How Does Aspartate Aminotransferase-to-Platelet Ratio Index (APRI) Hold Up in Predicting Adverse Outcomes and Prognosis among Patients with Chronic Liver Disease Compared to Other Liver Scoring Systems?

Siddharth Gosavi[1], Samarth Sangamesh[2], Amogh Ananda Rao[3], Shashank Shastry[4], Aishwarya Hulikal[5], Ayushi Mendiratta[6]

[1, 2, 3, 4, 5, 6] Department of General Medicine, J.J.M. Medical College, Davangere, Karnataka, India.

ABSTRACT

BACKGROUND

Chronic liver disease is the progressive destruction of liver for 6 months thereby impairing clotting factor formation, bile metabolism, and protein synthesis. Child-Pugh-Turcotte (CTP) score, model for end-stage liver disease (MELD) and MELD–sodium (Na) are well established calculated parameters to predict prognosis in chronic liver disease (CLD) patients. This study was conducted to determine as to how aspartate aminotransferase : platelet ratio index (APRI) fares in predicting adverse outcomes and prognosis among patients with chronic liver disease compared to other liver scoring.

METHODS

This was a cross-sectional hospital-based study of inpatients admitted in the department of General Medicine at Chigateri General Hospital. MELD, MELD-Na, Child-Pugh-Turcotte score, and APRI index, were applied and calculated on all the 50 patients to stage the chronic liver disease, and were followed up for 3 months.

RESULTS

19 patients survived and 31 patients died. Among the 31 dead patients, 24 had MELD score of greater than 21.5 points. Sensitivity of MELD & MELD-Na in predicting mortality was 77.42 %. Diagnostic accuracy for both scores was 74 %. All patients who died had a Child Pugh score of greater than 10. The sensitivity of CTP scoring was 100 % and diagnostic accuracy was 98 %. 76 % of our patients experienced severe fibrosis according to APRI index. 4 % experienced significant fibrosis. 20 % of the patients did not have significant fibrosis. The least sensitivity (61.29 %) and diagnostic accuracy (62 %) was observed with APRI. However, positive predictive value was 73.08 % and diagnostic accuracy was 65 % for mortality.

CONCLUSIONS

Given the minimal investigations required in calculating APRI, it can be used as a fair indicator predicting status of the patient especially in resource limited settings.

KEYWORDS

Child Pugh Turcotte Score, APRI Index, MELD Score, MELD Na Score

Corresponding Author:
Dr. Amogh Ananda Rao,
General Medicine,
J.J.M. Medical College,
Dental College Road,
MCC B- Block, Davangere - 577004,
Karnataka, India.
E-mail: amoghanand7596@gmail.com

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BACKGROUND

Chronic liver disease is the progressive destruction of the liver for 6 months thereby impairing clotting factor formation, bile metabolism and protein synthesis. It is characterised by sequential fibrosis of the liver with modification in hepatic architecture and regenerative nodule formation. It is an irreversible breakdown of the liver with transplantation being the only treatment.

Numerous aetiologies for chronic liver disease have been described, which include toxins, long term alcohol abuse, infections, autoimmune diseases, genetic and metabolic disorders.

If left untreated, complications like variceal haemorrhage, portal hypertensive gastropathy, ascites, spontaneous bacterial peritonitis, hepatorenal syndrome, hepato-pulmonary syndrome, hepatic hydrothorax, portopulmonary syndrome, cirrhotic cardiomyopathy, hepatic encephalopathy, hepatocellular carcinoma and portal vein thrombosis may occur.[1,2]

Child Pugh Turcotte Score			
Criteria	**1**	**2**	**3**
Encephalopathy	None	Mild to moderate	Severe
Ascites	none	Mild to moderate	Severe
Bilirubin	< 2	2 – 3	> 3
Albumin	> 3.5	2.8 – 3.5	< 2.8
Prothrombin time	< 4	4 – 6	> 6
INR	< 1.7	1.7 – 23	> 2.3
Table A. Child Pugh Turcotte Score			
Class A = 5 to 6 points Class B = 7 to 9 points Class C = 10 to 15 points			

