Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

MELD XI (MODEL FOR END STAGE LIVER DISEASE EXCLUDING INR) SCORE IN CRITICALLY ILL CASES IN ICU-PROGNOSTIC SIGNIFICANCE

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Abstract

Background: There are variety of scores for risk stratification and mortality prediction in critically ill patients like APACHE, SAPS 2, SOFA which are being used widely. APACHE II and SAPS 2 used for severity of illness prediction in all patients in critical care units. SOFA score predicts organ dysfunction and used for prediction of outcome in sepsis patients. These scores are well validated, but difficult to calculate. Their calculation cannot be done easily on bedside basis in ICU, as the parameters required to calculate them may not be known at time of admission, and are highly variable like respiratory rate, heart rate, body temperature, and manual error chances are high. This emphasis the need for a scoring system that compensate these drawbacks. MELD score has been evaluated as a predictor for clinical outcome in patients suffering from liver disease. It utilizes logarithmic function including serum creatinine, total serum bilirubin, and INR and It has been shown that MELD score can also serve as indicator of multi organ dysfunction. As it is including INR it cannot be used in patients on anticoagulant therapy. Therefore, modification of the MELD score excluding INR (MELD-XI score) was designed and it has been shown that the MELD-XI score is comparable to the MELD score even after omitting INR from the equation. This MELD XI score requires only serum creatinine and bilirubin, it can be easily calculated and not time consuming. This study is undertaken to assess MELD XI SCORE's prognostic significance in critically ill ICU cases, as other scoring systems are complex to calculate.

Keywords: MELD-XI score, SOFA, SAPS2, Organ Dysfunction.

Introduction

Scoring systems for use in intensive care unit were developed over the last 30 years. They help in assessment of the severity of disease and in providing an estimate of in-hospital mortality. This is achieved by collecting routinely measured data specific to a patient. Weightage is applied to each variable, and the sums of the weighted individual scores are used to calculate the severity score. Various factors have been shown to increase the risk of

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

in-hospital mortality after admission to ICU, like increasing age and severity of acute illness, certain pre-existing medical conditions and emergency admission to ICU. Before the 1980s, there were no scoring systems applicable to critical care populations which would allow outcomes from different critical care units to be compared. Since then, many scoring systems have been developed.[1] Physiology-based scoring systems are applied to critically ill patients and have advantages over diagnosis-based systems. Any patient admitted to ICU can have single or multiple organ failure and therefore cannot categorised to a clearly defined diagnostic group. Sometimes, no diagnosis can be made, either on admission or retrospectively. Scoring systems essentially consists of two parts: a severity score and a calculated probability of mortality. Mostly, this is the risk of in-hospital mortality. In order to develop a scoring system, a database incorporating a large amount of patient data from many ICUs, and ideally from many different countries, is required. Most critical care severity scores are calculated from data obtained on the first day of ICU admission. Other scoring systems are repetitive and collect data sequentially throughout the duration of ICU stay or over the first few days. Both first day and sequential scoring systems can be further divided into subjective and objective scores. Subjective scores are produced by taking variables that have been agreed by a panel of experts, and then applying a numerical weighting to each variable to produce a subjective score. Objective scores are developed from a large database of clinical data taken from many ICUs. A computer-based multipurpose probability model is then used to determine which variables to use and the weighting to be applied to each variable.

Assessment of Scoring Systems

Once a scoring system has been produced, its performance should be assessed and validated. This process refers to the ability of the score to predict mortality, and must be carried out on a different population to that used to assemble the score. This can occur by randomly splitting the original population into two groups: the first to produce the score and the other to validate the model, or by using a completely separate population.

Model Calibration

Calibration assesses the degree of correspondence between the estimated probability of mortality and that actually observed. This can be tested using a goodness of fit test, like the Hosmer–Lemeshow C statistic. Over the range of probabilities, the expected and observed mortality are compared and a P-value derived. Calibration is considered to be good if the predicted mortality is close to the observed mortality.

Model Discrimination

Model discrimination reviews the ability of the scoring model to discriminate between patients who die from those who survive, based on the predicted mortalities. Methods include calculation of the area under the receiver operating characteristic (ROC) curve or by using a classification matrix.

Issues Related to Model Assessment

Despite the methods of validating a scoring system, there remain a number of issues related to the design and assessment of the models that could affect their reliability. The populations on which the model is developed and validated are split randomly or chosen at random. As significant length of time it can take for a data required to develop and validate a scoring system, chance that many factors might have changed during this period. Thus, if poor

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goodness-of-fit is obtained during validation, it may be difficult to state for certain if this due to sample or model problems. Sample size also has a major influence on the validity of the scoring system: too small a population, risk of the score being unable to distinguish and assess reliably between different patient groups is high. Thus, a large population is required. In addition, a scoring system must be modelled and validated against a real cohort of patients.

