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Non-Invasive Assessment Of Liver Fibrosis In Patients With Non-Alcoholic Fatty Liver Disease In A Tertiary Care Hospital

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ABSTRACT

Aims :To compare the NAFLD fibrosis score and FIBROSIS 4 score to fibroscan, and affirm whether the scores shall be used as a screening tool for liver fibrosis, in place of fibroscan. Methodology: It was a cross-sectional study. Patients with fatty liver on ultrasonological examination with 200 sample size. After obtaining the informed consent the following details were collected socio-demographic details, history, co-morbidities, anthropometric measurements, Laboratory investigations. Results: the ROC curve analysis of fibroscan reveals the area under curve of 0.499 and based on the cut off value of 4.50Kpas the sensitivity and specificity was found to be 85.7% and 83.5% respectively. The ROC curve analysis of fibrosis-4 reveals the area under curve of 0.495 and based on the cut off value of 0.80 the sensitivity and specificity was found to be 91.9% and 92.1% respectively. Analysis of NAFLD fibrosis score reveals the area under curve of 0.476 and based on the cut off value of -1.53 the sensitivity and specificity was found to be 93.1% and 93.9% respectively. Conclusion: Henceforth the study suggests that NAFLD fibrosis score shall be used as a non - invasive bedside assessment of liver fibrosis in high risk population and hence guiding their follow up for prevention of morbidity in resource limited settings.

KEYWORDS: NAFLD, fibrosis, fibroscan 3

INTRODUCTION

Occurring commonly in the world is nonalcoholic fatty liver disease (NAFLD), a disease that is yet to be recognized as a potential disease". Defined as fat in the liver that exceeds 5-10% by weight, ranges as a spectrum from a simple fatty steatosis to an inflammatory form of steatohepatitis where there is a cellular ballooning, necrosis, apoptosis, inflammation associated with fibrosis that may progress to cirrhosis in 15 –20%". [1]

The current view states that previously what was much classified as cryptogenic cirrhosis could have largely been a part of unrecognized non-alcoholic fatty liver disease that has progressed to cirrhosis". The association of diabetes and NAFLD goes hand in hand that, 40- 60% of NAFLD patients have T2DM and 35-75% of diabetic patients are found to have NAFLD. [2] Both could be linked together with probable common share of factors such as the genetics, obesity and sedentary lifestyle with dietary influences. [3]

The term NASH or Non-alcoholic steatohepatitis was introduced by Ludwig et al., who defined it in those patients who had liver diseases from steatosis to cirrhosis with history of non -significant or no alcohol consumption.[3] Those who consumed less than 210 g/ week in men and less than 140g/week in women were taken to be non-alcoholic in nature. The gold standard for confirming the cirrhosis of liver and assessing its fibrotic nature is by biopsy of liver. However, it is not routinely performed due to its invasiveness, cost, and potential complications. [4, 5] Just as in any other field recently, new non-invasive techniques have been developed to assess the degree of liver fibrosis.

Alternative methods of 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 Fibrosis 4 (FIB-4) score and NAFLD fibrosis score (NFS). In this study, Fibrosis 4 score and NAFLD fibrosis score are going to be weighed against the values of fibroscan scores to assess the accuracy of these inexpensive and readily available scoring systems for detecting fibrosis in NAFLD patients.

Objectives: 1) To assess for the presence or exclude the absence of liver fibrosis in patients with nonalcoholic fatty liver disease using NAFLD fibrosis score, FIBROSIS 4 score and fibroscan. 2) To compare the NAFLD fibrosis score and FIBROSIS 4 score to fibroscan, and affirm whether the scores shall be used as a screening tool for liver fibrosis, in place of fibroscan.

MATERIAL AND METHODS

Study design: This is a Cross sectional observational study. Study setting: Our study was conducted in Government

Royapettah Hospital /Government Kilpauk, Medical College, Chennai. For the period of one year. Study population and sample size**:** Patients with fatty liver on ultrasonological examination with 200 sample size. Inclusion criteria:Patients >30 years of age both sexes, with fatty liver on ultrasound were included in the study. Also, patients with or without diabetes mellitus (type 1 and type 2) and hypertension were included in the study. Exclusion criteria: Patients with history of significant alcohol consumption that is ethanol intake of <210 g/wk for men and < 140 g/wk for women, Patients with other causes of chronic liver disease as hepatitis B and hepatitis C, Wilson and autoimmune hepatitis, Patients on hepatotoxic drugs as amiodarone, methotrexate, HAART, Patients with cardiac failure, renal failure, thyroid disorders and hepatic congestion.

