Document heading doi: 10.21276/apjhs.2018.5.4.3 Original Article

To Study the Etiology and Predicting Scores of Patients with acute on chronic liver failure

Rachit Magazine[1*], Vijant Singh Chandail[2], Shahzad Qureshi[3]

[1]Post Graduate, Department of Medicine, Government Medical College, Jammu, India
[2]Lecturer Department of Medicine, Government Medical College, Jammu, India
[3]Lecturer Department of Medicine, Government Medical College, Jammu, India

Received: 1-09-2018 / Revised: 30-09-2018 / Accepted: 25-10-2018

ABSTRACT

Aim: To study the aetiology, precipitating insults of patients presenting with acute on chronic liver failure and predictors of mortality of acute chronic liver failure. **Methods:** The prospective study was carried out in 100 patients admitted with acute on chronic liver failure for a period of 1 year in the Department of Medicine of Government medical college and Hospital, Jammu. **Results**: ACLF has a predominant male preponderance i.e 92 %. The mean age of patients presenting with ACLF was 45.39 ± 1.1 yrs. Among causes of chronic liver disease alcohol was commonest (79 %) followed by Alcohol + Hepatitis C (4.0 %) ,Alcohol + hepatitis B (1 %), Hepatitis B (1 %), Hepatitis C (3 %), NASH related (4 %) and Auto immune (5 %).Etiologyof acute precipitants included alcohol (43%) followed by Alcohol with Hepatitis B/C (9 %), alcohol with Hepatitis E (4%), alcohol with hepatitis E + Dengue (2%), Hepatitis E (8%), Hepatitis B (8 %) and Hepatitis C (6%) ,Hepatitis E + Leptospirosis (2%), leptospirosis (1%) and gastrointestinal bleed + others etiology (14%) were other causes of acute etiology in patients of acute on chronic liver failure. The mean SOFA, MELD and MDF scores were found to be **better** predictors of mortality. **Conclusion**: ACLF carries a high mortality rate. Alcohol was found to be the most common cause of chronic etiology of Chronic liver disease as well as acute insult. Scoring systems such as SOFA, MELD and MDF scores were considered to better predictors of mortality.

Keywords: Alcohol, Chronic Liver failure, etiology, mortality.

Introduction

Acute on chronic liver failure (ACLF) is an intense deterioration of a chronic liver disease distinct from acute liver failure and decompensated chronic liver ailment [1]. This term was first employed in 1995 to depict a condition in which two insults to liver are operatingat the same time, one of them being ongoing and chronic and the other acute [2].There have been different reports and definitions of what precisely comprises of ACL.

**Correspondence*
Dr. Rachit Magazine
Post Graduate, Department of Medicine, Government Medical College, Jammu, India.
E-Mail: rachitmagazine27@gmail.com

Asian Pacific Association for the Study of the Liver (APASL) explained it as "acute hepatic insult establishing as jaundice (defined as serum bilirubin level ≥5 mg/dL) and coagulopathy (defined as international normalized ratio ≥1.5), complicated within 4 weeks by ascites and/or encephalin a patient with previously diagnosed or undiagnosed chronic liver disease (Sarin S et al 2014)[3]. In terms of precipitating events, primary hepatitic insult counting reactivation of hepatitis B virus (HBV) as well as secondary viral insults with hepatitis E virus (HEV) and hepatitis A virus (HAV) frame a major cause in the east, and APASL definition per se prohibits bacterial infection as a precipitating event [4]. More current components like dengue fever and malaria infection are too being considered as acute etiological factors in Acute on chronic liver failure. A recent EASL-CLIF consortium prospectively analyzeda expansive cohort of patients to particularly characterize various organ failures, to survey different variables anticipating mortality and to create a prognosticating model [5-7]. The consortium

moreover modified the existing Sequential Organ Failure Assessment (SOFA) score utilized byintensivists and formulated a new CLIF-SOFA score to address various issues particularly related with liver failure and cirrhosis.In such circumstances, research and advancement of various proprietary artificial and bio artificial liver devices to supplement liver functions in settings of ACLF may make a modern skyline [8]. Studies on ACLF are limited, heterogeneous, and mostly retrospective. It is pertinent to study the etiological profile of ACLF patients, factors predicting their mortality, for understanding the natural course of ACLF and developing newer treatment modalities to lessen the mortality.

