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Research Article

Clinical Profile of Patients with Acute-on-Chronic Liver Failure

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Abstract

Background: Acute-on-Chronic Liver Failure (ACLF) is defined as sudden deterioration of liver functions due to acute insult in patients with known or unknown chronic liver disease. Its main feature is the reversibility, and high short term mortality due to Multi-Organ Failure (MOF).

Aims/Objectives: To study the clinical, laboratory, etiological profile and outcome of patients with ACLF.

Methods: This prospective observational study was conducted on 120 consecutive ACLF patients (WGO working party definition) admitted in department of gastroenterology, M.G Hospital, Dr S.N. Medical College from March 2016 to august 2016. Their clinical, laboratory, etiological profile and outcome were studied.

Results: Mean age ± standard deviation was 37.61 ± 8.54 years and 80% of patients were male. The most common aetiology of underlying chronic liver disease was alcohol (79.16%). Most common acute insult was alcoholic hepatitis (49.16%). Type C ACLF constitutes 70% of patients. Remaining 30 % of patients were of Type A/B ACLF. Twenty eight days mortality was 43.33% (52/120). Most patients who died had ≥1 organ failure, MELD score of 31 ± 5.75 and CLIF-SOFA score of 11.96 ± 2.82. Eighty nine patients (74.16%) had one or more organ failure. Of these, 51 (57.30%) died. Whereas, of the remaining thirty one patients without organ failure, only one died. The presence of 1, 2, ≥3 organ failure was seen in 18.33%, 23.33% and 32.5% of patients respectively. Mortality increases with the number of organ failure. The most common Organ Failure (OF) was liver failure in 34.66% of patients followed by coagulation failure in 18.6%. The other OF such as kidney, cerebral, circulatory and respiratory were seen in 16.8, 15.11, 8.88 and 5.7% respectively. Out of 52 patients who died, 39/52(75%) were not decompensate (WGO A/B) prior to illness. Mortality was more in alcoholic CLD 37/52(71.15%) in comparison to CLD patients of non alcoholic aetiology 15/52(28.84%). Independent predictors of mortality are low haemoglobin, high bilirubin, high MELD score and aetiologies of acute hepatic insult.

Conclusion: Most common cause of acute insult in ACLF was continued alcohol consumption leading to alcoholic hepatitis, which is preventable. Prognosis was worst in patients who were decompensated prior to illness (WGO-C), had multiple organ failure, and high MELD and SOFA score. Mortality increases with the number of organ failure.

Keywords: Chronic liver disease; Acute insult; Organ failure

Abbreviations

AASLD: American Association for the Study of Liver Diseases; ACLF: Acute On Chronic Liver Failure; ALT: Alanine Aminotransferase; ANA: Anti Nuclear Antibody; Anti HBc: Antibody Against Hepatitis B Core Antigen; Anti LKM1: Anti Liver Kidney Microsomal Antibody; APASL: Asia Pacific Association for the Study of Liver Disease; ASMA: Anti Smooth Muscle Antibody; AST: Aspartate Aminotransferase; ATT: Anti Tubercular Treatment; CANONIC: CLIF Acute on Chronic Liver Failure in Cirrhosis; CLIF-SOFA: Chronic Liver Failure -Sequential Organ Failure Assessment; CLD: Chronic Liver Disease; DILI: Drug Induced Liver Injury; ELISA: Enzyme Linked Immune Sorbent Assay; GI: Gastro Intestinal; HAV: Hepatitis A Virus; HBV: Hepatitis B Virus; HBsAg: Hepatitis B Surface Antigen; HRS: Hepatorenal Syndrome; INASL: Indian National Association for the Study of Liver; INR: International Normalized Ratio; MELD: Model for End Stage Liver Disease; MOF: Multi Organ Failure; NASH: Non Alcoholic Steato Hepatitis; SBP: Spontaneous Bacterial Peritonitis

Introduction

The world gastroenterology organization consensus defines ACLF as "a syndrome in patients with CLD with or without previously diagnosed cirrhosis which is characterized by acute hepatic decompensation resulting in liver failure (jaundice and prolongation of INR)" and one or more extra hepatic organ failure

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Table 1: CLIF Consortium organ failure score.

