Section: General Medicine

Original Research Article

# AN INVESTIGATION ON SEPSIS AND ITS BIOMARKERS IN PATIENTS WITH RENAL FAILURE UNDERGOING HAEMODIALYSIS

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## Abstract

**Background:** The present study was conducted to study the markers of sepsis and inflammation in renal failure patients on haemodialysis, along with correlation of haematological abnormalities with sepsis in such patients.

**Materials and Methods:** At the Department of Medicine, 200 patients of both sexes were diagnosed with renal failure, including acute kidney injury (AKI) and Chronic Kidney Disease (CKD), based on clinical history, examination, biochemical markersand haemodialysis advice.

**Result:** In a study of 200 renal failure patients on haemodialysis, the mean age was 45.65±12.48 years, with 140 male patients. Out of 200 patients, 44 (22%) had positive blood and catheter tip culture and 156 (78%) had negative. Of 44 sepsis patients, 9 were 15–25 years old, 9 were 26–35 years old, 6 were 36–45 years old, and 20 were above 45. All 44 patients experienced fever with chills and rigor. 20 had redness and discomfort at the haemodialysis catheter site. 14 were confused, disoriented or unconscious and 8 had hypotension. None of 44 renal failures with sepsis patients had TLC less than 4.8/cumm (leukopenia), 12 had 4.8–10.8/cumm and 32 had more than 10.8/cumm.Staphylococcus aureus was detected in 35 (79.54%) individuals, E. coli in 5 (11.36%), Acinetobacter in 2 (4.54%) and Candida in 2 (4.54%). In 44 renal failure patients on haemodialysis with sepsis10 (22.72%) had internal jugular lines, 4 (9.09%) had subclavian lines and 30 (68.18%) had femoral lines.

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

## INTRODUCTION

Sepsis is defined as the dysfunction of organs caused by an unregulated response to infection. Septic shock is characterized by persistent hypotension despite adequate fluid resuscitation, the need for vasoactive drugs to maintain a mean arterial pressure (MAP) of at least 65 mmHg and an elevated plasma lactate level exceeding 2 mmol/L.Approximately 60% of individuals with sepsis get acute kidney injury (AKI).[1,2] The precise mechanism of sepsis-associated acute kidney damage (SA-AKI) remains incompletely understood.Multiple mechanisms, including inflammation,complement activation, mitochondrial dysfunction and microcirculatory dysfunction, are likely tocontribute to the development of AKI.[3] The presence of AKI is associated with a significantly elevated mortality risk in comparison to sepsis alone.[4]

Considering that an excess of fluid might lead to negative outcomes, it is essential to customize the administration of fluids for each individual and determine it based on their fluid responsiveness. The selection of fluid for resuscitation has undergone much examination and discussion. Prior studies suggest that the use of 0.9% saline solution might result in hyperchloremia - a condition that can cause acute kidney damage (AKI) and negatively impact patient outcomes.[6] However, recent studies have shown that saline may be used without any adverse effects.[7] Due to the contradictory research results, this issue remains a topic of contention. Nevertheless, according to the current study, it seems that administering a maximum of 4 liters of saline is not associated with any adverse patient-centered outcomes.[8]

Every patient diagnosed with sepsis should be considered to have an increased susceptibility to acute kidney damage (AKI), whereas individuals with certain comorbiditiessuch as chronic renal disease are at an even higher risk of developing AKI in such situations. The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines advocate for


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the meticulous monitoring of kidney function via the assessment of blood creatinine levels and urine output. This enables prompt identification and classification of renal illness.[9] However, the KDIGO definition of Acute Kidney Injury (AKI) has certain limitations. It is crucial to establish a starting point for serum creatinine levels in order to identify any increase. However, there is presently no consensus on how to establish a baseline serum creatinine level before the onset of acute kidney injury (AKI) in the absence of direct evidence.[10] Furthermore, changes in serum creatinine levels are often delayed particularly in instances of sepsis when the production of creatinine may reduce by 50% and the concentration of creatinine may be diluted as a result of fluid resuscitation.[11]

Although urine output is a significant component of the AKI criteria, it is not a precise indication and can only be accurately evaluated in patients using a urinary catheter. Multiple observational cohort studies have shown that the same stage of acute kidney injury (AKI), as defined by either serum creatinine or urine output, may exhibit different degrees of risk for morbidity and mortality. [12,13]

The present study sought to examine the markers of sepsis and inflammation in individuals with renal failure who are receiving hemodialysis.