Materials and Methods

The present observational, cross-sectional analytical study was conducted on patients defined by Asian Pacific Association for the Study of the Liver (APASL GUIDELINES) 2014 [3]admitted with acute on chronic liver failure for a period of 1 year in the Post graduate Department of Internal Medicine, Government Medical College and Associate Hospitals, Jammu, a tertiary care hospital w.e.f November 1st 2016 to October 31st, 2017.Informed consent was taken from the first degree relatives (FDRs) of the patient for enrollment in the trial. The study was presented for approval, to the Institutional Ethical Committee, prior to the enrollment of patients into the study.

Method of collection of data

Acute hepatic insult (1 or more) were defined from the following etiologies such as Infectious etiology (Hepatotropic and non-hepatotropic viruses, reactivation of Hepatitis B (overt or occult) or Hepatitis C and other infectious agents afflicting the liver) and non infectious etiology (Alcohol: active drinking within the last four weeks, use of hepatotoxic drugs, herbs, flare of autoimmune hepatitis or Wilson's disease, surgical intervention, variceal bleeding and Unknown hepatotoxic etiology.

Chronic liver disease was based on clinical, radiologic and endoscopic criteria. The presence of any of the following was taken as evidence of underlying chronic liver disease: ascites with high serum-ascites albumin gradient, presence of esophagealvarices, hepatic venous pressure gradient (HVPG) >10 mm Hg, stage >2 fibrosis on histological analysis, or portal vein >13 mm on ultrasonography[9]

Inclusion criteria

Consecutive patients with ACLF as defined by APASL were included. Every consecutive patient with previously diagnosed or undiagnosed chronic liver disease, Jaundice [serum bilirubin level >5mg/dL] and coagulopathy (international normalized ratio >1.5 or prothrombin activity < 40%) with onset of ascites and/or encephalopathy occurring within 4 weeks of the acute insult,sudden onset of acute liver disease on presentation with evidence of chronic liver disease confirmed after evaluation and age group older than 16 years.

Exclusion criteria

Age younger than 16 years, sudden onset of acute liver disease on presentation with no evidence of chronic liver disease, patients of decompensated chronic liver disease in whom the presence of acute hepatic insult cannot be defined, patients with sepsis and patients with Hepato renal syndrome (HRS)

Assessment of severity and organ dysfunction

Prognostic Scores including Maddrey's discriminant function (MDF) (Maddrey WC et al., 1978)[10], Model for end stage liver disease (MELD) (Malinchoc M et al., 2000[11]) and Sequential organ failure assessment score (SOFA) (Vincent JL et al., 1998)[12] were calculated for all patients as per defined by above guidelines.

Statistical analysis

All results are expressed as mean±standard deviation (SD), median (range), or frequency (in percent). Quantitative variables, expressed as means ±SD, were compared with the use of the Student's t test. Qualitative variables, expressed as percentages, were compared with the use of a chi-square test. A p value of <0.05 was considered statistically significant. Analysis was performed using SPSS software version 23 for Windows and Microsoft Excel for Windows.

Result and discussion

Acute on chronic liver failure (ACLF) is a critical condition and approximately two-thirds of patients may die in the absence of liver transplantation. Most patients already have multi-organ failure at presentation which has a spiraling downhill effect leading to high mortality in these patients. The present study was conducted at Government Medical College and Associated Hospitals, Jammu and a total of 100 patients were included in the study.

The age of the patients in our study ranged from 22 years to 68 years. Most of the patients belonged to age group of 40-49 and 51-60 years of age respectively (table 1). In a study from GB Pant hospital Delhi the median age of the patients was 36 years (range 15 to 80) years with a predominance of males (74% vs 24%)

[13]. Our results were also in agreement with Moreau et al who reported that the mean age of patients presenting with acute on chronic liver failure was 56 years [14]. Majority of the patients were males (n= 93) compared to (n= 7) females (table 2). The male preponderance is due to the fact that major cause of chronic liver disease in our region is alcohol intake and use of alcohol is much more common in males than females (Table 2). Male patients consisted of 74%, 86%, 86%, in different studies [3,4,15]. The sex distribution of ACLF patients is similar to that of in cirrhotic patients presenting to our hospital.

