

Predictors of Acute Kidney Injury in Chronic Liver Disease: Role of Hemodynamic Instability, Infections, and Drug Exposure

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ABSTRACT

Background: Acute kidney injury (AKI) is a common and clinically important complication in chronic liver disease patients (CLD). This study was carried out to examine the major clinical predictors associated with AKI in patients with chronic liver disease, with particular attention to hemodynamic instability, infection, and drug exposure as identifying these key predictors is essential for early intervention and prevention.

Methods: This observational cross-sectional study was carried out in the department of Medicine at Hamidia Hospital, Bhopal, a tertiary care center in central India and included 150 patients with chronic liver disease and AKI. Demographic details, risk factors, clinical, laboratory, and treatment-related variables were recorded. The factors specifically assessed were hypotension, gastrointestinal bleeding, infectious complications, and drug exposure. Statistical analysis was performed using EPI Info 7.0, and a p value of less than 0.05 was considered statistically significant.

Results: The mean age of the patients was 49.63 ± 11.74 years, and most belonged to the 51-60 year age group. Males constituted 76% of the study patients. Hypotension was present in 28% of patients. Upper gastrointestinal bleeding was the most frequent associated factor and was seen in 40.67% of cases. Infectious causes included sepsis in 28% and spontaneous bacterial peritonitis in 12%. Drug exposure was also common, particularly diuretic use (36%) and nephrotoxic drug combinations (21.33%). Most patients had advanced liver disease, with 56.67% classified as Child-Turcotte-Pugh class C.

Conclusion: AKI in chronic liver disease was commonly seen in the setting of hemodynamic instability, infection, bleeding, and drug exposure, usually on a background of advanced liver dysfunction. Recognition of these common clinical settings may help in earlier management and prevention of further renal injury.

Keywords: Acute kidney injury, chronic liver disease, predictors, hypotension, sepsis, diuretics.

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Introduction

Acute kidney injury is one of the most important complications seen in patients with chronic liver disease, usually after decompensation sets in. Once renal dysfunction develops in cirrhosis, hospital stay becomes more complicated, short-term outcomes worsen considerably and healthcare burden increases significantly (1,2). For this reason, clinicians are more concerned with the clinical setting in which AKI develops, identification of the precipitating factors

and whether the precipitating factors can be corrected early.

As per the literature and published studies the mechanisms are well recognized that initiates with portal hypertension and splanchnic vasodilation leading to reduction in effective arterial blood volume and set the stage for renal hypoperfusion (6,7). Systemic inflammation, infection and nephrotoxic drug exposure like NSAIDs further aggravate this process and may contribute directly to renal injury

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(8,9). In clinical practice, AKI in patients with cirrhosis develop following an initiating event rather than spontaneously without and acute event or trigger. And the most common triggers are infections-including sepsis and spontaneous bacterial peritonitis, that are well recognized (10,11). In patients with advanced liver disease upper gastrointestinal bleeding is a very important cause of sudden hemodynamic instability that can precipitate AKI. Previous studies have reported AKI in a significant proportion of hospitalized patients with chronic liver disease, usually between 20% to 50%, with more chances in patients with advanced liver disease that is Child-Turcotte Pugh C and patients with higher MELD scores (3,4,11). Significant decrease in urine output and even minimal rise in levels of serum creatinine have prognostic significance in these patients as early detection of renal injury can prevent the further complexity of treatment, improve clinical outcomes and reduce hospital stay (2,5). Severity of liver disease is commonly assessed using scores such as Child-Turcotte-Pugh (CTP) and MELD in patients with advanced liver dysfunction (14). Drug exposure is also an important preventable contributor to renal injury in CLD patients. Diuretics, one of the essential medications in prescription of CLD patients for management of ascites is one of the common drug contributor for renal injury as it can cause hypovolemia if used in excess or in unstable patients. Nephrotoxic medications like NSAIDs, aminoglycosides can further impair renal perfusion or cause direct renal injury. In most patients, multiple precipitating factors are present at the same time, making the clinical picture more complex and increasing the risk of AKI. The broad pathophysiology leading to AKI in patients with liver disease is similar, but the relative contribution of these factors may differ across hospitals and patient populations. The present study was therefore undertaken to assess the major clinical predictors of acute kidney injury in patients with chronic liver disease admitted to a tertiary care centre in Central India, with specific emphasis on hemodynamic instability, infections, bleeding, and drug exposure.

