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Evaluation of Clinical and Laboratory Profile among Patients with Acute on Chronic Liver Disease–A Cross-Sectional Study

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ABSTRACT

Background: Acute-on-chronic liver failure (ACLF) is defined as an acute hepatic insult shown as jaundice and Coagulopathies, which is exacerbated within 4 weeks by ascites and/or encephalopathy in patients with previously recognised or undetected chronic liver diseases.

Methods: A prospective study was done on 200 patients with an ACLF diagnosis, as well as an equal number of age-matched controls (non-ACLF). Demographic characteristics, clinical profiles, risk factors, and biochemical indicators were assessed in both ACLF and non-ACLF patients.

Results: The majority of the patients (46%) were above the age of 50, with men accounting for 87%. In ACLF, alcoholic liver disease was the most common (85.7%), followed by cirrhosis caused by the Hepatitis B virus (8.2%). Jaundice was seen in all cases, followed by ascites in 94.3% of patients. Oesophageal varices (66%), Splenomegaly (60%), hepatic encephalopathy (46%), acute malnutrition (32%), hepatomegaly (30%), and fever (20%). The triggering reasons included acute flare-ups of Hepatitis B infection in 60% of patients with Hepatitis B-related cirrhosis, recent drug use (44.8%), sepsis (28.9%), spontaneous bacterial peritonitis (14.7%), urinary tract infections (14.7%), acute hepatitis A in 2%, and acute hepatitis E in 1.2% of patients. High mortality was found to be significantly linked with hepatic encephalopathy, inadequate salt, and a high International Normalised Ratio (INR).

Conclusion: ACLF is distinguished by rapid deterioration, especially when multiorgan failure develops as a result of specific triggering circumstances in a previously recognised or unknown chronic liver ailment.

Key-words: Acute chronic liver failure, Alcoholic liver cirrhosis, Clinical profile, Biochemical parameters

INTRODUCTION

Acute Chronic Liver Failure (ACLF) refers to an acute decrease in liver function in people with Chronic Liver Disease (CLD).

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Acute-on-chronic liver failure (ACLF) is a clinical condition characterised by sudden hepatic decompensation, one or more extra-hepatic organ failures, and an increased risk of death in those who already have chronic liver disease [1,2]. ACLF is defined as a rapidly worsening course of a chronic liver disease that may be reversible and is either previously recognised or unknown [3]. ACLF has a high short-term mortality rate (50–90%) [4]. There are now two widely accepted working definitions of ACLF. "Acute hepatic insult manifesting as jaundice (defined as serum bilirubin level >5 mg/dl) and Coagulopathies (defined as international normalised ratio >1.5), complicated within 4 weeks by ascites and/ or

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encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease," according to the Asia Pacific Association for the Study of Liver (APASL) [5]. In 2013, the American Association for the Study of Liver Disease (AASLD) and the European Association for the Study of Liver (EASL) published an alternative definition of ACLF: "Acute deterioration of pre-existing chronic liver disease usually related to a precipitating event and associated with increased mortality at 3 months due to multi-system organ failure [6]. Being a dynamic illness, ACLF can improve, deteriorate, or have a moderate, prolonged course that allows us to evaluate the likelihood of a liver transplant. The aetiology of the precipitating event that induces ACLF has little bearing on the prognosis [7]. Systemic inflammation is one of the characteristics of ACLF. Consequently, compared to patients without ACLF, those with ACLF had higher white cell counts, plasma levels of C-reactive protein (CRP), and pro-inflammatory chemicals such as interleukin (IL)-6, IL-1β, and IL-8 [8]. In ACLF, triggering causes may be viral or non-infectious. Hepatitis B virus (HBV) infection reactivation is a common infectious aetiology, especially in Asia. Infection with the hepatitis E virus is very common, especially on the Indian subcontinent [9]. The APASL definition does not include bacterial infection as a precipitating event, even though it is a significant contributing factor to the development of ACLF in the West. Some of the non-infectious causes of ACLF include hepatotoxic drugs, herbal indigenous treatments, severe variceal haemorrhage, and major surgery [10]. The current study evaluates the clinical and biochemical spectrum, underlying chronic liver disease, different precipitating events, and characteristics that predict death in individuals with ACLF.

MATERIALS AND METHODS

Study design- This was a prospective cross-sectional hospital-based study conducted at the Department of General Medicine, Amaltas Institute of Medical Sciences, Dewas, Madhya Pradesh, India from Jan 2024- Nov 2024.

