Clinical profile and outcome of patients with ACLF at a tertiary care centre

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Abstract Background and Objectives: Acute-on-chronic liver failure (ACLF) is a syndrome characterised by acute decompensation of chronic liver disease associated with organ failures and high short term mortality. we carried out this study to analyse aetiology, clinical profile and outcome of patients with ACLF at a tertiary care centre. Methods: This is a prospective study of 72 patients satisfying APASL definition of ACLF admitted at our institute which is a tertiary care centre. Aetiology of acute precipitating insult and chronic liver disease and outcomes were assessed. Severity of disease and prognosis were assessed by CTP and MELD score. Results: Among acute insults Hepatitis E virus infection in 45.8% of patients was the most common trigger at our centre followed by alcohol binge in 30.5%. Alcohol was found to be the most common aetiology of CLD in 72.2% of patients. In hospital mortality was 31.9%. Conclusion: This study highlights that hepatitis E virus infection is the most common acute insult. Leucocytosis, altered serum creatinine, impaired INR and MELD score were found to be the independent predictors of mortality among the patients of ACLF. Alcoholic Liver disease was the most common underlying CLD. Key Word: ACLF, CLD.

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INTRODUCTION

Acute-on-chronic liver failure (ACLF) is an acute deterioration of liver function in patients with chronic liver disease, either secondary to superimposed liver injury or due to extra-hepatic precipitating factors such as infection culminating in the end-organ dysfunction. There are two consensus working definitions for this syndrome exists. The first was put forward by the APASL "Acute hepatic insult manifesting as jaundice and coagulopathy, complicated within 4 weeks by ascites and/or encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease"¹. The second was at EASL-AASLD single topic symposium "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". The latter definition gives more importance to organ failure"² ACLF is a specific clinical entity in terms of its rapid progression, the requirement for multiple organ supports and a high incidence of short and medium term mortality of 50–90%¹.Scoring system for the prognosis of ACLF need to be used at the early stage to allow beneficial intervention³.

AIIMS AND OBJECTIVES

- To study aetiology of patients with ACLF.
- To study clinical features & laboratory parameters of these patients.
- To study outcome of patients with ACLF at the end of hospitalization.

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MATERIALS AND METHODS

A prospective study was carried out on 72 patients admitted with ACLF at B.J. Medical College And Civil Hospital, Asarwa; Ahmedabad which is a tertiary care setup. Eligibility criteria are as follows

Inclusion criteria:

- All cases of ACLF diagnosed as per APASL criteria.
- A. Jaundice (serum bilirubin>5 mg/dl)
- B. Coagulopathy (INR >1.5 or prothrombin activity <40%)
- C. Ascites and/or encephalopathy as determined by physicalexamination.
- Age >12 yrs.
- All patients presenting with previously diagnosed or newly diagnosed compensated liver

parenchymal disease or acutely decompensated liver parenchymal disease.

• Patients of ACLF referred from other centers are also included in the study.

Exclusion criteria:

- Critically ill patients
- Pregnant patients
- Hepatic carcinoma
- Patients who did not consent

The cases selected were subjected to detailed physical as well as systemic examination & then investigated for various lab parameters. Haematological and biochemical investigations were performed and special investigations such as viral markers, ascitic fluid analysis and serum ammonia were performed on patients as and when required.

RESULTS

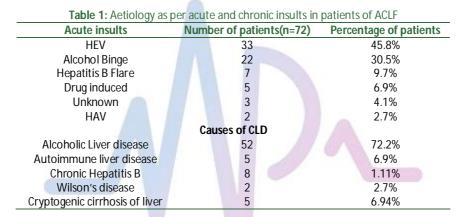


Table 2: Haematological parameters in patients of ACLF

		Number of patients (n=72)	Percentageof patients
	<9	38	52.7%
Haemoglobin level (g/dl)	9-11.99	29	40.2%
	>12	5	6.9%
	<11,000	26	36.1%
Total WBC count	11,000-14,999	17	23.6%
(cells/microliter)	15,000-19,999	19	26.3%
	>20,000	10	13.8%
	30,000-49,999	10	13.8%
Platelets (per microliter)	50,000-1,49,999	18	25%
	1,50,000-4,49,999	44	61.1%

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Table 3: Biochemical parameters in patients of ACLF				
		Number of Patients	Percentage of	
		(n=40)	patients	
Serum Total Bilirubin	5-9.99	26	36.1%	
(mg/dl)	10-14.99	14	19.4%	
	>15	32	44.4%	
	<2.5	37	51.3%	
Serum albumin (g/dl)	2.5-3.5	28	38.8%	
	>3.5	7	9.7%	
	1.50-1.99	22	30.5%	
PT INR	2-2.99	21	29.16%	
	>3	29	40.27%	
C. Creatining (mg/dl)	<1.5	32	44.4%	
S. Creatinine (mg/dl)	>1.5	40	55.5%	

Table 2. Dischamical parameters in patients of ACLE

*The normal range of INR is 0.8 to 1.2 as per kit used at our centre

Table 4: CTP Score in patients of ACLF

Number of patients (n=40)	Percentageof patients
Nil	0%
8	11.1%
64	88.8%
	(n=40) Nil 8

MELDScore	Number ofpatients (n=40)	Percentageof patients		
<10	Nil	0%		
10-19	4	5.5%		
20-29	34	47.2%		
30-39	22	30.5%		
>40	12	16.6%		

_	Outcome of patients	With Complications	Without Complications
	Survived(n=49)	36.7%(n=18)	63.2%(n=31)
	Expired(n=23)	95.6% (n=22)	1.38%(n=1)

