International Journal of Advances in Medicine
Mukherjee T et al. Int J Adv Med. 2019 Jun;6(3):932-939
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: http://dx.doi.org/10.18203/2349-3933.ijam20192267

Original Research Article

Comparison of Model for End Stage Liver Disease-Na score and Model for End Stage Liver Disease score in predicting in-hospital mortality in patients with end stage liver disease: an observational study

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Received: 01 April 2019
Accepted: 02 May 2019

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ABSTRACT

Background: Model for End-stage Liver Disease (MELD) score was originally developed to predict mortality after trans jugular intrahepatic portosystemic shunt. Hyponatremia is the most common electrolyte abnormality in End Stage Liver Disease (ESLD). Incorporating serum sodium into MELD score increases its predictive accuracy.
Methods: This is an observational study conducted on 50 patients of ESLD admitted from October 2012 to September 2014. Study population was divided into survivor and non-survivor groups. MELD score and Model for End Stage Liver Disease-Na (MELD-Na) score was calculated and compared between the groups.
Results: Out of 50 participants, 20 (40%) died in the hospital due to cirrhosis related complications. The average age was 44.7±12.040 years in the survivor group and 54.1±9.910 years in the non-survivor group. 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. Majority of the patients in survivor group had MELD score between 10-19 (43.3%) and 30-39 (36.7%). In the non-survivor group majority of patients had score of more than 20 (80%). MELD-Na score has better sensitivity (90%) compared to MELD score (80%) at a cut off value above 22. However, MELD score has better specificity (60%) compared to MELD-Na score (43.3%) at the same cut off value.
Conclusions: MELD-Na score was higher in non-survivor group with good predictability for in-hospital mortality and there was good correlation between both the scores in terms of degree of agreement and MELD-Na score was more sensitive compared to MELD score.

Keywords: Cirrhosis, MELD, MELD-Na

INTRODUCTION

Cirrhosis is the final common end point of all progressive liver diseases of various etiologies.[1] End stage liver disease (ESLD) is one of the leading causes of death in India and worldwide.[2] According to the latest WHO data published in 2017 liver disease deaths in India reached 259,749 or 2.95% of total deaths. The natural history of cirrhosis is variable depending on the etiology and interventions. Annual rate of decompensation is approximately 4% and 10% respectively for viral hepatitis C and hepatitis B. Decompensation in alcoholic

liver disease is even more rapid with the continued alcohol usage. 5-year mortality is more than 85% once decompensation sets in, irrespective of the etiology.[3] Various scoring systems have been developed to assess the severity and prognosticate the liver disease. Child-Turcott-Pugh (CTP) score, is a simple scoring system with a fairly good predictive value. (C) 1-year survival for patients with CTP class A, B and C are 100%, 80% and 45% respectively.[4] The model for end-stage liver disease (MELD) score was developed to define medical urgency for transplantation. The MELD, originally developed to predict mortality after trans jugular intrahepatic portosystemic shunt.[5] MELD score is calculated using serum total bilirubin, the international normalized ratio (INR), and serum creatinine and it correlates well with short-term mortality risk in ESLD.[6-8] It has been observed in various studies that hyponatremia is the most common electrolyte abnormality due to various pathogenetic mechanisms. Hyponatremia has been associated with hepatorenal syndrome ascites and cirrhosis related mortality.[9-18] Hyponatremia which occurs due to free water retention correlates well with the mortality in cirrhosis especially, in those with low MELD score.[19,20] For each millimole decrease in serum sodium between 125 and 140 mmol/L, the mortality increases by 5%.[21] Incorporating serum sodium into the MELD score increases its predictive accuracy especially, for patients with ascites.[22-24] As serum sodium is a readily available, cost-effective test, its incorporation into MELD score led to the development of MELD-Na score. This study was undertaken to evaluate the prognostic value of MELD-Na score in comparison with the conventional MELD score in patients with end stage liver disease.

