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AST to platelet ratio index for predicting the in-hospital mortality in chronic liver disease patients in tertiary care hospital

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ABSTRACT

Background: Liver cirrhosis is the end result of chronic liver injury. Cirrhosis of liver may progressively deteriorate from a well-compensated state to decompensated conditions. **Aims and Objective:** Our study aims at evaluating the AST to Platelet Ratio Index (APRI) for predicting the in-hospital mortality and also comparing APRI, MELD and albumin for predicting in hospital mortality in chronic liver disease. **Materials and Methods:** Data of Patients with Chronic liver disease were retrospectively reviewed. MELD and APRI scores were calculated for the patients and results from ROC curves were analysed. **Results:** In our study conducted on 299 patients, the age distribution was between 18-64 years with mean age of patients being 46.47 +/-10.9 years, sex ratio Male: Female: 266:37 with mortality rate of 17.7%. The Area under curves of ROC of APRI, MELD and Albumin are 0.63, 0.76 and 0.55. **Conclusion:** APRI is an independent predictor of mortality. The prognostic performance of all 3 was comparable but MELD has better prognostic significance than APRI score.

Key words: Aspartate aminotransferase to platelet ratio index; Model of end stage liver disease; Area under curve; Alanine transaminase; Hepatitis C virus

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INTRODUCTION

Liver cirrhosis is the end result of fibrogenesis that occur with chronic liver injury and tissue repair due to any etiology.[1] Alcohol is one of the common aetiology, alcohol related liver disease is the commonest cause of death, accounting for 2.5 million/yr.[2] A cirrhotic liver may progressively deteriorate from compensated state to decompensated conditions. 5-year survival rate of 84% in compensated cirrhosis, 14% to 35% decompensated cirrhosis.[3-5] Although a preferable treatment option for decompensated liver cirrhosis is liver transplantation, shortage of donor livers and high cost make this approach impracticable in most cases.[5-6] Therefore, identifying a marker associated with disease severity helps in improving clinical management. Aspartate aminotransferase to platelet ratio index (APRI) was initially proposed as a predictive marker for liver fibrosis and cirrhosis in hepatitis C virus (HCV)-infected patients.[7] Recent studies show that APRI predicted liver related mortality in alcoholic liver disease individuals.[8]

APRI was calculated using the formula= AST (U/L)/ (upper limit of the normal range) ×100/platelet count (10^9/L). The 40 U/L of AST was used as the upper limit of the normal range. It is a mathematical formula using only two parameters, based on routine blood tests and is compared to MELD score and albumin level. APRI reflect extent of liver injury and compensatory state of hepatic function which is simpler, cost effective and easier to calculate than MELD score.[7]

Herein we conducted a retrospective data analysis to determine APRI, the association of APRI with the progression of chronic alcoholic liver disease and mortality and to compare the prognostic significance of the APRI score with MELD score and albumin level.

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AIMS AND OBJECTIVES

1) To evaluate the AST to Platelet Ratio Index (APRI) for predicting the in-hospital mortality in chronic liver disease patients.
2) To compare APRI, MELD and albumin for predicting hospital mortality in chronic liver disease.

MATERIALS AND METHODS

The study was conducted at Bowring and Lady Curzon Hospital (Attached to Bangalore Medical College and Research institute). Chronic liver disease patients secondary to ethanol between 2016 January and 2016 December were retrospectively reviewed.

Inclusion criteria

1) All patients aged above 18 years with chronic liver disease.
2) Chronic liver disease as evidenced by abdominal ultra sound and liver profile derangement.

Exclusion criteria

1) Chronic liver disease due to hepatitis B, C, malignancy, metabolic causes, autoimmune hepatitis.

Method of collection of data

History, clinical Examination and Routine CBP, RFT, LFT, serum electrolytes, HIV, HBsAg, HCV, VDRL serology, prothrombin time, APTT, Ultrasound of abdomen, upper GI endoscopy and other relevant investigations were noted.

Chronic liver disease is evidenced by: abdominal ultrasound and liver profile derangement.

Complications like anaemia, hepatic encephalopathy, renal dysfunction and mortality noted.

APRI = AST (U/L)/(upper limit of the normal range) ×100/platelet count.

The 40 U/L of AST was used as the upper limit of the normal range.

MELD= (10 * ((0.957 * ln (Creatinine)) + (0.378 * ln (Bilirubin)) + (1.12 * ln (INR))) + 6.43

Method of Statistical analysis

All statistical analysis were performed using the Medcalc software. Continuous Data were expressed as the mean+/- standard deviation (SD) and median with minimum and maximum. Categorical data were expressed as the frequency. Receiving-operative characteristics curve analysis was performed to identify the discriminative ability of the APRI, MELD score and albumin levels in predicting in-hospital mortality. Areas under the ROC curves were calculated and compared. The best cut off value was selected as the sum of sensitivity and specificity was maximal. Then sensitivity, specificity, positive likelihood ratio, negative likelihood ratio were reported.

