A Study to Investigate the Correlation between Non-Invasive Markers of Liver Fibrosis and Cirrhosis (APRI, MELD and Child Pugh Score)

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ABSTRACT

Introduction: Cirrhosis, a final pathway for a wide variety of chronic liver disease (CLD), is a pathological entity defined as diffuse hepatic fibrosis with replacement of normal liver architecture by nodules. Aspartate aminotransferase to platelet ratio index (APRI) has originally been considered as a non-invasive marker for detecting hepatic fibrosis in patients with chronic hepatitis B and C. Subsequently various studies have attempted to extend this marker for assessing other liver diseases. Study aimed to calculate APRI INDEX, Child Pugh score and MELD score in liver cirrhosis patients and to find the correlation between them.

Material and methods: A total of 100 patients having liver cirrhosis were selected. All the patients personally subjected to detailed history and systemic examination. Blood investigations was done, APRI index, CPT score and MELD calculated. Statistical methods applied and differences between variables were evaluated using ANOVA tests.

Results: 100 cirrhotic patients were divided into 3 groups for further analysis based on APRI levels: group A (APRI < 1.0)30, group B (>1.0, but <2.0)24, and group C (>2.0)46. Highly elevated APRI was associated with higher frequencies of clinical complications such as ascites, variceal bleeding, esophageal varices encephalopathy and mortality. Mean MELD score was Higher in patients in group C than in groups A and B. Mean Child Pugh score was Higher in patients in group C than in groups A and B. Mean AST was Higher in patients in group C than in groups A and B. Platelet count was lower in patients in group C than in groups A and B. Positive correlations between APRI and Child Pugh score and MELD scores were detected in cirrhotic patient.

Conclusion: In this study, APRI was identified as an independent predictor for mortality in patients with cirrhosis. In this present study, a positive correlation between the MELD score, Child Pugh score and APRI was identified Our study demonstrates that APRI is a simple and non-invasive scoring system that could predict risk for the development of liver-related complications and mortality in patients with cirrhosis.

Keywords: Aspartate Aminotransferase to Platelet Ratio Index (APRI), Child Pugh Score, MELD Score

INTRODUCTION

Cirrhosis, a final pathway for a wide variety of chronic liver disease (CLD), is a pathological entity defined as diffuse hepatic fibrosis with replacement of normal liver architecture by nodules. Cirrhosis is one of the leading causes of mortality in United States and particularly affects person in the most productive years of their lives.[1] Most of this increase in CLD mortality has been reported from the countries of Asia and Africa.[2] Deaths from cirrhosis have been estimated to increase and would make it as the 12th leading cause of death in 2020.[3] Today, even in Asian countries like India, alcohol is emerging as the commonest cause of chronic liver disease.[4] The median survival in patients with compensated cirrhosis is 9 to 12 years, compared with 2 years in those with decompensated cirrhosis. Prognosis depends not only on the clinical stage of the disease but also on the presence of comorbidities.[5]

Clinical features, biochemical tests, and hepatic imaging studies are helpful in assessing stage but generally become abnormal only in the middle to late stages of cirrhosis. Combinations of blood test results have been used to create models for predicting advanced liver disease. Scoring systems are employed to assess compensated versus decompensated disease and prognosis. A reliable staging system is the modified Child-Pugh classification, with a scoring system of 5–15: scores of 5 and 6 represent Child-Pugh class A (consistent with "compensated cirrhosis"), scores of 7–9 represent class B, and scores of 10–15 represent class C. Recently, the Child-Pugh system has been replaced by the Model for End Stage Liver Disease (MELD) system for the latter purpose. This score is calculated from three non-invasive variables: the prothrombin time expressed as the international normalized ratio (INR), the serum bilirubin level, and the serum creatinine concentration.[6]