METHODS

This is an observational study conducted on 50 patients of cirrhosis of liver admitted in the department of general Medicine, Kempegowda institute of medical sciences, from October 2012 to September 2014. Informed consent was obtained from all the participants or their care takers (of those who were not in a position to give consent due to their critical illness or due to encephalopathy). Cirrhosis of liver (End stage liver disease) was diagnosed based on clinical history and examination, biochemical tests, and ultrasonology of liver. Patients aged less than 18 years, who were on diuretic therapy and anti-coagulation therapy were excluded from the study. Demographic details, thorough clinical history and examination findings, complete blood count (CBC), liver function tests (LFT), prothrombin time (PT), activated partial thromboplastin time (APTT), International normalized ratio (INR), renal function tests, serum electrolytes, and abdominal ultrasonography findings were recorded. All patients were screened for subclinical hepatic encephalopathy using psychometric testing. Serum ammonia levels were tested in those with clinical/subclinical hepatic encephalopathy. All patients with ascites were subjected for ascitic fluid analysis to rule out spontaneous bacterial peritonitis (SBP). All previous health records of previous 6 months were screened for evidence of esophageal varices and those who had not undergone upper GI endoscopy within past 6 months were subjected for the same to look for esophageal varices. All patients were screened for hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infection. Those with evidence of possible hepatocellular carcinoma on ultrasonography were subjected for computerized tomography (CT) abdomen.

Child-turcott-pugh (CTP) score was calculated for all patients. Patients were grouped into class A, B and C according to total CTP score of 5-6,7-9 and 10-15 respectively. MELD score was calculated at admission. The participants were followed until discharge or death in the hospital and were observed for any cirrhosis related complications.

MELD Score was calculated using the following formula

0.957×log (serum creatinine in mg/dl) +0.378×log (Serum bilirubin in mg/dl) +1.12×log (INR)+0.643

The score is multiplied by 10 and rounded to the nearest whole number.

Serum sodium levels were obtained for all patients and the following formula was used to calculate MELD-Na score.

MELD-Na: MELD + 1.32 × (137-Na) -(0.033 × MELD × (137-Na))

Statistical methods

The following methods of statistical analysis have been used in this study. Data was entered in Microsoft excel and analyzed using SPSS (Statistical Package for social science, Ver.10.0.5) package. The results were averaged (mean± standard deviation) for continuous data and number and percentage for dichotomous data are presented in (Table and Figure). Normality of data was tested using Shapiro-Wilk test. Proportions were compared using chi-square (χ^2) test of significance. Proportion of cases belonging to specific group of parameters or having a particular problem was expressed in absolute number and percentage. The student 't' test was used to determine whether there was a statistical difference between groups in the parameters measured if the data is normal. A non-parametric test (distribution-free) used to compare two independent groups of sampled data. Unlike the parametric t-test, this non-parametric makes no assumptions about the distribution of the data (e.g., normality). A receiver operating characteristic (ROC) curve analysis was used to assess the accuracy of MELD and MELD-Na for identifying risk factor (death), or for identifying each factor separately. A comparison of the diagnostic abilities for each test was performed using

the area under the curves (AUC). The optimal cutoff points were obtained from the point on the ROC curve which was closest to (0,1). This point was calculated as the minimum value of the square root of ((1-sensitivity)2+(1-specificity)2). In all the above tests "p" value of less than 0.05 was accepted as indicating statistical significance.

RESULTS

Out of 50 study participants with end stage liver disease, 20 (40%) died in the hospital due to cirrhosis related complications. For the purpose of analysis, the study population was divided into survivor group and non-survivor group and the parameters were compared between each group.

Table 1: Characteristics of study population.