## MATERIALS AND METHODS

The study was conducted in the Department of Medicine and included a total of 200 patients of both sexes who were diagnosed with renal failure. This included both acute kidney injury (AKI) and chronic kidney disease (CKD), based on clinical history, examination, and biochemical markers. These patients were advised to undergo hemodialysis and were included in the study.

The research used the RIFLE criteria which included risk, injury, failure, loss of kidney functionand end-stage renal disease to assess AKI.[14] The kidney disease outcomes quality initiative (KDOQI) defines chronic kidney disease (CKD) as the presence of kidney damage or a reduced glomerular filtration rate (GFR) of less than 60 ml/min/1.73 $m^2$ for a duration of at least three months.[15]

The criteria for the systemic inflammatory response syndrome (SIRS) have been derived from the consensus conference of the American College of Chest Physicians and the Society of Critical Care Medicine.[16]

**Inclusion Criteria**

**1.**Patients with renal failure who recently had a subclavian venous catheter, internal jugular venous catheteror femoral catheter inserted for hemodialysis.

**2.**Patients must have developed systemic signs and symptoms of sepsissuch as fever, chills, rigor, rapid heart rate, rapid breathing, low blood pressure, confusion, disorientation and agitation after the catheter insertion and hemodialysis.

**3.**Additionally, patients with local swelling, redness, pain, or pus discharge at the site of the hemodialysis catheter are also included.

**Exclusion criteria**

**1.** Patients with renal failure caused either by septicemia or post-operatively.

**2.**History of previous hemodialysis present.

**3.** A known source of infection such as diabetic foot, pyelonephritis, bedsore, or those with an A-V fistula.

**Methodology**

After enrolling patients for the study, we collected their clinical history and conducted relevant blood and radiological tests. These tests included measurements of hemoglobin, total leucocyte count (TLC), differential leucocyte count (DLC) and platelet count. We also assessed renal function through tests measuring serum creatinine, blood urea and serum electrolyte levels. Additionally, we measured serum phosphorus, C-reactive protein, and liver function through tests measuring serum bilirubin, serum total protein, serum albumin and alkaline phosphatase levels. Furthermore, we evaluated thyroid function through tests measuring FT3, FT4 and Thyroid Stimulating Hormone (TSH) levels. Lastly, we conducted urine tests including routine and microscopy analysis as well as urine culture and sensitivity testing. Tests including blood culture, sensitivity analysis of central line catheter tip culture, chest X-ray posteroanterior (P/A) view(CXR), abdominal and kidney ultrasonography (USG) and kidney, ureter and bladder (KUB) ultrasonography were conducted. Before inserting the catheter, a leukocyte count and blood culture were performed. Additionally, a single sample was obtained from the peripheral vein to check for any existing bacteremia. If the patient tested positive, they were eliminated from the research. Furthermore, 72 hours after the implantation, two 5 ml blood samples were obtained. One sample was taken from the peripheral vein while the other was retrieved from the catheterafter a minimum of 12 hours of hemodialysis.

Subcultures were performed in the laboratory by transferring samples from Hartley's broth onto blood agar (BA) and MacConkey medium. This was done after incubating the samples overnight at a temperature of 37°C. Subcultures were also performed on the 2nd, 4th and 7th day. If the results were negativethe subcultures were discarded.

A mid-stream urine sample was obtained using aseptic techniques and placed in a sterile vial containing boric acid. The sample was then transferred to the microbiology laboratory. A bacterial culture was prepared by streaking 0.002 ml of urine collected mid-stream onto MacConkey agar and 5% sheep blood agar plates. The plates were then incubated at 37°C for 24 hours in the presence of oxygen. The resulting colonies were counted using a colony counter. A sample that produced a pure bacterial growth of at least $10^5$ colony-forming units per milliliter (cfu/ml) was considered to have a


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considerable presence of bacteria in the urine. Levels ranging from $10^4$ to $10^5$cfu/ml are classified as positive.Levels less than or equal to $10^4$ cfu/ml were considered as negative.

The catheter tip was retrieved only from individuals who had their catheter removed at the end of their hemodialysis session or if they exhibited any indications of infection. The specimen was cultivated using Maki's standard semi-quantitative technique on blood agar and then transferred to Trypticase Soy Broth (TSB).