Model for end stage liver disease score:

$$MELD = 3.78 \times log\ serum\ bilirubin\ (mg\ /\ dL) + 11.20 \times log\ INR\ + 9.57 \times log\ serum\ creatinine\ (mg/) + 6.43\ (constant)$$

APRI Index:

$$APRI = \frac{\text{AST / AST (upperlimit of normal)} \times 100}{\text{Platelet count (109/L)}}$$

The Child-Pugh score was proposed by Child and Turcotte (1964). Initially, it was used as a predictor of variceal bleeding in patients undergoing portosystemic shunt surgeries. Child and Turcotte included ascites, hepatic encephalopathy, nutritional status, total bilirubin and albumin. Pugh added prothrombin time instead of nutrition in the scoring system (1972) (Graph 1).[3]

Model for end-stage liver disease score (MELD score) was initially proposed in patients undergoing trans-jugular intrahepatic portosystemic shunt. The parameters now described are international normalised ratio (INR), total bilirubin, serum creatinine and need for dialysis (at least twice in the past 1 week) (Graph 1). It is particularly useful in planning liver transplant, predicting mortality after transjugular intrahepatic portosystemic shunt (TIPS) surgery, cirrhotic patients undergoing non-transplant surgical procedures, acute alcoholic hepatitis and acute variceal haemorrhage. However, hyponatremia and malnutrition are not accounted for in the MELD score.[4]

The triumvirate complications like refractory ascites, hyponatremia and the hepatorenal syndrome were incorporated to bring out a new scoring system known as the MELD-Na scoring system. It gave a better account of the prognosis of cirrhosis and graft allocation system became much easier. The only limitation of this scoring is diuretic use and intravenous (IV) fluid administration that alters serum sodium levels. However, this was found to be better than MELD score.[5,6]

The accuracy of Child Pugh Turcotte and MELD scoring systems have been adequately emphasised in literature. Although performing the tests required to calculate the scores are expensive which is significant especially in a resource limited setting like India.

APRI index (Table 1, 2 and 3) uses aspartate transaminase (AST) and platelet count to estimate liver fibrosis, which is an extension of liver damage and compensatory state of hepatic function. It is cost-effective and non-invasive.[7]

There have been few previous studies comparing all the 4 above mentioned scoring systems.[8] This study was conducted to compare the predictive values of all 4 scoring systems, i.e. to know how does aspartate aminotransferase : platelet ratio index (APRI) hold up in predicting adverse outcomes and prognosis among patients with chronic liver disease compared to other liver scoring.

METHODS

This was a prospective cross-sectional hospital-based study of inpatients admitted in the Department of General Medicine at Chigateri General Hospital, JJM Medical College, Davangere, between March 2020 and August 2020. The inclusion criteria were defined as patients diagnosed with chronic liver disease, aged between 18 to 85 years with informed written and oral consent. Patients with malignancies and patients on immunosuppressive drugs were not included in the study. The size of the sample was 50 patients. The study was started after obtaining a clearance from the institutional ethics committee.

Sample size was calculated using the formula:

$$N = Z^2 P\ (1 - P) d^2$$

Where Z = level of confidence (95 %); d = precision (0.04)

P = approximate prevalence of disease (0.05 %) (population served by the hospital was approximately 1,00,000. There were 65 new cases of CLD diagnosed during the study period. 5 patients fit the exclusion criteria (2 – malignancy, 3 – immunosuppressant therapy). 10 patients did not give consent to be included in the study.

Since there were no pilot studies performed to estimate the prevalence, the incidence per month was multiplied by 180 to account for the past 15 years and adjusted for mortality. This gives an approximate prevalence of 0.05 %.