	Type of Complications	Number of patients Survived with complications (n=18)	Number of patients Expired with complications (n=22)
Complications	Septicemia	55.5%(n=10)	54.5%(n=12)
	HRS	16.6%(n=3)	31.8%(n=7)
	Haematemesis	11.1%(n=2)	-
	SBP	11.1%(n=2)	-
	Dual complications*	5.5%(n=1)	13.6% (n=3)

Dual complications include septicemia with haematemesis, HRS with SBP*, HRS withhaematemesis.**HRS**: Hepatorenal Syndrome **SBP**: Spontaneous Bacterial Peritonitis

Table 7: Comparison of Variables between survivors and non survivors

Variable	Survived(n=49)	Non-survivors(n=23)	p value
Haemoglobin(gm/dl)	9.26	9.23	0.074
Total WBC count(per cu mm)	13,180	17,243	<0.001
Platelet count(per cu mm)	1.98 lac	1.42lac	0.861
INR	2.23	3.2	<0.001
Serum creatinine(mg/dl)	0.8	3.8	<0.001

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Serum total bilirubin(mg/dl)	11.7	19.7	0.043
Serum albumin(g/dl)	2.57	2.7	0.754
CTP score	11.2	12.5	0.01
MELD	23.5	38.7	<0.001
Acute insult			
HEV	24(82.7%)	9(39.13%)	
Alcohol	8(16.32%)	12(52.1%)	
HBV flare	5(10.2%)	2(8.6%)	
DILI	5(10.2%)	-	
HAV	3(6.1%)	-	
Unknown	2(4.08%)	-	
Causes of CLD			
Alcoholic Liver disease	17(65.38%)	20(85.7%)	
Autoimmune liver disease	2(7.6%)	-	
Chronic Hepatitis B	3(11.5%)	2(8.6%)	
Wilson's disease	3(11.5%)	-	
Cryptogenic cirrhosis of liver	1(3.8%)	-	

DISCUSSION

This is a prospective study of 72 patients with ACLF admitted at our institute. In this study Hepatitis E virus infection was the most common acute insult at our centre in 45.8% of patients followed by alcohol binge in 30.5% of patients. Alcoholic Liver disease was found to be the most common cause of CLD in our study. We studied the laboratory parameters of patients with ACLF.

- Marked anaemia with haemoglobin level of <9 g/dl was present in 52.7% (n=38) of patients.
- Leucocytosis was seen in 63.8% (n=46) of patients.
- Most of the patients in this study were having normal platelet count (1.5 to 4.5 lakhs) with frequency of 61.1% (n=44).
- 44.4% of patients admitted for ACLF had severe hyperbilirubinemia with total bilirubin >15mg/dl.
- Marked hypoalbuminemia with serum albumin of <2.5 g/dl was seen in 51.3% (n=37) of patients.
- 30.5% (n=22) of patients were having mildly deranged PT INR in range of 1.50 to 1.99 and 40.27%(n=29) of patients were having markedly deranged PT INR of >3.
- Majority of patients were having normal serum creatinine (<1.5 mg/dl) with frequency of 55.5% (n=40) and 44.4% (n=32) of them had impaired creatinine (>3).
- In our study, 88.8% (n=64) of patients were having CTP CLASS C(score 10-15) and 11.1% (n=8) were from CTP CLASS B(score 7-9).
- 47.2% of the patients had MELD score between 20-29 followed by 30.5% of patients with MELD score between 30-39.
- In this study, 36.7% (n=18) of survived patients were having complications and 95.6% (n=22) of expired patients were having complications.

- Septicemia was found to be present with nearly equal frequency in both survived and expired groups of patients.
- Hepatorenal syndrome was seen in 31.8% (n=7) of expired patients and 16.6% (n=3) of patients who survived.
- Single complications like haematemesis & SBP were found to be more common among patients who survived with equal frequency of 11.1% (n=2).
- Dual complications were significantly higher among patients who expired with frequency of 13.6% (n=3) as compared to that in 5.5% (n=1) of patients in the survived group.
- In hospital mortality was 31.9% in our study.

ACLF is characterized by an acute insult leading to decompensation of underlying CLD, previously diagnosed or undiagnosed. Precipitating factors include both hepatic and extrahepatic insults. In the CANONIC trial-which included 303 ACLF patients with hepatic or extrahepatic acute precipitants-bacterial infection (32.6%), gastrointestinal bleeding (13.2%), and active alcoholism (24.5%) were common acute precipitants, while no precipitating event was found in 43.6% of patients⁴. In the present study, a higher proportion of viral hepatitis infections were found as an acute precipitating event, which is not unexpected because both HAV and HEV are endemic in India and are major causes of both sporadic and epidemic forms of acute hepatitis. Alcohol was reported as the most common etiology of cirrhosis in the CANO-NIC study (49.2%). In India, the average consumption of alcohol has increased, and the average age of consumption of alcohol has decreased⁵. Even in our study alcohol was found to be the most common cause of CLD in 72.2% of patients. As shown in table 7, we can conclude that among laboratory parameters; Leucocytosis, altered serum creatinine, impaired INR and MELD score were associated with poor outcome in patients of ACLF while platelet count & serum albumin had no significant impact on the outcome of patients. The mean CTP score of expired as well as survived patients was >10 indicating that most of them were from CTP class C. Mean MELD score of expired patients was >30 while that of survived patients was <30. This concludes that MELD score is a better liver prognostic index than CTP score. We also observed that complications such as septicaemia, SBP, Hepatorenal syndrome were independent predictors of outcome in patients with ACLF.

CONCLUSION

This study highlights that hepatitis E virus infection is the most common acute insult and alcoholic liver disease is the most common cause of CLD. The high mortality is a matter of concern. Leucocytosis, altered serum creatinine, impaired INR and MELD score were found to be the significant predictors of mortality. There is a need for further research into the prognostic factors, and future efforts are needed to define patients who are going to best benefit from liver transplantation.

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