## RESULTS

In our study among 200 patients of renal failure on hemodialysis the mean age in our study was 45.65±12.48 years with 140 male patients. Out of 200 patients 44 (22%) had positive blood and catheter tip culture and 156 (78%) of patients had negative blood and catheter tip culture. [Table 1]

Out of 44 sepsis patients 9 were between 15 and 25, 9 were between 26 and 35, 6 were between 36 and 45, and 20 were beyond 45. Fever with chills and rigor affected all 44 patients. 20 experienced redness and discomfort at the hemodialysis catheter site. 14 were confused, disorientedor unconsciousand 8 had hypotension. None of 44 renal failures with sepsis patients had TLC less than 4.8/cumm (leucopenia), 12 had 4.8–10.8/cumm and 32 had more than 10.8/cumm. [Table 2]

S. aureus was detected in 35 (79.54%) individuals, E. coli in 5 (11.36%), Acinetobacter in 2 (4.54%), and Candida in 2 (4.54%). [Table 3]

In 44 renal failure patients on hemodialysis with sepsis, 10 (22.72%) had internal jugular lines, 4 (9.09%) had subclavian lines and 30 (68.18%) had femoral lines. [Table 4]

Catheter duration of 7-14 days was found in 7 patients. 7 patients had catheterfor 14–21 days and 30 patients had it for >21 days. Out of 44 patients of renal failure on hemodialysis with sepsis none hadserum phosphate level less than 3.5 mg/dl. 10 had serum phosphorus level between 3.5–5.5 mg/dl and 34 patients had serum phosphorus level >5.5 mg/dl.Albumin level less than 3.4 gm/dl was found in 26 patients, 18 had serum albumin level more than 3.4 gm/dl. [Table 5]

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

| Parameter | Renalfailurepatientsonhemodialysis withsymptomsofsepsis | |
|---|---|---|
| | N=200 | % |
| Positive blood/Cathetertipculture | 44 | 22 |
| Negative blood/Cathetertipculture | 156 | 78 |
| Total | 200 | |
| Gender | | |
| Male | 140 | 70 |
| Female | 60 | 20 |

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

| Age groups | N |
|---|---|
| 15-25 years | 9 |
| 26-35 years | 9 |
| 36-45 years | 6 |
| >45 years | 20 |
| Symptoms | |
| Fever with chills and rigor | 44 |
| Redness and Pain at hemodialysis catheter site | 20 |
| Confused, Disoriented or comatose | 14 |
| Hypotension | 8 |
| TLC | |
| Less than 4.8/cumm (leucopenia) | 0 |
| Between 4.8–10.8/cumm | 12 |
| More than 10.8/cumm | 32 |

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

| Type of bacteria | Renal failure patients on hemodialysis with sepsis | |
|---|---|---|
| | N=44 | % |
| S.aureus | 35 | 79.54 |
| E.coli | 5 | 11.36 |
| Acinetobacter | 2 | 4.54 |
| Candida | 2 | 4.54 |
| Total | 44 | 100 |

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

| Site of hemodialysis catheter | Renal failure patients on hemodialysis with sepsis | |
|---|---|---|
| | N=44 | % |
| Internal Jugularvenouscatheter | 10 | 22.72 |
| Femoral catheter | 30 | 68.18 |
| Subclavian catheter | 4 | 9.09 |


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| | | |
|---|---|---|
| Total | 44 | 100 |

**Table 5: Distribution of patients according to Catheter duration,Serum phosphate and Albumin levels**

| Catheter duration | N |
|---|---|
| 7-14 days | 7 |
| 14-21 days | 7 |
| >21 days | 30 |
| Serum phosphate levels | |
| Less than 3.5 mg/dl | 0 |
| Between 3.5–5.5 mg/dl | 10 |
| >5.5 mg/dl | 34 |
| Serum albumin levels | |
| Less than 3.4 gm/dl | 26 |
| More than 3.4 gm/dl | 18 |

## DISCUSSION

Sepsis is a potentially fatal condition characterised by a widespread inflammatory response to an infection which may lead to organ damage, shock or death.[20,21] Sepsis is the 10th most common cause of mortality in the United States and it is responsible for 10% of all admissions in the intensive care unit (ICU).[22]Chronic kidney disease (CKD) is becoming more prevalent as a significant public health issue in the 21$^{st}$century. According to the recommendations set by the national renal foundation disease outcomes quality initiative, chronic kidney disease (CKD) is defined as either kidney damage or a glomerular filtration rate (GFR) of less than 60 ml/min/ 1.73 $m^2$ for a minimum of 3 months.[23]