The study group patients were divided into 3 subgroups on basis of presentation viz subgroup A (Not a known CLD presenting with acute decompensation), sub group B (Known compensated CLD presenting with acute decompensation) and sub group C (Known decompensated CLD presenting with rapid deterioration of liver function). Most of the patients belonged to sub group A. Thus undiagnosed cirrhosis was already present in most of the patients with ACLF. (Table 3)

The etiology of chronic liver disease as well as acute insult was studied. In our study the most common cause of etiology of chronic liver disease was found to be to be alcohol related (79 %), Alcohol + Hepatitis C (4.0 %), Alcohol + hepatitis B (1 %), Hepatitis B (1 %), Hepatitis C (3 %), NASH related (4 %) and auto immune (5 %) were the other common causes of chronic liver disease (Table 4). In a study from Osmania Medical College, Hyderabad, the most common cause of underlying liver disease is alcoholic liver disease (76 %) followed by hepatitis B (6 %). Among the alcoholic liver disease super added alcoholic hepatitis is the most common (36.8%) cause followed by acute hepatitis E (18.4%) [16]. In the western world alcoholic cirrhosis constitutes 50-70 % of all the underlying chronic liver diseases and Hepatitis B constitutes about 10-15 % of all cases [17-19]. However in the Asian countries Hepatitis B constitutes 70 % and alcohol only about 15% of the etiology of chronic liver disease. In study published from Delhi the most common etiology of chronic liver disease was Hepatitis B followed by chronic alcohol abuse [13] In a recent study stated from western India [20] the most common etiologies of CLD were hepatitis B (29.6 %) and cryptogenic (27.7%). The cause of chronic liver disease was due to alcohol in 79% of our patients. Alcohol as a cause of CLD in relation to other causes was studied and it was not found to be having significant correlation with mortality in this subgroup of patients. In another study by different studies, alcohol wasfounf to be most common insult followed by viral hepatitis and autoimmune hepatitis[21].

Coming on to the acute etiology in patients of acute on chronic liver failure, alcohol (43%) constituted the most common etiology of acute decompensation. Alcohol with Hepatitis B/C (9 %), alcohol with Hepatitis E (4%) and alcohol with hepatitis E + Dengue (2%) also constituted causes of acute etiology. Hepatitis E (8%), Hepatitis B (8 %) and Hepatitis C (6%) are other common causes of acute etiology. Hepatitis E + Leptospirosis (2%), leptospirosis (1%) and gastrointestinal bleed + others etiology (14%) were other causes of acute etiology in patients of acute on chronic liver failure (Table 5). Our results were in coherent with another study in which the etiology of underlying cirrhosis was alcohol in majority of patients (59%) with alcoholic hepatitis being the most common acute precipitating event, occurring in 43% of patients [22].In another study [15]which statedthat alcoholic liver disease (68%) was the most common etiology of cirrhosis in ACLF. Similar pattern of acute decompensation was found again like western world with alcohol being the most common causei.e 25% [23].Thus, there is a significant difference between etiologies of acute as well as chronic disease among northern and western India; alcohol being the major contributing factor in our population group.

The prognostic factors determining the outcome of patients with cirrhosis and multi-organ failure are currently under evaluation. In our study,the mean SOFA score was 7.63 in patients with poor clinical outcome (death) and 6.57 in patients with good clinical outcome (alive)and had a significant correlation with the mortality and clinical outcome of the patients.. The mean MELD score was 32.31 and 27.17 in patients with poor and good clinical outcome respectively. The mean MDF score was 71.84 in patients with poor clinical outcome as compared to 51.28 in patients with good clinical outcome (Table 6).In a similar study conducted it was observed that sequential assessment of organ dysfunction (SOFA) during the first few days of ICU admission is a good indicator of prognosis. Both the mean and highest SOFA scores are particularly useful predictors of outcome[24].In aanalogousstudy 50 patients admitted to a six bed multidisciplinary ICU with SIRS were consecutively enrolled in the study and SOFA scores were calculated at zero hour, after 48 hrs, and after 96 hrs and patients were followed till discharge from hospital[25]. Hence, the SOFA scoring system was found to be useful in predicting outcomes in ICU and thus help in proper utilization of ICU resources