Organ system	Score = 1	Score = 2	Score = 3
Liver, bilirubin (mg/dl)	<6	6-≤12	**>12**
Kidney, creatinine (mg/dl)	<2	**2-<3.5**	**≥3.5 or renal replacement**
Brain, grade (West-Haven)	0	1-2	**3-4**
Coagulation, INR	>2.0	2.0-<2.5	**≥2.5**
Circulation, MAP (mmHg)	≥70	<70	**Vasopressors**
Respiratory PaO_2/FiO_2	>300	≤300 and >200	**≤200**
or SpO_2/FiO_2	>357	>214 and ≤357	**≤214**

The highlighted area in light blue reflects the definition of each organ/system failure.
INR: International normalized ratio; MAP: Mean arterial pressure; PaO2/FiO2: ratio of arterial oxygen partial pressure to fractional inspired oxygen; SpO2: Oxygen saturation

Table 2: The demographic, clinical feature, biochemical parameters, prognostic scores and mortality of ACLF patients (n=120).

Parameters	Total (n=120)	WGOA/B (n=36)	WGO-C (n=84)	P value
Age	37.61±8.54	37.5±9.1	37.66±8.34	0.922
Male: Female Ratio	4:1	1.7:1	6.3:1	0.006
Hepatic encephalopathy (Gr 1-2)	11.66%	8.33%	13.09%	0.549
Hepatic encephalopathy (Gr 3-4)	28.33%	5.55%	38.09%	0.0001
Hb (gm/dl)	8.75±2.28	9.7±2.6	8.34±2	0.002
Total leukocyte count/mm^3	12506±9822	9751±4943	13687±11105	0.043
Platelets ($x10^3/mm^3$)	94.73±41.14	122±39	83±36.26	<0.0001
Total bilirubin (mg/dl)	11.63±5.33	10.5±5.4	12.11±5.25	0.131
Creatinine (mg/dl)	1.75±0.8	1.8±0.9	1.72±0.76	0.607
Aspartate aminotransferase (U/L)	428±604	915±914	219±155	<0.0001
Alanine aminotransferase (U/L)	384±684	982±1003	127±159	<0.0001
Albumin (gm/dl)	2.26±0.44	2.35±0.48	2.2±0.43	0.143
International normalized ratio	2.23±0.61	2.05±0.42	2.3±0.67	0.042
MELD score	28.46±5.529	27.19±4.8	29.01±5.75	0.099
SOFA score	10.5±2.7	9.36±1.9	11±2.84	0.002
28 days mortality	43.33%	36.11%	46.42%	0.321
Aetiology (chronic liver disease)				
Alcohol	79%	61.11%	86.90%	0.002
NASH	9%	5.55%	10.71%	0.502
Hepatitis B virus	8%	25%	1.2%	<0.0001
Cryptogenic	3%	8.33%	1.2%	0.080

Data are presented as mean ± SD or number of patients (%), MELD: Model for end stage liver disease; SOFA score: Sequential organ failure score; MDF Score: Maddreys Discriminant Function Score; NASH: Non alcoholic steato-hepatitis

that is associated with increased mortality within a period of 28 days and up to 3 months from onset [1].

ACLF occurs in about 30% of patients with an acute decompensation of cirrhosis and it has a significantly higher short term mortality of 30-50% than expected with decompensated liver disease [1,2].

It is usually associated with a precipitating event which can be reversed if diagnosed early. The causes of acute insult in ACLF are variable; they can be both hepatotropic and non-hepatotropic, infectious or non-infectious. Causes of acute insult are variable and depend on geographical area. The present study is conducted to evaluate the clinical, laboratory, etiological profile and outcome of patients with ACLF.

Materials and Methods

This study was conducted in Department of Gastroenterology, Dr S.N. Medical College, Jodhpur, Rajasthan. This is a prospective observational study conducted from March 2016 to august 2016. Written informed consent was taken from all patients before enrolment, except from patients with altered sensorium in whom consent was taken from a relative. The study was approved by the college ethical committee.

120 consecutive patients with ACLF as defined by WGO working party [1] were included. They were categorised into three different subtypes: Type A ACLF- non cirrhotic CLD with an acute flare; often

indistinguishable from acute or sub acute liver failure. Type B ACLF-well compensated cirrhosis with an acute insult. Type C ACLF-cirrhosis with previous hepatic decompensation.

Work-up for aetiology of acute hepatic injury and underlying CLD

Presence of cirrhosis, chronic hepatitis, metabolic liver disease or cholestatic liver disease was defined as chronic liver disease. Diagnosis of cirrhosis was made using combination of following criteria:

1. Previous liver biopsy findings if available

2. Clinical evaluation

3. Radiological (heterogenous echotexture of liver with irregular outline, altered liver size or porto-systemic collaterals).