Objectives

1. To Assess prognostic significance of MELD –XI SCORE critically ill ICU cases
2. To calculate optimal cutoff value for MELD –XI score for prognostic assessment.
3. To compare MELD-XI to well accepted score, like APACHE II

Material and Methods

Source of Data: Patients admitted in critical care unit under Department of General Medicine, Kempegowda Institute of Medical Sciences, and Bangalore considering inclusion and exclusion criteria.

Study Design: Prospective Observational cross-sectional study.

Study Period: 18 months

Sample Size: 100 subjects admitted in intensive care unit under Department of general medicine.

No: of diseased subjects needed-89

Total sample size for present study marginally increased to 100.

Note: The sensitivity of newer test was obtained based on previous literature.

Inclusion Criteria:

- Age more than 18 years
- Patient/attenders willing to give informed consent.
- All critically ill cases admitted in ICU, under Department of General Medicine, Kempegowda Institute of Medical Sciences, Bangalore.

Exclusion Criteria:

- Patients/attenders not willing to give informed consent
- Age Less Than 18yrs
- Pregnancy
- Patients Referred to Other Hospitals and discharges against medical advice.

Methods of Data Collection

- 100 patients fulfilling the inclusion criteria and exclusion were enrolled for the study after approval and clearance from the institutional ethics committee.
- Informed consent was taken from the patient
- A pre-structured and pretested proforma was used to collect data
- Detailed history from the patients like, general patient profile, presenting complaint, history of presenting illness, past history, family history, treatment history, & personal history were collected
- General physical examination, systemic examination was done.

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- Investigations include- Hemoglobin, total count, differential count, blood sugar levels, LFT, RFT, Electrolytes, ABG (all laboratory values were obtained from standard in hospital laboratory).
- MELD-XI Score at time of admission to ICU and APACHE II score for each patient was calculated. The patients were followed up till discharged from hospital or till death in hospital and follows exclusion criteria.

Calculation of Meld-XI Score:

- 5.11 x ln (serum bilirubin in mg/dL) ±11.76 x ln(serum creatinine in mg/dL) ± 9.4.
- The endpoint of the study was mortality or discharge from hospital after recovery.

Outcome Measures:

- Study subjects were divided in to two cohorts based on the MELD XI score and optimal cut off value for the score was calculated and evaluated the score for its prognostic relevance regarding survival of the patient.
- Comparison of Meld XI (Model for end Stage Liver Disease Excluding INR) score with APACHE II score.
- Data recorded are statistically analysed.
- Confidentiality of information obtained maintained.

Statistical Analysis: Statistical Package for Social Sciences [SPSS] for Windows Version 22.0 Released 2013. Armonk, NY: IBM Corp. will be used to perform statistical analyses.

Results

A total of 100 cases were enrolled in the study and following are the inferences from this study.

Table 1: Gender Distribution of Study Group

Variable		Category	n	%
Gender		Males	61	61%
		Females	39	39%

As shown in Table 1, 61 % (n=61) were males and 39 % (n=39) of study population were females.

Table 2: Age Distribution of Study Group

Variable	Category	n	%
Age (in years)	20-29	10	10%
	30-39	12	12%
	40-49	13	13%
	50-59	16	16%
	60-69	30	30%
	70-79	17	17%
	80-89	2	2%
		Mean	SD
	Mean & SD	54.36	16.69
	Range	20 – 88	

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[Table 2] describes age distribution of cases selected for the study. Age is calculated in years. Age ranges from 20-88 years. Majority of patients were in age group 60-69 years, accounts for 30 percent (n=30). Only 2 % of the study population belongs to age group of 80-89 years.17% of patients belongs to age group of 70-79,16 % of patients had age ranging from 50-59 years.13 % had age ranging from 40-49 years.12 % of study population had age 30-39 years and 10 % of them had age ranging from 20-29 years. On an average, they belong to age of 54 years with standard deviation of 16.69.

Table 3: Distribution of Study Population Based on Survival

Distribution of study population based on Survival Status			
Variable	**Category**	**n**	**%**
Survival	Non-Survivor	43	43%
	Survivor	57	57%

[Table 3] describes the distribution of study subjects based on survival status. Among 100 cases studied, 43% (n=43) were non-survivors and 57%, (n=57) were survivors.

