

Clinical Profile, Etiologies, and Outcomes of Acute on Chronic Liver Failure: A Prospective Observational Study from a Tertiary Center in North India

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Abstract:

Background: Acute on chronic liver failure (ACLF) is a multifactorial syndrome with intensive short-term mortality. It is defined by acute worsening of liver function in a patient with underlying liver disease.

Objectives: To establish the clinical profile, precipitating causes, etiologies, and 30-day, 90-day, and 6-month outcomes of ACLF.

Methods: A prospective observational study was carried out at Government Medical College, Srinagar between 2019 and 2021. Sixty patients fulfilling APASL and/or EASL-CLIF criteria were enrolled. Clinical, biochemical, etiological, and outcome information were assessed.

Results: Mean age was 56.8 years; 81.7% of patients were male. Symptoms that were most common included jaundice (100%) and ascites (91.6%). NASH (38.3%) and hepatitis B (23.3%) were most common chronic etiologies. Sepsis (50%) and hepatitis B reactivation (21.7%) were most common acute insults. ACLF grade 3 was present in 53.3% of patients. 30-day, 90-day, and 6-month mortality were 53.3%, 65%, and 75%, respectively.

Conclusion: ACLF has significant mortality, especially with grade 3 involvement. There should be early detection of precipitating events and aggressive management measures.

Keywords: ACLF, NASH, sepsis, hepatitis B, liver failure, India, short-term mortality.

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Introduction

Acute on chronic liver failure (ACLF) is a rapidly progressive syndrome in individuals with pre-existing chronic liver disease.

Described by multiorgan failure and short-term high mortality, ACLF is acknowledged by leading hepatology societies like APASL, EASL, and AASLD.

Regional differences in definition represent variant epidemiology, with Asian definitions portraying more hepatic insults and Western definitions focusing on multiorgan failure.

High mortality of the syndrome requires region-specific research to enhance clinical management.

Materials and Methods

Study Design and Setting: A two-year prospective observational study was conducted from August 2019 through August 2021 at Government Medical College, Srinagar.

Inclusion Criteria: Patients meeting APASL and/or EASL-CLIF criteria for ACLF, all age groups, both genders, informed consent taken.

Exclusion Criteria: CKD, HIV infection, malignancies (except HCC).

Clinical Evaluation: History, physical examination, and laboratory investigations were done. Encephalopathy graded with West-Haven criteria. Organ failures scored on CLIF-SOFA.

Data Analysis: SPSS v26.0 for statistical analysis. Categorical data are presented as frequencies/percentages, continuous variables as mean \pm SD.

Results

Demographics: 81.7% of the 60 enrolled patients were male. Mean age was 56.8 ± 10.8 years. Majority of the patients (46.7%) were between 40 and 59 years.

Table 1: Age and Gender Distribution of Patients

| Age (years) | Male | | Female | | Total | |
|-------------|-----------|------------|-----------|------------|-----------|------------|
| | Frequency | Percentage | Frequency | Percentage | Frequency | Percentage |
| 20-39 | 5 | 10.2 | 0 | 0 | 5 | 8.3 |
| 40-59 | 24 | 49 | 4 | 36.3 | 28 | 46.7 |
| ≥60 | 20 | 40.8 | 7 | 63.7 | 27 | 45 |
| Total | 49 | 81.7 | 11 | 18.3 | 60 | 100 |

Clinical Presentation: Jaundice was present in all patients; ascites was present in 91.6%. Encephalopathy occurred in 88.3%.

Table 2: Clinical history of patients with ACLF

| Symptom | Frequency | Percentage |
|--------------|-----------|------------|
| Jaundice | 60 | 100 |
| Ascites | 55 | 91.6 |
| Anorexia | 33 | 55 |
| Fatigue | 17 | 28.3 |
| Fever | 30 | 50 |
| Pruritis | 7 | 11.6 |
| Pedal edema | 20 | 33.3 |
| Pain abdomen | 12 | 20 |
| Oliguria | 15 | 25 |
| Weight loss | 12 | 20 |
| GI bleed | 6 | 10 |
| Alcohol | 1 | 1.7 |

Etiology of CLD: NASH (38.3%), hepatitis B (23.3%), cryptogenic (25%), autoimmune hepatitis (5%), and alcoholic (1.7%).

