

Original Research Article

An observational study of the evaluation of fatty liver in non-alcoholics with metabolic syndrome using fatty liver index and its correlation with USG elastography

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Received: 12 February 2020

Revised: 13 February 2020

Accepted: 12 March 2020

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ABSTRACT

Background: NAFLD (Non Alcoholic Fatty Liver Disease) is being considered the hepatic component of metabolic syndrome. It is now the most common cause of chronic liver disease worldwide and needs to be addressed urgently as it is asymptomatic and widely prevalent and can progress to cirrhosis and hepatocellular carcinoma. There is a need for simpler methods to diagnose the condition in modern day practice which will help in identifying vulnerable subjects and in bringing about awareness and lifestyle modifications focused on reversal of the condition. Aim of this study was to check the applicability of the fatty liver index in modern day out patient practice using formula based FLI calculator.

Methods: It was a cross sectional study on patients with metabolic syndrome in a tertiary care hospital. 60 patients with metabolic syndrome, both male and female above the age of 30 years and who were non-alcoholics were enrolled in the study. BMI, waist circumference, lipid profile and GGT were obtained and FLI calculated. It was compared with the ultrasound and Elastography reports. Chi square test, Independent t test and ANOVA test were used for comparing parameters. A p value of <0.05 was considered statistically significant.

Results: Among 60 patients all had fatty liver which emphasizes that fatty liver is the hepatic component of metabolic syndrome. There is a significant correlation between BMI (Body Mass Index) and waist circumference in predicting fatty liver and to some extent its grade. Patients with higher BMI had a greater grade of fatty liver.

Conclusions: The fatty liver index is a reliable predictor of fatty liver in people with metabolic syndrome. The grade of fatty liver increases with increase in waist circumference and increased BMI. Ultrasound and Elastography are reliable non invasive methods of detecting fatty liver. BMI and Waist circumference are strong predictive factors for fatty liver.

Keywords: Metabolic syndrome, Fatty liver index, Non alcoholic fatty liver disease, Elastography, USG, Correlation

INTRODUCTION

Non-alcoholic fatty liver disease is a major cause of chronic liver disease worldwide.¹ Its prevalence in Indian population ranges from 5 to 28%, which is comparable to the West.² Metabolic syndrome is a cluster of conditions that increase the risk of heart disease, stroke and diabetes.

Occurrence of fatty liver in people with metabolic syndrome is now very common because of increased urbanization and changing food habits and sedentary lifestyle.³ Obesity and its adverse associations, especially type2diabetes and hypertriglyceridemia, are the main factors responsible for the current epidemic.⁴ Non-alcoholic fatty liver disease (NAFLD) is now considered

the hepatic equivalent of metabolic syndrome.⁵ Excess fat in the body is stored in our liver cells in >5 to 10% manifests as fatty liver. This condition which is called as Non Alcoholic Steato hepatitis leads to liver inflammation which in turn leads to scarring -irreversible damage –cirrhosis –liver failure

During the last two decades, NAFLD has become the most common chronic liver disease in North America and Europe, but until recently what was thought to be uncommon (perhaps due to the lack of adequate studies in Asia).² Fatty liver can be identified on imaging modalities (ultrasonography, computed tomography scans, and magnetic resonance imaging, Elastography and liver biopsy).⁶ The fatty liver index calculator takes into account the BMI, Waist circumference, Triglycerides and GGT of an individual and using the algorithm formulated by Bedogni et al, detects fatty liver.¹

This article attempts to highlight our current knowledge of the prediction of fatty liver in non-alcoholics with metabolic syndrome, using the fatty liver index (FLI).The FLI is correlated with USG and Elastography findings of the liver.

METHODS

It is a cross sectional observational study conducted at a rural tertiary care hospital in Pondicherry, India. The study period was 18 months and has been approved by the institutional ethics committee and all standard procedures were adopted according to the ethical committee guidelines.

