ISSN: 0975-3583,0976-2833 VOL14, ISSUE 10, 2023

Fibroscan as A Noninvasive Tool in the Assesment of Fibrosis in Non Alcoholic Fatty Liver Disease (NAFLD) And It's Correlation with Fibrosis 4 Score (FIB4) and NAFLD Fibrosis Score(NFS)

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Received Date: 15/09/2023 Acceptance Date: 08/10/2023

Abstract

Background: Non alcoholic fatty liver disease(NAFLD) is emerging as an important cause of liver disease in India. The prevalence of NAFLD in Indian population is reported to be between 9-32% which is almost comparable to the Western countries. NAFLD is considered the hepatic manifestation of the metabolic syndrome and shares a strong association with Type 2 diabetes mellitus. **Materials and methods -** It is aProspective Observational study, conducted between October 2018 to April 2020 on 200 NAFLD patients detected with fatty liver on abdominal ultrasound examination. **Results-** In our study, the mean age of NAFLD patients is 47. 9 years. The prevalence of NAFLD increases with increasing age. The prevalence of NAFLD in men is higher with 117(58. 5%) males and 87(41. 5%) female. The prevalence of components of metabolic syndrome,i. eObesity/overweight, hypertension, dyslipidemia and T2DM is 39. 5%, 18. 5%, 69% and 46% respectively. Based on Fibroscan examination the mean stiff ness score is 7. 09 (SD 5. 07) kpa. **Conclusion**– The combined use of Fibroscan with other non invasive biomarkers is useful in detecting the advanced fibrosis in NAFLD patients and also for the follow up of patients with minimal disease, thus avoiding the need for liver biopsy.

Keywords: NAFLD, Fibroscan, FIB 4 score, Diabetes, Liver fibrosis

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Introduction

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in many parts of the world, including the United States. Population- based abdominal imaging studies have demonstrated fatty liver in atleast 25% of American adults[1].

NAFLD is emerging as an important cause of liver disease in India. The prevalence of NAFLD in Indian population is reported to be between 9-32% which is almost comparable to the Western countries[2]. The term 'NASH' or non- alcoholic steatohepatitis was introduced by Ludwig et al., describing the lesion in various degrees of severity in patients without significant ethanol exposure.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 10, 2023

NAFLD is characterized by increased liver fat content, with a threshold of > 5%, in the absence of significant alcohol consumption or other secondary cause of steatosis, including alcohol consumption (characterized as 30g/day for men and 20g/day for women)
NAFLD is considered the hepatic manifestation of the metabolic syndrome and shares a strong association with type 2 diabetes mellitus, obstructive sleep apnea (OSA), and cardiovascular disease. The global obesity epidemic has dramatically increased the prevalence of NAFLD and made it the leading cause of chronic liver disease in Western nations.
The assessment of liver fibrosis is essential for predicting the prognosis and outcome of all forms of chronic liver disease. The diagnosis can be accomplished by history, physical examination and liver imaging [1,3]. NAFLD is usually discovered incidentally because of elevated liver biochemical test levels or an incidental finding of hepatic steatosis on imaging[4]. Liver biopsy remains the 'gold standard' but there are practical limitations, which include life-threatening complications.
So alternative methods, simple and noninvasive, quantitative laboratory tests and radiological testing for the assessment of liver fibrosis in NAFLD have evolved to estimate the presence of steatohepatitis or hepatic fibrosis during the past decade and these methods may be able to overcome the limitations of liver biopsy. [5. 6]
Fibroscan is an ultrasound- based test that measures liver stiffness as a surrogate marker of fibrosis. This new tool will likely be used serially to monitor fibrosis progression and regression in NAFLD patients[7].

Objectives

- To look for the Liver stiffness score in the patients with NAFLD.
- To compare patients with High Fibrosis Scores with FIB-4 score and NAFLD Fibrosis Score.

All ethical guidelines for research were followed, and ethical committee clearance was obtained forthisstudy.