Table 1: Age group wise distribution of the patients (n=100)

Age group	Number	Percentage
20-29	10	10.00
30-39	19	19.00
40-49	31	31.00
50-59	31	31.00
60-69	9	9.00
Total	100	100.00
Mean age	45.39	
SD age	10.72	

Table 2: Sex distribution (n=100)

Sex	Number	Percentage
Male	93	93.00
Female	7	7.00
Total	100	100.00

Table 3: Distribution of patients according to group (n=100)

	Group	Number	Percentage
Subgroup A	Not a known CLD presenting with acute decompensation	53	53.00
Subgroup B	Known compensated CLD presenting with acute decompensation	37	37.00
Subgroup C	Known decompensated CLD presenting with rapid deterioration of liver function	10	10.00
Total		100	100.00

Table 4: Etiology of Chronic Disease in Patients of acute on Chronic Liver Failure (ACLF) (n=100)

Chronic Disease Etiology	Number	Percentage
Alcohol (AL)	79	79.00
Alcohol + Hepatitis B (AL+B)	1	1.00
Alcohol + Hepatitis **C** (AL+**C**)	4	4.00
Hepatitis B (B)	1	1.00
Hepatitis **C (C)**	3	3.00
NASH (N)	4	4.00
Auto immune (Al)	5	5.00
Unknown (U)	3	3.00
Total	100	100.00

Table 5: Etiology of Acute Disease in Patients of Acute on Chronic Liver Failure (ACLF) (n=100)

Acute disease etiology	Number	Percentage
Alcohol (AL)	43	43.00
Alcohol + Hepatits E (AL+E)	4	4.00
Alcohol + Hepatitis B/C (AL+B/C)	9	9.00
Alcohol + Hepatits E + Dengue fever (AL+L+D)	2	2.00
Acute Hepatitis B (B)	8	8.00
Acute Hepatitis C (C)	6	6.00
Acute Hepatitis E (E)	8	8.00
Hepatitis E + Leptospirosis (E+L)	2	2.00
Hepatits A + Hepatitis E (A+E)	1	1.00
Leptospirosis (L)	1	1.00
Liver abscess (LA)	1	1.00
GI bleed + Other etiology (GIB+OTH)	14	14.00
Unknown (U)	1	1.00
Total	100	100.00

Table 6: Relation of Scoring Systems MDF, MELD and SOFA to clinical Outcome in Patients of Acute on Chronic Liver Failure (n=100)

	MDF		MELD		SOFA	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Alive	51.28	26.94	27.17	7.83	6.57	3.08
Death	71.84	47.71	32.31	9.58	7.63	2.90
Total	62.38	40.68	29.95	9.14	7.14	3.02
t-value	-2.5920		-2.9060		-1.7765	
P value	0.0110*		0.0045*		0.0788	

References

1. Jalan R, Gines P, Olson JC, Mookerjee RP, Moreau R, Garcia-Tsao G, et al. Acute-on chronic liver failure. J Hepatol. 2012;57:1336- 1348.
2. Ohnishi H, Sugihara J, Moriwaki H, Muto Y. Acute-on-chronic liver failure. Ryoikibetsu Shokogun Shirizu. 1995; 7(2):217-19.
3. Sarin SK, Kedarisetty C, Abbas Z, Amarapurkar D, Bihari C, Chan A. Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific Association for the Study of the Liver (APASL). Hepatol Int 2014; 8(4):453-71.
4. Khatun UF, Sayeed A, Hussain SMB, Paul S, Kawsar NM, Al-Azad. Etiological study of acute on chronic liver failure among patients admitted in medicine

ward in Chittagong medical college hospital JAFMC Bangladesh 2013; 9:77-82.