Study Procedure: After getting consent from patient or patient's relatives, the following data was collected from all patients with fatty liver on ultrasound examination. Socio-demographic details, presence or absence of diabetes, type of diabetes mellitus, duration of diabetes, treatment details including oral hypoglycemic drugs and insulin, history of consumption of alcohol, intake of hepatotoxic drugs, presenting symptoms, and detailed clinical examination was done along with anthropometric measurements. Laboratory investigations such as complete blood count, renal and liver function tests, urine routine examination, serum electrolytes, anti-hepatitis B and C, fibroscan was done.

Results obtained were computed as per application of NAFLD fibrosis score and fibrosis 4 score and results were compared against fibroscan.FIB-4 was determined by using the following formula:

$$\textbf{FIB} - \textbf{4} = \frac{\textbf{Age (years)} \times \textbf{AST Level (U/L)}}{\textbf{Platelet count} \times \sqrt{\textbf{ALT (U/L)}}}$$

NAFLD fibrosis score was determined by following formula:

$$NAFLD\ fibrosis\ score = -1.675 + 0.037 \times age(year) + 0.094 \times BMI + 1.13 \times IFG/diabetes\ (yes = 1, no = 0) + 0.99 \times AST/ALT\ ratio - 0.013 \times platelet\ count(\times 109/L) - 0.66 \times albumin\ (g/dL)$$

Data Collection:Data was collected using Pre-designed proforma, after getting clearance from Ethical committee. Written Informed consent of participants was taken.

Statistical Analysis:Descriptive analysis was used to report mean (S.D). The diagnostic accuracy of fibroscan, Fibrosis-4 score and NAFLD fibrosis score was evaluated using ROC analysis and sensitivity and specificity were reported. The association between fibroscan stage and Fibrosis-4 score and NAFLD fibrosis score were done using one way ANOVA. The association between fibroscan stage (<F2 and >F2) and Fibrosis-4 score and NAFLD fibrosis score were done using Independent student t test. The SPSS v 24 were used for the data analysis.

RESULT

In our study, out of 200 patients, 84 (42%) were males and 116 (58%) were females. Female preponderance was observed in the study. The mean age of the study participants was 45.39±9.5 years. Out of 200 patients, diabetes was present in 154 (77%) cases and absent in 46 (23%) cases. Around hypertension was present in 16 (8%) patients and absent in 184 (92%) patients. CAD was present in 3 patients and absent in 197 patients. Thyroid illness was present in 4 patients and absent in 196 patients.

Regarding the anthropometric measurements, The mean height of the study population was 159.64 ± 6.30 cm. The mean weight of the study population was 60.98 ± 8.9 kg. The mean BMI of the study population was 23.98±3.69 Kg/m2.

The mean AST and ALT level in the present study was found to be 75.67±19.05 IU and 62.07±19.89 IU. The mean AST/ALT ratio among the study participants was found to be 1.26±0.33. The mean serum albumin in the present study was 4.40±2.39 g/dl. The mean platelet count in the present study was found to be 2.69±0.69 lakhs/cu.mm.

The mean fibrosis-4 score in the present study was found to be 1.76±0.76. Based on the fibrosis- 4 NAFLD staging, out of 200 patients 10 patients were positive, 78 patients were negative and 112 patients were inconclusive. The mean NAFLD fibrosis score in the present study was found to be 0.50±0.02. Based on the NAFLD fibrosis score staging 2 patients were negative, 92 patients were positive and 106 patients were intermediate. The mean fibroscan score in the present study was found to be 6.92±2.02 Kpas. Based on the fibroscan score staging, 91 patients were F0, 23 patients were F1 and 86 patients were F3.

As seen in the Table 1, the ROC curve analysis of fibroscan reveals the area under curve of 0.499 and based on the cut off value of 4.50Kpas the sensitivity and specificity was found to be 85.7% and 83.5% respectively.

