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Child-Turcotte-Pugh versus Model for End Stage Liver Disease Score for Predicting Survival in Hospitalized Patients with Decompensated Cirrhosis

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ABSTRACT

Background: Short term and medium term survival predictive value of the Child-Turcotte-Pugh (CTP) and Model for End Stage Liver Disease (MELD) score has been established but their usefulness in predicting survival of hospitalized patients with decompensated cirrhosis is lacking. We compared the survival predictive value of these scoring systems in hospitalized patients of decompensated cirrhosis and other associated factors.

Methods: A prospective, observational study in 216 consecutive cases of decompensated cirrhosis admitted in medical ward, were enrolled if the inclusion criteria were fulfilled. All cases were investigated and treated as per standard guidelines and clinician's judgment. CTP and MELD score were calculated for each case at the time of admission and followed throughout the hospital stay till discharge/death. The accuracy of the different score systems for predicting survival was evaluated through the area under ROC curve.

Results: CTP and MELD score were higher (12.44±1.07, 31.91±4.92) in expired cases than who improved and discharged (11.32±1.28, 23.97±5.36) respectively with significant p-value (<0.001). Area under ROC curve for serum creatinine, MELD score, blood urea and CTP score for predicting hospital survival were 0.887, 0.864, 0.836 and 0.738 respectively.

Conclusions: MELD score is superior to CTP score in predicting survival at the time of discharge in hospitalized patients with decompensated cirrhosis. Renal failure in patients with decompensated cirrhosis carries poor prognosis and has a good outcome prognostic value, even superior to MELD/CTP scoring.

Keywords: Child-Turcotte-Pugh Score; decompensated cirrhosis; model for end stage liver disease score; receiver operator characteristic curve.

INTRODUCTION

Decompensated cirrhosis has a poor prognosis and the mortality rate is much higher when cirrhotic patients require hospital admission due to recurrent episodes of liver decompensation and extrahepatic complications.[1] The poor survival of cirrhotics has driven physicians to a search for good short and long term prognostic markers.[2] The Child-Turcotte classification modified by Pugh has been widely applied prognostic markers in patients with cirrhosis and commonly used clinical instruments to risk-stratify cirrhotic patients.[3,4] The Model for End-stage Liver Disease (MELD) score is a new liver-specific prognostic model, currently used in donor liver allocation systems in USA.[5] Both have been validated for short and long-term survival in cirrhotics but its accuracy has never been evaluated in admitted cirrhotic patients.[1,6]

Our aim was firstly to evaluate and compare survival predictability of CTP and MELD score for decompensated cirrhosis in hospitalized patients and to identify the other predictive factors for mortality.

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METHODS

A prospective cross sectional study was conducted in Department of Medicine, B.P. Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal. Total 216 cases of decompensated cirrhosis, except patients with age below 18 years and severe primary cardiopulmonary failure or intrinsic kidney disease were studied from August 2007 to September 2008. Ethical approval from institutional review board was taken for the study along with the informed verbal consent from all patents. All cases were investigated and treated as per standard guidelines and clinician's judgment.

According to our routine clinical practice, detailed clinical history including demographic profile, presenting features, etiology and cause of admission were recorded from the patients and/or guardian in the predesigned proforma along with relevant clinical examination and laboratory investigations to establish the diagnosis and management of the patients. The case of clinical cirrhosis was diagnosed by having at least one clinical sign of hepatocellular failure and one of portal hypertension along with at least three USG findings suggestive of cirrhosis and /or liver biopsy.[7] In this study, the diagnosis of decompensated cirrhosis is based on clinical, laboratory and radiological signs of cirrhosis with at least one sign of liver decompensation: ascites,variceal bleeding, hepatic encephalopathy, non-obstructive jaundice. The cause of cirrhosis was considered to be chronic hepatitis B virus infection in cases with long standing(>6 months) HBsAg positivity; chronic hepatitis C virus (HCV) infection in cases with detectable antibodies against HCV (anti-HCV); alcoholic liver disease in cases with a compatible history with a significant amount of alcohol intake, AST/ALT ratio more than one and absence of other causes of liver injury; primary biliary cirrhosis in cases with elevated alkaline phosphatase, positive anti-mitochondrial antibodies and/or compatible previous histological findings; primary sclerosing cholangitis in cases with elevated alkaline phosphatase and compatible radiological and/or histological findings. Spontaneous bacterial peritonitis(SBP) was diagnosed when the ascitic fluid culture grows pathogenic bacteria or the ascitic fluid neutrophils count >250 cells/mm^3 and there is no evidence of surgically treatable intra-abdominal sources of infection.[8,9]

