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Original Research Article

Clinical profile of acute on chronic liver failure patients in a tertiary care hospital: a cross-sectional study

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ABSTRACT

Background: Acute-on-chronic liver failure (ACLF) is characterized by the sudden worsening of chronic liver disease (CLD) and high short-term mortality. This study evaluated the clinical profiles, outcomes, and predictors of early mortality.
Methods: A cross-sectional study was conducted in 51 patients with ACLF at Tirunelveli Medical College Hospital from April 2023 to April 2024. Clinical features, aetiologies, triggering factors, and prognostic scores such as model for end-stage liver disease (MELD), MELD-Na, chronic liver failure - organ failure (CLIF-OF), chronic liver failure - consortium acute-on-chronic liver failure (CLIF-C ACLF), APASL ACLF Research Consortium (AARC) were recorded. Outcomes, including intensive care unit (ICU) admission, readmission, early mortality, and transplant-free survival (TFS), were analyzed.
Results: Ethanol-related CLD was most common in males 43 (84.3%), and CAM-related factors were the leading trigger 26 (51%). The clinical features included jaundice (100%), ascites (98%), and encephalopathy (56.9%). Early mortality occurred in 13 (25.5%), overall mortality in 15 (29.4%), ICU admission in 40 (78.4%), and readmission in 22 (43.1%). TFS was 72.5% at 28 days, 66.6% at 3 months, 58.8% at 6 months, and 52.9% at 1 year. Non-survivors had significantly higher MELD-Na (31.5±3.6 versus 27.9±3.6; p=0.0028), AARC (11.2±1.9 versus 8.1±1.3; p<0.0001), CLIF-OF (11.2±1.0 versus 8.9±1.1; p<0.0001), and CLIF-C ACLF scores (52.4±5.5 versus 42.4±5.1; p<0.0001). Among 5 cases receiving PLEX, early mortality was 20% versus 26.1% without plasma exchange (PLEX) (p=1.000), and 28-day TFS was 100% versus 69.6% (p=0.300). Higher MELD-Na and AARC scores were associated with increased risk of death (p=0.011 and p=0.033, respectively).
Conclusion: Ethanol-related CLD was the predominant cause of ACLF, with complementary and alternative medicine (CAM)-related triggers. Higher MELD, MELD-Na, CLIF-OF, CLIF-C ACLF, and AARC scores predicted early death.

Keywords: AARC score, Acute-on-chronic liver failure, MELD-Na, Mortality, PLEX therapy

INTRODUCTION

Acute-on-chronic liver failure (ACLF) is an acute worsening of chronic liver disease (CLD), frequently triggered by hepatic or extrahepatic insults, leading to rapid deterioration and multi-organ failure with high short-term mortality.[1] Recognizing ACLF as a distinct clinical syndrome has become increasingly important for early diagnosis and tailored management strategies.[2] In India, studies at tertiary care centres have consistently shown that alcohol and viral hepatitis (notably hepatitis B) are the predominant aetiologies underlying CLD in patients with ACLF, with acute triggers such as sepsis or hepatitis reactivation amplifying the risk of poor outcomes.[3,4] A study from eastern India reported that sepsis, hyponatraemia, renal failure, and coagulopathy at admission were significantly associated with short-term mortality in ACLF patients.[5]

Data from a multicentre Indian cohort (INASL consortium) further substantiated that the number and type of organ failures, particularly renal dysfunction, advanced

hepatic encephalopathy, and the need for ventilator support, were independent predictors of in-hospital mortality in ACLF, with over 40% of patients dying during hospitalisation.[6] Furthermore, investigations in western India revealed that encephalopathy and elevated model for end-stage liver disease (MELD) scores (especially >27) were strong independent predictors of mortality, while other factors such as leukocytosis, serum bilirubin, and Child–Pugh scores were also correlated with outcomes in univariate analyses.[7]

