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Original Research Article

Predicting the immediate outcome in patients with acute on chronic liver disease by comparison of CLIF-C ACLF scores and MELD scores

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ABSTRACT

Background: Acute on chronic liver disease is determined by the acute deterioration of liver function over a short period of time. It leads to an increase in morbidity and mortality, hence scores like model for end-stage liver disease (MELD) and chronic liver failure-sequential organ failure (CLIF-C ACLF) are identified to determine prognosis. A comparison would help us in determining which score is better for predicting immediate outcomes.
Methods: In this single centre study, patients of both genders, >18 years of age, >48 hours hospital stay with organ failure either ≤1, defined as, an increase in serum creatinine by 50% or more (1.5-fold from baseline), hepatic encephalopathy (HE) graded III/IV according to West haven criteria, liver failure, bilirubin ≥5 mg/dl, international normalized ratio (INR) ≥1.5 were enrolled after which relevant lab investigations and imaging was done and MELD and CLIF-C ACLF scores were applied, they were compared and analyzed.
Results: Among 50 patients, 62% had grade 2, 36% had grade 3 and only 1 had grade 4 HE. Mean MELD score and CLIF- C ACLF scores were significantly high in patients who expired (both $p<0.05$), and the mean PaO_2/FIO_2 ratio was considerably low in patients with mortality ($p=0.00$). Sensitivity and specificity for CLIF-C ACLF score is much higher (90.9% and 100% respectively, with cut off value of 59), compared to the MELD score (77.3% and 60.7% respectively, with cut-off value of 25.50)
Conclusions: CLIF-C ACLF score is a better predictor of mortality and for survival in ACLF than the MELD score in changing the outcome of the patient.

Keywords: Acute on chronic liver disease, CLIF-C ACLF scores, MELD score

INTRODUCTION

Acute-on-chronic liver failure (ACLF) is a recently recognized syndrome in cirrhosis characterized by 'acute deterioration in liver function over a short period (up to four weeks) associated with a precipitating event' 'in patients with previously well-compensated liver disease'.[1] Patient would have organ failure, and high short-term mortality. Organ failure is determined by either the chronic liver failure-sequential organ failure (CLIF-SOFA) score or its abbreviated chronic liver failure-organ failure assessment (CLIF-OF) score.[2] They consist of 6 types of organ failure: "liver, coagulation, renal, cerebral, circulatory and respiratory". When hospitalized for AD, almost one-third of patients already have ACLF or develop it during their stay. A triggering event is frequently present in a closed connection with acute-on-chronic liver failure.[2] ACLF is divided into three stages based on the number of organ failures: ACLF-1 refers to a single renal failure or a single non-renal organ failure that is associated with renal dysfunction and/or cerebral dysfunction; ACLF-2 refers to two organ failures; and ACLF-3 refers to three to six organ failures with a CLIF-C ACLF score ≤ 64 an increasing 28-day mortality rate

(from 23% to 74%) organ failures and ACLF-4 as 4 organ failures with a CLIF-C ACLF score ≤ 64 respectively. At any point during the clinical course of the disease, acute-on-chronic liver failure may develop. Patients who have never had acute decompensation develop a severe form of ACLF.[2] When a trigger event like bacterial illness, acute alcohol, or drug-induced or viral hepatitis occurs, ACLF frequently follows in a closed-sequence fashion. However, only about 40% of people can identify the absence of a precipitating event. In situations without predisposing factors, intestinal translocation of bacteria or bacterial metabolites may also occur. The mechanisms of ACLF include systemic inflammation brought on by infections, and acute liver injury. Liver and kidney failures are the most common organ failures, followed by brain, circulatory, coagulation, and respiratory failures.[3] There are numerous prognosis-evaluating scores available for these patients, including the "MELD score," the "MELD score refined to take into account serum sodium level (MELD-Na)," the CLF-OF score," the "CLIF consortium acute-on-chronic liver failure (CLIF-C ACLF) score," and the "child-Turcotte-Pugh classification". Comparing CLIF-C ACLF and MELD scores for choosing patients with high mortality was the purpose of this investigation.[4]

MELD score=3.78*$\log_e$ serum bilirubin (mg/dl) +11.20*$\log_e$ INR+9.57*$\log_e$ serum creatinine (mg/dl)+6.43 (constant for liver disease etiology).

