ORIGINAL ARTICLE

Comparison of Different Scores in Predicting Mortality in Patients with Acute on Chronic Liver Failure Admitted to the Intensive Care Unit of a Tertiary Care Hospital

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Abstract

Background:

The illness known as acute-on-chronic liver failure (ACLF) was just recently identified and characterized which is linked to morbidity and deaths. Several prognostic models are available to stratify these patients.

Objective:

The objective was to compare the performance of different non-invasive available models in predicting one-month and six months mortality in ACLF.

Methods:

This retrospective observational study included patients of age range 8-70 years of any gender having liver cirrhosis and fulfilling the criteria of ACLF from January 2019 to December 2022. The predesigned formula was used to calculate scores based on different models. The outcome was noted in terms of one month and six months of mortality in each patient. The receiver operative curve was constructed for six prognostic models available for predicting 30-day and six months mortality in ACLF patients. These scores were subjected to multivariable cox-regression analysis to determine the independent determinants of both short- and long-term mortality in ACLF patients.

Results:

A total of 235 patients were studied in this retrospective investigation. A one-month mortality rate of 78 patients (33.2%) and a six-month mortality rate of 155 patients (66%) were recorded, respectively. CTP score, MELD score, LBi, CLIF-SOFA, and CLIF-ACLF were independent predictors of one-month mortality on multivariate cox-regression analysis, but only CTP score, MELD score, and LBi were independent predictors of mortality at six months.

Conclusion:

Among the six prognostic scores used for the ICU-admitted ACLF patients, LBi was the most efficient predictor of both one-month and six months mortality while CLIF-C SOFA and CLIF ACLF were good predictors of both mortalities. CTP and MELD scores were useful in forecasting six months' mortality.

Keywords: Acute on Chronic liver failure, prognostic models, mortality.

INTRODUCTION

Acute Chronic Liver failure (ACLF) is a sequela of chronic liver disease (CLD) that develops in cirrhosis and is characterized by an event of liver decompensation along with one or more extrahepatic organ dysfunction and is linked to a higher death rate of approximately 30-35% at one month and more than 50% at three months [1].

In the presence of cirrhosis and decompensation, ACLF is triggered by an acute insult. This results in activation of the cascade that causes excessive release of inflammatory mediators resulting in organ failure (OF) that can be multifactorial but likely occurs due to organ hypoperfusion [2-4].

The absence of organ failure in decompensated cirrhosis distinguishes it from ACLF. Organ Dysfunction can result

*Corresponding author: Raja Taha Yaseen Khan, Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan, Email: raja_taha101488@hotmail.com Received: March 18, 2023 Revised: May 12, 2023 Accepted: May 15, 2023 DOI: https://doi.org/10.37184/jlnh.2959-1805.1.8 in high morbidity and mortality in this population. Despite of activation of a lethal cascade of processes in these patients, there is still some component of reversibility that can be addressed with good medical support and treatment and removal of the inciting factor [5, 6].

Lately, many models have been proposed and utilized for mortality anticipation in ACLF cases. However, due to differences and variations in the ACLF characterization by various liver societies, none of these models have attained universal acceptance. The models have been categorized into two categories: the one used for the evaluation of hepatic dysfunction and secondly, the global prognostic scores that in addition to the heaptic dysfunction also forecast the other organ failure. These scores include Child Turcotte Pugh Score (CTP), Chronic Liver Failure Consortium Acute on Chronic Liver Failure (CLIF-C ACLF) score, Model for End-stage Liver Disease score (MELD), APACHE II, Chronic Liver Failure-sequential Organ Failure Assessment (CLIF SOFA), ACLF Research Consortium (AARC) score,

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Lactate to Bilirubin Index (LBi), Platelet to White Blood Cell Ratio (PWR), *etc.* [1, 7-19].

The severity of the global prognostic scores over liver-specific scores in projecting death (particularly short-term) in ACLF cases has been shown in several studies. However, the optimal performance of these scores in forecasting long-term (six months) mortality is yet to be defined. This knowledge will allow us to identify the scores that can help us in the early referral of the patients for liver transplantation in our population (especially in those patients who are at low risk of one-month mortality but have a high six-month mortality rate). Therefore, we aimed to compare the utility of different non-invasive scores in anticipating one-month and six months mortality in ACLF.

METHODS

It was a retrospective observational study carried out in Karachi, Pakistan, at the Sindh Institute of Urology and Transplantation's Department of Hepatogastroenterology. All patients of age range 18-70 years of age gender having liver cirrhosis and fulfilling the criteria of ACLF as per the APASL [17] from January 2019 to December 2022 were taken in this investigation. While, cases with missing data, those with lost follow-up, or patients with a history of Hepatocellular Carcinoma, prior liver transplantation, life-threatening comorbidities (renal failure, ischemic heart disease), seizures, cardiac arrest, heart failure, mesenteric ischemia, acute pancreatitis, diabetes ketoacidosis, renal failure and other causes of increased lactate such as sepsis were omitted from this study.

