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CLIF-SOFA SCORING SYSTEM IN PREDICTING SHORT- TERM MORTALITY IN PATIENT WITH LIVER CIRRHOSIS

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ABSTRACT

Background: Patients of Liver Cirrhosis who are hospitalized for decompensation and organ failure are at high risk of short term death. Mortality rates at 28 days and 90 days in patients with acute decompensation are 33.9% and 51.2% respectively. In this study we aimed to assess the outcome of Cirrhosis patient according to CLIF-SOFA scoring system and to compare CLIF-SOFA scoring system with three conventional prognostic models [MELD, MELD-Na and Child Turcotte-Pugh (CTP)]) in predicting short term mortality in Cirrhotics. **Methodology:** All the patients admitted with a diagnosis of Liver Cirrhosis from 1st March 2015 to 30th April 2016 were enrolled and evaluated in detail. The CLIF-SOFA score, Child Turcotte-Pugh, MELD and MELD-Na scores was calculated in each patient within 24 hours and patient were followed for 4 weeks to determine 4 week mortality. **Results:** Among 95 patients of Liver cirrhosis, 20 (21%) patients died during 4 week period. The mortality rates in different CLIF SOFA stages were I- 0%, II- 13.3%, III- 69.2%, IV- 90% (p value <0.001). This study showed that CLIF-SOFA outperforms all 3 scoring system in predicting 4 week mortality by displaying highest area under the ROC curve .974 (95 confidence interval- .947- 1.000). Area under the ROC curve for MELD-Na, MELD and CTP were .864 (.758- .970), .851 (.749- .953) and .711 (.602- .819) respectively. Thus CLIF-SOFA is the best measure of predicting short term (4 week) mortality followed by MELD-Na, MELD and CTP scores respectively. **Conclusion:** CLIF SOFA score is better than MELD- Na, MELD score, and CTP class in predicting 4 week mortality.

KEYWORDS: Liver Cirrhosis, CLIF SOFA score, MELD score, MELD- Na score, CTP class.

INTRODUCTION

Cirrhosis is defined by the World Health Organization (WHO) as a diffuse process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules.[1] Common causes of Chronic Liver Disease are Alcohol, Hepatitis B and Hepatitis C infection. Chronic liver disease and cirrhosis are important causes of morbidity and mortality in the world and the burden of chronic liver disease is projected to increase, due in part to the increasing prevalence of end-stage liver disease and HCC secondary to NAFLD and HCV.[2] The main causes of deaths among patients with cirrhosis followed up for up to 16 years constituted liver failure (24%), liver failure with gastrointestinal bleeding (13%), gastrointestinal bleeding (14%), primary liver cell carcinoma (4%), other liver-related causes (2%), infections (7%), cardiovascular diseases (22%), extra hepatic malignancies (9%), and other non-liver-related causes (5%).[3]

A number of prognostic tools devised for end-stage liver disease have been validated, namely the Model for End-stage Liver Disease (MELD), MELD-Na, Child Turcotte-Pugh (CTP).[4,5,6] The above prevailing scoring methods unfortunately gauge mortality at 12 weeks or 1 year, ignoring the first 4 weeks of an acute episode.[4,5,6] Consequently, they are of limited value in predicting short term mortality. Mortality rates at 28 days and 90 days in patients with acute decompensation are 33.9% and 51.2% respectively.[7,8]

The Chronic Liver Failure-Sequential Organ Failure Assessment (CLIF-SOFA) scoring system was formulated by the EASL-CLIF Consortium to predict mortality in patients by addressing six functional failures (hepatic, renal, cerebral, coagulatory, circulatory and respiratory), each weighted by severity from 0 to 4, for a total score between 0 and 24.[8] The prevalence of organ failure in Cirrhosis is 32.9% and the presence of organ failure is associated with increased mortality 14.6% for 1 organ failure, 32% for 2 organ failure, 68% for 3 organ failure and 88.4% for >3 organ failure.[8]

The aim of this study is to 1) assess the outcome of Cirrhosis patient according to CLIF-SOFA scoring

system, 2) To compare CLIF-SOFA scoring system with three conventional prognostic models [MELD, MELD-Na and Child Turcotte-Pugh (CTP)]) in predicting short term mortality in Cirrhotics.

MATERIAL AND METHODS

This was a hospital based, Prospective, Observational study done in the Department of Internal Medicine Wards and Medical ICU of BPKIHS for a duration of 1 year (March 2015 to April 2016). Sample size was calculated by the formula $Z^2 \times P \times (1-P)/d^2$ (where Value of Z in 95% confidence interval is 1.96, P is estimated prevalence of mortality at 4 weeks in acute decompensated Cirrhosis, d is precision i.e Margin of error which is taken about 10% in my study). The value of estimated prevalance of mortality rates at 4weeks in patients with acute decompensated cirrhosis was taken as are 33.9%.[7,8] Thus the sample size came out to be 86 and to adjust various biases sample size was chosen as 95.

