



## STUDY OF CLINICAL PROFILE OF PATIENTS WITH ACUTE KIDNEY INJURY IN LIVER DISEASES. IN TERTIARY CARE CENTRE OF NORTH INDIA

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### ABSTRACT

**Background:** The clinical profile of patients with acute kidney injury in liver diseases has many causes. Among them Pre renal AKI is superior to Acute tubular necrosis and Hepato- Renal syndrome. Acute kidney damage in patients with liver cirrhosis is linked to a significant in-hospital death rate.

**Aim:** To study the clinical profile of patients with acute kidney injury in liver diseases.

**Material & Methods:** From December 1, 2022, to November 30, 2023, the gastroenterology patient department at the MM Institute of Medical Sciences Mullana, Ambala, was the site of this prospective observational study. The study comprised 100 cases of individuals who were older than 18 years old & had been diagnosed with either acute or chronic liver disease with signs of acute kidney injury according to KIDGO criteria. Complete hemogram, conjugated & unconjugated bilirubin, serum total bilirubin, serum albumin, serum globulin, serum PT (prothrombin time)/INR, blood urea (BU), alkaline phosphatase, serum creatinine (sCr) at admission & every day until the patient gets better or is discharged, & baseline reports were recorded during the hospital stay.

**Results:** Of the individuals, 37% had a history of prerenal azotemia (PRA), 34% of acute tubular necrosis (ATN), & 29% had a history of hepatorenal syndrome (HRS). Subjects with PRA had the highest mean serum creatinine levels, whereas subjects with HRS had higher mean blood pressure. The participants with PRA, HRS, & ATN had mean hospital stays of 9.78±1.13, 12.55±1.09, & 10.02±1.14, respectively. 38% of the patients indicated their overall mortality. The participants with ATN had the highest recorded death rate (55.88%), followed by HRS (44.83%).

**Conclusion:** Acute kidney damage in patients with liver cirrhosis is linked to a significant in-hospital death rate. The two main indicators of in-hospital mortality are oliguria & a greater stage of AKI at presentation. The outcome of pre-renal AKI is superior to that of ATN or HRS.

**Keywords:** AKI, ATN, HRS, Liver Disease, Mortality, PRA

**Introduction:** Known as the abrupt impairment of kidney function, acute kidney injury (AKI) is a term used to describe a diverse range of conditions that share common diagnostic features, such as elevated blood urea, serum creatinine (SCr) concentration, &/or nitrogen concentration. Rather than

being categorized as a single disease, these conditions can be combined under this umbrella. This is frequently connected to a decrease in urine volume<sup>1</sup>. Up to 30% of patients to the intensive care unit & 5–7% of acute care hospital admissions are complicated by acute kidney injury (AKI)<sup>2</sup>. Between 3% & 7% of hospitalized patients & 25% to 30% of intensive care unit (ICU) patients experience acute kidney injury (AKI); 5% to 6% of these patients required dialysis<sup>3</sup>. Precipitating events such diuretic overdose, large-volume paracentesis without albumin replacement, bacterial infections, & gastrointestinal bleeding frequently cause it to occur<sup>4</sup>.

Life-threatening consequences can arise from cirrhosis, a common liver condition that progresses over time as the liver loses its ability to compensate. In an Indian multicentric research, of 13,014 patients of chronic liver disease (CLD), 33.9% had decompensated cirrhosis.<sup>5</sup> The most common cause of cirrhosis was alcoholism (34.3%), while the primary cause of CLD overall (33.3%) & noncirrhotic CLD (40.8%)<sup>6</sup> was hepatitis B. In recent years, there have been numerous changes to the diagnosis of AKI in cirrhosis. To improve these patients' prognosis, consensus standards have emerged to detect it early, gain a better knowledge of the etiology, & start therapy as soon as possible. Renal impairment in cirrhosis was previously defined as a 50% rise in serum creatinine (SCr) with a final result more than 1.5 mg/dL. By using this criterion, patients who have less severe renal failure are not receiving early therapy because they are not being diagnosed<sup>7</sup>.

The major causes of AKI in LC are pre-renal AKI, acute tubular necrosis, & the hepatorenal syndrome type of AKI (HRS-AKI). Studies describing AKI in hospitalized individuals with LC are quite rare. AKI has a substantial negative influence on the prognosis of cirrhosis patients, thus it's critical to stop it from developing whenever feasible & to find the source as soon as possible to start the right kind of treatment. In order to assess the clinical profile of individuals with acute renal injury in hepatic disorders, this study was carried out. The following are the study's goals & objectives:

1. To research the causes of acute kidney injury (AKI) in individuals with acute, chronic, & combined liver disorders.
2. To research patients with acute liver illness, acute on chronic liver disease, & chronic liver disease on the clinical & biochemical profile of AKI
3. Investigating the effects of AKI in patients with acute, acute-onset chronic, & chronic liver diseases.