Data Collection

Clinical data were recorded using predesigned proforma including baseline laboratory investigations and liver disease etiology. The laboratory investigations included complete blood count, prothrombin time, serum creatinine, serum Bilirubin, serum albumin, and serum lactate levels. The CLD etiology was noted considering viral hepatitis, alcoholic liver disease, auto-immune hepatitis, Wilson Disease, Budd Chiari Syndrome, and Non-alcoholic Fatty liver disease was noted. The cause of acute insult was also observed including the use of any herbal or hepatotoxic medications and infection by hepatotropic viruses. The predesigned formula was used to calculate CTP, MELD score, LBi, AARC score, CLIF-C ACLF, and CLIF SOFA in each patient. The outcome was noted in terms of one month and six months mortality in each patient by phone call.

SPSS software version 23.0 was utilized to perform an analysis of retrieved data. Average and data spread (standard deviation) were used for the expression of

continuous variables while frequency and percentages were calculated for categorical variables. Student t-test was used to analyze numerical variables while categorical variables were evaluated using the Chi-square test. The area under the receiver operating curve (AUROC) was obtained to identify scores utility in anticipating 30-day and six months mortality. Later on, an optimal cut-off was taken using AUROC at a point of optimal sensitivity and specificity (major increment of 0.2). These scores were subjected to multivariable cox-regression analysis to determine the independent determinants of both short and long-term mortality in ACLF patients. P-value less then or equal to 0.05 was taken as statistically significant.

RESULTS

Retrospectively, a total of 302 patients with ACLF diagnoses were initially enrolled in the study. Out of them, 38 patients were omitted to missing data, and 29 patients were excluded as they fall in the exclusion criteria (Fig. 1). After exclusion, 235 records were lastly subjected to analysis.

Among 235 cases, 140 (59.6%) were males. A frequent source of CLD was hepatitis C in 63 (26.8%), followed by hepatitis B in 54 (22.9%), autoimmune hepatitis (AIH) in 48 (20.4%), alcoholic liver disease in 31 (13.2%), Wilson disease in 18 (7.7%), cryptogenic cirrhosis in 9 (3.8%), non-alcoholic fatty liver disease and primary biliary cirrhosis each in 6 (2.6%) patients respectively. While the commonest root for acute insult was viral hepatitis which was observed in 96 (40.9%)patients. Among them, 48 (50%) patients were infected with hepatitis E, 17 (17.7%) patients with hepatitis A, 22 (25%) patients with hepatitis D, and 7 (7.3%) patients with cytomegalovirus. Drug-induced liver injury was the second-ranked source of acute insult, occurring in 76 (32.3%) patients, followed by an AIH flare in 21 (8.9%), alcoholic hepatitis in 19 (8%) patients, Wilsonian crises in 12 (5.1%) patients, and acute insults with no known origin in 11 (4.7%) patients. On presentation, ascites were observed in 202 (86%) patients, hepatorenal syndrome in 15 (6.4%), and portosystemic encephalopathy in 123 (52.3%) patients respectively. Multiple organ failure was observed in 93 (39.6%) patients. On admission, the mean Child-Pugh score, MELD score, LBi, AARC score, CLIF-SOFA, and CLIF-C ACLF scores were 11.1+1.9, 27.8+8.3, 11.7+1.3, 9.2+2.4, 10.6+3.9 and 10.1+2.7 respectively. One-month mortality was noted in 78 (33.2%) while 155 (66%) patients had mortality at six months (Table 1).

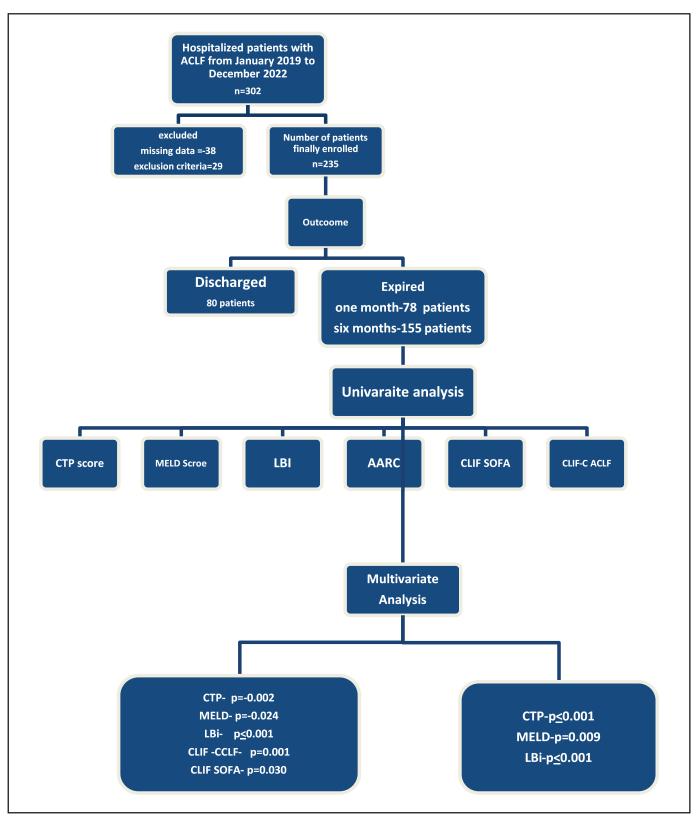


Fig. (1): Flow chart of the study.

ACLF-Acute on Chronic liver failure; CTP-Child Turcotte Pugh; MELD-Model for End Stage Liver Disease; LBi-Lactate to Bilirubin; AARC-APASL ACLF research consortium; CLIF-SOFA-chronic liver failure-sequential organ failure assessment; CLIF-C-chronic liver failure consortium.