Inclusion criteria comprised of people above the age of 30 years (non-alcoholics) who presented for master health check-up who fit into the metabolic syndrome criteria, i.e. with Waist circumference of >100cm (men) and >88 cm (women), BP >130/85 mm Hg. or on hypertensive medications, Fasting blood sugars of >100 mg/dl, HDL<40mg/dl in men, <50 in women, BMI equal to or more than 30 kg/sq.m. Subjects excluded were alcoholics and people with pre-existing liver pathology eg: Hepatitis B,C infections.

Sample size was worked to 60 subjects with a precision error of 3% SD of 1.96. 60 patients were recruited after obtaining an informed consent. History regarding DM/HTN/Dyslipidemia and treatment details were obtained. Blood samples for LFT, FLP (Fasting lipid profile) were obtained and all previous treatments were continued. FLI (Fatty liver index) calculated using the FLI calculator.

FORMULA:FLI = $(e^{0.953 \cdot \log_e(\text{triglycerides})} + 0.139 \cdot \text{BMI} + 0.718 \cdot \log_e(\text{ggt}) + 0.053 \cdot \text{waist circumference} - 15.745) / (1 + e^{0.953 \cdot \log_e(\text{triglycerides})} + 0.139 \cdot \text{BMI} + 0.718 \cdot \log_e(\text{ggt}) + 0.053 \cdot \text{waist circumference} - 15.745) * 100$ (1)

The same patients then proceeded for Ultrasound imaging and Elastography. Using Siemens Acuson S2000

Machine was used and correlations of Fatty liver index to USG and Elastography findings were done

Statistical method

Sampling was done by simple random sampling. Statistical analysis was carried out using SPSS version 17.0(IBM SPSS, US) software with regression models installed and Microsoft Word and Excel have been used to generate graphs, tables etc.

Results on continuous measurements such as BMI, Waist circumference, HDL-C, TGL,GGT and FLI are presented on Mean±SD (min/max) and results on categorical measurements such as grade of fatty liver are presented in percentage (%). Significance is assessed at 5% level .Chi square/Independent t test/ANOVA test were used to find the significance of the study parameters.

Operational definitions

BMI

Body Mass Index is a person's weight in kg, divided by his or her height in metres squared. The National Institute of Health now defines normal weight, overweight, and obesity according to BMI rather than the traditional height/weight charts. Overweight is a BMI of 27.3 or more for women and 27.8 or more for men.

Waist circumference

Waist circumference is a measurement taken around the abdomen at the level of the umbilicus. It is used to screen patients for possible weight related health problems. In my study men with >90 cm and women with >80cm waist circumference will be chosen as subjects as it is included in the metabolic syndrome criteria

Triglyceride level

An ester form of Glycerol with three fatty acid groups. It is the main constituent of natural fats and oils. In metabolic syndrome a high triglyceride level is found. Normal is <150 mg/dl

GGT

Gamma glutamyltransferase is a liver enzyme that is found to be deranged in liver disease. It is a diagnostic marker of liver disease. Normal value is 9 to 48 units per liter.

FLI

The fatty liver index is an algorithm based on Waist circumference, Body mass index (BMI), Triglyceride (TGL) and Gamma glutamyl transferase (GGT) for the prediction of fatty liver ,and is easy to employ as its each individual component is a routine measurement in clinical practice .

FLI formula:

FLI is thus calculated as:

$$FLI = (e^{0.953 \cdot \log_e(\text{triglycerides})} + 0.139 \cdot \text{BMI} + 0.718 \cdot \log_e(\text{ggt}) + 0.053 \cdot \text{waist circumference} - 15.745) / (1 + e^{0.953 \cdot \log_e(\text{triglycerides})} + 0.139 \cdot \text{BMI} + 0.718 \cdot \log_e(\text{ggt}) + 0.053 \cdot \text{waist circumference} - 15.745) * 100 (1)^1$$

USG

Ultrasound is a non-invasive radiological investigation by which the size, echo-texture of the abdominal organs can be visualized. It picks up abnormalities in the viscera and guides in diagnosis.

Elastography

Elastography is a medical imaging modality that maps the elastic properties and stiffness of soft tissue. The main idea is that whether the tissue is hard or soft will give diagnostic information about the presence or status of disease. It is a non-invasive radiological investigation, which in our study was used for correlation of findings and to substantiate fatty liver in the subjects studied. It is conclusive for fatty liver in this study and complements the USG findings.