Table 7: Likely etiology of underlying chronic component

| Etiology | Frequency | Percentage |
|-------------|-----------|------------|
| NASH | 23 | 38.3 |
| Hepatitis B | 14 | 23.3 |
| Hepatitis C | 3 | 5 |
| Cryptogenic | 15 | 25 |
| Autoimmune | 3 | 5 |
| Alcohol | 1 | 1.7 |
| Budd-Chiari | 1 | 1.7 |
| Total | 60 | 100 |

Precipitating Causes: Sepsis (50%) was the most common precipitant, followed by reactivation of hepatitis B (21.7%), drug-induced liver injury (16.7%), and GI bleed (10%). Out of infections, SBP was the most frequent (40%).

Table 8: Precipitating factors for ACLF

| Precipitant | Frequency | Percentage |
|--------------------------|-----------|------------|
| Sepsis | 30 | 50 |
| Hepatitis B Reactivation | 13 | 21.7 |
| DILI | 10 | 16.7 |
| GI bleed | 6 | 10 |
| Alcohol | 1 | 1.7 |
| Total | 60 | 100 |

ACLF Criteria Compliance: EASL-CLIF alone (48.3%), APASL alone (25%), and both (26.7%).

Table 10: Patients satisfying different ACLF Criteria

| Criteria | Frequency | Percentage |
|---------------------|-----------|------------|
| APASL | 15 | 25 |
| EASL-CLIF | 29 | 48.3 |
| APASL and EASL-CLIF | 16 | 26.7 |
| Total | 60 | 100 |

ACLF Grading: Grade 1 (15.6%), Grade 2 (31.1%), Grade 3 (53.3%).

Table 11: Grading of Patients by CLIF-SOFA score

| ACLF grade | Frequency | Percentage |
|------------|-----------|------------|
| Grade 1 | 7 | 15.6 |
| Grade 2 | 14 | 31.1 |
| Grade 3 | 24 | 53.3 |
| Total | 45 | 100 |

Results: Mortality at 30 days was 53.3%, at 90 days 65%, and at 6 months 75%.

Table 12: Outcome of ACLF patients

| Outcome | Survivors | Non-survivors | Percentage mortality |
|----------|-----------|---------------|----------------------|
| 30 days | 28 | 32 | 53.3 |
| 90 days | 21 | 39 | 65 |
| 6 months | 15 | 45 | 75 |

Discussion

This prospective observational study compared the clinical profile, etiologies, precipitating causes, and outcomes of North Indian ACLF patients. Male predominance and mean age follow international patterns.

NASH as the most common etiology followed by alcohol reflects changing lifestyle patterns with obesity and metabolic syndrome becoming more relevant. Sepsis was the most common precipitating cause, of which SBP was predominant. This underscores the importance of infection control in CLD patients.

Severe mortality, particularly in ACLF grade 3, emphasizes the need for ICU management, liver supportive care, and a potential transplant. The usefulness of CLIF-SOFA scoring in prediction and stratification is emphasized in the study. Limitations are small sample size and lack of transplant facility at the study site.

Conclusion

ACLF remains an acute high-risk syndrome with very high short-term mortality. Sepsis, NASH, and hepatitis B were the most frequent etiologies within the current series. Early recognition, risk stratification, and aggressive treatment of precipitating causes are needed to minimize mortality.