Materials And Methods

Study Period, Population and Design

The present study is Prospective Observational study, conducted between October 2018 to April 2020 on 200 NAFLD patients detected with fatty liver on abdominal ultrasound examination outpatient and in-patient department of General Medicine,Basaveshwara Teaching and General Hospital, Kalaburagi attached to Mahadevappa Rampure Medical College, Kalaburagi.
Patients are selected for study according to all inclusion and exclusion criteria. The purpose of the study was explained to the patient and informed consent was obtained in patient's own vernacular language. A detailed history, clinical and laboratory data of these patients was recorded as per the Proforma. Fibroscan was be performed on the patients in whom Fatty liver has been detected on the ultrasound examination. The Fibroscan scores were then correlated with Nonalcoholic fatty liver disease Fibrosis Score and Fibrosis- 4 Score.

Inclusion Criteria

- Patients who are diagnosed with Fatty liver on Ultrasound examination.
- Patients 8 to 80 years of age of either sex.

Exclusion criteria

- Alcohol intake > 20 gm per day
- HBsAg reactive

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 10, 2023

- Positive for anti HCV
- HIV
- Tuberculosis
- Chronic drug usage
- Pregnancy

Statistical analysis

Descriptive and inferential statistical analysis has been carried out in the present study. The results were analysed by using SPSS version 18 (IBM Corporation, SPSS Inc., Chicago, IL, USA). Results on continuous measurements were presented on Mean±SD (Min-Max) and results on categorical measurements were presented in Frequency (Percentage). Inferential statistics like Chi-square test/Fischer Exact test, Independent t test and Pearson correlation was used. P value less than 0. 05 was considered to be statistically significant.

The AST/ALT ratio was measured, and the FIB 4 score and NFS score was determined by using the following equations.

$$\boldsymbol{FIB-4=\frac{Age(year)\times AST(\frac{U}{L})[EQUATION\ 1]^{8}}{Platelet\ count(10^{9}/L)\times ALT^{\frac{1}{2}}(\frac{U}{L})}}$$

NAFLD fibrosis score = [−1. 675 + 0. 037 – age (years) + 0. 094 – BMI (kg/m^2) + 1. 13 × IFG/diabetes (yes = 1, no = 0) + 0. 99 × AST/ALT ratio – 0. 013 × platelet count (×10^9/l) – 0. 66 × albumin (g/dl)]

Results

In our study, the mean age of NAFLD patients is 47. 9 years. Male patients are 117 (58. 5%) and 87 are female (41. 5%).

Table No 1: Gender distribution

Gender	Frequency	Percentage
Female	83	41. 5
Male	117	58. 5
Total	200	100

Table No2: Risk Factors

Risk factors	Frequency	Percentage
Hypertension	21	10. 5
T2DM	76	38
Hypertension + T2DM	16	8

In our study, 76 patients have Diabetes, 21 NAFLD patients (10. 5%) have Hypertension, and 16 (8%) have both hypertension and diabetes.

In our study,121(60. 5%) NAFLD patients were found to have BMI of < 25 and 79 (39. 5) patients had BMI of > 25 who were overweight/obese. Hypertriglyceridemia was seen in 138 (69%) NAFLD patients.

The patients with advanced fibrosis have higher Serum Triglyceride levels with mean value 265. 10 (P value 0. 001, significant) compared to patients with mild disease. The prevalence of components of metabolic syndrome, i. e. Obesity/overweight, hypertension, dyslipidemia and T2DM were 39. 5%, 18. 5%, 69% and 46% respectively. In our study there is no

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 10, 2023

statistically significant association (P value = 0. 062) observed between age and grade of fibrosis.

Table No 3: Laboratory Investigations

Test	**Mean ± SD**
Platelet count	2. 76 ± 0. 88
ALT, U/L	33. 30 ± 21. 74
AST, U/L	26. 15 ± 18. 83
Triglycerides	209. 15 ± 57. 93

Test	**Mean ± SD**
Platelet count	2. 76 ± 0. 88
ALT, U/L	33. 30 ± 21. 74
AST, U/L	26. 15 ± 18. 83
Triglycerides	209. 15 ± 57. 93

The mean Alanine transaminase(ALT) levels is 33. 30 U/L. The normal range considered is less than 40 IU/L. Normal levels of ALT in 146 patients (73%) NAFLD patients, 54 (27%) patients had values higher than 40IU/L. There is no statistical difference of ALT levels between the patients of mild-moderate fibrosis and advanced fibrosis.
The mean platelet count is 2. 76. The mean platelet count in NAFLD patients with mild to moderate fibrosis and advanced fibrosis is 2. 92 and 1. 86 respectively. There is no statistical difference in platelet count between two groups (P = 0. 251).