Table 4: Distribution of Age Groups among Non-Survivors in the Present Study

Age	**N**	**%**
20-29	2	4.7%
30-39	6	14.0%
40-49	7	16.3%
50-59	5	11.6%
60-69	15	34.9%
70-79	7	16.3%
> 80	1	2.3%
Total	43	100.0%

[Table 4] explains distribution of Age groups among non-survivors in the present study. Total number of non survivors were 43 in a study population of hundred. It is observed that maximum deaths are seen in patients having age range of 60-69 years, fifteen patients died (34.9 %) followed by age group of 70-79 and 40-49 years, seven death (16.3%). This is followed by 30-39 years age group having six (14%)and 50-59 years age group having five deaths(11.6%) followed by 20-29yrs and more than 80 years age having two (4.7%) and one death (2.3%)respectively.\

Table 5: Age Wise Comparison of mean MELD Xi Score

Age wise comparison of mean Meld XI scores among study population using Mann Whitney Test					
Age	**N**	**Mean**	**SD**	**Mean Diff**	**P-Value**
< 60 yrs.	56	17.91	7.63	0.11	0.75
> 60 yrs.	44	17.80	6.37		

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[Table 5] explains age wise comparison of mean MELD XI score among study subjects using Mann Whitney Test. It shows that number of cases below 60 years are n=56 and had an average MELD XI score 17.91 (SD=7.63) and those above 60 years are n=44 and had an average MELD XI score of 17.80(SD=6.37) with a mean difference of 0.11 with a p value 0.75.

Table 6: Gender Wise Comparison of Mean MELD Xi Scores

Gender wise comparison of mean MELD XI scores among study population using Mann Whitney Test					
Gender	N	**Mean**	**SD**	**Mean Diff**	**P-Value**
Males	61	19.28	7.40	3.64	0.02*
Females	39	15.64	5.96		

[Table 6] describes gender wise comparison of mean MELD XI scores among study group using Mann Whitney Test. Among n=61 males, mean MELD XI score is 19.28 and in n=39 females MELD XI score is 15.64 with standard deviation 7.40 and 5.96 respectively with a mean difference of 3.64 and is statistically significant with P -value 0.02.

Table 7: Comparison of Mean Meld Xi Scores Based On the Diagnosis

Comparison of mean MELD XI scores based on the diagnosis using Kruskal Wallis Test						
Diagnosis	**N**	**Mean**	**SD**	**Min**	**Max**	**P-Value**
Sepsis	17	20.35	5.88	9	30	<0.001*
CLD	12	24.33	9.28	9	40	
Acute GE	18	17.50	4.88	9	25	
IHD	19	19.47	6.39	9	26	
Pneumonia and ARDS	13	13.15	4.34	9	22	
Meningoencephalitis	5	10.20	1.79	9	13	
OP Poisoning	7	11.57	2.70	9	17	
CKD	4	26.00	0.00	26	26	
Acute Exacerbation of COPD	5	11.20	2.28	9	14	

In [Table 7], further the cases were categorised and mean MELD-XI score is calculated for each category of cases using Kruskal Wallis test and found to have different values for different category. Chronic kidney disease group had mean MELD XI score (n=4) of 26. All category of disease group had minimum score of 9 except CKD where minimum score is also 26. Maximum score of 40 was calculated for chronic liver disease patients, 30 for sepsis patients, 25 for acute gastroenteritis patients, 26 for IHD and CKD patients, 22 for pneumonia and ARDS cases, 13 for meningoencephalitis cases, 17 for op poisoning, and 14 for acute exacerbation of COPD. Average MELD XI score also vary among the different category with approximately 20.35(+/-5.88) for sepsis ,24.33(+/-9.28) for CVA,17.50(+/-4.88) for acute gastroenteritis,19.47(+/-6.39) for IHD,13.15 (+/-4.34) for pneumonia and ARDS,10.20(+/-1.79) for meningoencephalitis,11.57(+/-2.70) for OP poisoning cases,11.20(+/-2.28) for Acute exacerbation of COPD. This comparison is statistically

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significant with p value <0.001. Thus, MELD XI is significantly increased in chronic kidney disease and CVA cases followed by sepsis then in ischemic heart disease cases, compared to others.

Table 8: Cut Off For Meld Xi Score between Survivors and Non Survivors

ROC Curve analysis for MELD XI scores for determining the cut-off between Survivors and Non-Survivors									
Variable	**AUC**	**Std. Error**	**95% Conf. Interval**		**P-Value**	**Cut off**	**Youden Index**	**Sn (%)**	**Sp (%)**
			Lower	Upper					
MELD XI	0.59	0.06	0.48	0.68	0.13	> 15	0.24	69.8	54.40

[Table 8 and graph 1] describes a cut off value for MELD XI score for survivors and non survivors and it is calculated with Youden index 0.24 and ROC analysis done. The cut off value for MELD XI between survivors and non survivors in this study is 15. Area under the ROC curve is 0.59, 95% CI ranging from 0.48-0.68, with a sensitivity of 69.8% and specificity of 54.40% with p-value 0.13 and is marginally significant.

