



CLINICAL PROFILE, PRECIPITATING FACTORS, AND OUTCOMES OF ACUTE-ON-CHRONIC LIVER FAILURE: A PROSPECTIVE STUDY FROM NORTHEAST INDIA

Monush Senar*

Post Graduate Trainee, Department of General Medicine, Assam Medical College & Hospital (AMCH), Dibrugarh, Assam *Corresponding Author

Dr. Anup Kumar Das

Professor, Department of General Medicine, Assam Medical College & Hospital (AMCH), Dibrugarh, Assam

Dr. Chimanjita Phukan

Professor & Head, Department of Microbiology, Assam Medical College & Hospital (AMCH), Dibrugarh, Assam

ABSTRACT **Background:** Acute-on-chronic liver failure (ACLF) is an acute deterioration of pre-existing chronic liver disease, triggered by various precipitants and associated with systemic inflammation, multiple organ dysfunction, and high short-term mortality. The condition shows striking geographic variability, with alcohol being the leading precipitant in Asia, while infections predominate in Western cohorts. Understanding regional patterns of ACLF is critical for designing prevention and management strategies. In this prospective observational study, 60 ACLF patients fulfilling APASL 2019 criteria were recruited between November 2023 and October 2024 at Assam Medical College, Dibrugarh. **Results:** The mean age was 41 ± 9 years, with strong male predominance (86.7%). Alcohol was the leading precipitant (53.3%), followed by variceal bleed (11.7%), infections including spontaneous bacterial peritonitis, cellulitis, urinary tract infection, and lower respiratory tract infection (collectively ~27%), herbal medications (6.7%), and hepatitis E (1.7%). Overall 28-day mortality was 28.33%. **Conclusion:** ACLF in Northeast India primarily affects young to middle-aged men, with alcohol as the most common precipitant. Mortality is unacceptably high, underscoring the need for public health interventions focusing on alcohol misuse prevention, early management of infections, and improved critical care support.

KEYWORDS : ACLF, precipitating factors, alcohol, infection, epidemiology, India

INTRODUCTION

Acute-on-chronic liver failure (ACLF) has emerged as a distinct clinical syndrome that occupies an intermediate position between acute liver failure and decompensated cirrhosis. It is characterized by an acute hepatic insult superimposed on chronic liver disease, leading to jaundice, coagulopathy, ascites, and encephalopathy within a short period. Importantly, ACLF is associated with exaggerated systemic inflammation, multiple organ dysfunction, and a high risk of short-term mortality.⁴

The definition of ACLF varies across regions. The Asian Pacific Association for the Study of the Liver (APASL) defines ACLF as an acute hepatic insult manifesting as jaundice and coagulopathy, complicated by ascites and/or encephalopathy within 4 weeks, in a patient with pre-existing chronic liver disease or cirrhosis.¹ The European Association for the Study of the Liver–Chronic Liver Failure (EASL-CLIF) consortium definition emphasizes multi-organ failure and mortality risk. Despite differences, both recognize ACLF as a distinct syndrome with high mortality.³

Globally, the precipitating factors of ACLF vary considerably. In Asia, alcohol remains the predominant trigger, accounting for more than half of the cases, as reported by Sarin et al. and subsequent APASL cohorts. In contrast, the CANONIC study from Europe and the NACSELD study from North America identified bacterial infections as the leading triggers.² Viral hepatitis, gastrointestinal bleeding, and drug-induced liver injury also contribute variably. These differences reflect not only epidemiology but also lifestyle, healthcare systems, and socioeconomic factors.

In India, alcohol-related liver disease is increasing due to changing drinking patterns, earlier age of initiation, and widespread availability of alcohol. This makes alcohol an especially relevant precipitant for ACLF in the Indian context. In addition, infections such as spontaneous bacterial peritonitis, urinary tract infections, and cellulitis are common triggers due to cirrhosis-associated immune dysfunction.⁵

There is limited data from Northeast India regarding the clinical profile and precipitants of ACLF. This region has a high prevalence of alcohol use, unique dietary and cultural practices, and limited healthcare resources, all of which may influence the epidemiology of ACLF. Therefore, this study was undertaken to evaluate the clinical profile, precipitating factors, and outcomes of ACLF patients in this region.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department

of Medicine, Assam Medical College and Hospital, Dibrugarh, over a period of 12 months (November 2023 – October 2024). A total of 60 patients were included based on the following inclusion criteria: (1) age above 18 years, (2) diagnosis of ACLF as per APASL 2019 criteria. Exclusion criteria included patients with hepatocellular carcinoma or other malignancies, and those with severe unrelated comorbidities.