Based on the admission data, the CTP score (range: 5-15) and CTP class were estimated for each patient according to the suggestion by Pugh et al,[4] while the MELD score (range: 6-40) was calculated according to the formula proposed by Kamath et al,[5] and followed throughout the hospital stay till discharge/death.

All data were analyzed using the statistical program SPSS (PC+) version 11.0. Results were expressed as mean values (±SD) or as median values (range). Qualitative variables were compared by corrected x^2 test and quantitative variables by t-test. The accuracy of the different score systems for predicting short-term survival was evaluated through the urea under the receiver operating characteristic (ROC) curve. The accuracy of the different models as predictors of survival was evaluated by the concordance (c)-statistics (equivalent to the area under the ROC curve). Each model was considered to have prognostic accuracy in case of a c-statistics >0.70 and excellent prognostic accuracy in case of a c-statistics >0.80.

RESULTS

The study from August 2007 to September 2008 enrolled a total of 216 cases; mostly from eastern part of Nepal with mean age was 51.31 years and male/female ratio of 1.88:1. Baseline characteristics features of all cases are presented in (Table 1).

In only 18 patients, other acute illness was present in addition to features of hepatic decompensation at the time of admission. In 13 patients, pneumonia was present whereas 5 patients was suffering from urinary tract infection. There were 30 patients who were diagnosed having decompensated cirrhosis for the first time at the time of admission whereas 104 cases were having cirrhosis for ≤6 months, 77 patients for 7-12 months and 5 patients for more than 12 months. Thirty one patients were with diabetes mellitus, 27 with hypertension, 8 with chronic obstructive pulmonary disease and 2 with congestive cardiac failure with underlying heart disease. Only 5 patients were suffering from both diabetes mellitus and hypertension. In 110 (50.9%) patients urea was raised and maximum was upto 216 mg/dl whereas 93 patients (43.1%) was having raised creatinine and maximum upto 4.1 mg/dl but in two cases dialysis was done later. Rest was managed conservatively. In our patients with cirrhosis,dyselectrolytemia was very common and upto 192 (88.9%) patients were having hyponatremia and 36 (16.7%) patients had severe hyponatremia (<120 meq/L).

Mortality

There was total 68 death including 32 cases left against the medical advice. Most common cause of death in our cirrhotic patients was GI bleed 13 (19.11%) leading to shock and followed by renal failure 12 (17.64%) and hepatic coma 7 (10.29%). Only 4 (5.8%) patients died due to ongoing sepsis.Thirty Four patients expired out of 113 who presented with GI bleed, 43 out of 83 patients in case of HE, 8 out of 26 patients in case of SBP, 24 out of

142 patients in case of esophageal varices (10% in grade -I, 15.1% in grade-II, 25.1% in grade-III).

Factors associated with mortality

(Table 2 A and B) show variables associated with death of patients with decompensated cirrhosis. The variables significantly associated with in mortality are increasing age, longer duration of cirrhosis, low blood pressure at the time of presentation, increased respiratory rate, HE, presence of coagulopathy, impaired renal function, hyponatremia, more CTP and MELD score at the time of admission.

Table 1. Baseline characteristics of 216 patients with decompensated cirrhosis.

