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Original Research Paper

Diagnostic and Prognostic Utility of Model for End-Stage Liver Disease (MELD) and MELD-Na in Short Term Three Month Mortality of Patients with Chronic Liver Disease.

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ABSTRACT:
Background: A late stage of progressive hepatic fibrosis known as cirrhosis is characterized by the formation of regenerative nodules and distortion of the liver's architecture. In its advanced stages, it is commonly thought to be irreversible, making liver transplantation the only option for treatment. This study aimed to evaluate the MELD and MELD-Na in relation to the short-term mortality of patients with liver cirrhosis. **Material & Method**: This prospective observational study was conducted in patients who were hospitalized with complications due to chronic liver disease at Yenepoya Medical College, Mangalore. Patients aged more than 18 years of age with chronic liver disease were included. Patients diagnosed with hepatocellular carcinoma, SIADH, on antiviral treatment, congestive cardiac failure, patients on thiazide diuretics and pancreatic injuries were excluded from study. Patients with clinical and imaging features consistent with a diagnosis of chronic liver disease and the blood parameters were measured and the Child-Pugh score, MELD score and MELD-Na score was measured. The data were entered in MS Excel spreadsheet and analysed using SPSS v21 operating on windows 10. **Result**: A total of sixty four patients who were enrolled had a mean age of 49.68±9.89yrs. Among them 62 were males. There was a significantly higher mean level of renal parameters, Child-Pugh score, MELD score, MELD-Na and MELD plus score in patients who died, when compared to the patients who survived ($p<0.05$). This study also showed significant positive strength of association of Child-Pugh score with MELD score ($r=0.669$), MELD Na score ($r=0.718$). **Conclusion**: Study documented the utility of MELD and MELD-Na in predicting the mortality among patients with liver cirrhosis.

Keywords: Cirrhosis, MELD, MELD-Na score, Mortality, Prediction.

INTRODUCTION:

Liver cirrhosis is defined as an "anatomically diffuse process with fibrosis and nodule formation." Global prevalence of cirrhosis from autopsy studies ranges from 4.5% to 9.5% of the general population.[1] Cirrhosis was estimated to kill 771,000 people worldwide in 2001, ranking 14th and 10th as the leading cause of death in the world and developed countries, respectively.[2] The Global Health Observatory statistics from the World Health Organisation indicate that cirrhosis is responsible for 22.2 deaths per 100,000 people in India.[3] A late stage of progressive hepatic fibrosis known as cirrhosis is characterized by the formation of regenerative nodules and distortion of the liver's architecture. In its advanced stages, it is commonly thought to be irreversible, making liver transplantation the only option for treatment. Following treatment of the underlying cause, many types of liver disease have reversed cirrhosis in its early stages.[4,5] Patients with cirrhosis have a significantly decreased life expectancy and are more likely to experience a number of complications. Due to the constant shortage of donors, several prognostic scoring systems have developed out of the need to prioritize patients for liver transplantation. Even in the healthcare industry, these scores are now widely used for predicting outcomes. While the Child-Pugh classification has been around for quite a while, Model for End-stage Liver Disease (MELD) and its variant, which incorporates sodium values (MELD-Na) have only recently gained recognition.[5–9] Further validation of Indian data regarding the accuracy of these scores is required. This study attempted to evaluate the MELD and MELD-Na in relation to the short-term mortality of patients with liver cirrhosis.

MATERIAL AND METHOD:

This prospective, observational study was conducted in patients who were hospitalized with complications due to chronic liver disease at Yenepoya Medical College, Mangalore. Patients aged more than 18 years of age with chronic liver disease were included. Patients diagnosed with hepatocellular carcinoma, SIADH, on antiviral treatment, congestive cardiac failure, patients on thiazide diuretics and pancreatic injuries were excluded from study.

A diagnosis of chronic liver disease was limited to cases with laboratory and clinical findings. For the sake of our study chronic liver disease was defined as clinical and/or biochemical and/or imaging features evidenced for 6 months or more. Patients with clinical and imaging features consistent with a diagnosis of chronic liver disease. Patients with hepatocellular carcinoma present at admission and during the follow-up period were excluded. Patients using thiazide diuretics were excluded and antiviral drugs at any time of survival 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.

All tests were ordered as a part of the routine care, by the treating physician, in a typical case of chronic liver disease. Blood samples were not stored or utilised for any further or future research and the samples were disposed of as per the policy of the central laboratory of YMCH.

