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ORIGINAL ARTICLES

Correlation between FibroScan and AST/ALT ratio and splenic size in NASH patients in a tertiary care center

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Abstract: *Background: Non-Alcoholic Steatohepatitis (NASH) is an aggressive form of Non-Alcoholic Fatty Liver disease (NAFLD), with liver inflammation and scarring. Due to a lack of clinical biomarkers and asymptomatic nature, NASH is often under-diagnosed. It is the most common cause of chronic liver disease in the USA. Liver biopsy is the gold standard to diagnose NASH, but it is invasive and life-threatening and histologic evaluation of a liver biopsy sample is imperfect as a reference because of sampling variability due to the irregular distribution of fibrosis. Aim: Validating AST/ALT ratio as a stand-alone scoring system in NASH is scarce and so this study aims to establish a correlation between FibroScan values and AST/ALT ratio. Methodology: All NASH patients, who underwent FibroScan were included. Their demographics, FibroScan, AST, ALT values were recorded in M S Excel and Pearson correlation between FibroScan values and AST/ALT ratios of 150 NASH patients was calculated using SPSS. Results: Out of 150 NASH patients, 72% were males and 57.33% belonged to 40-50 years age group. FibroScan values and AST/ALT ratio showed positive Pearson correlation of 0.245, (p value=0.003). FibroScan values and splenic size also showed a positive Pearson correlation of 0.289 (p value<0.001). Conclusion: Males of 40-50 years age group had higher distribution of NASH, so middle aged males should be screened routinely as they are at a higher risk. FibroScan value with AST/ALT ratio and splenic size showed a positive correlation, thus showing that AST/ALT ratio and splenic size increases with increase in liver stiffness.*

Keywords: *NAFLD, NASH, FibroScan, Elastography, AST/ALT*

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is a broad term used for a range of liver conditions affecting people who drink little to no alcohol, and is the most common cause of chronic liver disease in the United States of America [1], affecting approximately 90% of the obese population and 15-40% of the general population [2]. As the name implies, the main characteristic of NAFLD is excessive fat stored in the hepatic cells of the liver [1]. It consists of a spectrum of conditions: benign steatosis or non-alcoholic fatty liver (NAFL), steatosis accompanied by inflammation and fibrosis or nonalcoholic steatohepatitis (NASH), and finally cirrhosis [3].

The rising prevalence of NAFLD globally may be accounted for by changes in dietary habits and an increase in sedentary lifestyle [4]. Insulin resistance and oxidative stress play an important role in NAFLD development and progression [5]. Due to the lack of clinical biomarkers as well as its asymptomatic nature, NASH is often under-diagnosed and most commonly found incidentally during routine Ultrasound of the abdomen [3]. No highly sensitive and specific tests are available to differentiate NASH from simple steatosis, but diagnostic accuracy can be improved by combining blood biomarkers [6]. It is an aggressive form of fatty liver disease, marked histologically by liver

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inflammation and may progress to advanced scarring (cirrhosis) and liver failure, which is similar to the damage caused by heavy alcohol use. The number of people at risk for NAFLD is even greater given the increasing prevalence of obesity, diabetes and metabolic syndrome [1]. Although steatosis can be a significant cofactor in progression of established CLD, or even hepatocellular carcinoma (HCC), only steatohepatitis indicates the presence of progressive liver disease in patients with NAFLD. Benign and malignant liver tumors have been more frequently reported with the increasing prevalence of obesity and diabetes [7]. Early identification and targeted treatment of patients with NASH are needed to improve patient outcomes, directing patients toward intensive lifestyle modification to promote weight loss as well as for referral for bariatric surgery as indicated [8]. In NAFLD, HCC frequently develops in a not-yet cirrhotic liver; ss there are no surveillance programs for these patients, diagnosis often occurs at a tumor stage beyond curative options, further marking the importance of its early diagnosis [9]. According to a recent study done by Edenvik et al. [10], NAFLD and alcoholic liver disease were more commonly associated with deficient surveillance for HCC, and therefore early diagnosis was missed.