Study Population			n (%)
Mean Age (years	±S.D)		41 <u>+</u> 16
Gender	Male		140(59.6)
Ochuci	Fem	ale	95(40.4)
	HCV		63(26.8)
	HBV		54(22.9)
	Alcohol		31(13.2)
Etiology of Chronic	Autoimmune		48(20.4)
Liver Disease	Wilson disease		18(7.7)
	NAI	FLD	6(2.6)
	PB	BC	6(2.6)
	Unknowr	n cause	9(3.8)
	Viral	HEV	48(50%)
	Viral	HAV	17(17.7)
	Hepatitis	HDV	22(25)
	96(40.9)	CMV	7(7.3)
Cause of Acute Liver Injury	DI	LI	76(32.3)
	AIH	flare	21(8.9)
	Alcoholic Hepatitis		19(8)
	Wilsonian Crises		12(5.1)
	Unkn	own	11(4.7)
A	Present		202(86)
Ascites	Absent		33(14)
	Present		123(52.3)
Hepatic Encephalopathy	Absent		112(47.7)
II (10 1	Present		15(6.4)
Hepatorenal Syndrome	Absent		220(93.6)
	Present		93(39.6)
Multi-organ failure	Absent		142(60.4)
Hemoglobin (g/dL)		10±2.3
Total Leucocyte Coun			12.9±8.9
· · · · · · · · · · · · · · · · · · ·	x10 ⁹ /L)		153±113
Serum Creatinine	,		1.9±2.2
Total Bilirubin (µ			15.2±9.1
Alkaline Phosphatas			279±512
Aspartate Transaminase	(IU/L) (AST)(IU/L)		348±676
Alanine Transaminase			216±380
	(ALT)(IU/L))	
Albumin (g/			2.3±0.7
`	nmol/L)		0.9±1.3
Child Turcotte Pug			<u>11.1+1.9</u>
MELD score			<u>27.8+8.3</u>
LBi Index			<u>11.7 +1.3</u>
AARC score			9.2 <u>+</u> 2.4
CLIF SOF			10.6+3.9
CLIF-C AC			<u>10.1 +2.7</u>
30 days mortality	Present		78(33.2)
	Absent		157(76.8)
6 months mortality	Present		155(66)
	Absent	80(34)	

 Table 1: Baseline characteristics of ACLF patients included in the study (n=235).

On univariate analysis, age, International Normalized Ratio, total leucocyte count, total bilirubin, serum creatinine, Aspartate Transaminase, and Alanine Transamnase were considerably raised in the non-survivors relative to the survivors while platelet count and albumin were significantly lesser in the former. The scores calculated such as CTP score, MELD score, LBi, AARC score, CLIF-SOFA, and CLIF-C ACLF were considerably inflated in the non-survivors group (**Table 2**). Similarly, the presence of >3 organ failure, hepatic encephalopathy and hepatorenal syndrome at presentation resulted in increased mortality in ACLF patients (**Table 3**).

 Table 2: Comparison of continuous variables in terms of overall mortality (n=235).

Variable	Non Survivors (n-155) Mean ± SD	Survivors (n-80) Mean ± SD	p-value
Age	41.5±16.1	33.9 ± 17.2	0.002
Hemoglobin (g/dL)	9.7 ±2.1	10.2 ± 2.4	0.188
Total Leucocyte Count (x10 ⁹ /L)	15.7 ± 12.5	11 ±6	0.001
Platelet Count (x10 ⁹ /L)	115 ± 54.7	171 ± 128	≤0.001
Total Bilirubin (µmol/L)	323.1±161.8	208.8 ± 130.7	≤0.001
Aspartate Transaminase (AST)(IU/L)	658±1070	193±218	≤0.001
Alanine Transaminase (ALT)(IU/L)	290±417	178±355	0.003
Serum Albumin (g/dL)	2.4±0.9	3.1±1.2	≤0.001
Serum Creatinine	2.6±1.8	1.6±2.3	≤0.001
Serum Lactate levels (mmol/L)	3.2±1.9	0.7±0.3	≤0.001
International Normalized Ratio (INR)	2.3±0.96	1.2±0.8	≤0.001
CTP score	12.3±1.5	10.5±1.7	≤0.001
MELDScore	32.9±8.2	25±7	≤0.001
LBi	13.1±0.89	11.1 ± 0.8	≤0.001
AARC score	11.5 <u>+</u> 1.9	8.1 <u>+</u> 1.8	≤0.001
CLIF-C ACLF	12.3 <u>+</u> 2.3	8.9 <u>+</u> 2.1	≤0.001
CLIF SOFA	14.5 <u>+</u> 3.6	8.6 <u>+</u> 2.4	≤0.001

CTP-Child Turcotte Pugh; MELD-Model for End Stage Liver Disease; LBi-Lactate to Bilirubin; AARC-APASL ACLF research consortium; CLIF-SOFA-chronic liver failure-sequential organ failure assessment; CLIF-C-chronic liver failure consortium.

Table 3: Comparison of categorical variables in terms of mortality in studied population.

