Section: Medical Gastroenterology

Original Research Article

STUDY OF FIBROSCAN VERSUS OTHER NONINVASIVE SCREENING TOOLS IN PREDICTING FIBROSIS IN NONALCHOLIC FATTY LIVER DISEASE PATIENTS FROM SOUTH INDIA

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Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is now considered to be the commonest liver disease in the world affecting 15-40% of general population. There is also increased evidence of fibrosis and cirrhosis in these patients. However, data regarding the prevalence liver fibrosis in Indian individuals are scarce. We studied the prevalence of fibrosis with non-invasive tests and clinical profile of NAFLD patients from south India. The aim is to study clinical profile of NAFLD patients and compare fibroscan with other non invasive screening tools in predicting fibrosis in nonalcholic fatty liver disease patients from south India. **Materials and Methods:** We conducted an analytical cross-sectional study of 100 consecutive adults with NAFLD at Stanley hospital Chennai from June 2022 to December 2022. After general and systemic clinical examination routine blood tests, fibroscan, NAFLD fibrosis score (NFS), APRI was performed. Liver stiffness measurement (LSM) by transient elastography of ≥7 kPa was taken as cutoff suggesting fibrosis. **Result:** A total of 100 patients were included in this study with 60% males & 40% females. The Mean age of the study participants was 46.08 +10.27 years. 58% patients were symptomatic with vague symptoms of abdominal pain, bloating and dyspepsia. Higher body mass index (BMI, P = 0.022), increased alanine aminotransferase (ALT), type 2 DM, hypertension, aging was independently associated with fibrosis. The prevalence of fibrosis was 23% using fibroscan. AUC for NFS (0.51) was better as compared to APRI **Conclusion:** These results support screening of all patients with NAFLD and other risk factors like hypertension, diabetes dyslipidemia and altered liver function parameters. NFS was better screening tool to detect fibrosis than APRI in absence of fibroscan.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is now considered to be the commonest liver disease in the western world affecting 15-40% of general population. The prevalence of NAFLD is approximately 9-32% within the general population of India.[1] By definition, there is accumulation of fat in liver in absence of recent or ongoing intake of significant amount of alcohol. The significant amount of alcohol has been defined variably but a cut-off intake of more than 20g/d in females and 30g/d in males. NAFLD is more common among men than women.[2] The fat deposition in liver is best defined histo-pathologically on liver biopsy as macrovesicular steatosis occupying at least 5% of the hepatocytes, however it is impractical to do liver biopsy in all patients of NAFLD. Patients with NAFLD have a higher incidence of cardiovascular diseases, cerebrovascular diseases and liver-disease related morality such as cirrhosis and hepatocellular carcinoma as compared to general population.[3,4] Various studies have shown that early intervention in NAFLD patients such as diet control, exercise and weight loss leads to an improvement in the histological grade of NAFLD.[5] Hence, early identification of fibrosis in NAFLD is vital. Transient elastography (TE) is a widely used modality that can be performed in clinic and provides a quick assessment of liver stiffness. Transient elastography is an ultrasound-based technique for fibrosis risk assessment. It generates

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two parameters: controlled attenuation parameter (CAP), which gives information of liver steatosis, and liver stiffness measurement (LSM), which gives information of liver fibrosis.[6] Fibroscan (transient elastography) measures liver stiffness through estimation of velocity of propogation of a shear wave transmitted through the liver tissue. Transient elastography accurately diagnoses cirrhosis(F4) and useful for distinguishing advanced fibrosis (F2 or greater) from no or minimal fibrosis(F0). The NAFLD fibrosis score (NFS) is another noninvasive method to detect liver fibrosis and uses parameters like age, body mass index, liver enzymes, platelet count and serum albumin to calculate a composite score. AST to platelet ratio index (APRI) determines the likelihood of hepatic fibrosis and cirrhosis. This study is designed to study the clinical profile of patients with NAFLD diagnosed by ultrasonography, and comparison of fibroscan versus other non-invasive test of fibrosis NAFLD fibrosis score (NFS), aspartate aminotransferase (AST)/platelet ratio (APRI).

MATERIALS AND METHODS

This hospital based analytical cross-sectional study was conducted at Government Stanley hospital department of medical gastroenterology, Chennai, India over a period of 6months from July 2022 to December 2022. Total 100 participants underwent ultrasound abdomen to assess the presence of steatosis. Informed consent from the enrolled participants and approval from Institutional Ethics Committee were obtained.

Inclusion criteria: All patients were above 18 years of age with diagnosis of fatty liver on ultrasonography without significant alcohol consumption which was defined as alcohol consumption more than 20 g/day for women and 30 g/day for men

Exclusion criteria: patients Age< 18 years. Patients with significant alcohol consumption, patients diagnosed with hepatitis C and hepatitis B were excluded.