Although liver biopsy is considered the gold standard to diagnose NASH, only those patients with a high risk of NASH or advanced fibrosis require this evaluation, since it is an invasive and potentially life threatening procedure. Non-invasive tools for diagnosis and disease staging are required, reserving liver biopsy for those patients where it offers clinically relevant additional information only [11]. The use of non-invasive tests to stage the severity of liver disease (ie. scarring) is now well established in the management of patients with chronic liver disease since the assessment of liver scarring provides prognostic information and establishes treatment priorities [12]. Techniques such as transient elastography, magnetic resonance elastography and acoustic radiation force imaging are becoming more established in detecting fibrosis in a variety of chronic liver conditions in addition to NAFLD, as reviewed by Fitzpatrick E et al. [13]

One such technique, transient elastography (TE), is a simple, safe and efficient way to estimate liver scarring which is done using FibroScan, and is the most popular non-invasive device used to assess liver 'hardness' (or stiffness) via TE. Liver hardness is evaluated by measuring the velocity of a vibration wave (also called a 'shear wave') generated on the skin [12]. The main clinical indication for liver elastography is fibrosis staging of chronic liver disease and detect advanced fibrosis. Histologic evaluation of a liver biopsy sample is an imperfect reference standard because some degree of sampling variability is inevitable due to the irregular distribution of fibrosis in chronic liver disease.

FibroScan can be easily performed at the bedside or in the outpatient clinic with immediate results for the diagnosis of significant fibrosis and cirrhosis in nonalcoholic fatty liver disease chronic hepatitis C, in recurrence of hepatitis C after liver transplantation, in co-infected HIV-HCV patients, in chronic hepatitis B, in chronic cholestatic diseases, in alcoholic disease [14]. FibroScan evaluates liver stiffness, inflammation and portal hypertension and the values have to be interpreted according to clinical, biological and morphological data. FibroScan® results range from 2.5 kPa to 75 kPa. Between 90–95% of healthy people without liver disease will have a liver scarring measurement <7.0 kPa (median is 5.3 kPa) [12].

The usual observed biochemical pattern in hepatic steatosis due to NAFLD is of increased levels of transaminases, with alanine aminotransferase (ALT) levels exceeding those of aspartate aminotransferase (AST). This classical pattern differentiates between hepatic steatosis from NAFLD and alcoholic liver injury, with the latter normally associated with a high AST/ALT ratio [15]. Generally, the AST to ALT ratio increases with the severity of the necroinflammatory and fibrotic changes [16].

Data validating the use of the AST/ALT ratio as a stand-alone scoring system in NASH is scarce. This study aims to establish a correlation between FibroScan values and AST/ALT ratio. Given the high prevalence of NAFLD in the general population, these noninvasive methods could be used in clinical practice to screen patients with NAFLD [17]. Lifestyle modifications to reduce weight are a major factor in the treatment of NAFLD. No pharmacological substances are as yet approved for the indication NASH [18].

MATERIALS AND METHODS

Out of a total of 2000 patients diagnosed with NASH over a period of 3 years (January 2017 to December 2019) in Amrita Institute of Medical Sciences and Research Centre, Kochi, 150 patients who underwent Transient Elastography Scan (FibroScan) is selected. Inclusion criteria consists of abnormal liver function tests, fatty liver infiltration on ultrasonography (US), undergone FibroScan etc. Exclusion Criteria are patients with a history of alcohol intake, hepatitis B and C, history of hepatotoxic drug intake and other liver diseases. Ethics Comittee of Amrita Institute of Medical Sciences has approved the study.

The mean of 10 elastography values is taken as the FibroScan value. Patient details like their demographics, USG findings, AST/ALT ratio, Neutrophil/Lymphocyte ratio, LFT etc were

obtained using their hospital numbers from Amrita Health Information System and recorded in MS Excel.