From the table Table 2, the ROC curve analysis of fibrosis-4 reveals the area under curve of 0.495 and based on the cut off value of 0.80 the sensitivity and specificity was found to be 91.9% and 92.1% respectively.

From the table Table 3, the ROC curve analysis of NAFLD fibrosis score reveals the area under curve of 0.476 and based on the cut off value of -1.53 the sensitivity and specificity was found to be 93.1% and 93.9% respectively.

The mean NFS between F0 and F3 was found to be significant (0.78±0.12 vs 0.24±0.09; p=0.04). Further, the mean NFS score between F0 and F1 was also found to be significant (0.78±0.18 vs 0.39±0.1; p=0.04). However, the NFS score between the fibroscan stage between F1 and F3 was found to be non-significant (P>0.05). Thus, based on the one-way ANOVA, the results shows that there was a significant association between fibroscan stage and NFS score and thus retains the hypothesis.

There was no significant difference (P>0.05) in the fibroscan score and fibroscan stage (F0, F1 and F3). Thus, based on the one way ANOVA, the results shows that there was no significant association between fibroscan stage and fibroscan-4 score and thus rejects the null hypothesis.

The fibroscan stage was classified as <F2 and > F2 and the NFS score between these groups compared using students t test. The results of the analysis showed that there was a significant difference in NFS score between the two fibroscan stages <F2 and >F2 (0.701±0.20 vs 0.241±0.05; p= 0.03) and this it retains the null hypothesis. fibroscan stage was classified as <F2 and > F2 and the fibrosis-4 score between these groups were compared using students t test. The results of the analysis showed that there was a no significant difference in fibrosis-4 score between the two fibroscan stages <F2 and >F2 (1.78±0.75 vs1.72±0.78; p= 0.54) and this it rejects the null hypothesis.

Parameter	Cut off value	Area under curve	Sensitivity	Specificity
Fibroscan	4.5 (Kpas)	0.499	85.7%	83.5%

Table 1: ROC curve analysis of Fibroscan

Param-eter	Cut off value	Area under curve	Sensi-tivity	Speci-ficity
Fibrosis-4	0.80	0.495	91.9%	92.1%

Table 2: ROC curve analysis of Fibrosis-4

Parameter	Cut off value	Area under curve	Sensi-tivity	Speci-ficity
NAFLD fibrosis score	-1.53	0.476	93.1%	93.9%

Table 3: ROC curve analysis of NAFLD fibrosis score

DISCUSSION

In this study, we compared FIB-4 and NFS values to fibroscan scores to assess the accuracy of these inexpensive and readily available scoring systems for detecting fibrosis in NAFLD patients. In our study, the ROC curve analysis of fibroscan reveals the area under curve of 0.499 and based on the cut off value of 4.50Kpas the sensitivity and specificity was found to be 85.7% and 83.5%.