4. Laboratory (low serum albumin, AST/ALT ratio >1).

5. Endoscopy (oesophageal varices > 5mm in size).

All patients were thoroughly evaluated to find out the aetiology of chronic liver disease and acute insults. All patients were investigated with HBsAg, anti-HBc IgM and anti-HCV by ELISA. Tests for hemochromatosis, wilsons disease and autoimmune liver disease (ANA, ASMA, anti-LKM1, ceruloplasmin, 24 Hr urinary copper and ferritin) were done.

Diagnosis of alcoholic hepatitis was made in a patient with a history of alcohol abuse within a span of 28 days of symptoms, typical symptoms and physical findings, abnormal compatible liver enzyme levels. Maddrey's Discriminant Function was calculated to assess for severity of alcoholic hepatitis as follows:

[4.6 × (patient's prothrombin time - control prothrombin time, in seconds)] + Serum bilirubin level, in milligrams per decilitre

Diagnosis of acute viral hepatitis was based on the clinical presentation, LFT and a positive viral serology (IgM Anti HEV, IgM Anti HAV by ELISA). Diagnosis of autoimmune hepatitis was based on the simplified criteria for AIH and that of hepatitis B flare based on AASLD.

MELD score was calculated to assess the severity. MELD score was calculated as follows: logarithmic equation (0.957 × log [creatinine mg/dl] + 0.378 × log [bilirubin mg/dl] + 1.120 × log [international normalized ratio] + 0.643).

The organ failure were defined as per the CLIF-sequential OF assessment score [1] (Table 1).

Management

As per uniform management protocol, antibiotics were given to patients with sepsis first empirically and then as per sensitivity reports of blood, urine and ascitic fluid analysis.SBP and HRS was managed as per AASLD recommendations [3].

Therapeutic paracentesis was done when indicated. Renal replacement therapy and assisted ventilation were provided when appropriate. HBV infection was treated with antiviral therapy. Anti hepatic encephalopathy regimen was used to treat patients with hepatic encephalopathy. Ionotropes were used to maintain blood pressure in patients with hypotension.

Table 3: Distribution based on age and sex.

Age group (yrs)	Cases	
	Number	Percentage (%)
≥20	1	0.83
21-30	21	17.5
31-40	54	45
41-50	33	27.5
>50	11	9.16
Total	120	100
Mean ± SD	37.61±8.54	
Sex		
Female	24	20
Male	96	80
Total	100	100

≤: Less than or equal; >: More than, SD: Standard Deviation

Follow up

Patients were followed for duration of 28 days and the development of organ failure, infection and mortality were recorded.

Stastical analysis

Results are expressed as mean ± Standard Deviation (SD) or frequency (in percentage). Quantitative variables, expressed as mean ± SD, were compared using student's t test. Qualitative variables, expressed as percentage were compared with the use of Z-test. A p value of < 0.05 was considered as statistically significant. Univariate analysis was performed to compare survivors and non survivors'. Variables significant on univariate analysis was analysed by backward removal method using multiple logistic regression. Receiver operating characteristic (AUROC) were drawn to compare different scores for predicting mortality.

Results

During the study period, 120 consecutive patients with ACLF were included.

Demographic, Clinical and biochemical profile (Table-2/3)

In the present study it was observed that the mean age ± standard deviation was 37.61 ± 8.54 years and 80% of patients were male. Clinical profile, haematological and laboratory parameters are shown in Table 2. Type C ACLF constitutes 70% (84/120) of patients. Remaining 30 % of patients were of Type A/B ACLF

Aetiology of acute insult in ACLF and aetiology of underlying chronic liver disease (Figure 1, 2)

The commonest aetiology of acute insult leading to ACLF was continues alcohol consumption leading to alcoholic hepatitis in 49.16% of patients. Second most common cause was viral infection in 17.82% of patients (HEV superinfection= 14, HBV reactivation= 4, HAV superinfection= 3, HBV superinfection= 1). Sepsis, upper G.I. bleed and ATT induced DILI were implicated in 14.16%, 13.33% and 4.16% respectively.

Most common aetiology of CLD was alcohol in 79.16%% of patients. HBV, NASH and cryptogenic cause constitutes 8.33, 9.16 and 3.33% respectively.