Aspartate aminotransferase to platelet ratio index (APRI) has originally been considered as a non-invasive marker for detecting hepatic fibrosis in patients with chronic hepatitis B and C. APRI has been used for predicting liver-related mortality in patients with chronic hepatitis C virus infection or alcoholic liver disease.[7] The APRI is simple to use and cheap. An 86% negative predictive value (NPV) and 88% positive predictive value (PPV) were reported to predict the presence of significant fibrosis and a 98% NPV and a 57% PPV were reported to predict the presence of cirrhosis.[8]

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Subsequently, various studies have attempted to extend this marker for assessing other liver diseases.Although its clinical value has been questioned by controversial findings, APRI remains an attractive and frequently used marker for assessing a patient's prognosis. APRI is a simple, non-invasive, and easy to calculate index that helps clinicians identify individuals in need of greater care, especially in outpatient clinics.[9-13] This study aimed to investigate the correlation between non-invasive markers of liver fibrosis and cirrhosis (APRI INDEX) and MELD and Child Pugh Score.

Study aimed to calculate APRI, Child Pugh score and MELD score in liver cirrhosis patients and to find the correlation between APRI, MELD score and Child Pugh Score.

MATERIAL AND METHODS

The present study was conducted among 100 patients who were treated in the department of General Medicine, R.N.T. Medical College Udaipur Rajasthan. All the patients personally subjected to detailed history regarding name, age, sex, occupation, socioeconomic status, general physical examination and systemic examination. At baseline, all demographic and clinical characteristics were collected including the model for end-stage liver disease (MELD) score, AST platelet ratio index (APRI) score, and Child Pugh score. 100 cirrhotic patients were divided into 3 groups for further analysis based on APRI levels: group A (APRI < 1.0), group B (>1.0, but <2.0), and group C (>2.0). All three groups were compared with all demographic and clinical characteristics. APRI SCORE, MELD SCORE, and Child Pugh score were compared and were analysed

Inclusion Criteria

- Patients with cirrhosis of liver between age 18-75 years.
- Cirrhosis of liver was confirmed by ultrasound and biochemical reports.
- Cirrhosis due to alcohol, Hepatitis B, Hepatitis C, NAFLD leading to cirrhosis were included in the study.

Exclusion Criteria

Age less than 18 years
Age more than 75 years
Primary haematological disorders
Acute infectious diseases

STATISTICAL ANALYSIS

All continuous variables were expressed as mean standard deviation (SD) or medians (range), and categorical data were calculated as percentages. Differences between variables were evaluated using ANOVA tests. Statistical analysis was performed using SPSS and P<0.05 was statistically significant.

RESULTS

Out of hundred cases, the age distribution was between 18-75 years with mean age of patients being 46.85±13.42 years. There were no significant differences detected in age among the 3 groups. Out of these patients 80 were males and 20 were females. There were no significant differences detected in gender among the 3 groups.

Out of hundred cases 71 were alcoholic, HBsAg related (HBS) cirrhosis were 14, Hepatitis C (Hep C) related cirrhosis were 2, 7 were related to autoimmune (AIH) and 6 were idiopathic. (Chart 1)

The mean albumin in group A was 2.85±0.69, 2.48±0.67 in group B and 2.21±0.50 in group C. The mean INR in group A was 1.25 ±0.25, 1.33±0.30 in group B and 1.71±0.66 in group C. The mean Bilirubin in group A was 1.82±1.77, 1.82±0.95, in group B and 5.13±5.34 in group C. The mean AST in group A was 43.13±18.40, 67.92±28.66 in group B and 175.22±253.24 in group C. The mean platelets in group A was 214.93±30.00, 116.71±24.00 in group B and 81.91±46 in group C. The difference in values of mean albumin, mean INR, mean Bilirubin, mean AST and mean Platelets is statistically significant with a p-value of <0.001. Mean creatinine in group A was 1.31±0.76, 1.25±0.60 in group B and 1.47±1.18 in group C respectively. There were no significant differences detected in creatinine levels among 3 groups. (Table 1)

Highly elevated APRI was associated with higher frequencies of clinical complications such as encephalopathy and ascites. The number of cases with encephalopathy in group A is 60%, 87.50% in group B and 78.26% in group C. The results are significant with a p value of< 0.05. (Table 2) The number of cases with ascites in group A is 90%, 66.66% in group B and 86.95% in group C. The number of cases with ascites in the group C is higher than the group B and those in group A presented with mild ascites. The results are significant with a p value of< 0.05.(Table 3)

