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RESEARCH ARTICLE
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A COMPARATIVE STUDY OF MODEL FOR END-STAGE LIVER DISEASE- SODIUM (MELD- NA) VS. MODEL FOR END-STAGE LIVER DISEASE (MELD) IN PREDICTING SHORT-TERM MORTALITY IN DECOMPENSATED LIVER DISEASE.

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Abstract:

Introduction: In cirrhotic individuals with ascites, dilutional hyponatremia is a commonly observed occurrence that is linked to increased mortality rates during hospitalisation. Model for end-stage liver disease (MELD) is a highly reliable indicator of 3-month mortality in cirrhotic patients who are scheduled for orthotopic liver transplantation. Additionally, the study aimed to determine if incorporating serum sodium into the MELD would enhance the accuracy of the score used to estimate waitlist mortality.

Methodology: A comparative study was done in 100 patients on two prediction modalities (MELD and MELD Na) in patients with cirrhosis of liver in department of general medicine over a period of 24 months. After obtaining permission from the institutional ethics committee, informed consent will be taken from the patient and their attendees. A semistructured case proforma was used to collect the data. History and clinical examination will be done and relevant laboratory tests will be performed. Based on the serum sodium values, patients are divided into three groups. Group A - Sr sodium > 135, Group B – Sr sodium 131 - 135 and Group C – Sr sodium < 130. The presence of complications and its frequency in all 3 groups were studied and analysed. Statistical analysis was done using SPSS, Med calc is used for the calculation of predictive accuracy statistics of MELD and MELD – Na values.

Results: Overall, alcohol-related liver disease was the leading cause across all groups, followed by viral hepatitis and other causes, with a progressive decline in total cases from Group A (40) to Group C (28). while age and gender were comparable among groups, disease severity as reflected by MELD and MELD-Na scores increased significantly from Group A to Group C thus showing the

association with hyponatraemia. Hepatic encephalopathy, hepatorenal syndrome, spontaneous bacterial peritonitis, variceal bleeding, and mortality at 3 months were analyzed as complications of liver cirrhosis across the three groups. The frequency and severity of complications increased significantly from Group A to Group C, indicating a clear association between disease progression and adverse outcomes. In predicting mortality MELD-Na achieved greater accuracy (87.92%) than MELD (75.83%).

Conclusions: Incorporation of serum sodium in prediction models accounts for the detrimental effects of dilutional hyponatraemia, a recognized marker of circulatory dysfunction and poor prognosis in cirrhosis.

Keywords: Model for end-stage liver disease (MELD), MELD Na, prediction model, cirrhosis of liver, complications, mortality.

Introduction:

The model for end-stage liver disease (MELD) relies on three biochemical variables that are easily accessible, replicable, and unbiased: serum bilirubin, serum creatinine, and the international normalized ratio (INR) of prothrombin time. The study has revealed that MELD is a highly reliable indicator of 3-month mortality in cirrhotic patients who are scheduled for orthotopic liver transplantation (OLT) [1]. The MELD score has been utilised as the basis for allocating organ donors, except for patients with fulminant hepatic failure and those requiring emergency transplantation who are classified as United Network for Organ Sharing status, cirrhotic patients are categorised on the waiting list. They are given priority for organ transplantation based on their MELD scores [2].

Recent data has indicated a decline in mortality rates and the number of individuals removed from the waiting list due to insufficient health for orthotopic liver transplantation (OLT). [3] Notwithstanding the use of MELD, it is pertinent to inquire whether the efficacy of the score can be further enhanced, particularly for certain patient groups. The presence of ascites is a significant consequence of cirrhosis, thereby necessitating the use of OLT [4]. The serum creatinine used in the MELD formula However, the elevation of serum creatinine levels occurs later in individuals diagnosed with ascites. Arroyo et al. [5] reported at the Consensus Conference of the International Ascites Club that the elevation of serum creatinine happens chronologically, namely after the commencement of salt retention and impaired ability to excrete free water. Furthermore, individuals diagnosed with type 1 hepatorenal syndrome may experience a swift and gradual deterioration of their kidney function, leading to a higher likelihood of illness and death after undergoing organ transplantation [6,7]. Prior research has demonstrated that biomarkers that assess systemic hemodynamic and renal function are more accurate indicators of survival in individuals with cirrhosis and ascites compared to commonly used measures of hepatic function. Several examples of these parameters are glomerular filtration rate, urinary sodium excretion, plasma renin activity, renal water excretion following a water load test, dilutional hyponatremia, mean arterial pressure and norepinephrine concentration [6,10].

