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Original Research Article

# Study of Sepsis and its Markers in Renal Failure Patients on Hemodialysis

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**Conflict of interest: Nil**

**Abstract:**

**Aim:** The present study was conducted to study the presence of bacteremia, markers of sepsis and Inflammation in renal failure patients on hemodialysis, along with correlation of hematological abnormalities with sepsis in such patients.

**Material & Methods:** The present study was conducted at department of General medicine for one year and total of 100 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.

**Results:** In our study among 100 patients of renal failure on hemodialysis the mean age in our study was 44.76±14.46 years with 65 male patients. Out of 100 patients 20 (20%) had positive blood and catheter tip culture and 80 (80%) of patients had negative blood and catheter tip culture. Out of 20 patients with sepsis 4 (20%) were in the age group between 15–25 years, 4 (20%) were in the age group between 26–35 years, 3 (15%) were in the age group 36–45 years and 9 (45%) were above 45 years of age. All 20 (100%) patients had episode of fever with chills and rigor, 9 (45%) patients had redness and pain at hemodialysis catheter site, 6 patients (30%) were confused, disoriented or comatose and 4 (20%) patients had hypotension. Among 20 patients of renal failure with sepsis, none had TLC less than 4.8/cumm (leucopenia), 5 (25%) patients had count between 4.8–10.8/cumm and 15 (75%) patients had TLC more than 10.8/cumm.

**Conclusion:** Patients requiring hemodialysis, who are having non modifiable risk factors like age, sex other risk factors for infection should be controlled to reduce incidence of infection.

**Keywords:** Sepsis, Chronic kidney disease, Hemodialysis, Blood stream infection



## Introduction

Sepsis is a life-threatening systemic inflammatory response to an infection that might result in organ injury, shock, or death. [1,2] In the United States, sepsis ranks as the 10th leading cause of death, and it accounts for 10% of all ICU admissions. [3] Chronic kidney disease (CKD) is fast emerging as a major public health problem in the 21st century. The National Kidney Foundation Disease Outcomes Quality Initiative guidelines defined CKD as kidney damage or a glomerular filtration rate of less than 60 ml/min per 1.73 $m^2$ for at least 3 months. [4] The CKD population is predisposed to adverse infectious events because of overwhelming uremia, which is associated with alterations in primary host defense mechanisms and increases the risk of bacterial infections and three most commonly seen infectious complications are urinary tract infections (UTI), pneumonia, and sepsis. [5] Sepsis-associated acute kidney injury (S-AKI) is a common complication in hospitalized and critically ill patients, which increases the risk of developing chronic comorbidities and is associated with extremely high mortality. AKI of any origin is associated with higher risk of developing sepsis. [6] The diagnosis of AKI is currently based on an increase serum creatinine concentration and/or a decrease in urine output. [7,8] As in other forms of AKI, serum creatinine can be an insensitive indicator of kidney injury, and oliguria can be nonspecific in S-AKI. One of the most serious and life-threatening infections in dialysis patients is septicemia. The sepsis is complicated by the use of immunosuppressive drugs to treat and control underlying diseases and exacerbated by nutritional deficiencies, the dialysis procedure and the disruption of cutaneous or mucosal barriers to infection. [9] It accounts for over three fourths of deaths caused by infections. [10] The annual percentage of mortality secondary to sepsis is

approximately 100 to 300 fold higher in dialysis patients. [11] 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. [12] Uremia often results in immune deficiency. [13] Malnourishment and older age may interact with uremia to impair the immune system. 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. [14,15] In peritoneal dialysis (PD), infection may occur through either the catheter entrance through the skin or the peritoneal cavity. [13] In hemodialysis (HD) patients, infection may occur from the need for intravascular catheters to perform dialysis. [13] Infection may also depend on the type of vascular access used to conduct HD, reuse practices, and membrane selection. [16] 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. [17]

The present study was conducted to study the presence of bacteremia, markers of sepsis and Inflammation in renal failure patients on hemodialysis, along with correlation of hematological abnormalities with sepsis in such patients.

## Material & Methods

The present study was conducted at department of General medicine Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India for 1 years and total of 100 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. [18] 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 m2 for 3 or more months. [19] Criteria for the systemic inflammatory response syndrome, adapted from the American college of chest physicians/society of critical care medicine consensus conference. [20]

**Inclusion Criteria:**

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.

**Exclusion Criteria;**

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.

