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Dr. Krishna Kartik
Department of Radio-Diagnosis, Medical College and S.S.G. Hospital, Vadodara, Gujarat, India

Dr. Chetan M Mehta
Department of Radio-Diagnosis, Medical College and S.S.G. Hospital, Vadodara, Gujarat, India

Corresponding Author:
Dr. Krishna Kartik
Department of Radio-diagnosis, Medical College and S.S.G. Hospital, Vadodara, Gujarat, India

Ultrasonographic evaluation of fatty liver disease and cardiovascular disease in type ii diabetics

Dr. Krishna Kartik and Dr. Chetan M Mehta

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Abstract
Purpose: The current study is an attempt at ultrasonographic evaluation of risk factors of nonalcoholic fatty liver disease (NAFLD) in Type 2 diabetic patients and its correlation with cardiovascular risk in the same in comparison to healthy controls. This study aims to evaluate these risk factors in a cost effective and non-invasive manner using ultrasonography.
Materials and methods: Study was carried out on 151 diabetic patients and 150 age and sex matched controls on whom ultrasonographic evaluation was performed by single radiologist and the following parameters were examined: Liver echogenicity, Portal vein doppler study, Mesenteric fat pad thickness, Carotid artery grey-scale study for assessing atherosclerotic changes.
Results: Among the parameters assessed among the type 2 diabetic patients age, BMI, Liver echogenicity, Portal vein velocity, Paraumbilical Mesenteric Fat Thickness and bilateral carotid artery intima medial thickness showed significant association with Non-alcoholic fatty liver disease**.** ($p = <0.001$). Portal Vein Velocity and Paraumbilical Mesenteric Fat Thickness were the best parameter for predicting Fatty Liver Disease with a high sensitivity (>70%) and specificity (>86%).
Conclusion: Non-alcoholic fatty liver disease is fast reaching epidemic proportions worldwide and in the Indian subcontinent. The morbidity and mortality related to NAFLD is expected to rise with the upsurge of obesity and type 2 diabetes mellitus, so the need of the hour is to ultrasound based devise low cost, accurate, reproducible, and non-invasive techniques and means of estimating Non-alcoholic fatty liver

Keywords: Ultrasound, Fatty liver, Non-alcoholic fatty liver, cardiovascular disease, atherosclerosis

1. Introduction
Non-alcoholic fatty liver disease (NAFLD) is a common condition characterised by excess deposition of fat in liver which ranges from simple steatosis to steatohepatitis, cirrhosis and hepatocellular carcinoma (HCC) in the absence of excessive alcohol intake [2]. Metabolic syndrome and conditions associated with it like diabetes, obesity and dyslipidaemia are predisposing factors of NAFLD [1].
NAFLD is becoming a major public health problem due to rising incidence of obesity and type II diabetes. The overall prevalence of NAFLD is 15 to 40% in western countries while 9-40% in Asian countries [1]. The data from Asian countries derived from various published series where there was no uniformity in definition of NAFLD and population studied. Prevalence of the disease is estimated to be around 9-32% in the general Indian population, with a higher incidence rate amongst obese and diabetic patients. NAFLD is a common cause of chronic liver disease and liver transplantation in western countries [2]. Increasing incidence of NAFLD has been well documented from Asian countries like Japan, China and the Indian subcontinent [3]. Diabetes mellitus (DM), obesity, hyperinsulinemia are predisposing factors NAFLD. There is increase in incidence of DM, obesity and insulin resistance in India in last two decades [4]. Hence it is logical to expect increase in incidence of NAFLD in India.

2. Review of literature
While there is abundant literature on association of NAFLD with CVD, there is sparse literature regarding the screening for NAFLD in patients with diabetes mellitus and CVD. The association of NAFLD with CVD is related to the common metabolic risk factors such as obesity, diabetes mellitus (DM), hypertension, and dyslipidemia; however, multiple

studies have shown that NAFLD is also independently associated with CVD despite presence of confounders (metabolic risk factors). CVD has been shown to be the most common cause of death in patients with NAFLD, and this risk is more in patients with NASH as compared with simple steatosis or NAFL [3, 5-8]. Majority of these studies have shown that risk of mortality is more in these patients as compared with controls, while few studies have shown independent association with CVD but not higher risk of mortality [6-9].