		Survivors (N=30)		Non-survivors (N=20)		Total (N=50)		'p' value
Age	(Mean± SD)	44.7±12.040		54.1±9.910		48.5±12.056		0.006
	(Min-Max)	(26-80)		(35-73)		(26-80)		
Gender	Male	24	80.0%	17	85.0%	41	82.0%	0.652
	Female	6	20.0%	3	15.0%	9	18.0%	
Presentation at admission	Jaundice	18	62.1%	16	80.0%	34	69.4%	0.181
	Abdominal distension	21	70.0%	16	80.0%	37	74.0%	0.430
	Pedal oedema	20	66.7%	12	60.0%	32	64.0%	0.630
	Alcohol consumption	22	73.3%	17	85.0%	39	78.0%	0.329
	Hypotension	4	13.3%	9	45.0%	13	26.0%	0.012
	Anemia	23	76.7%	17	85.0%	40	80.0%	0.470
	Thrombocytopenia	25	83.3%	15	75.0%	40	80.0%	0.470
Peripheral smear	Dimorphic anaemia	9	30.0%	3	15.0%	12	24.0%	0.438
	Macrocytic anaemia	2	6.7%	1	5.0%	3	6.0%	
	Microcytic hypochromic anaemia	1	3.3%	4	20.0%	5	10.0%	
	Normocytic hypochromic anaemia	2	6.7%	1	5.0%	3	6.0%	
	Normocytic normochromic anaemia	13	43.3%	11	55.0%	24	48.0%	
	Pancytopenia	1	3.3%	0	0.0%	1	2.0%	
Raised ESR		10	33.3%	10	50.0%	20	40.0%	0.239
Impaired glucose tolerance		5	16.7%	3	15.0%	8	16.0%	0.875
USG/CT abdomen	Cirrhosis of liver	30	100.0%	20	100.0%	50	100.0%	1.000
	Splenomegaly	20	66.7%	12	60.0%	32	64.0%	0.630
	Ascitis	20	66.7%	12	60.0%	32	64.0%	0.630
	PV thrombosis	2	6.7%	0	0.0%	2	4.0%	0.239
Complications	Hepatorenal syndrome	7	23.3%	6	30.0%	13	26.0%	0.599
	Hemodialysis	1	3.3%	5	25.0%	6	12.0%	0.021
	Esophageal varices	27	90.0%	15	75.0%	42	84.0%	0.156
	Spontaneous bacterial peritonitis (SBP)	11	36.7%	1	5.0%	12	24.0%	0.010
	Portal hypertension	30	100.0%	19	95.0%	49	98.0%	0.216
	Hepatic encephalopathy	12	40.0%	14	70.0%	26	52.0%	0.038
	Gastrointestinal tract bleed	6	20.0%	3	15.0%	9	18.0%	0.652
	Hepatocellular carcinoma	0	0.0%	1	5.0%	1	2.0%	0.216
Etiology	Alcohol	22	73.3%	16	80.0%	38	76.0%	0.752
	Hepatitis B	1	3.3%	1	5.0%	2	4.0%	
	Other non-alcoholic causes	7	23.3%	3	15.0%	10	20.0%	

The average age was 44.7±12.040 years in the survivor group and 54.1±9.910 years in the non-survivor group. The age span was 26-80 years in survivor group and 35-73 years in non-survivor group.

There was male preponderance in both the study groups with male to female ratio of 4:1 in survivor group and 5.6:1 in non-survivor group. Gender difference with respect to in-hospital mortality was not statistically significant.

Table 2: Comparison of lab values between survivors and non-survivors group.

	Outcome	N	Mean	SD	Median	Min.	Max.	'p' value
Serum creatinine	Survivors	30	1.10	0.833	0.70	.30	4.20	0.002
	Non -survivors	20	3.18	3.387	1.65	.30	11.60	
	Total	50	1.93	2.432	1.00	.30	11.60	
Total bilirubin	Survivors	30	8.230	9.981	2.585	.37	31.20	0.267
	Non-survivors	20	11.719	11.850	7.500	.60	41.80	
	Total	50	9.626	10.788	4.270	.37	41.80	
Serum albumin	Survivors	30	2.293	0.652	2.300	1.00	3.90	0.472
	Non-survivors	19	2.153	0.675	2.000	1.00	3.40	
	Total	49	2.239	0.658	2.000	1.00	3.90	
International normalized ratio	Survivors	30	2.4410	1.19054	1.9800	1.10	5.72	0.867
	Non-survivors	20	2.3860	1.03482	2.2250	1.17	5.38	
	Total	50	2.4190	1.12019	2.1450	1.10	5.72	
Serum sodium	Survivors	30	131.23	6.377	132.50	119	144	0.505
	Non-survivors	20	132.50	6.771	132.00	120	145	
	Total	50	131.74	6.499	132.00	119	145	
Serum potassium	Survivors	30	4.0400	.76771	4.1000	2.90	5.90	0.901
	Non-survivors	20	4.0050	1.21805	3.6500	1.80	7.00	
	Total	50	4.0260	.96146	4.1000	1.80	7.00	
SGOT	Survivors	30	101.90	85.240	85.00	19	346	0.232
	Non-survivors	20	135.50	110.563	123.50	28	459	
	Total	50	115.34	96.523	92.00	19	459	
SGPT	Survivors	30	58.63	105.558	31.50	10	605	0.721.
	Non-survivors	20	49.90	31.271	40.50	19	138	
	Total	50	55.14	83.621	35.50	10	605	
Serum ammonia	Survivors	13	123.75	77.7160	92.00	62.0	340.0	0.452
	Non-survivors	14	107.24	21.6609	105.00	68.0	163.0	
	Total	27	115.19	55.6135	102.00	62.0	340.0	