Prognostic scoring systems tailored to ACLF have emerged to guide clinical practice. For example, the CLIF-C ACLF score has demonstrated superior accuracy over MELD, MELD-Na, and Child-Pugh scores in predicting short-term mortality among admitted patients with ACLF.[8] Aligning with, O'Leary et al developed the North American Consortium for the study of end-stage liver disease (NACSELD)-ACLF score, which effectively predicted 30-day survival in hospitalised patients with cirrhosis and ACLF.[9]

A study examining broader clinical profiles has highlighted common presentations such as jaundice, ascites, and hepatic encephalopathy, with in-hospital mortality rates ranging from 45% to 70%, depending on the severity and number of organ failures.[10] A single-centre study in eastern India found that 71% of ACLF patients died within three months.[11] Another prospective study from Northern India showed a combined 1-month and 3-month mortality of around 60%.[12] Similarly, a study from southern India reported a 43.1% mortality rate, with a sharp increase in deaths among patients having multiple organ failures.[13] Given the regional variations in disease burden and clinical presentation, it is vital to characterize the local patient profile and determinants of early mortality and treatment outcomes in this population. Therefore, this study aimed to describe the clinical profile of patients with ACLF, identify factors associated with early mortality, and determine variables predicting treatment outcomes.

METHODS

Study design and setting

This cross-sectional observational study was conducted with 51 patients with ACLF in the Department of Medical Gastroenterology, Tirunelveli Medical College Hospital, Tamil Nadu, over a period of one year from April 2023 to April 2024. Approval for the study was obtained from the Institutional Ethics Committee, and written informed consent was obtained from all patients before enrolment.

Inclusion criteria

All patients admitted to the Department of Gastroenterology during the study period who were diagnosed with ACLF based on the diagnostic definitions provided by the Asia-Pacific Association for the Study of the Liver (APASL) and European Association for the Study of the Liver-Chronic Liver Failure (EASL-CLIF) guidelines were included in the study.

Exclusion criteria

Patients with previously diagnosed hepatic decompensation, hepatocellular carcinoma, other systemic malignancies, portal vein thrombosis, or those aged >80 years were excluded.

Methodology

All eligible patients were admitted and underwent detailed evaluation at the time of presentation. A thorough clinical history and complete physical examination were conducted, focusing on identifying the underlying cause of CLD and any precipitating events of acute-on-chronic liver failure. The diagnostic workup included complete blood count, liver function tests, renal function tests, and coagulation profile with prothrombin time (PT) and international normalized ratio (INR). Cardiopulmonary assessment was performed using electrocardiography (ECG) and chest radiography.

Etiological screening was performed to identify the causes of CLD and precipitating factors for ACLF, including viral markers, autoimmune profiles, metabolic screening, and alcohol-related evaluations. Imaging studies, such as ultrasonography, computed tomography (CT), or magnetic resonance imaging (MRI) of the abdomen, were performed when required to assess liver morphology, ascites, and associated complications. Upper gastrointestinal endoscopy was performed to evaluate the varices and other possible sources of gastrointestinal bleeding. Additional investigations included ascitic fluid analysis, arterial blood gas (ABG) measurements, and urine, sputum, and blood cultures, whenever clinically indicated. In selected cases, liver biopsy was performed to assist in the etiological diagnosis.

The sequential organ failure assessment (SOFA) score was used to assess organ dysfunction, and a score of >3 points in any individual organ system was considered significant for organ failure. Prognostic scoring systems, including the MELD, MELD-Na, CLIF-C ACLF, CLIF-OF, and AARC scores, were calculated for each patient at admission and during follow-up to determine their predictive value for short-term outcomes.

Statistical analysis

All collected data were entered into Microsoft Excel and analyzed using IBM statistical package for the social sciences (SPSS) software v23. Continuous variables are expressed as mean±standard deviation (SD), whereas categorical variables are presented as frequencies and percentages. Statistical comparisons between categorical variables were performed using the chi-square test, while continuous variables were analyzed using the independent sample t-test. Statistical significance was set at $p<0.05$.

