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Original Research Article.

Serum Lactate & Cystatin C Based Model of End Stage Liver Disease (MELD) As Prognostic Factors in Patients with Liver Cirrhosis in Intensive Care Unit

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ABSTRACT

Background: Cirrhotic patients admitted to the intensive care unit (ICU) usually have multi-organ failure. Multiple organ failure entails a very poor outcome in all intensive care patients .The use of prognostic models for patients admitted to ICU is of great importance, since they provide an objective evaluation for a group of patients with potentially high mortality rates and cost. The advanced stage of liver failure and presence of cirrhotic complications contribute to poor prognosis of cirrhotic patients admitted to ICU.

Objective: To determine whether serum lactate level and MELD based cystatin C score give any predictive value for cirrhotic patient prognosis and mortality in ICU and also to determine whether MELD based cystatin C is better than the usual MELD score in the prognostic performance.

Methods: In all the patients enrolled, a diagnosis of cirrhosis was confirmed by resorting to clinical, laboratory, and ultrasonographic findings. During this period, patients with cirrhosis were admitted to the ICU with varying indications. Child-Turcotte-Pugh (CTP), Model for End-stage Liver Disease (MELD), cystatin c based Model for End-stage Liver Disease (MELD-cys), Acute Physiology and Chronic Health Evaluation (APACHE II) and Sequential Organ Failure Assessment (SOFA) scores and lactate were compared between deceased and discharged patients.

Results: A total of 89 consenting patients were enrolled in this study. The mean age of all the patients was 59.9± 10.25. The etiological factors for cirrhosis were mainly HCV and HBV. Lactate level, CTP, APACHE II, MELD, MELD -cys and SOFA scores were significantly higher inpatients who died than in those who were discharged from the ICU (*p* values were <0.001, 0.31, < 0.001, < 0.001,<0.001 and < 0.001 respectively).

Conclusion: Serum lactate and MELD-cys score are good prognostic factors and have a high mortality prediction in liver cirrhosis patients who were admitted to ICU. Substitution of creatinine by cystatin C does not improve the predictive power of MELD score. In terms of prognostic value, SOFA score, APACHE II score and lactate level are superior to the MELD cys, MELD and CTP scores (in the same order) in predicting mortality in liver cirrhosis patients in ICU.

Keywords: Serum Lactate, Cystatin C, End Stage Liver Disease, Liver Cirrhosis.

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INTRODUCTION

Cirrhotic patients admitted to the intensive care unit (ICU) usually have multi-organ failure. Multiple organ failure entails a very poor outcome in all intensive care patients .The use of prognostic models for patients admitted to ICU is of great importance, since they provide an objective evaluation for a group of patients with potentially high mortality rates and cost. The advanced stage of liver failure and presence of cirrhotic complications contribute to poor prognosis of cirrhotic patients admitted to ICU.[1]

Several scores have been developed for cirrhotic patients admitted to ICU based on combination of prognostic indicators. Of

the models used like, child turcotte-pugh (CTP), model of end stage liver disease (MELD) for patients with liver disease, while acute physiology & chronic health evaluation (APACHE II) and sequential organ failure assessment (SOFA) are valid for use in different patient groups admitted to ICU.[2]

The level of lactate is made normally by muscle tissue and red blood cells. When the oxygen level in the body is normal, carbohydrate breaks down into water and carbon dioxide. When the oxygen level is low, carbohydrate breaks down for energy and makes lactic acid.[3] Lactic acid levels get higher when strenuous exercise or other conditions such as heart failure, a severe infection (sepsis), or shock which lowers the flow of blood and oxygen throughout the body. Lactic acid levels can also get higher when the liver is severely damaged or diseased, because the liver normally breaks down lactic acid.[4] Cystatin C, a potent inhibitor of cysteine proteases, is found mainly in extracellular fluids such as blood, cerebrospinal fluid, and seminal plasma. Its low molecular weight and stable production rate indicate that the blood concentration of cystatin C is determined mainly by glomerular filtration. The production rate of cystatin C is less altered by non-renal factors than is the production of creatinine.[5] The patients with liver cirrhosis, particularly with Child-Pugh class C, should have regular estimation of serum cystatin C level for prognosis, dosage assessment of potentially nephrotoxic drugs and recognition of changes in glomerular filtration rate (GFR) to detect early affection of their renal functions.[6] The model of end stage liver disease (MELD) includes serum creatinine, which is a poor surrogate marker of renal function in patients with cirrhosis. Especially in women and patients with advanced disease as creatinine underestimates true renal function.[7]