NAFLD is now acknowledged to be the commonest liver condition in the world, largely because of the considerable increase in metabolic diseases such as obesity and diabetes [9]. It is clear that NAFLD leads to liver related morbidity and mortality in a subset of people, particularly those who are obese, diabetic, and who have NASH. However, a better understanding of the natural history of NAFLD will permit better identification of at risk patients who should be targeted for long term and potentially expensive treatment, as CVD is more common cause of death in NAFLD, role of cardiovascular risk screening is important. The current study discusses the utility of ultrasonographic screening tools in the screening of NAFLD and CVD in patients with diabetes.

2.1 Epidemiology of NAFLD

Non-alcoholic fatty liver disease (NAFLD) is a clinical diagnosis that includes the presence of 5% or more hepatic steatosis as determined by liver imaging or biopsy in the absence of secondary causes of hepatic fat accumulation. NAFLD spans the spectrum of simple steatosis or non-alcoholic fatty liver (NAFL) to non-alcoholic steatohepatitis (NASH) which is defined histologically as hepatic steatosis, hepatic inflammation, and hepatocellular ballooning with or without fibrosis. NASH can progress to cirrhosis a known causes of secondary hepatic steatosis and hepatocellular carcinoma.

Current studies show that NAFLD affects 30% of the United States (US) population; 32% of the Middle East population; 30% of the South American population; 27% of Asian populations (highest in East Asians); 24% of the European population; and 13% of the African population. Hispanic Americans have a higher prevalence of NAFLD compared with Caucasians; while African-Americans have the lowest prevalence among all racial and ethnic groups in the US [10]. In India the prevalence is approximately 9-36% [11]. The etiology of this racial and ethnic disparity is likely multi-factorial and includes contributions from genetic, behavioural and socio-economic factors [12].

NAFLD is a metabolic disease which involves the complex interactions between hormonal, nutritional and genetic factors, few of which have been briefly discussed below.

