Positive blood/catheter tip culture | 9 | 18 |
| Negative blood/catheter tip culture | 41 | 82 |
| Total | 50 | 100 |

**Table 2: Type of organism found in blood culture among 15 patients of renal patients on hemodialysis with sepsis.**

| Type of bacteria | Renal failure patients on hemodialysis with sepsis | |
|---|---|---|
| | N | % |
| *S. aureus* | 5 | 55.6 |
| *E. coli* | 2 | 22.2 |
| *Acinectobacter* | 1 | 11.1 |

| | | |
|---|---|---|
| *Candida* | 1 | 11.1 |
| Total | 9 | 100 |

**Table 3: Site of hemodialysis catheter among 15 patients of renal patients on hemodialysis with sepsis.**

| Site of hemodialysis catheter | Renal failure patients on hemodialysis with sepsis | |
|---|---|---|
| | N | % |
| Internal jugular venous catheter | 02 | 22.2 |
| Femoral catheter | 06 | 66.7 |
| Subclavian catheter | 01 | 11.1 |
| Total | 09 | 100 |

## Discussion

One of the most serious and life threatening infections in dialysis patients is septicemia. Several clinical, treatment, and sociodemographic characteristics make end stage renal diseases (ESRD) patients particularly susceptible to septicemia. Uremia often results in immune deficiency [21]. Malnourishment and older age may interact with uremia to impair the immune system further and to increase the risk of infection in patients with ESRD [22]. Risk may also vary according to the presence of comorbid conditions such as diabetes mellitus (DM) and disruptions of dermal barriers to gain access for dialysis. In peritoneal dialysis (PD), infection may occur through either the catheter entrance through the skin or the peritoneal cavity [23]. In hemodialysis (HD) patients, infection may occur from the need for intravascular catheters to perform dialysis [24]. Infection may also depend on the type of vascular access used to conduct HD, reuse practices, and membrane selection.

CRBSI and catheter colonization (CC) are two complications among HD patients that lead to increased morbidity and mortality. In our study the incidence of CRBSI was 18% which was similar to studies by Hung et al and Abid et al who reported CRBSI as 21.4% and 25% respectively [25, 26]. Nagarika et al conducted study in 210 patients and found that bacteremia occurred in 36 cases (17.14%) [27]. Powe et al found that 11.7% of haemodialysis patients had septicemia [28]. Gupta et al conducted a prospective analysis among 100 patients found that catheter related bacteremia (CRB) was diagnosed in 15 patients (15%) [29].

Gram positive cocci (GPC) (68%) were the predominant group was associated with sepsis in study of Hoen et al [30]. Parameswaran et al found 64% of the pathogens causing CRBSI were gram-positive and 36% were gram-negative [31]. The commonest pathogen causing CRBSI was S. aureus. In our study we found that most common organism isolated from blood culture was GPC.

Nagarika et al in 2006-2007 conducted a study in 210 patients and found that bacteremia occurred in 17 (47.22%) patients with femoral catheter, 8 (22.22%) patients with subclavian catheter and 11 (30.55%) patients with jugular hemodialysis catheter [27]. A study conducted on 100 patients by Gupta et al shown that CRBSI was higher (29.4%) with femoral vein usage as compared to 12.2% with internal jugular vein for haemodialysis [29]. So we observe that in our study sepsis was common in patients with femoral haemodialysis catheter which is similar to above mentioned studies. Oliver et al had shown that incidence of bacteremia was 5.4% after three weeks of placement in internal jugular vein and 10.7% after one week in femoral vein [32]. The incidence of bacteremia was 1.9% one day after the onset of an exit site infection but increased to 13.4% by the second day

if the catheter was not removed. Napalkov et al show catheter-related complications occurred most often during the first 90 days of catheter placement [33].

Among HD patients, low serum albumin at baseline was also an identifiable risk factor for septicemia. Low serum albumin may represent nutritional deficiency in dialysis patients and has previously been shown to be a strong predictive risk factor for death [34]. Our findings suggest that prevention and treatment of dialysis associated malnutrition through nutritional counseling, avoiding low-protein diet months before implementation of renal replacement therapy, and increasing the dose of dialysis to improve appetite and correct acidosis may eventually decrease the risk of septicemia in this vulnerable population. [35]

**Conclusion:**

Use of vascular access to deliver haemodialysis therapy in renal failure patients has increased due to which they are prone to infections because of risk factors like advanced age, male sex, diabetes, anemia, hypoalbuminemia, hyperphosphatemia and prolonged duration of hemodialysis. Gram positive cocci (S. aureus) is the commonest cause of sepsis. Sepsis was most common in patients with prolonged duration of dialysis (>21 days).

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