AIMS AND OBJECTIVES

To determine whether serum lactate level and MELD based cystatin C score give any predictive value for cirrhotic patient prognosis and mortality in ICU and also to determine whether MELD based cystatin C is better than the usual MELD score in the prognostic performance.

PATIENTS & METHODS

This study was held at the intensive care unit of Theodor Belhars Research Institute between 2016 and 2017 with the approval of the local ethics committee. Informed consent was obtained from lucid patients or from the next of kin of incapacitated patients. All adult cirrhotic patients (with age of 21 years or above), of both sexes, who were admitted to ICU for more than 24 hours with varying indications like hepatic encephalopathy secondary to spontaneous bacterial peritonitits or upper GIT bleeding. Diagnosis of liver cirrhosis was confirmed by abdominal ultrasound findings which reveal the presence of liver cirrhosis of any degree in the abdominal ultrasound study. Patients aged less than 21 years old, Patients with hepatocellular carcinoma diagnosed by documented previously done histopathological analysis, patients discharged from the ICU during the first 24 hours, chronic kidney disease with creatinine clearance < 30 mL/min/1.73 m^2 and heart failure whatever the etiology were excluded from the study.

All patients were subjected to the following after admission: Thorough history with clinical examination, Vital signs on admission (HR, SBP, DBP, MAP, RR, temperature), conscious level using Glasgow Coma Scale (GCS), Liver function tests: serum transaminases, serum bilirubin (total and direct) International normalized ratio and serum albumin. Also, complete blood count, serum urea, creatinine levels, arterial blood gas. Serum sodium, serum potassium levels, serum cystatin c, serum lactate and abdominal ultrasonography. All laboratory investigations were done on admission to ICU through a blood sample taken from a peripheral vein after sterilization of the skin with povidone iodine. Arterial blood gas sample was done through about 1ml of blood taken from radial artery after sterilization of the skin.

In addition, APACHE II, CTP, MELD, MELD-CYS and SOFA score were calculated for each patient. All these scores besides serum lactate were compared between deceased and discharged patients.

Statistical Analysis

The statistical analysis was performed using a standard SPSS software package version 17 (Chicago, IL).Normally distributed numerical data are presented as mean ± SD or median + IQR. Differences between groups were compared using the independent Student's *t*-test, categorical variables were analyzed using the χ^2 test or fisher exact test and are presented as absolute number. The area under the receiver operator curve (AUC) was presented for each prognostic factors with95% confidence interval. $P < 0.05$ is considered statistically significant.

Table 1: Patient's Characteristics

	Overall (n=89)	Discharge (n= 67)	Deceased (n=22)	p-value
Age (years)	59.9±10.25	58.6± 9.35	61.8± 11.98	0.38
Sex(M/F)	50/39	37/30	13/9	0.81
HCV	88	66	22	0.75
Cirrhosis	89	67	22	1
DM	38	27	11	0.46
HTN	14	9	5	0.322
Esophageal Varices	49	36	13	0.3
Spontaneous Bacterial Peritonitis	30	25	5	0.3
Others	10	6	4	0.3

HCV hepatitis C virus, DM diabetes milietus, HTN hypertension, others e.g: pancreatitis, urinary tract infection and hypovolemic shock. (data are presented as mean ± SD)