Sample size was calculated by applying the formula Z^2pq/d^2 . Considering 95% confidence interval and taking 35% prevalence of ACLF, 15% absolute error, the sample size was calculated to be 39 and taking 30% non-response rate, the sample size came out at 50.7 which was rounded off to 60.⁶

All patients underwent a detailed clinical evaluation including history of alcohol intake, drug or herbal medication use, recent infections, gastrointestinal bleeding, and other potential triggers. Physical examination assessed for jaundice, ascites, hepatic encephalopathy, and signs of infection. Laboratory investigations included complete blood count, liver function tests, renal function tests, coagulation profile, and viral hepatitis markers. Imaging studies such as abdominal ultrasound and upper gastrointestinal endoscopy were used to detect features chronic liver disease, ascites and esophageal varices. Patients were followed for 28 days to document survival or mortality.

RESULTS

A total of 60 patients with ACLF were included in the study. The mean age was 41.01 ± 9.06 years, and the majority of patients (86.7%) were male, reflecting the high prevalence of alcohol-related liver disease in men in this region.

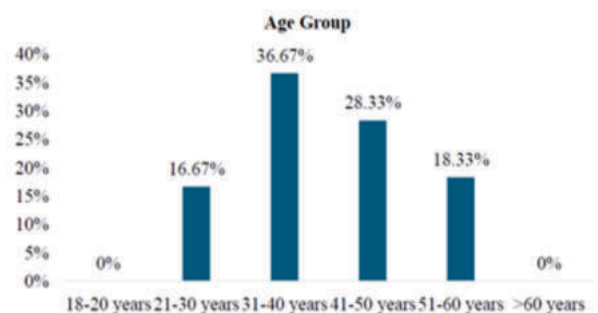


Figure 1: Age Distribution of ACLF Patients (n=60)

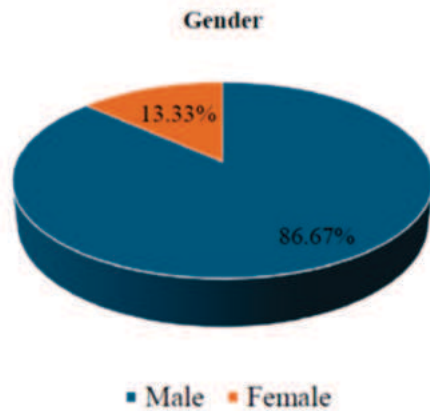


Figure 2: Gender Distribution of ACLF Patients (n=60)

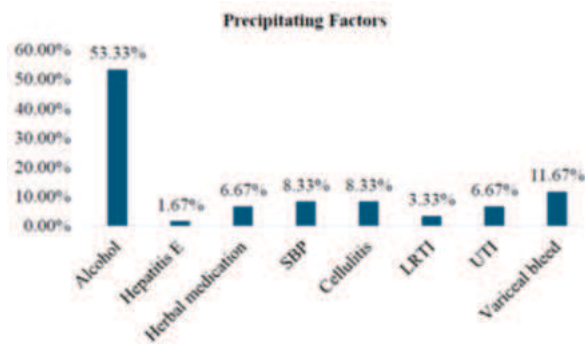


Figure 3: Distribution of Precipitating Factors in ACLF (n=60)

Alcohol accounted for more than half of the cases (53.3%). Variceal bleed was the next most frequent precipitant (11.7%). Infections, including spontaneous bacterial peritonitis (SBP), cellulitis, urinary tract infection (UTI), and lower respiratory tract infection (LRTI), collectively contributed to approximately 27% of cases. Herbal medication use and hepatitis E were less common precipitants. These findings highlight the central role of alcohol in precipitating ACLF in this region, with infections as important secondary triggers.



Figure 4: 28-day Mortality Outcomes in ACLF Patients (n=60)

Overall, 28-day mortality was 28.33%, with 17 patients succumbing to ACLF and 43 surviving beyond 28-day period.

DISCUSSION

This prospective study provides valuable insights into the clinical profile and precipitants of ACLF in Northeast India. The findings demonstrate that ACLF predominantly affects young to middle-aged men, with alcohol as the leading precipitant, followed by infections and variceal bleed. The demographic profile is consistent with earlier studies from India, which have reported younger age of onset compared to Western populations.⁹

The male predominance (86.7%) underscores the gendered pattern of alcohol consumption in India, where heavy drinking is far more common among men. This finding aligns with previous Indian and Asian cohorts but differs from some Western studies where gender

distribution is more balanced. The mean age of 41 years highlights the devastating impact of ACLF on individuals in their most productive years, contributing significantly to socioeconomic burden.