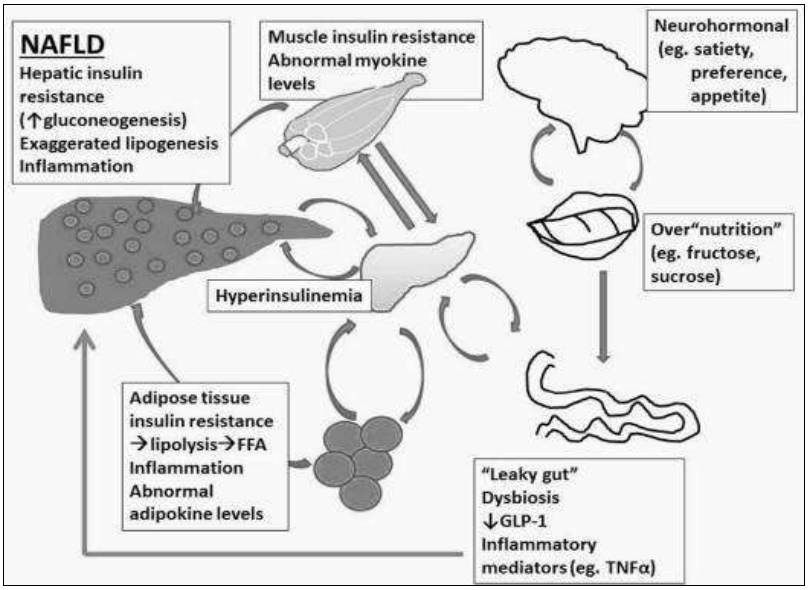

Fig 1: Image depicting the Multifactorial etiology of fatty liver disease

2.2 Role of insulin resistance, lipotoxicity, and hepatic inflammation- transition from steatosis to steatohepatitis

Both hyperinsulinemia and insulin resistance are central to NAFLD pathophysiology [14]. Under normal conditions, pancreatic beta cells secrete insulin primarily in response to circulating glucose levels. Insulin acts on several metabolic tissues, including adipose tissue to promote esterification of fatty acids and storage into lipid droplets while inhibiting the opposing process of lipolysis. In hepatocytes, insulin activates key regulators of *de novo* lipogenesis. In NAFLD patients, the development of insulin resistance results in 1) increased adipocyte lipolysis and high circulating free fatty acids available for subsequent hepatic uptake, 2) reduced hepatic glycogen storage and 3) and increased gluconeogenesis. Perhaps in response to systemic insulin resistance, hyperinsulinemia develops which augments hepatic *de novo* lipogenesis pathways. The net effect is increased intra-hepatic lipid accumulation (steatosis) and accentuated triglyceride secretion in the form of very-low density lipoprotein. The increased lipid load circulates to adipose tissue, thus compounding the already reduced ability of adipocytes to store these lipids in lipid droplets.

In hepatocytes, the inability to accommodate neutral lipids within lipid droplets exposes cells to lipotoxic bioactive lipids. Lipotoxicity further impairs insulin signalling, causes oxidative damage, and promotes inflammation and fibrosis through a number of mechanisms. Cell injury may occur when the capacity of hepatocytes to safely store fat is overwhelmed by continued uptake, local synthesis, or impaired egress of fatty acids; these fatty acids then become toxic to the cell in a pathobiological process termed lipotoxicity [15]. The fatty liver is predisposed to forms of

injury that involve oxidant stress. Steatosis could therefore provide the setting (or "first hit") for NASH, but a "second hit" may be needed to cause cellular injury or recruit inflammation.

The "two-hit" model of NASH pathogenesis was proposed in response to the experimental observations that endotoxin causes focal cytolysis and inflammation with exaggerated release of TNF alpha in rodent models of Steatosis, and the livers of patients with NASH as well as animal models of metabolic steatohepatitis over-express CYP2E1, a microsomal fatty acid oxidase that generates reactive oxygen species.

2.3 relation of NAFLD and CVD

NAFLD and cardiovascular disease are associated with metabolic syndrome, they are also independently associated through several common risk factors and hence NAFLD is important for the pathogenesis of CVD. These independent risk factors could accelerated atherogenesis and they possibly include genetic factors, atherogenic dyslipidaemia, chronic inflammation, and imbalance of procoagulant and anticoagulant factors. Along with NAFLD, insulin resistance, oxidative stress, and adiponectin imbalance also contribute to CVD. Atherogenic dyslipidemia is characterized by high triglycerides and low high-density lipoprotein (HDL), which is frequently present in NAFLD. Nigam *et al*. from Delhi (India) showed that increase of hs-CRP level by 1 mg/dl was associated with risk of having NAFLD by 1.7 times as when compared with controls [13]. NAFLD is associated with increase in proinflammatory cytokines that promote lipolysis [tumor necrosis factor alpha (TNF-a)] causes insulin resistance).These proinflammatory cytokines may also cause endothelial dysfunction [16]. Adiponectin works as insulin sensitizer, anti-atherosclerotic, and anti-inflammatory agent. NAFLD is associated with low adiponectin which is associated with more extensive necroinflammation [3]. In the study by Tripodi *et al*. showed that patients with NAFLD had a procoagulant imbalance that increases from the less severe (steatosis) to more severe (NASH and cirrhosis) forms of the disease. This imbalance was caused by increased factor VIII and reduced protein C. This imbalance may also play a role in the causation of CVD in patients with NAFLD.

2.4 Carotid artery disease in NAFLD

The intima-media thickness (IMT) of the carotid artery can be measured non-invasively by ultrasound techniques. An increased IMT has been shown to be a risk factor for myocardial infarction and stroke. A metanalysis by Cai J *Et al* of 7 studies on Carotid IMT has shown that the IMT in NAFLD patients increased 0.16 mm compared with the control group, and risk of carotid plaque was 3.73 times than that of the controls [17]. Wang *et al* study further showed that ALT level is proportionally associated with the risk of carotid IMT in subjects with fatty liver [18]. Furthermore, the severity of liver histopathology among NAFLD patients is strongly associated with early carotid atherosclerosis, independent of age, sex, BMI, smoking, LDL cholesterol, insulin resistance, and the presence of metabolic syndrome [19]. Carotid intima media thickness (CIMT) is a well-studied phenotype of atherosclerosis. Using B mode ultrasound the CIMT can be assessed quickly, non-invasively at relatively low cost [20].

