

Original Research Article

Study of sepsis and its markers in renal failure patients on hemodialysis

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ABSTRACT

Background: Patients with chronic kidney disease have impaired immunity due to disease per se and because of immunosuppressant treatment used for their disease. Catheters used for hemodialysis acts as conduit for microorganisms to cause infections. This leads to increase in morbidity and mortality.

Methods: 100 patients of renal failure requiring hemodialysis were selected. Relevant pathological and radiological investigation done to rule out already existing infection, later on tests were repeated after catheter insertion and hemodialysis to check for infection and sepsis. Using appropriate statistical analysis was done and p value <0.05 was taken as significant.

Results: Out of 100 patients underwent study, 15 developed catheter related blood stream infection. Older age, history of diabetes, male sex, diabetes, anemia, hypoalbuminemia, hyperphosphatemia, prolonged duration of hemodialysis and site of hemodialysis catheter were found to be risk factor for infection.

Conclusions: 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

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 m² for at least 3 months.¹ New classification system standardizes categories for the various stages of kidney damage. Three intermediary stages follow, with kidney failure or end-stage renal disease (ESRD), as the final stage, defined by a glomerular filtration rate of less than 15 ml/min per 1.73 m². Hemodialysis (HD) acts wonders by improving the quality of life in patients of end stage renal disease. HD machine removes wastes from the blood stream and regulates the body's fluid and chemical balances. 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. Neutrophils exhibit impaired chemotaxis, oxidative metabolism, phagocytic activity, degranulation, intracellular killing, and dysregulated programmed cell death. These patients had a higher risk of contracting bacterial infections and three most commonly seen infectious complications are urinary tract infections (UTI), pneumonia, and sepsis.² These immunologic abnormalities are 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.³ The annual percentage of mortality secondary to sepsis is approximately 100 to 300 fold higher in dialysis patients.⁴ 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.⁵ 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 micro-organisms. The gold standard is the combination of a positive blood culture with the same organism isolated from the catheter.⁶

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.

METHODS

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.⁷ 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.¹ Criteria for the systemic inflammatory response syndrome, adapted from the American college of chest physicians/society of critical care medicine consensus conference.⁸ 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 °C and also on the 2nd, 4th and 7th days and were then discarded, if negative.⁹ 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 °C for 24 hours, under aerobic conditions and the colonies was counted by a colony counter. Sample that yielded pure bacterial growth of $\geq 10^5$ cfu/ml was regarded as significant bacteriuria. Counts between 10^4 and 10^5 cfu/ml repeated while counts $\leq 10^4$ cfu/ml considered as negative.¹⁰ 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.⁹ If the same organisms grew from both peripheral and central venous catheter (CVC) blood cultures confirmation was done by the pour-plate quantitative method.¹¹ Association and correlation assessment were done by statistical package for the social sciences (SPSS).

RESULTS

In our study among 100 patients of renal failure on hemodialysis the mean age in our study was 43.86 ± 13.52 years with 66 male patients. Out of 100 patients 15 (15%) had positive blood and catheter tip culture and 85 (85%) of patients had negative blood and catheter tip culture (Table 1). Out of 15 patients with sepsis 3 (20%) were in the age group between 15–25 years, 3 (20%) were in the age group between 26–45 years, 2 (13.33%) were in the age group 36–45 years and 7 (46.67%) were above 45 years of age. All 15 (100%) patients had episode of fever with chills and rigor, 7 (46.66%) patients had redness and pain at hemodialysis catheter site, 5 patients (33.33%) were confused, disoriented or comatose and 03 patients had hypotension. 11 (11%) patients had urinary tract infection, 15 (15%) patients diagnosed as catheter related blood stream infection (CRBSI) and 2 (2%) patients had pneumonia. Among 15 patients of renal failure with sepsis, none had TLC less than 4.8/cumm (leucopenia), 4 (26.67%) patients had count between 4.8–10.8/cumm and