Table No 4: Stages of liver fibrosis based on Fibroscan

Stages of liver fibrosis (kpa)	**Frequency**	**Percentage**
F0 (0-5. 9)	87	43. 5
F1 (6-6. 9)	40	20
F2 (7-9)	44	22
F3 (9. 1-10. 3)	14	07
F4 (>10. 4)	15	7. 5
Total	200	100

In our study of 200 NAFLD patients, based on Fibroscan examination the mean stiffness score is 7. 09 (SD 5. 07) kpa. 87(43. 5%) showed no fibrosis (F0), 84 (42%) showed mild to moderate fibrosis(F1-F2), 29 (14. 5%) showed severe fibrosis (F3-F4). The mean stiffness score in male patients is 7. 58kpa and females is 6. 10kpa.

Table No 5: Fibrosis 4 Score (FIB 4 Score)

FIB 4 SCORE	**Frequency**	**Percentage**
< 1. 45	169	84. 5
1. 45 – 3. 25	27	13. 5
>3. 25	4	2
Total	200	100

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The Mean FIB 4 score is 0. 92. Majority of the NAFLD patients 169 (84. 5%) showed normal or mild fibrosis with FIB 4 score < 1. 45, moderate fibrosis seen in 27 (13. 5%) patients and advanced fibrosis (>3. 25) is seen in 4 (2%) patients.

NAFLD FIBROSIS SCORE

Based on NAFLD Fibrosis score, in our study 136 patients (68%) had score less than(– 1. 45) indicating no fibrosis or minimal fibrosis, 53 patients (26. 5%) had indeterminant score and about 11 patients (5. 5%) had score of > 0. 675 indicating advanced stages of fibrosis.

Table No. 6: Correlation between Fibroscan and other variables

Fibroscan	Correlation Coefficient	P value
NFS	0. 482	0. 001*
FIB4	0. 790	0. 001*
AST/ALT	0. 267	0. 001*