Table 2: Vital Data Analysis

	Overall (n=89)	Discharge (n= 67)	Deceased (n=22)	p-value
SBP (mmHg)	91.11±17	96.1±15.9	75.9±9.59	<0.001*
DBP (mmHg)	55.6±11.56	59.85±8.2	42.68±10.7	<0.001*
MAP (mmHg)	67.24±13.62	72.19±8.83	52.14±14.65	<0.001*
Heart rate (HR) Beat/minute	109.3±14.4	105.5±13.3	120.68±11.35	<0.001*
Respiratory rate(RR) Breath/minute	21.8±7.3	19.88±6.119	27.9±7.47	<0.001*
Temperature(c)	37.3±3.85	37.56±1.23	36.6±7.53	0.572
GCS	11(9-13)	11(11-13)	8(8-9)	<0.001*

SBP systolic blood pressure, DBP diastolic blood pressure, MAP mean arterial pressure,
GCS Glasgow coma scale (data are presented as mean ± SD or median + IQR)

RESULTS

A: Patient's Characteristics

This study was held at the intensive care unit of Theodor Belhars Research Institute. A total of 89 consenting Egyptian patients were enrolled in this study 50 (56.2 %) of which were men and 39 (43.8 %) were women. From 89 patients, (67) patients were discharged while (22) patients were dead (deceased). The percentage of discharged males is 74% while the percentage of the deceased males is 26%. The percentage of discharged females is 76.9% while the percentage of the deceased females is 23.1%.

The mean age of patients in this study was 59.9±10.25 years. The mean age of patients who were discharged was 58.6±9.35 years, while the mean age of patients who died was 61.8±11.98 years in patients who died. The etiological factor for cirrhosis in this study was mainly HCV in 88 patients (98.87%) and HBV was only one case (1.13%). The causes of the ICU admission were the complications for decompensated liver cirrhosis e.g esophageal varices bleeding and spontaneous bacterial peritonitis.

B: Vital Signs

Systolic blood pressure (SBP) showed statistically significant difference between the discharged patients (mean: 96.1 ±15.9 mmHg) and the deceased patients (mean: 75.9±9.59 mmHg) with the P-value <0.001. Diastolic blood pressure (DBP) showed statistically significant difference between the discharged patients (mean: 59.85±8.2mmHg) and the deceased patients (mean: 42.68±10.7 mmHg) with the P-value <0.001. Mean arterial pressure (MAP) showed statistically significant difference between the discharged patients (mean: 72.19± 8.83 mmHg) and the deceased patients (mean: 52.14± 14.65 mmHg) with the P-value <0.001.

Glasgow coma scale (GCS) showed statistically significant difference between the deceased patients (median: 8(8-9)) and the discharged patients (median: 11(11-13)) with the P-value <0.001. Heart rate showed statistically significant difference between the deceased patients (mean: 120.68±11.35beat per minute) and the discharged patients (mean: 105.5±13.3beat per minute) with the P-value <0.001.

Respiratory rate showed statistically significant difference between the deceased patients (mean: 27.9±7.47breath per minute) and the discharged patients (mean: 19.88± 6.119 breath per minute) with the P-value <0.001.

Table 3: Laboratory Analysis For Complete Blood Count and INR.

	Overall (n=89)	Discharge (n= 67)	Deceased (n=22)	p-value
HB (g/dl)	9.7± 2.6	9.7± 2.25	9.66± 3.58	0.93
HCT (%)	28.37± 8.1	28.47±7.17	28.09±10.93	0.856
WBCs (10^9/L)	11.79± 7.6	10.09± 5.72	16.97±10.1	<0.001*
PLT (10^9/L)	131.9± 110.2	128.6± 102.67	142±132.8	0.623
INR	1.66±0.53	1.44± 0.29	2.37± 0.48	<0.001*

HB:hemoglobin, HCT: hematocrit value, WBCs: white blood cell*1000 count, PLT: platelets count*1000,
INR: international normalized ratio (data are presented as mean ± SD).

Table 4: Laboratory Analysis For Liver Function Tests.