Variable		Non-survivors (n-155) n (%)	Survivors (n-80) n (%)	p-value	
Gender	Male	95(61.3)	45(56.3)	0.456	
Gender	Female	60(38.7)	35(43.7)		
Hanataranal Symdroma	Yes	15(9.7)	0(0)	0.016	
Hepatorenal Syndrome	No	140(90.3)	80(100)		
Organ Failura	<3	86(55.5)	68(85)	< 0.001	
Organ Failure	>3	69(44.5)	12(15)	≥ 0.001	
A	Yes	19(12.3)	14(17.5)	0.072	
Ascites	No	136(87.7)	66(82.5)	0.273	
Dortogratamia Enconholonothy	Yes	90(58.1)	6(7.5)	< 0.001	
Portosystemic Encephalopathy	No	65(41.9)	74(92.5)	≥0.001	

AUROC was obtained for the studied scores and all the scores were significant predictors of both one-month and six months mortality. AUROC for CTP score, MELD score, LBi, AARC score, CLIF-SOFA, and CLIF-C ACLF was 0.772, 0.755, 0.956, 0.897, 0.897, and 0.845 respectively in predicting one-month mortality (Fig. 2).

While, in predicting six months mortality in ACLF patients, AUROC for CTP score, MELD score, LBi Index, AARC score, CLIF-SOFA and CLIF-C ACLF were 0.774, 0.676, 0.865, 0.763, 0.725, 0.731 respectively (Fig. 3).

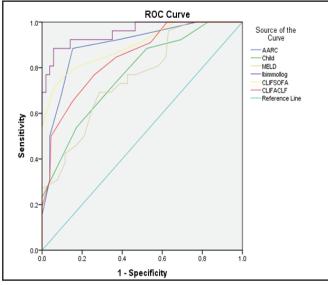


Fig. (2): Area under the receiver operating curve for CTP score, MELD score, LBi, AARC score, CLIF SOFA and CLIF-C ACLF in predicting one month mortality in ACLF.

ACLF-Acute on Chronic liver failure; CTP-Child Turcotte Pugh; MELD-Model for End Stage Liver Disease; LBi-Lactate to Bilirubin; AARC-APASL ACLF research consortium; CLIF-SOFA-chronic liver failure-sequential organ failure assessment; CLIF-C-chronic liver failure consortium.

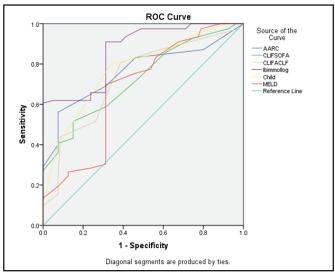


Fig. (3): Area under the receiver operating curve for CTP score, MELD score, LBi, AARC score, CLIF SOFA and CLIF-C ACLF in predicting six months mortality in ACLF.

ACLF-Acute on Chronic liver failure; CTP-Child Turcotte Pugh; MELD-Model for End Stage Liver Disease; LBi-Lactate to Bilirubin; AARC-APASL ACLF research consortium; CLIF-SOFA-chronic liver failure-sequential organ failure assessment; CLIF-C-chronic liver failure consortium.

On multivariate cox-regression analysis, CTP score, MELD score, LBi Index, CLIF-SOFA, and CLIF-ACLF

were observed to be forecasters of one-month mortality while at six months, only MELD score, LBi, and CTP score were independent mortality predictors (**Tables 4** and **5**).

Table 4: Multivariate Cox-regression analysis showing independentprognostic predictors of one month mortality in ACLF patients.

Variables	p-value	Odds ratio	CI (95%)		
v al lables	p-value	Ouus ratio	Lower Limit	Upper Limit	
CTP score	0.002	0.089	0.02	0.406	
MELD score	0.024	1.571	1.062	2.323	
LBi	≤0.001	2.432	1.867	5.43	
AARC score	0.507	1.571	0.443	5.198	
CLIF SOFA	0.001	0.149	0.48	0.461	
CLIF - C ACLF	0.030	7.62	1.22	47.9	

CTP-Child Turcotte Pugh; MELD-Model for End Stage Liver Disease; LBi-Lactate to Bilirubin; AARC-APASL ACLF research consortium; CLIF-SOFA-chronic liver failure-sequential organ failure assessment; CLIF-C-chronic liver failure consortium.

Table 5: Multivariate Cox-regression analysis showing independent prognostic predictors of six months mortality in ACLF patients.

Variables p-value	n_valua	Odds ratio	CI (95%)		
	Ouusiano	Lower Limit	Upper Limit		
CTP score	≤0.001	0.424	0.291	0.617	
MELD score	0.009	1.171	1.041	1.318	
LBi	≤0.001	0.032	0.011	0.091	
AARC score	0.909	1.036	0.567	1.89	
CLIF SOFA	0.159	1.253	0.916	1.714	
CLIF-C ACLF	0.293	1.253	0.823	1.906	

CTP-Child Turcotte Pugh; MELD-Model for End Stage Liver Disease; LBi-Lactate to Bilirubin; AARC-APASL ACLF research consortium; CLIF-SOFA-chronic liver failure-sequential organ failure assessment; CLIF-C-chronic liver failure consortium.

The diagnostic accuracy was highest for LBi in anticipating short and long-term mortality followed by CLIF-SOFA and CLIF-C ACLF scores were good in the prediction of short-term mortality and MELD and CTP scores were good for long-term mortality anticipation (Table 6).