RESULTS

The mean age was 41.7±6.8 years old. Of the 51 patients, 46(90.2%) were male and 5 (9.8%) were female. Among the etiological factors, ethanol-related CLD was the most common, seen in 43 (84.3%) patients, followed by metabolic dysfunction-associated fatty liver disease (MAFLD) in 4 (7.8%), Wilson's disease in 2(3.9%), and hepatitis B in 2 (3.9%). Regarding triggering factors, CAM-related causes were observed in 26 (51%) patients, alcoholic hepatitis in 15 (29.4%), cellulitis in 4 (7.8%), and other causes, including UGI bleeding, SBP, and sepsis in 6 (11.8%). Clinically, jaundice was present in 51 (100%), ascites in 50 (98%), encephalopathy in 29 (56.9%), sepsis in 7 (13.7%), and organ failure in 8 (15.7%) (Table 1).

Table 1: Baseline demographics, etiological causes, triggering factors, and clinical features of ACLF patients.

Parameters	N (%)
Baseline demographics and etiological factors	
Age (years) (mean±SD)	41.7±6.8
Male	46 (90.2)
Female	5 (9.8)
Ethanol-related CLD	43 (84.3)
MAFLD	4 (7.8)
Wilson's disease	2 (3.9)
Hepatitis B	2 (3.9)
Triggering factors	
CAM-related	26 (51)
Alcoholic hepatitis	15 (29.4)
Cellulitis	4 (7.8)
Others (UGI bleed, SBP, sepsis)	6 (11.8)
Clinical features	
Jaundice	51 (100)
Ascites	50 (98)
Encephalopathy	29 (56.9)
Sepsis	7 (13.7)
Organ failure	8 (15.7)

The mean MELD score was 27.3±6.1, and the mean MELD-Na score on day 1 was 28.7±3.9. The mean CLIF-C ACLF score on day 1 was 44.9±6.1, and the mean CLIF-OF score on day 1 was 9.35±2.0. The mean AARC score on day 1 was 9.5±1.8 (Table 2).

Among the 51 patients with ACLF, index admission mortality was observed in 13 (25.5%), while the overall mortality during follow-up was 15 (29.4%). A total of 40 (78.4%) patients required ICU admission, and 22 (43.1%) were readmitted. The transplant-free survival (TFS) rates were 37 (72.5%) at 28 days, 34 (66.6%) at 3 months, 30 (58.8%) at 6 months, and 27 (52.9%) at 1 year (Table 3).

Table 2: Baseline prognostic scores of ACLF patients.

Scores	Mean±SD
MELD	27.3±6.1
MELD-Na (day 1)	28.7±3.9
CLIF-C ACLF (day 1)	44.9±6.1
CLIF-OF (day 1)	9.35±2.0
AARC score (day 1)	9.5±1.8

Table 3: Overall outcomes and survival of ACLF patients.

Outcome	N (%)
Index admission mortality	13 (25.5)
Overall mortality (follow-up)	15 (29.4)
ICU admission	40 (78.4)
Readmission	22 (43.1)
TFS	
28 days	37 (72.5)
3 months	34 (66.6)
6 months	30 (58.8)
1 year	27 (52.9)

Among the patients, early mortality (n=13) was strongly associated with disease severity. Organ failure was significantly more common among patients who died (53.8%, 7 cases) than among survivors (2.6%, 1 case) ($p<0.001$). The MELD-Na score on day 1 was higher in non-survivors (31.54±3.64) than in survivors (27.88±3.65) ($p=0.0028$). On day 14, non-survivors also had higher AARC scores (11.18±1.89 versus 8.09±1.26), CLIF-OF scores (11.20±1.03 versus 8.94±1.14), and CLIF-C ACLF scores (52.45±5.48 versus 42.38±5.10), all with $p<0.0001$ (Table 4).

Table 4: Predictors of early mortality in ACLF patients.