Among the various clinical presentations, the incidence of jaundice (80% vs 62.1%), ascites (80% vs 70%), anemia (85% vs 76.7%) and hypotension (45% vs 13.3%) was higher in the non-survivor group. A statistically significant difference was noted with respect to hypotension with a p-value of 0.012. The incidence of thrombocytopenia was found to be lower in non-survivor group (75%) compared to survivor group (83.3%). However, there was no significant statistical difference with respect to thrombocytopenia (Table 1).

Comparison of ultrasonology findings of abdomen is shown in the (Table 2).

Splenomegaly was noted in 32 (64%) patients of whom 20 (66.7%) patients belonged to survivor group and 12(60%) patients belonged to non-survivor group. Ascites was found in 32 (64%) patients of whom 20 (66.7%) patients belonged to survivor group and 12 (66.7%) patients belonged to non-survivor group. 2 (4%) patients both of whom in the survivor group had evidence of portal vein thrombosis (Table 1).

Among the cirrhosis related complications, portal hypertension was the most common complication observed in 49 (98%) patients. Oesophageal varices was observed in 42 (84%) patients of whom 27 (90%) belonged to survivor group and 15 (75%) belonged to non-survivor group. Hepatic encephalopathy was observed in 26 (52%) patients the incidence of which was found to higher in non-survivor group (70%) compared to survivor group (40%) and was statistically significant with a p value of 0.038. Hepatorenal syndrome was observed in 13(26%) patients the incidence of which was found to be higher in non-survivor group (30%) compared to survivor group (23.3%). However, there was no statistical significance difference between the two

groups. Spontaneous bacterial peritonitis was observed in 11 (36.7%) patients compared to 1 (5%) patients in non-survivor group. This was found to be statistically significant with a p value of 0.010. GI bleed was noted in 9(18%) of patients. Hepatocellular carcinoma was seen in 1(2%) patient who died in the hospital (Table 1).

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 (Table 3).

Table 3: Comparison of meld and model for end-stage liver disease-Na score between survivors and non-survivors group.

	Outcome	N	Mean	SD	Median	Min.	Max.	'p' value
MELD	Survivors	30	22.03	10.759	19.00	7	44	0.002
	Non-survivors	20	28.50	8.488	28.00	15	44	
	Total	50	24.62	10.329	25.00	7	44	
MELD Na	Survivors	30	25.67	9.466	25.50	10	43	0.061
	Non-survivors	20	30.45	7.222	30.00	15	43	
	Total	50	27.58	8.880	27.50	10	43	

Table 4: Distribution of model for end-stage liver disease score among survivors and non-survivors.

Outcome	MELD					Total	χ^2 value	'p' value
	<9	10-19	20-29	30-39	≥40			
Survivors	3	13	2	11	1	30	8.929	0.063
	10.0%	43.3%	6.7%	36.7%	3.3%	100.0%		
Non-survivors	0	4	6	8	2	20		
	0.0%	20.0%	30.0%	40.0%	10.0%	100.0%		
Total	3	17	8	19	3	50		
	6.0%	34.0%	16.0%	38.0%	6.0%	100.0%		

Majority of the patients in the survivor group had MELD score between 10-19 (43.3%) and 30-39 (36.7%). In the non-survivor group majority of the patients had score of more than 20 (80%). So, the MELD score was significantly higher in non-survivor group compared to survivor group (Table 4).

Table 5: Distribution of model for end-stage liver disease-Na score among survivors and non-survivors.

