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Original Research Article

CLINICAL STUDY OF ACUTE KIDNEY INJURY IN PATIENTS WITH CHRONIC LIVER DISEASE

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Abstract

Background: Acute kidney injury (AKI) is a serious event which commonly occurs in patients with chronic liver disease (CLD) and is associated with significant morbidity and mortality. The study aimed to assess the etiological aspect of AKI in cirrhosis, clinical profile and mortality in relation to kidney disease improving global outcomes staging and Child Turcotte Pugh (CTP) score. **Material & Methods:** This prospective, cross-sectional study was conducted at Department of Medicine and Nephrology at Gauhati Medical College and Hospital for a period of one year from 1st August 2014 to 31st July 2015. The study enrolled patients aged >12 years of either sex with diagnosis of AKI with CLD. Data was collected at baseline and patients were followed up for at least 3 months. **Results:** A total of 148 patients were included in the study with mean age of 53.5 years. Majority of patients were in group C (55.4%) and in KDIGO stage 2 (38.5%) according to CTP score and KDIGO criteria, respectively. The most common symptom reported was decreased urine output (98.6%). Ascites was observed in majority of patients (95.9%). Infections was the most common etiology of AKI in patients with CLD (42.2%). Death was recorded in 39.2% of patients. Patients with KDIGO stage 3 and CTP class C had highest mortality. **Conclusion:** AKI was associated with increased mortality in patients with CLD. Infection was the most common cause of AKI therefore early diagnosis of infection may prevent the progression of AKI and hence can improve the prognosis.

INTRODUCTION

Acute kidney injury (AKI) commonly develops in individuals with preexisting chronic liver disease (CLD) and cirrhosis, and it manifests in various ways. Renal dysfunction occurs in 20% of patients with cirrhosis admitted to hospital, often linked with other complications of cirrhosis such as variceal bleeding and spontaneous bacterial peritonitis.[1] The occurrence of AKI in CLD has serious implications, leading to higher rates of morbidity and mortality. Therefore, it is crucial to promptly recognize and accurately diagnose the renal dysfunctions associated with both noncirrhotic and chronic liver diseases, such as prerenal hepatorenal syndrome and acute tubular necrosis (ATN), in order to provide optimal management. Accurate differentiation has utmost importance as the approach towards treatment vary significantly. Hepatorenal syndrome-associated AKI and ATN require specific and different treatment strategies and are associated with high in-hospital mortality rates.[2] Recent progress in understanding the relationship between CLD and acute renal dysfunction in cirrhosis patients has resulted in significant advancements, including improved classification, nomenclature, and consideration of the underlying pathophysiology.[3]

Several risk factors for the development of AKI in critically ill patients have been identified through clinical studies. These include advanced age, the presence of sepsis, administration of contrast agents, diabetes, pre-existing kidney disease, hypovolemia, and shock.[4]

Due to the high occurrence of AKI and its negative impact on the prognosis of patients with liver failure, it is crucial to closely monitor renal function as an essential aspect of proper clinical care. Careful monitoring of hemodynamic and renal parameters, as well as electrolyte levels, acid/base balance, and glucose levels, is necessary.[5]

There have been very few Indian studies which have evaluated patients with AKI and cirrhosis, and no such study has ever been performed in North-East till date. The present study will assess the etiological

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aspect of AKI in cirrhosis, clinical profile, and mortality in relation to KDIGO staging and child pugh score.

MATERIALS AND METHODS

Study design

This was a prospective, cross-sectional study conducted at Department of Medicine and Nephrology at Gauhati Medical College and Hospital from 1st August 2014 to 31st July 2015. The study was approved by institutional ethics committee, and was performed in accordance with the Declaration of Helsinki and the International Conference on Harmonization guidelines. Written informed consent was obtained from all the participants prior to enrollment in this study.

Study participants

Patients of either sex aged >12 years, suffering from AKI with CLD were included in this study. Patients with preexisting renal disease, AKI without CLD, acute viral hepatitis, acute liver injury with AKI and patients with hypertension, diabetes mellitus and thyroid dysfunction were excluded from the study.

Data collection

Patients who met the eligibility criteria were undergone thorough clinical examination and relevant investigations were performed with detailed history to confirm the diagnosis of AKI in cirrhosis and also to determine the presence of various complications. The staging of AKI was done by kidney disease improving global outcomes (KDIGO) criteria and staging of cirrhosis by Child Turcotte Pugh (CTP) score. Renal biopsy was done in selected cases.

Staging of AKI and CLD

KDIGO

The KDIGO criteria classify AKI into three stages based on changes in serum creatinine levels or urine output.

Stage 1: A rise in serum creatinine to 1.5–1.9 times the baseline value or an increase of 0.3 mg/dl (26.5 mmol/l) from baseline, along with a urine output of less than 0.5 ml/kg/h for 6–12 hours.

Stage 2: A rise in serum creatinine to 2.0–2.9 times the baseline value and a urine output of less than 0.5 ml/kg/h for over 12 hours.