Based on their USG findings, patients with NAFLD were included. After general and systemic clinical examination, routine blood investigation fibroscan, NAFLD fibrosis score (NFS), APRI was performed. Liver stiffness measurement (LSM) by transient elastography of ≥7 kPa was taken as cut off suggesting fibrosis .In a recent study from north India of comparative evaluation of fibroscan, liver biopsy and non invasive serum markers of hepatic fibrosis by Marwah et al the accuracy of fibroscan in evaluation of fibrosis was comparable to liver biopsy.[7] Hence in our study due to increased complication and cost associated with liver biopsy we have taken fibroscan as best tool for detection of fibrosis.

Statistical Analysis

Analysis was done in R software (Version-3.3). Quantitative & Categorical variables were expressed in Mean (SD) and percentages respectively. With 95% CI, p value <0.05 was considered significant Confusion matrix was done to calculate specificity, sensitivity, PPV & NPV. ROC curve was plotted to find out the efficiency between the test by comparing the area under curve (AUC) values.

RESULTS

A total of 100 NAFLD patients were Included 60% male and 40% female Mean age was 46.08+_10.27years. Mean BMI was 27.19+_2.6kg/m2.gerneral characteristics of study participants are shown in [Table 1].

58% patients were symptomatic with vague symptoms of pain abdomen, bloating and dyspepsia. Comorbid conditions like hypertension, diabetes and dyslipidemia were seen in 18%,21% and 27% of the study population. Transaminitis was seen in 9 % of population [Table 2].

The prevalence of fibrosis among studied population was 23% using transient elastography and 3 % for NAFLD fibrosis score (NFS). [Table 3]

[Table 3 and 4] shows comparison of NFS and APRI with fiboscan.

[Table 5] represents the performance characteristics of two diagnostic tests, NFS Test and APRI test used in our study. The sensitivity of both tests is quite low, with NFS Test having a sensitivity of 0.13 and APRI Test having a sensitivity of 0.08. However, the specificity of both tests is high, with NFS Test having a specificity of 1 and APRI Test having a specificity of 1. The positive predictive value (PPV) of both tests is quite low, with NFS Test having a PPV of 0.13 and APRI Test having a PPV of 0.08. However, the negative predictive value (NPV) of both tests is moderate to high, with NFS Test having an NPV of 0.79 and APRI Test having an NPV of 0.78. The accuracy of both tests is relatively high, with NFS Test having an accuracy of 80% and APRI Test having an accuracy of 79%. However, the detection rate of both tests is quite low, with NFS Test having a detection rate of 0.03 and APRI Test having a detection rate of 0.02. In conclusion, while both tests have a high specificity and accuracy, their low sensitivity and PPV suggest that they may not be reliable for diagnosing the condition at early stage.

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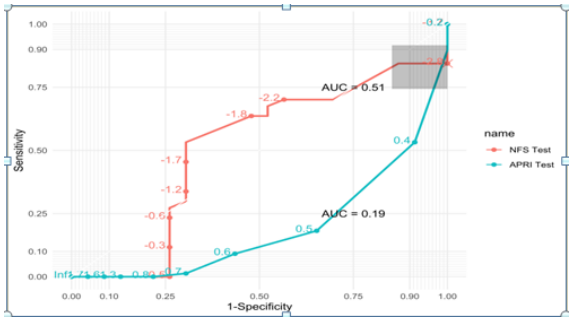

Figure 1: The ROC curve compared the efficiency of the test by comparing the AUC values. The AUC for NFS (0.51) was better as compared to APRI test (0.19) [Figure 1].

Table 1: Baseline characteristics of study population

Characteristics	Overall (N=100)
Age (years)	
Mean (SD)	46.08 (10.27)
Range	28.00 - 68.00
Sex	
Female	40 (40.0%)
Male	60 (60.0%)
Weight (Kg)	
Mean (SD)	78.67 (7.82)
Range	64.00 - 98.00
Height(cm)	
Mean (SD)	170.44 (7.89)
Range	154.00 - 184.00
BMI(Kg/m2)	
Mean (SD)	27.19 (2.64)
Range	23.50 - 34.70

Table 2: Clinical profile of the study participants

Characteristics	Overall (N=100)
Clinical Presentation	
Asymptomatic	42 (42.0%)
Symptomatic	58 (58.0%)
Blood pressure(>120/80 mm Hg)	
Hypertension	18 (18.0%)
Normal	82 (82.0%)
Blood glucose(rbs>200mg/dl)	
Diabetic	21 (21.0%)
Normal	79 (79.0%)
Lipid profile(blood cholestrol>200mg/dl)	
Dyslipidemia	27 (27.0%)
Normal	73 (73.0%)
Liver function test(ALT>40IU/L	
Abnormal	9(9%)
Normal	91(91%)

Table 3: Comparison of Fibroscan findings with NFS test

		Fibroscan Results			
		Liver Fibrosis (N=23)	**Normal (N=77)**	**Total (N=100)**	**P value**
Finding as per NFS value (cutoff point= 0.67)	Liver Fibrosis	3 (3.0%)	0 (0.0%)	3 (3.0%)	0.001
	Normal	20 (20.0%)	77 (77.0%)	97 (97.0%)	
	Total	23(23.0%)	77(77.0%)	100(100%)	