Table 9: Comparison of Mortality Rate Based on the Cut-Off Values of MELD XI Scores

Variables	**Category**	**Non-Survivors**		**Survivors**		**P-Value**
		N	**%**	**n**	**%**	
MELD Cut-off	< 15	13	30.2%	31	54.4%	0.02*
	> 15	30	69.8%	26	45.6%	

[Table 9 and bar diagram 1] compares mortality rates based on cut off values of MELD XI score using chi square tests. It is observed that n=43 were non-survivors and n=57 were survivors. Among non survivors, 30.2 % had MELD XI score <15 and 69.8% had MELD XI score >15.Whereas, 54.4% of survivors had MELD XI score <15 and 45.6% of survivors had MELD XI score > 15 and this difference is statistically significant with p- value 0.02*.

Table 10: Comparing Mean Values of Different Parameters Based on Cut off Value of MELD XI for Mortality

Parameters	**MELD XI**	**N**	**Mean**	**SD**	**Mean Diff**	**P-Value**
Arterial Pressure of CO_2	< 15	44	42.79	21.44	12.75	0.11
	> 15	56	30.05	12.70		
Mean Arterial Pressure	< 15	44	92.59	20.45	8.97	<0.001*
	> 15	56	83.63	24.96		
Heart Rate	< 15	44	97.39	20.52	-3.61	0.14
	> 15	56	101.00	21.90		
Respiration Rate	< 15	44	27.27	6.70	0.72	0.08
	> 15	56	26.55	5.91		

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Arterial Ph	< 15	44	7.36	0.13	0.05	0.06
	> 15	56	7.31	0.18		
Serum Bicarbonate	< 15	44	22.83	6.90	7.74	0.52
	> 15	56	15.10	5.58		
Packed Cell Volume	< 15	44	37.87	9.04	4.42	0.99
	> 15	56	33.45	11.07		
White Blood Cell Count	< 15	44	14188.95	5601.95	-1687.12	0.33
	> 15	56	15876.07	8269.35		
Glasgow Coma Scale	< 15	44	12.39	3.77	0.53	<0.001*
	> 15	56	11.86	4.91		
Rectal temp	< 15	44	100.55	1.31	0.47	0.75
	> 15	56	100.08	1.58		
Serum Sodium	< 15	44	137.16	7.79	0.82	0.03*
	> 15	56	136.34	8.34		
Serum Potassium	< 15	44	4.48	0.87	-0.45	0.68
	> 15	56	4.93	0.95		
Comparison of mean values of different parameters based on the Cut-off values of MELD XI scores using Mann Whitney Test						
Parameters	**MELD XI**	**N**	**Mean**	**SD**	**Mean Diff**	**P-Value**
Total Bilirubin	< 15	44	0.84	0.54	-1.85	0.04*
	> 15	56	2.69	5.32		
Serum Creatinine	< 15	44	1.03	0.32	-2.67	0.04*
	> 15	56	3.70	2.73		
Mortality (%) Apache II Score	< 15	44	36.11	19.42	-17.40	<0.001*
	> 15	56	53.52	24.90		
AST(Sgot)	< 15	44	43.75	35.26	-112.18	0.04*
	> 15	56	155.93	368.89		
ALT(Sgpt)T	< 15	44	30.77	21.66	-76.89	0.008*
	> 15	56	107.66	287.83		
Hb	< 15	44	12.56	3.25	1.96	0.11
	> 15	56	10.59	3.63		
Lactate	< 15	44	2.15	2.06	-0.69	0.13
	> 15	56	2.84	3.08		

From the above [Table 10], it is observed that cases with MELD XI score < 15 have Mean arterial pressure (n=44) 92.59 (SD=20.45) and those with MELD XI score>15 have MAP 83.63(SD=24.96) with a statistically significant difference of 8.97 with p-value <0.001. Similarly, a statistically significant difference of p-value <0.001 is observed with Glasgow Coma Scale for MELD XI score </> 15 with values that averages 12.39(SD=3.77) and 11.86(SD=4.91) with significant difference of 0.53 with p value < 0.001. Serum sodium values for the same two categories of MELD XI score shows statistically significant difference of 0.82 with p value 0.03 with serum sodium 137.16 (SD=7.790) for MELD XI

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<15 and 136.34 (SD=8.34) for MELD XI >15. Similarly, cases with MELD XI >15 have high total bilirubin levels (2.69+/-5.32 vs 0.84+/-0.54), high serum creatinine (3.70+/-2.73 vs 1.03+/-0.32), high AST (155.93+/368.89 vs43.75+/-35.26), high ALT (107.66+/-287.83 vs 30.77+/-21.66), high mortality percent as per APACHE II score (53.52+/-24.90 vs 36.11+/-19.42) with significant difference of p -value 0.04 for serum bilirubin, serum creatinine, and AST and 0.008 for ALT and <0.001 for mortality percentage.However, other study parameters compared between MELD XI score </> 15 did not showed any significant difference.