Pearson correlation of FibroScan values with AST/ALT ratio and splenic size and Receiver Operative Characteristic (ROC) is used to find out optimal cut off for AST/ALT and Splenic diameter, as well as their sensitivity, specificity, and predictive values, using SPSS.

RESULTS

The majority of cases were seen among males (Figure 1). 74% (111) of cases were above 40 years (Table 1 and Figure 2).

Table 1: Distribution of age

Age Group (years)	Frequency	Percent Distribution
11-20	1	0.6
21-30	15	10
31-40	23	15.3
41-50	38	25.3
51-60	48	32
61-70	22	14.6
71-80	3	2
Total	150	100

Figure 1: Distribution of gender

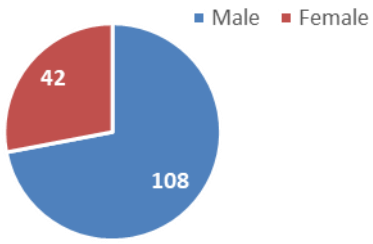
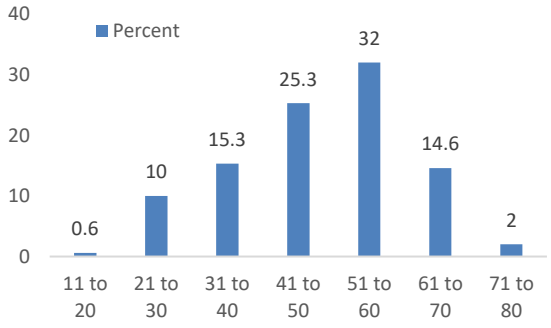


Figure 2: Distribution of age



Mean laboratory values are given in Table 2.

Table 2: Demographics and laboratory characteristics

Mean Age	48.4 years
Gender (Males)	108 (72%)
Mean HDL	46.68 mg/dl
Mean LDL	127.34 mg/dl
Mean TG	136.52 mg/dl
Mean AST	72.18 IU/L
Mean ALT	103.72 IU/L
FibroScan	7 kPa
Splenic Size	9.7 cm
Neutrophil	54.12%
Lymphocytes	35.5%
NEU/LYM	2.02

In order check the correlation between FibroScan and AST/ALT (Figure 3), Pearson correlation was used. Positive correlation of 0.245 with a statistically significant P value of 0.003 was obtained. Positive correlation of 0.298 with a statistically significant P value of <0.001 was obtained between FibroScan and Splenic Diameter (Figure 4).