RESULTS

Among the 60 study patients, mean age of patients is 47.9±9.3 years and age distribution wise most of the patients nearly 40% belonged to the age group of 41-50 years, with equal distribution of male and female, 77% were diabetic and 61.7% were hypertensive. GGT range of 12-58 (U/L), with value of 58 in only one patient outlier who was confirmed to be a non alcoholic and not known to suffer from any other causes of hepatic inflammation (Table 1).

Table 1: Distribution of different parameters and their mean and standard deviation.

	Mean±SD
BMI	32.6±2.9
WC	106.9±8.0
HDL-C	40.5±7.4
TGL	168.5±38.7
GGT*	22±16-27.5
FLI	77.7±14
*MEDIAN	(IQR)

The variables required to calculate the Fatty liver index were analysed and found to be statistically significant. Subjects with waist circumference of 101-110 cm had a mean of 75.9 and SD of 14.6 and subjects with waist circumference of >110cm had a mean of 91.3 and SD of 6.2 and a p value of <0.001 was obtained. Based on USG

findings grade I fatty liver was present with a mean of 64.2 and SD of 15.3, grade II fatty liver was present with a mean of 78.1 and SD of 7.6 and grade III fatty liver was present with a mean of 93.5 and SD of 4.0 and p value of <0.001 was obtained (Table 2).

Table 2: FLI and its association with fatty liver and distribution of different grades of fatty liver visualized with USG and elastography.

FLI	USG/Elastography No. of patients	Percentage
Grade I	16	26.7
Grade II	31	51.7
Grade III	13	21.6
Total	60	100

According to the American Gastroenterology Association fatty liver in USG is graded as the following,

- Grade 1: Increased hepatic echogenicity along with visible periportal and diaphragmatic echogenicities.
- Grade 2: Increased hepatic echogenicity along with imperceptible periportal echogenicity, with no obstruction of the diaphragm.
- Grade 3: Increased hepatic echogenicity along with imperceptible periportal echogenicity and obstruction of the diaphragm.⁷



Figure 1: Elastography images of grade II fatty liver.

Elastography images using Acoustic Radiation Force Impulse Imaging (ARFI) which shows increased mean shear wave velocity (m/s) of the liver parenchyma consistent with fatty liver (Figure 1).

DISCUSSION

Study shows that BMI and waist circumference are significant predictive factors of fatty liver and to a certain extent the grade of fatty liver which was supported by ultrasound and Elastography findings. Authors were able to observe that people leading sedentary lifestyles were showing a higher incidence of metabolic syndrome and fatty liver.

Statistically 60 patients with Metabolic Syndrome were taken up for the study. In a study conducted by Kotronen A et al, 90% of participants with NAFLD had atleast one component of Metabolic syndrome and 33% subjects had all components of Metabolic syndrome, supporting the definite association between both conditions which are interrelated and share a common causative factor primarily insulin resistance.⁸ All 60 patients had a BMI of $>30\text{kg/m}^2$ and were obese. In a study conducted by Angulo P et al, it was found that 30-100% of individuals with NAFLD were obese and hepatic steatosis was found to be 4.6 times higher than the normal population.⁹

In this study almost 30 % of participants were housewives and 17% were engineers which was closely followed by businessmen who constituted 11%. It further emphasizes on the sedentary lifestyle of such individuals who form a major cohort in the fatty liver spectrum which is consistent with the findings of Pardhe et al, and their study on physical activity and nutrition in subjects with NAFLD.¹⁰