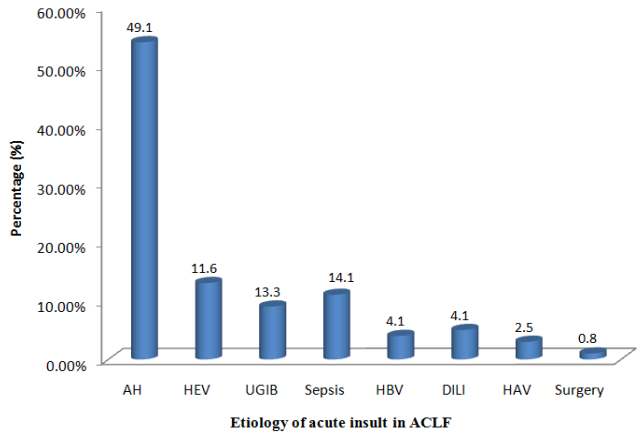

Figure 1: Aetiology of acute insult in ACLF.

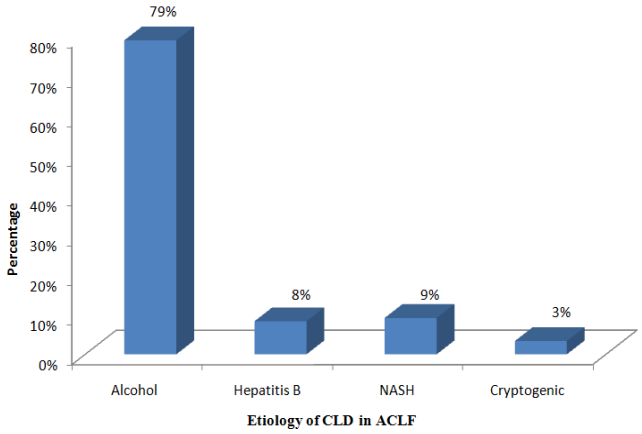

Figure 2: Aetiology of CLD in ACLF.

Liver Disease Status in ACLF

Among 120 patients 36(30%) had Type A/B ACLF and 84(70%) had Type C ACLF. The mean age, serum bilirubin, creatinine, albumin and MELD score are similar (p value >0.05) in both the groups. Males were significantly more in WGO-C group (p value-0.006). HE grades I/II are similar in both groups in comparison to HE III/IV which is significantly (p value-0.0001) more in WGO-C group. Haemoglobin and platelets are significantly low, whereas TLC, AST, ALT, INR and SOFA score are significantly more in WGO-C group. Most common aetiology of CLD in both group was alcohol but it was significantly (p value-0.002) more in WGO-C group in comparison to WGO -A/B group in which cryptogenic and NASH are the predominant cause of CLD.

Organ failure and 28 days mortality (Figure 3)

Among 120 patients of ACLF, 52 died within 28 days. 89 patients (74.16%) had one or more organ failure. Of these, 51 (57.30%) died. Whereas, of the remaining 31 patients without organ failure, only one died. The presence of 1, 2, ≥3 organ failure was seen in 18.33%, 23.33% and 32.5% of patients respectively. The most common Organ Failure (OF) was liver failure in 34.66% of patients followed by coagulation failure in 18.6%. The other OF such as kidney, cerebral, circulatory and respiratory were seen in 16.8, 15.11, 8.88 and 5.7% respectively.

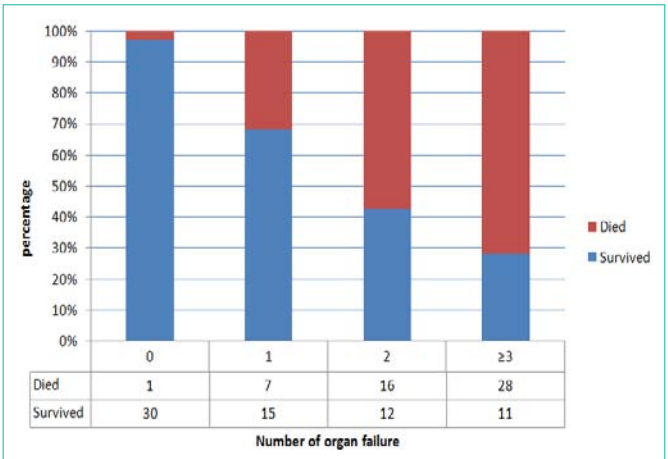

Figure 3: Organ failure and twenty eight days mortality.

Mortality increases with the increase in number of organ failure. Multi-organ failure (≥2 OF) was the major cause of death.