Stage 3: A rise in serum creatinine to 3.0 times the baseline value or an increase to 4.0 mg/dl (353.6 mmol/l), or the initiation of renal replacement therapy. In patients over 18 years of age, it also includes a decrease in estimated glomerular filtration rate (eGFR) to less than 35 ml/min per 1.73 m² or a urine output of less than 0.3 ml/kg/h for 24 hours or anuria- for 12 hours.

CTP score

The CTP score is a widely used scoring system for assessing the severity and prognosis of CLD, particularly cirrhosis.

Ascites, hepatic encephalopathy, serum bilirubin level, serum albumin level, prothrombin time are the five parameters considered in the CTP score. Each parameter is assigned a score ranging from 1 to 3, with higher scores indicating more severe abnormalities. The individual scores for these parameters are then added together to calculate the CTP score, which ranges from 5 to 15. Based on the CTP score, patients are categorized into different classes indicating the severity of liver disease and the associated prognosis:

Class A: CTP score 5-6 (mild), Class B: CTP score 7-9 (moderate), Class C: CTP score 10-15 (severe).

Follow-up

Follow-up was done for 3 months and mortality was assessed according to staging of AKI and cirrhosis.

RESULTS

A total of 148 patients were included in the study. As per assessment of CTP score, 2 (0.01%) patients were belonged to class A, 64 (43.2%) patients were belonged to class B and 82 (55.4%) patients were belonged to class C (Table 3). According to KDIGO criteria 46 (31.1%) patients were in stage 1, 57 (38.5%) patients in stage 2 and 45 (30.4%) patients were in stage 3. The mean (SD) age of study population was 53.5 (11.2) years with majority of patients (34.5%) belonging to age group of 55-64 years. [Table 1]

On examination decreased urine output was the most common symptom in 98.6% of the patients followed by jaundice (58.7%), leg swelling (49.3%), distension of abdomen (47.3%), fever (33.1%), abdominal pain (29.7%), constipation (25%), upper gastrointestinal bleed (26.4%). Altered sensorium was observed in 22.3% of patients; however, 6.08% of patients had bleeding manifestations. Moreover, many patients have reported more than one symptom. Ascites was the majorly reported finding in 95.9% of patients followed by pedal edema (68.2%), splenomegaly (66.2%), icterus (63.5%), pallor (60.8%), abdominal tenderness (38.5%), and hypotension (36.5%). Asterixis was reported in 22.3% of the patients, while 17.6% had hepatomegaly and 8.1% of patients had petechie or purpura.

The most common etiology of AKI in patients with CLD was infections (42.2%), out of which urinary tract infection was diagnosed majorly in 19.6% of patients. [Table 2]

Death was recorded during 90 days of follow up in 39.2% of patients. Patients with AKIN stage 3 had highest mortality with an in-hospital mortality of 28.8 % and 90-days total mortality of 55.5%. CTP class C had highest mortality with in-hospital mortality of 28% and 90-days total mortality of 50% (Table 3). In patients with hepatorenal syndrome (HRS), 90-days mortality was found to be 49%.

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Table 1: Age-wise distribution of patients

Age (years)	No. of Patients (N=148)
15-24	1 (0.7)
25-34	8 (5.4)
35-44	25 (16.9)
45-54	33 (22.3)
55-64	51 (34.5)
65-74	25 (16.9)
75-84	5 (3.4)
Data presented as n (%).	

Table 2: Etiologies of AKI in CLD

Etiology of AKI	N= 148
Infection	64 (42.2)
UTI	29 (19.6)
SBP	14 (9.4)
Sepsis (Unknown source)	11 (7.4)
Lung infections	7 (4.7)
Cellulitis	3 (2)
HRS	46 (31)
Hypovolemia induced renal failure	27 (18.2)
ATN	10 (6.7)
IgA Nephropathy	1 (0.7)
Data presented as n (%). AKI, acute kidney injury; ATN, acute tubular necrosis; HRS, hepatorenal syndrome; IgA, immunoglobulin A; SBP, Spontaneous bacterial peritonitis; UTI, urinary tract infection.	

Table 3: Frequency of mortality in patient population

	In-hospital mortality	Mortality after 90 days
Staging of AKI (KDIGO)		
Stage 1 [n=46]	3 (6.5)	9 (19.6)
Stage 2 [n=57]	8 (14)	24 (42)
Stage 3 [n=45]	13 (28.8)	25 (55)
CTP score		
A [n=2]	0	0
B [n=64]	3 (4.7)	17 (26.5)
C [n=82]	23 (28)	41 (50)
Data presented as n (%). KDIGO, kidney disease improving global outcomes; CTP, child turcotte pugh.		

DISCUSSION

In the present study, the key observations reported were: 1) Infection was the most common cause of AKI in patients with CLD, 2) KDIGO stage 3 had highest overall mortality, 3) Patients with CTP class C had highest mortality.

