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Assessment of the Predictors and Mortality in Patients of Acute on Chronic Liver Failure; A Prospective Study

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ABSTRACT

Objective: To evaluate the predictors of short-term mortality in patients with acute-on-chronic liver failure (ACLF).

Methodology: This prospective study was conducted at the gastroenterology department of the Asian Institute of Medical Sciences Sindh, Pakistan from January 2018 to December 2018. All the patients with acute-on-chronic liver failure (ACLF) aged more than 25 years and of either gender were included. A complete history was obtained including demographic profile and specifics on clinical characteristics (jaundice, ascites, gastro-intestinal bleed, grade of encephalopathy, records of vital parameters etc.). Serum electrolytes, viral serology, autoimmune profile, liver function tests, serum creatinine, prothrombin time, and INR were among the laboratory tests performed on each patient.

Results: A total of 99 patients were studied; their average age was 40.90+13.93 years; and there was a male predominance (73.5%). HCV and HBV+HDV were the most common etiological factors. According to the frequency of organ failure, hepatic failure was in 59.8% of the cases, renal failure was in 43.6% of the cases, CNS failure was in 38.5% of the cases, 41.0% of the cases had circulatory failure, coagulation failure was in 55.6% of the cases, and respiratory failure was seen in 17.1% of the cases. Overall, the 30-day mortality rate was 61.5%. Hepatic failure, renal failure, CNS failure, coagulation failure, SBP, and grading of ACLF were significantly associated with short-term survival rate (p= <0.05). While gender, etiology, circulatory failure and respiratory failure were statistically insignificant (p= >0.05). MELD score >28, CTP score >13, organ failure >3 and ACLF grade II and III were also highly significantly linked to short term survival rate (p-0.0001).

Conclusion: According to the study's findings, hepatic failure, renal failure, CNS failure, coagulation failure, and ACLF grading, CTP score > 13, MELD score > 28, and the presence of hepato-renal syndrome were found to be significant predictors of short-term mortality in patients with Acute On-Chronic Liver Failure (ACLF).

Key words: ACLF, mortality, etiology, predictors

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Introduction

Acute-on-chronic liver failure (ACLF) is a syndrome accompanied by chronic liver disease' (CLD) acute decompensation related to the failures of the organs, either hepatic or extr-ahepatic.[1,2] It is a specific syndrome linked to a high rate of short-term mortality.[3] It seems to be a distinguishable syndrome that affects individuals who have CLD, whether or not they have cirrhosis. It is marked by acute hepatic decompensation (GI bleeding,

encephalopathy, ascites, and bacterial infection), as well as single or even more extrahepatic organ impairments, and it has a high short-term (28 days) mortality rate of 33% and at 90 days, 51% mortality. [3,4] In the vast majority of cases, ACLF caused the acute incident that adds an inflammatory surge to the baseline chronic inflammation prevalent in those who have cirrhosis of the liver and the decompensation. Failure of the organ is caused by a number of processes, which include an increase in inflammatory mediators and organ hypoperfusion. Furthermore, approximately 40% of people with ACLF had no apparent acute incident prior to the onset of ACLF. [3,4] Regardless of the absence of prospective data to characterize this, there has been a substantial amount of credible evidence that this ailment is a unique clinical phenomenon.[6] From such a pathophysiologic standpoint, alterations in the host's reaction to injuries and infection are crucial towards its progression.[6] Many different scoring systems have indeed been established, but the majority of these are based on the clinical signs that are present during the diagnosis in order to evaluate the ACLF prognosis. Common types include the scoring of Model of End-stage Liver Disease (MELD), and the score of Child–Turcotte–Pugh 'CTP'.[5-7] Other examples include the more subsequent score of the CLIF-SOFA and the score of CLIFC ACLF, both of which were recommended by the European Organization for the study of Chronic hepatic failure.[6,8] Both the baseline features and the dynamic changes of prognostic factors are helpful in predicting prognosis in ACLF because of the nature of the condition, which is changing rapidly.[9] Early diagnosis of the poor prognosis associated with ACLF is important for reducing ineffective and costly treatments as well as for judicious resource allocation for the transplantation of the liver.[10] There have been a substantial number of studies conducted all over the world regarding it. [11] Nevertheless, there haven't been found more local studies to determine the factors that are linked to death in this particular suffering population. Therefore, this study has been done to assess the predictors and mortality in patients with acute-on-chronic liver failure (ACLF).

