

Clinical spectrum of AKI in chronic liver diseases


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Introduction: Acute kidney injury (AKI) is a heterogeneous syndrome of different aetiologies, and often multifactorial. Occurrence of Acute kidney injury in patients with chronic liver disease is frequent finding which makes prognosis of CLD even poorer. **Material and methods:** A prospective cohort observational study on 100 adult patients of chronic liver disease with AKI conducted over a period of 24 months from August 2016 to August 2018 at Sri Aurobindo medical college and postgraduate institute. Detailed clinical examination and biochemical tests were done. Univariate and multivariate logistic regression (odds ratio) analyses were used. **Result:** 87% are males and 13 % are females. The most common cause of cirrhosis is alcoholic 77% followed by hepatitis B virus related 10%, unknown etiology 7%, hepatitis C 3%, NASH 2%, Wilson 1. The most common sign of decompensation of liver is jaundice 78% followed by ascites 70%, hepatic encephalopathy 37% and upper GI bleed 30%. Distribution of child class as a prognostic indicator showed the maximum no. of patients found in class C 56% followed by class B 34% and class A 10%. **Conclusion:** Acute kidney injury is very common in chronic liver disease patient in our hospital and majority of them have intrinsic cause of AKI.

Keywords: Acute kidney injury, Chronic liver disease, Kidney function

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Introduction

Incidence of AKI varies from 3% to 7% in hospitalized patient and 25% to 30% in intensive care unit (ICU) patient, approximately 5% to 6% patients who develop AKI, had to undergo dialysis. Chronic liver disease (CLD) is also a common clinical problem afflicting mankind. Its association with disease of other important organ kidney makes it a more devastating disease [1].

As AKI significantly impacts the outcome of patients with cirrhosis, it is important to prevent the development of AKI if possible and to identify the cause early enough so that appropriate treatment measures can be instituted [2,3,4].

Occurrence of Acute kidney injury in patients with chronic liver disease is frequent finding which makes prognosis of CLD even poorer [5,6]. Physiological changes that occur in CLD place these patients at high risk for AKI [6]. Cirrhosis is an immunocompromised state, and these patients are at increased risk of infection [7]. Therefore, early evaluation and treatment of infection is imperative for patients with cirrhosis who develop an AKI [8].

Material and Methods

The present study is a hospital-based observational study conducted over a period of 24 months from August 2016 to August 2018 at Sri Aurobindo medical college and postgraduate institute, Indore. Consecutively admitted 100 adult patients of chronic liver disease with AKI were chosen for the study.

Study Design: Observational Study

Inclusion Criteria

01. Age more than 18 years.
02. Diagnosed case of chronic liver disease.
03. Patient of acute kidney injury in chronic liver disease.

Exclusion Criteria

01. Known case of CKD.
02. Patients of chronic diseases such as active tuberculosis, malignancy.

Collection of data- Detailed clinical interview and physical examination were done at the time of admission. Clinical events (infection, AKI, bleeding, ascites, and encephalopathy) were carefully evaluated, then these patients were subjected to appropriate investigations.

During hospitalization complete hemogram, serum Total bilirubin, unconjugated bilirubin and conjugated bilirubin, serum total protein serum albumin, serum globulin, PT (Prothrombin time)/INR, alkaline phos-phatase, Blood urea (BU), serum creatinine (sCr) at admission and daily till patient improve or discharge & baseline report noted if available, serum electrolytes and ABG (arterial blood gas analysis) done at admission and done whenever required, viral markers (HBsAg & Anti HCV, HIV) were investigated.

Culture of ascitic fluid, blood, urine, and sputum were performed when an infection is suspected. Urine routine microscopy, urine electrolytes whenever relevant, ascitic fluid microscopy done when patients have ascites, Ultrasonography of Whole abdomen, chest x ray, and the other lab investigation which were required for evaluation and treatment of patients.

The diagnosis of cirrhosis was based on clinical evaluation by a hepatologist using laboratory values, liver imaging, endoscopy, and (when available) liver biopsy [24]. Cirrhosis staged clinically by Child-Pugh classification (CPC) with scoring system of 5-15 score of 5 to 6 being CPC-A, 7 to 9 CPC-B and 10 to 15 being CPC -C [9].

Serum creatinine (sCr) measured at admission and daily till patient improve or discharge which ever earlier & baseline report noted if available. During hospitalisation peak sCr value noted and compared with baseline sCr for staging of AKI.

Statistical analysis plan: Continuous variables were described as means (95% confidence interval) and the difference was observed by using T test. ANOVA was carried out for >2 groups.

Differences for categorical variables were assessed by the chi-square test. Univariate and multivariate logistic regression (odds ratio [OR]) analyses were used to identify those variables associated with AKI and mortality. *p*value < 0.05 was considered significant.

Results

Table 1: Sex wise distribution of cases.