Present study demonstrated infection (42.2%) as the commonest cause of AKI including UTI (19.6%), spontaneous bacterial peritonitis (9.4%), sepsis of unknown source (7.4%), lung infection (4.7 %), and cellulitis (2%), followed by HRS (31 %), hypovolemia including upper gastrointestinal bleed (18.2%), ATN (6.7%) and IgA nephropathy (0.7%). Similar findings were reported by Martin L et al which included 463 hospitalized patients of AKI with CLD. The most frequent cause was bacterial infection (46%) followed by other causes like hypovolemia-induced renal failure (32%), HRS (13%), parenchymal nephropathy (9%), drug-induced renal failure (7.5%).[6] A study by Ji-Tseng Fang et al. also reported that infection was the major cause of AKI in patients with cirrhosis.[7]

Hartleb M et al. demonstrated that bacterial infection was responsible for 30-60% of cases of AKI, while HRS occurs in 40-50% of individuals with CLD and ascites. Furthermore, intrinsic renal injury, specifically ATN, might account for approximately 40% of cases of AKI in cirrhotic patients with ascites.[8] In a study by Andrew S. Allegretti et al., where 120 participants who had both cirrhosis and AKI were analyzed. Among them, 40 individuals (33%) were diagnosed with prerenal azotemia, 35 (29%) with HRS, 36 (30%) with ATN and 9 (8%) had other causes of AKI.[9]

In the present study, the in-hospital mortality for KDIGO stage 1 was 6.5%, and the overall mortality within 90 days was 19.6%. For KDIGO stage 2, the in-hospital mortality was 14%, with a total mortality of 42.1% within 90 days. The most critical condition was found in KDIGO Stage 3 with in-hospital mortality of 28.8% and a total mortality of 55.6% within 90 days. Comparatively, patients in stage 3 had a significantly higher mortality rate when compared to those in stages 1 and 2. In a prospective study conducted by Robert Scott et al. among the 110 patients with cirrhosis who experienced AKI, 44 patients (40%) were classified as AKI stage 1, 32 patients (29.1%) as stage 2, and 34 patients (30.9%) as stage 3. The in-hospital mortality was highest in patients with AKI stage 3 (43.2%) as compared to those in stage 2 (37.8%) and stage 1 (13.5%). It was observed that mortality increased with increased severity of AKI1. The overall comparison of

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survival among patients categorized according to AKI stage was found to be statistically significant in a study by Claudia Fagundes et al.[10] Patients with stage 3 AKI showed highest mortality; however, it was observed that there was no statistically significant difference between patients with stage 2 and stage 3 AKI in terms of survival outcome. In the study conducted by Andrew S. Allegretti et al., the combined total mortality in AKI stage 1 and 2 was 32.5%, while for stage 3, it was 52.3% within the 90-day follow-up period.[9] Findings from the study by Shetty S et al.2 demonstrated that there was a clear association between the severity of AKI stages and mortality rates. Among the participants, the mortality rate was 15.8% for stage 1 AKI, 27.3% for stage 2 AKI, and notably higher 60.6% for stage 3 AKI.

Present study demonstrated that there was no mortality during the in-hospital period in patients with CTP class A. For class B, the in-hospital mortality rate was 4.7%, and the overall mortality within 90 days was 26.5%. However, for class C, the results were concerning, as it had the highest in-hospital mortality at 28% and an overall mortality of 50% within 90 days. These findings were comparable to findings from the study by Scott RA, et al.[1] where the results indicate a progressive increase in mortality with the advancement of liver disease, with class C (32.8%) having the highest mortality rate as compared to classes A (3.1%) and B (23.6%). In the study conducted by Belcher JM et al., the distribution of Child-Pugh classes among the patients was class A (2%), class B (31%), and class C (65%). During the 90-day follow-up period, patients in class C had the highest mortality rate of 36.8%, indicating a significant correlation between more advanced liver disease and increased mortality.[11]

In the current study involving 148 cases, the overall mortality rate, combining in-hospital and 90-day mortality, was found to be 39.2%. Similarly, the study conducted by Scott RA et al.1, where 110 patients with cirrhosis and AKI had a total mortality of 31.8%. Additionally, another study conducted by Andrew S. Allegretti et al.[9] with 120 patients showed a total mortality rate of 46.7% with cirrhosis and AKI.

As per the observations in the current study the mortality rate associated with HRS within a 90-day period was 49%. Similar findings were reported by Fagundes C et al. where the mortality rate of patients with HRS was observed as 47%.[10] Marta ML et al. also reported that patients with HRS had poor prognosis and survival rate6. Moreover, another study showed that the mortality rate was higher (44.4%) in patients associated with HRS.[2]

CONCLUSION

The occurrence of AKI in patients with cirrhosis is a frequent and concerning event, as demonstrated in the current study. In this population AKI is associated with a deterioration of prognosis and increased mortality. The study identified infection as the most prevalent cause of AKI in these patients. Early detection and diagnosis of infections in patients with CLD could potentially help to prevent the complications associated with AKI and improve the overall prognosis in this vulnerable population. Timely management and intervention may play a crucial role in reducing the impact of AKI in patients with cirrhosis which can ultimately lead to improved outcomes.

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