ORIGINAL RESEARCH

To assess the diagnostic accuracies of APRI and FIB4 in predicting various stages of liver fibrosis in patients with NAFLD and their correlation with Fibroscan

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ABSTRACT

Aim: To assess the diagnostic accuracies of APRI and FIB4 in predicting various stages of liver fibrosis in patients with NAFLD and their correlation with Fibroscan. **Materials and methods:** The current investigation was a prospective, observational study done among 50 patients with non-alcoholic fatty liver disease (NAFLD). The patients were identified using ultrasound imaging and both males and females were included in the study. All patients who were diagnosed with non-alcoholic fatty liver disease (NAFLD) were included in this research. The laboratory test results that were evaluated included those in the hospital information. All results were obtained within one month of a Fibroscan examination. **Results:** Mean APRI and FIB-4 among the study subjects was 0.89±0.12 and 1.59±0.45 respectively. NAFLD fibrosis was reported among 48% of the subjects i.e. G1, G2, G3 and G4 was revealed in 24%, 8%, 10% and6% of the subjects respectively. Based on FibroScan results, 50% were classified as F1, 32% as F2, 12% as F3 and 6% as F4. Mean AST/ALT, APRI and FIB-4 was found to be more in F3+F4grade as compared to F1+F2 grade. When mean AST/ALT, APRI andFIB-4 was compared according to fibroscan results, significant difference was found w.r.t. APRI and FIB-4 as $p<0.05$. FIB-4 has the best sensitivity while APRI has the best specificity in predicting different stages of liver fibrosis among patients of NAFLD. Hence APRI and FIB-4 was comparable in this study to predict liver fibrosis. AST/ALT has the worst sensitivity and specificity in predicting different stages of liver fibrosis among patients of NAFLD. **Conclusion:** Our findings indicate that APRI is the most effective marker for predicting advanced liver fibrosis, surpassing the AST/ALT ratio and showing similar performance to FIB-4. Additionally, APRI exhibits the highest connection with FibroScan results. Thus, in situations where there are limited resources and FibroScan is not accessible, APRI serves as a suitable indicator for predicting significant liver fibrosis.

Keywords: APRI, AST, FibroScan, NAFLD

INTRODUCTION

Assessing the prevalence of chronic liver disease (CLD) and the resulting hepatic fibrosis is a difficult task. According to recent data from an epidemiology database, 37.2% of patients were found to have either obvious or hidden chronic liver disease (CLD) based on assessments of liver function and imaging techniques[1]. The progression of liver fibrosis in chronic liver disease (CLD), including non-alcoholic fatty liver disease (NAFLD), determines the patient's total morbidity and mortality. A greater level of fibrosis indicates a worse prognosis[2]. Nonalcoholic fatty liver disease (NAFLD) encompasses a range of liver damage, ranging from the accumulation of fat in liver cells (steatosis) to persistent inflammatory damage (non-alcoholic steatohepatitis [NASH]). The degree of liver fibrosis is directly associated with the likelihood of developing liver cirrhosis and issues connected to the liver in both viral and non-viral chronic liver disease (CLD)[3]. Therefore, the evaluation of liver fibrosis is essential for determining treatment options and forecasting results.

The assessment of fibrosis is most accurately done using liver biopsy, which is considered the most reliable method. Nevertheless, liver biopsy is subject to many constraints, such as its high cost, potential

difficulties, and the variability that might arise due to differences between observers, within the sample, and in the sampling procedure used by the gastroenterologist[4]. Hence, the emergence of noninvasive indicators for detecting fibrosis in patients with non-alcoholic fatty liver disease (NAFLD) has gained significance in the field of medical practice[5]. Several non-invasive panels and scoring systems have been created, each with varying levels of accuracy.

Novel approaches to non-invasive laboratory and radiographic diagnostics for evaluating liver fibrosis in NAFLD have emerged in recent years, potentially addressing the drawbacks of liver biopsy. These techniques include the AST platelet ratio index (APRI) and the Fibrosis 4 (FIB-4) score[6-8]. The ultrasound-based methodology is widely used and well proven as a non-invasive tool for evaluating liver fibrosis[6]. Nevertheless, obesity restricts the diagnostic yield in around one-third of patients[9,10]. Hence this study was conducted to analyse the results of liver fibrosis assessments using ultrasound are compared to the FIB-4 scores and APRI scores for NAFLD patients.

MATERIALS AND METHODS

The current investigation was a prospective, observational study done among 50 patients with non-alcoholic fatty liver disease (NAFLD). The patients were identified using ultrasound imaging and both males and females were included in the study. The research was done at the department of medicine, after approval from the Institutional Ethical Committee. All patients who were diagnosed with non-alcoholic fatty liver disease (NAFLD) were included in this research. The research excluded patients with evidence of other chronic liver illnesses such as hepatitis B or C, alcoholic liver disease, and those using hepatotoxic drugs.