In cirrhotic individuals with ascites, dilutional hyponatremia is a commonly observed occurrence that is linked to increased mortality rates during hospitalization [11,12]. In addition, hyponatremia has been identified as a separate factor that can predict long-term survival and hepatorenal syndrome. It is also seen as a substitute indicator for circulatory dysfunction after large-volume paracentesis [6-12], this study aimed to examine the predictive significance of blood sodium and hyponatremia in patients with cirrhosis who were listed for orthotopic liver transplantation (OLT). Additionally, the study aimed to determine if incorporating serum sodium into the Model for End-stage Liver Disease (MELD) would enhance the accuracy of the score used to estimate waitlist mortality.

AIM: This study aims to show that MELD - Na is a better predictor of mortality than the standard MELD score among patients suffering from end-stage liver disease.

OBJECTIVES:
1. To determine the prevalence of hyponatremia in decompensated liver disease.
2. To calculate MELD and MELD – Na scores in patients with decompensated liver disease.

Methodology: A comparative study was done in 100 patients on two prediction modalities in patients with cirrhosis of liver in department of general medicine over a period of 24 months. The study was approved by IEC of Osmania Medical College, and the study was conducted in Osmania Medical College, Hyderabad.

Inclusion criteria:
All the patients diagnosed with cirrhosis of liver and more than 18years of age.

Exclusion criteria:
a. Patients with cardiac failure.
b. Patients with chronic kidney disease
c. Patients on drugs like SSRI, TCA, MAO inhibitors, cytotoxic drugs etc.
d. Unwillingness of participation.

Study procedure:
After obtaining permission from the institutional ethics committee, the study was done in Osmania General Hospital. Informed consent will be taken from the patient and their attendees. A semistructured case proforma was used to collect the data. History and clinical examination will be done and relevant laboratory tests will be performed. History and findings of clinical examination recorded were duration of alcoholism, jaundice, ascites, oliguria, pedal oedema and gastrointestinal bleeding, splenomegaly, variceal bleed, hepatic encephalopathy, spontaneous bacterial peritonitis and hepatorenal syndrome. Platelet count, PT-INR, and liver function tests were estimated. Based on the serum sodium values, patients are divided into three groups.
1. Group A - Sr sodium > 135
2. Group B – Sr sodium 131 - 135
3. Group C – Sr sodium < 130.

The presence of complications and its frequency in all 3 groups were studied and analysed. An ultrasonogram abdomen and Doppler study of the portal venous system, the portal vein and spleen diameter along with echo texture of the liver, spleen size and direction of blood flow, and ascites was noted. MELD score and MELD - Na is calculated for each patient and compared. Patients are followed up for three months for complications and short-term mortality.

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Statistical analysis:
SPSS (version 28.0) programme was used to analyse data. The qualitative data were described in terms of numbers and percentages. Non- parametric analysis chi-square test/ binomial was used. The quantitative data were described using the range, mean, standard deviation, and median. Mean across groups was compared using student t test. The obtained results were considered significant at the 95% level. MEDcalc is used for the calculation of predictive accuracy statistics of MELD and MELD – Na values

OBSERVATIONS AND RESULTS

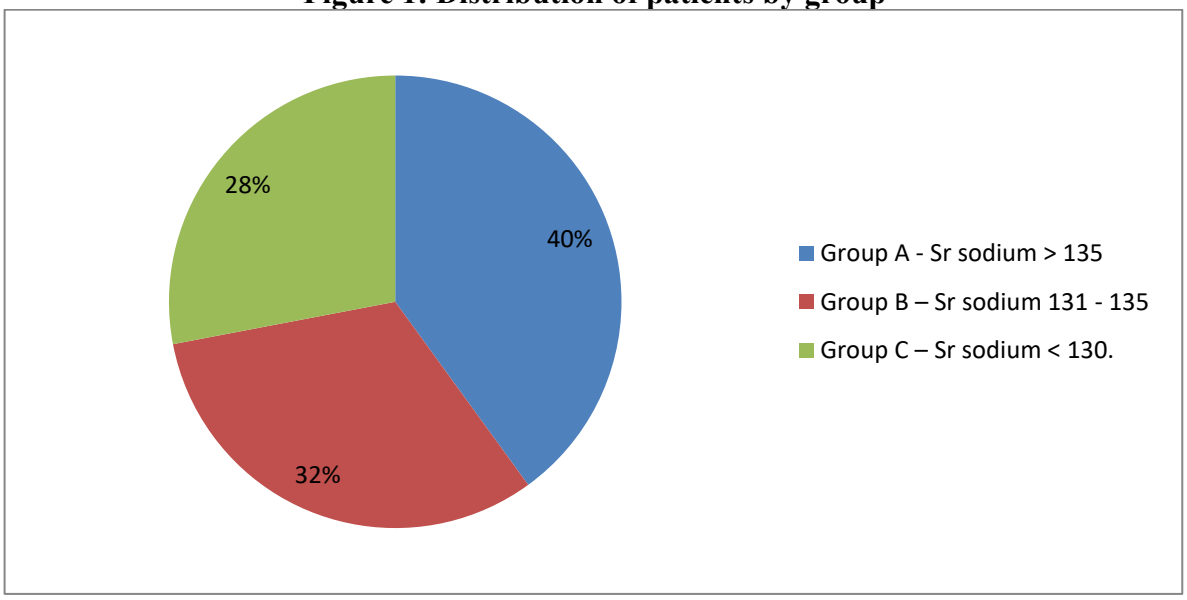
Among the 100 adult patients with cirrhosis of liver included in the analysis, 72% were male and 28% patients were female with sex Ratio = 72/28 = 2.57. Age ranges from 34 to 68 years, with mean age being 47.32. Most patients are aged 41-50 years, making up 47% of the sample, followed by 31-40 years at 25% (shown in table 1).