Table 11: Comparison of Comorbidities and Other Factors with MELD XI Score for Mortality Based On Chis-Square Test

Variables	**Category**	**< 15**		**> 15**		**P-Value**
		n	**%**	**n**	**%**	
Inotropes	Yes	13	29.5%	28	50.0%	0.04*
	No	31	70.5%	28	50.0%	
Ventilator any time	Yes	27	61.4%	31	55.4%	0.55
	No	17	38.6%	25	44.6%	
Diabetes Mellitus	Yes	19	43.2%	24	42.9%	0.97
	No	25	56.8%	32	57.1%	
COPD	Yes	8	18.2%	4	7.1%	0.09
	No	36	81.8%	52	92.9%	
Hypertension	Yes	19	43.2%	23	41.1%	0.83
	No	25	56.8%	33	58.9%	
Chronic Kidney Disease	Yes	1	2.3%	15	26.8%	0.001*
	No	43	97.7%	41	73.2%	
Cancer	Yes	0	0.0%	1	1.8%	0.37
	No	44	100.0%	55	98.2%	
Chronic Liver Disease	Yes	1	2.3%	4	7.1%	0.27
	No	43	97.7%	52	92.9%	
Old Tuberculosis	Yes	1	2.3%	4	7.1%	0.27
	No	43	97.7%	52	92.9%	
Old Cerebrovascular Accident	Yes	1	2.3%	4	7.1%	0.27
	No	43	97.7%	52	92.9%	
Pulmonary Thrombo-Embolism	Yes	0	0.0%	1	1.8%	0.37
	No	44	100.0%	55	98.2%	
Old COVID	Yes	0	0.0%	1	1.8%	0.37
	No	44	100.0%	55	98.2%	
Retroviral Disease	Yes	0	0.0%	1	1.8%	0.37
	No	44	100.0%	55	98.2%	
Comparison of different Predisposing Factors / Comorbidities based on the Cut-off values of MELD XI scores using Chi Square Test						
Variables	**Category**	**< 15**		**> 15**		**P-Value**

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		n	%	n	%	
Old Ischemic Heart Disease	Yes	7	15.9%	8	14.3%	0.82
	No	37	84.1%	48	85.7%	
Hypothyroidism	Yes	4	9.1%	3	5.4%	0.47
	No	40	90.9%	53	94.6%	
Hyperthyroidism	Yes	0	0.0%	0	0.0%	..
	No	44	100.0%	56	100.0%	

[Table 11] compares MELD XI score for mortality cut off with comorbidities and use of inotropes and ventilators. It is observed that cases with MELD XI score>15 were 56. Among them 50 % (n=28) on inotropes and other half not on inotropes. Whereas, among those with MELD XI <15, 29.5% were on inotropes and 70.5% were not on inotropes and this difference is statistically significant with p-value 0.04.Among all the comorbidities compared, there is a statistically significant difference with p -value 0.001 observed when MELD XI cut-off value for mortality is compared for chronic kidney disease with, patients having MELD XI score >15 were 26.8% (n=15) and 2.3% (n=1) for those with MELD XI<15. However, other study parameters compared between MELD XI score </> 15 did not show any significant difference.

Table 12: Significance of Association of MELD XI Score with Mortality after Correction of Relevant Confounders

MELD XI scores was still associated with Mortality (HR 1.12, 95% 0.78-1.95; P=0.03*) in an adjusted model after correction for relevant confounders by using Cox Regression Model								
Parameters	**Univariate HR**				**Multivariate HR**			
	HR	**95.0% CI for HR**		**P-Value**	**HR**	**95.0% CI for HR**		**P-Value**
		Lower	**Upper**			**Lower**	**Upper**	
MAP	0.98	0.97	1.00	0.02*	1.00	0.99	1.01	0.98
GCS	0.88	0.83	0.93	<0.001*	0.89	0.81	0.97	0.007*
Na	1.05	1.02	1.09	0.005*	0.99	0.95	1.03	0.57
T. Bilirubin	0.90	0.81	1.01	0.06	0.82	0.69	0.98	0.03*
S. Creatinine	0.64	0.52	0.79	<0.001*	0.38	0.26	0.57	<0.001*
AST Sgot	1.01	1.02	1.06	0.01*	1.00	0.99	1.00	0.01*
ALT Sgpt	1.01	1.03	1.08	0.02*	1.01	1.00	1.01	0.02*
Ionotropes	2.88	1.47	5.62	0.002*	2.31	0.97	5.52	0.04*
CKD	1.94	0.61	2.17	0.02*	1.72	0.58	5.12	0.33

* - Statistically Significant

In [Table 12], it is observed that MELD XI score is still associated with mortality with (HR 1.12, 95% 0.78-1.95; P=0.03*) and is statistically significant with p=0.03. In the study population on univariate cox regression analysis, it is observed that those on inotropes haveHR-2.88(95% CI 1.47-5.62) for mortality with increase in MELD XI >15 and is