	Overall (n=89)	Discharge (n= 67)	Deceased (n=22)	p-value
AST (U/L)	163.8±409.8	79±80.8	422±768.55	<0.001*
	60(41-97)	55(38-82)	79(50-468)	
ALT (U/L)	69.3±110.67	48.2±67.36	133.64±176.96	0.001*
	32(22-60)	31(22-54)	56(27-140)	
T.Bil.(mg/dl)	4.56±5.1	3.84±4.49	6.77±6.38	0.02*
D.Bil. (mg/dl)	2.23±2.8	1.89±2.52	3.26±3.4	0.04*
Albumin (g/dl)	2.33±0.5	2.39±0.52	2.14±0.58	0.057

AST: aspartate transaminase, ALT: alanine transaminase, T.Bil: total bilirubin, D.Bil: direct bilirubin

Table 5: Laboratory Analysis for Renal Function Tests.

	Overall (n=89)	Discharge (n= 67)	Deceased (n=22)	p-value
Urea(mg/dl)	77.37±45.06	70.63± 42.14	97.87±48.48	0.013*
Creatinine(mg/dl)	1.4±0.75	1.3± 0.75	1.7±0.67-	0.024*
Sodium(mEq/l)	134.8±7.28	134.69±7.35	135.23±7.2	0.76
Potassium(mEq/l)	4.37±0.82	4.36±0.77	4.4±0.95	0.831
Creatinine clearance(ml/min)	77.76±42.41	86.44±44.9	51.3±14.77	<0.001*
Cystatin c(mg/dl)	0.25 (0.2-0.4)	0.25 (0.2-0.37)	0.27(0.2-0.39)	0.842

(Data are presented as mean ± SD or median + IQR).

Table 6: ABG, Mechanical Ventilation Requirement and Length of Stay.

	Overall (n=89)	Discharge (n= 67)	Deceased (n=22)	p-value
PH	7.4±0.09	7.44±0.07	7.35± 0.124	0.005*
Co2 (mmHg)	31.4±6.9	32.66± 6.27	27.4± 7.4	0.002*
Po2 (mmHg)	88.7±20.5	92.25± 19.59	77.9±20.2	0.004*
HCo3 (mmol/L)	21.14±5.6	22.5± 4.95	16.75±5.6	<0.001*
SaO2 (%)	96.4±2.4	97.13± 1.7	94.09±2.7	<0.001*
FiO2 (%)	29.9±7.6	28.79± 6.5	33.33± 9.59	0.015*
MV	26	4	22	<0.001*
LOS (days)		4.48± 2.04	9.9± 5.23	<0.001*

PO2:partial pressure of oxygen,PCO2:partial pressure of carbon dioxide,Hco3:bicarbonate,SO2: oxygen saturation, FIO2: fraction of the inspired oxygen , MV: mechanical ventilation ,LOS:length of stay (data are presented as mean ± SD)

Table 7: Lactate and Scoring Systems between Discharged and Deceased Patients.

	Overall (n=89)	Discharge (n= 67)	Deceased (n=22)	p-value
Lactate (mmol/L)	4.36± 3.2	3.32± 2.17	7.7± 3.54	<0.001*
CTP	11(10-13)	11(10-13)	12(10-13)	0. 498
MELD		16.4± 6.11	27.7± 8.01	<0.001*
	17(12-24)	16 (12-21)	27(22-32)	
MELD-CYS		14.12± 5.1	22.9± 5.45	<0.001*
	15(11-20)	13(11-16)	21(18-25)	
APACHE II		17.2± 4.49	27.95± 5.2	<0.001*
	19(15-24)	16(14-20)	28(25-31)*	
SOFA		6.79± 2.3	11.8± 2.15	<0.001*
	8(6-10)	7(6-8)	11(10-13)	

CTP child-turcotte-pugh; MELD model for end-stage liver disease; APACHE II acute physiology and chronic health evaluation; SOFA sequential organ failure assessment; (Data are presented as mean ± SD or median +IQR).