In addition, those who could not undergo Fibroscan examinations because of very high BMIs or for other reasons, and those withclinical or ultrasound evidence of decompensated cirrhosis, was also prevented from participating in the study. The laboratory test results that were evaluated included those in the hospital information. All results were obtained within one month of a Fibroscan examination. The laboratory reference normal range of serum alanine aminotransferase (ALT) is 30 - 65 U/L. Normal upper serum ALT limits were defined as 45.25 U/L for males and 30.47 U/L for females. The serum aspartate aminotransferase (AST) normal reference range is 15-37 U/L, and the normal reference range for platelet counts is 150 - 400 k/uL.Liver enzymes were measured using a dimension clinical chemistry system (Flex Reagent Cartridge). For each patient, the AST/ALT ratio was measured, and the APRI score will be determined using the following equation:

FIB-4 was determined by using the following formula:

$$FIB-4 = \frac{Age(y) \times AST(U/L)}{Platelet\ Count 10^9/L \times \sqrt{ALT(U/L)}}$$

$$APRI = \frac{AST\ Level/(/ULN)}{Platelet\ Counts(10^9/L) \times 100}$$

DIAGNOSTIC CRITERIA

NAFLD fibrosis was graded as grade (G) 1, fibrosis in zone 3 and perisinusoidal and/or pericellular fibrosis; grade 2, fibrosis in zone 3 and periportal fibrosis; grade 3, bridging fibrosis; and grade 4, nodule formation and cirrhosis. The cutoff values used for the diagnosis of severe fibrosis were: APRI>1, NAFLD score>0.676 and FIB-4 score>3.25.

USG Findings

US B-mode imaging allows to subjectively estimate the degree of fatty infiltration in the liver. It is graded as follows: Absent (score 0) when the echotexture of the liver is normal; mild (score 1), when there is a slight and diffuse increase of liver echogenicity with normal visualization of the diaphragm and of the portal vein wall; moderate (score 2), in case of a moderate increase of liver echogenicity with slightly impaired appearance of the portal vein wall and the diaphragm; severe (score 3), in case of marked increase of liver echogenicity with poor or no visualization of portal vein wall, diaphragm, and posterior part of the right liver lobe.

Data Analysis

The data obtained was transferred to spread sheets and analysed using SPSS version 24.0. The results are presented as means ± standard deviation, percentages, and tables. Continuous variables were compared using the Student's t- test, while categorical parameters were analyzed with the Chi-square test or two tailed Fischer's exact test as appropriate. A P- value of 0.05 or less was considered statistically significant.

RESULTS

Among the 50 individuals, 35 were male and 15 were female. Therefore, there was a prevalence of male participants in this research. The average age of the participants in the research was 48.52±2.87 years. Obesity was detected in 70% of the participants. The prevalence of hypertension, diabetes, and hyperlipidemia among the individuals was 36%, 20%, and 10% correspondingly, as shown in table 1.

Table 1: Gender, Overweight and co-morbidities among the NAFLD patients

Gender	Number	Percentage
Male	35	70
Female	15	30
Age in years (Mean±SD)	48.52±2.87	
Overweight+Obese	35	70
Diabetes	10	20
Hypertension	18	36
Hyperlipidemia	5	10

Mean APRI and FIB-4 among the study subjects was 0.89±0.12 and 1.59±0.45 respectively. NAFLD fibrosis was reported among 48% of the subjects i.e. G1, G2, G3 and G4 was revealed in 24%, 8%, 10% and6% of the subjects respectively. Based on FibroScan results, 50% were classified as F1, 32% as F2, 12% as F3 and 6% as F4 (table 2).

Table 2: APRI, FIB-4, NAFLD fibrosis and fibroscan results among the study subjects

Variables	Mean	SD
APRI	0.89	0.12
FIB-4	1.59	0.45
Grade	**Number**	**Percentage**
GO	26	52
G1	12	24
G2	4	8
G3	5	10
G4	3	6
Fibroscan		
F1	25	50
F2	16	32
F3	6	12
F4	3	6

Mean AST/ALT, APRI and FIB-4 was found to be more in F3+F4grade as compared to F1+F2 grade. When mean AST/ALT, APRI andFIB-4 was compared according to fibroscan results, significant difference was found w.r.t. APRI and FIB-4 as $p<0.05$ (table 3).