CLIF-C ACLF=10×(0.33×CLIF- OFs + 0.04 x Age + 0.63×$\log_e$ (WBC count)-2).

A CLIF-C ACLF score ≥ 70 at 48 hours can accurately predict mortality, indicating poor prognosis, which was remarkably higher than MELD scores of 30, 40, and 50 at 48 hours, according to a comparison of the two scores. The significant mortality predictors were the need for supportive care and organ dysfunction.[4] Interesting findings from the CANONIC trial reveal that the mortality rate for patients with prior decompensation (type C ACLF) was much lower than that of patients without prior decompensation (type B ACLF). Further research is needed to determine the source of this difference; however, it may lead to a reduction in the vital organ's capacity to tolerate a response that is inflammatory in patients with no prior decompensation.[5] A comparison of MELD and CLIF-C ACLF would help us in determining which score is better for predicting immediate outcomes. This could help in changing the course for further treatment and help us in deciding candidates for liver transplantation early on, thereby reducing the disease burden due to hepatic failure from society. The present study was conducted to do a comparative analysis of CLIF-C ACLF and MELD scores in patients with acute on chronic liver failure for determining the better predictor of the immediate outcome.

Aim

Aim of the study was to do a comparative analysis of CLIF-C ACLF and MELD scores in patients of acute on chronic liver failure for determining the better predictor of the immediate outcome.

Objectives

Objectives of the study was to assess the immediate outcome in the patients with acute on chronic liver failure by the MELD score, and to assess an immediate outcome in the patients with acute on chronic liver failure by the CLIF-C ACLF score, also to compare the above-mentioned scores and to determine the better predictor of immediate outcome in patients with acute on chronic liver failure.

METHODS

Source of data

The study was started after approval of the IEC (Institutional ethics committee) and IRC (Institutional review committee) a study was conducted on "acute on chronic liver disease" patients admitted.

Type of study

Comparative observational cross-sectional study type was used.

Sample size, design, and assumptions

That study was started in March 2021 and data collection was done till November 2022.

The sample size (n) was calculated using "Slovin's formula" which is as follows.

$$N=\frac{N}{1+Ne^2}$$

"Where n=sample size, N=population size, e=margin of error (0.05)".

Therefore, 50 cases were studied considering significance and error.

Inclusion criteria

Both male and female genders, patients >18 years of age, patients >48 hours of hospital stay having organ failure (either one or more, as defined below), Increase in serum creatinine 50 percentages or more (1.5-fold from baseline), HE graded III/IV according to the West haven criteria, liver failure, defined as bilirubin ≥ five mg/dl, international normalized ratio was (INR) ≥ 1.5 were included in the study.

Exclusion criteria

Patients having a known history of pre-existing renal failure (chronic kidney disease), patients having a known history of neuro-deficit and neurological disease such as CVA/seizure disorder, patients having a known history of/ pre-existing lung pathology such as ILD/COPD/cystic fibrosis, and others.

Method of collection of data

All patients satisfying the criteria of "acute on chronic liver failure" were enrolled in this study, valid, and written, and Informed Consent was taken in the patient's own language. Relevant lab investigations and imaging findings during the course of in-hospital treatment were recorded in the study MELD scoring was applied CLIF-C ACLF scoring was applied comparison of MELD and CLIF-C ACLF scores to measure the immediate outcome data collection and master chart preparation analysis of the collected data.

Analysis of result

Data was compiled using MS excel (master chart preparation) and analysed using statistical package of social science. Data were analysed using the Chi-square test, mean standard deviation, standard error of the mean, students' t test, and ANOVA. Specific statistical tests were applied by data comparison to determine the statistical significance of the comparisons. Quantitative variables were compared using mean values and qualitative variables using proportions. The significance level was fixed at $p<0.05$.

RESULTS

The 62% of patients had grade 2, 36% had grade 3 and only one patient had grade 4 "HE".