2.5 NAFLD and portal vein flow dynamics.

Duplex Doppler sonography is a major diagnostic method for the non-invasive assessment of the hemodynamics of hepatic vessels [21]. Many reports indicate that hepatic vascular hemodynamics are altered in parenchymal liver diseases [22]. Recent studies have suggested that hepatic artery and hepatic vein flow characteristics are altered in fatty liver. Reduced parenchymal and vascular compliance is suggested as the cause of monophasic venous flow in hepatic steatosis [23, 24]. In addition, the limited distensibility of the liver capsule leads to the compression of hepatic veins by the increased volume of hepatocytes due to fat deposition and has been suggested as the reason for flattened hepatic vein flow waveforms [23].

It is well known that portal vein Mean Flow Velocity (MFV) decreases in chronic liver diseases and may even reverse in cases with severe fibrosis [25]. An increase in hepatocyte volume associated with fat deposition in the cytoplasm leads to a decrease in hepatic sinusoidal space up to 50%. Sinusoidal compression due to steatosis and expansion of hepatocytes have been suggested as factors involved in the decrease in portal blood flow [25].

2.6 NAFLD and mesenteric fat thickness

It is now well recognized that visceral adipose tissue, notably mesenteric fat, drained by the portal circulation is metabolically more active than nonportal adipose tissues such as subcutaneous and preperitoneal fat deposits. The increased free fatty acids from these adipocytes can lead to reduced fat oxidation and ectopic fat deposition in liver and muscle, resulting in reduced glucose uptake.(26) Furthermore, visceral adipocytes can secrete a large number of cytokines and vasoactive peptides, including interleukin-6, tumor necrosis factor, angiotensin II, plasminogen activator inhibitor-1, etc., all of which can increase cardiovascular risks [27].

2.7 ultrasound as a screening tool

Ultrasound represents a non-invasive, widely available, and fairly accurate tool in the detection of NAFLD. Although there is limited data available to support the use of ultrasound as a screening tool, ultrasound can be a powerful tool in the setting of known liver abnormality. Ultrasound should be used as the first-line diagnostic test in patients with abnormal liver enzymes. Standardized, characteristic sonographic findings are able to reliably identify patients with NAFLD. Clinical risk factors, when used with ultrasound findings, have high utility in identifying NAFLD patients and initiating an early plan of care. Singh *et al* demonstrated that the sensitivity of USG in detecting hepatic steatosis ranges from 60 to 94% and the specificity from 84 to 95% [28]. Ultrasound can be easily incorporated into the training of clinicians and used in hepatology practices at outpatient visits.

Riley *et al* demonstrated that clinical providers could be trained to identify ultrasound images consistent with NAFLD after a brief 20-min session. Healthcare providers were subsequently able to reliably identify NAFLD using the prototype image with substantial inter-observer agreement, $\kappa = 0.76$ [29].

3.0 Material and Methods

Study was carried out on 151 patients from the inpatients admitted to the medicine wards and outpatients visiting the

medicine outpatient clinics with type 2 diabetic and on treatment within 26 to 80 years of age who were fulfilling the inclusion and exclusion criteria and 150 healthy age and sex matched control population. Institute ethical committee clearance was obtained prior to the study. A total of 151 patients were recruited of which 15 patients had to be excluded as 5 of them were tested HbsAg positive and 10 patients had history of chronic alcoholism with intake of >40 g/day for past 10 years (>4 drinks/ day)

3.1 Inclusion criteria
The Inclusion Criteria include:-_All the OPD/ IPD patients with Type 2 diabetic patients aged 26-80 years visiting the hospital were included.

