

**A STUDY TO COMPARE THE EFFICACY OF ASPARTATE AMINOTRANSFERASE
PLATELET RATIO INDEX TO FIBROSCAN AS A MARKER FOR EARLY FIBROSIS IN
– NON ALCOHOLIC FATTY LIVER DISEASE**¹*Dr. G. S. Ramya, ²Dr. Rajshekar, ³Dr. Banda Naveen¹(Post Graduate), ²(Associate Professor), ³(Post Graduate)

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ABSTRACT

Introduction: Liver disease represents a rapidly increasing health burden globally. Analyses of liver parameters are now the third most common type of biochemical test. NAFLD is a spectrum of liver diseases, from fatty infiltration to steatohepatitis, fibrosis, and cirrhosis. There is immediate need of non-invasive procedure like aminotransferase platelet ratio index (APRI) and fibroscan in the early diagnosis of liver fibrosis. The present study was undertaken to assess the efficacy of APRI to fibroscan as a marker for early fibrosis in cases with nonalcoholic fatty liver diseases. **Objectives:** Study to assess the relation between Aspartate aminotransferase and platelet count in patients with pre cirrhosis and compare the efficacy of aspartate aminotransferase platelet ratio index to that of fibroscan in early fibrosis. **Materials and methods:** A hospital based prospective study conducted on all ultrasound defined newly diagnosed 100 NAFLD patients attending outpatient department in RIMS, Raichur fulfilling inclusion criteria and exclusion criteria during the study period.. Fibroscan was done for all NAFLD patients. Serum AST level and platelet count was measured in those patients and APRI calculated. Data analysis was done by using SPSS Ver. 26 software. Chi square test for consolidated data and Pearson correlation for correlation coefficient to test the significance of difference between variables. A 'p' value less than 0.05 was taken to denote significant relationship. **Results:** The mean age was 49.4 years, and most patients were in the age group 45-55 years. High incidence of NAFLD in males (61%) compared to females. The mean APRI score was 1.09. 14 patients having APRI index between 0.7 to 1.0 had a fibro scan score between 7.0 to 8.9 denotes mild to moderate fibrosis according to the metavir scoring system. The association between APRI score and fibroscan was statistically significant ($p=0.0214$) and there was good correlation between fibroscan and APRI. Pearson correlation coefficient calculated was 0.92. showed very strong positive correlation. **Conclusion:** The APRI score can be a useful non-invasive alternative for the exclusion and inclusion of significant liver fibrosis. The use of APRI >0.7 would avoid the need for fibroscan.

KEYWORDS: Liver disease; NAFLD; Fibrosis; Fibroscan; APRI; AST.**INTRODUCTION**

Liver disease represents a rapidly increasing health burden globally. The prevalence of Non-alcoholic fatty liver disease (NAFLD) is around 9-32% of general population in India. Clinico-pathological studies show that NAFLD is an important cause of unexplained rise in hepatic transaminases, cryptogenic cirrhosis and cryptogenic hepatocellular carcinoma in Indian patients.^[1] The invention of new diagnostic noninvasive markers of nonalcoholic fatty liver disease (NAFLD) is a major preference in clinical research. Analyses of liver parameters are now the third most common type of biochemical test.^[2,3]

Non-alcoholic fatty liver disease is considered an increasing public health problem, owing to its close association with type 2 diabetes mellitus, obesity, and metabolic syndrome, as well as their undeniable epidemics worldwide. NAFLD is a spectrum of liver diseases, from fatty infiltration to steatohepatitis, fibrosis, and cirrhosis.^[4] Progression of NAFLD leads to hepatic inflammation and fibrosis. Liver fibrosis is associated with an increased risk of complications, such as cirrhosis, hepatic failure, hepatocellular carcinoma, and even death.