S.No	Sex	No.of Patients
1	Female	13
2	Male	87
Total		100

Above table shows that males are predominant in our study than females i.e 87% are males and 13% are females.

Table-2: Cause of Cirrhosis.

S.No.	Cause of cirrhosis	No. of patients
1	Unknown etiology	7
2	Alcoholic cirrhosis	77
3	Hepatitis B Virus related	10
4	Hepatitis C Virus related	3
5	NASH	2
6	Willson's disease	1
Total		100

The most common cause of cirrhosis is alcoholic in 77% followed by hepatitis B virus related 10%, unknown etiology 7%, hep C 3%, NASH 2%, Wilson 1

Table-3: Decompensation of liver.

S. No.	Complication	No. of patients Present	No. of patient absent
1	Hepatic encephalopathy	37	63
2	Ascites	70	30
3	Jaundice	78	22
4	h/o UGI Bleed	30	70
Total		100	100

The above table shows that the most common sign of decompensation of liver is jaundice 78% followed by ascites 70%, hepatic encephalopathy 37% and upper GI bleed 30%.

Table-4: Distribution according to CHILD class

S. No.	CHILD Class	No. patients
1	A	10
2	B	34
3	C	56
Total		100

Distribution of child class as a prognostic indicator as shown in above table the maximum no of patients found in class C 56% followed by class B 34% and class A 10%.

Table-5: Stage of AKI

S No.	Stages Of AKI	No. of Patients
1	AKI-1	36
2	AKI-2	24
3	AKI-3	40
Total		100

Above table shows that maximum no. of patients found in AKI stage III 40% followed by stage I 36% then stage II 24%.

Table-6: Precipitating factors for AKI.

S No.	Factors	No. Of Patients
1	Sepsis-CN1	33
2	Bacteraemia	4
3	Candidiasis	1
4	UTI	8
5	Pneumonia	4
6	SBP	18
7	UGI Bleed	10
8	Paracentesis	4
9	Diarrhea	4
10	Vomiting	4
11	Diuretics	9
12	Aminoglycosides (Amikacin)	1
Total		100

- Sepsis culture negative (blood, urine, ascitic fluid, sputum)

Above table shows the most common precipitating factor was sepsis 33% followed by SBP 18%, UGI bleed 10%, diuretics 9%, UTI 8%, paracentesis, Diarrhea, vomiting, bacteraemia, pneumonia 4% each, and aminoglycosides 1%.

Table 7: Etiological classification of AKI with cirrhosis patients.

S.No.	Classification	Number of patients
1	Pre-Renal	28
2	HRS-AKI	33
3	Intrinsic	39
4	Other	0
Total		100

Above study shows the etiological classification of AKI in cirrhosis patients in which the majority are of intrinsic AKI 39% followed by HRS-AKI 33% and pre renal AKI 28%.

Discussion

This study is an observational hospital-based study. In this study we studied the clinical spectrum of AKI in cirrhosis patients i.e. causes of AKI, precipitating factors for AKI in cirrhosis and the outcome of AKI in cirrhosis patients. In our study, out of 100 patients of cirrhosis with AKI, there are 87 males and 13 females, male to female ratio being 6.6: 1. In several other studies males are more predominantly involved than females like Andrew S et al [10] found that Median (quartile1, quartile 3) age of the entire cohort was 58 (50, 65) years. The majority of participants were male (71%), white race (93%), and of non-Hispanic ethnicity (87%).

Jaiganesh et al [11] found mean age was 48.32 ± 10.19 years. Of these, majority were male (95% (95/100)) and females were only 5% (5/100).

Fleming KM et al [12] who also found an increased incidence of chronic liver disease with increase in age. This study showed that the majority of patients were male which is similar to our study. The study also found that the incidence was over 50% higher in men compared with women. In our study, alcoholic cirrhosis is the most common aetiology of cirrhosis that is 77% followed by hepatitis B (10%) then hepatitis C (3%) then NASH (2%) and then Wilson's disease (1%).

Similarly Jaiprakash et al [13] found the Most common aetiology of cirrhosis was chronic alcoholism (29.8%) followed by cryptogenic (25.3%) and chronic hepatitis B (24.1%). Other less common causes included chronic hepatitis C (7.3%), primary biliary cirrhosis, non-alcoholic fatty liver disease, and autoimmune hepatitis, combined effects of alcoholism and hepatitis B, and Wilson's disease, in decreasing order of frequency.

Jaiganesh et al [11] found that, the most common aetiology of cirrhosis was alcohol 85% (85/100), followed by Hepatitis B (11% (11/100)) and C virus 4% (4/100)). Renal dysfunction was observed in 33.3% (5/15) of cirrhotic cases with viral aetiology. There is no significant association between the etiology of cirrhosis and renal disorders ($P = 0.25$). Of which 17 (20%) alcohol related 5% of hepatitis B&C develop AKI.