Participants and Study Setting- In a tertiary care Indian hospital, the Department of Medicine and the Department of Biochemistry collaborated to perform this prospective cross-sectional study. The study included 200 individuals with ACLF based on the Asia-Pacific Association for the Study of the Liver (APASL) criteria.[11]

Inclusion criteria

- Patients of both sexes who are older than 18 years.
- Individuals with an ACLF diagnosis based on APASL criteria
- Individuals who gave the study their written informed consent.

Exclusion criteria

- The patients were younger than eighteen.
- Patients with hepatocellular carcinoma, portal vein thrombosis, and pregnant women.
- Patients who refuse to participate in the research.

Methodology- The study covered all subjects who satisfied the eligibility requirements. Patient demographics, BMI, clinical presentation, aetiology, precipitating variables, test data, and endoscopic features were all documented. Nutritional status was evaluated using nutritional assessment scores. Patients with ACLF were further evaluated for the presence of precipitating causes, including acute hepatitis A and E virus infection, alcoholic hepatitis, infection, medication toxicity, and an abrupt flare-up of chronic hepatitis B. Haemogram estimation, liver and renal function tests, serum electrolyte (Na/K) measurements, viral serology (HIV/HBsAg/Anti-HCV/IgM HAV/IgM HEV), microscopic examination of the urine, chest X-ray, and abdominal ultrasonography were performed on these patients. The ACLF and non-ACLF groups were compared in every laboratory parameter.

Statistical Analysis- An Excel sheet was used to enter all of the data. SPSS 22 software was used to do the statistical analysis. For the relevant variables, the mean and median were determined. Multivariate analysis was used to compare variables that were significant in univariate analysis. A P value of less than 0.05 was considered significant.

RESULTS

In this study, 100 individuals with an ACLF diagnosis were enrolled and examined. With a mean age of 43.6±4.3 years, the majority of patients (46%) were over 50. Eighty-seven percent were men, 61% lived in rural areas, and 45% were from lower socioeconomic classes. Of the patients, 42% were overweight and 44% had completed primary school (Table 1).

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Table 1: Socio-Demographic features, among ACLF patientsat admission

Demographic features		Frequency (N:100)	Percentage (%)
Age group (years)	<30	17	17
	31-50	37	37
	>50	46	46
Mean±SD= 43.6±4.3 years			
Gender	Male	87	87
	Female	13	13
Residential status	Rural	61	61
	Urban	39	39
socio-economic class	Lower	45	45
	Middle	35	35
	Upper	20	20
Education	Illiterate	30	30
	Primary school	44	44
	Secondary school	21	21
	Graduate	5	5
Body mass index (Kg/m^2)	Normal	33	33
	Overweight	42	42
	Obese	25	25

In Fig. 1, the typical clinical manifestations are compiled. Ninety-three percent of patients had abrupt onset ascites, and 99 percent of patients had jaundice. 61% of patients had esophageal varices (>grade 2), 60% had Splenomegaly, 40% had hepatic encephalopathy, 32% had severe malnutrition, 33% had hepatomegaly, and 23% had fever.