NAFLD is also important as a cause of liver-related mortality and morbidity. Therefore, early identification of fibrosis in children is crucial.^[5] Currently, liver biopsy

is the gold standard assessment method to investigate hepatic fibrosis and inflammation. However, due to the invasiveness of liver biopsy, it may not be recommended for use in children. Also, it is challenging to use liver biopsy as a reoperation for therapeutic and follow-up purposes.^[6]

Therefore, an accurate noninvasive procedure to detect the degree of hepatic fibrosis in NAFLD is needed. A noninvasive, rapid, painless, and reproducible technique, transient elastography (FibroScan) has been developed to measure liver stiffness.^[7] Liver stiffness and the severity of liver fibrosis in patients with NAFLD have a significant and positive correlation with the results of liver biopsies. With this there is immediate need of non-invasive procedure like aminotransferase platelet ratio index (APRI) and fibroscan in the early diagnosis of liver fibrosis. Fibroscan has good sensitivity, specificity and diagnostic accuracy.

FibroScan can be a useful and objective method to assess the degree of liver fibrosis in NAFLD patients. However, the high cost of FibroScan equipment and the need of skillful specialists limit its broad use, especially in medical practices.^[8] For this reason, the development of simpler and easier clinical and laboratory indices for medical practice are needed to identify advanced fibrosis in patients with NAFLD. The aspartate aminotransferase (AST)-to-platelet ratio index (APRI) has been proposed as a simple and noninvasive predictor to evaluate hepatic fibrosis in several liver diseases. The assessment predictors of biological liver function include simple blood parameters such as AST and platelets are easy to use and estimate. Therefore, APRI could be a good alternative diagnostic method to FibroScan or liver biopsy.^[7]

Hence, the present study was undertaken to assess the efficacy of APRI to fibroscan as a marker for early fibrosis in cases with nonalcoholic fatty liver diseases.

OBJECTIVES

Study to assess the relation between Aspartate aminotransferase and platelet count in patients with pre cirrhosis and compare the efficacy of aspartate aminotransferase platelet ratio index to that of Fibroscan in early fibrosis.

MATERIALS AND METHODS

A hospital based prospective study conducted on all ultrasound defined newly diagnosed 100 NAFLD patients attending outpatient department in RIMS, Raichur fulfilling inclusion criteria and exclusion criteria during the study period. The inclusion criteria included all newly diagnosed cases of ultrasound defined NAFLD in the age group 25-65 years. Patients were excluded if liver biopsy was not useful for fibrosis staging, or if liver injury was due to hepatitis B virus, coronary artery disease or other cause of chronic liver diseases or inflammation.

Informed consent was obtained from all patients to be enrolled for the study and patients relevant information will be collected in a predesigned proforma. The patients were selected based on clinical examinations, biochemical tests and ultrasound abdomen. Weight, height, and body mass index were recorded. All patients had a liver biopsy and a platelet count performed the same day as the biopsy. They also had an AST determination within a month before/after the biopsy. Fibroscan was done for all NAFLD patients. Serum AST level and platelet count was measured in those patients and APRI calculated. APRI was correlated with fibroscan in assessing the early fibrosis. All liver biopsies were reviewed by a single pathologist. Fibrosis was staged according to the METAVIR scale.

The APRI score will be calculated by using the formula

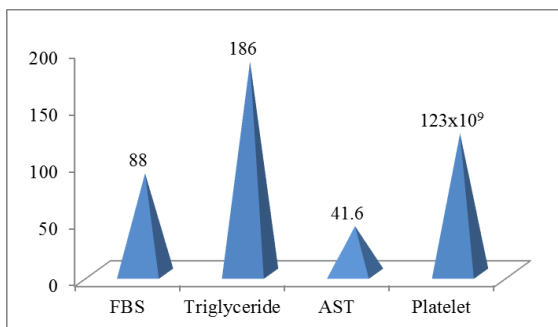
$$\text{APRI} = \{(\text{AST level} / \text{ULN}^*) / \text{PLATELET COUNT}(10^9/\text{L})\} \times 100$$

*ULN, AST upper level of normal (or 56 IU/L)