Characteristics		Mean (% Range)	Std. Deviation
Age (yr)		51.31 (30-89)	11.5
Sex, male		141 (65.3)	
Duration of cirrhosis (months)		5.25 (0-24)	4.13
Cause of cirrhosis	Alcohol	208 (96.3)	
	HBV	5 (2.3)	
	HCV	3 (1.4)	
Presenting features on admission	Ascites	211 (97.7)	
	GI Bleeding	113 (52.3)	
	Encephalopathy	83 (38.4)	
	Jaundice	213 (98.6)	
SBP on admission		26 (12.0)	
Blood Pressure (mmhg)	Systolic BP	109.31 (70-160)	18.93
	Diastolic BP	72.19 (50-100)	11.86
PulseRate (/min)		103.75 (59-136)	13.51
Respiratory Rate(/min)		22.74 (14-36)	3.70
Hemoglobin (gm/dl)		9.768 (3.7-14)	1.783
White blood Count (/mm^3)		9,174.54 (4,100-28,900)	3962.41
Platelet Count (/mm^3)		1,43,796.30 (14,000-5,60,000)	58741.97
Prothrombin Time (sec)		35.96 (13-100)	13.07
INR*		2.75 (1-8)	1.02
Urea (mg/dl)		50.35 (23-133)	24.85
Creatinine (mg/dl)		1.532 (0.4-4.1)	0.699
Sodium (meq/L)		127.79 (108-143)	6.84
Potassium (meq/L)		4.16 (2-6)	0.72
Bilirubin (mg/dl)		5.72 (1-22)	3.6
Albumin (mg/dl)		2.662 (1.8-4.0)	0.465
AST (IU/L)		138.12 (38-659)	66.02
ALT (IU/L)		74.63 (19-224)	37.70
CTP score		11.68(8-15)	1.32
CTP class	B	11 (5.1)	
	C	205 (94.9)	
MELD score		26.47 (9-40)	6.3

*INR- International Normalized Ratio, AST-AspartateTransaminase, ALT- AlanineTransaminase

Table 2A. Parameters associated with survival (quantitative variables) comparison by *t*-test.

Variables	Outcome	n	Mean±Std.Dev.	Mean Diff (95%CI)	P Value
Age(yrs)	Improved, Discharged, Expired	148 68	50.13±11.35 53.90±12.56	-3.77 (-7.16--0.38)	0.03*
Durationof disease (months)	Improved, Discharged, Expired	148 68	4.86±4.30 6.10±3.62	-1.24 (-2.35-0.13)	0.04*
SystolicBP(mmhg)	Improved, Discharged, Expired	148 68	112.95±18.83 101.38±16.70	11.56 (6.31 - 16.82)	<0.001*
DiastolicBP(mmhg)	Improved, Discharged, Expired	148 68	74.18±11.59 67.88±11.35	6.29 (2.97-9.62)	<0.001*
Pulse rate (/min)	Improved, Discharged, Expired	148 68	102.75±12.01 105.94±16.20	-3.19 (-7.08 - 0.70)	0.107
Resp. rate (/min)	Improved, Discharged, Expired	148 68	22.18±3.69 23.94±3.42	-1.76 (-2.80--0.72)	0.001*
Hemoglobin (g/dl)	Improved, Discharged, Expired	148 68	9.733±1.895 9.844±1.519	-0.111 (-0.627 - 0.405)	0.672
White blood cell (/ mm^3)	Improved, Discharged, Expired	148 68	8852.03±3747.82 9876.47±4339.96	-1024.44 (-2163 - 114.12)	0.078
Platelet Count (/mm^3)	Improved, Discharged, Expired	148 68	152128.38±61052.48 125661.76±49.68.52	26466.61 (9842.28 - 43090.95)	0.002*
Blood sugar(R) (mg/dl)	Improved, Discharged, Expired	148 68	107.91±28.20 105.65±22.50	2.27 (-5.4 - 9.93)	0.561
Urea(mg/dl)	Improved, Discharged, Expired	148 68	40.39±17.71 72.03±24.46	-31.64 (-37.43--25.84)	<0.001*
Creatinine (mg/dl)	Improved, Discharged, Expired	148 68	1.224±0.415 2.203±0.724	-0.979 (-1.132--0.825)	<0.001*
Sodium(mmol/l)	Improved, Discharged, Expired	148 68	128.85±6.55 125.47±6.94	3.38 (1.45 - 5.31)	0.001*
Potassium(mmol/l)	Improved, Discharged, Expired	148 68	4.12±0.67 4.25±0.81	0.13	0.207
Albumin(mg/dl)	Improved, Discharged, Expired	148 68	2.742±0.474 2.488±0.393	0.254 (0.124 - 0.384)	<0.001*
AST(IU/l)	Improved, Discharged, Expired	148 68	136.22±71.53 142.26±52.31	-6.05 (-25.14 - 13.04)	0.533
ALT (IU/l)	Improved, Discharged, Expired	148 68	72.75±37.64 78.71±37.78	-5.96 (-16.84 - 4.93)	0.533