Alcohol was identified as the most common precipitant in this study (53.3%). This is consistent with APASL data, where alcohol accounted for more than half of ACLF cases.⁷ In contrast, the CANONIC study from Europe found bacterial infections to be the predominant triggers, followed by alcohol. These regional differences may reflect varying patterns of alcohol use, differences in healthcare systems, and genetic susceptibility to liver injury. Infections collectively accounted for more than a quarter of cases in this study, including spontaneous bacterial peritonitis (SBP), cellulitis, urinary tract infection (UTI), and lower respiratory tract infection (LRTI).¹⁰ This supports the concept of cirrhosis-associated immune dysfunction, where patients are more vulnerable to infections due to impaired innate and adaptive immune responses.¹¹

Variceal bleed was another important precipitant (11.7%). Gastrointestinal bleeding can lead to hemodynamic instability, bacterial translocation, and worsening of hepatic function, acting as a major trigger for ACLF. Herbal medications, though less common (6.7%), represent an emerging concern in India, as unregulated use of indigenous remedies can lead to hepatotoxicity.

The high short-term mortality (28.33%) observed in this study mirrors global reports, underlining the severity of ACLF.⁸ Unfortunately, liver transplantation, the definitive therapy, remains inaccessible for most patients in this region due to cost and infrastructure limitations.

This study has several important implications. First, public health policies must address harmful alcohol use, which remains the dominant precipitant of ACLF in this region. Second, early detection and prompt treatment of infections are essential to improve outcomes. Third, greater awareness about the hepatotoxic potential of herbal remedies is required.

The limitations of this study include its single-center design, relatively small sample size, and short follow-up period of 28 days. However, it provides valuable baseline data for Northeast India, where studies on ACLF are scarce. Future research should focus on multi-center cohorts, long-term outcomes, and evaluation of therapeutic interventions.

In conclusion, this study highlights the predominance of alcohol as a precipitant of ACLF in Northeast India, the significant role of infections and variceal bleed, and the unacceptably high short-term mortality.

CONCLUSION

ACLF in Northeast India primarily affects young to middle-aged men, with alcohol as the leading precipitant, followed by infections and variceal bleed. The 28-day mortality of 28.3% highlights the serious short-term prognosis of the condition. Preventive strategies targeting alcohol misuse, timely management of infections, and improved critical care are urgently needed to reduce mortality.

REFERENCES

- Sarin SK, et al. Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific Association for the Study of the Liver (APASL). *Hepatol Int*. 2019;13:353–90.
- Moreau R, et al. Acute-on-chronic liver failure is a distinct syndrome: results from the CANONIC study. *Gastroenterology*. 2013;144(7):1426–37.
- Jalan R, et al. Toward an improved definition of acute-on-chronic liver failure. *Gastroenterology*. 2014;147(1):4–10.
- Arroyo V, et al. Pathophysiology of ACLF: the role of systemic inflammation. *J Hepatol*. 2021;74(4):670–85.
- Albillos A, et al. Cirrhosis-associated immune dysfunction: systemic inflammation and acute-on-chronic liver failure. *J Hepatol*. 2014;61(6):1385–96.
- Mezzano G, Juanola A, Cardenas A, Mezey E, Hamilton JP, Pose E, et al. Global burden of disease: acute-on-chronic liver failure, a systematic review and meta-analysis. *Gut*. 2022;71(1):148–55.
- Sarin SK, Choudhury A. Acute-on-chronic liver failure: terminology, mechanisms and management. *Nat Rev Gastroenterol Hepatol*. 2016;13(3):131–49.
- Olson JC, Kamath PS. Acute-on-chronic liver failure: concept, natural history, and prognosis. *Curr Opin Crit Care*. 2011;17(2):165–9.
- Bernal W, Jalan R, Quaglia A, Simpson K, Wendon J, Burroughs A. Acute-on-chronic liver failure. *Lancet*. 2015;386(10003):1576–87.
- Clària J, Arroyo V, Moreau R. The systemic inflammatory response in decompensated cirrhosis and acute-on-chronic liver failure. *Nat Rev Gastroenterol Hepatol*. 2016;13(2):59–71.
- Katoonzadeh A, Laleman W, Verslype C, Wilmer A, Maleux G, Roskams T, et al. Immune dysregulation in acute-on-chronic liver failure: pathophysiological insights and clinical relevance. *Liver Int*. 2016;36(4):467–75.