Figure 3: Scatter Plot of FibroScan and AST/ALT

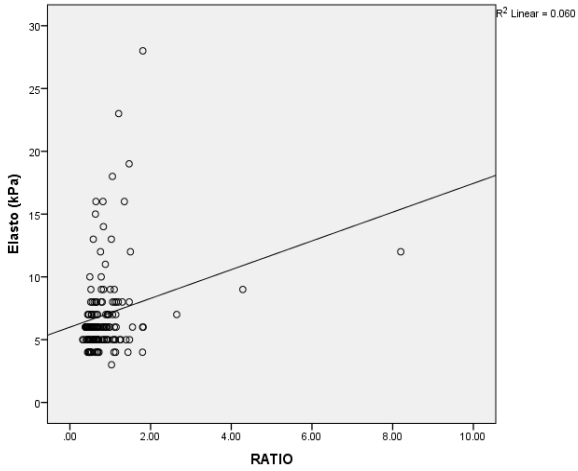


Figure 4: Scatter Plot of FibroScan and splenic size

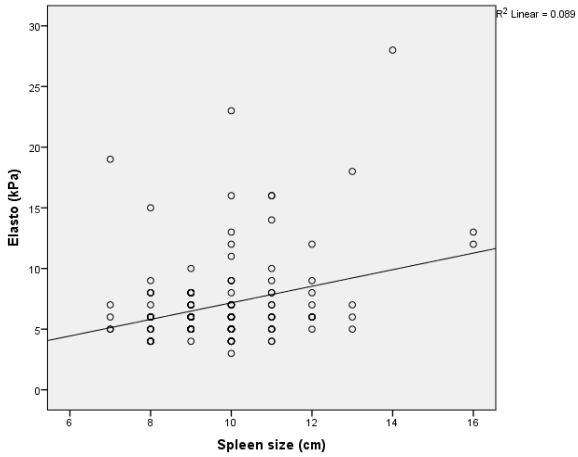
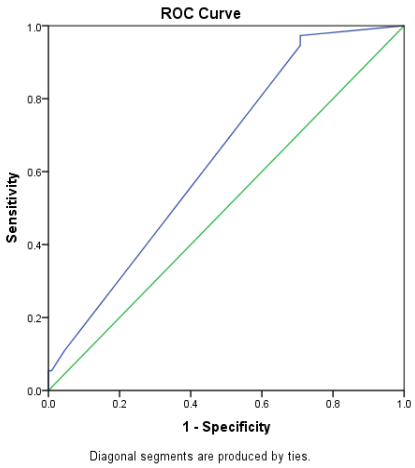


Table 3: Demographics and laboratory characteristics

		AST/ALT	Splenic size
Fibroscan	Pearson corrrelation	0.245	0.298
	p-value	0.003	<0.001

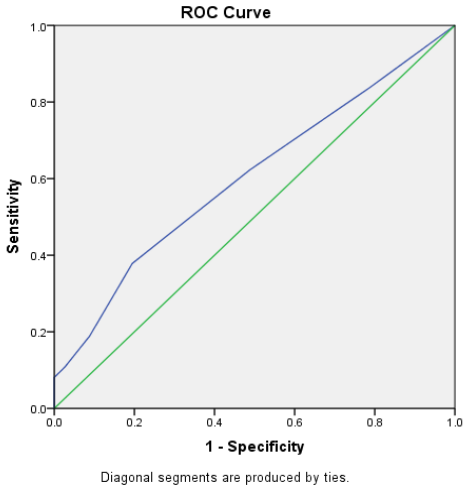
ROC curves were used to check the diagnostic accuracy of AST/ALT (Figure 5) which showed an AUROC of 0.641, ASTAST/ALT cut off 0.32 (P value 0.01), with a sensitivity and specificity of 97.3% and 29.2%. ROC for Splenic Diameter (Figure 6) showed an AUROC of 0.60, cut off of 9.5cm (P value 0.06), with a sensitivity and specificity of 62% and 51.3%.

Figure 5: ROC curve for AST/ALT



Area	0.641
AST/ALT	0.32
P value	*0.01*
Sensitivity	97.3%
Specificity	29.2%

Figure 6: ROC curve for Splenic Size



Area	0.603
SS	9.50
P value	*0.061*
Sensitivity	62%
Specificity	51.3%

CONCLUSION

Males of age more than 40 years had higher distribution of NASH, so middle aged males should be screened routinely as they are at a higher risk for developing NASH. FibroScan value with AST/ALT ratio and splenic size showed a statistically significant positive correlation, thus showing that AST/ALT ratio and splenic size increases with increase in liver stiffness. Thus our study shows that AST/ALT ratio can also be used for prompt diagnosis and management of NASH patients.

Contribution of authors

Varsha Somakumar, V S Srikanth, Cibi Manoharan – Concepts, design, definition of intellectual content, literature search, data acquisition, data analysis, Manuscript preparation, editing and review; Vishal Marwaha, VR Mujeeb, M.G.K.Pillai - Concepts, design, definition of intellectual content, Manuscript editing and review.

The manuscript has been read and approved by all the authors, and each author believes the manuscript represents honest work. There is no conflict of interest among the authors.

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