Elevated APRI was also associated with higher frequencies of clinical complications such as oesophageal varices, variceal bleeding and mortality. Oesophageal varices were seen in 78.26% in group C, 62.50% and 50% in group B and A respectively. Similarly, 45.65% in group C had variceal bleeding while in group A and B was 16.67% and 37.50% respectively. Mortality in group C was 21.74%. (Table 4)

Blood Parameter	Group A (n-30)	Group B (n-24)	Group C (n-46)	Total (n-100)
Serum Albumin	2.85±0.69	2.48±0.67	2.21±0.50	2.47±0.66
INR	1.25±0.25	1.33±0.30	1.71±0.66	1.48±0.53
Serum Bilirubin	1.82±1.77	1.82±0.95	5.13±5.34	3.34±4.11
Serum AST	43.13±18.40	67.92±28.66	175.22±253.24	109.84±182.21
Platelets	241.93±30	116.71±24	81.91±46	130.7±100
Serum creatinine	1.31±0.76	1.25±0.6	1.47±1.18	1.37±0.94

Table-1: Distribution of APRI values according to blood investigations

Encephalopathy (Y/N)	Grp A (n=30)		Grp B (n=24)		Grp C (n=46)		N=100	
	0-1		1-2		>2		Total	
	No.	%	No.	%	No.	%	No.	%
No	12	40.00%	3	12.50%	10	21.74 %	25	25%
Yes	18	60.00%	21	87.50%	36	78.26 %	75	75%
Total	30	100%	24	100%	46	100%	100	100%

Table 2: Distribution of APRI values on clinical characteristic: **Encephalopathy**

Ascites (Y/N)	Grp A (n=30)		Grp B (n=24)		Grp C (n=46)		N=100	
	0-1		1-2		>2		Total	
	No.	%	No.	%	No.	%	No.	%
Yes	27	90.00%	16	66.66%	40	86.95%	83	83%
No	3	10.00%	8	33.33%	6	13.04%	7	7%
Total	30	100%	24	100%	46	100%	100	100%

Table 3: Distribution of APRI values on clinical characteristic: **Ascites**

	Grp A (n=30)		Grp B (n=24)		Grp C (n=46)		N=100		
	0-1		1-2		>2		Total		P VALUE
	No.	%	No.	%	No.	%	No.	%	
Mortality	2	6.66%	1	4.16%	10	21.74%	7	7%	<0.05
Variceal bleeding	5	16.67%	9	37.50%	21	45.65%	40	40%	<0.05
Esophageal varices	15	50%	15	62.50%	36	78.26%	66	66%	<0.05

Table 4: Distribution of APRI Values according to clinical complications

The Child Pugh Score in group A was 8.23±1.92, 8.92±1.38 in group B and 10.46±1.67 in group C. Increased APRI was associated with higher Child –Pugh Score (p-value of <0.001). (Chart 2)

The MELD Score in group A was 13.17±7.12, 13.46±5.55 in group B and17.28±6.55 in group C. Increased APRI was