Table 8: Comparison between Serum Lactate, APACHEII, SOFA, MELD, MELD-cys and CTP scores to Predict Mortality.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV	AUC (95% CI)	p-value
Lactate (mmol/L)	100	73	33.3	96.2	0.887 (0.816-0.92)	<0.001*
APACHE II	95.5	60.7	40.4	97.3	0.93 (0.87-0.99)	<0.001*
SOFA	100	76	29.7	100	0.95 (0.9-0.991)	<0.001*
MELD	86.4	69	47.5	93.9	0.875 (0.8-0.947)	<0.001*
MELDcys	87	66	45	94	0.8 (0. 68-0.911)	<0.001*
CTP	66.7	44.8	27.5	78.9	0.553 (0.418-0.687)	0.498

PPV positive predictive value; NPV negative predictive value; AUC area under curve.

C: Laboratory findings: Table 3,4,5,6

D: Lactate and Scoring Systems Analysis

Lactate level showed statistically significant difference between the deceased patients (mean: 7.7± 3.54 mmol/l) and discharged patients (mean: 3.32±2.17 mmol/l) with the P-value <0.001.

CTP didn't show statistically significant difference between the deceased patients (median: 12 (10-13)) and the discharged patients (median: 11 (10-13)) with the P-value 0.498.

APACHE II score showed statistically significant difference between the deceased patients (mean: 27.95±5.2) and the discharged patients (mean: 17.2±4.49) with the P-value <0.001.

MELD score showed statistically significant difference between the deceased patients (mean: 27.7±8.01) and the discharged patients (mean: 16.4±6.11) with the P-value <0.001.

MELD-cys score showed statistically significant difference between the deceased patients (mean: 22.9±5.45) and the discharged patients (mean: 14.12±5.1) with the P-value <0.001.

SOFA score showed statistically significant difference between the deceased patients (mean: 11.8±2.15) and the discharged patients (mean: 6.79±2.3) with the P-value <0.001.

E: ROC (Receiver Operating Characteristic) Curve Analysis

ROC curve was performed to describe the prognostic performance for the serum lactate, CTP, MELD, MELD-cys, SOFA and APACHEII scores.

SOFA score at the level of (≥6) showed specificity of (76%), sensitivity of (100%) and AUC (Area under curve) of (0.95).

APACHEII score at the level of (≥15) showed specificity of (60.7%), sensitivity of (95.5%) and AUC (Area under curve) of (0.93).

Serum lactate at the level of (≥2.2mmol/l) showed specificity of (73%), sensitivity of (100%) and AUC (Area under curve) of (0.887).

MELD score at the level of (≥20) showed specificity of (69%), sensitivity of (86.4%) and AUC (Area under curve) of (0.875).

MELD-cys score at the level of (≥20) showed specificity of (66%), sensitivity of (87%) and AUC (Area under curve) of (0.8).

CTP score at the level of (≥10) showed specificity of (44.8%), sensitivity of (66.7%) and AUC (Area under curve) of (0.553).

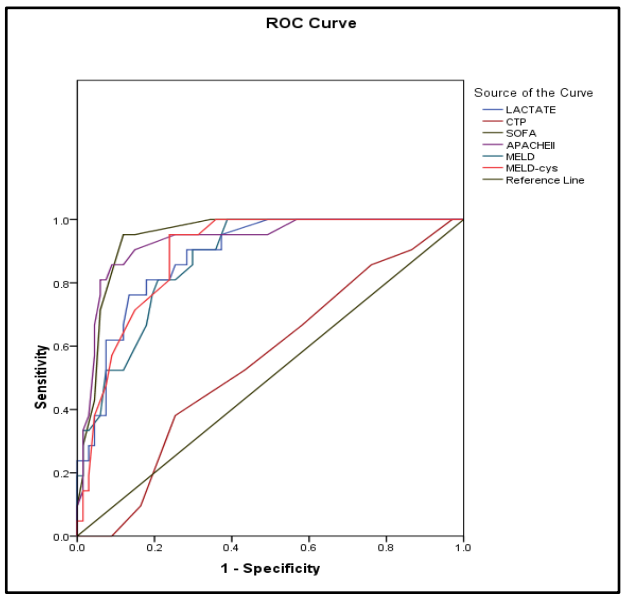

Figure 1: Receiver operating characteristic (ROC) Analysis for Prognostic Performance forLactate, MELD, MELD cys, SOFA, CTP and APACHEII Scores in Cirrhotic Patients.