5. Radha Krishna Y, Saraswat VA, Das K et al. Clinical features and predictors of outcome in acute hepatitis A and hepatitis E virus hepatitison cirrhosis. Liv. Int.: Off. J. Int. Assoc. Study Liv. 2009; 29 (3):392–8.

6. Kumar Acharya S, Kumar Sharma P, Singh R et al. Hepatitis E virus (HEV) infection in patients with cirrhosis is associated with rapid decompensation and death. J. Hepatol. 2007; 46 (3):387–94.

7. Jha AK, Nijhawan S, Rai RR, Nepalia S, Jain P, Suchismita A. Etiology, clinical profile, and inhospital mortality of acute-on-chronic liver failure: a prospective study. Indian J. Gastroenterol: Off. J. Indian Soc. Gastroenterol. 2013; 32 (2):108–14.

8. Laleman W, Wilmer A, Evenepoel P, Elst IV, Zeegers M, Zaman Z. Effect of the molecular adsorbent recirculating system and Prometheus devices on systemic haemodynamics and vasoactive agents in patients with acute on- chronic alcoholic liver failure. Crit Care 2006; 10(4):108.

9. Monga R, Garg S, Tyagi P, Kumar N. Superimposed acute hepatitis E infection in patients with chronic liver disease. Indian J Gastroenterol 2004; 23:50-52.

10. Maddrey WC, Boitnott JK, Bedina MS, Weber FL, Mezey E, White RI. Corticosteroid therapy of alcoholic hepatitis. Gastroenterology 1978; 75(2): 193-99.

11. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, Ter Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. Hepatol 2000; 31(4):864-71.

12. Vincent JL, de Mendonca A, Contrane F. Moreno R, Takalo J, Stter PM et al. SOFA Score to assess the incidence of organ dysfunction/failure in Intensive Care Unit: results of multicenter prospective study. Crit Care Med 1998; 26(11):1793-800

13. 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. Dig Liver Dis 2012; 44(2):166-71.

14. Moreau R, Jalan R, Gines P, Pavesi M, Angeli P, Cordoba J. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. Gastroenterol 2013; 144(7):1426-37.

15. 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(40):14934-41.

16. Kumar BR, Rahul D, Prabhakar B. A study of clinical profile in patients with acute on chronic liver failure in a tertiary hospital. Asian Pac J Health Sci 2016; 3(2):47-57.

17. Zauner C, Schneeweiss B, Schneider B, Madl C, Klos H, Kranz A. Short-term prognosis in critically ill patients with liver cirrhosis: an evaluation of a new scoring system. Eur J Gastroenterol Hepatol 2000; 12:517-22.

18. Zauner CA, Apsner RC, Kranz A, Kramer L, Madl C, Schneider B. Outcome prediction for patients with cirrhosis of the liver in a medical ICU: a comparison of the APACHE scores and liver-specific scoring systems. Intensive Care Med 1996; 22:559-63.

19. Cholongitas E, Senzolo M, Patch D, Kwong K, Nikolopoulou V, Leandro G. Risk factors, sequential organ failure assessment and model for end-stage liver disease scores for predicting short term mortality in cirrhotic patients admitted to intensive care unit. Aliment PharmacolTher 2006; 23:883-93.

20. Khot AA, Somani P, Rathi P, Amarapurkar A .Prognostic factors in acute-on-chronic liver failure: A prospective study from western India. Indian J Gastroenterol 2013; 12:56-62

21. 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(40):14934-41.

22. Jain R, Thakur MB. Acute on chronic liver failure: Casuative factors & comparison of prognostic scores. J Liver Res DisordTher 2016; 1:15-28.

23. Amarapurkar D, Dharod MV, Chandnani M. Acute-on-chronic liver failure: A prospective study to determine the clinical profile, outcome, and factors predicting mortality. Indian J Gastroenterol 2015; 34: 216-24.

24. Ferreira FL, Bota DP, Brass A, Melot C, Vincent JL. Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA 2001; 286:1754-8.

25. Acharya SP, Pradhan B, Marhatta MN. Application of "the Sequential Organ Failure Assessment (SOFA) score" in predicting outcome in ICU patients with SIRS Kathmandu University. Med Jr 2007; 5:475-48.

Conflict of Interest: None
Source of Support: Nil