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Original Research Article

Comparison of the model for end-stage liver disease and disease sodium values in prognosticating short term 3-month mortality in chronic liver disease

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ABSTRACT

Background: Chronic liver disease (CLD) cirrhosis of liver is one of the common non communicable disease, accounting for significant morbidity and mortality in developing countries like India. several prognostic scoring systems have evolved from the need to prioritize patients for liver transplantation model for end-stage liver disease (MELD) and its variant, which includes sodium values (MELD-Na) have been recently popularized.
Methods: Prospective observational study with follow-up telephone call every month for 3 months, with ppurposive sampling done on 60 patients admitted to AIMS BG Nagara Mandya district Karnataka India. Statistical analysis included the strength of association was assessed using Pearson's correlation and the ROC curve was drawn to assess the accuracy and diagnostic utility of the two models. A $p<0.05$ was considered statistically significant.
Results: In the present study, the mean age of patients was 49.68±9.89 years of age. The strength of association between the MELD score and MELD-Na score was found to be a very strong positive strength of association ($r=0.904$, $p<0.05$). The mean MELD score and MELD-Na score was found to be higher in non-survivors' group (28.5 and 30.5) compared to survivors group (22.03 and 25.67) which was statistically very significant.
Conclusions: MELD-Na score was higher among the patients with outcome of death compared to the MELD score among the patient. The ROC curve showed a comparable result with MELD and MELD-Na scores. There was a relation of severity of hyponatremia with the child-Pugh scores.

Keywords: Mortality in CLD, MELD score, MELD-Na score

INTRODUCTION

Chronic liver disease (CLD) is a progressive deterioration of liver functions for more than six months, CLD is the tenth most common cause of death in adults, cirrhosis is a final stage of CLD. Liver cirrhosis is defined as an anatomically diffuse process with fibrosis and nodule formation. The global health observatory statistics from the World health organization indicate that cirrhosis is responsible for 22.2 deaths per 100,000 people in India.[1] Cirrhosis is a late stage of progressive hepatic fibrosis characterized by hepatic architecture distortion and the development of regenerative nodules. It is commonly thought to be irreversible in its advanced stages, at which point liver transplantation may be the only treatment choice. Cirrhosis (in its early stages) has been reversed in many types of liver disease following treatment of the underlying cause. Cirrhotic patients are predisposed to a number of complications and their life expectancy is significantly shortened. Several prognostic scoring systems have evolved from the need to prioritize patients for liver transplantation, since there is always a shortage

of donors. These scores are now widely used for prognosticating even in the domain of health care. While the child-Pugh classification has been around for some time, MELD and its variant, which includes sodium values (MELD-Na) have been recently popularized.

In a study by Kim et al the serum sodiumlevel was found to be closely linked to the degree of liver function dysfunction as calculated by the child-Pugh and MELD scores ($p<0.0001$). Also, hyponatremia, especially serum levels of 130 mmol/L, may indicate the presence of severe complications related to liver cirrhosis.[2]

In study by Samuel et al there was a major interaction between the MELD score and the serum sodium concentration, the combination of the MELD score and serum sodium concentration was significantly higher than the MELD score alone in 32 of the patients who died (7%). Thus, prioritisation based on the MELD score combined with serum sodium concentration may have resulted in transplantation and saved lives.[3]

In a study by Londono et al it was noted that- serum sodium and MELD were found to be independent predictors of survival in cirrhotic patients undergoing liver transplantation.[4]

In a study by Hsu et al it was noted that for patients with acute decompensated hepatitis, MELD-Na and MELD-Na have higher prognostic accuracy than MELD. The result of these patients is determined by the adequacy of their liver reserve.[5]

In a study by Ruf et al it was noted that adding serum sodium to MELD established a subset of patients with bad outcomes more effectively than MELD alone and greatly improved the score's effectiveness in predicting waitlist mortality.[6]

In a meta-analysis by Peng et al it was noted that in patients with acute-on-chronic liver failure, the child-Pugh score was more sensitive but less specific than the MELD score. MELD score had a lower negative probability ratio and higher sensitivity than child-Pugh score in ICU patients. In patients undergoing surgery, the child-Pugh score was more specific than the MELD score.[7]

In a study by Laderas et al it was noted that the MELD-Na score (OR=1.069, 95% CI=1.014-1.127), age >60 years (OR=2.479, 95% CI=1.226-5.015), and LTR height<163 cm (OR=4.092, 95% CI=2.115-7.917) were identified as independent predictors of early mortality.[8]