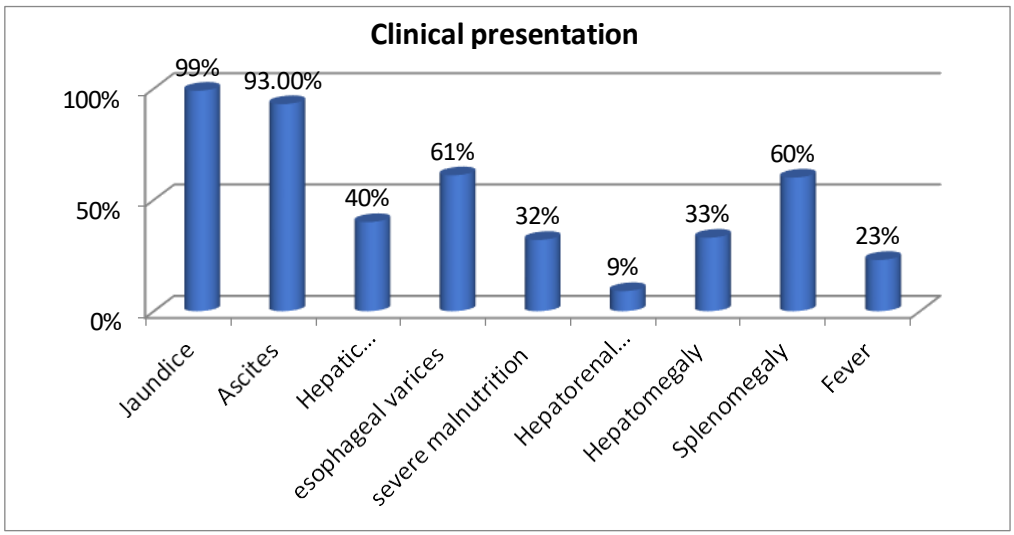

Fig. 1: Clinical presentation and prognostic variables among ACLF patients

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Acute flare-ups of Hepatitis B caused acute insults in 60% of patients with Chronic Hepatitis B-related cirrhosis while alcohol-related cirrhosis caused acute insults in 47% of patients with ACLF. In 28% of cases, sepsis was identified as the triggering cause. Of those, 44% reported recent drug usage. Two percent had hepatitis A, and two percent had acute hepatitis E. Multiple acute predisposing insults were found in 98 (40%) of the patients, of whom 32% had two insults at the same time and 19 (7%) had three or more insults. One acute insult occurred in 98 individuals (40%) of the total. There was no discernible triggering factor in 49 individuals (20%). Patients who received more than one insult died at a considerably higher rate than those who only received one (Fig. 2).

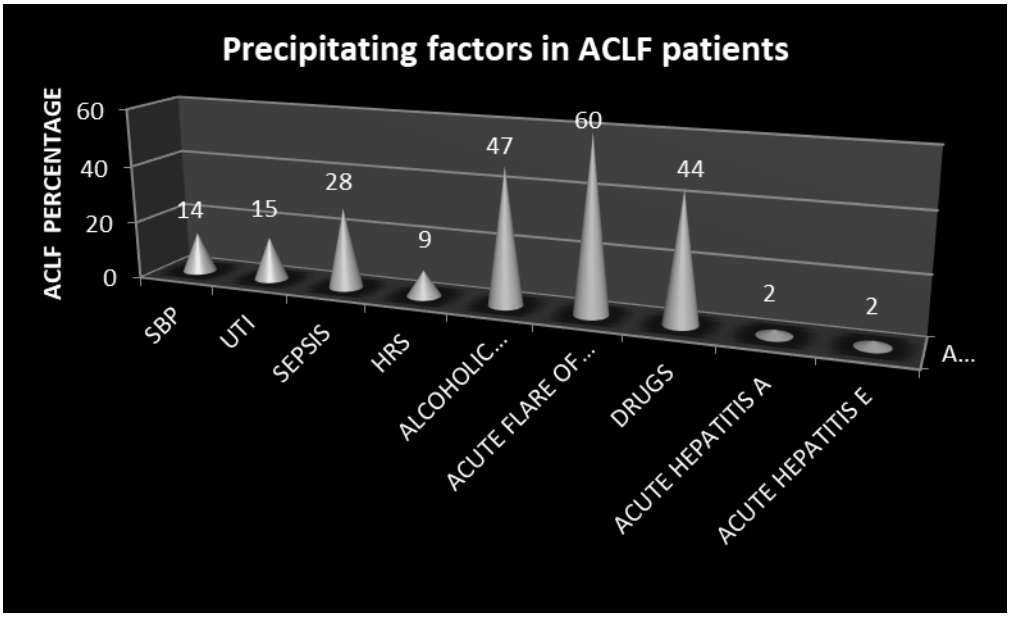

Fig. 2: Precipitating factors in ACLF patients

SBP: Spontaneous Bacterial Peritonitis, UTI: Urinary Tract Infection, HRS: Hepatorenal Syndrome, UGIB: Upper Gastrointestinal Bleed.

Among the laboratory parameters, mean total bilirubin level, AST, ALT, ALK, Prothrombin time, INR, TLC and serum Creatinine were significantly increased among ACLF patients as compared to non-ACLF, whereas Serum Albumin, Sodium and potassium were significantly lower among ACLF patients as compared to non ACLF cases ($p<0.05$) as shown in Table 2.