Outcome	MELD Na					Total	χ^2 value	'p' value
	<9	10-19	20-29	30-39	≥40			
Survivors	0	10	8	11	1	30	6.489	0.090
	0.0%	33.3%	26.7%	36.7%	3.3%	100.0%		
Non-survivors	0	1	9	8	2	20		
	0.0%	5.0%	45.0%	40.0%	10.0%	100.0%		
Total	0	11	17	19	3	50		
	0.0%	22.0%	34.0%	38.0%	6.0%	100.0%		

Majority of patients had MELD-Na score of more than 10 in survivor group and score of more than 20 in non-survivor group. MELD-Na score was significantly higher in non-survivor group compared to survivor group (Table 5). There was a statistically significant agreement between MELD score and MELD-Na score in 21 out of 30 (70%) patients in the survivor group and 17 out of 20 (85%) patients in non-survivor group. Hence there was relatively better agreement between the two score in the non-survivor group (85%) compared to the survivor group (70%) (Table 6).

The mean hospital stay was 5.8 days in non-survivor group compared to 9.6 days in survivor group (Table 7).

Table 6: Agreement between meld and model for end-stage liver disease-Na score between survivors and non-survivors.

Outcome	MELD	MELD Na					Total
		<9	10-19	20-29	30-39	≥40	
Survivors	<9	0	3	0	0	0	3
		0.0%	100.0%	0.0%	0.0%	.0%	100.0%
	10-19	0	7	6	0	0	13
		0.0%	53.8%	46.2%	0.0%	.0%	100.0%
	20-29	0	0	2	0	0	2
		0.0%	0.0%	100.0%	0.0%	0.0%	100.0%
	30-39	0	0	0	11	0	11
		0.0%	0.0%	0.0%	100.0%	.0%	100.0%
	≥40	0	0	0	0	1	1
		0.0%	0.0%	0.0%	0.0%	100.0%	100.0%
	Total	0	10	8	11	1	30
		0.0%	33.3%	26.7%	36.7%	3.3%	100.0%
Non-survivors	<9	0	0	0	0	0	0
		0.0%	0.0%	0.0%	0.0%	0.0%	.0%
	10-19	0	1	3	0	0	4
		0.0%	25.0%	75.0%	0.0%	0.0%	100.0%
	20-29	0	0	6	0	0	6
		0.0%	0.0%	100.0%	0.0%	0.0%	100.0%
	30-39	0	0	0	8	0	8
		0.0%	0.0%	.0%	100.0%	0.0%	100.0%
	≥40	0	0	0	0	2	2
		0.0%	0.0%	0.0%	0.0%	100.0%	100.0%
	Total	0	1	9	8	2	20
		0.0%	5.0%	45.0%	40.0%	10.0%	100.0%

Table 7: Comparison of mean hospital days between survivor and non-survivor group.

Outcome	N	Mean	SD	Median	Min.	Max.	'p' value
Survivors	30	9.6	6.009	8.5	2	27	0.030
Non-survivors	20	5.8	5.981	4.0	1	25	
Total	50	8.1	6.240	7.0	1	27	

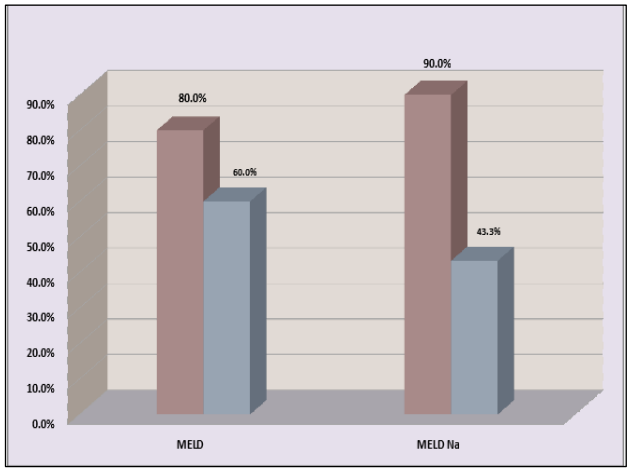

Figure 1: Sensitivity and specificity of MELD and model for end-stage liver disease Na score based on ROC.

MELD-Na score has better sensitivity (90%) compared to MELD score (80%) at a cut off value above 22. However, MELD score has better specificity (60%) compared to MELD-Na score (43.3%) at the same cut off value (Figure 2).