DISCUSSION

The survival rates are fifteen times lower in ACLF cases than in CLD patients presenting with acute decompensation without ACLF [15]. Thus, it becomes essential to distinguish such cases on admission using prognostic scores that can help in aggressive and priority-based management in these patients and also aid in prioritizing the patients regarding the need for urgent referral for liver transplantation.

In previous studies, an advanced life span and being male were meaningfully linked to increased mortality risk in ACLF patients. Zakareya *et al.* [20] reported that death rates were greater in Egyptian patients admitted with ACLF aged >55 years. Similarly, Dhiman *et al.* [21]. reported 45 years of average age in deceased ACLF cases. In our study, the patients who expired were slightly

Predictive model	AUROC	P-Value	Cutoff	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
	One Month Mortality							
CTP score	0.8	<u><</u> 0.001	<u>>13</u>	54%	82.8%	60.87%	78.31%	73.19%
MELD score	0.77	<u><</u> 0.001	<u>></u> 26	69%	76%	36%	93%	75%
LBi	0.98	<u><</u> 0.001	<u>></u> 11.8	92.3%	82.17%	72%	95.6%	86%
CLIF SOFA	0.897	<u><</u> 0.001	<u>>10</u>	84.6%	68%	56.9%	89.92%	73.62%
CLIF-C ACLF	0.845	<u><</u> 0.001	<u>></u> 10	84.62%	63.1%	53.2%	89.1%	70.21%
	Six Months Mortality							
CTP Score	0.774	<u><</u> 0.001	<u>></u> 13	41%	97%	92%	45%	58%
MELD Score	0.676	<u><</u> 0.001	<u>></u> 26	51.6%	86.1%	76%	67%	70.15%
LBi	0.865	<u><</u> 0.001	<u>></u> 11.8	62%	95%	96%	56.3%	73.1%

Table 6: Diagnostic accuracy of the prognostic scores in predicting short and long term mortality in ACLF patients (n=235).

CTP-Child Turcotte Pugh; MELD-Model for End Stage Liver Disease; LBi-Lactate to Bilirubin; AARC-APASL ACLF research consortium; CLIF-SOFA-chronic liver failure-sequential organ failure assessment; CLIF-C-chronic liver failure consortium

younger than those observed in the previous studies (mean age-41+16 years) which can be attributed to the delayed diagnosis of the primary disease in our population. This is unfortunately due to the lack of awareness regarding critical illnesses along with the poor socioeconomic status of our population.

In the previous studies performed in underdeveloped and developing countries, hepatitis C is the CLD cause. Zakareya *et al.* [20] reported HCV in 58% as a cause of chronic liver disease in the Egyptian population while Dhiman *et al.* [21] reported HCV in 10% as an etiology of CLD. In our population, the etiology of CLD was viral hepatitis in 50% of the cases, including hepatitis C in 27% and hepatitis B in 23% of cases respectively. After viral hepatitis, AIH-CLD was the common etiology observed in approximately 20% of our cases higher than that observed in a study done in an Indian population (6%) [21]. In our community, alcohol-related liver damage was seen in 13% of cases, which is close to the findings from Asian countries [21, 22-24].

The most frequent acute insult reason in the current investigation was viral hepatitis observed in 40% of the cases which is higher than that observed in the other coexisting studies [1, 20, 21]. Due to the patients' low socioeconomic status in this region of the world as well as the immunological dysfunction that develops in those with severe cirrhosis, this is the case. DILI was causing stood on second rank in this investigation accounting for 32% and included the use of over-the-counter, hakeemi, or homeopathic medications. Dihman *et al.* [21] reported AIH flare in 8% as a cause of acute insult in an Indian population presenting with ACLF, which is again comparable to our data as 9% of our patients had the diagnosis of AIH-flare at the time of presentation. Alcoholic

hepatitis was the cause of an acute insult in 25% of the patients in the study conducted by Dihman and his colleagues on an Indian population [21]. However, we had alcoholic hepatitis as a cause of acute insult in 8% of the cases. In our study, the cause of acute insult was unknown in 4.7% of cases which was much compared to that reported by Moreau *et al.* [1] in the European population, Zakariya *et al.* [20] in an Egyptian population, and Dihman *et al.* [21] in an Indian population *i.e.* 44%, 31% and 8% respectively.

The one-month mortality in ACLF is around 30-40% while three months mortality exceeds up to 60%. However, these findings are associated with regional variability. In South Asia, the estimated mortality rate for ACLF is around 68% [5, 25]. This high mortality rate in ACLF patients in this region is multifactorial and can be attributed to the unavailability of living donors for liver transplantation and decreased awareness regarding cadaveric transplantation. Secondly, multi-organ failure at the time of presentation especially renal failure is also one of the major reasons for delisting of the patient from the transplant list in this population.In the univariate analysis, the patients who died had significantly higher ages had increased mortality in our population. This finding is consistent with the previously available data [20, 26-30]. Similarly, increased mortality was noted in patients with higher TLC and lower platelet count. This finding was again consistent with the previous studies predicting mortality in ACLF patients [30-33]. In our study, INR and serum creatinine were also significantly higher while serum albumin levels were lesser among non-survivors than those who survived which was also reported in the previous studies [20, 30, 33-35]. In previous studies, no noteworthy changes in bilirubin levels

were observed between the survivors and non-survivors groups [30-34, 36]. However, in this study, serum bilirubin levels were meaningfully elevated in the non-survivors group. This high bilirubin in ACLF can be attributed to the impaired liver function in this population.

