e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2023; 15(8); 288-293

Original Research Article

Assessing Clinico-Etiological and Bacterial Profile in Patients with Sepsis and its Markers in Renal Failure on Hemodialysis

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Received: 21-12-2022 Revised: 25-01-2023 / Accepted: 23-02-2023

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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 200 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 200 patients of renal failure on hemodialysis the mean age in our study was 45.65±15.35 years with 140 male patients. Out of 200 patients 50 (25%) had positive blood and catheter tip culture and 150 (75%) of patients had negative blood and catheter tip culture. Out of 50 patients with sepsis 9 (18%) were in the age group between 15–25 years, 9 (18%) were in the age group between 26–35 years, 8 (16%) were in the age group 36–45 years and 24 (48%) were above 45 years of age. All 50 (100%) patients had episode of fever with chills and rigor, 24 (48%) patients had redness and pain at hemodialysis catheter site, 16 patients (32%) were confused, disoriented or comatose and 10 (20%) patients had hypotension. Among 50 patients of renal failure with sepsis, none had TLC less than 4.8/cumm (leucopenia), 10 (20%) patients had count between 4.8–10.8/cumm and 40 (80%) patients had TLC more than 10.8/cumm. 40 (80%) patients' blood culture was positive for S. aureus, and E. coli found in blood culture 6 (12%) patients, Acinectobacter in 2 (4%) patient and Candida in 2 (4%) patients. Among 50 patients of renal failure on hemodialysis with sepsis 12 (24%) patients had internal jugular line for hemodialysis, 4 (8%) had subclavian line and 34 (68%) had femoral line for hemodialysis.

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

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 defence 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]

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. [5] The diagnosis of AKI is currently based on an increase serum creatinine concentration and/or a decrease in urine output. [6,7] 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. [8] It accounts for over three fourths of deaths caused by infections. [9] The annual percentage of mortality secondary to sepsis is approximately 100 to 300 fold higher in dialysis patients. [10] 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. [11] Uremia often results in immune deficiency. [12] 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. [13,14]

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, Darbhanga Medical College and Hospital, Darbhanga, Bihar, India for one year and total of 200 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 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. [16]

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 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 0C and also on the 2nd, 4th and 7th days and were then discarded, if negative.[17] 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 37^0C 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.[18] 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.[17] If the same organisms grew from both peripheral and central venous catherer (CVC) blood cultures confirmation was done by the pour-plate quantitative method.[19] 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=200**	**%**
Positive blood/cathetertip culture	50	25
Negative blood/cathetertip culture	150	75
Total	100	
Gender		
Male	140	70
Female	60	30

In our study among 200 patients of renal failure on hemodialysis the mean age in our study was 45.65±15.35 years with 140 male patients. Out of 200 patients 50 (25%) had positive blood and catheter tip culture and 150 (75%) 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	9 (18)
26-35 years	9 (18)
36-45 years	8 (16)
>45 years	24 (48)
Symptoms	
Fever with chills and rigor	50 (100)
Redness and Pain at hemodialysis catheter site	24 (48)
Confused, Disoriented or comatose	16 (32)
Hypotension	10 (20)
TLC	
Less than 4.8/cumm (leucopenia),	0
Between 4.8–10.8/cumm	10 (20)
More than 10.8/cumm	40 (80)

Out of 50 patients with sepsis 9 (18%) were in the age group between 15–25 years, 9 (18%) were in the age group between 26–35 years, 8 (16%) were in the age group 36–45 years and 24 (48%) were above 45 years of age. All 50 (100%) patients had episode of fever with chills and rigor, 24 (48%) patients had redness and pain at hemodialysis catheter site, 16 patients (32%) were confused, disoriented or comatose and 10 (20%) patients had hypotension. Among 50 patients of renal failure with sepsis, none had TLC less than 4.8/cumm (leucopenia), 10 (20%) patients had count between 4.8–10.8/cumm and 40 (80%) patients had TLC more than 10.8/cumm.