All patients admitted to medicine ward and ICU with a diagnosis of Liver Cirrhosis were included till the sample size was met. Patient's not giving consent to participate in the study were excluded.

Cirrhosis was defined by either (1) biopsy or (2) clinical evidence of decompensation or varices or (3) radiological evidence of liver nodularity and intra abdominal varices in a patient with chronic liver disease.[9]

The CLIF-SOFA score, Child Turcotte-Pugh, MELD and MELD-Na scores was calculated in each patient. These scores were calculated within 24 hours of admission.

Acute decompensation was defined by acute onset of hepatic encephalopathy, ascites, gastrointestinal haemorrhage, bacterial infection or any combination of these.[10] Organ Failure was defined as per the guidelines in CLIF-Sofa scoring system.[8]

Patients were further stratified according to CLIF SOFA score, MELD score, MELD Na score and CTP score.

For CLIF SOFA[10]

- CLIF SOFA I- Total score of Less than or equal to 7
- CLIF SOFA II- Total score of 8-10
- CLIF SOFA III- Total score of 11-13
- CLIF SOFA- Total score of Greater than or equal to 14

For MELD score[11]

- MELD score less than or equal to 24
- MELD score greater than or equal to 25

For MELD Na score[12]

- MELD-Na score less than or equal to 22
- MELD-Na score greater than 22

For CTP score[13]

CLASS A: TOTAL SCORE OF 5-6
CLASS B: TOTAL SCORE OF 7-9
CLASS C: TOTAL SCORE OF 10 or More

Patients were followed up for duration of 4 week to determine short term (4 week) mortality. CLIF- SOFA scoring system was compared with three conventional prognostic models [MELD, MELD-Na and Child Turcotte-Pugh (CTP)] in predicting short term mortality (mortality within 4 weeks) in Cirrhosis.

Collected datas were entered in Microsoft Excel 2007. Error and Inconsistency was verified after checking source document (proforma). Descriptive analysis was used showing frequency, proportion, mean and standard deviation for quantitative variables. Chi- square test was used to examine the association between different categorical variables and ROC curve was used for accuracy in predicting mortality. P value < 0.05 was considered significant. Data was analyzed using Statistical package for social sciences SPSS for windows version 16.

Ethical clearance was obtained from Institutional Ethical Review Board.

RESULTS

The mean age of participants was (mean, SD) = 51.86 ± 11.98. The age distributions of 95 patients is shown in the following Table 1.

Table 1: Age distribution of 95 study participants.

Age of the patient (years)	Number of participants(n=95) (Percentage)
Less than 30	2 (2.1%)
30-39	14 (14.7%)
40-49	23 (24.3%)
50-59	32 (33.7%)
Greater than or equal to 60	24 (25.2%)

Out of 95 patients 50 (52.6%) were male and 45 (47.4%) were female. Among the patients included in our study, alcohol was the cause for liver disease in 80 (84.2%), Hepatitis B in 9 (9.5%), others in 6 (6.3%) of patients. Total number of patients who died during the 4 week follow-up was twenty (21%).

When compared for predicting 4 week mortality CLIF-SOFA outperformed all 3 scoring system in predicting 4 week mortality by displaying highest area under the ROC curve .974 (95% confidence interval- .947- 1.000).