**Material & Methods:** From December 1, 2022, to November 30, 2023, a one-year prospective observational study was carried out in the gastroenterology patient department at the MM Institute of Medical Sciences Mullana, Ambala. In all potential situations, institutional ethics clearance & written informed permission were obtained. Considering the following inclusion & exclusion criteria, a minimum of 100 cases with clinical data were included in the study:

### **Inclusion Criteria**

Patient older than 18 years old who has been diagnosed with either acute or chronic liver disease & shows signs of acute kidney injury according to KIDGO criteria

### **Exclusion Criteria**

1. Patients with a history of chronic kidney disease diagnosis.
2. Patients who decline to provide permission.
3. Patients who are younger than eighteen.
4. Patients who have received a kidney transplant.

### **Methodology:**

- a) The study comprised patients with renal failure who were admitted to MMIMSR Hospital or IPD & had underlying liver disorders that had been diagnosed.
- b) Liver disease was diagnosed based on the existence of the following:

**ALD** comprises the subsequent two classifications:

**ALI:** is characterized by a two-to three-fold increase in transaminases, a marker of liver damage, accompanied by coagulopathy & jaundice.

**ALF:** Severe acute liver injury (ALI) is the first clinical sign of acute liver failure (ALF). In a patient without a chronic liver illness, this is marked by a two- to three-fold elevation of transaminases, along with impaired liver function, such as coagulopathy, jaundice, & hepatic encephalopathy.

**CLD:** A group of illnesses collectively referred to as chronic liver disease (CLD) have a history of liver dysfunction lasting longer than six months & vary in the degree of intrahepatic inflammatory necrosis &/or fibrosis they produce.

**Liver cirrhosis:** Chronic liver inflammation results in diffuse hepatic fibrosis, which is characterized by the replacement of normal hepatic architecture by regenerating hepatic nodules. This process leads to liver cirrhosis.

(1) Compensated-Liver Cirrhosis: Individuals with cirrhosis who do not exhibit any signs or complications associated with the disease;

(2) Decompensated-Liver Cirrhosis: Individuals suffering from non-obstructive jaundice, ascites, variceal hemorrhage, or hepatic encephalopathy in addition to their cirrhosis.

Cirrhosis is diagnosed using one of the following methods:

(1) Cirrhosis with histology

(2) Ectopic varices in the digestive system or gastroesophageal varices, based on the exclusion of non-cirrhotic portal hypertension.

(3) Portal hypertension & cirrhosis are revealed by imaging.

**Acute On Chronic Liver Failure (ACLF):** In patients with previously diagnosed or undiagnosed chronic liver disease/cirrhosis, ACLF is an acute hepatic insult that presents as jaundice (serum bilirubin  $\geq 5$  mg/dL) & coagulopathy (INR  $\geq 1.5$ ). Within 4 weeks, the condition can worsen into clinical ascites &/or encephalopathy. ACLF is associated with a high 28-day mortality rate. The patient's clinical & laboratory results were documented in the proforma that is attached. KDIGO criteria were used to classify Acute Kidney Injury (AKI).

**Data collection:** At the time of admission, a thorough clinical interview & physical examination were performed. After a thorough evaluation of the clinical events (infection, AKI, bleeding, ascites, & encephalopathy), the patients underwent the necessary investigations.

Complete hemogram; serum total bilirubin, conjugated & unconjugated bilirubin; serum total protein; serum albumin; serum globulin; PT (Prothrombin time)/INR; alkaline phosphatase; blood urea (BU); serum creatinine (sCr); serum electrolytes; ABG (arterial blood gas analysis); &, if necessary, viral markers (HBsAg & Anti HCV, HIV) were investigated during the hospital stay.

When an infection is suspected, ascitic fluid, blood, urine, & sputum cultures are carried out. Regular microscopy of the urine, testing of the electrolytes, when necessary, ascites fluid microscopy performed on patients, whole abdominal ultrasonography, chest x-rays, & additional laboratory investigations for patient assessment & therapy.

After data was gathered, statistical analysis was performed.