References

- Jalan R, Gines P, Olson JC, et al. Acute-on-chronic liver failure. *J Hepatol* 2012; 57(6):1336–48.
- Dr. Supriya Sharma, Dr. Kamlesh Kumar, Dr. Samir Mohindra, Dr. Gaurav Pande, Dr. Vivek Anand Saraswat. Clinical profile of patients with acute-on-chronic liver failure (ACLF) and its prognostication. *International Journal of Medical and Health Research*, Volume 5, Issue 1, 2019, Pages 183-189
- Kumar R, Rana V, Koshy V, Gangadharan V, Koshy G. Descriptive study of clinical profile and outcome in patients of acute on chronic liver failure, at a tertiary care center in Northern India. *Int J Adv Med* 2020; 7:1687-94.
- Mikolasevic I, Milic S, Radic M, Orlic L, Bagic Z, Stimac D. Clinical profile, natural history, and predictors of mortality in patients with acute-on-chronic liver failure (ACLF). *Wien Klin Wochenschr.* 2015 Apr; 127(7-8):283-9. doi: 10.1007/s00508-015-0707-9. Epub 2015 Mar 28. PMID: 25821053.
- Amarapurkar D, Dharod MV, Chandnani M, Baijal R, Kumar P, Jain M, Patel N, Kamani P, Issar S, Shah N, Kulkarni S, Gautam S, Shah A, Doshi S. Acute-on-chronic liver failure: a prospective study to determine the clinical profile, outcome, and factors predicting mortality. *Indian J Gastroenterol.* 2015 May; 34(3):216-24. doi: 10.1007/s12664-015-0574-3. Epub 2015 Jun 18. PMID: 26080655.
- Mahmud N, Kaplan DE, Taddei TH, Goldberg DS. Incidence and Mortality of Acute-On-Chronic Liver Failure Using Two Definitions in Patients with Compensated Cirrhosis. *Hepatology.* 2019 May; 69(5):2150-2163. doi: 10.1002/hep.30494. Epub 2019 Mar 20. PMID: 30615211; PMCID: PMC6461492.
- Kulkarni S, et al. Acute on Chronic Liver Failure—In-Hospital Predictors of Mortality in ICU. *J Clin Exp Hepatol.* (2017), <https://doi.org/10.1016/j.jceh.2017.11.008>.
- Moreau R, Jalan R, Gines P, Pavesi M, Angeli P, Cordoba J, Durand F, Gustot T, Saliba F, Domenicali M, Gerbes A, Wendon J, Alessandria C, Laleman W, Zeuzem S, Trebicka J, Bernardi M, Arroyo V; CANONIC Study Investigators of the EASL–CLIF Consortium. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. *Gastroenterology.* 2013 Jun; 144(7):1426-37, 1437.e1-9. doi: 10.1053/j.gastro.2013.02.042. Epub 2013 Mar 6. PMID: 23474284.
- Choudhury A, Jindal A, Maiwall R, Sharma MK, Sharma BC, Pamecha V, Mahtab M, Rahman S, Chawla YK, Taneja S, Tan SS, Devarbhavi H, Duan Z, Yu C, Ning Q, Jia JD, Amarapurkar D, Eapen CE, Goel A, Hamid

SS, Butt AS, Jafri W, Kim DJ, Ghazianian H, Lee GH, Sood A, Lesmana LA, Abbas Z, Shiha G, Payawal DA, Dokmeci AK, Sollano JD, Carpio G, Lau GK, Karim F, Rao PN, Moreau R, Jain P, Bhatia P, Kumar G, Sarin SK; APASL ACLF Working Party. Liver failure determines the outcome in patients of acute-on-chronic liver failure (ACLF): comparison of APASL ACLF research consortium (AARC) and CLIF-SOFA models. *Hepatology*. 2017 Sep; 11(5):461-471. doi: 10.1007/s12072-017-9816-z. Epub 2017 Aug 30. PMID: 28856540.

10. El Sayed, M.L., Gouda, T.E.S., Khalil, E.L.S.A.M. et al. Clinical profile and outcome among patients with acute-on-chronic liver failure admitted in the intensive care unit. *Egypt J Intern Med* 33, 31 (2021). <https://doi.org/10.1186/s43162-021-00061-0>.