RESULTS AND ANALYSIS

The sample size in our study was 299 patients. The age distribution was between 18-64 years with mean age of patients being 46.47+/-10.9 years (Table 1). 267 were males and 32 were females (Table 2).

Among 299 patients, 53 were deaths and 246 were patients who showed improvement, with mortality percentage of 17.7 % (Figure 1).

Table 1: Age distribution of patients studied

Age in years	No. of patients	%
20-30	20	6.0
31-40	68	22.7
41-50	117	59.1
51-60	63	21.0
61-70	26	8.6
>70	5	1.6
Total	299	100.0

Mean ± SD: 46.47 ± 10.9

Table 2: Gender distribution of patients studied

Gender	No. of patients	%
Female	32	10.7
Male	267	89.2
Total	299	100.0

*Death: 53, Improved: 246

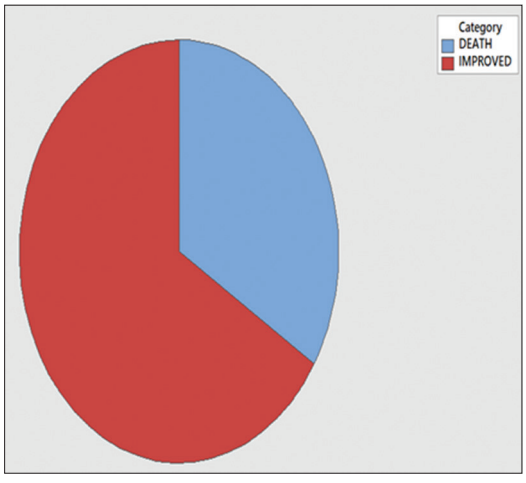

Figure 1: Outcome

Comparison of in-Hospital mortality with APRI, MELD and albumin level

The in-Hospital morality was 17.7%. The Area under curve (AUC) of the APRI score for predicting the in-hospital mortality was 0.631 (confidence interval: 95%: 0.574 -0.686) (Table 3). The best cut-off value of -0.743, with sensitivity of 77.9%, a specificity of 46.2%, positive likelihood ratio (PLR) of 1.72 and negative likelihood ratio (NLR) 1.66 (Figure 2).

The AUC of the MELD score for predicting the in-hospital mortality was 0.766 (confidence interval 95%: 0.713-0.812), with a sensitivity of 84.2%, a specificity of 75.6%, PLR of 1.7 and NLR of 1.6 (Figure 3).

The AUC of the Albumin level for predicting the in-hospital mortality was 0.559 (confidence interval 95% 0.500 -0.616), with a sensitivity of 89.8%, a specificity of 28.7%, PLR of 3.23 and NLR of 3.23 (Figure 4).

The AUC for predicting the in-hospital mortality was significantly different between the APRI, MELD score and albumin level (Figure 5). (APRI and MELD score –P= 0.0015; Albumin level and MELD P < 0.001) (Table 4).

ORDER: MELD score > APRI> Albumin level.

DISCUSSION

Cirrhosis of liver is associated with significant morbidity, mortality and health care costs. There are several biochemical markers that can reveal both liver function and the extent of liver injury.[9] APRI uses platelet count and AST levels to reflect insufficient liver function and new stress/damage to the liver. Decreased platelet

Table 3: Area under curve

Variable	AUC	Standard error	95% CI
ALBUMIN	0.559	0.0392	0.500 to 0.616
APRI_FINAL	0.631	0.0403	0.574 to 0.686
MELD_FINAL	0.766	0.0300	0.713 to 0.812