Table 1: Distribution of study participants by age and gender

Variables	Sub variable	Frequency	Percentage
Age group	31-40	25	25
	41-50	47	47
	51-60	19	19
	61-70	9	9
Gender	MALE	72	72
	FEMALE	28	28

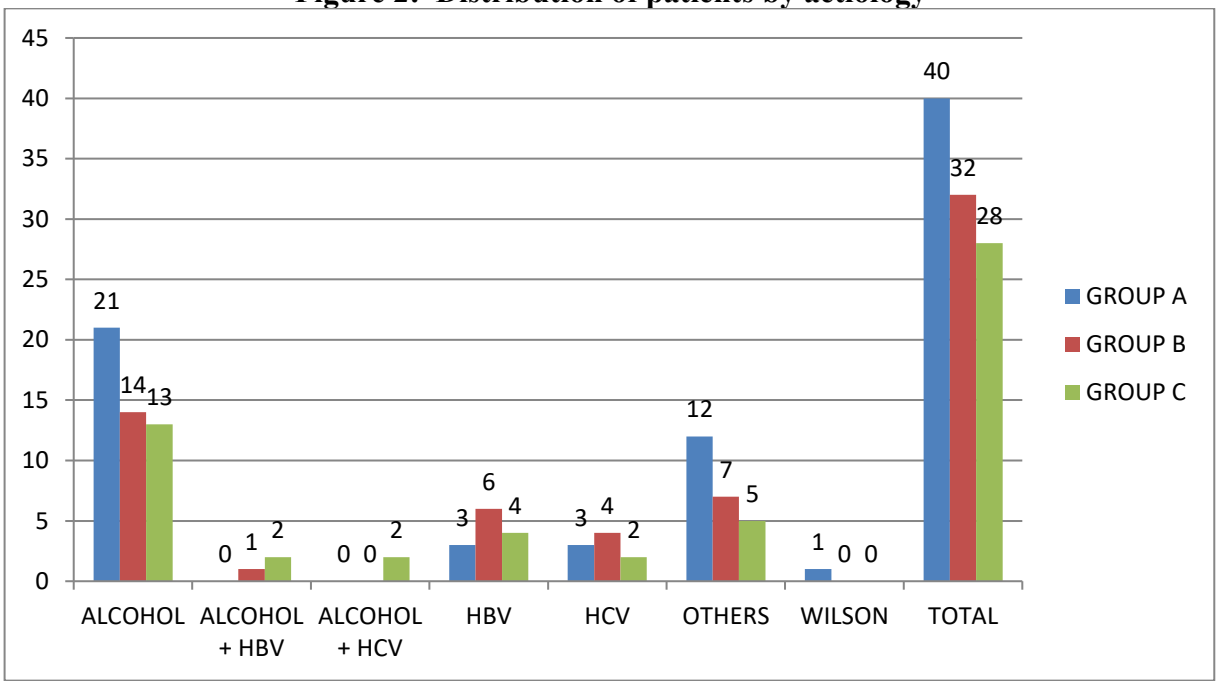
Patients belonging to group A, group B and group C were 40%, 32% and 28% respectively. (figure 2)