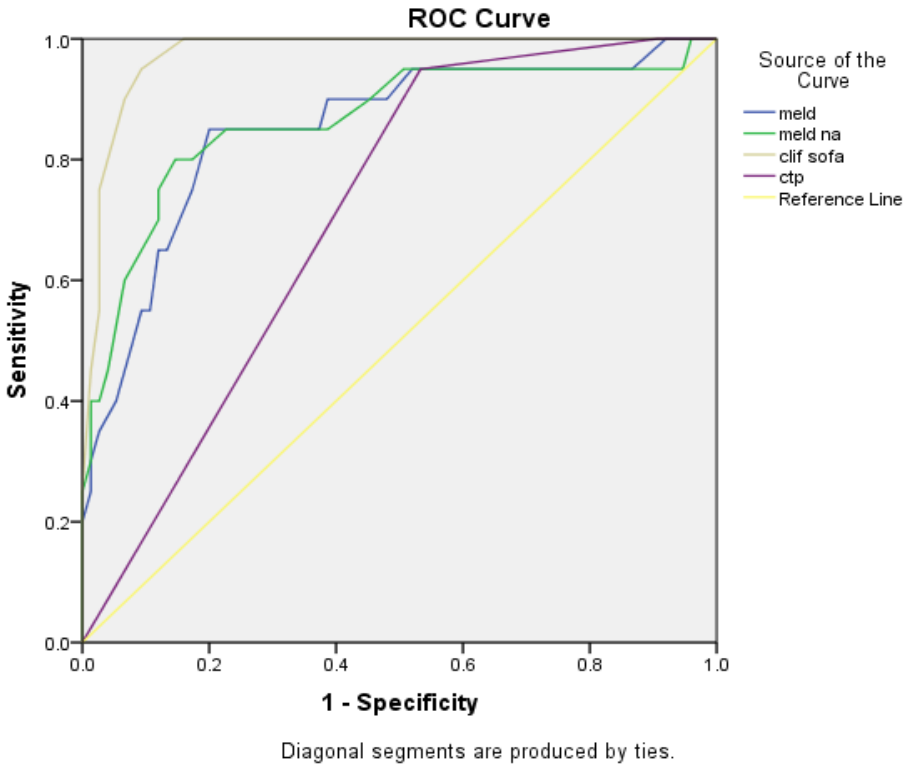

Figure 1: ROC curve of different predictive models in predicting 4 week mortality.

In this study when the patients were followed up to 4 weeks, there was no mortality in CLIF SOFA category I (score less than or equal to 7), 13.3% mortality in CLIF SOFA category II (score 8-10), 69.2% mortality in CLIF SOFA category III (score-11-13) and 90% mortality in CLIF SOFA category IV (score greater than or equal to 14). These results were statistically significant (p value- <0.001).

Table 2: Mortality in various CLIF SOFA stage.

CLIF SOFA stage	Total number of Patients	Number of Mortality	Percentage of Mortality	P value
I	57	0	0%	NA
II	15	2	13.3%	<0.001
III	13	9	69.2%	<0.001
IV	10	9	90%	<0.001

Similarly short term mortality (i.e. 4 week mortality) in patients with MELD score less than or equal to 24 was only 4.8% compared to 53.1% in patients with MELD score greater than or equal to 25 which was also statistically significant (p value- 0.001).

Table 3: Mortality in various MELD score.

MELD score	Number of patients	Number of mortality	Percentage of mortality	P value
Less than or equal to 24	63	3	4.8%	0.001
Greater than or equal to 25	32	17	53.1%	0.001

The short term mortality (i.e. 4 week mortality) in patients with MELD-Na score less than or equal to 22 was only 6.7% compared to 34% in patients with MELD score greater than 22 which was also statistically significant (p value- <0.001).

Table 4: Mortality in various MELD-Na score.

MELD-Na score	Number of patients	Number of mortality	Percentage of mortality	P value
Less than or equal to 22	45	3	6.7%	<0.001
Greater than 22	50	17	34%	<0.001

4 week mortality in patients who were in CTP class A was 0, those in CTP B was 3.4% and in patients with CTP class C it was 32.2% which was statistically significant (p value-0.003).

Table 5: Mortality in various CTP stage.

CTP class	Total number of Patients	Number of Mortality	Percentage of Mortality	P value
A	7	0	0%	NA
B	29	1	3.4%	0.003
C	59	19	32.2%	0.003

DISCUSSION

This study showed that Alcoholic liver disease was the most common cause of Chronic Liver disease 80 (84.2%) followed by Hepatitis B in 9 (9.5%) and others in 6 (6.3%) of patients. This is in contrast to other studies which showed that 60% of the patients had alcoholic cirrhosis, and 20% had hepatitis C virus–related cirrhosis[7,8] and study done by Shrestha SM which showed that Alcohol is responsible for 44.6% of cirrhosis, HBV and HCV accounted for 40% and 14% of the liver cirrhosis in Nepal.[14] This discrepancy is probably due to cultural factors leading to high alcohol intake in eastern part of Nepal.

The mean age of participants was 51.86 ± 11.98 out of which 53.6% were male and 46.4% patients were female. The male predominance and age group findings of our study are similar to studies done previously by Tafrel et al, in which mean age of patients was 53.10±12.5 years and male predominance of 64.3% and Demriel et al, in which the mean age of patients was 56.06±12.5 years and also showed the male predominance of 71.1%.

Majority of the patients (n= 32, 33.7%) were in the age group of 50-59 years. 14 (14.7%) patients were in the age group of 30-39 years out of which 11(78.5%) patients were diagnosed to have alcohol induced Liver cirrhosis. This may be due to the fact that other causes of cirrhosis like Wilsons disease, Biliary cirrhosis, Autoimmune hepatitis were not evaluated in detail because of the bias for significant history of alcohol consumption and lack of resources.