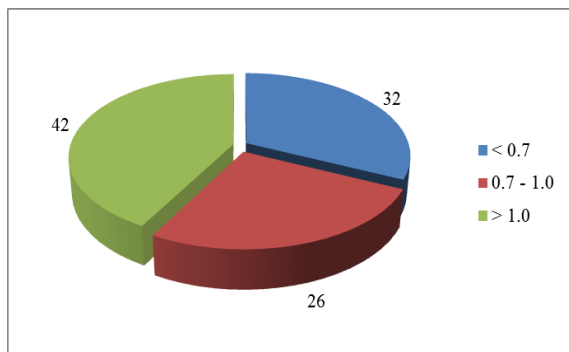
The data was recorded in Microsoft-Excel for analysis. Data analysis was done by using SPSS Ver. 26 software. Using SPSS software, percentages, means, standard deviations 'p' values were calculated by Student 't' test for raw data, Chi square test for consolidated data and Pearson correlation for correlation coefficient to test the significance of difference between variables. A 'p' value less than 0.05 was taken to denote significant relationship.

RESULTS

A total of 100 patients were included and analysed in this study. The mean age in the study group was 49.4 yrs. Most of the NAFLD patients were in the age group between 46-55 yrs (43%). Out of 100 cases, 61 were males, 39 were females. Among 100 patients having NAFLD, 42% of the patients were obese. The mean BMI was 29.6. Of 100 NAFLD patients, 33 % patients having FBS >100. The mean FBS was 88 mg/dl. In the study, 28% of the patients having triglyceride level >200mg/dl. The mean triglyceride value was 186mg/dl. Among NAFLD patients, 34% of patients had values between 41-50 IU, 20% of patients had >50 IU. The mean AST value was 41.6. Among 100 patients, 30 patients having platelet count < 100 × 10⁹ cells, 9 patients having platelet >200 × 10⁹ cells. The mean platelet count was 123 × 10⁹ cells. APRI was calculated for all NAFLD patients based on AST and platelet count. The mean APRI score was 0.84.

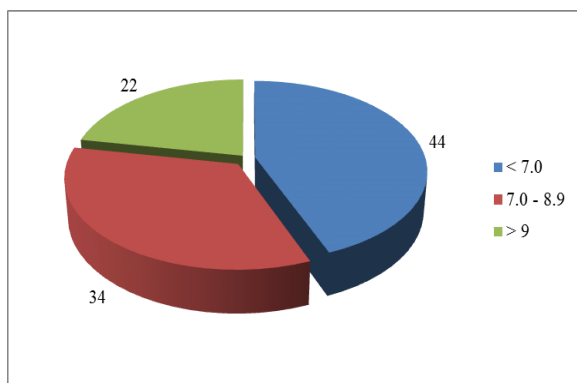


Graph 1: Mean values of laboratory investigations.



Graph 2: APRI distribution.

APRI <0.7 had no fibrosis. 0.7 -1.0 denotes mild to moderate fibrosis. APRI>1.0 denotes significant fibrosis. Among 100 patients 26 patients having APRI between 0.7 to 1.0.



Graph 3: Fibroscan distribution.

In Fibroscan, the values ranges from 3.2kpa to 16.9kpa. The mean value is 7.3kpa. 34% of patients have values between 7.0 to 8.9 kpa.

According to METAVIR scoring system, 7.0 to 8.9kpa represents moderate fibrosis.

Table 1: Correlation and association between fibroscan and APRI.

FIBROSCAN (Kpa)	APRI			p-value
	< 0.7	0.7 - 1.0	> 1.0	
< 7.0 (44)	32	12	0	p=0.0214 Significant
7.0 - 8.9 (34)	0	14	20	
> 9 (22)	0	0	22	
	32	26	42	

The association between APRI score and fibroscan was statistically significant (p=0.0214) and there was good correlation between fibroscan and APRI. Pearson correlation coefficient calculated was 0.92. showed very strong positive correlation.

DISCUSSION

Non-alcoholic fatty liver disease is often considered the hepatic manifestation of metabolic syndrome with insulin resistance playing a dominant role. In NAFLD, patients are asymptomatic, the diagnosis is often made by abnormal liver aminotransferases or during the evaluation of other diseases. Early and accurate assessment of the degree of liver fibrosis is essential in management and prognosis. Prognosis and treatment of chronic liver diseases is related to the degree of fibrosis. To evaluate fibrosis, liver biopsy has been the gold standard for many years. However, invasiveness, complications, inter- and intra-observer variations, and patient acceptability have limited its use, leading to search for new and noninvasive methods to diagnose liver fibrosis and cirrhosis.