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statistically significant p-value 0.002. Similarly, CKD patients had HR -1.94(95% CI 0.61-2.17) and is statistically significant with p value 0.02. Serum sodium had HR-1.05 for mortality, (95 % CI 1.02-1.09) with p value 0.005. Also, ALT and AST had HR 1.01(95% CI 1.03-1.08 and 1.02-1.06 respectively) and is statistically significant with p value 0.02 and 0.01 respectively. Other parameters for univariate regression analysis like MAP, Serum creatinine, Total bilirubin, GCS is observed to have less hazard risk of 0.98,0.64,0.90,0.88 respectively with p value 0.02, <0.001,0.06, <0.001 respectively. In presence of multiple confounders which establishes significant difference with MELD XI analysed under multivariate regression, those on inotropes still have significant HR2.31(95% CI 0.97-5.52) with p value 0.04 followed by significant HR for ALT (HR1.01,95% CI 1-1.01) p value 0.02. and AST, HR -1(95% CI 0.99-1) and is significant with p value 0.01. Others are found to have less hazardous risk.

Table 13: Comparing Mean APACHE II Score with MELD XI Score for Mortality Prediction

MELD XI		N	Mean	SD	Mean Diff	P-Value
< 15		44	20.09	7.63	-6.68	<0.001*
> 15		56	26.77	6.37		

[Table 13] compares MELD XI cut off score for mortality with mean APACHE II scores. It is observed that patients with MELD XI score more than 15 (n=56) have mean APACHE II score of 26.77 (approximately 27) and those with MELD XI score less than 15(n=44) had mean APACHE II score of 20.09(approximately 20) and have a difference of 6.68 and is statistically significant with p<0.001.

Table 14: Comparison of Mean Percentage of Mortality Based On APACHE II between Different Ages Groups among Nonsurvivors

Comparison of mean percentage of Mortality based on APACHE II Scores between different age groups among the non-Survivors using Kruskal Wallis Test						
Age	**N**	**Mean**	**SD**	**Min**	**Max**	**P-Value**
20-29	2	27.50	17.68	15	40	<0.001*
30-39	6	55.50	19.48	40	85	
40-49	7	43.00	23.24	25	73	
50-59	5	70.60	15.06	55	85	
60-69	15	64.20	20.36	25	85	
70-79	7	73.86	10.06	55	85	
> 80	1	73.00	.	73	73	

[Table 14] compares the mean percentage mortality based on PACHE II between different age groups among non survivors. It is observed that among non survivors belonging to age group of 70-79 years had high mean mortality percentage calculated as per APACHE II and is 73.86 and group (non survivors) with age more than 80 years were close by with mean mortality percentage of 73% followed by patients in age group of 50-59 years with mortality

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percentage of 70.60 %. Among non survivors in age group of 20-29, mortality % was 27.50 and is statistically significant with p value <0.001.

Table 15: Comparison of Percentage of Mortality Based on APACHE II Scores B/W Different Age Groups among Non-Survivors

Comparison of percentage of mortality based on APACHE II Scores b/w different age groups among non-Survivors using Chi Square Test									
Mortality (%) Apache II	**20-29**	**30-39**	**40-49**	**50-59**	**60-69**	**70-79**	**> 80**	**Total**	**P-Value**
15%	1	0	0	0	0	0	0	1	<0.001*
25%	0	0	4	0	1	0	0	5	
40%	1	3	0	0	2	0	0	6	
55%	0	1	1	2	5	1	0	10	
73%	0	1	2	1	1	4	1	10	
85%	0	1	0	2	6	2	0	11	
Total	2	6	7	5	15	7	1	43	

[Table 15] compares mortality percentage of APACHE II in our study with observed mortality in present study between different age groups. It is observed that maximum deaths are seen in patients having age of 60-69 years that is fifteen patients died. In that those with calculated mortality of 85 % were six followed by age group of 70-79 and 4049 years, seven deaths. Followed by 30-39year age group having six and 50-59year age group having five deaths followed by 20-29yrs and more than eighty years having two and one death respectively. Maximum mortality percentage of 85 based on APACHE II was observed in 11 cases died in this study. It was followed by 73 and 55 percent mortality observed in 10 cases each respectively whom died, followed by 40 percent mortality in six non-survivors followed by 25 percent and 15 percent mortality in total five and one non-survivor in this study respectively. It is observed that this data is statistically significant with p value <0.001.

Table 16: Comparison of Roc Curve Analysis of APACHE II and MELD XI Score to Determine the Prognostic Importance in Predicting Survival Outcome

Variable	**AUC**	**SE**	**95% Conf. Interval**		**MELD XI Scores**	
			Lower	**Upper**	**Diff**	**P-Value**
MELD XI	0.59	0.06	0.48	0.68	..	..
APACHE II	0.83	0.04	0.75	0.90	0.24	<0.001*

[Table 16 and graph 2] compares the ROC curve analysis for APACHE II and MELD XI to determine the prognostic significance in predicting the survival outcome.
Area under curve of MELD XI score is 0.59 and that of APACHE II score is 0.83 and the 95% CI of MELD XI score is 0.48-0.68 and APACHE II score is 0.75-0.90 and the difference is 0.24 and is statistically significant with p value<0.001.