Precision level of 0.04 was taken as advised by a study conducted by Pourhoseingholi et al.[9]

Fifty patients of chronic liver disease were subjected to blood investigations like complete blood count (CBC), red blood cells (Random Blood Sugar), renal function test (RFT), liver function test (LFT), serum electrolytes, human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), hepatitis B virus (HCV) and coagulation profile.

Electrocardiogram (ECG) and ultrasound abdomen and pelvis were also done for all the patients. Four scoring systems MELD, MELD-Na, Child-Pugh-Turcotte score and APRI index were applied and calculated on all the 50 patients to stage the chronic liver disease. The patients were observed for a week or till they died. The survivors were then followed up for up to 3 months.

Data analysis was conducted using International Business Machines Statistical Package for the Social Sciences (IBM SPSS) version 22. Descriptive statistics, Shapiro-Wilk test, chi-Square test and receiver operative curve analysis were all applied.

RESULTS

Mean age of the study population was 60.64 years (SD = 13.3 years) with a minimum age of 36 years and a maximum age of 82 years. There were 12 patients aged under 50 years and 38 patients above 50 years. There were 31 males and 19 females. 19 patients survived and were discharged, 31 patients died.

It is noteworthy that the total mortality amongst study subjects was high (62 %). This was since the hospital in which the study was conducted was a tertiary care centre and received such complicated cases. Alcoholism was the most important factor in development of chronic liver disease (only alcohol consumption history greater than 15 years was considered). 88 % of our patients were alcoholics. Baseline parameters associated with morality are described in Table 1.

	Parameter	Mortality Dead (N = 31)	Mortality Survived (N = 19)	P Value
	Age (Mean ± SD)	**59.9 ± 13.89**	**61.84 ± 12.55**	**0.622**
Age group	< 50 years	8 (25.81 %)	4 (21.05 %)	1.000
	> = 50 years	23 (74.19 %)	15 (78.95 %)	
Gender	Male	19 (61.29 %)	12 (63.16 %)	0.895
	Female	12 (38.71 %)	7 (36.84 %)	
Condition	CLD	0 (0 %)	2 (10.53 %)	*
	CLD with hepatitis C	0 (0 %)	2 (10.53 %)	
	CLD-alcohol	29 (93.55 %)	15 (78.95 %)	
	CLD-full blown Tb	2 (6.45 %)	0 (0 %)	
Score ± SD	MELD mean ± SD	25.94 ± 5.49	19.47 ± 4.86	< 0.001
	MELDNA mean ± SD	27.39 ± 5.96	20.26 ± 4.49	
	Child Pugh mean ± SD	12.35 ± 0.84	8.89 ± 0.66	< 0.001 < 0.001
	APRI score mean ± SD	3.59 ± 2.28	1.59 ± 1.77	0.002
	SGOT mean ± SD	126.97 ± 43.07	80.37 ± 59.15	0.002
	SGPT mean ± SD	44.65 ± 13.9	45.74 ± 15.46	0.797

Table 1. Comparison of Baseline Parameters between Mortality (N = 50) (Shapiro Wilk Test and Fisher's Exact Test were Used)

The mean MELD score of the study population was 23.48 ± 6.1. (Table 2). Mean MELD-Na score was 24.68 ± 6.43. (Table 2). Mean Child-Pugh score was 11.04 ± 1.86. (Table 2). Mean APRI index score was 2.83 ± 2.3. (Table 2).

Parameter	Mean ± SD	Minimum	Maximum
MELD	23.48 ± 6.1	14.00	34.00
MELD NA	24.68 ± 6.43	14.00	38.00
Child Pugh	11.04 ± 1.86	8.00	13.00
APRI score	2.83 ± 2.3	0.10	7.90

Table 2. Descriptive Analysis of Scores in Study Population (N = 50)

The mean serum glutamic-oxaloacetic transaminase (SGOT) of the population was 109.26 ± 54.25 units / L. The mean serum glutamic-pyruvic transaminase (SGPT) was 45.06 ± 14.36 units / L. Among the 31 patients who died, 24 had a MELD score of greater than 21.5 points. 7 patients had a MELD score of fewer than 21.50 points. Among the 19 surviving patients, 6 had a MELD score of greater than 21.5 points and 13 had a MELD score of fewer than 21.50 points. The sensitivity of MELD in predicting mortality was 77.42 % (Table 1).