Statistical Analysis:

All the data was entered in a MS Excel spreadsheet and analysed using SPSS v21 operating on windows 10. The mean difference between the continuous variables was analysed 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-value of <0.05 was considered statistically significant.

RESULTS:

Total of 64 patients fulfilling inclusion and exclusion criteria were included with mean age of 49.68±9.89yrs. Among the included patients 62 were male and 2 were female patients. Among the patients, 59.4% were with grade C cirrhosis, 35.9% with grade B cirrhosis and 4.7% with grade A liver cirrhosis.

Out of 64 patients who were included in study, follow up at the end of three months showed no mortality in 3 patients of Child Pugh Class-A, death of 2 patients out of 23 in Child Pugh Class-B (9%), and Child Pugh Class-C showed 10 deaths out of 38 patients (26%), establishing that the Child-Pugh score was predicting as expected (Table 1).

Table 1: Distribution of Child-Pugh grade of liver disease and outcome of patients

		Frequency	Alive	Expired
Child Pugh Grade	A	3	3	0
	B	23	21	2
	C	38	28	10

Table 2: Comparison of the study variables with outcome of patients

	Status				t-test (p-value)
	Alive		Expired		
	Mean	SD	Mean	SD	
Haemoglobin	10.38	2.35	9.62	2.81	0.33
Total Count	7.95	5.06	14.49	8.85	0.001**
Platelets	125.04	66.34	164.33	160.57	0.180
INR	1.47	.38	1.95	.62	0.001**

Sodium	131.69	4.90	132.00	2.92	0.836
Potassium	3.79	.62	3.65	1.19	0.572
Chloride	100.02	6.47	104.25	5.51	0.04*
Bilirubin	3.47	3.03	18.98	16.18	0.001**
Albumin	2.86	.69	2.34	.54	0.019*
Globulin	4.32	.66	4.12	.55	0.324
Protein	7.18	.97	6.77	.85	0.178
Urea	30.79	29.16	76.42	57.43	0.001**
Creatinine	1.02	.62	2.98	2.28	0.001**
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	.16	.14	.56	.23	0.001**

On assessment of the blood parameters level with outcome of the patients, there is a significant higher mean level of renal parameters, Child-Pugh score, MELD score, MELD-Na and MELD plus score in patients with death compared to the patients with survival.($p<0.05$)

Table 3: Pearson's correlation of various scores

		MELD Score	MELD Na Score
Child Pugh Score	r	.669**	.718**
	Sig	.001	.001
MELD Score	r	-	.904**
	Sig	-	.001

On pearson's correlation, there is strong positive correlation of Child-Pugh score with MELD-Na score and MELD score. The strength of correlation with MELD-Na was stronger compared to MELD score.