Table 4: Comparison of Fibroscan findings with APRI test

		Fibroscan Results			
		Liver Fibrosis (N=23)	**Normal (N=77)**	**Total (N=100)**	**P value**
Finding as per APRI value (cutoff point= 1.5)	Liver Fibrosis	2 (2.0%)	0 (0.0%)	2 (2.0%)	0.009
	Normal	21 (21.0%)	77 (77.0%)	98 (98.0%)	
	Total	23(23.0%)	77(77.0%)	100(100%)	

Table 5: Comparison table for two test (NFS & APRI)

Test	Sensitivity	Specificity	PPV	NPP	Accuracy	Detection Rate
NFS Test	0.13	1	0.13	0.79	80%	0.03
APRI Test	0.08	1	0.08	0.78	79%	0.02

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DISCUSSION

In our study of 100 patients of NAFLD diagnosed on ultrasonography at our centre were included. NAFLD is more prevalent among males compared to females in general population.60% were male & 40% female in our study. The Mean age of the study participants was 46.08 +10.27 years. 58% patients were symptomatic with vague of pain abdomen, dyspepsia .21% of our study population were diabetic and 27% had dyslipidaemia. Higher body mass index (BMI,
P = 0.022), alanine aminotransferase (ALT), aspartate aminotransferase, type 2 DM, hypertension was independently associated with fibrosis. Similar association of metabolic syndrome with NAFLD was seen in a study by Gaharwal et al from Madhya Pradesh, India.[8] More recently, a population-based study from coastal south India reported an overall NAFLD prevalence rate of 49.8%; urban domicile was found to be associated with a higher risk for NAFLD after adjusting for sex, body mass index (BMI), DM, and metabolic syndrome.[9] One of the multicentre studies across 101 Indian cities estimated the prevalence rate of NAFLD as 56.5% (n = 522) among 924 patients with type 2 DM.[10] Our study had lower diabetic population compared to other studies. In a study from India Metabolic syndrome was present in 43%, and at least one metabolic risk factor was present in 93% of patients with NAFLD (the commonest being central obesity in 84%).[11] Patients with non-alcoholic fatty liver disease (NAFLD) could present with many non-specific symptoms way before the diagnosis is made, although most patients are asymptomatic. Fatigue is one of the most common presenting symptoms. Sharp or dull aching upper abdominal pain, thirst, bloating and heartburn. In our study most patient had nonspecific symptoms of vague abdominal pain and heart burn, while few were asymptomatic. A study by khoonsari et al from iran had mostly asymptomatic patients of NAFLD.[12] After general and systemic clinical examination, routine blood investigation fibroscan, NAFLD fibrosis score (NFS), APRI was performed. Liver stiffness measurement (LSM) by transient elastography of ≥7 kPa was taken as cutoff suggesting fibrosis The prevalence of fibrosis was 23% using transient elastography. An interim analysis of an ongoing real-life, multicentric observational study (Indian Consortium on NAFLD [ICON-D]) in approximately 3000 patients with NAFLD showed the presence of significant fibrosis in 19%, 21%, and 29% of patients as assessed by Fibrosis-4 (FIB-4), aspartate aminotransferase (AST)-to-platelet ratio index (APRI), and FibroScan, respectively.[10] A recent meta-analysis by Xiao et al. reported that the highest diagnostic accuracy for determining the severity of fibrosis in NAFLD patients was magnetic resonance elastography and shear wave elastography. The authors also evaluated diagnostic accuracy of four non-invasive fibrosis scores, including APRI, FIB-4, BARD score, and NAFLD fibrosis score.[13] In another study by Tran et al from Vietnam, T2DM patients with NAFLD fibrosis was seen in 13% of study population by fibroscan.[14] Only 3 patients had significant fibrosis by NAFLD fibrosis score calculator used in our study population. Fibroscan was better test as compared to APRI and NFS in our study. Similar results were seen in study by Rogazzo T et al from Sao Paulo where fibroscan outweighed APRI, ELF, ARFI and FIB4.[15] In a study by Amernia et al APRI appears to be the most appropriate substitute of FibroScan for the detection of significant fibrosis in NAFLD patients.[16] In a study by Rungta S et al APRI and FIB-4 scores showed good performance in detecting patients without fibrosis as compared to fibroscan.[17]
There is growing evidence that fibrosis has a great influence on the hepatic and extra-hepatic mortality as compared to simple steatosis or even NASH without fibrosis.[2] Hence, it is vital that fibrosis be diagnosed at the earliest for NAFLD patients. It also recognises candidates for surveillance, such as endoscopic screening for gastroesophageal varices and surveillance for hepatocellular carcinoma. In addition, the presence of fibrosis may encourage the physician and the patient to make efforts at sustainable weight reduction and lifestyle modifications.

CONCLUSION

So according to our study findings in the era of increased burden of NAFLD it is recommended to screen all patients with nafld and other risk factors like hypertension, diabetes dyslipidaemia. NFS was better screening tool to detect fibrosis than APRI in absence of fibroscan.

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