AST/ALT	Improved, Discharged, Expired	148 68	1.99735±0.77591 1.95364±0.70995	-1.16 (-2.19--0.13)	0.693
Bilirubin (Total) (mg/dl)	Improved, Discharged, Expired	148 68	5.35±3.58 6.51±3.53	-6.61 (-10.28--2.93)	0.027*
ProthrombinTime (sec.)	Improved, Discharged, Expired	148 68	33.88±12.19 40.49±13.85	-0.51 (-0.8--0.22)	<0.001*
INR	Improved, Discharged, Expired	148 68	2.59±0.96 3.10±1.07	-1.12 (-1.47—0.76)	<0.001*
CTP Score	Improved, Discharged, Expired	148 68	11.32±1.28 12.44±1.07	-7.95 (-9.46--6.44)	<0.001*
MELD Score	Improved, Discharged, Expired	148 68	23.97±5.36 31.91±4.92	2.95 (2.11 - 3.79)	<0.001*
Duration of Hospital stay (days)	Improved, Discharged, Expired	148 68	6.42±2.94 3.47±2.80		<0.001*

Note: starred variables considered significant (p value <0.05).

Table 2B. Parameters associated with survival (qualitative variables) comparison by X^2 test.

Variables	N	n (%) deaths	p-value
Male	141	45 (31.91)	0.973
Female	75	23 (30.66)	
Ascites present	211	68 (32.22)	0.148
Ascites absent	5	0 (0)	
GI bleed present	113	34 (30.08)	0.753
GI bleed absent	103	34 (33)	
HE absent	133	25 (18.79)	<0.001*
HE present	83	43 (51.80)	
Jaundice present	213	68 (31.92)	0.320
Jaundice absent	3	0 (0)	
Alcoholic cirrhosis	208	66 (31.73)	0.513
Non alcoholic Cirrhosis	8	2 (25)	
HBsAg-	211	66 (31.27)	0.503
HBsAg+	5	2 (40)	
Anti HCV-	213	68 (31.92)	0.320
Anti HCV+	3	0 (0)	
Diabetes mellitus-	185	56 (30.27)	0.467
Diabetes mellitus+	31	12 (38.70)	
COPD absent	208	65 (31.25)	0.487
COPD present	8	3 (37.5)	
HTN absent	189	60 (31.74)	1.00
HTN present	27	8 (29.62)	
Pneumonia -	201	64 (31.84)	0.462
Pneumonia +	15	4 (26.66)	
SBP absent	148	54 (36.73)	0.734
SBP present	26	8 (30.76)	
Varices present	142	24 (16.9)	0.289
Varices absent	12	0 (0)	

**Note: starred variables considered significant (p value <0.05).*

Prognostic factors associated with mortality - Receiver operating characteristic curves

(Figure 1,2) and (Tables 3,4) show ROC curve for CTP and MELD scores, and other variables significantly associated with mortality of hospitalized patients with decompensated cirrhosis and area under ROC curve (AUROC/concordance or c-statistics). MELD score is significantly superior to CTP score in predicting survival in hospitalized patients with decompensated liver disease and AUROC are 0.864 and 0.734 respectively and among other variables creatinine(AUROC= 0.887)and urea(AUROC=0.836) has got good prognostic value.