Comparison of Patients who Died/Survived (Table 4)

On univariate analysis mean age, serum creatinine, serum bilirubin, INR, MELD score and SOFA score are significantly more in non-survivors than survivors. Patients who didn't survive have significantly low Hb, AST, ALT and albumin levels in comparison to survivors. No statistically significant difference between two groups in HE I/II but advanced HE i.e. grade III/IV was significantly more in non-survivors (p value<0.05). Although AH is the most common cause of acute insult in both group, it is significantly more common in patients who survived. UGIB and sepsis are significantly more common in patients who died. Rest all other causes of acute insult are similar in both groups. Although alcohol is the most common cause of CLD in both groups, all causes of CLD are similar in both groups.

Mortality according to aetiology and status of liver disease (Table 5)

Mortality was more in alcoholic CLD (72.72%) in comparison to CLD patients of non alcoholic aetiology (27.27%) which was statistically significant (p value <0.05). Mortality was significantly more (p<0.05) in patients who were having Type C ACLF (79.54%) in comparison to Type A/B ACLF patients (20.45%)

Comparison of various prognostic models among patients with ACLF (Table 6, Figure 4)

All the factors found significantly associated with mortality were analysed in backward removal method using multiple logistic regression and factors found most significantly associated with mortality are low haemoglobin, high bilirubin, high MELD score and acute aetiologies.

MELD and SOFA score are compared for predicting mortality using receiver operating curve. AUROC was 0.768 for SOFA and 0.740 for MELD. This concludes that SOFA score is better than MELD score for predicting mortality in ACLF patients.

Discussion

This is a prospective observational study done in a tertiary care centre to evaluate the clinical, laboratory, etiological profile and outcome of patients with ACLF.

Table 4: Comparison of patients who died and survived.

Variables	Mortality group (n=52)	Survival group (n=68)	p value
Mean age	39.76±8.7	35.97±8.07	0.015
Male : female ratio	3.7:1	4.2:1	0.820
Haemoglobin (gm%)	8.24±2.27	9.14±2.23	0.013
Platelet count /mm^3	90.63±40.41	97.86±41.72	0.342
Total leukocyte count/mm^3	13998±12191	11365±7428	0.146
Serum creatinine(mg/dl)	2.06±0.83	1.5±0.70	0.0002
Total bilirubin (mg/dl)	12.76±5.3	10.76±5.15	0.040
Aspartate amino transferase (IU/L)	275±408	544±700	0.015
Alanine amino transferase (IU/L)	257±492	480±790	0.076
Albumin (gm/L)	2.16±0.46	2.3±0.42	0.039
International normalized ratio (INR)	2.4±0.75	2.09±0.44	0.004
Hepatic encephalopathy (early/Gr 1-2)	15.38%	8.82%	0.390
Hepatic encephalopathy (advanced /Gr 3-4)	38.46%	20.58%	0.041
MELD score	31±5.75	26.52±4.5	<0.0001
SOFA score	11.96±2.82	9.39±2.01	<0.0001
Aetiology (acute insult)			
Alcoholic hepatitis	36.53%	58.82%	0.017
HBV Reactivation/ superinfection	1.92%	5.88%	0.387
HEV superinfection	5.76%	16.17%	0.092
HAV superinfection	3.84%	1.47%	0.578
Drug induced liver injury	1.92%	5.88%	0.387
Sepsis	23.07%	7.35%	0.018
Upper gastrointestinal bleeding	26.92%	2.94%	0.002
Surgery	0%	1.47%	1.000
Etiology (chronic liver disease)			
Alcohol	71.15%	85.29%	0.071
NASH	15.38%	4.41%	0.055
Hepatitis B virus	9.61%	7.35%	0.744
Cryptogenic	3.84%	2.94%	1.000

Data are presented as mean ± SD or number of patients (%), MELD: Model for end stage liver disease; SOFA score: Sequential Organ Failure Score; MDF Score: Maddreys Discriminant Function Score; NASH: Non Alcoholic Steato-Hepatitis

Table 5: Mortality according to aetiology and status of liver disease.

Aetiology	No. of cases	(%)	P value
Alcoholic	37/52	71.15%	<.05
Non alcoholic	15/52	28.84%	
Liver disease status			
Type C ACLF	39/52	79.54%	<.05
Type A/B ACLF	13/52	20.45%	

%: Percentage

Age and sex distribution

In the present study most of the patients were in age group 31-40 yrs (45%) followed by 41-50 yrs (27.5%) with mean age ± standard deviation of 37.61 ± 8.54 years. Study conducted by Dhiman RK et al. [4] reported that the mean age with standard deviation was 46 ± 13 years in ACLF patients. Sumana P V et al. conducted a study in ACLF patients, according to which mean age ± SD was 40.88 ± 1.1 [5]. The median age of the ACLF patients was 36 years (range 15-80) in a study done by H Garg et al. [6]. The mean (± SD) age of 1049 consecutive ACLF patients was 44.7 ± 12.2years [7].