31 (all) patients who died had a Child-Pugh score of greater than 10 points. Among the surviving patients (19), 18 patients had a score of fewer than 10 points (Table 1). 76 % of our patients experienced severe fibrosis according to APRI index. 4 % experienced significant fibrosis. 20 % of the patients did not have significant fibrosis. (Table 1) Among the dead group, 19 patients had an APRI score of greater than 2.05 points, 12 patients had an APRI index of fewer than 2.05 points. Among the survival group, 7 patients had an APRI score of greater than 2.05 points and 12 patients had an APRI index of fewer than 2.05 points (Table 1).

In our study, the sensitivity of Child-Pugh Turcotte (CTP) scoring was 100 % and diagnostic accuracy was 98 %. These findings agree with a study conducted by Gagandeep Acharya et al. In this study it was observed that Child-Pugh was superior to MELD and MELD-Na in predicting 3-month mortality.[9] Whereas the sensitivity of MELD and MELD-Na was 77.42 % and diagnostic accuracy for both was 74 %. MELD-Na was better than MELD as it considers the complications of cirrhosis.[4] The least sensitivity and diagnostic accuracy were observed with APRI index scoring (61.29 % & 62 % respectively). Table 3 compares the predictive validity of the 4 scoring systems used.

Parameter	Child Pugh Turcotte	MELD Meld	MELD Meld Na	APRI Index
Sensitivity	100.00 %	77.42 %	77.42 %	61.29 %
Specificity	94.74 %	68.42 %	68.42 %	63.16 %
False positive rate	5.26 %	31.58 %	31.58 %	36.84 %
False negative rate	0.00 %	22.58 %	22.58 %	38.71 %
Positive predictive value	96.88 %	80.00 %	80.00 %	73.08 %
Negative predictive value	100.00 %	65.00 %	65.00 %	50.00 %
Diagnostic accuracy	98.00 %	74.00 %	74.00 %	65.00 %
Area under ROC curve	0.994	0.826	0.834	0.802

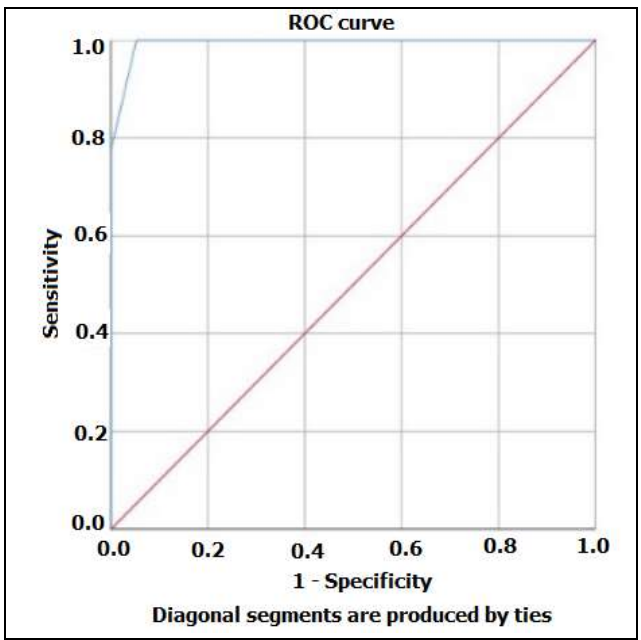
Table 3. Comparison of Predictive Validity of the 4 Scoring Systems in Predicting Mortality (N = 50)

Area under ROC curves of CTP, MELD, MELD Na, APRI index are 0.994, 0.826, 0.834, 0.802, respectively. This implies CTP score is the best among the systems.