In observational study by Mukherjee et al it was noted that the non-survivors' mean MELD score and MELD-Na score were found to be higher (28.5 and 30.5) than the survivors' community (22.03 and 25.67), which was statistically important, there was a good correlation between both scores in terms of degree of agreement, with MELD-Na score being more sensitive than MELD score.[9]

In a study by Mazumder et al it was noted that during the study period, 2137 (27%) patients died, with higher mortality rates for patients in the high MELD-Na category (19.4 (41.6%) versus 4.1 (12.6%) per 100 person-y, p=0.001). The high MELD-Na group died of a liver-related cause in 1142 of 1632 deaths (70%) compared to 240 of 505 deaths (47.5%) in the low MELD-Na group.[10]

Indian data on the accuracy of these scores needs further validation. We have attempted to assess the MELD and MELD-Na in the short-term mortality in liver cirrhosis patients.

METHOD

Study site

Patients who were hospitalized with complications due to chronic liver disease at Adichunchanagiri hospital and research center, AIMS BG Nagara Mandya district, Karnataka India

Study period

The study carried out in 1 year period between 1 January and 31 October 2021.

Study type

The study was of prospective observational study with follow-up telephone call every month for 3 months.

Source of data/sampling method

In-patient, outpatient based in Adichunchanagiri hospital and research center, AIMS BG Nagara Mandya district, Karnataka India, Purposive sampling of total 60 patients was done with following inclusion and exclusion criteria.

Methodology

A diagnosis of CLD was limited to cases with laboratory and clinical findings. For the sake of our study chronic liver disease is defined as clinical and/or biochemical and/or imaging features evidenced for 6 months or more. Patients with age >18 years, clinical and imaging features consistent with a diagnosis of chronic liver disease were included in the study, patients with hepatocellular carcinoma, patients on antivirals, SIADH as diagnosed by urine spot sodium and serum osmolality, patients on thiazide diuretics, congestive cardiac failure patients, patients gastrointestinal losses (Vomiting or diarrhoea), skin losses (exudative skin lesions or burns), sequestration of fluid into a "third space" (Example: severe pancreatitis, crush injuries) at admission and during the follow-up period were also excluded from the

current study. As causative factors for chronic liver disease, chronic hepatitis B was diagnosed in cases with detectable hepatitis B surface antigen, and chronic hepatitis C was diagnosed in patients positive for anti-HCV antibody. Patients who had chronically ingested alcohol, on a daily basis, in the absence of other causative factors such as drugs or evidence of a viral infection were defined as having alcoholic liver cirrhosis.

In addition to the standard tests done by the treating physician in a typical case of chronic liver disease, we ordered for serum sodium and PT INR (if it has not already been ordered by the treating physician). The patient paid for these blood investigation tests. Blood samples were not stored or utilized for any further or future research and the samples were disposed of as per the policy of the central laboratory of AIMS BG Nagara.

Statistical analysis

All the data was entered in excel sheet and analyzed using SPSS v21 operating on windows 10. The demographic details of the patients were summarized by frequency, percentage, mean and standard deviation, and demonstrated with help of tables, bar diagrams and pie charts. The mean difference between the continuous variables was analyzed using t-test and the categorical variables using the chi-square. The strength of association was assessed using Pearson's correlation and the ROC curve was drawn to assess the accuracy and diagnostic utility of the two models. A $p<0.05$ was considered statistically significant.

RESULTS

In the present study, a total of 64 patients were included in the present study after obtaining the informed consent. The mean age of the patients was 49.68±9.89 years and 62 were male and 2 were female patients.

Table 1: Mean age of the patients, (n=64).

Variable	Min	Max	Mean	SD
Age (Years)	28.0	68.0	49.68	9.89

The mean age of the patients was 49.68±9.89 years, minimum age of patients is 28 and maximum age is 68 with SD of 9.89.

Table 2: Distribution of gender in present study.

Gender	Frequency	Percent (%)
Female	2	3.1
Male	62	96.9
Total	64	100.0

Of total 64 patients 62 (96.9%) were male and 2 (3.1%) were female patients.

Table 3: The mean level of electrolytes, (n=64).

Variables	Minimum	Maximum	Mean	SD
Sodium	115.00	140.00	131.75	4.57
Potassium	1.70	5.20	3.76	0.74
Chloride	87.00	116.00	100.81	6.47

The mean level of electrolytes sodium is 131.75, potassium 5.20, chloride 100.81.

Table 4: The distribution of outcome among the patients.

Outcome	Frequency	Percent (%)
Alive	52	81.3
Expired	12	18.8
Total	64	100

Among 64 patients 12 (18.8%) patients expired and 52 (81.3%) patients were alive.

Table 5: Comparison of mean level of child-Pugh, MELD score, MELD-Na score and MELD plus score with outcome of the patients using t-test.