In the present study it was observed that 80% of patients were male. Male patients consisted of 74%, 86% and 81.8% in studies conducted by H Garg et al. [6], Dhiman RK et al. [4] and Deepak amarapurkar et al. [8] respectively.

Aetiology of chronic liver disease

The most common cause of CLD in this study was alcoholic liver disease (79.16%). Dhiman RK et al. reported that alcoholic liver disease (68%) was the most common aetiology of CLD in ACLF [4]. Deepak Amarapurkar et al. concluded in their study that alcohol was the most common cause of cirrhosis (56.8%) followed by cryptogenic/ NASH in 27.2% [8]. According to INASL consortium experience of 1049 ACLF patients alcohol was the commonest (56.7%) cause of CLD followed by cryptogenic and hepatitis virus [7]. In contrast to above

Table 6: Bivariate logistic regression influencing mortality.

	B	S.E.	Wald	df	Sig.	Odd ratio
Hb	-.329	.142	5.405	1	.020	.719
Bilirubin	.135	.064	4.539	1	.033	1.145
MELD	.138	.056	6.079	1	.014	1.149
Acute etiology			19.751	8	.011	
AH	-3.819	1.038	13.547	1	.000	.022
HBV R/S	-3.777	1.532	6.083	1	.014	.023
Covariates HEV	-1.213	1.966	.381	1	.537	.297
HAV	17.685	40192.970	.000	1	1.000	47898917.524
DILI	-3.979	1.241	10.279	1	.001	.019
Sepsis	-23.861	18964.188	.000	1	.999	.000
UGIB	-1.214	1.200	1.023	1	.312	.297
Surgery	-19.334	40192.970	.000	1	1.000	.000
Constant	-.016	1.782	.000	1	.993	.984

studies, a study conducted by Khatun UF et al. reported viral hepatitis (hepatitis B (50%), hepatitis C (26.67%) and alcohol (16.67%) as the cause of cirrhosis in ACLF [9]. 70% of patients were decompensated (WGO-C) prior to illness in comparison to 30% of patients who were not decompensated (WGO-A/B) prior to illness.

Aetiology of acute insult in ACLF

In present study the commonest aetiology of acute insult leading to ACLF was continues alcohol consumption leading to alcoholic hepatitis in 49.16% of patients. Second most common cause was viral infection in 17.82% of patients (HEV superinfection= 14, HBV reactivation= 4, HAV superinfection= 3, HBV super-infection= 1). Sepsis, upper G.I. bleed and ATT induced DILI were implicated in 14.16%, 13.33% and 4.16% respectively. Results of our study are comparable to INASL consortium experience [7] according to which aetiology of acute insult included alcohol in 35.7%, hepatitis virus (hepatitis A, hepatitis B, hepatitis E) in 21.4%, sepsis, variceal bleeding, drugs and cryptogenic in 16.6%, 8.4%, 5.7% and 9.9% respectively. Dhiman RK et al. in their study reported active alcohol intake as the most common acute insult leading to ACLF in 40% of cases [4]. Alcohol was also the commonest cause of acute insult leading to ACLF in 25% of cases according to study by Amarapurkar et al. [8]. Reactivation of hepatitis B was seen in 85% and only 4% in a study conducted by H Garg et al. [7] and Dhiman RK et al. [4] respectively.

Organ failure and Mortality

Presence of 1, 2, ≥3 organ failure was seen in 18.33%, 23.33% and 32.5% of patients respectively. 74.16% of patients had ≥1 organ failure, the results of which are comparable to the study conducted by Deepak Amarapurkar et al. [8] according to which 80.6% patients had at least 1 organ failure. Multi-organ failure was defined as ≥2 organ failure. 55.83% patients had ≥2 organ failure in comparison to a study conducted by H Garg et al. [6] in which organ failure was present in one third of patients. According to a study conducted by INASL consortium 14.96% had no organ failure, whereas 1,2,3,4 and 5 organ failure were recorded in 33.07, 22.57, 18.89, 7.34 and 3.14 respectively [7]. Mortality increases with the increase in the number of organ failure. In present study mortality was 0.83% with no organ failure,