3.2 Exclusion criteria
The exclusion criteria are as follow

1. Alcohol abuse or addiction
2. Use of drugs causing fatty damage to liver like amiodarone, sodium valproate, glucocorticoids, methotrexate etc (or intake of excess calorie diet which overwhelms the liver's ability to metabolize fat in a normal fashion, which results in fat accumulation and causes fatty damage to liver)
3. Hepatitis B and Hepatitis C positivity
4. Hypo or hyperthyroidism
5. Nephropathy
6. Other conditions like Celiac Sprue and Wilson's Disease
7. Any Malabsorption syndromes

3.3 Ultrasonography techniques
A brief history was taken of the patient's complaints and then the patients Random blood sugar and BMI values as recorded in the patients case paper were recorded and then ultrasonographic evaluation of the study subjects was performed by single radiologist and the following parameter were examined after obtaining consent- Liver echogenicity, Portal vein doppler study, Mesenteric fat pad thickness and Carotid artery doppler study. The following evaluation was done using both a curvilinear C6-2 (2-6 MHz) and linear array probe L5-12 50 (5-12 MHz) on a PHILIPS AFFINITI 50G USG machine in the Dept. of Radiology.

3.4 Liver echogenicity
The examination was performed using a 2-5 MHz convex transducer. The normal liver parenchyma has a homogeneous echotexture with echogenicity equal to or slightly greater than that of the renal cortex and spleen. The liver shows echogenicity higher than the renal cortex and spleen due to fatty infiltration [30]. Various (0-3) grades of steatosis have been proposed based on visual analysis of the intensity of the echogenicity, provided that the gain setting is optimum [Figure 2] [31].

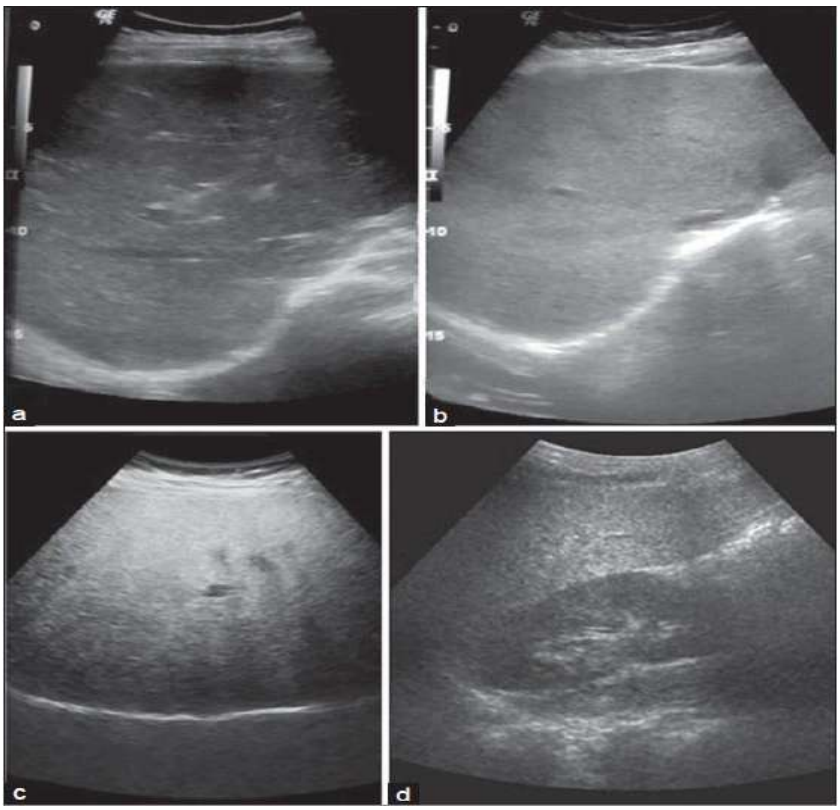

Fig 2: Grades of fatty liver on visual analysis. Ultrasound image shows (a) Normal liver echogenicity Grade 0 (b) Grade 1 fatty liver with increased liver echogenicity (c) Grade 2 fatty liver with the echogenic liver obscuring the echogenic walls of the portal venous branches (d) Grade 3 fatty liver in which the diaphragmatic outline is obscured.

3.5 Portal vein doppler study
Both the patients and control subjects had a routine liver parenchyma US examination US a single radiologist. All eight segments of the liver were carefully scanned, and subjects with vascular malformations or hepatic masses (e.g., cyst or hemangioma) were excluded. Doppler US of the portal vein showed a wide spectrum of different flow patterns and velocity in healthy patients. An important limitation of Doppler US is reproducibility or accurate measurements. To compensate for this limitation, we standardized each measurement.