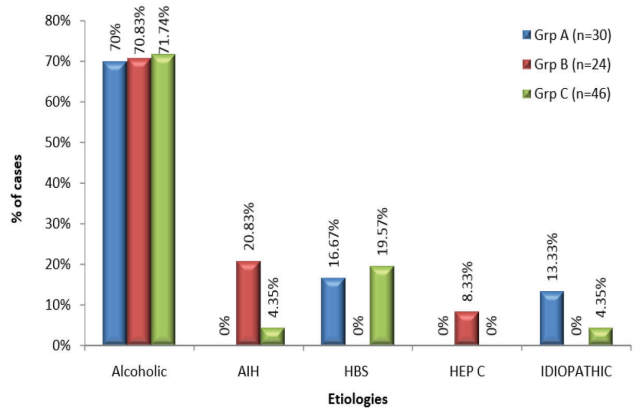

Chart-1: Distribution of cirrhotic patients on the basis of aetiology

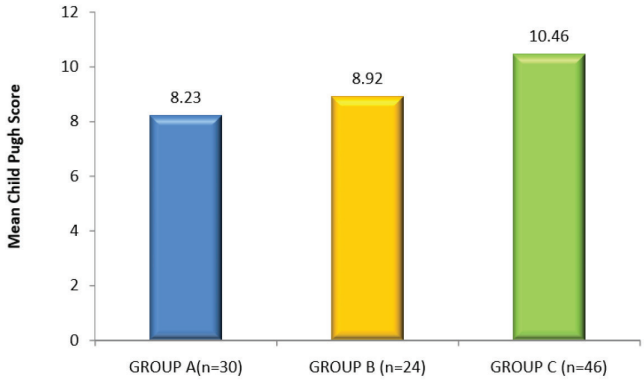

Chart-2: Distribution of APRI values according to Child Pugh Score

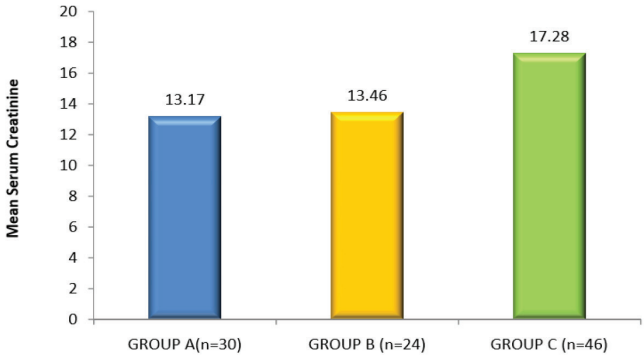

Chart-3: Distribution of APRI values according to MELD Score

associated with higher MELD Score (p-value of 0.001). (Chart 3)

DISCUSSION

In the present study, 100 cases of cirrhosis were studied in the medical wards of Maharana Bhupal Government Hospital, R.N.T. Medical College, Udaipur.

Out of hundred cases, the age distribution was between 18-75 years with mean age of patients being 46.85+/-13.42 years. This observation correlated closely with study conducted by Nagaraja BS et al[14] where mean age of patients being 46.47±10.9 years. There were no significant differences detected in age among the 3 groups, this observation correlated closely with study conducted by Weilin Mao et al.[7]

Out of hundred cases, 80 (80%) were males, and 20 (20%) were females This observation correlated closely with study Etiology and mode of presentation of chronic liver diseases in India[15]: A multi centric study by Partha S. Mukherjee, Sreenivas Vishnubhatla, Deepak N. Amarapurkar, Kausik Das, Ajit Sood, Yogesh K. Chawla, Chundamannil E. Eapen,Prabhakar Boddu, Varghese Thomas, Subodh Varshney, Diamond Sharma Hidangmayum, Pradip Bhaumik, Bhaskar Thakur, Subrat K. Acharya, Abhijit Chowdhury which showed male predominated across the etiologies.

Out of hundred cases, 71 were alcoholic, HBsAg related cirrhosis were 14, Hepatitis c Related cirrhosis were 2, 7 were related to autoimmune, and 6 were idiopathic. This observation correlated closely with A study on the etiology of cirrhosis of liver in adults living in the Hills of Himachal Pradesh, India[16] by Sharma B, Marwah R, Raina S, Sharma N, Kaushik M, Kaushal SS in which alcohol was the leading cause of cirrhosis (62.9%), hepatitis B was the second(10.1%), Non-Alcoholic Steatohepatitis (NASH) was the third (7.9%), and autoimmune the fourth (3.9%) most common cause for cirrhosis. Hepatitis C was present in 2.8% of patients as a cause of cirrhosis. Wilson disease and cardiac cirrhosis were present in one patient each. In 9.6% the etiology was cryptogenic.

In study conducted by Weilin Mao et al[7] detected the inverse correlation of APRI with serum albumin levels. Similar observations were seen in current study where albumin level was lowest in group C patients.