**Statistical analysis:** With the assistance of a statistician, the data was tabulated in an Excel sheet. For statistical analysis, the means & standard deviations of each group's measurements were employed. One way ANOVA was used to statistically analyze the data at each assessment point. The t test was utilized to ascertain the difference between the two groups, with a significance threshold of  $p < 0.05$ .

## Results:

The proportion of male & female individuals was 89% & 11%, respectively. This study had a male-dominated population as a result. Age groups  $>60$  years old accounted for the largest percentage of subjects (31%) & 51–60 years old (27%). The age range of the minimum subjects was 18 to 30 years old. Thus, an older age group was linked to this condition. Table 1 shows that 33%, 28%, & 39% of the individuals had AKI stages 1, 2, & 3.

Table 1: Gender, age & AKI distribution among the study subjects

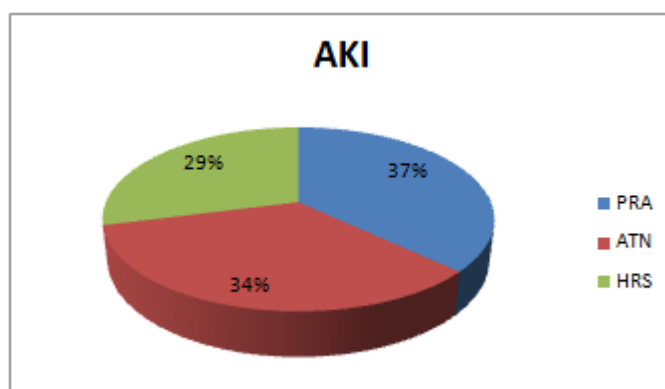
Gender	N	%
Male	89	89
Female	11	11
Age Group (in years)		
18-30	6	6
31-40	15	15
41-50	21	21
51-60	27	27
>60	31	31
AKI		
AKI-1	33	33
AKI-2	28	28
AKI-3	39	39
Total	100	100

Table 2 indicates that 81%, 9%, 3%, 2%, & 1% of the participants had cirrhosis due to alcohol, hepatitis C virus-related cirrhosis, hepatitis B virus-related cirrhosis, NASH, & Willson's disease, respectively.

Table 2: Cause of cirrhosis among the study subjects

Cause of Cirrhosis	N	%
Alcoholic cirrhosis	81	81
Hepatitis B Virus related	9	9
Unknown aetiology	4	4
Hepatitis C Virus related	3	3
NASH	2	2
Willson's disease	1	1
Total	100	100

Acute tubular necrosis (ATN), hepatic syndrome (HRS), & prerenal azotemia (PRA) were found in 37%, 34%, & 29% of the individuals, respectively (graph 1).



Graph 1: Etiological classification of AKI with cirrhosis patients

Table 3 presents the investigative profile of individuals with cirrhosis based on the etiology of AKI. Every one of the research parameters, i.e. It was discovered that the following values were abnormal: temperature (F), pulse (/min), SBP (mmhg), DBP (mmhg), Hb, TC (\*103/cumm), urea (mg/dl), & creatinine (mg/dl). Subjects with PRA had the highest mean serum creatinine levels, whereas subjects with HRS had higher mean blood pressure. Among participants with PRA, HRS, & ATN, no discernible difference was found in relation to the study's parameters.

Table 3: Investigative profile according to etiology of AKI in cirrhosis patients

Parameters	PRA		HRS		ATN		p value
	Mean	SD	Mean	SD	Mean	SD	
Temp (F)	99.82	1.26	98.73	1.17	99.95	1.13	0.18
Pulse (/min)	95.51	12.70	95.08	11.24	95.97	10.79	0.32
SBP (mmhg)	130.44	14.58	133.18	13.81	129.25	11.27	0.49
DBP (mmhg)	86.55	7.92	84.89	6.44	85.96	6.83	0.60
Hb	10.23	3.04	10.95	3.17	10.61	3.08	0.47
TC (*10 <sup>3</sup> /cumm)	21.38	7.30	21.02	7.64	21.90	6.76	0.26
Urea (mg/dl)	130.69	52.06	129.03	50.58	130.1	50.97	0.78
Creatinine (mg/dl)	3.58	1.81	3.21	2.06	3.12	2.05	0.29

The individuals with PRA, HRS, & ATN had mean Child-Pugh scores of 10.8±1.1, 10.96±1.07, & 11.39±1.04, respectively. Despite the fact that patients with ATN had higher Child-Pugh scores than those with HRS & PRA, no discernible difference was identified (p>0.05). The participants with PRA, HRS, & ATN had mean hospital stays of 9.78±1.13, 12.55±1.09, & 10.02±1.14, respectively. Despite the fact that participants with HRS required longer hospital stays (measured in days) than subjects with ATN or PRA, no discernible difference was identified (p>0.05). 38% of the patients indicated their overall mortality. The participants with ATN had the highest recorded death rate (55.88%), followed by HRS (44.83%). The participants with PRA had the lowest mortality rate. Using the chi square test, a statistically significant difference of p<0.05 was established when mortality in patients with cirrhosis was examined according to different etiologies of AKI (table 4).

