Acute-on-Chronic Liver Failure (ACLF) in Coastal Eastern India: ''A Single-Center Experience''

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Background and objectives: **Acute-On-Chronic liver failure (ACLF) is an emerging entity. The present study was undertaken to analyze the clinical profile and natural course of ACLF patients.** ***Patients and methods:*** **ACLF was defined as per Asia Pacific Association for the Study of Liver consensus criteria 2009. Patients fulfilling these criteria with some deviations were included and prospectively evaluated for clinical profile, etiologies of acute decompensation (AD) and underlying chronic liver disease, and short-term natural course [3 months].** ***Results:*** **Out of 123 patients with ACLF (mean age: 45.83 ± 12.05 years; male:female 109:14), 45.53% cases had prior history of AD, and 54.47% presented for the first time as ACLF. Etiologies of cirrhosis were alcohol, cryptogenic, and chronic hepatitis B virus infection in 65.04%, 23.57%, and 11.38% cases, respectively. Recent history of alcohol intake (within 4 weeks) [42.27%] followed by bacterial infections [36.58%] were the common etiologic precipitants for AD. Only 87 (70.73%) out of 123 cases could be followed up for a duration of 3 months; 62 (71.26%) cases died by 3 months. Most deaths occurred in the alcoholics compared to nonalcoholics [(43/53) 81.13% vs. (19/34) 55.88%; *P* = 0.01]. No significant difference in mortality rate was observed between ACLF cases with history of prior AD compared to newly diagnosed ACLF cases [30/40 (75%) vs. 32/47 (68.09%); *P* = 0.477]. The prognostic markers [MELD, MELD-Na, CTP] were not significantly different between survivors and nonsurvivors.** ***Conclusion:*** **ACLF patients in our population had high short-term mortality rates with majority of deaths in alcoholics. Alcohol intake and bacterial infections were mainly responsible for AD in our study. (J Clin Exp Hepatol 2016;6:26–32)**

Acute-on-chronic liver failure (ACLF) is an emerging entity denoting an acute deterioration of liver function in patients with chronic liver disease (CLD). However, there is lack of consensus on the definition of ''ACLF'' and its acute precipitants. This term was first used in 1995 to describe a condition in which two insults to liver are operating simultaneously, one of them being ongoing and chronic and the other one is acute.[1] A characteristic feature of ACLF is rapid progression and high short-term mortality, varying from 50 to 90%.[2] Currently, two consensus working definitions for this syndrome exist in the literature; the first one propounded by the Asia Pacific Association for the Study of the Liver (APASL) in 2009 defines ACLF as ''Acute hepatic insult manifesting as jaundice (serum bilirubin ≥5 mg/dl) and coagulopathy [International Normalized Ratio (INR) Prothrombin Time (PT) ≥1.5], complicated within 4 weeks by ascites and/or encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease.''[3] The second, put forth at the European Association for Study of Liver–American Association for Study of Liver Disease (EASL-AASLD) single topic symposium in 2013, defined ACLF as ''Acute deterioration of preexisting, chronic liver disease, usually related to a precipitating event and associated with increased mortality at 3 months due to multisystem organ failure''.[2,4,5] Alcohol and drugs constitute the majority of acute insults in the West, whereas infectious etiologies predominate in the East. Among the infectious etiologies, reactivation of hepatitis B virus (HBV) infection is one of the major causes of ACLF in Asia.[6,7] In India, superadded infection with hepatitis E virus (HEV) acts as an important acute precipitant leading to ACLF.[8–10] Among the noninfectious etiologies, active alcohol consumption is considered a major acute insult in the western countries[11,12]; consumption of hepatotoxic drugs and herbal indigenous medications act as an important acute precipitants in the Asia Pacific region.[13,14] There is paucity of prospective studies on ACLF and its short-term (3 months) natural outcome in our region, which is a

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Abbreviations: ACLF: acute-on-chronic liver failure; AD: acute decompensation; ALD: alcoholic liver disease; ALT: alanine transaminase; APASL: Asian Pacific Association for the Study of the Liver; CLD: chronic liver disease; CTP: Child-Turcotte-Pugh; EASL-AASLD: European Association for the Study of the Liver-American Association for the Study of Liver Diseases; HBV: hepatitis B virus; HE: hepatic encephalopathy; HEV: hepatitis E virus; HRS: hepatorenal syndrome; INR: International Normalized Ratio; MELD: Model for End-Stage Liver Disease; MELD-Na: Model for End-Stage Liver Disease Sodium; PT: prothrombin time; SD: standard deviation; SIRS: systemic inflammatory response syndrome

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region constrained with no facility for liver transplantation. The study was performed with an aim to assess the clinical and biochemical profile, etiologies of underlying CLD, acute insults, and factors affecting the short-term natural outcome of ACLF patients in Coastal Eastern India.