On univariate analysis, all the prognostic scores including CTP, MELD, LBi, AARC, CLIF-SOFA, and CLIF-C ACLF were also considerably inflated among non-survivors than those who survived. However, on multivariate Cox regression analysis, CTP score, MELD score, LBi, CLIF-SOFA, and CLIF-C ACLF were alone one-month mortality predictors. These findings are again consistent with previous studies. Zakariya et al. [20] reported CTP and CLIF-C ACLF as 28 days mortality predictors in ACLF patients and also predicted that CLIF-ACLF was better than CTP in short-term mortality anticipation (AUROC- 0.87 vs. 0.85). Similarly, a study done by Jalan et al. [37] showed the superiority of CLIF-C ACLF over other available scores including MELD and CTP scores (AUROC- 0.744 vs. 0.645 vs. 0.653). Chen et al. [38] also demonstrated similar results in the Taiwanese population as CLIF-C ACLF and CLIF OF scores were the finest short-term determinants in ACLF patients. In our study, CTP, MELD, and LBi were independent predictors of long-term mortality (AUROC- 0.774 vs. 0.676 vs. 0.865). Chen et al. [38] also demonstrated the highest AUROC for CTP, MELD score, and CLIF-C ACLF score in forecasting mortalities at six months (AUROC-0.766 vs. 0.738 vs. 0.757). However, in contrast, on multivariate analysis, CLIF-C ACLF and CLIF SOFA were not predictors of long-term death in Taiwanese patients with ACLF.

LBi is a novel score, recently utilized in a Chinese population to predict prognosis and deaths in critically-ill cirrhotic cases. Despite being simple it had good diagnostic accuracy in forecast ing 30-day mortality with a 51% and 82% sensitivity and specificity respectively. However, in comparison to the MELD score, it lacked accuracy in anticipating long-term mortality (3 months) [39]. In our study, we found that LBi Index had the highest AUROC curve for anticipating short and long-term deaths. Chen *et al.* [39] showed the highest accuracy of the MELD score for anticipation mortalities of short-term and long-term while the CTP score was merely an excellent model for short-term mortality prediction.

Certain limitations can be attributed to this study. At first, it was a retrospective study. Secondly, the small sample size interprets the data as difficult on large scales. Third, other scores such as APACHE III and IV and CLIF-OF were not compared in this study. It was a pioneer study from Pakistan comparing six prognostic scores predicting both short (one) month and long-term (six) month mortality in ACLF patients.

CONCLUSION

Among the six prognostic scores used for the ICU-admitted ACLF patients, LBi was an excellent predictor of both short and long-term mortality while CLIF-C ACLF and CLIF SOFA were good predictors of short-term mortality and CTP and MELD score were useful in predicting six months mortality. However, to quantify the value of these prognostic ratings in ACLF patients, which can help to prioritize the patients for liver transplantation, more prospective studies with bigger sample sizes are needed.

ETHICAL APPROVAL

The Helsinki Declaration and the institutional and / or national research committee's ethical guidelines were adhered to at all times when conducting studies involving human subjects.

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

Upon a fair request, the appropriate author will provide the data set.

FUNDING

Declared none.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

AUTHOR'S CONTRIBUTION

In the production of this work, all authors made an equal contribution.

REFERENCES

- 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(7): 1426-37.e1-9. DOI: https://doi.org/10.1053/j.gastro.2013.02.042 PMID: 23474284
- Moreau R. The pathogenesis of ACLF: the inflammatory response and immune function. Semin Liver Dis 2016; 36(2): 133-40.

DOI: https://doi.org/10.1055/s-0036-1583199 PMID: 27172355

3. Solé C, Solà E, Morales-Ruiz M, Fernàndez G, Huelin P, Graupera I, *et al.* Characterization of inflammatory response in

acute-on-chronic liver failure and relationship with prognosis. Sci Rep 2016; 6: 32341.

DOI: https://doi.org/10.1038/srep32341 PMID: 27578545

 Choudhury A, Kumar M, Sharma BC, Maiwall R, Pamecha V, Moreau R, *et al.* Systemic inflammatory response syndrome in acute on chronic liver failure - relevance of 'Golden Window': a prospective study. J Gastroenterol Hepatol 2017; 32(12): 1989-97.

DOI: https://doi.org/10.1111/jgh.13799 PMID: 28374414

- Arroyo V, Moreau R, Jalan R, Ginès P, EASL-CLIF Consortium CANONIC Study. Acute-on-chronic liver failure: a new syndrome that will re-classify cirrhosis. J Hepatol 2015; 62(1 Suppl): S131-43. DOI: https://doi.org/10.1016/j.jhep.2014.11.045 PMID: 25920082
- Gustot T, Fernandez J, García E, Ginès P, Moreau R, Jalan R, *et al.* Short-term (28-day) clinical course and transplant-free mortality in acute-on-chronic liver failure (ACLF): evidence for reversibility of ACLF (a study from the CANONIC database). J Hepatol 2014; 60:S228.
 DOL: https://doi.org/10.1016/S0168.8278(14)60628.2