For each duplex scanning, the sample gate was adjusted

between 6-10 mm with pulse repetition frequency set between 15 to 18 cm/s (depending on the diameter of the vessel). Moreover, the portal vein spectral analyses were always recorded for at least 2-3 cycles. The transducer was oriented along the longitudinal axis of the main portal vein using a paramedian or slightly oblique position.
The point of measurement was midway between the confluence of the splenic and superior mesenteric veins and the bifurcation of the portal vein during quiet inspiration by the same sonographer. The Doppler angle was always < 60º. The mean flow velocity were recorded in each patient and healthy subject and were photo documented. The pulsatility or the phasic variation of the spectral waveform was also recorded as present, absent or inconclusive.

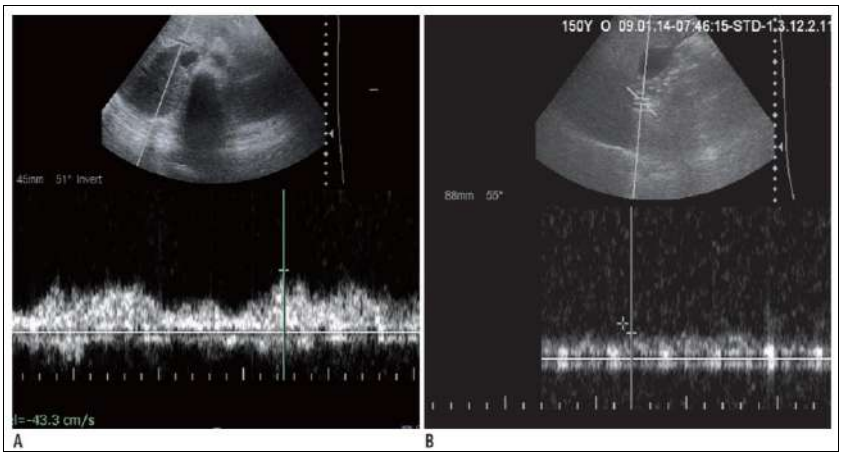

Fig 3: Spectral Doppter US of maximum velocities in portal veins of control subjects and patients with nonalcoholic steatohepatitis (NAFLD).A. Maximum velocity (V_{max} in portal vein of normal subject (43.30 cm/s). B. V_{max}. in portal veins of patients with NAFLD (18.10 cm/s).

3.6 Mesenteric fat pad thickness.

Abdominal fat thickness was measured by a single operator, using a 2-6MHz curvilinear transducer followed by a 5 to 12 MHz linear array transducer. A complete survey of the paraumbilical area was performed was performed in each subject with special attention to identify the mesenteric leaves (Figure 4). The mesenteric leaves appeared to be elongated structures with highly reflecting peritoneal surfaces. It had high-level echoes in the periphery and small vascular structures (1–2 mm in diameter) could be seen within it. The mesenteric leaves were divided from each other by specular echoes corresponding to their peritoneal surfaces. The mesenteries demonstrated no peristalsis, in contrast to small bowel loops attached to the distal end. Not all the mesenteries could be visualized on the scan as some of them might be obscured by bowel gas. When different mesenteric leaves were visualized, the maximum thickness was measured. Usually 6–10 measurements were made on each ultrasound examination, and the mean of the three thickest mesenteric leaves was used for the analysis.