Materials and Methods

Study design and setting: This observational cross-sectional study was conducted in the Department of Medicine, Hamidia Hospital, Bhopal.

Study population: A total of 150 patients with chronic liver disease and acute kidney injury were included in the study.

Inclusion criteria:

- Diagnosed cases of chronic liver disease
- Evidence of acute kidney injury AKI defined according to KDIGO criteria by the presence of any one of the following:
 - (i) Increase in serum creatinine by 0.3 mg/dL or more within 48 hours
 - (ii) Increase in serum creatinine to 1.5 times or more from baseline within 7 days
 - (iii) Urine output less than 0.5 mL/kg/hour for 6 hours

Exclusion criteria:

- Pre-existing chronic kidney disease

Data collection: Data was gathered regarding demographic details, clinical profile, blood pressure status with particular attention to hypotension, infection status including sepsis and spontaneous bacterial peritonitis, history or presence of gastrointestinal bleeding, and exposure to medications such as diuretics, nonsteroidal anti-inflammatory drugs, and other nephrotoxic drug combinations.

Outcome variable: The primary outcome was the identification of major clinical predictors associated with acute kidney injury in patients with chronic liver disease.

Statistical analysis: Data were analyzed using EPI Info 7.0. Categorical variables were expressed as percentages. Associations between predictors and AKI were evaluated using the chi-square test. A p value of less than 0.05 was considered statistically significant.

Results

A total of 150 patients with chronic liver disease complicated by acute kidney injury were included in the analysis. The study focused on the major clinical factors associated with AKI, particularly hemodynamic instability, infections, bleeding events, and drug exposure.

1. Demographic characteristics:

The mean age of the study population was 49.63 +/- 11.74 years. The largest proportion of patients belonged to the 51-60-year age group (27.33%) and there was a clear male predominance as male patients accounted for 76% of the study population.

Table-1: Age Distribution of Chronic Liver Disease Patients with Acute Kidney Injury

Age (Years)	No of cases	Percentage
18-30	10	6.67%
31-40	29	19.33%
41-50	40	26.67%

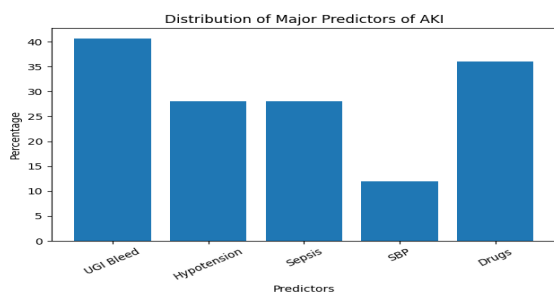
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51-60	41	27.33%
>60	30	20.00%
Total	150	100.00%
Mean ± SD	49.63 ± 11.74	

2. Major predictors of AKI

Table-2: Distribution of major likely predictors of AKI among Chronic Liver Disease Patients

Risk factors	No of cases	Percent age
SBP (Spontaneous bacterial peritonitis)		
No	132	88.00%
Yes	18	12.00%
Hypotension		
No	108	72.00%
Yes	42	28.00%
Total	150	100.00%
UGI Bleed		
No	89	59.33%
Yes	61	40.67%
Total	150	100.00%
Sepsis		
<4000	25	16.67%
4000-11000	83	55.33%
>11000	42	28.00%
Total	150	100.00%



3. Drug-related predictors: Drug exposure was frequently identified. Diuretic use

was present in 54 patients (36%), while drug combinations and other potentially nephrotoxic drug use (e.g – NSAIDS, lactulose, telmisartan) were noted in 32 patients (21.33%).