Variables	Status				P value
	Alive		Expired		
	Mean	SD	Mean	SD	
Child Pugh-score	9.54	1.78	12.25	2.09	0.001
MELD score	15.81	4.95	29.92	8.32	0.001
MELD Na score	20.23	4.89	32.42	6.91	0.001
MELD plus	0.16	0.14	0.56	0.23	0.001

Patients with mean child Pugh score of 9.54 were alive, mean score of 12.25 expired, mean MELD score 15.81 were alive, mean score of 29.92 expired, mean MELD-Na score of 20.23 were alive, mean score of 32.42 were expired, mean MELD PLUS score 0.16 were alive, mean score of 0.14 expired.

Table 6: Pearson's correlation of various scores in present study.

Variables		MELD score	MELD-Na score
Child Pugh score	R	0.669	0.718
	Sig	0.001	0.001
MELD score	R	1	0.904
	Sig		0.001

Pearson's correlation coefficient between child Pugh score and MELD, MELD-Na score is 0.669, 0.718

respectively, indicating strong positive correlation between the scores.

Table 7: Comparison of mean level of electrolytes with outcome of the studypatients.

Variables	Status				P value
	Alive		Expired		
	Mean	SD	Mean	SD	
Sodium	131.69	4.90	132	2.92	0.836
Potassium	3.79	0.62	3.65	1.19	0.572
Chloride	100.02	6.47	104.25	5.51	0.04

Above table shows comparison between mean S. electrolyte level between patient who were alive and those who expired mean sodium value among those who were alive is 131.69 and those expired is 132.

Table 8: Comparison of various scores in present study with outcome of thepatients.

Child Pugh grade (score)	Status				P value
	Alive		Expired		
	Mean	SD	Mean	SD	
A MELD	14.00	6.93	.	.	
B MELD	13.62	4.87	24.5	0.71	0.05
C MELD	17.64	4.20	31	8.76	0.05
A MELD Na	14.00	1.00	.		
B MELD Na	18.48	4.70	27.5	0.71	0.05
C MELD Na	22.21	4.25	33.4	7.20	0.05

There was a significantly lower mean score among the child Pugh score, MELD score, MELD-Na score and MELD plus score among the alive patients compared to the outcome of death among patients.

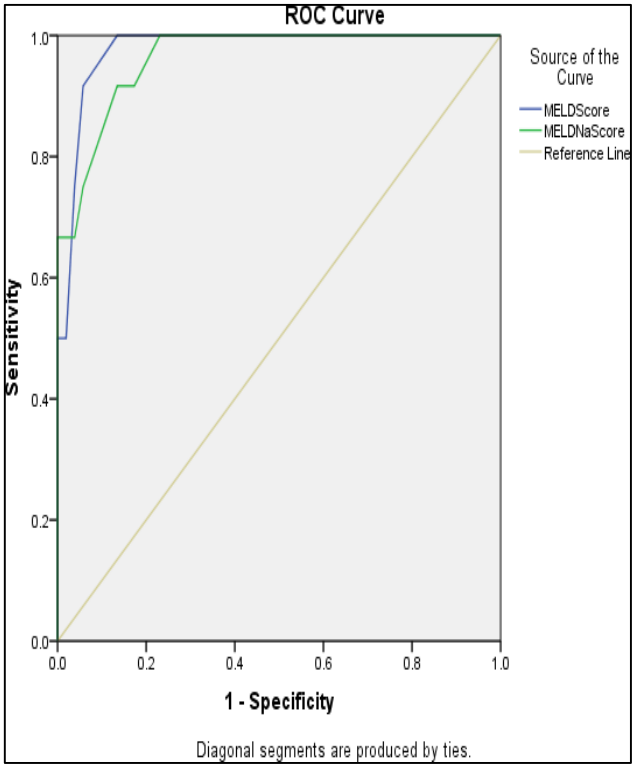

Figure 1: ROC curve of the AUC for MELD and MELD-Na.

Table 9: Area under the curve for meld score and meld-Na score.

Area under the curve					
Test results	Area	Std. error	Asymptotic sig.	Asymptotic 95% CI	
				Lower bound	Upper bound
MELD score	0.977	0.016	0.000	0.946	1.000
MELD-Na score	0.963	0.022	0.000	0.919	1.000

Area under the curve for MELD score (AUC=0.977, p<0.05) and MELD-Na score (AUC=0.963, p<0.05) was found to be comparable with Child Pugh score grading mentioned in the above comparison tablet.

Table 10: Comparison of child-Pugh grade with mean level of sodium.