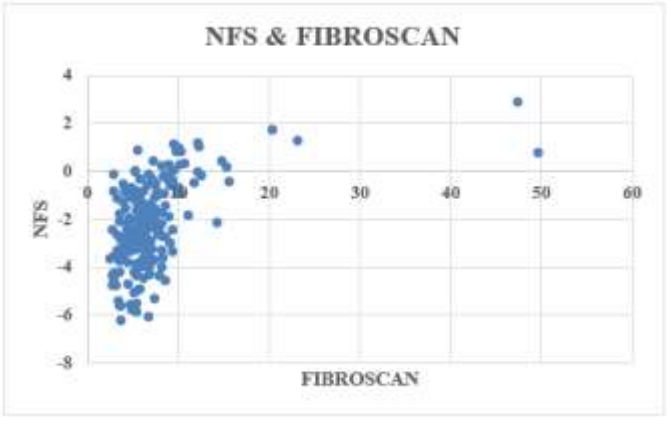

Figure 1

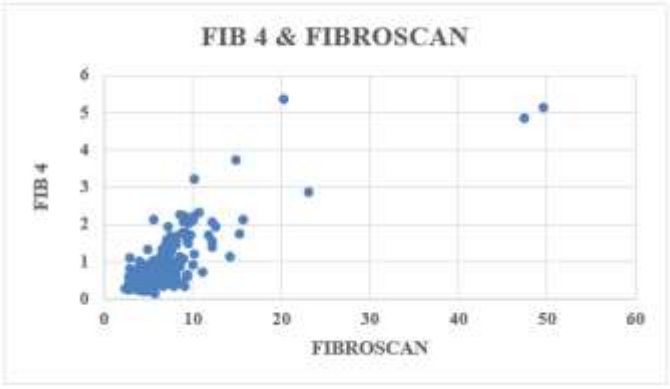

Figure 2

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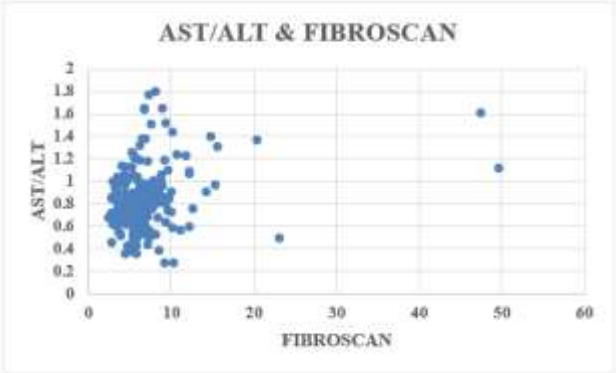

Figure 3

Statistically significant strong positive correlation is observed betweenFibroscan and FIB4. Statistically significant moderate positive correlation is observed between Fibroscan and NFS. Statistically significant mild positive correlation was observed between Fibroscan and AST/ALT.

Discussion

In our study, the mean age of NAFLD patients is 47. 9 years. The prevalence of NAFLD increases with increasing age and the peak prevalence (38. 5%) of NAFLD is between (46 – 60) years of age. However, it is difficult to generalise our results to the very old as only few patients with age > 65 years in study.

117 males (58. 5%) and 87 were female (41. 5%). The prevalence of NAFLD in men is higher, although NAFLD is also seen in females in significant number.

The prevalence of diabetes is seen in 92 (46%) NAFLD patients and 37 (18. 5%) patients have hypertension. Hence diabetes and hypertension are important risk factors for causing NAFLD. They independently act as a risk factor. Advanced stages of fibrosis is seen in 29 patients, out of which 22 patients (75%) have diabetes. This shows that presence of Diabetes leads to progression of liver disease. There is a complex bidirectional relationship between the progression of NAFLD and development of T2 DM and their interaction could result in an increase in both hepatic and diabetic mortalities in patients NAFLD and T2 DM [10].

NAFLD patients with BMI of < 25 are 121(60. 5%) and 79 (39. 5%) patients have > 25 who are overweight/obese. As seen, majority of the patients (60. 5%) are falling into normal BMI category, indicating that even people with normal weight can have NAFLD. This entity is referred to as NAFLD in lean. Among the 29 patients with advanced fibrosis 18 (62%) patients have BMI > 25. Thus indicating that Overweight leads to progression of liver fibrosis. Early measures to control the excess body weight in these NAFLD patients might be helpful in long run.

The prevalence of components of metabolic syndrome, i. e. Obesity/overweight, hypertension, dyslipidemia and T2DM were 39. 5%, 18. 5%, 69% and 46% respectively.

The patients with advanced fibrosis have higher Serum Triglyceride levels with mean value 265. 10 (P value 0. 001) compared to mild grades of fibrosis,which is statistically significant. Thus Serum Triglyceride levels can be used as a marker for advanced fibrosis.

The mean Alanine transaminase (ALT) levels is 33. 30 U/L. The normal range considered is less than 40 IU/L. Normal levels of ALT in 146 patients (73%) NAFLD patients, 54 (27%) patients having values higher than 40IU/L. There is no statistical difference of ALT levels between the patients of mild-moderate fibrosis and advanced fibrosis. Thus indicating that ALT levels are unhelpful in both diagnosis of NAFLD and determining the disease severity.

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The mean platelet count is 2. 76, Standard deviation 0. 88. The results showed, the mean platelet count in NAFLD patients with mild to moderate fibrosis and advanced fibrosis was 2. 92 and 1. 86 respectively. There was no statistical difference in platelet count between two groups (P = 0. 251). Platelet count cannot be used as a marker of severity of fibrosis.

Based on Fibroscan examination the mean stiffness score is 7. 09 (SD 5. 07) kpa and higher percentage 43. 5 % (87 patients) of the NAFLD patients exhibited no fibrosis, 84 patients (42%) mild to moderate fibrosis and 29 patients (14. 5%) had advanced fibrosis.