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Table 17: Correlation between MELD XI Score, APACHE II and Mortality %

Spearman's correlation b/w MELD XI, APACHE II Scores & % Mortality of APACHE II Scores					
Parameters	**N**	**APACHE II SCORE**		**Mortality (%)**	
		rho	**P-Value**	**rho**	**P-Value**
MELD XI	100	0.39	<0.001*	0.38	<0.001*

[Table 17] explains that there is a significant positive correlation of rho 0.39 and 0.38, with p value<0.001, between MELD XI score and APACHE II score and its mortality % respectively.

Discussion

This is prospective study involving 100 subjects. In this study we are assessing prognostic significance of MELD XI (Model for End Stage Liver Disease Excluding Inr) score in critically ill cases in intensive care units in predicting prognostic outcome. Also, MELD XI score is compared with APACHE II score. The clinical profile of 100 cases admitted in medical ICU is collected. In this study, MELD-XI Score calculated at time of admission to ICU. APACHE II score and mortality percentage is calculated, based on APACHE II score and also for our study population. Majority of the cohorts were males' 61% and 39% females. The age of the study subjects varied from 20-88 yrs. Mean age group was 54.36+/- 16.69. Majority of them belong to age group of 60-69 years, constituting 30% of total population. Among 100 cases studied, survivors were 57% and non-survivors were 43% on follow up. Maximum mortality is seen age group of 60-69 years (34.9 %) followed by age group of 70-79 and 40-49 years (16.3%).

In this study, for subjects with age <60 years, mean MELD XI score is 17.9+/-7.63, and for those with age >60 years, mean MELD XI score is 17.80+/-6.37 but difference is not statistically significant. 61 subjects were males and mean MELD XI score was 19.28+/7.40 and 39 were females, with mean MELD XI score is 15.64+/-5.96 with statistically significant difference of p<0.02. Thus, males had higher average MELD XI score.

Among category of cases selected for study, majority of them had IHD as primary diagnosis (19%), followed by Acute gastroenteritis (18%) followed by sepsis as primary diagnosis (17%) followed by 13% for pneumonia,12% for CLD, 7 % for Op Poisoning,5% for meningoencephalitis and Acute exacerbation of COPD and 4% for CKD. In this study, mean MELD XI score for the study population was 17.86+/-7.03 and the mean MELD XI score for each group of primary diagnosis differ with maximum value of 26 score for chronic kidney disease patients followed by chronic liver disease patients (24+/-9.28) followed by sepsis (20.35+/-5.85) followed by IHD (19.47 +SD 6.39), followed by Acute gastroenteritis (17.50+SD 4.88) and then Pneumonia (13.15+SD 4.34).

In a large centre study done by Wernly B, Lichtenauer M etal,[4] in 4381 patients admitted in ICU with critical illness, most common primary diagnosis was myocardial infarction (n = 2034), sepsis (n = 694), heart rhythm disturbance (846) and heart failure (n = 688). In this study, optimal cut off value for MELD XI is calculated by Youden index as 15 and area under curve is 0.59(95% CI 0.48-0.68) with sensitivity 69.8 and specificity 54.4% p-value

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0.13. On comparing mortality rate based on cut off value of MELD XI score,69.8% non-survivors had MELD XI score >15 and 54.4% survivors had score<15.Wernly B, Frutos-Viva etal,[3] investigated 11,091 critically ill patient. Median MELD-XI was 12 points, and the cohort was split into two subgroups, above (n = 5564) and below (n = 5527) MELD-XI of 12 points. AUC for prediction of 28-day-mortality was 0.63 (95%CI 0.62–0.64), the optimal cut-off using Youden Index was 12 points.

In the MELD-XI>12 cohort, in-hospital-mortality was significantly higher compared to the MELD≤12 group (46% vs 27%; HR 1.74 95%CI 1.63–1.86; p < 0.0001. Wernly B, Lichtenauer M etal,[4] by means of the Youden-Index calculated an optimal cut-off value for MELD XI score in their study population as 11.

In this study, while comparing different parameters with MELD XI cut off score of 15, significant difference between values were observed for mean arterial pressure (Mean difference 8.97 p < 0.001), GCS (Mean difference 0.53 P<0.001), serum sodium (mean difference 0.82 p=0.03), serum creatinine (-2.67 p=0.04), total bilirubin(mean difference -1.85 p-0.04),mortality percentage (mean difference -17.40,p<0.001),AST(mean difference -112.18 p=0.04),ALT(mean difference -16.89 p=0.008).[4]

In this study, 50% patients with MELD XI score >15 were on inotropes and 70.5% patients with score< 15 were not an inotropes and these are markers of multi organ failures. This signifies prognosis of multi organ failures according to MELD XI score.