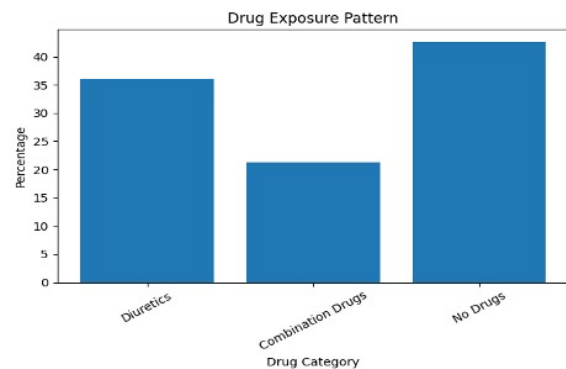
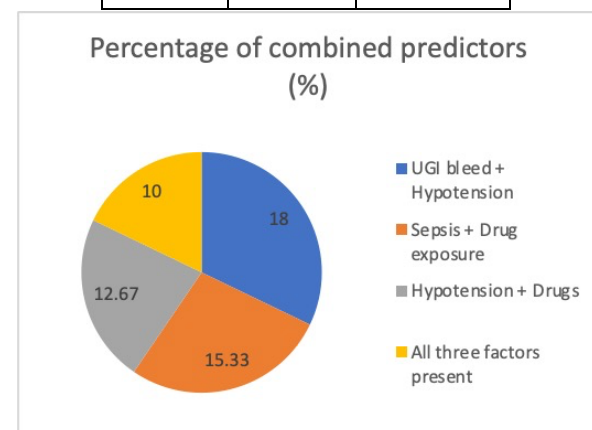


Table 3: Drug exposure

Drug Category	Number	Percentage (%)
Diuretics	54	36
Diuretics + combinations(NSAIDS, Lactulose , Telmisartan)	32	21.33
No drug exposure	64	42.67

4. Severity of liver disease: Most patients had advanced liver disease. CTP class C was the most common category, accounting for 56.67% of cases, followed by class B in 36% and class A in 7.33%.

CTP Class	Number	Percentage (%)
A	11	7.33
B	54	36
C	85	56.67



5. Combined predictor analysis:

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More than one associated factor was often present in the same patient. The most frequent combinations were upper gastrointestinal bleeding with hypotension (18.00%), sepsis with drug exposure (15.33%), and hypotension with drug exposure (12.67%). All three factors were present simultaneously in 10.00% of cases.

Combination	Percentage (%)
UGI bleed + Hypotension	18
Sepsis + Drug exposure	15.33
Hypotension + Drugs	12.67
All three factors present	10

Discussion

In this study, we examined the clinical pattern of AKI in patients with chronic liver disease, with particular attention to the factors present at the time kidney injury was first identified. A consistent pattern emerged: most patients were middle-aged men with advanced liver disease, and AKI frequently occurred in the setting of upper gastrointestinal bleeding, hypotension, infections, or exposure to certain medications. The findings highlight that AKI in CLD patients is most likely the result of acute precipitating factors superimposed on already compromised circulatory state, rather than a consequence of progressive liver dysfunction alone. The age and sex distribution in this study is not unexpected and is consistent with the previous studies data. Most patients belonged to the 51-60-year age group, and more than three-fourths were male. This pattern is likely linked to the burden of alcohol-related liver disease and to the fact that patients with longstanding cirrhosis often present only after decompensation has occurred. Once that stage is reached, even a relatively brief period of hemodynamic stress after any acute precipitating event like upper gastrointestinal bleeding, hypotension, infections may be enough to precipitate AKI.