Among the 200 patients with renal failure undergoing haemodialysis in our research, the average age was 45.65±12.48 years, and there were 140 male patients. Among the 200 patients, 44 (22%) tested positive for blood and catheter tip culture, whereas 156 (78%) tested negative.Each of the 44 patients had a bout of fever accompanied by chills and rigour.Additionally, 20 patients reported redness and discomfort at the site of their haemodialysis catheter. 14 patients exhibited symptoms of confusion, disorientation, or coma. Furthermore, 8 patients experienced hypotension. We observed a higher occurrence of sepsis in individuals aged above 45 years. Longitudinal cohort research undertaken by Powe et al revealed a higher prevalence of sepsis in the older age group.[24]

Research done in 2013 by Punit G on 45 patients with CKD revealed that the incidence of Catheter-Related-Bloodstream-Infection (CRBSI) in individuals aged 65 and above was 17.78%.[25] Our result aligns with previous research that has shown advanced age as a risk factor for CRBSI. Robinson et al discovered that fever was the predominant symptom seen at the beginning of CRBSI in 28 out of 32 individuals.[26]Kairaitis et al conducted a study on 105 haemodialysis catheters in 52 patients to determine patient outcomes and analyse the impact of patient and catheter factors on the occurrence of infectious complications. They discovered that exit-site infection was responsible for the removal of 8% of the catheters and the most prevalent clinical symptom was fever.[27]

Among the 44 patients diagnosed with sepsis, 9 were between the ages of 15 and 25, 9 were between the ages of 26 and 35, 6 were between the ages of 36 and 45, and 20 were above the age of 45. Each of the 44 patients had a bout of fever accompanied by chills and rigour. Additionally, 20 patients reported redness and discomfort at the site of their haemodialysis catheter. 14 patients exhibited symptoms of confusion, disorientation, or coma. Furthermore, 8 patients experienced hypotension. Out of the 44 patients with renal failure and sepsis, none had a total leukocyte count (TLC) less than 4.8/cumm (indicating leukopenia). 12 patients had a TLC between 4.8–10.8/cumm, whereas 32 patients had a TLC more than 10.8/cumm. Research done by Punit G on 45 patients with chronic kidney disease (CKD) who were undergoing haemodialysis found a correlation between catheter-related infections and total leukocyte count (TLC).Out of the total, 35 patients (79.54%) had a positive blood culture for S. aureus. E. coli, was discovered in the blood culture of 5 patients (11.36%), Acinetobacter in 2 patients (4.54%)and Candida in 2 patients (4.54%).

In 2006-2007, Nagarika et al performed research including 210 patients. The study revealed that 47.22% of patients with a femoral catheter had bacteraemia, whereas 22.22% of patients with a subclavian catheter and 30.55% of patients with a jugular haemodialysis catheter experienced the same condition.[28] Out of a group of 200 patients with renal failure who were undergoing haemodialysis, sepsis was present in 44 patients. Out of the total number of 44 patients, 10 (22.72%) had an internal jugular venous line for haemodialysis, 4 (9.09%) had a subclavian line, and 30 (68.18%) had a femoral line for haemodialysis. Oliver et al demonstrated that the occurrence of bacteraemia was 5.4% after three weeks of insertion in the internal jugular vein and 10.7% after one week in the femoral vein.[29]

Seven individuals had a catheter length of 7-14 days, while another 7 patients had it for a period of 14-21 days. Additionally, 30 patients had a catheter for more than 21 days. Out of the 44 patients with renal failure on haemodialysis with sepsis, none had a serum phosphate level below 3.5 mg/dl. 10


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patients had a serum phosphorus level between 3.5–5.5 mg/dland 34 patients had a serum phosphorus level over 5.5 mg/dl. Out of the total number of patients, 26 had an albumin level below 3.4 gm/dlwhereas 18 had a serum albumin level above 3.4 gm/dl. Research done by Plantinga found a significant correlation between elevated phosphorus levels and infection in dialysis patients, which too aligns with our study.[30] The presence of hypoalbuminemia has been shown to be associated with an elevated risk of catheter-related infection, which is consistent with the findings of Powe et al. [24] He proposed that hypoalbuminemia is prevalent in catheter-related bloodstream infections.

## CONCLUSION

The prevalence of renal failure necessitating haemodialysis has risen, leading to a corresponding increase in the use of vascular access for the administration of haemodialysis treatment. Patients who need haemodialysis are susceptible to infections due to many risk factors such as older age, male gender, diabetes, anaemia, low levels of albumin in the blood, high levels of phosphates in the blood and lengthy periods of undergoing haemodialysis. The location where vascular access is obtained is a significant contributing factor to the likelihood of developing sepsis. Staphylococcus aureus is the most prevalent cause of sepsis.

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