The mean stiffness score in male patients is 7. 58kpa and females is 6. 10kpa. Among the NAFLD patients with Advanced fibrosis (N =29), 18 (62. 06%) were male and 11 (37. 9%) female. The mean stiffness score in male patients with advanced fibrosis is 16. 9 kpa whereas in females it is 10. 5kpa. Male patients exhibited higher stiffness scores than female patients. It shows that male patients are more likely to suffer from advanced fibrosis than female patients. This phenomenon could be due to the protective effect of female sex hormones on the progression of hepatic fibrosis. Our results are similar to study carried out by HindI. Fallatah in 2016[9]. In our study there is no statistically significant association (P value = 0. 062) observed between age and grade of fibrosis. Hence age of the patient cannot be used as a predictor of hepatic fibrosis in NAFLD.

The FIB 4 identified the absence or presence of advanced fibrosis with using the threshold value of 3. 25 for the presence of advanced fibrosis. With cut off 1. 45 the Positive Predictive value(PPV)is 100%, the NPV 13. 79%. Thus indicating that FIB 4 score can diagnose the minimal grades of fibrosis with high accuracy (PPV 100%) but can't exclude the minimal grades(NPV 13. 79%). An FIB 4 index higher than 3. 25, PPV was 100% with specificity 100% and NPV 87. 24%. Advanced fibrosis can be excluded (NPV 87. 24%) and diagnosed with high accuracy(PPV 100%).

For NFS scores, PPV for lower grades of fibrosis was 100% and NPV was 87. 24%. Thus NFS can be used to accurately diagnose and exclude mild disease. For fibrosis stages 3-4, PPV is 91. 67% and NPV 90. 43%. With good NPV, the score can be used to exclude advanced disease.

Conclusion

As the prevalence of obesity and alcohol abuse have created a new era with NAFLD and alcoholic liver disease (ALD) becoming the leading causes of chronic liver disease worldwide. The Noninvasive assessment of liver disease offer a safe, cost effective and practical approach to hepatic fibrosis and steatosis quantification.

Our study has shown that the combination of Fibroscan, NFS, and FIB-4 methods provides a valuable approach for assessing liver fibrosis in NAFLD patients. Using these scoring systems in combination with imaging studies is more reasonable and a significant proportion of patients at low risk of fibrosis could avoid an unnecessary liver biopsy. These scores can also be used for follow up of the patients.

References

1. Manal F, Abdelmalek et al Non-alcoholic fatty liver disease. Harrisons 20th Edition Chapter 336- 2401-2404.
2. Duseja A. Nonalcoholic fatty liver disease in India – a lot done, yet more required! Indian J Gastroenterol. 2010;29:217-25
3. Sebastiani G, et al. Performance of noninvasive markers for liver fibrosis is reduced in Chronic hepatits C. J Viral Hepat. 2008; 15:212-218.
4. Dawn M. Torres, Stephen A. Harrison, Nonalcoholic Fatty Liver Disease, SLEISENGER, 11th Edition, Chapter 87, 1358-1359.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 10, 2023

5. Fallatah HI. Non invasive biomarkers of liver fibrosis: ano verview. Adv Hepatol. 2014;2014.
6. Machado MV, Cortez-Pinto H. Non-invasive diagnosis of non-alcoholic fatty liver disease. A critical appraisal. J Hepatol. 2013;58(5):1007–19. doi: 10. 1016/j. jhep. 2012. 11. 021. [PubMed: 23183525].
7. Nobili V, Vizzutti F, Arena U et al. Accuracy and reproducibility of transient elastography for the diagnosis of fibrosis in pediatric nonalcoholic steatohepatitis. **Hepatology** 2008;48(2):442–448.
8. Shah AG, Lydecker A, Murray K, et al. Comparison of noninvasive markers of fibrosis in patients with nonalcoholic fatty liver disease. Clin Gastroenterol Hepatol 2009; 7:1104.
9. HindI. Fallatah et al, Fibroscan Compared to FIB-4, APRI, and AST/ALT Ratio for Assessment of Liver Fibrosis in Saudi Patients with Nonalcoholic Fatty Liver Disease Hepatitis Monthly July 2016 DOI: 10. 5812/hepatmon. 38346
10. Ming- Feng Xia et al NAFLD and Diabetes: Two Sides of the Same Coin? Rationale for Gene Based Personalized NAFLD Treatment. Front Pharmacol. 2019; 10: 877.