DISCUSSION

This study was a cross section prospective observational study was held at the intensive care department of Theodor Belhars Research Institute. A total of 89 consenting patients were enrolled in this study. The patients were 50 males (56.2 %) and 39 females (43.8 %).

In this study, high SOFA, APACHE II, MELD, MELD-cys, SOFA and CTP scores as well as increase of lactate were all found to be associated with a higher mortality rate in cirrhotic patients who were admitted to the intensive care unit.

By using Receiver Operating Characteristics (ROC) curve statistical analysis, results of our study have shown the SOFA score to be the best prognostic model, among the scoring systems studied, at predicting prognosis in cirrhotic patients with SOFA score at the cutoff level of (≥6) showed specificity of (76%), sensitivity of (100%) and AUROC (Area ROC curve) of (0.95).

The SOFA score is an excellent model which may be used to provide objective information to patients and their relatives regarding the prognosis of the disease. SOFA scores is currently the most often used score for evaluation of multiple organ dysfunction. Its sequential use demonstrated optimal accuracy to predict mortality in several scenarios, including subgroups of cirrhotic patients.[8]

Our study agrees with a study on 160 patients with cirrhosis admitted to the ICU done by Tsai et al. in 2004 demonstrated that the SOFA score was better than the CTP score in predicting mortality. It showed significantly progressive increase in mortality rate was associated with high SOFA scores ($p < 0.001$) and (AUROC) was 0.892 which is nearly similar to (AUROC) in our study was (0.95) while Child-Pugh scores clearly performed more poorly (AUROC 0.712) which is nearly similar to results of our study (AUROC of CTP: 0.553).[9]

These results confirm those noticed by Cholongitas et al. in 2008 on 128 patients admitted to ICU. SOFA score had the best discriminative ability (higher AUC), compared to the other scores (APACHE II, CTP, MELD) on admission and at 48 h had the best calibration ability.CTP, MELD, APACHE II, SOFA performed better at 48 h (AUC: 0.78, 0.86, 0.78 and 0.88 respectively) than at baseline (AUC: 0.75, 0.78, 0.75 and 0.81 respectively) while in our study they were done on admission only which demonstrated that AUC for CTP, MELD, APACHE II and SOFA were (0.553, 0.875, 0.93 and 0.95) respectively.[10]

In contrary to our study, a study by Juneja et al. in 2009 on 104 patients admitted to a specialty liver ICU in India, higher SOFA is good prognostic model in predicting 30-day mortality, observed mortality in ICU and at 30 days was 75.3% and 87.7%, respectively. Area under curve was 0.77 (95% CI, 0.65-0.86) for APACHE II, 0.94 (95% CI, 0.85-0.98) for SOFA, 0.83 (95% CI, 0.7-0.96) for CTP, and 0.93 (95% CI, 0.85-0.98) for MELD. SOFA and MELD scores were the best prognostic model in this study while in our study SOFA and APACHE II scores are the best prognostic model which could be attributed to difference in study design as it described the observed mortality on admission and at 30 days mortality.[11]

Results of our study have shown the APACHE II score at the cutoff level of (≥15) showed specificity of (60.7%), sensitivity of (95.5%) and AUROC (Area under ROC) of (0.93) to be highly effective as prognostic model next to the SOFA score.