The APRI score correlates significantly to fibrosis stage in patients with NAFLD. It is based on two routine laboratory tests and is, therefore, a promising tool with limited expense and widespread availability.^[9] It is known that platelet counts decrease and AST levels increase with the progression of liver fibrosis. Platelet generation diminishes secondary to a decreased production of thrombopoietin by hepatocytes.^[10,11]

Also, platelets are sequestered and destructed in the spleen as liver fibrosis advances and portal hypertension develops. As to AST, ongoing liver injury increases its release from mitochondria, and fibrosis decreases its clearance.^[12]

We here-in evaluated the performance of the APRI score in the diagnosis of fibrosis in NAFLD patients.

In our study population of 100 NAFLD cases was diagnosed with the help of ultrasound and various parameters were measured. The following observations are made from this study. In this study, the mean age was 49.4 years, and most patients were in the age group 45-55 years. In a similar study by Dhananjay K et al^[13], majority of the cases belonged to 41-50 years (56.67%). A study by Habis YZ^[14], noticed that an age of greater than 40 years was associated with significantly higher fibrosis compared with age 40 years or younger. There was a significant correlation between age and Fibroscan fibrosis score. This shows NAFLD was more prevalent in middle age groups.

There was a high incidence of NAFLD in males (61%) compared to females in this study. Sowmya et al^[16], reported NAFLD in males (60%).

The value of triglyceride was 42% between 150-200mg/dl range. A study by Dhananjay et al^[13], triglyceride value was 45.83% between 150-200mg/dl similar to our study. The mean triglyceride value was 186mg/dl. Our study shows fasting triglyceride value was high in patients with NAFLD, which reflects the increased prevalence of metabolic syndrome in NAFLD cases.

The levels of BMI was >30 in 41% cases, in between 26-30 in 36% cases and <25 in 23% cases. The mean BMI in NAFLD cases in our study is 29.6. This observation is consistent with the study done by Dhananjay et al^[13], BMI was >30 in 42.5% cases, in between 26-30 in 48.33% cases and <25 in 9.16% cases. Hence our study shows an increased prevalence of obesity in NAFLD which might be a component of metabolic syndrome.

The reference value of AST is 45 IU, cut off for cirrhosis in fibroscan in 14Kpa. The mean AST value was 41.6 IU. 34% of patients have values between 41-50 IU, and 20% of patients have >50 IU. The mean platelet count among 100 cases was 123×10^9 cells. APRI was calculated based on these AST and platelet values. Fibroscan was done for those patients and correlated with APRI. The mean APRI score was 1.09. 14 patients having APRI index between 0.7 to 1.0 had a fibro scan score between 7.0 to 8.9 denotes mild to moderate fibrosis according to the metavir scoring system.

The association between APRI score and fibroscan was statistically significant ($p=0.0214$) and there was good correlation between fibroscan and APRI. A study by Habis YZ et al^[14], noticed significant correlation for patients who had moderate or advanced fibrosis on fibroscan.

In patients with NAFLD, the APRI score seldomly reached the value of 1, but a tendency towards higher values in patients with advanced stages of fibrosis was observed. This could be explained by gradual increases of AST in the presence of normal platelet counts. Patients with NAFLD characteristically present mild to moderate increases in transaminase levels. Many studies have been done in chronic Hepatitis B and C patients regarding APRI and fibroscan, so further studies need to be done in NAFLD patients to strengthen this association. The need of sex and age specific APRI thresholds warrants further evaluation.

CONCLUSION

Aspartate aminotransferase to platelet ratio index is a cheap, blood-test based scoring system that can predict liver fibrosis. The APRI score can be a useful non-invasive alternative for the exclusion and inclusion of significant liver fibrosis. The use of APRI >0.7 would avoid the need for fibroscan. In patients with NAFLD, the APRI score appears to increase with a higher METAVIR score, suggesting that it might also be useful to diagnose fibrosis in this disease.

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