11 (73.33%) patients had TLC more than 10.8/cumm. Twelve (80%) patients' blood culture was positive for *S. aureus*, and *E. coli* found in blood culture 1 (6.66%) patient, *Acinetobacter* in 1 (6.66%) patient and *Candida* in 1 (6.66%) patient (Table 2). Among 15 patients of renal failure on hemodialysis with sepsis 04 (26.66%) patients had internal jugular line for hemodialysis, 1 (6.67%) had subclavian line and 10 (66.67%) had femoral line for hemodialysis (Table 3). Catheter duration of 7-14 days was found in 2 (13.33%), 2 (13.33%) patients had central line between 14–21 days, and 11 (73.34%) 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 (26.67%) had serum phosphorus level between 3.5–5.5 mg/dl and 11 (73.33%) patients had serum phosphorus level >5.5 mg/dl. Albumin level less than 3.4 gm/dl was found in 9 patients, 6 (40%) had serum albumin level more than 3.4 gm/dl. Table 1 showing patients with positive blood/catheter tip culture among 100 patients of renal failure patients on hemodialysis. Table 2 showing type of organism found in blood culture among 15 patients of renal patients on hemodialysis with sepsis. Table 3 showing site of hemodialysis catheter among 15 patients of renal patients on hemodialysis with sepsis.

Table 1: Patients on hemodialysis with sepsis.

Parameter	Renal failure patients on hemodialysis with symptoms of sepsis	
	N=100	%
Positive blood/catheter tip culture	15	15
Negative blood/catheter tip culture	85	85
Total	100	

Table 2: Bacteria found on patients with sepsis.

Type of bacteria	Renal failure patients on hemodialysis with sepsis	
	N=15	%
<i>S. aureus</i>	12	80
<i>E. coli</i>	1	6.66
<i>Acinetobacter</i>	1	6.67
<i>Candida</i>	1	6.67
Total	15	100

Table 3: Most common catheter site associated with infection.

Site of hemodialysis catheter	Renal failure patients on hemodialysis with sepsis	
	N=15	%
Internal jugular venous catheter	04	26.66
Femoral catheter	10	66.67
Subclavian catheter	01	6.67
Total	15	100

DISCUSSION

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 15% which was similar to studies by Hung et al and Abid et al who reported CRBSI as 21.4% and 25% respectively.^{12,13} Nagarika et al conducted study in 210 patients and found that bacteremia occurred in 36 cases (17.14%).¹⁴ Powe et al found that 11.7% of haemodialysis patients had septicemia.¹⁵ Gupta et al conducted a prospective analysis among 100 patients found that catheter related bacteremia (CRB) was diagnosed in 15 patients (15%).¹⁶ In our study we found similar incidence of CRBSI. 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.¹⁵ 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.¹⁷ So, our study conforms with other studies, who had shown that advanced age is risk factor for CRBSI. Robinson et al found that fever was the most consistent symptom at onset of CRBSI (28 of 32 cases).¹⁸ 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.¹⁹ These observations support that fever was most common symptom in patients with sepsis, which similar with above observations. Diabetes is a major risk factor for bacterial and fungal infections Jean G et al. (2002)²⁰ had found CRBSI in 33% of diabetic patients. Gupta Pooja et al. (2011)¹⁶ had found 44.4% diabetic patients suffered from CRBSI. Similar to these observations, we noted 40% diabetic patients developed CRBSI. A study conducted by Gupta on 45 CKD patient on haemodialysis, catheter related infections were correlated with TLC.¹⁷ The value of TLC less than 10.8/cumm were seen in 42.8% of patient and value of TLC more than 10.8/cumm seen in 57.1% of patient with CRBSI. So as above observations we found that higher TLC associated with infection which is similar as above mentioned study. Gram positive cocci (GPC) (68%) were the predominant group was associated with sepsis in study of Hoen et al.²¹ Parameswaran et al found 64% of the pathogens causing CRBSI were gram-positive and 36% were gram-negative.²² 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.¹⁴ 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.¹⁶ 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.²³ 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.

Thus in our study it was found that sepsis was common in patients with prolonged duration of dialysis (>21 days) which is similar to above mentioned studies. A study conducted by Plantinga had shown high phosphorus level was associated with infection in dialysis patients which supports our finding too.²⁴ We noted hypoalbuminemia is contributing to increased risk of catheter related infection matches with studies of Powe et al.¹⁵ 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. Prevention of CRBSI by encouraging AV Fistula, minimizing the use of CVCs, use of preventive measures for *S. aureus* carriers and aggressive management of hyperphosphatemia with phosphate binding agents can reduce incidence of CRBSI.

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