Our study results were similar to the study by Chiavone et al. in 2005 on 94 patients admitted to ICU. Higher APACHE II scores were reported to be associated with higher mortality rates.[12]

Also in agreement with our results, a study by Ho et al. in 2004 on 135 patients with complicated cirrhosis who required intensive care, higher CTP and APACHE II scores were both found to be correlated with increased mortality, the APACHE II score being of

better prognostic value.The overall hospital mortality rate was 66.6%. Furthermore, by using the areas under receiver operating characteristic (AUROC) curve, the APACHE II scores demonstrated a better discriminative power (AUROC 0.833) than Child-Pugh scores (AUROC 0.75) (P=.024). This investigation confirms the grave prognosis for the cirrhotic patients admitted to the ICU. While both Child-Pugh and the APACHE II scores can satisfactorily predict the outcomes for critically ill cirrhotic patients, APACHE II is more powerful in discriminating the survivors from the non-survivors.[13] Against to our study, a study done by Hannah et al. 2017 revealed that the APACHE IV score showed good discrimination and calibration in predicting in-hospital and 1 year mortality after liver transplantation and better than APACHE II, MELD, MELD-Na,SAPS-3 and CTP. APACHE IV has a very good prognostic model but with difficult applicable usage so, APACHE II was used in our study because of its simplicity and capability of classifying severity of illness and predicting hospital mortality.[14]

MELD is a liver specific prognostic model, used to predict short-term survival in cirrhotic patients and to prioritize recipients for transplantation.[15]

In our study, the MELD-cys score at the cutoff level of (≥20) showed specificity of (66%), sensitivity of (87%) and AUROC (Area under ROC) of (0.8) has been shown to be equivalent or less accurate than the MELD score at the cutoff level of (≥20) which had specificity of (69%), sensitivity of (86.4%) and AUROC (Area under ROC) of (0.875) to estimate short-term survival among cirrhotic patients.

The MELD cys score includes the same parameters such as MELD except cystatin c instead of creatinine.[16]

In agreement with our study, a study by Finkenstedt et al. in 2012 on 429 patients admitted to a speciality liver ICU, higher MELD cys is good prognostic model in predicting short term mortality but Substitution of creatinine by cystatin C does not improve the predictive power of MELD.Unfortunately, there were no more studies discussing the predictive mortality for MELD cys score.[16]

In contrary to our study, a study done by Dorde et al. 2014 on 63 patients with liver cirrhosis concluded that values of cystatin C between patients with different stages of liver cirrhosis according to Child-Pugh (P = 0.01), and a significant correlation with model of end stage liver disease (MELD) score (r s = 0.527, P < 0.001) and Cystatin C may be a more reliable marker for assessment of liver insufficiency. While in our study there no statistical significance for cystatin C (P < 0.482) between the discharged and the deceased patients which could be attributed to different study designs, sample size and patients category with unstable hemodynamics and subsequent deterioration.[17]

Also, a study done by Chung et al. 2010 on 53 patients with liver cirrhosis found that The accuracy in predicting acute kidney injury and short-term mortality in comparison for MELD and MELD-Na was higher for a serum cystatin C level of >1.23 mg/L (P<00.1) than for the serum creatinine concentration in patients with cirrhosis (P<00.1). While in our study there no statistical significance difference for cystatin C (P < 0.482) between the discharged and the deceased patients and there is statistical significance difference (P: 0.24). This could be explained by different sample size and the patients usually had unstable hemodynamics in our study.[18]

Against to our study, a study done by Bilyana and Emiliya in 2014 showed that Serum Cystatin C could be used as a good prognostic marker in patients with cirrhosis and normal Cr levels and showed significant statistical difference between the survivors and non survivors (P:0.02). This difference could be explained by the difference in patient criteria as in our study, most of the patients are in acute kidney injury as they were admitted in acute illness.[19]

Regarding MELD score, in agreement with our study, a study by Tu et al. in 2011 demonstrated on 202 critically ill cirrhotic patients as a prognostic model, the MELD score was superior to the CTP.[20]

In agreement with our study, Papeatheodoridis et al. in 2005 demonstrated that the predictive accuracy of MELD score was always superior offering the greatest benefit in the prediction of 12- and 24-mo survival.Both MELD and CTP scores can accurately predict short-term (3- and 6-months) survival in patients with decompensated cirrhosis, while MELD appears to have a slight advantage in predicting medium-term (12- and 24-months).[21]

Against our study, Cholongitas et al. in 2006 on 312 cirrhotic patients demonstrated that MELD score showed high discrimination (AUROC: 0.81), almost the same as SOFA score (AUROC: 0.83) and superior to APACHE II (AUROC: 0.78) and CTP (AUROC: 0.72). this could be explained by different study design as in the previous one it evaluatesonly 6-week mortality in cirrhotic patients admitted to an ICU, and to compare general and liver-specific prognostic scores and different sample size.[22]

Results of our study have shown the CTP score at the cutoff level of (≥10) showed specificity of (44.8%), sensitivity of (66.7%) and AUROC (Area under ROC) of (0.553). It is the least accurate score in predicting mortality in cirrhotic patients.