Figure 1: Distribution of patients by group



Alcohol was the predominant etiology across all groups, accounting for 21 cases in Group A, 14 in Group B, and 13 in Group C. Viral causes such as hepatitis B and C, either alone or in combination with alcohol, were less frequent. HBV alone was seen in 3, 6, and 4 cases respectively, while HCV alone occurred in 3, 4, and 2 cases. Combined etiologies of alcohol with HBV or HCV were rare, with a few cases noted only in Groups B and C. Other miscellaneous causes contributed 12, 7, and 5 cases in Groups A, B, and C, respectively, while Wilson's disease was observed in only one case in Group A. Overall, alcohol-related liver disease was the leading cause across all groups, followed by viral hepatitis and other causes, with a progressive decline in total cases from Group A (40) to Group C (28). (figure 2)

Figure 2: Distribution of patients by aetiology



The comparison of baseline variables among the three groups showed no significant difference in mean age or gender distribution. The mean age was 46.97 years in Group A, 46.78 years in Group B, and 48.43 years in Group C (**p = 0.785**). Males predominated across all groups, with 30 in Group A, 23 in Group B, and 19 in Group C, while females constituted 12, 10, and 6 cases respectively (**p = 0.86**), indicating no gender-based difference. However, the mean MELD score showed a significant increase from Group A (19.15) to Group B (21.5) and Group C (23.28) (**p = 0.001**). Similarly, the mean MELD-Na score rose markedly across the groups—14.07, 23.22, and 28.89 respectively—with a highly significant difference (**p < 0.001**). These findings suggest that while age and gender were comparable among groups, disease severity as reflected by MELD and MELD-Na scores increased significantly from Group A to Group C thus showing the association with hyponatraemia (table 2).

Table 2: Baseline study variables across the groups

Variable		Group A	Group B	Group C	P value
age	Mean	46.97	46.78	48.43	0.785
Gender	Male (72)	30	23	19	0.86
	Female (28)	12	10	6	
MELD	Mean	19.15	21.5	23.28	0.001
MELD Na	Mean	14.07	23.22	28.89	< 0.001

Hepatic encephalopathy, hepatorenal syndrome, spontaneous bacterial peritonitis, variceal bleeding, and mortality at 3 months were analyzed as complications of liver cirrhosis across the three groups. Hepatic encephalopathy was significantly more frequent in Group C, with 18 cases, compared to 8 in Group B and only 2 in Group A (**p < 0.001**). Similarly, hepatorenal syndrome showed a progressive increase from 3 cases in Group A to 7 in Group B and 11 in Group C (**p = 0.007**). Spontaneous bacterial peritonitis was observed in 4, 10, and 14 cases in Groups A, B, and C, respectively (**p = 0.001**). Variceal bleeding was also more common in Group C (12 cases), followed by Group B (6 cases) and Group A (4 cases), showing a statistically significant difference (**p = 0.005**). Mortality at 3 months was notably higher in Group C, with 9 deaths, compared to 1 in Group B and none in Group A (**p < 0.001**). Overall, the frequency and severity of complications increased

significantly from Group A to Group C, indicating a clear association between disease progression and adverse outcomes. (table 3)

Table 3: Complication across groups

Complication in cirrhosis of liver	Sub variable	**Group A**	**Group B**	**Group C**	**P Value**
Hepatic. Encephalopathy	Absent	38	32	10	<0.001 Significant
	Present	2	8	18	
Hepato Renal Syndrome	Absent	37	25	17	0.007/ significant
	Present	3	7	11	
Systemic Bacterial Peritonitis	Absent	36	22	14	0.001 /significant
	Present	4	10	14	
Variceal bleed	Absent	36	26	16	0.005/ significant
	Present	4	6	12	
Mortality at 3 months	Absent	40	31	19	< 0.001/ significant
	present	0	1	9	

Both MELD and MELD-SODIUM scores shows positive correlations with mortality at 3 months, with correlation coefficients of 0.646, 0.736 and statistical significance at the 0.01 level (2-tailed), indicating their association with MELD Na being better in assessing liver disease severity (table 4).

Table 4: MELD and MELD- Na versus mortality

		Mortality at 3 months
MELD	Spearman Correlation	.646
	Sig. (2-tailed)	.014
	N	100
MELD-Na	Spearman Correlation	.736
	Sig. (2-tailed)	<.001
	N	100

In predicting mortality among patients with liver cirrhosis, the MELD-Na **score** demonstrated superior diagnostic performance compared to the MELD score. MELD-Na showed a higher sensitivity (92.83%) **and** specificity (69.57%)**,** whereas MELD had lower sensitivity (87.33%) and specificity (52.29%). The positive predictive value (PPV) and negative predictive value (NPV) were also higher for MELD-Na (88.25% and 87.89%, respectively) compared to MELD (79.95% and 62.29%). Overall, MELD-Na achieved greater accuracy (87.92%) than MELD (75.83%). These findings indicate that MELD-Na is a more reliable predictor of mortality in cirrhotic patients, offering improved sensitivity, specificity, and overall prognostic accuracy. (table 5)