Table 4: Outcome according to etiology of AKI in cirrhosis patients

	PRA		HRS		ATN		p value
	Mean	SD	Mean	SD	Mean	SD	
Child-Pugh score	10.8	1.1	10.96	1.07	11.39	1.04	0.22
Hospital stay (in days)	9.78	1.13	12.55	1.09	10.02	1.14	0.07
	<b>N=37</b>	<b>%</b>	<b>N=29</b>	<b>%</b>	<b>N=34</b>	<b>%</b>	
Mortality	6	16.22	13	44.83	19	55.88	0.004*

\*statistically significant.

**Discussion:**

Several research have looked into the incidence of AKI in people with cirrhosis. The most recent systematic review, which included 30 studies & 18,474 subjects overall, found that 29% of people with cirrhosis also had AKI.<sup>8</sup> This assessment showed a great deal of variability, which may have resulted from variations in the diagnostic criteria used to characterize & categorize AKI. In order to analyze the clinical profile of patients with acute kidney injury in liver diseases, the current prospective observational research was carried out among 100 cases diagnosed with acute or CLD with evidence of ACI as per KIDGO criteria & with an age greater than 18 years in the patient “department of Gastroenterology at MM Institute of Medical sciences Mullana, Ambala”. The study took place over the course of one year, from December 1, 2022, to November 30, 2023.

Age groups >60 years old accounted for the largest percentage of subjects (31%) & 51–60 years old (27%). The age range of the minimum subjects was 18 to 30 years old. Thus, an older age group was linked to this condition. 89% & 11% of the participants were male & female, respectively. This study had a male-dominated population as a result. In their work, Purohit A et al<sup>9</sup>. demonstrated a similar male dominance. Male involvement is higher than female involvement in several other studies. For example, Andrew S et al.<sup>10</sup> reported that the cohort's median age was 58 (50, 65) years. Seventy-one percent of the participants were men. The mean age, according to Jaiganesh et al.<sup>11</sup>, was 48.32 ± 10.19. Of these, there were only 5% (5/100) girls & 95% (95/100) males. Fleming KM et al<sup>12</sup> discovered that as people age, the incidence of chronic liver disease rises. Similar to our study, this

one also revealed that men made up the majority of the patient population. Additionally, the study discovered that the incidence in men was more than 50% higher than in women<sup>1</sup>.

In the current study, 81%, 9%, 3%, 2%, & 1% of the participants reported having cirrhosis as a result of alcohol, hepatitis B virus-related, hepatitis C virus-related, NASH, & Willson's disease, respectively. In a similar vein, Jaiprakash et al<sup>13</sup> discovered that chronic alcoholism (29.8%) was the most common cause of cirrhosis, followed by cryptogenic disease (25.3%) & chronic hepatitis B (24.1%). According to Jaiganesh et al<sup>12</sup>, alcohol was the most ordinary cause of cirrhosis, accounting for 85% (85/100 cases), followed by hepatitis B (11% (11/100 cases) & the C virus (4% (4/100 cases). In 33.3% (5/15) of cirrhotic cases with a viral etiology, renal impairment was noted.

In this study, sepsis was the most frequent precipitating cause, followed by elevated blood pressure & UTI. Similar results were also found in the meta-analysis conducted by Nall S et al<sup>14</sup>. Our study also revealed a substantial correlation between AKI & sepsis or septic shock in cirrhosis patients, which is in line with the findings of Tariq et al<sup>15</sup>. This correlation can be explained by the intricate interactions among cirrhosis-related reduced immune function, systemic inflammation, & the possibility of bacterial infections exacerbating pre-existing liver & kidney damage. Severe immunological reaction to infection, known as sepsis, can aggravate organ dysfunction, particularly renal impairment, & alter hemodynamics in cirrhosis patients. Patients with cirrhosis may be particularly vulnerable to the deleterious effects of sepsis on renal function due to their weakened physiological state<sup>16</sup>.