Table 3: Comparison of AST/ALT, APRI and FIB-4 score among the study subjects according to fibroscan outcome

Variables	F1+F2		F3+F4		t test	p value
	Mean	SD	Mean	SD		
AST/ALT	0.76	0.54	0.95	0.66	1.05	0.26
APRI	0.39	0.25	1.20	0.71	4.22	0.002
FIB-4	0.99	012	2.61	1.94	7.14	0.01

A statistically significant positive correlation was observed between APRI, FIB-4 when compared to Fibrosis stages as statistically confirmed using Pearson correlation test (table 4)

Table 4: Correlation of fibroscan with AST/ALT, APRI and FIB-4

Variables	r value	p value
AST/ALT	0.23	0.25
APRI	0.54	0.01
FIB-4	0.70	0.01

FIB-4 has the best sensitivity while APRI has the best specificity in predicting different stages of liver fibrosis among patients of NAFLD. Hence APRI and FIB-4 was comparable in this study to predict liver fibrosis. AST/ALT has the worst sensitivity and specificity in predicting different stages of liver fibrosis among patients of NAFLD (table 5)

Table 5: Diagnostic efficacy of AST/ALT, APRI and FIB-4 considering fibroscan as gold standard

Variables	Sensitivity	Specificity
AST/ALT	61.25	75.61
APRI	83.58	90.45
FIB-4	97.02	78.22

DISCUSSION

This research aimed to determine the diagnostic accuracies of APRI and FIB 4 in predicting various stages of liver fibrosis in patients with non-alcoholic fatty liver disease (NAFLD), and to assess their connection with fibroscan results. The study design was prospective and observational. A total of 50 patients with non-alcoholic fatty liver disease (NAFLD), identified by ultrasound examination, were selected for the research. The patients included both males and females. Among the 50 individuals, 35 were male and 15 were female. Therefore, there was a prevalence of male participants in this research. The average age of the participants in the research was 48.52±2.87 years. In a research conducted by Adams LA [15], a total of 73 patients were discovered. Among them, there were 45 males with an average age of 50.24 ± 15.71 and 28 females with an average age of 57.28 ± 15.07. In their research, Ome Z. Pérez-Gutiérrez et al[16] found that there was an equal distribution of males and females, with a mean age of 48.6 ± 12.7 years. In a research conducted by Hind I. Fallatah et al[17], it was found that 53.3% of the participants were male, with an average age of 50.2 years. The results of our investigation were comparable to their findings. Male patients often have more severe liver disorders across many causes compared to females. The observed phenomena may be attributed to the protective influence of female sex hormones on the advancement of hepatic fibrosis. Based on FibroScan results, 50% were classified as F1, 32% as F2, 12% as F3 and 6% as F4. Mean AST/ALT, APRI and FIB-4 was found to be more in F3+F4 grade as compared to F1+F2 grade. When mean AST/ALT, APRI and FIB-4 was compared according to fibroscan results, significant difference was found w.r.t. APRI and FIB-4 as $p<0.05$. A statistically significantpositive correlation was observed between APRI, FIB-4 when compared to Fibrosis stages as statistically confirmed using Pearson correlation test in this study. Adams LA et al[15] in their study described that 29 patients were classified as F0 (Normal), 13 as F0-F1 (Normal-Mild Fibrosis stage), 14 as F2-F3 (Mild-Moderate Fibrosis stage), 5 as F3-F4 (Moderate-Severe Fibrosis stage) and 12 as F4 (Cirrhosis). Similarly Hind I. Fallatah et al[17] in their study showed that there was a significant difference in the results of the stiffness scores for APRI and the FIB- 4 calculations between patients with advanced fibrosis of more than F2 at 44 (36%) and those with mild to moderate fibrosis of F2 or under at 78 (64%). According to Ome Z. Pérez-Gutiérrez et al[16], the ALT and AST levels did not differ significantly between groups.FIB-4 has the best sensitivity while APRI has the best specificity in predicting different stages of liver fibrosis among patients of NAFLD. Hence APRI and FIB-4 was comparable in this study to predict liver fibrosis. AST/ALT has the worst sensitivity and specificity in predicting different stages of liver fibrosis among patients of NAFLD. According to Hind I. Fallatah et al[17], there was a significant positive correlation between the Fibroscan results and the AST/ALT ratios, the APRI scores and the FIB-4 results. These findings are similar to our study. The AST/ALT ratio was the least likely among the numerous non-invasive methods in this study to indicate a difference between mild to moderate and advanced fibrosis. Ome Z. Pérez-Gutiérrez et al[16] in their studyrevealed similar findings too. Extrapolating these results to our population and comparing the diagnostic accuracy suggest that APRI can reliably exclude the presence of severe fibrosis. The APRI has an advantage in that it uses two variables available in routine practice and a simple formula for the calculation, although it is unable to obtain values for indeterminate fibrosis.

CONCLUSION

Our findings indicate that APRI is the most effective marker for predicting advanced liver fibrosis, surpassing the AST/ALT ratio and showing similar performance to FIB-4. Additionally, APRI exhibits the highest connection with FibroScan results. Thus, in situations where there are limited resources and FibroScan is not accessible, APRI serves as a suitable indicator for predicting significant liver fibrosis. This aids in making decisions regarding additional evaluations, referral to higher levels of care, and potentially implementing lifestyle changes or prescribing medications.

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