DOI: https://doi.org/10.1016/S0168-8278(14)60638-3

- Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. Br J Surg 1973; 60(8): 646-9. DOI: https://doi.org/10.1002/bjs.1800600817 PMID: 4541913
- Silva PESE, Fayad L, Lazzarotto C, Ronsoni MF, Bazzo ML, Colombo BS, *et al.* Single-centre validation of the EASL-CLIF Consortium definition of acute-on-chronic liver failure and CLIF-SOFA for prediction of mortality in cirrhosis. Liver Int 2015; 35(5): 1516-23.
 DOL: https://doi.org/10.1111/jij.12507.PMID: 24840673

DOI: https://doi.org/10.1111/liv.12597 PMID: 24840673

9. Gao F, Sun L, Ye X, Liu Y, Liu H, Geng M, *et al.* Development and validation of a prognostic model for acute-on-chronic hepatitis B liver failure. Eur J Gastroenterol Hepatol 2017; 29(6): 669-78.

DOI: https://doi.org/10.1097/meg.00000000000854 PMID: 28195876

- 10. Yi ZQ, Lu MH, Xu XW, Fu XY, Tan DM. A novel prognostic score for acute-on-chronic hepatitis B liver failure. J Huazhong Univ Sci Technolog Med Sci 2015; 35(1):87-92.
 DOI: https://doi.org/10.1007/s11596-015-1394-5 PMID: 25673199
- Mookerjee RP. Prognosis and biomarkers in acute-on-chronic liver failure. Semin Liver Dis 2016; 36(02): 127-32. DOI: https://doi.org/10.1055/s-0036-1583200 PMID: 27172354
- 12. Karvellas CJ, Pink F, McPhail M, Austin M, Auzinger G, Bernal W, *et al.* Bacteremia, acute physiology and chronic health evaluation II and modified end stage liver disease are independent predictors of mortality in critically ill non transplanted patients with acute on chronic liver failure. Crit Care Med 2010; 38(1): 121-6.

DOI: https://doi.org/10.1097/ccm.0b013e3181b42a1c PMID: 19770744

13. Duseja A, Choudhary NS, Gupta S, Dhiman RK, Chawla Y. APACHE II score is superior to SOFA, CTP and MELD in predicting the short-term mortality in patients with acute-on-chronic liver failure (ACLF). J Dig Dis 2013; 14(9):484-90.

DOI: https://doi.org/10.1111/1751-2980.12074 PMID: 23692973

- Zhang Y, Nie Y, Liu L, Zhu X. Assessing the prognostic scores for the prediction of the mortality of patients with acute-on-chronic liver failure: a retrospective study. PeerJ 2020; 8:e9857. DOI: https://doi.org/10.7717/peerj.9857 PMID: 32983642
- 15. Grochot RM, Luz LB, Garcia R, Balbinot RA, Balbinot SS, Soldera J. CLIF-SOFA is superior to other liver-specific scores for predicting mortality in acute-on-chronic liver failure and decompensated cirrhosis. Austin J Gastroenterol 2019; 6(2):1105
- 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. Doi: 10.3748/wjg.v20.i40.14934.
- Sarin SK, Choudhury A, Sharma MK, Maiwall R, Al-Mahtab M, Rahman S, *et al.* Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific association for the study of the liver (APASL): An update. Hepatol Int 2019; 13(4): 353-90. DOI: https://doi.org/10.1007/s12072-019-09946-3 PMID: 31172417
- Chen XF, Zhao Y, Chen WZ, Shao XT, Huang ZM. Lactate and bilirubin index: a new indicator to predict critically III cirrhotic patients' prognosis. Can J Gastroenterol Hepatol 2021; 2021: 6624177.
 DOL: https://doi.org/10.1155/2021/6624177

DOI: https://doi.org/10.1155/2021/6624177

- Khan RTY, Tasneem AA, Laeeq SM, Ismail H, Metlo HA, Bajaj K, et al. Platelet to white cell count ratio (PWR) in prediction of mortality among patients with acute on chronic liver failure (ACLF). Adv Res Gastroentero Hepatol 2021; 18(1): 555981. DOI: http://dx.doi.org/10.19080/ARGH.2021.18.555981
- Zakareya T, Akl M, Shibl S, El-Mazaly M, Abdel-Razek W. Utility of prognostic scores in predicting short-term mortality in patients with acute-on-chronic liver failure. Egypt Liver J 2022; 12: 21.

DOI: https://doi.org/10.1186/s43066-022-00183-2

- 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. DOI: https://doi.org/10.3748%2Fwjg.v20.i40.14934 PMID: 25356054
- Mann RE, Smart RG, Govoni R. The epidemiology of alcoholic liver disease. Alcohol Res Health 2003; 27(3): 209-19. PMID: 15535449
- Lucey MR, Mathurin P, Morgan TR. Alcoholic hepatitis. N Engl J Med 2009; 360(26): 2758-69. DOI: https://doi.org/10.1056/nejmra0805786 PMID: 19553649
- Louvet A, Mathurin P. Alcoholic liver disease: mechanisms of injury and targeted treatment. Nat Rev Gastroenterol Hepatol 2015; 12(4): 231-24.
 DOI: https://doi.org/10.1038/nrgastro.2015.35 PMID: 25782093
- Mezzano G, Juanola A, Cardenas A, Mezey E, Hamilton JP, Pose E, *et al.* Global burden of disease: acute-on-chronic liver failure, a systematic review and meta-analysis. Gut 2022; 71(1): 148-55. DOI: https://doi.org/10.1136/gutjnl-2020-322161 PMID: 33436495