Methodology

This prospective study was conducted at gastroenterology department of Asian Institute of Medical Sciences Sindh Pakistan. The study duration was one year from January 2018 to December 2018. All the patients with acute-on-chronic liver failure (ACLF) aged more than 25 years and of either gender were included. All the cases who had a previous history of hepatic decompensation, were not matched to ACLF criteria, who suffered from hepatocellular carcinoma as well as any other form of cancer or portal vein thrombosis, and those who did not agree to take part in the study were excluded. ACLF was defined Asian Pacific Association for the Study of Liver "APASL" 2014, as the immediate manifestation of a severe hepatic impairment like coagulopathy, jaundice "total bilirubin >5 mg/dL", complications developed within a period of four weeks like encephalopathy and/or ascites among cases who seems to have "CLD", either of which has been diagnosed or not diagnosed previously.[11,12] In order to determine the etiology of chronic liver disease as well as the acute triggering event, a complete history was obtained including demographic profile and specifics on clinical characteristics (jaundice, ascites, gastro-intestinal bleed, grade of encephalopathy, records of vital parameters etc.). Serum electrolytes, autoimmune profile, liver function tests, serum creatinine, prothrombin time, and INR were among the laboratory tests performed on each patient. A detailed history of previous consumption of the hepatotoxic agents has been obtained and additional serological tests for hepatitis A, hepatitis B, HCV, HBV, and HCV were done if indicated, in order to determine the source of the acute hepatic injury. The patients were monitored for one month or until any in-hospital deaths occurred. All the data was collected via a pre-designed study proforma and the analysis of the data was done by using SPSS version 26.

Results

A total of 99 patients were studied; their average age was 40.90±13.93 years, and the male predominance (73.5%). HCV and HBV+HDV were the commonest etiological factors. According to the frequency of organ failure, hepatic failure was in 59.8% of the cases, renal failure was in 43.6% of the cases, CNS failure was in 38.5% of the cases, 41.0% of the cases had circulatory failure, coagulation failure was in 55.6% of the cases, and respiratory failure was seen in 17.1% of the cases. Overall, 30 days mortality rate was 61.5%, while acute insult and number of the organs failure presented in table I

Hepatic failure, renal failure, CNS failure, coagulation failure, SBP, and grading of ACLF were significantly associated with short-term survival rate ($p = <0.05$).

Table I: Descriptive statists of demographic characteristics, etiology, organ failure and mortality (n=99)

Variables		Descriptive statistics	
Age (mean)		40.90±13.93 years	
CTP score		13.34 ± 1.20	
MELD score		33.20 ± 5.37	
Gender	Male	86	73.5
	Female	31	26.5
	Total	117	100.0
Etiological factors	HCV	42	35.9
	HBV	23	19.7
	ALCOHOLIC	6	5.1
	NASH	3	2.6
	HBV+HDV	24	20.5
	HBV+HCV	8	6.8
	HCV+ALCOHOLIC	3	2.6
	UNKNOWN	6	5.1
	AIH	2	1.7
Acute insult	ATT	4	3.4
	DAA	1	.9
	IFN	2	1.7
	SEPSIS	76	65.0
	HEV	7	6.0
	HBV FLARE	4	3.4
	HDV	5	4.3
	ALCOHOL BINGE	4	3.4
	SURGERY	2	1.7
	ACUTE PVT	2	1.7
	UGIB	1	.9
	UNKNOWN	9	7.7
Organ failure	Hepatic failure	70	59.8
	Renal failure	51	43.6
	CNS failure	45	38.5
	Circulatory failure	48	41.0
	Coagulation failure	65	55.6
	Respiratory failure	20	17.1
Number of organ failure	0	7	6.0
	1	22	18.8
	2	31	26.5
	3	30	25.6
	4	12	10.3
	5	13	11.1
	6	2	1.7
In hospital mortality (28 days)	Expired	72	61.5
	Survived	45	38.5