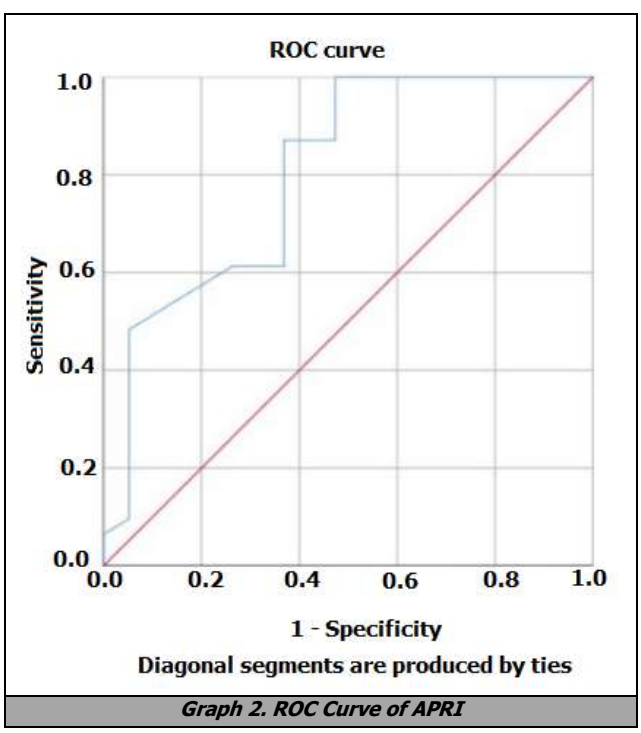
Though APRI ranks inferior in comparison, it has 73 % positive predictive value and 65 % diagnostic accuracy for mortality. Given the minimalistic investigations required in

calculating APRI, it can be used as a fair indicator into the status of the patient especially in low resource settings.

To further compare, ROC curves drawn for CTP score and APRI score and the results are as follows (Graph 1, 2). Area under ROC for APRI was 0.802 with P-value < 0.001. Area under ROC for CTP score was 0.994 with P-value < 0.001. This implies that CTP is superior to APRI.



Graph 1. ROC Curve for CTP Score



Graph 2. ROC Curve of APRI

The end-stage liver disease leads to a rise in morbidity and mortality, with most preventable cases attributed to excessive alcohol consumption, viral hepatitis or non-alcoholic fatty liver disease (NAFLD). Single or multifactorial damage to the liver results in cirrhosis. The most common factors being alcohol abuse, chronic hepatitis C and obesity with concomitant NAFLD. In a study conducted by Shrestha et al. at a tertiary care centre in Nepal, 130 patients diagnosed with liver disease were analysed; most of the patients were in the range of 41 – 50 years of age, followed by those at 31 – 40 years of age.[8]

Our findings agree with the findings of that study since most of the patients were above 40 years of age.

DISCUSSION

Among the 31 patients who died, 24 had a MELD score of greater than 21.5 points. 7 patients had a MELD score of fewer than 21.50 points. Among the 19 surviving patients, 6 had a MELD score of greater than 21.5 points and 13 had a MELD score of fewer than 21.50 points. The sensitivity of MELD in predicting mortality was 77.42 % (Table 1).

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Whereas the sensitivity of MELD and MELD-Na was 77.42 % and diagnostic accuracy for both was 74 %. MELD-Na was better than MELD as it considers the complications of cirrhosis.[4]

In our study, the least sensitivity and diagnostic accuracy were observed with APRI index scoring (61.29 % & 62 % respectively).

CONCLUSIONS

The CTP score was superior to the MELD and MELD-Na scores and APRI index in predicting 3-month mortality outcomes. APRI index may be considered as a useful screening tool especially in low resource settings due to its simplicity. The performance of any scoring method for end-stage liver disease may depend on the variable clinical settings, and aetiologies of liver disease occurring in the different regions.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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