- 26. Yang SS, Cheng KS, Lai YC, Wu CH, Chen TK, Lee CL, *et al.* Decreasing serum alpha-fetoprotein levels in predicting poor prognosis of acute hepatic failure in patients with chronic hepatitis B. J Gastroenterol 2002; 37(8): 626-32. DOI: https://doi.org/10.1007/s005350200099 PMID: 12203078
- 27. Yu JW, Wang GQ, Li SC. Prediction of the prognosis in patients with acute-on-chronic hepatitis using the MELD scoring system. J Gastroenterol Hepatol 2006; 21(10): 1519-24. DOI: https://doi.org/10.1111/j.1440-1746.2006.04510.x PMID: 16928211
- 28. Huang K, Hu JH, Wang HF, *et al.* Survival and prognostic factors in hepatitis B virus-related acute-on-chronic liver failure. World J Gastroenterol 2011; 17(29): 3448-52. DOI: https://doi.org/10.3748%2Fwjg.v17.i29.3448 PMID: 21876637
- 29. Xu Z, Ren X, Liu Y, Li X, Bai S, Zhong Y, *et al.* Association of hepatitis B virus mutations in basal core promoter and precore regions with severity of liver disease: an investigation of 793 Chinese patients with mild and severe chronic hepatitis B and acute-on-chronic liver failure. J Gastroenterol 2011; 46(3): 391-400

DOI: https://doi.org/10.1007/s00535-010-0315-4 PMID: 20848146

30. Sun QF, Ding JG, Xu DZ, Chen YP, Hong L, Ye ZY, *et al.* Prediction of the prognosis of patients with acute-on-chronic hepatitis B liver failure using the model for end-stage liver disease scoring system and a novel logistic regression model. J Viral Hepat 2009; 16(7): 464-70. DOI: https://doi.org/10.1111/j.1365-2893.2008.01046.x PMID: 19413694

- 31. Garg H, Sarin SK, Kumar M, Garg V, Sharma BC, Kumar A. Tenofovir improves the outcome in patients with spontaneous reactivation of hepatitis B presenting as acute-on-chronic liver failure. Hepatology 2011; 53(3): 774-80. DOI: https://doi.org/10.1002/hep.24109 PMID: 21294143
- 32. Zheng MH, Shi KQ, Fan YC, Li H, Ye C, Chen QQ, *et al.* A model to determine 3-month mortality risk in patients with acute-on-chronic hepatitis B liver failure. Clin Gastroenterol Hepatol 2011; 9(4): 351-6.e3.

DOI: https://doi.org/10.1016/j.cgh.2010.12.027 PMID: 21195790

 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.

DOI: https://doi.org/10.1016/j.dld.2011.08.029 PMID: 21978580

 Katoonizadeh A, Laleman W, Verslype C, Wilmer A, Maleux G, Roskams T, *et al.* Early features of acute-on-chronic alcoholic liver failure: a prospective cohort study. Gut 2010; 59(11): 1563-11.

DOI: https://doi.org/10.1136/gut.2009.189639 PMID: 20675694

- Krishna YR, Saraswat VA, Das K, Himanshu G, Yachha SK, Aggarwal R, *et al.* Clinical features and predictors of outcome in acute hepatitis A and hepatitis E virus hepatitis on cirrhosis. Liver Int 2009; 29(3): 392-8. DOI: https://doi.org/10.1111/j.1478-3231.2008.01887.x PMID: 19267864
- 36. Zhai S, Zhang L, Dang S, Yu Y, Zhao Z, Zhao W, *et al.* The ratio of Th-17 to Treg cells is associated with survival of patients with acute-on-chronic hepatitis B liver failure. Viral Immunol 2011; 24(4): 303-10.
 POL https://libia.com/10.1000/circ.2010.0125_PMUD: 21721021

DOI: https://doi.org/10.1089/vim.2010.0135 PMID: 21721931

 Jalan R, Saliba F, Pavesi M, Amoros A, Moreau R, Ginès P, *et al.* Development and validation of a prognostic score to predict mortality in patients with acute-on-chronic liver failure. J Hepatol 2014; 61: 1038-47.
 DOL: https://doi.org/10.1016/j.jbap.2014.06.012.PMID: 4050482

DOI: https://doi.org/10.1016/j.jhep.2014.06.012 PMID: 4950482

- 38. Chen BH, Tseng HJ, Chen WT, Chen PC, Ho YP, Huang CH, et al. Comparing eight prognostic scores in predicting mortality of patients with acute-on-chronic liver failure who were admitted to an ICU: a single-center experience. J Clin Med 2020; 9(5): 1540. DOI: https://doi.org/10.3390/jcm9051540 PMID: 32443729
- Chen XF, Zhao Y, Chen WZ, Shao XT, Huang ZM. Lactate and bilirubin index: a new indicator to predict critically Ill cirrhotic patients' prognosis. Can J Gastroenterol Hepatol 2021; 2021: 6624177.

DOI: https://doi.org/10.1155/2021/6624177