Table 1: HE grades.

Grade	Frequency	Percent (%)
2	31	62
3	18	36
4	1	2
Total	50	100

Table 2: Comparison of mean clinical parameters and scores between patient outcomes.

Variables	Outcome				P
	Death		Discharge		
	Mean	SD	Mean	SD	
PaO_2/FIO_2	106.8	57.36	330.92	161.7	0.0*
MELD	30.73	7.69	23.89	5.34	0.0*
CLIF C ACLF	66.59	7.04	46.57	9.87	0.0*

*Indicates significant $p<0.05$.

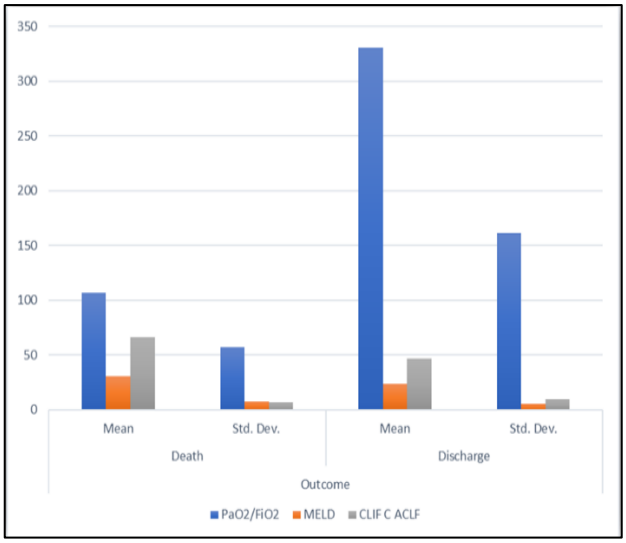

Figure 1: Comparison of clinical parameters and CLIF- C ACLF and MELD scores for predicting outcome.

Mean MELD score and CLIF C ACLF scores were significantly high in patients who expired (both $p<0.05$) and the mean PaO_2/FIO_2 ratio was considerably low in patients with mortality ($p=0.000$).

Table 3: Association of history of "renal replacement therapy" and grades of "HE".

H/o renal replacement therapy	HE grades, N (%)			Total, n (%)	P value
	2	3	4		
Yes	0 (0)	7 (38.9)	0 (0)	7 (14)	0.00*
No	31 (100)	11 (61.1)	1 (100)	43 (86)	
Total	31 (100)	18 (100)	1 (100)	50 (100)	

Indicates significant $p<0.05$.

Out of 18 patients with "grade 3 HE", 7 (38.9%) had a history of renal replacement therapy, and none of the patients with "grade 2 HE" had history of renal replacement therapy. Association significant ($p=0.00$).

Table 4: Comparison of sensitivity and specificity of scores.

Scores	Sensitivity (%)	Specificity (%)	Cut-off value
CLIF C ACLF	90.9	100	59.00
MELD	77.3	60.7	25.50

"Sensitivity and specificity" for "CLIF C ACLF score" is much higher (90.9% and 100% respectively, with cut off value of 59), compared to those for MELD score (77.3 and 60.7% respectively, with cut-off value of 25.50)

DISCUSSIONS

Predictive scores are important to be created to detect patients with a high risk of mortality, enabling early management to reduce mortality.[13] The most efficient score is important for predicting mortality in patients for clinical treatment. A comparison of MELD and CLIF-C ACLF would help us in determining which score is better for predicting immediate outcomes. This could help in changing the course for further treatment and help us in deciding candidates for liver transplantation early on, thereby reducing the disease burden due to hepatic failure from society. The present study was conducted to do a comparative analysis of CLIF-C ACLF and MELD scores in patients of acute on chronic liver failure for determining the better predictor of the immediate outcome.

HE grades

The 62% of patients had "grade 2", 36% had "grade 3" and only 1 patient had "grade 4" "HE". Zhang et al showed that the ACLF patient distribution was grade 2 (30.4%), grade 3 (44.1%), and grade 4 (25.5%).[6]

Mortality among patients

The mortality of ACLF patients in our study was 44%, which was similar to the previous research.[7] Ramzan et al showed that there is greater mortality (66.67%) of ACLF patients.[8]

Yue Zhang et al found that when compared with surviving patients, non-surviving patients had a higher MELD score and CLIF-ACLF score ($p<0.050$).[6] Statistically significant differences were found for the MELD score and CLIF-ACLF score at 3 months and 6 months ($p<0.050$).