Child Pugh grade	Sodium		P value
	Mean	SD	
A	134.33	1.15	0.140
B	132.91	3.92	
C	130.84	4.92	

Above table shows comparison between child Pugh grade and mean sodium levels, patients with higher grade of child Pugh (grade c had lower sodium levels that is 130.84), and was statistically significant with p=0.140.

DISCUSSION

The child-Pugh score and the MELD score have been commonly used in the assessment of cirrhotic prognosis; however, the shortcomings of subjective variable implementation in the child-Pugh score and unsuitability to all stages of liver cirrhosis in the MELD score limit their prognostic values.

Continuous attempts have been made in recent years to investigate the prognostic value of body fluid bio-markers for cirrhotic patients, with positive results recorded. Fluid bio markers may be ideal indicators for predicting the prognosis of cirrhosis because collection of fluid specimens is easy, noninvasive, and repeatable.[11-13] The present study, aimed to compare MELD-Na. versus MELD in prognosticating 3 month mortality in chronic liver disease patients.

In the present study, the mean age of patients was 49.68±9.89 years of age. Among them 96.9% were male and 3.1% were female, with male preponderance. The mean level of haemoglobin was found to be 10.23±2.43, and the INR of mean 1.55±0.46. The mean level of serum sodium was 131.75±4.57, potassium was 3.76±0.74 and chloride was 100.81±6.47. In study by Mukherjee et al found a significant higher mean level of INR, creatinine and sodium among the patients with the death outcome.[9,14]

Among the included patients, the child Pugh grade A were 3 patients (4.7%), 23 were in B grade (35.9%) and 38 were with C grade (59.4%) Among the included patients, on follow-up, 12 patients (18.8%) expired and 52 were alive (81.3%). In the present study, there was a significantly higher mean of the blood parameters in the study. The mean level of total leucocyte count, bilirubin, albumin, INR, urea and creatinine were significantly higher among the patients who expired compared to the alive patients.

There was a significantly lower mean score among the child Pugh score, MELD score, MELD-Na score and MELD plus score among the alive patients compared to the outcome of death among patients. Child Pugh score was 9.54±1.78 in alive patients and 12.25±2.09 among death, MELD score was 15.81±4.95 in alive patients and 29.92±8.32 among death, MELD-Na score was 20.23±4.89 in alive and 32.42±6.91 in death and MELD plus score among the alive patients was 0.16±0.14 and 0.56±0.23 among the death patients. All these findings were significantly higher among the patients with death outcomes. In a study by Mazumder et al the high MELD-Na group died of a liver-related cause in 1142 of 1632 in the expired outcome group (70%) compared to 240 of 505 deaths (47.5%) in the low MELD-Na group.[10,15] Ina study by Mukherjee et al non-survivors' mean MELD score and MELD-Na score were found to be higher (28.5 and 30.5) than the survivor's community (22.03 and 25.67), which was statistically important. The majority of patients in the survivor group had MELD ratings ranging from 10 to 19 (43.3%) and 30-39 (43.3%) (36.7%).[9,14]

On correlation between various scores taken in present study, the study showed significant positive strength of association of Child Pugh score with MELD score ($r=0.669$, $p<0.05$), MELD Na score ($r=0.718$, $p<0.05$), and MELD Plus score ($r=0.687$, $p<0.05$). The strength of association between the MELD score and MELD-Na score was found to be a very strong positive strength of association ($r=0.904$, $p<0.05$). The mean MELD score and MELD-Na score was found to be higher in non-survivors' group (28.5 and 30.5) compared to survivors' group (22.03 and 25.67) which was statistically very significant, in study by Mukherjee et al.[9,14]

Among the patients with each grade of child Pugh score, it was found to be a significantly higher mean of the MELD score and MELD-Na score among the patients with death outcome compared to the alive patients. In present study, the MELD score and MELD-Na were assessed to predict the death outcome using the ROC curve. It was found that the area under the curve for MELD score (AUC=0.977, $p<0.05$) and MELD-Na score (AUC=0.963, $p<0.05$) was found to be comparable. Similar to the present study, Mukherjee et al., found a significant association between the MELD and MELD-Na, also the ROC curve showed the comparable outcome and cutoff for the death of the patients.[9,14,16]

Limitations

More and more research is required with larger sample size to decide whether adding serum sodium to MELD improves its prognostic accuracy, as in the current study there were limitations like-small sample size, very few females, very few child-Pugh class A, few confounding variables which are not accounted for.

CONCLUSION

MELD-Na score was higher among the patients with outcome of death compared to the MELD score among the patient. This was consistent with the child-Pugh grade among them.

The ROC curve showed a comparable result with MELD and MELD-Na scores. There was a relation of severity of hyponatremia with the child-Pugh scores.

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