Hemodynamic instability due to multiple causes emerged as one of the most important predictors in the present study. Hypotension was observed in a significant proportion of patients and add on to the already reduced effective arterial blood volume,

which is a central mechanism in the pathogenesis of AKI in cirrhosis (6,7). Cirrhotic patients exhibit marked splanchnic vasodilation and impaired vascular responsiveness, resulting in renal hypoperfusion. Even transient episodes of hypotension can significantly compromise renal blood flow and precipitate AKI. These findings are consistent with previous studies that have demonstrated the critical role of circulatory dysfunction in renal impairment in CLD (1,3)

Upper gastrointestinal bleeding was the most common factor seen in this study. This is important because it is common in advanced liver disease, and even small blood loss can quickly reduce renal blood flow and resulting in prerenal azotemia (12). If not managed early, this may progress to acute tubular necrosis. The presence of hypotension in many patients supports this explanation. Overall, it appears that most cases of AKI were due to reduced blood flow rather than direct kidney damage.

Infections were also an important part of the clinical picture. Sepsis was seen in 28% of patients, while spontaneous bacterial peritonitis was present in 12%. These findings are consistent with the well-known role of infections in triggering kidney dysfunction in cirrhosis, mainly through inflammation, vasodilation, and reduced organ perfusion (8-11). From a clinical perspective, this highlights a simple but important point: in cirrhotic patients with fever, suspected infection, or spontaneous bacterial peritonitis, renal function should be monitored closely, even before clear signs of AKI appear.

Drug exposure emerged as another unavoidable precipitating factor. Diuretics were used in over one-third of patients, can lead to excessive fluid loss and hypovolemia if not monitored carefully (13). Nephrotoxic drugs like NSAIDs use were also common which impairs renal perfusion by inhibiting prostaglandin mediated vasodilation, further increasing the risk of AKI. This finding is easy to understand in routine practice. Patients with chronic liver disease often require diuretics for ascites and may also be exposed to analgesics or antibiotics. When drug exposure occurs together with bleeding, hypotension, or infection, the cumulative effect on renal function may be substantial. These findings underscore the importance of cautious drug use and regular monitoring in patients with CLD. The CTP profile of this study is also worth noting. More than half of the patients were in class C, indicating advanced hepatic dysfunction. Severe liver disease does not by itself explain every episode of

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AKI, but it is associated with profound circulatory and metabolic disturbances, which predisposes for renal dysfunction(14). In that sense, the data suggest that advanced cirrhosis lowers the threshold at which bleeding, infection, or drug exposure results in renal injury.

The analysis of combined predictors supports the same overall interpretation. Combinations such as upper gastrointestinal bleeding with hypotension, sepsis with drug exposure, and hypotension with drug exposure were commonly observed, and about 10% of patients had all three factors together. This likely reflects real-world clinical practice more accurately than considering any single factor alone. In cirrhosis, AKI usually develops due to multiple overlapping insults rather than a single isolated cause.

The broader clinical relevance of these observations is consistent with evidence showing that AKI in cirrhosis is closely linked to adverse outcomes (15). This study has limitations. It was cross-sectional, conducted at a single centre, and did not include long-term outcome assessment. It therefore describes associations rather than prognosis or causality. Even so, it provides a practical view of the clinical settings in which AKI was encountered in this patient population.

Conclusion

In this observational cross sectional study of patients with chronic liver disease, AKI was most often seen in patients with upper gastrointestinal bleeding, hypotension, infection, and drug exposure. Diuretic use and nephrotoxic drug combinations were common, and many patients had more than one associated factor at the same time. Most patients had advanced liver disease and were in Child–Turcotte–Pugh class C. Overall, these findings suggest that AKI in chronic liver disease typically develops on a background of severe liver dysfunction and is then triggered by acute factors such as hemodynamic instability, infections, or treatment related insults.

Careful early clinical assessment remains important. Attention to upper gastrointestinal bleeding, blood pressure, infection, and medication history may help identify patients at risk before renal injury progresses and early intervention to be initiated if renal injury ensues. Further prospective multicentre studies are needed to clarify the relative contribution of these factors and their effect on outcomes.

Limitations

- Cross-sectional design

- No long-term outcome assessment
- Single-center study

Future

- Prospective multicenter studies
- Development of predictive scoring systems
- Evaluation of preventive interventions

Directions

Declarations

Funding: None
Conflict of Interest: None
Ethical Approval: Obtained
Consent: Taken

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