International Journal of Medicine Research
ISSN: 2455-7404; Impact Factor: RJIF 5.42
www.medicinesjournal.com
Volume 1; Issue 4; June 2016; Page No. 56-60

An observational assessment of sepsis and its markers in renal failure patients on hemodialysis

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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 on 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±15.65 years with 140 male patients. Out of 200 patients 42 (21%) had positive blood and catheter tip culture and 158 (79%) of patients had negative blood and catheter tip culture. Out of 42 patients with sepsis 11 (26.19%) were in the age group between 15–25 years, 26–35 years, 7 (16.66) were in the age group 36–45 years and 13 (30.95) were above 45 years of age. All 42 (100%) patients had episode of fever with chills and rigor, 20 (47.61) patients had redness and pain at hemodialysis catheter site, 14 (33.34) were confused, disoriented or comatose and 10 (23.80) patients had hypotension. Among 42 patients of renal failure with sepsis, none had TLC less than 4.8/cumm (leucopenia), 13 (30.95) patients had count between 4.8–10.8/cumm and 29 (69.05) patients had TLC more than 10.8/cumm. 34 (80.95%) patients' blood culture was positive for S. aureus, and E. coli found in blood culture 4 (9.52%) patient, Acinectobacter in 2 (4.76%) patient and Candida in 2 (4.76%) patients.
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-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 [1-4]. 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. Identifying the exact onset of injury in sepsis is nearly impossible, leading to difficulty in timely intervention for prevention of renal injury.

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. However, in sepsis, oliguria appears to carry increased significance, and even by 3 to 5 hours, an association between oliguria and AKI may be detectable [8, 9]. Serum creatinine is also limited by the absence of baseline value in many patients, and a consensus is lacking as to the best way to handle this missing information [10, 11]. Most sepsis studies have looked at the general population and have not looked at high-risk populations. Recently, two studies looked at the toll of sepsis on ESRD patients. A retrospective study done by Abou Dagher *et al*. found that the in-hospital mortality of septic haemodialysis patients (n=90) was 26% and it was as high as 40% when they examined the subset of patients with septic shock [12]. Lowe *et al*. looked at the mortality of haemodialysis patients in septic shock (n=137) and found that their ESRD patients had a mortality of 20.4% vs. 17% in non-ESRD patients [13].

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 [14]. 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 [15]. The annual percentage of mortality secondary to sepsis is approximately 100 to 300 fold higher in dialysis patients [16].

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 on 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 [17]. 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 [18].

Criteria for the systemic inflammatory response syndrome, adapted from the American college of chest physicians/society of critical care medicine consensus conference [19].

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 [20]. 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 [21]. 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 [20]. If the same organisms grew from both peripheral and central venous catherer (CVC) blood cultures confirmation was done by the pour-plate quantitative method [22]. 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

Parameter	Renal failure patients on hemodialysis with symptoms of sepsis	
	N=200	%
Positive blood/catheter tip culture	42	21
Negative blood/catheter tip culture	158	79
Gender		
Male	140	60
Female	60	30

In our study among 200 patients of renal failure on hemodialysis the mean age in our study was 45.65±15.65 years with 140 male patients. Out of 200 patients 42 (21%) had positive blood and catheter tip culture and 158 (79%) 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	11 (26.19)
26-35 years	11 (26.19)
36-45 years	7 (16.66)
>45 years	13 (30.95)
Symptoms	
Fever with chills and rigor	42 (100)
Redness and Pain at hemodialysis catheter site	20 (47.61)
Confused, Disoriented or comatose	14 (33.34)
Hypotension	10 (23.80)
TLC	
Less than 4.8/cumm (leucopenia),	0
Between 4.8–10.8/cumm	13 (30.95)
More than 10.8/cumm	29 (69.05)

Out of 42 patients with sepsis 11 (26.19%) were in the age group between 15–25 years, 26–35 years, 7 (16.66) were in the age group 36–45 years and 13 (30.95) were above 45 years of age. All 42 (100%) patients had episode of fever with chills and rigor, 20 (47.61) patients had redness and pain at hemodialysis catheter site, 14 (33.34) were confused, disoriented or comatose and 10 (23.80) patients had hypotension. Among 42 patients of renal failure with sepsis, none had TLC less than 4.8/cumm (leucopenia), 13 (30.95) patients had count between 4.8–10.8/cumm and 29 (69.05) 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=42	%
S. aureus	34	80.95
E. coli	4	9.52
Acinectobacter	2	4.76
Candida	2	4.76

34 (80.95%) patients' blood culture was positive for S. aureus, and E. coli found in blood culture 4 (9.52%) patient, Acinectobacter in 2 (4.76%) patient and Candida in 2 (4.76%) patients.

Table 4: Most common catheter site associated with infection

Site of hemodialysis catheter	Renal failure patients on hemodialysis with sepsis	
	N=42	%
Internal jugular venous catheter	12	28.57
Femoral catheter	29	69.04
Subclavian catheter	1	2.38

Among 42 patients of renal failure on hemodialysis with sepsis 12 (28.57%) patients had internal jugular line for hemodialysis, 1 (2.38%) had subclavian line and 29 (69.04%) 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	6 (14.28)
14-21 days	6 (14.28)
>21 days	30 (71.42%)
Serum phosphate levels	
Less than 3.5 mg/dl	0
Between 3.5–5.5 mg/dl	8 (19.05)
>5.5 mg/dl	34 (80.95)
Serum albumin levels	
Less than 3.4 gm/dl	26 (61.90)
More than 3.4 gm/dl	16 (38.10)

Catheter duration of 7-14 days was found in 6 (14.28), 6 (14.28) patients had central line between 14–21 days, and 30 (71.42%) 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, 8 (19.05) had serum phosphorus level between 3.5–5.5 mg/dl and 34 (80.95) patients had serum phosphorus level >5.5 mg/dl. Albumin level less than 3.4 gm/dl was found in 26 (61.90) patients, 16 (38.10) 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 [23-25]. 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 [26].

Out of 42 patients with sepsis 11 (26.19%) were in the age group between 15–25 years, 26–35 years, 7 (16.66) were in the age group 36–45 years and 13 (30.95) were above 45 years of age. All 42 (100%) patients had episode of fever with chills and rigor, 20 (47.61) patients had redness and pain at hemodialysis catheter site, 14 (33.34) were confused, disoriented or comatose and 10 (23.80) 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 [27]. 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 [28]. 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) [29]. 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 [30].

Among 42 patients of renal failure with sepsis, none had TLC less than 4.8/cumm (leucopenia), 13 (30.95) patients had count between 4.8–10.8/cumm and 29 (69.05) 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.[28] 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 [31].

Among 42 patients of renal failure on hemodialysis with sepsis 12 (28.57%) patients had internal jugular line for hemodialysis, 1 (2.38%) had subclavian line and 29 (69.04%) 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 [32].

Catheter duration of 7-14 days was found in 6 (14.28), 6 (14.28) patients had central line between 14–21 days, and 30 (71.42%) 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, 8 (19.05) had serum phosphorus level between 3.5–5.5 mg/dl and 34 (80.95) patients had serum phosphorus level >5.5 mg/dl. Albumin level less than 3.4 gm/dl was found in 26 (61.90) patients, 16 (38.10) 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 [33]. 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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