Table 3: Bacteria found on patients with sepsis

Type of bacteria	Renal failure patients on hemodialysis with sepsis	
	N=50	%
S. aureus	40	80
E. coli	6	12
Acinectobacter	2	4
Candida	2	4

40 (80%) patients' blood culture was positive for S. aureus, and E. coli found in blood culture 6 (12%) patients, Acinectobacter in 2 (4%) patient and Candida in 2 (4%) patients.

Table 4: Most common catheter site associated with infection

Site of hemodialysiscatheter	Renal failure patients onhemodialysis with sepsis	
	N=50	%
Internal jugularvenous catheter	12	24
Femoral catheter	34	68
Subclavian catheter	4	8

Among 50 patients of renal failure on hemodialysis with sepsis 12 (24%) patients had internal jugular line for hemodialysis, 4 (8%) had subclavian line and 34 (68%) 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	8 (16)
14-21 days	8 (16)
>21 days	34 (68)
Serum phosphate levels	
Less than 3.5 mg/dl	0
Between 3.5–5.5 mg/dl	10 (20)
>5.5 mg/dl	40 (80)
Serum albumin levels	
Less than 3.4 gm/dl	30 (60)
More than 3.4 gm/dl	20 (40)

Catheter duration of 7-14 days was found in 8 (16%), 8 (16%) patients had central line between 14–21 days, and 34 (68%) patients had central line >21 days. None patients had serum phosphate level less than 3.5 mg/dl, 10 (20%) had serum phosphorus level between 3.5–5.5 mg/dl and 40 (80%) patients had serum phosphorus level >5.5 mg/dl. Albumin level less than 3.4 gm/dl was found in 30 (60%) patients, 20 (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. [20-22] As individual syndromes, sepsis and acute kidney injury (AKI) render the host susceptible to each other. Sepsis has a complex and unique pathophysiology, which makes S-AKI a distinct syndrome from any other phenotype of AKI. [23]

In our study among 200 patients of renal failure on hemodialysis the mean age in our study was 45.65±15.35 years with 140 male patients. Out of 200 patients 50 (25%) had positive blood and catheter tip culture and 150 (75%) of patients had negative blood and catheter tip culture. Out of 50 patients with sepsis 9 (18%) were in the age group between 15–25 years, 9 (18%) were in the age group between 26–35 years, 8 (16%) were in the age group 36–45 years and 24 (48%) were above 45 years of age. All 50 (100%) patients had episode of fever with chills and rigor, 24 (48%) patients had redness and pain at hemodialysis catheter site, 16 patients (32%) were confused, disoriented or comatose and 10 (20%) patients had hypotension. Among 50 patients of renal failure with sepsis, none had TLC less than 4.8/cumm (leucopenia), 10 (20%) patients had count between 4.8–10.8/cumm and 40 (80%) patients had TLC more than 10.8/cumm. 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. [24] 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. [25] 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). [26] 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. [27]

40 (80%) patients' blood culture was positive for S. aureus, and E. coli found in blood culture 6 (12%) patients, Acinectobacter in 2 (4%) patient and Candida in 2 (4%) patients. 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. [28] 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. [29]

Among 50 patients of renal failure on hemodialysis with sepsis 12 (24%) patients had internal jugular line for hemodialysis, 4 (8%) had subclavian line and 34 (68%) had femoral line for hemodialysis. Catheter duration of 7-14 days was found in 8 (16%), 8 (16%) patients had central line between 14–21 days, and 34 (68%) patients had central line >21 days. None patients had serum phosphate level less than 3.5 mg/dl, 10 (20%) had serum phosphorus level between 3.5–5.5 mg/dl and 40 (80%) patients had serum phosphorus level >5.5 mg/dl. Albumin level less than 3.4 gm/dl was found in 30 (60%) patients, 20 (40%) had serum albumin level more than 3.4 gm/dl. The 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. [30] 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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