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 bilurubin, 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 0C and also on the 2nd, 4th and 7th days and were then discarded, if negative. [21] 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 37 $^0$C 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. [22] 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).

**Statistical Analysis**

A colony count of ≥15 was considered significant for cultures done by Maki's method. [21] If the same organisms grew from both peripheral and central venous catherer (CVC) blood cultures confirmation was done by the pour-plate quantitative method. [23] Association and correlation assessment were done by statistical package for the social sciences (SPSS).

**Results**

**Table 1: Patients on hemodialysis with sepsis and gender distribution**

| | Renal failure patients onhemodialysis with symptoms of sepsis | |
|---|---|---|
| **Parameter** | **N=100** | **%** |
| **Positive blood/cathetertip culture** | 20 | 20 |
| **Negative blood/cathetertip culture** | 80 | 80 |
| **Total** | 100 | |
| **Gender** | | |
| **Male** | 65 | 65 |
| **Female** | 35 | 35 |

In our study among 100 patients of renal failure on hemodialysis the mean age in our study was 44.76±14.46 years with 65 male patients. Out of 100 patients 20 (20%) had positive blood and catheter tip culture and 80 (80%) of patients had negative blood and catheter tip culture.

**Table 2: Distribution of patients according to age groups, symptoms and TLC**

| **Age groups** | **N%** |
|---|---|
| 15-25 years | 4 (20) |
| 26-35 years | 4 (20) |
| 36-45 years | 3 (15) |
| >45 years | 9 (45) |
| **Symptoms** | |
| Fever with chills and rigor | 20 (100) |
| Redness and Pain at hemodialysis catheter site | 9 (45) |
| Confused, Disoriented or comatose | 6 (30) |
| Hypotension | 4 (20) |
| **TLC** | |
| Less than 4.8/cumm (leucopenia), | 0 |
| Between 4.8–10.8/cumm | 5 (25) |
| More than 10.8/cumm | 15 (75) |

Out of 20 patients with sepsis 4 (20%) were in the age group between 15–25 years, 4 (20%) were in the age group between 26–35 years, 3 (15%) were in the age group 36–45 years and 9 (45%) were above 45 years of age. All 20 (100%) patients had episode of fever with chills and rigor, 9 (45%) patients had redness and pain at hemodialysis catheter site, 6 patients (30%) were confused, disoriented or comatose and 4 (20%) patients had hypotension. Among 20 patients of renal failure with sepsis, none had TLC less than 4.8/cumm (leucopenia), 5 (25%) patients had count between 4.8–10.8/cumm and 15 (75%) patients had TLC more than 10.8/cumm.

**Table 3: Bacteria found on patients with sepsis**

| | Renal failure patients on hemodialysis with sepsis | |
|---|---|---|
| **Type of bacteria** | **N=20** | **%** |
| S. aureus | 16 | 80 |
| E. coli | 2 | 10 |
| Acinectobacter | 1 | 5 |
| Candida | 1 | 5 |
| **Total** | 20 | 100 |

16 (80%) patients' blood culture was positive for S. aureus, and E. coli found in blood culture 2 (10%) patient, Acinectobacter in 1 (5%) patient and Candida in 1 (5%) patient.

**Table 4: Most common catheter site associated with infection**

| Site of hemodialysiscatheter | Renal failure patients onhemodialysis with sepsis | |
|---|---|---|
| | N=20 | % |
| Internal jugularvenous catheter | 5 | 25 |
| Femoral catheter | 14 | 70 |
| Subclavian catheter | 1 | 5 |
| Total | 20 | 100 |

Among 20 patients of renal failure on hemodialysis with sepsis 5 (25%) patients had internal jugular line for hemodialysis, 1 (5%) had subclavian line and 14 (70%) had femoral line for hemodialysis.

**Table 5: Distribution of patients according to catheter duration and serum phosphate and albumin levels**

| Catheter duration | N% |
|---|---|
| 7-14 days | 3 (15) |
| 14-21 days | 3 (15) |
| >21 days | 14 (70) |
| **Serum phosphate levels** | |
| Less than 3.5 mg/dl | 0 |
| Between 3.5–5.5 mg/dl | 4 (20) |
| >5.5 mg/dl | 16 (80) |
| **Serum albumin levels** | |
| Less than 3.4 gm/dl | 12 (60) |
| More than 3.4 gm/dl | 8 (40) |

Catheter duration of 7-14 days was found in 3 (15%), 3 (15%) patients had central line between 14–21 days, and 14 (70%) patients had central line >21 days. 15 patients of renal failure on hemodialysis with sepsis none had serum phosphate level less than 3.5 mg/dl, 4 (20%) had serum phosphorus level between 3.5–5.5 mg/dl and 16 (80%) patients had serum phosphorus level >5.5 mg/dl. Albumin level less than 3.4 gm/dl was found in 12 (60) patients, 8 (40%) had serum albumin level more than 3.4 gm/dl.