Most of the patients in our study mostly presented in CTP C (63%) followed by CTP B (30%) and CTP A (n=7%) which was consistent with previous study in which 52% of the presenting patients were in CTP C.[15]

This study showed that increasing scores of CLIF SOFA scoring system was positively associated with short term mortality (i.e mortality within 4 weeks) which achieved the level of statistical significance (Less than or equal to 7- mortality 0%, 8-10- mortality 13.3%, 11-13- mortality 69.2%, Greater than or equal to 14- mortality 90% (p value <0.001). The higher mortality seen in our study in score greater than 11 is in contrast to other study of similar kind in which Lee et al. concluded that- 4 weeks mortality according to CLIF SOFA score[10] (Less than or equal to 7- 2.8%, 8-10- 10.4%,11-13- 36.8%, Greater than or equal to 14- 75.8%). The higher mortality seen in our study in CLIF SOFA score 11-13 (69.2% versus 36.8%) and greater than or equal to 14 (90% versus 75.8%) is probably because of the small sample size (95) in our study.

This study also showed that increasing MELD scores was positively associated with 4 week mortality which also achieved the level of statistical significance. (MELD score less than or equal to 24- Mortality- 4.8%, MELD score greater than or equal to 25- Mortality- 53.1% (p value- 0.001)). Gleisner, AL etal stratified the survival rates on the waiting list versus one-year post-liver transplant survival on the basis of MELD score. (MELD 10: 90 percent waiting list survival versus 83 percent 1-year post-liver transplant survival ($p<0.05$), MELD 15: 81 versus 80 percent, respectively ($p = 0.70$), MELD 20: 63 versus 78 percent, respectively ($p<0.05$), MELD 25: 42 versus 74 percent, respectively ($p<0.05$, MELD 30: 21 versus 71 percent, respectively ($p<0.05$)).[16] Similarly patients awaiting liver transplantation with a MELD score ≤15 points has a predicted three-month survival of approximately 95 percent, while a patient with a MELD score of 30 points has a predicted three-month survival of approximately 65 percent. However direct comparison of our study with these studies should not be done as these previous studies have gauzed mortality at 3 months and/or 1 year ignoring the first 4 weeks and our study has calculated only the mortality at 4 weeks. This was also one of the limitations of this study. As the patients were not followed up for longer duration mortality trends and 3 months and 1 year survival rate could not be obtained.

This study also showed that increasing MELD- Na scores was positively associated with 4 week mortality which also achieved the level of statistical significance. (MELD-Na score- Less than or equal to 22- Mortality- 6.7%, MELD-Na score- Greater than 22- Mortality- 34% (p value- <0.001)). Since MELD-Na score has been used

to predict 3 months mortality[4] direct comparison of previous study findings with our study remained elusive. Nevertheless this study was successful in establishing the association of MELD-Na score with 4 week mortality.

Similarly CTP class was also shown to be positively associated with 4 week mortality which also achieved the level of statistical significance (CTP A- mortality 0%.

CTP B- mortality-3.4%, CTP C- mortality-32.2% (p value- 0.003). Comparison of our study finding with previous studies couldn't be done because CTP class is traditionally used to predict 1 year survival.[13]

This study showed that CLIF-SOFA outperforms all 3 scoring system in predicting 4 week mortality by displaying highest area under the ROC curve .974 (95 confidence interval- .947- 1.000). Area under the ROC curve for MELD-Na, MELD and CTP were .864 (.758- .970), .851 (.749- .953) and .711 (.602- .819) respectively. Thus CLIF-SOFA is the best measure of predicting short term (4 week) mortality followed by MELD-Na, MELD and CTP scores respectively. This result is similar to study done by Lee at al. in which it was found that in predicting short-term mortality at Week 4, CLIF-SOFA scoring system was better than MELD, MELD-Na and Refit MELD. (Lee, M 2015.). Thus patients with higher CLIF-SOFA score should be managed aggressively and should be considered for liver transplantation earlier.

CONCLUSION

Based on this study it can be concluded that CLIF-SOFA scoring system is the best method of predicting short term mortality (4 week mortality) in patients with Liver cirrhosis. It can also be concluded that increasing CLIF SOFA score, MELD score, MELD- Na score, CTP class is associated with increase in mortality. However studies with larger sample size is needed to further validate this findings.

This study is subjected o certain limitations. 1) Liver biopsy for histological confirmation of Liver Cirrhosis was not performed in any of the patient. 2) Complete workup in patient to rule out metabolic causes in patients with significant alcohol consumption was not done. This may have accounted for higher prevalence of alcohol as the cause of Chronic Liver Disease. 3) Patients were only followed up for 4 weeks only.

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