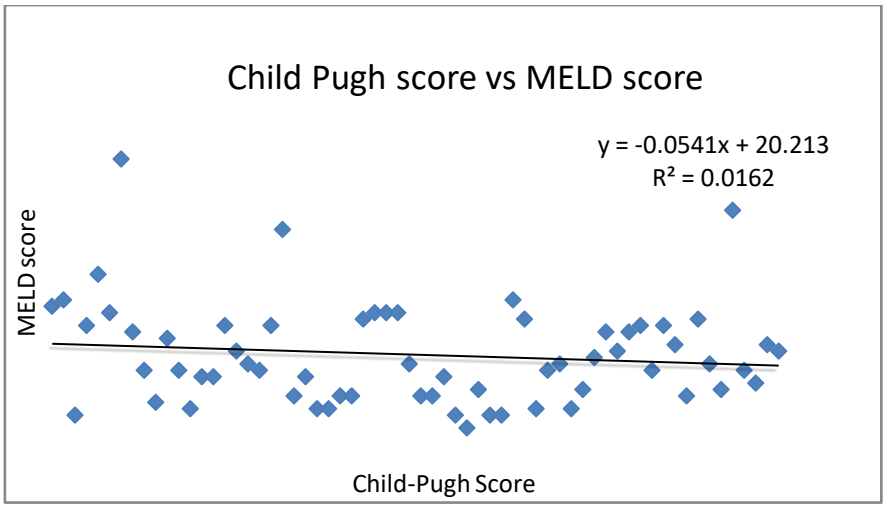

Figure 1: Pearson's correlation of Child-Pugh score with MELD scores

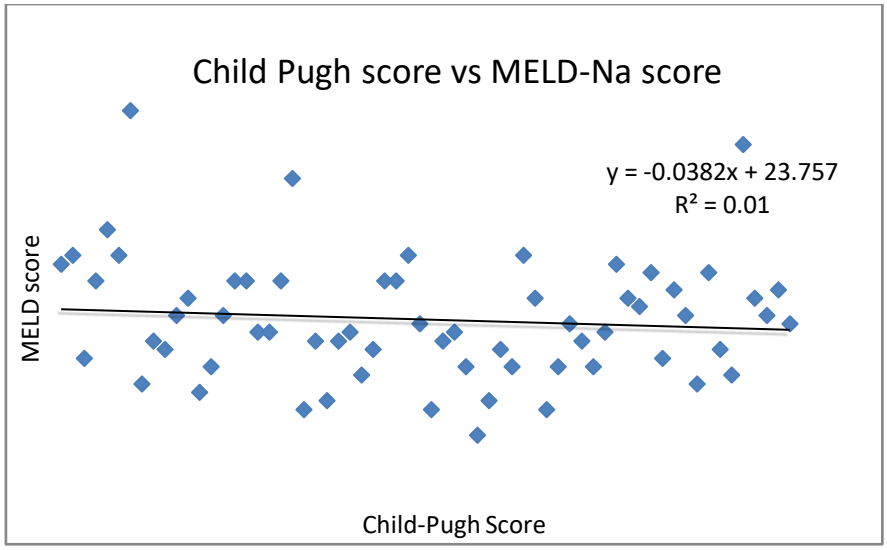

Figure 2: Pearson's correlation of child-Pugh score with MELD-Na scores

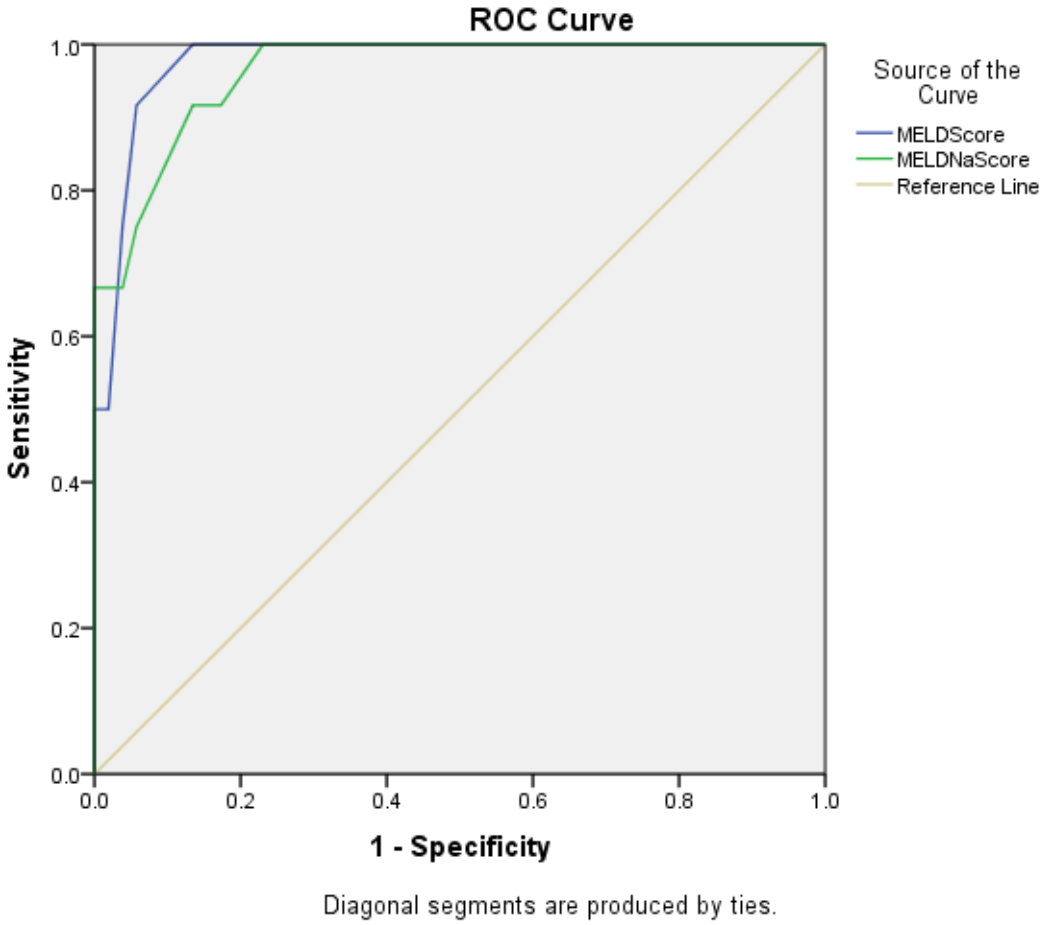

Figure 3: ROC curve showing the AUC for MELD and MELD-Na

Table 4: Area Under the Curve for MELD and MELD-Na score					
Test Result Variable(s)	**Area**	**Std. Error[a]**	**Asymptotic Sig.[b]**	**Asymptotic 95% Confidence Interval**	
				Lower Bound	**Upper Bound**
MELD Score	.977	.016	.000	.946	1.000
MELD-Na Score	.963	.022	.000	.919	1.000

In our study the MELD score and MELD-Na were assessed to predict death outcome using ROC curve. It was found that the area under the curve for MELD score (AUC=0.997, p<0.05) and MELD-Na score (AUC=0.963, p<0.05) was found to be comparable.

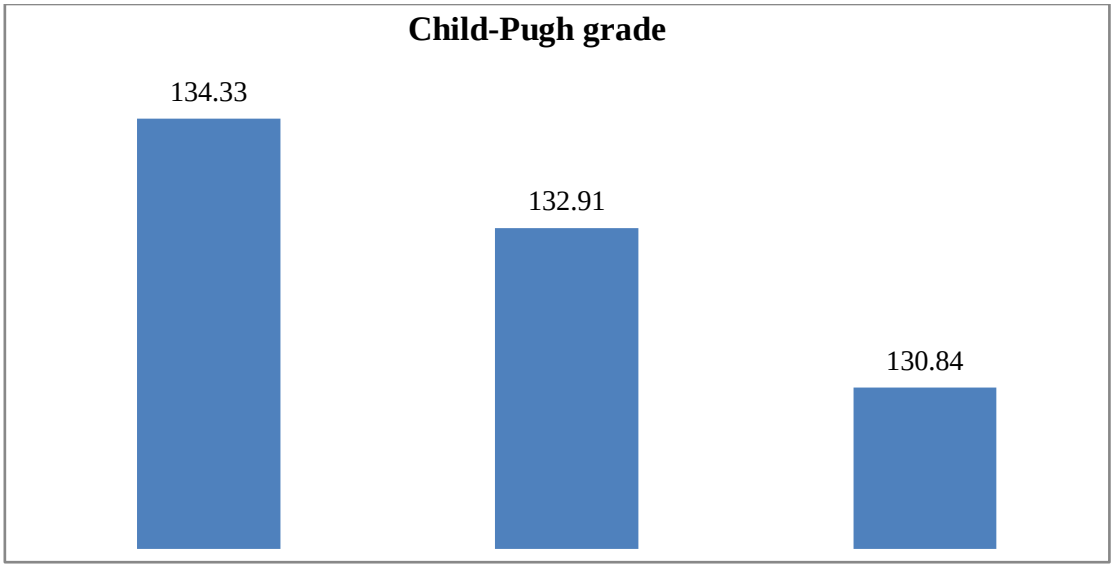

Figure 4: Hyponatremia among the grades of Child-Pugh

In our study when mean serum sodium levels were compared across all 3 classes of Child Pugh staging, it was found that as the severity of cirrhosis worsened with increase in Child Pugh classification, there was worsening/ decrease in mean serum sodium levels.

DISCUSSION:

Continuous attempts have been made in recent years to investigate the prognostic value of body fluid biomarkers for cirrhotic patients, with positive results recorded. Fluid biomarkers may be ideal indicators for predicting the prognosis of cirrhosis because collection of fluid specimens is easy, non-invasive, and repeatable.[10] The Child-Pugh score and the model for end-stage liver disease (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. The present study, aimed to compare MELD-Na. versus MELD in prognosticating 3 month mortality in chronic liver disease patients.

The mean age of patients was 49.68±9.89yrs 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 death outcome.[11]

In our study, 3 patients were in Child Pugh grade A class (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%). Also there was a significantly higher mean of the blood parameters in the study in the group that expired during the study period. 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 expired group. 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.[12] In a 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 survivors' 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 percent) and 30-39 (43.3 percent) (36.7 percent).[11]

Pearson's correlation between various scores found with a 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.[11]

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.[11]

CONCLUSION:

This study documented the utility of MELD and MELD-Na in predicting the mortality among patients with liver cirrhosis. 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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