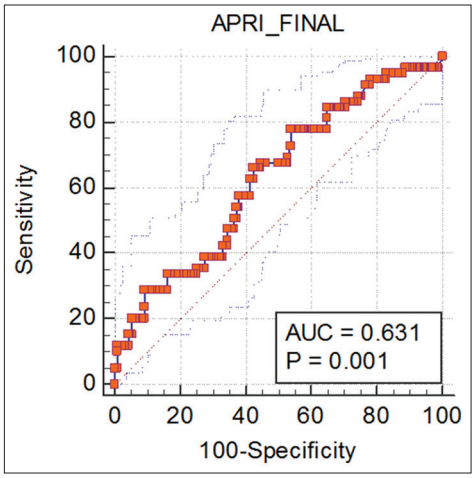

Figure 2: Area under curve for APRI

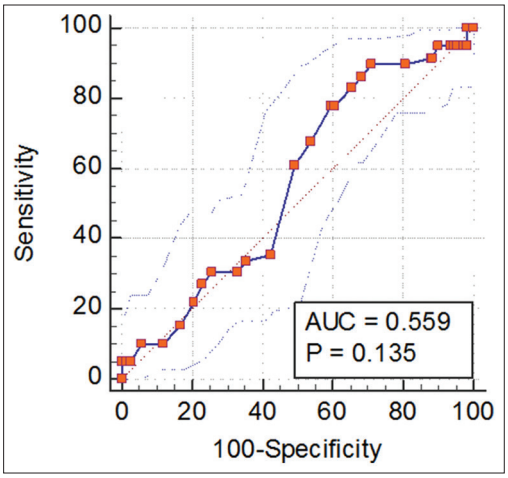

Figure 4: Area under curve for Albumin

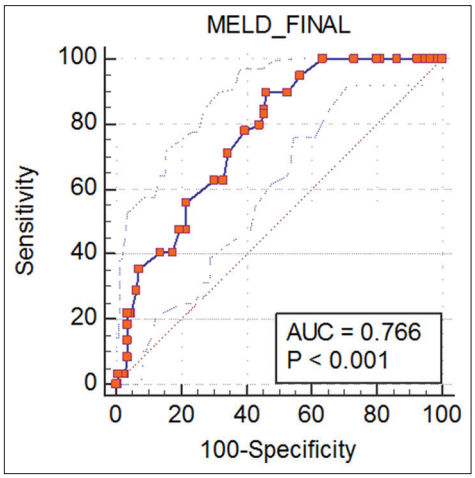

Figure 3: Area under curve for MELD score

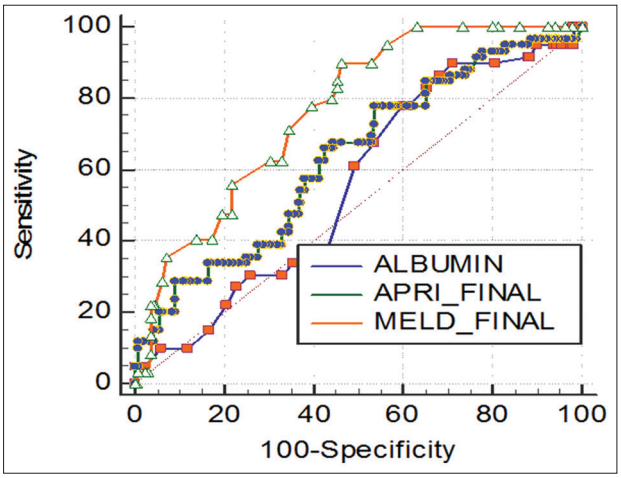

Figure 5: comparing AUC for albumin, MELD and APRI

Table 4: Pairwise comparison of ROC curves	
ALBUMIN~APRI_FINAL	
Difference between areas	0.0730
Standard Error[a]	0.0557
95% Confidence Interval	-0.0361 to 0.182
z statistic	1.311
Significance level	P=0.1899
ALBUMIN~MELD_FINAL	
Difference between areas	0.207
Standard Error[a]	0.0461
95% Confidence Interval	0.117 to 0.297
z statistic	4.491
Significance level	P<0.0001
APRI_FINAL~MELD_FINAL	
Difference between areas	0.134
Standard Error[a]	0.0423
95% Confidence Interval	0.0512 to 0.217
z statistic	3.171
Significance level	P=0.0015

count and increased AST levels are known as clinical manifestations of progression of liver cirrhosis. A reduction in platelet count can be caused by the accelerating destruction of an enlarged spleen which is termed as "hypersplenism" secondary to portal hypertension in cirrhosis.[10-12] AST is more abundantly present in the mitochondria and cytoplasm relative to ALT.[13] Fibrosis of liver may reduce the clearance of AST, leading to the retention of AST in blood.[13-15] Therefore, high AST levels combined with low platelet count may be used to predict the severity and progression of liver injury in cirrhotic patients.

In our study, we tried to explore the prognostic performance of the APRI score for the assessment of the in-hospital mortality of chronic liver disease.

We found that the prognostic performance of the APRI score was comparable to that of MELD score and albumin level. In this study, MELD score had the largest AUC, followed by APRI and albumin level. Therefore, MELD score has better prognostic performance compared to APRI and albumin level.

Study done by Weilin Mao et al, On 193 chronic HBV-infected patients. Mortality that occurred within 90 days of hospital stay was compared, which concludes that APRI is an independent predictor for mortality in patients with cirrhosis and they found positive correlation between the MELD score and APRI.[9]

In a study conducted by Lieber CS1 et al, on 1308 patients, APRI has low sensitivity and specificity for the diagnosis of significant fibrosis in patients with alcoholic liver disease.[8]

Limitation of the study

1) Long term follow up was unavailable so this study couldn't evaluate the role of APRI for predicting long term Prognosis.
2) APRI score is not dynamically measured.
3) Retrospective study, needs prospective study for better understanding of correlation.

CONCLUSION

APRI is an independent predictor of mortality. Highly elevated APRI was associated with higher frequencies of clinical complications such as ascites and encephalopathy

The prognostic performance of all 3 variables were comparable but MELD score has better prognostic significance than APRI score

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Authors Contribution:
NBS- Concept and Design of the study, Manuscript preparation, Statistically analysed and interpreted, critical revision of the manuscript; **MR-** Concept and Design of the study, Statistically analysed and interpreted, critical revision of the manuscript; **AHR-** reviewed the literature, helped in preparing first draft of Manuscript, collected data; **UKJ -** collected data, Statistically analysed and interpreted, helped in preparing draft of manuscript.

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