The CTP scoring system has some subjective components but does not score factors such as cardiovascular, renal and pulmonary dysfunction, which may explain its low prognostic efficiency in patients with liver cirrhosis admitted in intensive care.[23]

Despite involving numerous subjective parameters and its limited scope of definition, CTP is still the most commonly used scoring system in the determination of prognosis in cirrhotic patients. Some investigators have suggested that higher CTP scores and the presence of more complications were associated with higher mortality rates.[24]

A metaanalysis by Aggarwall et al in 2001 on 118 patients showed that higher CTP scores were associated with higher mortality rates.[25] Cellular metabolism under anaerobic conditions converts to lactate from pyruvate. Lactic acid levels relate to the oxygen debit corresponding to the extent of tissue hypoperfusion.[26]

Results of our study have shown the lactate level at the cutoff level of (≥2.2 mmol/l) showed specificity of (73%), sensitivity of (100%) and AUC (Area under curve) of (0.887). It was found that lactate level was better than MELD, MELD cys and CTP in predicting mortality in cirrhotic patients in ICU.

Plasma lactate levels are currently used in risk stratification of patients with sepsis, trauma and pulmonary embolism.[27]

Similar to our study, a study by Noval-Padillo et al. in 2011 on 16 patients found that increased lactic acid that occurs is an early predictor of postoperative complications among cardiopulmonary bypass (CBP) patients.[28]

In agreement with our study, a study by Ludhmila et al. 2013, on 502 patients found that Hyperlactatemia 6 hours after ICU

admission is an independent risk factor for worse outcomes in adult patients after cardiac surgery.[29]

Similarly, another study by Hadem et al. 2008 on 102 patients found that serum lactate (AUROC: 0.73) had better prognostic performance than MELD score (AUROC: 0.71) in patients with acute liver failure.[30]

Against our study, a study by Lee et al. in 2012 on a total of 170 patients who were admitted to the emergency department with acute paraquat poisoning shows that the arterial lactate had similar discriminative power to the APACHE II score while in our study APACHEII score had better performance than lactate. This difference may be attributed to different patient categories and sample size.[31]

In contrary to our study, a study by adnan et al in 2012 on 90 patients high lactate levels (AUROC:0.942) was associated with higher mortality rate in cirrhotic patient in intensive care units and better as a prognostic factor than SOFA score (AUROC:0.813). This could be explained by different patient criteria as in that study, only the elderly cirrhotic patients were included. Also, different cut off values for serum lactate and SOFA score.[32]

CONCLUSION

Many factors may be useful as a predictor of mortality in ICU on patients with cirrhosis. Firest, MELD-cys score and serum lactate are good prognostic factors and have a high mortality prediction in liver cirrhosis patients who were admitted to ICU. Second, Substitution of creatinine by cystatin C does not improve the predictive power of MELD score. Third, In terms of prognostic value, SOFA score, APACHE II score and lactate level are superior to the MELD cys, MELD and CTP scores (in the same order) in predicting mortality in liver cirrhosis patients in ICU.

RECOMMENDATIONS

Based on our study results, SOFA score is the most reliable mortality predictor for all critically ill patients and especially in cirrhotic patients, so it should be used broadly in ICU. Although CTP is simple and popular, it had less reliable in mortality prediction for liver cirrhosis patient. Serial following up of serum lactate as a reliable mortality predictor in cirrhotic patients is highly recommended. Recommendations for further research to other scores like APACHE III and APACHE IV in predicting mortality in cirrhotic patients.

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