In this study, it is observed that cases with low GCS (11.86+/-4.91) had MELD XI >15 and those with high GCS (12.39+/-3.77) at time of admission had low MELD XI score of<15.Studies has shown that Glasgow coma scale at admission is an independent predictor of mortality.[5] Similarly, serum sodium levels were slightly lower (136.34+/-8.34) in cases with MELD XI >15 compared to cases with MELD XI<15 (137.16+/7.79). Abnormalities in serum electrolytes levels are the biochemical parameter that decides the clinical manifestations in events such as sepsis, vascular, hormonal events, medications, events in renal system etc.[6]

Wernly B, Frutos-Viva etal,[3] investigated 11,091 critically ill cases. Group with MELDXI>12 points were clinically sicker as per higher SAPS2 scores (52 ± 19 vs 42 ± 17; p < 0.001). Group with MELD-XI>12 evidenced increased hospital (46% versus 27%; p <0.001), ICU (39% versus 22%; p < 0.001) and 28-day mortality (39% versus 22%).

It is observed in this study that 56% of population had haemoglobin around 10.59 and had MELD XI score more than 15. It is proved that cases having critical illness admitted to ICU are prone for inflammatory process. This is shown in a study by Corwin H L etal that 56 % of patients had anaemia and required blood transfusion.[7]

In this study, maximum mortality percentage of 85% by APACHE II score was observed in 11 cases who died followed by 73 and 55 percent mortality observed in 10 cases died followed by 40 percent mortality in six non-survivors followed by 25 percent and 15 percent mortality in five and one non survivor respectively. Thus, as the mortality percentage of APACHE II score increases in critically ill patients in ICU, their chance of survivability decreases and thus is a good prognostic score.[2]

It is observed in this study that non survivors belonging to age group of 70-79 years had high mean mortality percentage of 73.86 calculated as per APACHE II and non survivors with age more than 80 years were close by with mean mortality percentage of 73% followed by cases

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

in age group of 50-59 years with mortality percentage of 70.60 %. Among non survivors in age group of 20-29, mortality % was 27.50. Thus, age is a determining factor in assessing prognosis of illness in critical illness with chance of mortality is high in patients with age more than 50 yrs.

In this study, 30.2 % of non survivors had MELD XI score <15 and 69.8% had MELD XI score >15.Whereas, 54.4% of survivors had MELD XI score <15 and 45.6% of survivors had MELD XI score > 15 and this difference is significant and thus mortality is high in cases with MELD XI more than 15.[4]

It is observed that cases with MELD XI score more than 15 (n=56) had average APACHE II score of 26.77 (approximately 27) and those with MELD XI score less than 15(n=44) had mean APACHE II score of 20.09 (approximately 20) and have a difference of 6.68 and is statistically significant. Thus, APACHE II score is higher among patients with MELD XI >15 and is significant. Deepak CL and Bhat S had found that mean APACHE II score was 24.2 in cases died compared to patients who recovered from illnesses (18.5, p value 0.002).[2,8]

In this study it is also observed that cases with MELD>15 had high mortality percentage as predicted by APACHE II (53.52%) and those with MELD XI score < 15 had low mortality percentage 36.1% and difference is statistically significant. MELD XI score is still associated with mortality (HR 1.12, 95% 0.78-1.95; P=0.03) after correction of relevant confounders by univariate and multivariate cox regression analysis.[4] Spearman's correlation b/w MELD XI, APACHE II Scores & % Mortality of APACHE II Scores explains that there is a weak positive correlation of rho 0.39 and 0.38, which is statistically significant with p value<0.001, between MELD XI score and APACHE II score and mortality % respectively so that when MELD XI score is increasing, proportionate increase in APACHE II and mortality percentage based on APACHE II also increases. AUC analysis of APACHE II score is 0.83 (95% CI 0.75-0.90) and MELD XI score is 0.59(95% CI 0.48-0.68) and difference is 0.24 and is statistically significant. Thus, MELD XI score can be used as a prognostic marker at the time of admission of critically ill cases to ICU in predicting mortality though APACHE II is better score than MELD XI score with more sensitivity and specificity.

Conclusion

It is concluded from this study that MELD XI (MODEL FOR END STAGE LIVER DISEASE EXCLUDING INR) score can be used as a prognostic marker in assessing prognostic outcome in critically ill cases admitted to intensive care units as it is simple to calculate, not time consuming and is not variable like that of APACHE II. Optimal cut off of MELD XI score is obtained as 15 in this study, to predict the prognosis of critically ill cases admitted in intensive care units. Although APACHE II is a better score than MELD XI score with more sensitivity and specificity.

Acknowledgement:

The author is thankful to Department of General Medicine for providing all the facilities to carry out this work.

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