While gender, etiology, circulatory failure and respiratory failure were statistically insignificant (p= >0.05). The MELD score, CTP, organ failure >3 and ACLF grades II and III were also highly significantly linked to short term survival rate (p-0.0001). Table II

Table II: Descriptive statists of predictors of mortality in Acute-On-Chronic Liver Failure (n=99)

Predictors		Mortality		Total	p-value
		Expired	Survived		
Gender	Male	54	32	86	0.643
	Female	18	13	31	
Etiology	HCV	25	17	42	0.879
	HBV	14	9	23	
	Alcoholic	5	1	6	
	NASH	1	2	3	
	HBV+HDV	14	10	24	
	HBV+HCV	5	3	8	
	HCV + alcoholic	2	1	3	
	Unknown	5	1	6	
	AIH	1	1	2	
SBP	Yes	25	16	41	0.046
	No	47	29	76	
Liver failure	Yes	48	22	70	0.056
	No	24	23	47	
Renal failure	YES	38	13	51	0.011
	No	34	32	66	
CNS failure	yes	39	6	45	0.001
	No	33	39	72	
Circulatory failure	YES	32	16	48	0.342
	NO	40	29	69	
Coagulation failure	YES	46	19	65	0.022
	NO	26	26	52	
Respiratory failure	YES	14	6	20	0.393
	NO	58	39	97	
Number of organ failure	0	0	7	7	0.0001
	1-3	50	33	83	
	4-6 or >6	22	5	27	
CTP score	>13	56	30	86	0.001
	<13	16	15	31	
MELD score	>28	58	23	81	0.001
	<28	14	22	36	
In Hospital mortality	ACLF=0	4	14	18	0.0001
	ACLF=1	5	6	11	
	ACLF=2	18	13	31	
	ACLF=3	45	12	57	

Discussion

A distinctive illness known as acute-on-chronic liver failure (ACLF) is linked to a high rate of short term (30 days) mortality. Early detection of the cases at high risk is crucial to determining whether they require an ICU and the need of organ transplantation.[3] In this study a total of 99 cases of ACLF were studies to assess the predictors and mortality in patients of Acute-On-Chronic Liver

Failure (ACLF). In this study the men age of the patients was 40.90±13.93 years and males were in majority (73.5%). Consistently Tasneem AA et al[11] reported that the patients' mean age was 47.8 ±8.7 years and males were 66.4% out of all study subjects. In the line of this study Zakareya T et al[3] also reported that the mean was 53.9 ± 12.8 years of their study participants and males were 71.1%. Male predominance may because of the protective effects of sex hormones among females and the decreased occurrence of cofactors like alcohol consumption for the growth of fibrosis are may responsible for this variation.[13]

In this study HCV and HBV+HDV were the commonest etiological factors. In the comparison of our findings, Ayele AG et al[14] demonstrated that the Hepatitis B was found in 35.8% of individuals clinically classified to have CLD, and anti-HCV antibodies were found in 22.5% of those individuals. Like this study, on the other hand it is reported that in Pakistan, the causative factors for CLD are different from those in the world's other countries.[15] These risk factors are including viral hepatitis (HCV and HVB), non-alcoholic steatohepatitis (NASH). Although the Autoimmune hepatitis, haemochromatosis, Wilson disease and the alcoholism are, seems to be the unusual causes of CLD.[15] However Tasneem AA et al[11] also reported that, the most prevalent cause of the CLD was hepatitis B, which was found in 25% cases, following by cirrhosis associated to hepatitis C, which was found in the 23.6% of the cases.