## Discussion

Sepsis-associated acute kidney injury (S-AKI) is a common complication in hospitalized and critically ill patients, which increases the risk of developing chronic comorbidities and is associated with extremely high mortality. [24-26] As individual syndromes, sepsis and acute kidney injury (AKI) render the host susceptible to each other. Although sepsis is the most common contributing factor for developing AKI, AKI of any origin is associated with higher risk of developing sepsis.5 Sepsis has a complex and unique pathophysiology, which makes S-AKI a distinct syndrome from any other phenotype of AKI. [27]

Out of 20 patients with sepsis 4 (20%) were in the age group between 15–25 years, 4 (20%) were in the age group between 26–35 years, 3 (15%) were in the age group 36–45 years and 9 (45%) were above 45 years of age. All 20 (100%) patients had episode of fever with chills and rigor, 9 (45%) patients had redness and pain at hemodialysis catheter site, 6 patients (30%) were confused, disoriented or comatose and 4 (20%) patients had hypotension. We noted the incidence of sepsis was more in patients of age group greater than 45 years of age. Longitudinal cohort study conducted by Powe et al showed that sepsis was more common in older age group. [28] In 2013 a study conducted by Gupta in 45 patients of CKD showed that the prevalence of CRBSI was 17.78% in patients above 65 years of age. [29] So, our study conforms with other studies, who had shown that advanced age is risk factor for CRBSI. Robinson et al found that was fever was the most consistent symptom at onset of CRBSI (28 of 32 cases). [30] Kairaitis et al conducted a study of 105 haemodialysis catheters in 52 patients in order to identify patient outcomes and to analyse the effect of patient and catheter factors on the incidence of infectious complications, they found that exit-site infection was the cause for removal in 8% and most common clinical symptom was fever. [31]

Among 20 patients of renal failure with sepsis, none had TLC less than 4.8/cumm (leucopenia), 5 (25%) patients had count between 4.8–10.8/cumm and 15 (75%) patients had TLC more than 10.8/cumm. A study conducted by Gupta on 45 CKD patient on haemodialysis, catheter related infections were correlated with TLC. [29] 16 (80%) patients' blood culture was positive for S. aureus, and E. coli found in blood culture 2 (10%) patient, Acinectobacter in 1 (5%) patient and Candida in 1 (5%) patient. 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. [32] Among 20 patients of renal failure on hemodialysis with sepsis 5 (25%) patients had internal jugular line for hemodialysis, 1 (5%) had subclavian line and 14 (70%) had femoral line for hemodialysis. 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. [33]

Catheter duration of 7-14 days was found in 3 (15%), 3 (15%) patients had central line between 14–21 days, and 14 (70%) patients had central line >21 days. 15 patients of renal failure on hemodialysis with sepsis none had serum phosphate level less than 3.5 mg/dl, 4 (20%) had serum phosphorus level between 3.5–5.5 mg/dl and 16 (80%) patients had serum phosphorus level >5.5 mg/dl. Albumin level less than 3.4 gm/dl was found in 12 (60) patients, 8 (40%) had serum albumin level more than 3.4 gm/dl. study conducted by Plantinga had shown high phosphorus level was associated with infection in dialysis patients which supports our finding too. [34] We noted hypoalbuminemia is contributing to increased risk of catheter related infection matches with studies of Powe et al. [28] He suggested hypoalbuminemia was common in catheter related blood stream infection.

## Conclusion

Incidence of renal failure requiring hemodialysis has increased and accordingly use of vascular access to deliver haemodialysis therapy has increased. The patient requiring haemodialysis are prone to infections because of risk factors like advanced age, male sex, diabetes, anemia, hypoalbuminemia, hyperphosphatemia and prolonged duration of hemodialysis. The site of vascular access is an important risk factor for development of sepsis. GPC (S. aureus) is the commonest cause of sepsis.

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