Table 2: Biochemistry in patients with ACLF and NonACLF

Parameters	ACLF	Non ACLF	p-value
Total Bilirubin(mg/dl)	11.4±6.8	1.9±1.1	0.001
AST (U/l)	175.8±192.7	100.4±90.4	0.001
ALT(U/l)	96.5±148.4	56.9±58.5	0.001
ALK (U/l)	227±139	217.9±183.3	0.021
Albumin (gm/dl)	2.5±0.5	2.7±0.6	0.001
Prothrombin time (sec)	23.6±9	17.8±6.6	0.001
INR	2.2±1.1	1.7±4.7	0.01
TLC (10^3 /ul)	10.4±6.6	6.8±5.8	0.002
Haemoglobin(gm/dl)	8.8±2.1	8.7±2.3	0.530

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Platelet count(10^3/ul)	128±5	144±325	0.054
Sodium(mmol/l)	133.3±7.7	134.9±9	0.003
Potassium(mmol/l)	2.8±0.8	5.3±1.4	0.01
Creatinine (mg/dl)	2.1±1.1	1.1±0.8	0.000

AST: Aspartate Transaminase, ALT: Alanine Transaminase, ALK phos: Alkaline phosphatase, INR: International Normalized Ratio, TLC: Total Leukocyte count

DISCUSSION

Most people with compensated cirrhosis develop decompensated illness, which is typified by coagulopathy and jaundice. There are four stages of cirrhosis: compensatory cirrhosis with unblemished varices, ascites without bleeding, variceal bleeding, and cirrhosis without either varices or ascites. It has been suggested that the fifth stage of cirrhosis is cirrhosis with sepsis. Chronic liver disease naturally progresses to ACLF. A higher death rate and the possibility of multiple organ failure are present [12].

The majority of the ACLF patients in this prospective trial were senior men; Duseja and Singh [13] reported similar results. In line with the findings of Saxena *et al.* [14] and Khatun *et al.* [15], who found that alcohol consumption is the most frequent cause of underlying liver cirrhosis, all the cases in our study had underlying cirrhosis. Persistent Hepatitis B Virus infection was the second most common cause of this condition. Hepatitis B flare-ups, which mostly happened with hepatitis B infection, followed by alcoholic hepatitis, drug-induced hepatitis, and sepsis, were the most common precipitating variables in our analysis. A study by Garg *et al.* [16] found that a Hepatitis B flare-up was responsible for 85% of the cases.

Nonetheless, most of the literature identifies alcoholic hepatitis, sepsis, and upper gastrointestinal haemorrhage as the usual triggering causes [17]. Jaundice, which is present in every case, and acute onset ascites are the most common clinical presentations in the current investigation. Fever, severe malnutrition, hepatic encephalopathy, esophageal varices (>grade 2), Splenomegaly, hepatomegaly, Bhattacharyya *et al.* [18] and Kumar *et al.* [19] showed similar outcomes to ours.

According to Dhiman *et al.* studies, 46% of our ACLF patients experienced acute insult due to alcoholic hepatitis [20]. Because of hyperdynamic circulation and portal hypertension, the current clinical definition of sepsis and SIRS may not be entirely applicable. As a result, a high index of suspicion and careful consideration were used to identify sepsis in our patients.

Our findings were correlated with Das *et al.* [21] when fever, SIRS, and a high total leukocyte count were considered. Chandigarh-based Duseja *et al.* discovered that alcohol was the most frequent insult, followed by autoimmune and viral hepatitis [22].

Our findings were consistent with research by Anand *et al*. [23] that found that biochemical markers such as serum bilirubin, AST, ALT, and alkaline phosphatase were considerably higher in ACLF patients than in non-ACLF patients. Infection and its consequences are more common in patients with alcoholic liver disease. Mookerjee *et al.* [24] have noted that these patients have impaired phagocytosis and neutrophil activity. The increased oxidative burst in these neutrophils indicates a malfunction.

CONCLUSIONS

ACLF is a debilitating syndrome that often has a high death rate because acute triggering insults not only cause multi-organ failure but also further damage the liver, which has underlying chronic liver disease. Since multiorgan failure has been associated with a fatality rate of approximately 90%, identifying the modifiable triggering factors and organ failure as soon as possible is essential to improving patient outcomes. A more precise definition of the illness will aid future researchers in developing innovative management strategies, as existing therapy options are symptomatic.

CONTRIBUTION OF AUTHORS

Research concept- Kiran Yadav, Pankaj Kumar Jain, Ranjana Mandal
Research design- Kiran Yadav, Pankaj Kumar Jain
Supervision- Ranjana Mandal
Materials- Kiran Yadav

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Data collections- Kiran Yadav, Pankaj Kumar Jain
Data analysis and interpretation- Pankaj Kumar Jain, Ranjana Mandal
Literature research- Kiran Yadav, Ranjana Mandal
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Critical review- Kiran Yadav, Pankaj Kumar Jain
Article editing- Pankaj Kumar Jain, Ranjana Mandal
Final approval- Kiran Yadav, Pankaj Kumar Jain, Ranjana Mandal

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