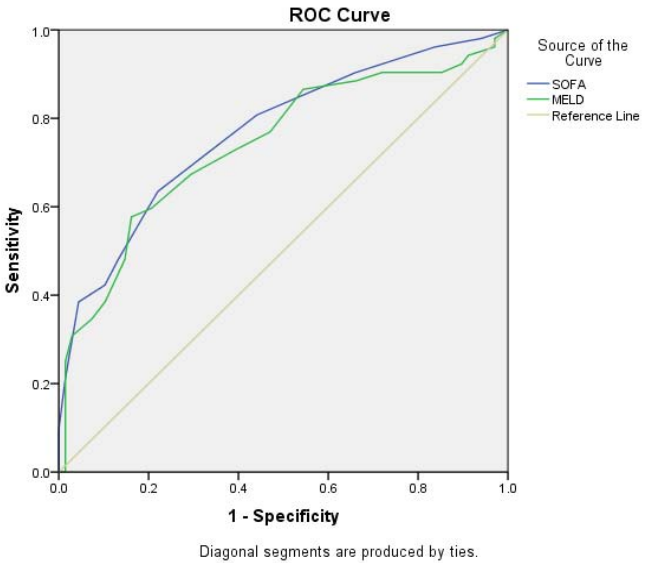

Figure 4: Receiver Operating Characteristic (ROC) curve of MELD and mortality (AUC 0.740) and SOFA and mortality (AUC 0.768).

31.81, 57.14 and 71.79% with 1, 2 and ≥3 organ failure respectively which are comparable to INASL consortium experience, according to which mortality increased progressively with increasing number of organ failure (12.3% with no OFs and 83.3% with five OFs) [7]. The most common Organ Failure (OF) was liver failure in 34.66% of patients followed by coagulation failure in 18.6 %. The other OF such as kidney, cerebral, circulatory and respiratory were seen in 16.8, 15.11, 8.88 and 5.7 % respectively. Results are comparable to a study conducted by Shalimar et al. [10] according to which most common OF was hepatic failure seen in 65.3% followed by coagulation failure seen in 31.9%. Other OF including kidney, cerebral, circulatory and respiratory seen in 28.2, 17.2, 15 and 19.75% of patients.

In present study, 7days, 14 days and 28 days mortality was 29%, 41% and 44%. The results are different from experience of INASL consortium 2016 [7], according to which 42.6% (447/1049) patients died during a median hospital stay of 8 days. Results of our study are similar to a study conducted by H Garg et al. [6] according to which 33.33% of patients died within first week and another 37.03% died in second week. Results comparable to a study conducted by Mikolasevic I et al. [11] according to which 50% of patients died within 28 days of admission: 71.7% within 14 days and 17.8% within 7 days of admission. These data suggests that initial 1-2 weeks are very crucial in the management of patients with ACLF and is known as "Golden Window". Early diagnosis and management during this period prevents organ failure and provides an opportunity for reversal of hepatic injury. Liver transplantation in spite of indication was not feasible, due to lack of an organ or a donor or other socio economic status.

Mortality according to liver disease status

Mortality was significantly more (p value <0.001) in Type C ACLF patients (79.54% {35/44}) in comparison to Type A/B ACLF patients (20.45% {9/44}) and this was comparable to a study conducted by Rajiv jalan et al. [12] according to which patients who had a previous episode of decompensation requiring hospital admission within

the previous six months were more than twice as likely to die if they developed organ failure. Contrarily, in the CANONIC study [1], patients with ACLF and no prior acute decompensation had a higher prevalence of organ failure and more severe grade of ACLF as compared to those with acute decompensation in the past with higher mortality at 28 days in former group (42.2% *vs.* 29.6%; p=0.03).

Comparison of patients with WGO-A/B and WGO-C

WGO-C group constitutes predominantly male patients, and this can be explained by the fact that alcohol was the cause of CLD in around 85% of patients in WGO-C group and they were predominantly male. HE grade I/II and HE grade III/IV were seen in 13% and 38% in WGO-C group in comparison to 8% and 5% in WGO-A/B group. The explanation for above mentioned result is that the hepatic reserve is less in WGO-C group, so more chances of encephalopathy. One interesting finding was that AST and ALT was significantly more in patients in WGO-A/B group than in WGO-C group. The possible reason is better residual liver reserve in WGO-A/B group .Above mentioned results are comparable to a study conducted by Shalimar et al. [10] in which AST and ALT were higher in silent CLD in comparison to overt CLD. Similarly males predominate the overt CLD group.