Parameters	Died (n=13)	Survived (n=38)	P value
Organ failure present	7 (53.8%)	1 (2.6%)	<0.001
MELD-Na (day 1)	31.54±3.64	27.88±3.65	0.0028
AARC score (day 14)	11.18±1.89	8.09±1.26	<0.0001
CLIF-OF score (day 14)	11.20±1.03	8.94±1.14	<0.0001
CLIF-C ACLF score (day 14)	52.45±5.48	42.38±5.10	<0.0001

Among the 51 ACLF cases, early death occurred in one (20%) and 12 (26.1%) patients in the PLEX and non-PLEX groups, respectively ($p=1.000$). ICU admission was required in 5 (100%) versus 35 (76.1%) patients ($p=0.570$). Readmissions were noted in 3 (60%) versus 19 (41.3%) ($p=0.640$), and transplant-free survival at 28 days

was achieved in 5 (100%) versus 32 (69.6%) (p=0.300). Higher MELD-Na (p=0.011) and AARC scores were significantly associated with an increased risk of death (p=0.033) (Table 5).

Table 5: Comparison of outcomes between plex and no plex groups in ACLF patients.

Outcome	PLEX (n=5) (%)	No PLEX (n=46) (%)	P value
Early mortality	1 (20)	12 (26.1)	1.000
ICU admission	5 (100)	35 (76.1)	0.570
Readmission	3 (60)	19 (41.3)	0.640
TFS at 28 days	5 (100)	32 (69.6)	0.300

DISCUSSION

In our study, ACLF primarily affected middle-aged men, mostly due to alcohol-related liver disease, with MAFLD, Wilson's disease, and hepatitis B being less common. Triggers included infections, alcoholic hepatitis, cellulitis, and complications such as bleeding or sepsis. Clinically, all patients had jaundice, most had ascites, over half had encephalopathy, and a few developed sepsis or organ failure. Similarly, Hareesh et al studied 40 patients with ACLF (mean age 43.3±12.2 years; 88% male) with alcoholic cirrhosis in 80%, triggered by previous decompensation or infection.[14] In another study, Zhang et al analysed 102 patients (mean age 56.96±12.18 years; 67% male), with variceal bleeding as the main cause of decompensation (68.6%) and ascites in most patients (moderate 27.5%, severe 24.5%). Treatments included endoscopic haemostasis (48%), mechanical ventilation (40.2%), and vasopressors (64.7%).[15] Likewise, Chetwood et al reviewed 615 patients (median age 57; 67.5% male) with cirrhosis due to hepatitis C virus (HCV) (36.3%), alcohol (35.5%), and non-alcoholic steatohepatitis (NASH) (13.5%). Common admissions were ascites (32.7%), hepatic encephalopathy (22.6%), and gastro intestinal (GI) bleeding (21.3%); 34% had ACLF (grade 1:20.6%, grade 2:29.7%, grade 3:49.8%).[16] Overall, both our study and previous reports show that ACLF mostly occurs in middle-aged men, is often triggered by alcohol-related liver disease or infections, and presents with jaundice, ascites, and encephalopathy.

In our study, the patients had high severity scores among MELD, MELD-Na, CLIF-OF, CLIF-C, ACLF, and AARC, reflecting advanced liver disease and notable organ dysfunction. Likely, Reddy et al. reported that non-survivors had higher MELD scores (30.04±2.37 versus 25.53±1.81) and that advanced Child-Pugh class C and higher EASL-CLIF grades were linked to increased mortality.[17] Likewise, Zhang et al found that non-survivors had higher CTP, MELD, CLIF-C OF, CLIF-SOFA, and CLIF-ACLF scores, with all scores predicting 3- and 6-month mortality; MELD-Na was higher in non-survivors but not significant at 28 days.[15] Similarly, Chetwood et al. reported median admission MELD 21 and MELD-Na 25, with CLIF-C ACLF showing AUROC 0.77 for 90-day transplant-free mortality; MELD and MELD-Na had AUROCs of 0.72 and 0.73.[16] In the same way, Hareesh et al found higher CLIF-C ACLF and CLIF-C OF scores in non-survivors, more frequent coagulation failure (62% versus 21%), and ACLF grade III in 42.9% of non-survivors.[14] Comparably, Chen et al. reported median ICU scores of CTP 9, MELD 23, CLIF-C OF 10, and CLIF-C ACLF 49.2, with APACHE III and CLIF-C ACLF showing the highest predictive accuracy for overall mortality.[18] These findings indicate that higher severity scores MELD, MELD-Na, CLIF-OF, CLIF-C, ACLF and AARC consistently predict worse outcomes in ACLF, with multiple scoring systems effectively identifying patients at greater risk of mortality.