Quresi et al [14] found, Majority of the patients had their liver disease secondary to hepatitis C with a mean MELD and Child-Pugh score of 17.4 ± 4.6 and 10 ± 2 , respectively. Etiological finding of our study is similar to study done by Das et al [15] except with frequency, they found Alcohol, Hepatitis B, Hepatitis C and non-alcoholic fatty liver disease (NAFLD) were among the causes of cirrhosis. Present study showed most common cause was alcohol followed by Hepatitis B and Hepatitis C.

Other studies done on cirrhosis patients also found alcohol was the most common cause of cirrhosis in Brij Sharma et al [16] alcohol in 62.9%, HBV related 10.1% and NASH found in <10% cases, in a study done by Apurva Shah et al [17] found alcohol in 48%, NASH in 26% HBV in 10% HCV in 6% and 7% have others causes of cirrhosis. In present study the most common cause of cirrhosis is alcohol followed by HBV, HCV NASH, Wilson ds.

Which is similar to other studies, and in 7 cases aetiology of cirrhosis is unknown. Present study included 100 patients of cirrhosis with AKI admitted in our hospital, Number of cases in previous studies are as follows-

Kirk B et al [18] included 206 cirrhotic patients in which they studied renal dysfunction, Das et al [15] included 61 patients were admitted with chronic liver disease but among them 11 were not included in the study as they had existing kidney disease. Qun-Qun Jiang et al [19] studied 280 patients of cirrhosis with AKI. Jai Prakash et al [13] studied total of 404 cases of cirrhosis of liver in which One hundred and seventyeight patients were diagnosed to have different forms of renal diseases.

Jaiganesh mohan et al [11] studied retrospectively reviewed medical records of 100 cirrhotic patients admitted in three month period. Kulkarni et al [20] studied 120 patients of cirrhosis of liver with acute kidney injury. In present study maximum AKI patients are found in Child Class C 56%, in Child class B 34% and in Child class A 10% patients found it is similar to other study as Child class increases patients of cirrhosis have more incidence of AKI. similar to our study are-

Jaiprakash et al [13] proportionate increase in the incidence of renal disease with increase in the severity of liver disease as determined by Child-Pugh classification. The incidence of renal diseases was 15.7% in class A, 50% in class B, and 54.8% in class C of Child-Pugh classification.

These findings were also supported by Attia et al [21] found the incidence of renal disease was 6.7%, 13.5%, and 33.9% in patients with Child-Pugh class A, B, and C cirrhosis, respectively. Which also similar to present study.

Jaiganesh mohan et al [11] There is an increase in the number of renal disorder with increase in the severity of cirrhosis. In the cirrhotic patients with higher severity of cirrhosis (Child Pugh class B and C), renal dysfunction was developed much more (OR=3.37; CI=1.08-10.5; $P = 0.03$). This also similar to our study as the severity of liver disease increases no. of patients having renal dysfunction increases.

In present study hepatic encephalopathy were found in 37% cases, ascites in 70% cases, jaundice in 78% cases, H/O UGI bleed in 30% cases, Jaiganesh et al [11] found Among the renal dysfunction cases studied 45.5% (10/22) had hepatic encephalopathy

Factor such as hepatic encephalopathy has been associated with the progression of AKI [22].

HRS is exclusively found in patients with cirrhosis with ascites, in our study 70 cases have ascites of which 33 cases i.e. 47.1% (33/70) were found to have HRS-AKI. Which is contrary to our study, HRS-1 affects about 7% of hospitalised cirrhotic patients, both HRS1&2 affecting approximately 10% of cirrhotic patients with ascites [22]. Precipitating factors of AKI in cirrhosis patients in our study were sepsis 33%, SBP 18%, upper GI bleed 10%, diuretics 9%, UTI 8%, bacteremia 4%, pneumonia 4%, diarrhoea 4%, vomiting 4%, paracentesis 4%, candidiasis 1%, and aminoglycosides 1%, in which the commonest cause is sepsis followed by SBP rest in decreasing order respectively.

There are many studies in which sepsis is one of the commonest cause of AKI in cirrhosis patients while rest of the other cause are in different orders similar finding also observe by Jaiprakash et al [13], in his study sepsis is the most common cause of AKI. So we conclude that AKI in cirrhosis is commonly due to Intrinsic AKI followed by HRS AKI & pre renal AKI in decreasing order, and sepsis is most common precipitating factors for AKI. Others factors are Spontaneous Bacterial Peritonitis, Upper Gastro-Intestinal Bleed, Urinary Tract Infection, Diuretics use, diarrhoea, vomiting, and bacteraemia.

Conclusion

Acute kidney injury is very common in chronic liver disease patient in our hospital and majority of them have intrinsic cause of AKI. It is observed that frequency of renal disease keeps on increasing with increase in severity of liver disease. Further study and multicentre clinical trials are needed to help clinicians better diagnose and improve outcomes in this critically ill group of patients.

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