Comparison of various prognostic models among patients with ACLF

In present study factors found most significantly associated with mortality are low haemoglobin, high bilirubin, high MELD score and aetiologies of acute hepatic insult .According to a study conducted by Shalimar et al. [10] independent predictors of mortality included HE(early and advanced) ,serum creatinine ≥ 1.5,CLIF-SOFA score >8 and aetiology of acute hepatic insult (alcohol, cryptogenic).In the CANONIC study encephalopathy and renal failure were important determinants of mortality [1]. In a study conducted by Kumar et al. [5] blood urea, serum creatinine, PT/INR and CRP levels were significantly higher in the patients who died compared to who survived.

In present study AUROC was 0.768 for SOFA and 0.740 for MELD which concluded that SOFA score is better than MELD score for predicting mortality in ACLF patients. Kumar et al. [5] concluded that AUROC was significantly higher for SOFA (0.932) score compared to MELD (0.857) and CTP score (0.858). Study conducted by H Garg et al. showed that amongst all severity scores studied MELD, SOFA and APACHE-II scores had AUROCs of >0.8 which was significantly higher than that of CTP score.

There are few imitations in our study. Firstly, study conducted in a single tertiary care centre so chances of referral bias are there. Secondly, only 28 days mortality was evaluated instead of 90 days, so the follow up is not adequate. Lastly the results of this study cannot be generalized due to geographical variations in the aetiology of acute insult and CLD.

Conclusion

Most common cause of acute insult in ACLF was continued alcohol consumption leading to alcoholic hepatitis, which is preventable. Prognosis was worst in patients who were decompensated prior to illness (WGO-C), had multiple organ failure, and high MELD and SOFA score. Mortality increases with the number of organ failure.

References

1. Moreau R, Jalan R, Gines P, Pavesi M, Angeli P, Cordoba J, et al. Acute-on chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. Gastroenterology. 2013; 144: 1426-1437.
2. Duseja A, Chawla YK, Dhiman RK, Kumar A, Choudhary N, Taneja S. Non-hepatic insults are common acute precipitants in patients with acute on chronic liver failure (ACLF). Dig. Dis. Sci. 2010; 55: 3188-3192.
3. Bruce A Runyon. Management of Adult Patients with Ascites due to Cirrhosis: Update 2012. American Association for the Study of Liver Diseases. 2012.
4. Dhiman RK, Agrawal S, Gupta T, Duseja A, Chawla Y. Chronic Liver Failure- Sequential Organ Failure Assessment is better than the Asia-Pacific Association for the Study of Liver criteria for defining acute-on-chronic liver failure and predicting outcome. World J Gastroenterol. 2014; 20: 14934-14941.
5. B Ramesh Kumar, D Rahul, B Prabhakar. A study of clinical profile in patients with acute on chronic liver failure in a tertiary hospital Asian Pac. J Health Sci. 2016; 3: 47-57.
6. Garg H, Kumar A, Garg V, Sharma P, Sharma BC, Sarin SK. Clinical profile and predictors of mortality in patients of acute on- chronic liver failure. Digestive and Liver Disease. 2012; 44: 166-171.
7. Shalimar, Saraswat V, Singh SP, Duseja A, Shukla A, Eapen CE, et al. Acute on chronic liver failure in India: the INASL consortium experience. J Gastroenterol Hepatol. 2016; 31: 1742-1749.
8. Amarapurkar D, Dharod MV, Chandnani M, Baijal R, Kumar P, Jain M, et al. Acute-on- chronic liver failure: A prospective study to determine the clinical profile, outcome, and factors predicting mortality. Indian J Gastroenterol. 2015; 34: 216-224.
9. Khatun UF, Sayeed A, Hussain SMB, Paul S, Kawsar NM, Al-Azad MAS. Etiological study of acute on chronic liver failure among patients admitted in medicine ward in Chittagong medical college hospital. JAFMC, Bangladesh. 2013; 9.
10. Shalimar, Kumar D, Vadiraja PK, Nayak B, Thakur B, Das P, et al. Acute on chronic liver failure because of acute hepatic insults: Aetiologies, course, extra-hepatic organ failure and predictors of mortality. Journal of Gastroenterology and Hepatology. 2016; 31: 856-864.
11. 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; 127: 283-289.
12. Jalan R, Stadlbauer V, Sen S, Cheshire L, Chang YM, Mookerjee RP. Role of predisposition, injury, response and organ failure in the prognosis of patients with acute-on-chronic liver failure: a prospective cohort study. Critical Care. 2012; 16: 227.

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