Original Research Article

Diagnostic Accuracies of APRI and FIB4 For Predicting Different Stages of Liver Fibrosis In Patients of NAFLD and its Correlation With Fibroscan

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Abstract

Aim: To analyse the diagnostic Accuracies of APRI and FIB4 for predicting different stages of liver fibrosis in patients of NAFLD and its correlation with Fibroscan. **Material and methods**: The present study prospective, observational study was conducted among 100 NAFLD patients, diagnosed by USG of both genders were recruited for 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 cutoff values used for the diagnosis of severe fibrosis were: APRI>1, NAFLD score>0.676 and FIB-4 score >3.25. **Results**: Mean AST/ALT, APRI and FIB-4 was found to be more in F3+F4 grade as compared to F1+F2 grade. A statistically significant positive correlation was observed between APRI, FIB- 4 when compared to Fibrosis stages as statistically confirmed using Pearson correlation test. 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. **Conclusion**: We found APRI to be the best index to predict advanced liver fibrosis compared to AST/ALT ratio while comparable with FIB-4, with this index having the strongest correlation with FibroScan results.

Keywords: AIDS, clinicopathology, cutaneous lesions, HIV.

Introduction

The prevalence of chronic liver disease (CLD) and consequent liver fibrosis is challenging to assess. Recently, epidemiological database revealed that 37.2% of patients had either overt or occult CLD based on liver function and imaging modalities[1-4]. The stages of liver fibrosis in CLD, such as NAFLD, define the patient's overall morbidity and mortality; the higher the stage of fibrosis, the worse the prognosis[5]. Nonalcoholic fatty liver disease (NAFLD) refers to a broad spectrum of liver damage that varies from fat deposition in the hepatocytes (steatosis) to chronic inflammatory damage (non-alcoholic steatohepatitis [NASH]). The amount of liver fibrosis is correlated with the risk of developing liver cirrhosis and liver-related complications in viral and non-viral CLD[6]. The assessment of liver fibrosis is thus crucial in making therapeutic decisions and predicting outcomes.

Liver biopsy is the gold standard for assessing fibrosis. However, liver biopsy has several limitations, including its cost, complications, and variability between observers, within the sample and the gastroenterologist's sampling technique[7,8]. Therefore, the development of noninvasive markers for the diagnosis of fibrosis in patients with NAFLD has become important in clinical practice[9]. Many non-invasive panels and scoring systems have been developed with variable accuracy.

Alternative methods of non-invasive laboratory and radiological testing for the assessment of liver fibrosis in NAFLD have evolved during the past decade, and these methods may be able to overcome the limitations of liver biopsy. These methods include the AST platelet ratio index (APRI), and the Fibrosis 4 (FIB-4) score[10-12].

Ultrasound-based technique, is one of the most extensively used and well validated non- invasive methods for the assessment of liver fibrosis[10]. However, the diagnostic yield is limited by obesity in approximately one-third of patients[13,14].

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 present study prospective, observational study was conducted among 100 NAFLD patients, diagnosed by USG of both genders were recruited for the study. The study was conducted in the department of medicine, CSS Hospital, Subharti Medical College, Meerut from December 2020 to August 2022 after taking permission from the Institutional Ethical Committee of CSS Hospital, Subharti Medical College, Meerut.

Eligibility criteria

a. Inclusion criteria

All patients diagnosed with NAFLD was included in this study.

b.**Exclusion criteria**

1. Evidence of other chronic liver diseases, including hepatitis B or C or alcoholic liver disease.
2. Patients on hepatotoxic medications.
3. Advanced liver disease
4. Cardiac failure
5. Acute fatty liver of pregnancy

In addition, those who could not undergo Fibroscan examinations because of very high BMIs or for other reasons, and those with

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clinical 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[15]:

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

FIB-4 was determined by using the following formula:

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

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[16-18]

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

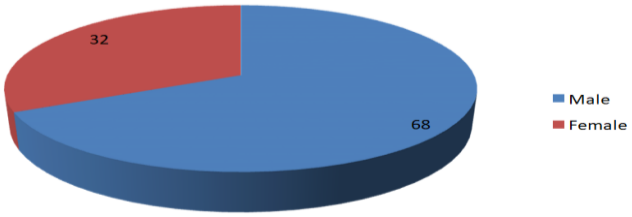
The data obtained was transferred to spread sheets and analysed using SPSS version 20.0. The results are presented as means ± standard deviation, percentages, and tables. Continuous variables were compared using the Student's *t*- test, while categorical parameters were analyzed with the Chi-square test or two tailed Fischer's exact test as appropriate. A *P*- value of 0.05 or less was considered statistically significant.

Results

Out of 100 subjects, 68 were males and 32 were females. Hence there was male dominancy in this study. Mean age among the study subjects was 47.6±9.31 years. Overweight was revealed in 71% of the subjects. Hypertension, diabetes and hyperlipidemia was reported among 34%, 21% and 12% of the subjects respectively (table 1).