In this study hepatic failure was in 59.8% of the cases, renal failure was in 43.6% of the cases, CNS failure was in 38.5% patients, 41.0% cases had circulatory failure, coagulation failure was in 55.6% cases and respiratory failure was seen in 17.1% of the cases. Although in the study conducted in Northern India, a predictive model was developed based on the presence of hepatic encephalopathy, electrolyte imbalance, and kidney failure. This model included patients who had ACLF as a consequence of cirrhosis caused by a variety of different causes.[16] Nevertheless, the parameters may be extremely diverse in individuals having ACLF whom present with renal failure as in these cases, the circulatory alterations can be the most prominent symptom in some people, while an enhanced pro-inflammatory mediators' synthesis, might be the most prominent symptom in others, or the both.[8] On the other hand it is reported that the multi - organ dysfunction progresses, systemic and hepatic hemodynamics significantly change, and liver function deteriorates. Microbial evacuation, along with pathogenic bacteria, is the leading frequent trigger of deterioration brought on by the systemic inflammatory response and it is essential in the transition from compensated to decompensated cirrhosis.[17]

In this study the overall, 30 days mortality rate was 61.5% in the patients of acute-on-chronic liver failure. Consistently Zakareya T et al[3] the death rate was 74.3% in the patients of ACLF. On other hand in the other studies reported that a considerable short-term mortality of 50 to 90% occurs in individuals having ACLF.[11,18] In the study of Kulkarni S et al[20] reported that the short term (28 days) mortality rate was 43.75%, while individuals having sepsis had the highest mortality rate 67.8%. These differences in the mortality rates could be explained by differences in the definition of ACLF and recommendations employed in these various settings, the diversity of patient characteristics and ethnic backgrounds, and the relative variability in the reversibility of the intense predisposing insult in addition to the grades of the ACLF.[3] An improper inflammatory response and immune system dysfunction that makes people more susceptible to infections are likely the causes of the increased mortality rate linked to ACLF.[11]

In this study hepatic failure, renal failure, CNS failure, coagulation failure and grading of ACLF were significantly associated to short term survival rate (p= <0.05). Similar to our findings Tasneem AA et al[11] reported that the mortality is common in individuals with ACLF, and it is more likely when there are three or more organ failure, urosepsis, encephalopathy and the renal failure. Although Kulkarni Set al[20] reported that the sepsis individuals had the greatest rate of death (67.85%). On the other hand, it is reported that the significant impairment of the hepatic, renal, nervous system, clotting, circulatory, and pulmonary systems could define organ failure and are the predictors of mortality.[21] In this study the MELD score, CTP, organ failure >3 and ACLF grade II and III were also highly significantly linked to short term survival rate (p-0.0001). In the line of this study Tasneem AA et al[11] also reported that, among patients of ACLF had higher mortality rate those having CTP score of >13 and the MELD score of > 30. Similar findings have been found in an Indian study, which revealed that a MELD score of 27 or above was linked to a significant mortality rate among individuals having ACLF.[22] According to the Tasneem AA et al[11], the institute did not immediately provide its patients with the option the hepatic transplant, which was among the study's limitations that contributed to the higher rate

of mortality. There were also some other limitations like limited sample size and single centre study. Additionally, only one time in this investigation was short-term mortality predicted using a number of variables. In critically ill patients like ACLF, sequential measurements may have been more informative in forecasting the outcomes.

Conclusion

As per study conclusion, Hepatic failure, renal failure, CNS failure, coagulation failure and grading of ACLF, CTP score >13, MELD score >28 and presence of hepato-renal syndrome were observed to be the significant predictors of the of the short-term mortality in patients of Acute-On-Chronic Liver Failure (ACLF). Further large scale and multicentral studies are recommended on such subject.

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