The mean BMI was 32.6 and the mean waist circumference was 106.9 further supporting the conclusions of Dasarathy et al, and Bellatani et al, that BMI and waist circumference are independent predictors of fatty liver and metabolic syndrome supported by ultrasound evidence.^{11,4} Mean triglyceride was 168.5 ± 38.7 mg/dl which is similar to the results obtained by Bedogni et al, in their study which identified raised TGL levels to be an independent risk factor in predicting the incidence of fatty liver.¹² Mean FLI in this study was 77.7 ± 2.9 . The average GGT was 22 and 50% of participants had values ranging between 16-27.5. Mean HDL was 40.5 ± 7.4 mg/dl in this study which was consistent with a similar study done by Pardhe et al, where amongst all metabolic components studied HDL-C had the highest frequency of 69.8% closely followed by TGL with frequency of 60.27%.¹⁰ It was also concluded that an increase in TGL and a decrease in HDL-C correlated with the development and progression of NAFLD. They also studied about the levels of total cholesterol and LDL-C between different grades of fatty liver and found it to be of no great significance, which was not done in this study. In a study done by Kirovski et al, they arrived upon the conclusion that reduced HDL-C levels were indeed associated with greater degree of steatosis.¹³ Another study by Marchesini et al, found that hypertriglyceridemia was present in 64% and low HDL-C was present in 42% of the study population who had NAFLD.¹⁴ In contrary to results a study conducted by Mahaling et al, with a p value of <0.05 arrived upon the conclusions that TC/HDL/LDL and VLDL increase were associated with an increase in grade of fatty liver, however increase or decrease in TGL did not contribute to be an independent risk factor.¹⁵ This study showed that there was a significant association of FLI with waist circumference. The mean fatty liver index in patients with waist circumference upto 100 cm was 68.3. It was 75.9 among patients with waist circumference of 101-110

cm and 91.3 for waist circumference above 110cm. In a study done by Bedogni et al, with parameters involved being AST/ALT/BMI/Waist circumference /Sum of 4 sites skinfolds /Glucose/Insulin and TGL, insulin levels was found to be the strongest predictor after BMI.¹² When insulin was removed it was found that waist circumference in the final model indicated that waist circumference is an independent factor in the prediction of fatty liver. The mean FLI among patients with grade I fatty liver was 64.2, grade II 78.1 and grade III 93.5, both in ultrasound and Elastography findings. About 52% of participants had grade II fatty liver. One fourth (27%) had grade I and 22% had grade III fatty liver. It is important to note that both Ultrasound and Elastography had similar findings for all patients. In a similar study conducted by Pardhe et al, in Nepal on 429 subjects with a mean age of 56 ± 10 years the incidence of grade I fatty liver was 54%, grade II was 39% and grade III was 7%.^{14,10}

They found a significant correlation between increased BMI, Waist circumference, SBP and DBP with a p value of <0.001 . In the frequency of distribution of metabolic parameters highest incidence was that of HDL-C (69.8), TGL (60.27), Overweight (57.5), HTN (56.1). However liver enzymes particularly ALT values were markedly increased with increasing grade of fatty liver, which is a limitation in our study as LFT was not included for analysis in our subjects. On the contrary a similar study done by Cordeiro et al, showed that there was no significant discrepancies between ALP, ALT and AST in individuals with hepatic steatosis.¹⁶

In this study 83% were non smokers, probably because 50% of the study group were females and smoking amongst females in the Indian subcontinent is fairly uncommon and that all participants in the study were non alcoholic. It is commonly noted that smoking and alcohol co-exist in the same individual .

In view of small sample size and the female subjects in the study are non smokers so the association between smoking and FLI could not be properly assessed.

In future a larger sample can be studied and results compared with similar studies by others.

CONCLUSION

Based on the results and methodology employed we have concluded that BMI and Waist circumference are strong predictive factors for fatty liver. Diabetes, dyslipidemia and hypertension as components of metabolic syndrome are strong predictive factors of fatty liver. The fatty liver index is a reliable predictor of fatty liver in people with metabolic syndrome even without the aid of radiological investigations. The grade of fatty liver increases with increase in waist circumference and BMI. Ultrasound and Elastography are reliable non-invasive methods of detecting fatty liver.

ACKNOWLEDGEMENTS

Authors would like to acknowledge the Vice Chancellor Sri Balaji Vidhyapeeth (Deemed to be University), India, the Dean MGMCRI Puducherry, India and Prof. Dr. Lokesh HOD Department of General Medicine for their invaluable assistance.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Danasekaran V, Narayanan M. An observational study of the evaluation of fatty liver in non-alcoholics with metabolic syndrome using fatty liver index and its correlation with USG elastography. *Int J Adv Med* 2020;7:673-7.