Table 3. Area Under the ROC Curve (AUROC) for CTP and MELD score.

Test Result Variable(s)	Area
MELD score	0.864
CTP score	0.738

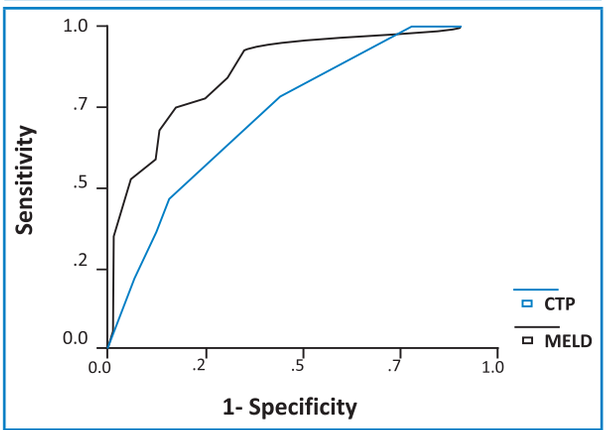

Figure 1. ROC Curve for CTP and MELD score.

Table 4. Area Under ROC Curve (AUROC) for other prognostic variables.

Test Result Variable(s)	Area
Duration of cirrhosis	0.617
Systolic BP	0.303
Diastolic BP	0.355
RespiratoryRate	0.661
Platelet Count	0.364
Urea	0.836
Creatinine	0.887
Sodium	0.361
Albumin	0.320
Total Bilirubin	0.609
Prothrombin Time	0.651
INR	0.649

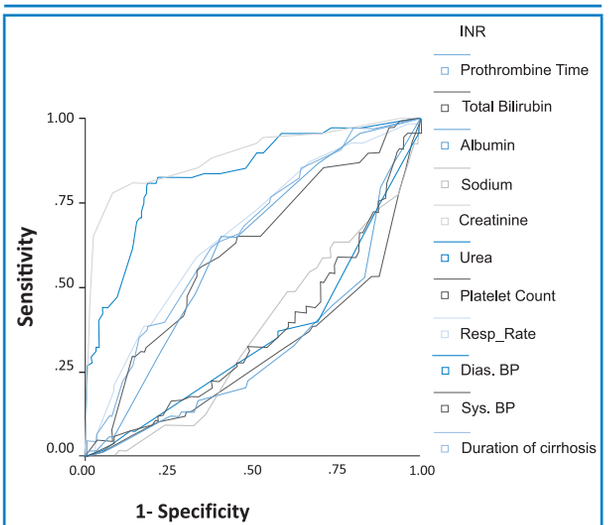

Figure 2. ROC Curves for other prognostic variables.

DISCUSSION

Accurate prognostic indicators for decompensated cirrhosis for survival in ward are important and help to guide clinical decision making, talking to families of patients. This is particularly relevant in cirrhotic patients, as mortality remains high despite intensive support.[1] In our study, we evaluated predictors from patients' clinical and laboratory variables available at the time of admission to generate a useful prognostic model for cirrhotic patients who require inpatient care. From Nepal, as far as we aware, this is the first study on comparison of survival predictability of CTP and MELD score for decompensated cirrhosis in hospitalized patients.

Total Hospital mortality was 68 in which 36 patients expired in hospital and 32 patients left against medical advicebecause of deteriorating health condition or no improvement during hospital stay. Case fatality rate was 31.5% and only 5 patients got intensive care unit (ICU) care during treatment. Cause of high mortality rate could be due to lack of bed in ICU at the time of admission, reluctation of patients' relatives to afford for treatment after knowing prognosis and nature of end stage liver disease.

Highest mortality rate was found in case of gastrointestinal bleed patients 19.4% and more severe bleeding with increasing grade of oesophageal varices, may be due to unavailability of emergency variceal band ligation in our institution and lack of early blood transfusion due to scarcity of blood in our blood bank and high cost of octreotide, followed by deteriorating renal failure with no response to conservative management and even dialysis support in two cases and increasing severity of hepatic encephalopathy.