DISCUSSION

In present study, out of 50 patients with end stage liver disease, 20 patients died within the hospital accounting for 40% in-hospital mortality. In a study conducted by Cholangitas E et al, mortality was seen up to 65%. High mortality in their study was probably due to higher incidence of life-threatening upper GI bleed (172 out of 312 patients).[21] Of these 172 patients, 115 patients already had complications such as aspiration pneumonia, severe infection or organ failure. Authors also observed that higher age was associated with increased mortality. Most common presenting features in present study was

abdominal distension (74%) followed by jaundice (69.4%), swelling of lower limbs (64%) and hypotension (26%). Authors observed that the mean serum creatinine was higher in death group and when serum creatinine was solely compared with the mortality, p value was found to be significant. The development of renal failure in cirrhotic patients indicates a catastrophic reduction in survival probability, such that it is the predominant factor in end stage cirrhosis. Mean serum sodium was 131.74mEq/dl as compared to 137mEq/dl in Cholangitas E et al, study. Even though mean bilirubin was relatively higher in non-survivor group compared to survivor group it was not statistically significant in predicting mortality.[21] Similarly, serum sodium levels were not statistically significant.

MELD score and MELD-Na score was calculated for each patient and the mean value for survivor and non-survivor group was calculated. Authors observed that mean MELD score was found to higher in non-survivor group which was statistically significant with a p value of 0.002. MELD-Na score was also higher in non-survivor group but was not statistically significant. The best cut-off point for MELD score calculated using Youden index (sensitivity + specicity-1) was found to be 22 above which the mortality is higher. Similarly, authors calculated mean value for MELD-Na score and compared with the study done by Serste T et al, in France in 2012.[25] The best cut-off value for MELD-Na came to be 22 similar to MELD score. To study the correlation between MELD score and MELD-Na score authors used the degree of agreement between the 2 scores. There was statistically significant agreement between the two scores in 21 out of 30 (70%) patients in the survivor group and 17 out of 20 (85%) patients in non-survivor group.

Table 8: Agreement between meld and Meld-Na score between survivors and non-survivors groups.

Outcome MELD		MELD NA					Total
		0.<9	**10-19**	**20-29**	**30-39**	**≥40**	
Survivors	<9	0	3	0	0	Z0	3
		0.0%	100.0%	0.0%	0.0%	0.0%	100.0%
	10-19	0	7	6	0	0	13
		0.0%	53.8%	46.2%	0.0%	0.0%	100.0%
	20-29	0	0	2	0	0	2
		0.0%	0.0%	100.0%	0.0%	0.0%	100.0%
	30-39	0	0	0	11	0	11
		0.0%	0.0%	0.0%	100.0%	0.0%	100.0%
	≥40	0	0	0	0	1	1
		0.0%	0.0%	0.0%	0.0%	100.0%	100.0%
	Total	0	10	8	11	1	30
		0.0%	33.3%	26.7%	36.7%	3.3%	100.0%
Non-survivors	<9	0	0	0	0	0	0
		0.0%	0.0%	0.0%	0.0%	0.0%	.0%
	10-19	0	1	3	0	0	4
		0.0%	25.0%	75.0%	0.0%	0.0%	100.0%
	20-29	0	0	6	0	0	6
		0.0%	0.0%	100.0%	0.0%	0.0%	100.0%
	30-39	0	0	0	8	0	8
		0.0%	0.0%	0.0%	100.0%	0.0%	100.0%
	≥40	0	0	0	0	2	2
		0.0%	0.0%	0.0%	0.0%	100.0%	100.0%
	Total	0	1	9	8	2	20
		0.0%	5.0%	45.0%	40.0%	10.0%	100.0%

At cut off value more than 22, MELD-Na score has better sensitivity (90%) compared to MELD score (80%). However, in terms of specificity, MELD score is better than MELD-Na score (60% vs 43.3%) (Table 8).

CONCLUSION

MELD-Na score was higher in non-survivor group with good predictability for in-hospital mortality and there was good correlation between both the scores in terms of degree of agreement and MELD-Na score was more sensitive compared to MELD score.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Mukherjee T, Nataraju KT, Rakesh BM, Dandothi SD. Comparison of Model for End Stage Liver Disease-Na score and Model for End Stage Liver Disease score in predicting in-hospital mortality in patients with end stage liver disease: an observational study. Int J Adv Med 2019;6:932-9.