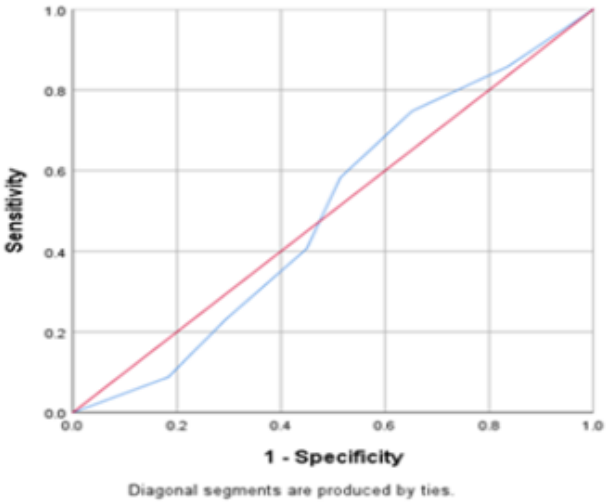

Figure 1: ROC curve analysis of fibroscan

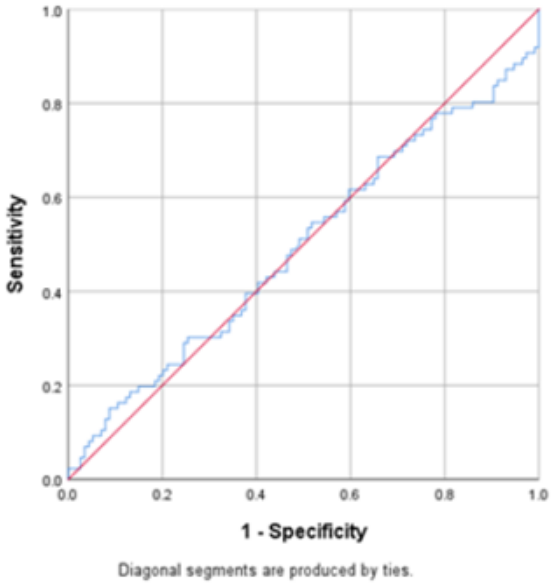

Figure 2: ROC curve analysis of fibrosis

ROC curve analysis of fibrosis-4 reveals the area under curve of 0.495 and based on the cut off value of 0.80 the sensitivity and specificity was found to be 91.9% and 92.1% respectively. The ROC curve analysis of NAFLD fibrosis score reveals the area under curve of 0.476 and based on the cut off value of -1.53 the sensitivity and specificity was found to be 99.1% and 93.9%.

In the present study, when compared to fibroscan, the sensitivity and specificity of NFS score was higher as compared to fibroscan and Fibrosis-4. Meanwhile the sensitivity and specificity Fibrosis-4 score was high as compared to fibroscan score. The present study report was comparable with the previous studiesTable 4.

Methods	Present study		Anastasiou et al (2016) [6]		Tuong and Duc (2018) [7]	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Fibrosis-4 score	91.9%	92.1%	81.8%	92.9%	69.2%	56.7%
NAFLD fibrosis 4 score	93.1%	93.1%	90%	87.1%	90.8%	75.2%
Fibroscan score	85.7%	83.5%	90.9%	59.5%	73.51%	82.8%

Table 4: Comparison of Sensitivity and Specificity with other studies

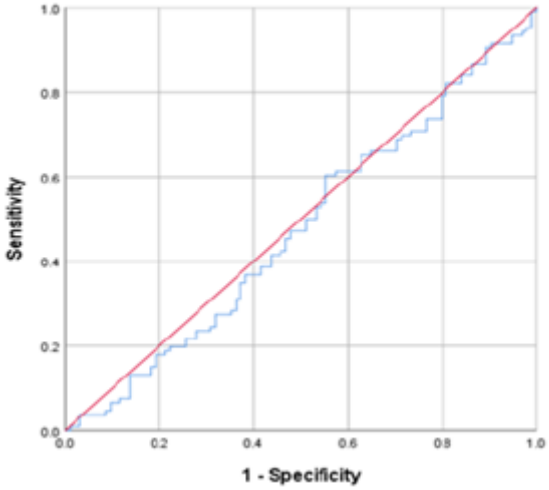

Figure 3: ROC curve analysis of NAFLD fibrosis score

Further, the ANOVA results comparing the fibroscan stage and NFS score and Fibroscan-4 score, the NFS score has significant association with fibroscan stage F1 and F3 as compared to F0 ($p<0.05$). Meanwhile, there was no significant association between the fibroscan stage and Fibrosis 4 ($p>0.05$). Further, the student t test result comparing the fibroscan stage (<F2 and >F2) and NFS score and Fibroscan-4 score, there was significant difference in the NFS score between <F2 and > F2 ($p<0.05$). Meanwhile, there was no significant association between the fibroscan stage (<F2 and >F2) and Fibrosis 4 ($p>0.05$).

CONCLUSION

When compared to Fibroscan and Fibrosis-4, NAFLD fibrosis score has good sensitivity and specificity in the prediction of fibrosis among the NAFLD patients. These findings suggest that the NFS can provide adequate reassurance to rule-out fibrosis in select patients, and has promising use in the primary care setting where fibroscan access is often limited. With a growing developing country like ours wherein the resource limited setups are seen and doctor patient ratio being less it is better to use tests that could be less monetary useful on a large scale as a screening test with good sensitivity. Henceforth, the study suggests that NAFLD fibrosis score shall be used as a non-invasive bedside assessment of liver fibrosis in high risk population and hence guiding their follow up for prevention of morbidity in resource limited settings.

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