In our study, index admission mortality was 13 (25.5%), and overall mortality during follow-up was 15 (29.4%). ICU admission occurred in 40 (78.4%) patients, and 22 (43.1%) were readmitted. Transplant-free survival rates were 72.5% at 28 days, 66.6% at 3 months, 58.8% at 6 months, and 52.9% at 1 year. Align with Reddy et al reported that 30 of 60 patients died within 3 months, with mortality closely linked to higher MELD scores and advanced ACLF grades.[17] Likewise, Chetwood et al found liver transplant (LT)-free mortality was higher in ACLF than AD patients (28-day 22.5% versus 10%, 90-day 55% versus 12.6%), with ICU admission in 52.6% and mortality rising with ACLF grade.[16] Overall, both our study and previous reports show that ACLF carries substantial early and short-term mortality, with ICU admission and disease severity strongly influencing outcomes.

In our study, early deaths were closely linked to more severe diseases. Patients who did not survive had more organ failures and higher severity scores throughout the first two weeks than those who survived. Similarly, Reddy et al. reported non-survivors had higher INR (>2.5 in 73.3% versus 16.6%), sepsis (60% versus 16%), renal failure (66.6% versus 16.6%), and hyponatremia (Na <130 mEq/l in 93.3% versus 46.6%).[17] In line with, Zhang et al found higher CTP, MELD, CLIF-SOFA, CLIF-ACLF, and CLIF-C OF scores in non-survivors, with CLIF-SOFA best predicting 28-day mortality (AUROC 0.805).[15] Likewise, Chetwood et al identified age, bilirubin, creatinine, INR, and white blood cell (WBC) as 90-day LT-free mortality predictors; AUROCs for 28-day mortality: MELD 0.81, MELD-Na 0.79, CLIF-C ACLF 0.78.16 Similarly, Hareesh et al observed higher CLIF-C ACLF (53.86±7.83 versus 44.11±6.62) and CLIF-C OF scores, more coagulation failure (62% versus 21%), and ACLF grade III (42.9% versus 5.3%) in non-survivors.[14] Chen et al reported higher MELD, CLIF-C OF, and CLIF-C ACLF in non-survivors, with APACHE III and CLIF-C ACLF superior for mortality prediction (p<0.001).[18] In Overall, early deaths in ACLF are consistently linked to greater disease severity, organ dysfunction, and higher predictive scores across different studies.

In our study, a small number of patients received PLEX therapy, whereas most did not. Early mortality, ICU admission, readmission, and short-term transplant-free survival rates were similar between the PLEX and non-PLEX therapy groups. Higher MELD-Na and AARC scores were associated with an increased risk of death. Accordingly, Chetwood et al. reported that among 209 recovered ACLF patients, 67.7% were readmitted within a median of 42 days, and 44.4% experienced a subsequent ACLF episode.[16] Align with this, Mukit et al compared 28 ACLF patients receiving PLEX or standard therapy, finding similar age, sex, and baseline scores; mortality was linked to higher bilirubin, MELD, MELD-Na, and AARC scores, with PLEX not significantly affecting outcomes ($p>0.05$).[19] Overall, both our study and previous reports indicate that PLEX does not significantly alter outcomes in ACLF, with patient prognosis largely determined by disease severity and key lab scores.

Limitations

This study was conducted at a single centre with a small sample size, which may limit the generalizability of the findings. The long-term outcomes were not assessed.

CONCLUSION

Ethanol-related CLD is the most common cause of ACLF, and CAM-related factors are the leading triggers. Higher MELD-Na, AARC, CLIF-OF, and CLIF-C ACLF scores were significant predictors of early mortality. Although PLEX therapy showed better short-term survival, the difference was not significant. Early identification of high-risk cases is essential for improving outcomes in patients with ACLF. Future studies with larger sample sizes and longer follow-up periods are needed to better evaluate the role of PLEX therapy and develop optimised strategies for early risk prediction and management.

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