The individuals with PRA, HRS, & ATN had mean Child-Pugh scores of  $10.8 \pm 1.1$ ,  $10.96 \pm 1.07$ , &  $11.39 \pm 1.04$ , respectively. Even though participants with ATN had higher Child-Pugh scores than those with HRS & PRA, this study did not find a significant difference ( $p > 0.05$ ). AKI risk is shown to be correlated with a high Child-Pugh score, as demonstrated by the Nall S et al<sup>14</sup> study. These results support the correlation between higher MELD scores, higher Child-Pugh scores, & a higher risk of developing AKI. They also align with the review of Tariq et al<sup>15</sup>. These correlations highlight the significance of monitoring & controlling kidney function, particularly in those with more advanced liver illness, & are useful in clinical settings, particularly for medical personnel caring for patients with liver disease. According to Purohit A et al.'s<sup>9</sup> study, the highest percentage of AKI patients are seen in Child Class C (56%), followed by Child Class B (34%), & Child Class A (10%) patients. These findings are consistent with previous research showing that as Child class increases, patients with cirrhosis have a higher frequency of AKI. Attia et al. also showed that individuals with Child-Pugh class A, B, & C cirrhosis had incidences of renal disease of 6.7%, 13.5%, & 33.9%, respectively.

Acute tubular necrosis (ATN), hepatorenal syndrome (HRS), & prerenal azotemia (PRA) were reported in 37%, 34%, & 29% of the study participants, respectively. In a similar vein, Meghna Vaidya et al<sup>17</sup> found that prerenal azotemia (38.37%) was the most common cause of acute kidney injury, followed by acute tubular necrosis (32.56%) & hepatorenal syndrome (29.07%).

The current study's individuals with PRA, HRS, & ATN had mean hospital stays (in days) of  $9.78 \pm 1.13$ ,  $12.55 \pm 1.09$ , &  $10.02 \pm 1.14$ , respectively. Even though participants with HRS required longer hospital stays (measured in days) than subjects with ATN or PRA, no discernible difference was identified ( $p > 0.05$ ). Meghna Vaidya et al<sup>17</sup> report that the average length of hospital stay for AKI patients with PRA was 7 days, compared to 15 days & 14 days for HRS & ATN patients, respectively. While the difference between HRS & ATN was not statistically significant, the difference between AKI owing to PRA vs HRS & PRA versus ATN was.

38% of the patients indicated their overall mortality. The participants with ATN had the highest recorded death rate (55.88%), followed by HRS (44.83%). In this study, the group of participants with PRA had the lowest mortality rate, with a statistically significant difference determined to be  $p < 0.05$ . 45 (52.33%) of the 86 instances of AKI with cirrhosis that were observed have survived. In contrast to HRS & ATN patients, which had survival rates of 44% & 46.43%, respectively, PRA cases had the highest survival rate; nevertheless, the difference was not statistically significant. The most frequent clinical manifestation among patients with documented mortality was encephalopathy, which was followed by hypotension & tight ascites (39.02% each). Meghna Vaidya et al.<sup>17</sup> noted in their study

that there was a statistically significant difference in the distribution of clinical features between the individuals that survived & those that died.

It is important to consider the constraints of our study when interpreting the results. This trial only involved one centre. Its participants were mostly men who were alcoholics, hence the results might not apply to other situations. In the Asian population, however, no current study has been published utilizing the updated 2015 Ascites Club Criteria. Therefore, we think that our findings have a significant impact on AKI patients who also have liver cirrhosis.

Our findings imply that, in comparison to PRA, people with cirrhosis & AKI who have HRS & ATN represent a seriously unwell population. Differentiating between these reasons is especially crucial for therapy & prognosis.

In conclusion, patients with liver cirrhosis frequently experience acute kidney injury (AKI), which is linked to a worsening of the prognosis. This calls for extra care in keeping an eye on these individuals' renal function. It may be possible to diagnose AKI sooner & modify treatment based on severity by using the RIFLE/AKIN classification to identify AKI & assess its severity. Improving outcomes requires early diagnosis & treatment of cirrhosis as well as recognition of the common causes of AKI. In conclusion, there is a substantial in-hospital death rate linked to acute renal damage in liver cirrhosis. The two main indicators of in-hospital mortality are oliguria & a greater stage of AKI at presentation. The outcome of pre-renal AKI is superior to that of ATN or HRS.

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