Mean duration of hospital stay was 5.49 days (SD±3.2) and range was 1 to 17 days but it was 6.42 days (SD±2.94) in who survived and discharged and 3.47days (SD±2.80) in who expired which was statistically significant with value <0.001.This could be explained by those who expired were more sick and expired early.

Parameters significantly associated with hospital mortality in decompensated cirrhosis were low systolic BP(P<0.001), low diastolic BP(P<0.001), high respiratory rate (P=0.001), low platelet count(P=0.002), high urea(P<0.001), high creatinine (P<0.001), low sodium(P=0.001), low albumin(P<0.001), high PT/INR(P<0.001), presence of HE(P<0.001).These findings are commonly associated with hospital mortality in any sick patients and have been found in many studies.

The mean CPT score (112.44 with SD±1.07) and MELD score (31.91 with SD±4.92) in expired patients were more than those who survived and discharged-CTP score (11.32 with SD±1.28), MELD score (23.97 with SD±5.36) and P value was <0.001 in both scoring.Our

data support that MELD score is significantly superior to CP score in predicting survival in hospitalized patients with decompensated liver disease. The concordance c-statistics (equivalent to the area under the ROC curve) for prediction of hospital survival by the MELD and CTP score are 0.864 and 0.738 respectively. Thus MELD has good prognostic accuracy(c-statistics>0.80).

In a study done by Markus W et al (2003) in patients admitted in ICU showed that short term prognosis is influenced by the degree of hepatic insufficiency and by dysfunction of extrahepaticorgan systems. Cumulative mortality rates were 36% in the ICU, 46% in the hospital. By using the area under receiver operating characteristic curves, the Sequential Organ FailureAssessment (SOFA) showed an excellent discriminative power (AUROC= 0.94), which was clearly superior to the Acute Physiology and Chronic Health Evaluation(APACHE) II (AUROC= 0.79) and the Child-Pugh system (AUROC= 0.74),[10] but similar study done by Serra MA et al. (2001) found that the prediction accuracy according to the area under the ROC curve was greater for the MELD scale than for serum creatinine.[11]

But in our study the concordance c-statistics for prediction of hospital survival by the serum creatinine, MELD score, blood urea and CTP score are 0.887, 0.864, 0.836 and 0.738 respectively. Thus showing renal failure in patients with decompensated cirrhosis carries poor prognosis and has a good prognostic value, comparable or even superior to MELD/CTP scoring.

Similar result was also seen in a study done by Michael S et al (2006) and they found that in patients with cirrhosis and renal failure, hepatorenal syndrome is associated with a worse prognosis than kidney dysfunction due to other conditions but only HRS type 1 has independent prognostic relevance in addition to the MELD score.[12]

The main drawbacks of the old CTP score are the inclusion of two subjective parameters, such as ascites and encephalopathy, and the estimation of three objective parameters, prothrombin time, serum bilirubin and albumin levels, as categorical variables.[4] Thus, in the CTP score, there may be significant interobserver variation in the assessment of the severity of ascites and encephalopathy, which may easily change by medical interventions, while an extended range of values of prothrombintime; bilirubin and albumin levels take the same points even if they may reflect different degrees of liver failure. Moreover, CTP score does not take into account the patient's renal function, which appears to be strongly associated with survival.[13] Limitations of our study are: other causes of cirrhosis could not be confirmed due to lack of liver biopsy in our institute, CTP class is not useful as in our study most of the cases were in class C, there are many cases of left against the medical advice which might have affected the result and high mortality may be due to inability to provide ICU care to the patients who needed it.

In conclusion, we can say MELD score is significantly superior to CTP score in predicting survival in hospitalized patients with decompensated cirrhosis in addition to usefulness in predicting short-term and medium-term survival in patients with decompensated cirrhosis. Renal failure in patients with decompensated cirrhosis carries poor prognosis and has a good prognostic value, comparable or even superior to MELD/CTP scoring.

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