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

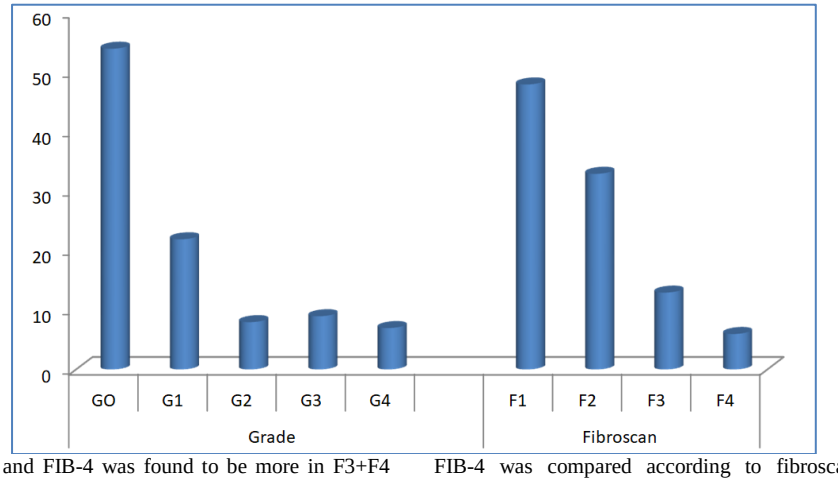
Gender	N	%
Male	68	68
Female	32	32
Total	100	100
Age in years (Mean±SD)	47.6±9.31	
Overweight+Obese	71	71
Diabetes	21	21
Hypertension	34	34
Hyperlipidemia	12	12



Mean APRI and FIB-4 among the study subjects was 0.91±0.64 and 1.63±1.17 respectively. NAFLD fibrosis was reported among 46% of the subjects i.e. G1, G2, G3 and G4 was revealed in 22%, 8%, 9% and 7% of the subjects respectively. Based on FibroScan results, 48% were classified as F1, 33% as F2, 13% 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	0.91	0.64
FIB-4	1.63	1.17
Grade	**N**	**%**
GO	54	54
G1	22	22
G2	8	8
G3	9	9
G4	7	7
Fibroscan		
F1	48	48
F2	33	33
F3	13	13
F4	6	6



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 (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	0.74	0.52	0.93	0.64	1.07	0.45
APRI	0.37	0.23	1.18	0.69	4.17	0.002*
FIB-4	0.98	1.03	2.59	1.92	7.02	<0.01*

*: statistically significant

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	0.21	0.23
APRI	0.52	<0.01*
FIB-4	0.68	<0.01*

*: statistically significant

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	60.2	74.7
APRI	82.4	89.5
FIB-4	96.8	77.6

Discussion

The present prospective, observational study was conducted to find the diagnostic accuracies of APRI and FIB 4 for predicting different stages of liver fibrosis in patients of NAFLD and its correlation with fibroscan findings.100 NAFLD patients, diagnosed by USG of both genders were recruited for the study. Out of 100 subjects, 68 were males and 32 were females. Hence there was male dominancy in this study. Mean age among the study subjects was 47.6±9.31 years. Similiarly Layal Al Danaf[19] in their study mentioned that total of 73 patients were identified, 45 males with mean age of 50.24 ± 15.71 and 28 females with mean age of 57.28 ± 15.07. Ome Z. Pérez-Gutiérrez et al[20] in their study revealed equal distribution of male and female with mean age of 48.6 ± 12.7 years. Hind I. Fallatah et al[21] in their study showed that 53.3% of the subjects were males with a mean age of 50.2 years. These findings were similar to our study. Male patients generally tend to have more severe liver diseases of most etiologies compared with females. This phenomenon may be explained by the protective effect of female sex hormones on the progression of hepatic fibrosis. Based on FibroScan results, 48% were classified as F1, 33% as F2, 13% 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 significant positive correlation was observed between APRI, FIB-4 when compared to Fibrosis stages as statistically confirmed using Pearson correlation test in this study. Layal Al Danaf[19] 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[21] 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[20], 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[21], 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[20] in their study

revealed 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.

Limitations

1. The number of included patients might be small in view of the national NADF prevalence data, but this could be compensated for by the strict inclusion criteria;
2. Liver biopsy, the gold standard of NAFLD diagnosis, was not used in this study, but due to the complications such a procedure can cause, it should not be recommended for every patient with NAFLD.

Conclusion

We found APRI to be the best index to predict advanced liver fibrosis compared to AST/ALT ratio while comparable with FIB-4, with this index having the strongest correlation with FibroScan results. Therefore, in the setting of limited resources where FibroScan is not available, APRI is an appropriate index for the prediction of significant liver fibrosis, contributing to decision making for further evaluations, referral to higher levels, and potentially lifestyle modifications or prescription of medications.

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