Since we tracked the study participants uptil one month after they were released from the hospital's critical care facility, our research cannot predict mortality rates that occur after this point. But given the high mortality rate among patients, we believe individuals who survived with high CLIF-C ACLF scores should be assessed for early liver transplantation in order to increase the survival rate.

Association of history of renal replacement therapy, grades of HE, and patient outcomes

The majority of the patients who died had a history of renal replacement therapy compared to patients who recovered. The association was significant ($p=0.02$). Out of 18 patients with "grade 3 HE", 7 had a history of renal replacement. The association was significant ($p=0.00$). Ramzan et al showed mortality was directly proportional to the grade of encephalopathy, and no statistically significant results were seen on mortality with respect to gender.[8]

As compared to the CANONIC cohort the ACLF grade 2 mortalities were much higher in our patients. This may be due to the management of multiple organ failure in the award, it can also be associated with the underestimation of the ACLF grade as the diagnosis of circulatory failure.[10]

There was also a greater incidence of "ACLF grade 2", possibly produced by an underestimation of the "ACLF grade" or related to the deprived clinical development of "ACLF grade 1" patients in the grant without monitoring intensively and treatment.

Comparison of "CLIF C ACLF" and "MELD scores" for prediction of outcome

AUC for both scores is significant for outcome prediction (both $p<0.05$) but AUC for the "CLIF C ACLF score" is quite higher compared to that for the "MELD score". So, the "CLIF C ACLF score" is a better predictor compared to the "MELD score". Sensitivity and specificity for CLIF C ACLF Score are much greater (90.9% and 100% respectively), compared to those for MELD Score (77.3% and 60.7% respectively).

Our analysis is also further corroborated by a study done in a Portuguese tertiary care hospital that involved 289 patients and found that the CLIF-C ACLF score was a better predictor of mortality than the MELD score (AUROC 0.79, $p=0.05$), which documented a specificity of 74% in contrast to our findings (specificity 54.17%, sensitivity 74.51%).[11] Ramzan et al in their study found that CLIF-C ACLF score ≥70 at 48 hours is more accurate (74.51% sensitive and 54.17% specific) in predicting mortality in ICU than a MELD score at 48 hours".[8]

In the journal of hepatology, a multicentre study was published in 2014 which showed that CLIF-C ACLF a score of ≤40 has 90% sensitivity, whereas CLIF-C ACLF score ≥ 60 has 94 % specificity".[17] Our data recommend that elevation in the MELD score is not a good predictor of mortality, increasing concerns about whether it should be used among the criteria for liver transplantation. The CLIF-C ACLF score may be considered a better parameter than the MELD score for selecting patients for liver transplantation in ACLF as it predicts mortality with more sensitivity and specificity at 48 hours. Similar findings were observed in a study by Zhang et al the AUROC of CLIF-SOFA is higher than other prognostic scores.[6] The CLIF-SOFA score provides a complete and effective evaluation of the severity of organ failure in ACLF patients and considers multiple systems, including the hepatic, renal, coagulation, respiratory, circulatory, and nervous systems; it was discovered by the European Liver Disease Collaboration Group for Liver Failure in 2013. Sy et al study indicated that the predictive value of the CLIF-SOFA score is better than those of the MELD score for short-term outcomes.[9]

CONCLUSION

We concluded that "sensitivity and specificity for CLIF C ACLF score" are much higher (90.9% and 100% respectively) as compared to those for MELD score (77.3% and 60.7% respectively). Hence, the CLIF-C ACLF score is a better predictor of mortality as well as for survival in ACLF than the MELD score. To give such patients a definitive treatment option, specialists should involve the transplant team and families early in the discussion of the possibility of "transplantation" and this could help in changing the further course of treatment, thus causing changes in the outcome of the patient.

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