Table 5: Predictive accuracy statistics of MELD versus MELD Na

Statistic	**MELD Na**	**MELD**
Sensitivity	92.83% (88.30 – 99.13)	87.33% (83.09 – 90.20)
Specificity	69.57% (51.71 – 81.15)	52.29% (39.19 – 68.53)
Positive Predictive Value (PPV)	88.25% (78.32 – 92.12)	79.95% (69.50 – 85.60)
Negative Predictive Value (NPV)	87.89% (73.10 – 95.12)	62.29% (44.82 – 75.27)
Accuracy	87.92% (78.02 – 93.66)	75.83% (62.78 – 83.23)

Discussion: Biggins et al. originally proposed the evidence-based incorporation of sodium into MELD (i.e., MELD-Na) based on increased risk of death at given MELD levels in hyponatraemic patients [14]. More recently, MELD-Na has been validated as superior to MELD for 90-day mortality prediction in liver transplant waitlists and in regional populations [15]. The advantage is particularly evident in patients with moderate MELD scores but significant hyponatraemia, in whom MELD alone may understate risk, hence this study was undertaken to confirm the same.

Among the 100 adult patients with cirrhosis of liver included in this study, 72% were male and 28% patients were female with sex Ratio = 72/28 = 2.57. Age ranges from 34.00 to 68.00 years, with mean age being 47.32. Most patients are aged 41-50 years, making up 47% of the sample, followed by 31-40 years at 25%. In study by Goyal P et al, a total of 716 hospitalized patients with cirrhosis were included. The mean age of patients was 54 ± 9.3 years (18–82 years), and male:female ratio was 5.7:1.[16]

In this study alcohol was the predominant etiology across all groups, accounting for 21 cases in Group A, 14 in Group B, and 13 in Group C. Viral causes such as hepatitis B and C, either alone or in combination with alcohol, were less frequent. HBV alone was seen in 3, 6, and 4 cases respectively, while HCV alone occurred in 3, 4, and 2 cases. Combined etiologies of alcohol with HBV or HCV were rare, with a few cases noted only in Groups B and C. Other miscellaneous causes contributed 12, 7, and 5 cases in Groups A, B, and C, respectively, while Wilson's disease was observed in only one case in Group A. In study by Goyal P et al, most common etiologies of cirrhosis were: alcohol (49.2%; n = 352), hepatitis C virus (HCV) infection (29.4%; 211), and nonalcoholic fatty liver disease (NAFLD) (13.6%; 98). Hepatitis B virus (HBV) infection was identified in 3.9% (n = 28) patients only. Other uncommon causes of cirrhosis were: autoimmune (n = 8; 1.1%), Wilson's disease (n = 5; 0.7%), celiac disease (n = 3; 0.4%), Budd–Chiari syndrome (BCS) (n = 1; 0.1%), and cryptogenic (n = 10; 1.4%) [16].

MELD **and** MELD-Na scores showed a significant stepwise increase from Group A to Group C ($p < 0.001$), demonstrating a progressive rise in disease severity and associated hyponatraemia in this study. Similar results were reported by Biggins et al**.** (2006) and Londoño et al. (2007), who established that the addition of serum sodium to MELD improves risk stratification in decompensated cirrhosis [14,17].

The analysis of complications revealed that hepatic encephalopathy, hepatorenal syndrome, spontaneous bacterial peritonitis, and variceal bleeding were significantly more frequent in Group C, indicating that complications increase with disease progression. Moreover, the present study demonstrated higher diagnostic accuracy for MELD-Na (87.9%) than for MELD (75.8%), with greater sensitivity (92.8% vs 87.3%) and specificity (69.6% vs 52.3%).This pattern mirrors findings from Wang S et al, Ge J et al, Sang J et al and Lim et al. (2018), who demonstrated that advanced liver dysfunction is strongly associated with higher rates of decompensating events and short-term mortality (18, 19, 20, 21).

Conclusions: These results collectively support the growing consensus that MELD-Na outperforms MELD in assessing liver disease severity and predicting short-term mortality. Incorporation of serum sodium accounts for the detrimental effects of dilutional hyponatraemia, a recognized marker of circulatory dysfunction and poor prognosis in cirrhosis. Consequently, many recent transplant allocation systems and clinical protocols have adopted MELD-Na as the preferred prognostic model.

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