Increased APRI was associated with higher MELD score. This observation correlated closely with study conducted by Weilin Mao et al.[7] Also, in study conducted by Dr Jithin George, Dr Yeshavanth. G[17] showed positive correlation between APRI INDEX and MELD SCORE. Hence APRI can also be used for predicting the mortality of liver cirrhosis patients and to know the prognosis as like other parameters. In study conducted by Nagaraja BS et al[14] evaluated APRI for predicting the in-hospital mortality and also comparing APRI, MELD for predicting in hospital mortality in chronic liver disease.

A European study by F Botta, et al[18] found the MELD score is an excellent predictor of both short- and medium-term survival. An increase in MELD score is associated with a decrease in residual liver function. In current study, it was found that Increased APRI was accompanied by increased MELD scores, which is an established marker for reflecting the severity of end-stage liver disease.

In the study conducted by Freeman RB Jr, Wiesner RH, Harper A, et al. The new liver allocation system: moving toward evidence-based transplantation policy.[19] The MELD score has been frequently used to predict patient survival with end-stage liver disease and to determine the urgency of liver transplantation. In this present study, a positive correlation between the MELD score and APRI was identified. Child-Pugh score/class is the first prognostic index widely employed for liver cirrhosis. The survival of cirrhotic patients is reduced, if Child-Pugh scores/classes are increased is shown in the studies by D'Amico G, Garcia-Tsao G, Pagliaro L; Natural history and prognostic indicators

of survival in cirrhosis: a systematic review of 118 studies.[20] In this study increased APRI was associated with worsened Child–Pugh grade suggesting poor prognosis if APRI is increased. Similar results were seen in study by Weilin Mao et al.[7] Study by Dr Jithin George, Dr Yeshavanth[17] also showed significant p value between APRI and Child Pugh Score. A reduction in platelet count can be caused by hypersplenism secondary to portal hypertension in cirrhosis. It can be also induced by reduced production. Liver fibrosis progression was associated with decreased production of thrombopoietin by hepatocytes, leading to reduced platelet production. Platelet count was lower in patients in group C than in groups A and B. Similar results were seen in study by Weilin Mao et al[7] in group A, B, C number of platelets (109/L) are 156.3±76.6, 83.4±54.5, 53.3±28.2 respectively. A cirrhotic liver can often be subjected to new stresses or insults from different etiologies. Reactivation of HBV replication represents a frequent cause for new liver injury in HBV-related cirrhosis.

Liver injury including mitochondrial injury results in the release of more AST, which is more abundantly present in the mitochondria and cytoplasm relative to ALT. Liver fibrosis progression may also reduce the clearance of AST, leading to the retention of AST in blood. Results of our study are comparable with study by Weilin Mao et al[7] in group A, B, C where AST levels (IU/L) are 29.2±12.6, 46.6±26.1,82.6±64.9 respectively. These data suggest that higher APRI in cirrhotic patients could be primarily attributed to increased AST levels and decreased platelet count.

There is positive correlations between APRI and Child Pugh score ($r=0.340$, $P<0.001$) and MELD scores ($r=0.490$, $P<0.001$), were detected in cirrhotic patient similar to study conducted by Weilin Mao et al[7] Therefore, high AST levels combined with low platelet count may be used to predict the severity and progression of liver injury in cirrhotic patients. Thus, APRI prediction is built on a sound pathologic foundation (increased hepatic necro-inflammatory activity and worsening liver function).

CONCLUSION

In this study, APRI was identified as an independent predictor for mortality in patients with cirrhosis. Child Pugh score is reliable predictor of survival in many liver diseases and predicts likelihood of complications. The MELD score has been frequently used to predict patient survival with end-stage liver disease and to determine the urgency of liver transplantation. In this present study, a positive correlation between the MELD score, CP score and APRI was identified. Our study demonstrates that APRI is a simple and non-invasive scoring system that could predict risk for the development of liver-related complications and mortality in patients with cirrhosis.

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