MATERIALS AND METHODS

Consecutive patients [total 123 patients] of ACLF fulfilling modified APASL Consensus criteria 2009 admitted to the Department of Gastroenterology, S.C.B. Medical College and Hospital, Cuttack between August 2012 and May 2014 were included and prospectively evaluated for 3 months, or till death, whichever occurred earlier. Patients with pregnancy, age <18 years, portal vein thrombosis, hepatocellular carcinoma, and unwillingness to participate in the study were excluded from the study protocol. The study was approved by the Institutional Ethics Committee. In the present study, cirrhosis was diagnosed on the basis of supportive history, clinical findings, biochemical abnormalities, ultrasonographic abnormalities [presence of heterogenous coarse shrunken liver with irregular margins and other signs of portal hypertension], and gastroscopic demonstration of varices. In the study, we also included cirrhotics with prior history of acute decompensation (AD), which is a departure from the APASL criteria that exclude patients with prior decompensation. Besides, we also included cases decompensating following insults like nonhepatotropic infections/sepsis and acute variceal bleeding. These are also deviations from the APASL 2009 criteria. AD was defined as rapid decompensation in the form of development of hepatic encephalopathy (HE) and/or ascites commensurate with the CANONIC study criteria.[4] Although, the role of nonhepatic acute insults (nonhepatotropic infections/sepsis and variceal bleeding) in ACLF has not been unambiguously defined in the APASL recommendations, we included them as acute precipitants because of their frequent inclusion as precipitating events in different studies from the West,[11,15] and their frequent association in our cirrhotic population. All the cases were searched for possible causes of AD including intake of hepatotoxic medication, active alcohol drinking (alcohol consumption within 4 weeks of onset of jaundice), infections (urinary tract infection, respiratory tract infection, gastrointestinal infection, etc.), variceal bleeding, viral hepatitis [hepatitis A virus (HAV), HEV, HBV flare], recent history of major surgery, etc. In our study, HBV flare was diagnosed when there was abrupt rise of alanine transaminase (ALT) >5 times upper limit of normal on a background of chronic hepatitis B related cirrhosis. Whenever suspected, the cases were also investigated for autoimmune liver disease, Wilson disease, and Hemochromatosis. In some patients, more than one acute insult was deemed to be responsible for the precipitation of ACLF; in such cases, they were considered as multiple acute insults. All the cases were also analyzed for the varied modes of presentation (jaundice, ascites, HE, upper gastrointestinal bleeding, etc.) and various related complications including hepatorenal syndrome (HRS), cardiorespiratory failure, septicemia, etc. The cases were further evaluated using prognostic scorings such as Child-Turcotte-Pugh (CTP) score, Model for End-Stage Liver Disease (MELD) score, and Model for End-Stage Liver Disease Sodium (MELD-Na) score at baseline.

Statistical Analysis

All the results were expressed as mean ± standard deviation (SD) or frequency (in percent). Normally distributed quantitative and categorical variables were compared using student's *t*-test and Chi-square test, respectively. Nonparametric unpaired data were compared using Mann–Whitney *U*-test. All the analyses were performed using SPSS 17 software. A '*P*-value of <0.05' was considered statistically significant.

RESULTS

The mean age of presentation of ACLF patients in our study was 45.83 ± 12.05 years; majority were males (male: female ratio 109:14). All 123 ACLF cases had cirrhosis of liver as underlying CLD. The etiologies of cirrhosis were alcohol, cryptogenic, and chronic HBV infection in 80 (65.04%), 29 (23.57%), and 14 (11.38%) cases, respectively. Fifty-six (45.52%) patients had cirrhosis of liver with prior history of AD, whereas the rest 67 (54.47%) patients had no prior history of AD. Mean duration of development of ascites from the onset of jaundice was 13.25 ± 7.66 days. Eighty-eight (71.54%) cases had single acute predisposing event, whereas the rest 35 (28.45%) had multiple acute insults (≥2 acute insults). Of the 35 cases with multiple acute predispositions, 30 had 2 acute predispositions and remaining 5 cases had 3 acute predisposing events. Recent history of active alcohol drinking followed by bacterial infections was the leading causes of acute insults. Most cases who decompensated following hepatotoxic medications had ingested indigenous drugs provided by quacks, while 2 cases were attributed to use of antitubercular drugs (ATT). Majority of cases (97.56%) presented with ascites followed by HE (40.65%) cases. Forty-seven (38.21%) cases presented with both ascites and HE. Sixty-four (52%) cases had portal hypertensive gastropathy. Baseline biochemical parameters and prognostic markers of all the cases [survivors as well as nonsurvivors] at the time of enrollment are shown in Table 1. Baseline clinical presentations, biochemical parameters, and prognostic markers in the cases with and without prior history of AD and with single and multiple acute predispositions are shown in Tables 2 and 3, respectively. Sixty-two (50.4%) cases died within 3 months,