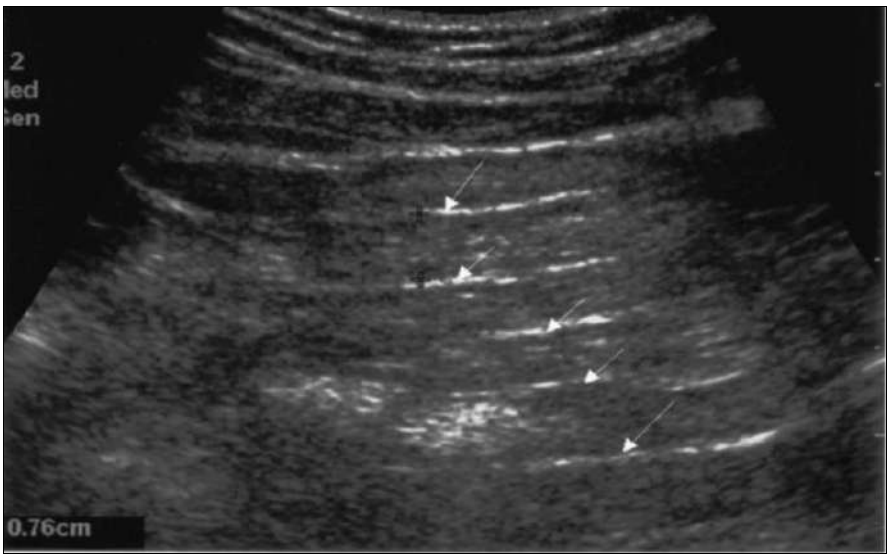

Fig 4: Ultrasonogram of mesenteric leaves. Each mesenteric leaf is indicated by highly reflecting peritoneal surfaces (arrows). The maximum mesenteric thickness on the image was measured with the callipers (+).

3.7 Carotid artery doppler study

High resolutions B mode ultrasonography of both common and internal carotid arteries were performed with an ultrasound machine (Philips Affiniti 50G) equipped with a 5-12 MHz linear array transducer. Patients were examined in the supine position with the head tilted backwards. After the carotid arteries were located by transverse scans, the probe was rotated 90° to obtain and record a longitudinal image of common carotid arteries. The maximum CIMT was measured at the posterior wall of the common carotid

artery, 2 cm before the bifurcation, as the distance between first and second echogenic lines of anterior and posterior arterial walls. The image was focused on posterior wall of common carotid artery and gain settings were used to optimize image quality. Measurement was performed vertical to arterial wall for accurate measurement of CIMT. Three measurements of CIMT were taken at each site and the average measurement was used. All of the sonograms of CIMT measurement were obtained the same radiologist who was performing the abdominal sonography. A cut off of 1 mm was considered as positive for cardiovascular disease.

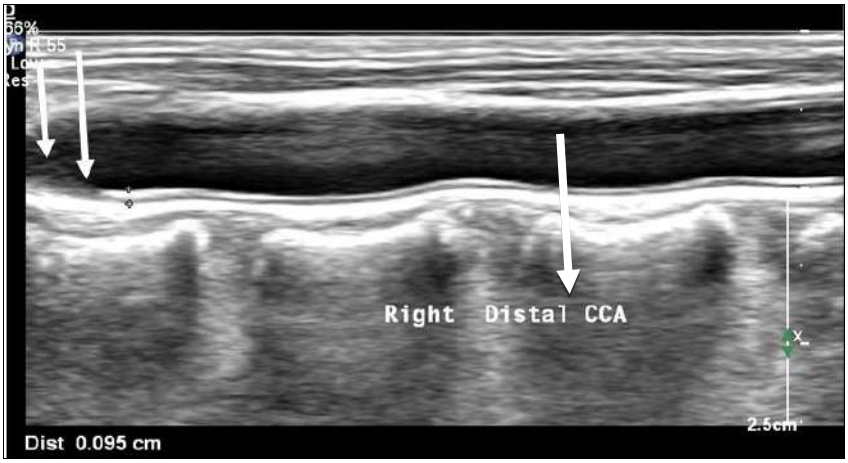

Fig 5: The distal carotid artery is the proper site for measuring the intima-media thickness. The two clearly visible hyperintense lines (arrows) that represent the interface between the blood pool and intima layer and the interface between the media layer and adventitial layer should be noted on the image. B. An example of manual intima-media thickness measurement is shown.

The presence of carotid intima medial thickening >1 mm in either common carotid arteries or presence of atherosclerotic plaque was taken as presence of cardiovascular disease.

3.7 Data analysis

- Data entry was done in Microsoft Excel for cases and controls.
- Data analysis was done using the SPSS software for calculating the statistical parameters.

4. Results and analysis

In our study a group of 135 (72- male; 63 -female) patients of mean age 51 years with diabetes were examined for fatty liver disease using ultrasound along with portal vein doppler, mesenteric fat thickness and carotid intima medial thickness. Carotid doppler study was done to study cardiovascular disease in the study subjects.

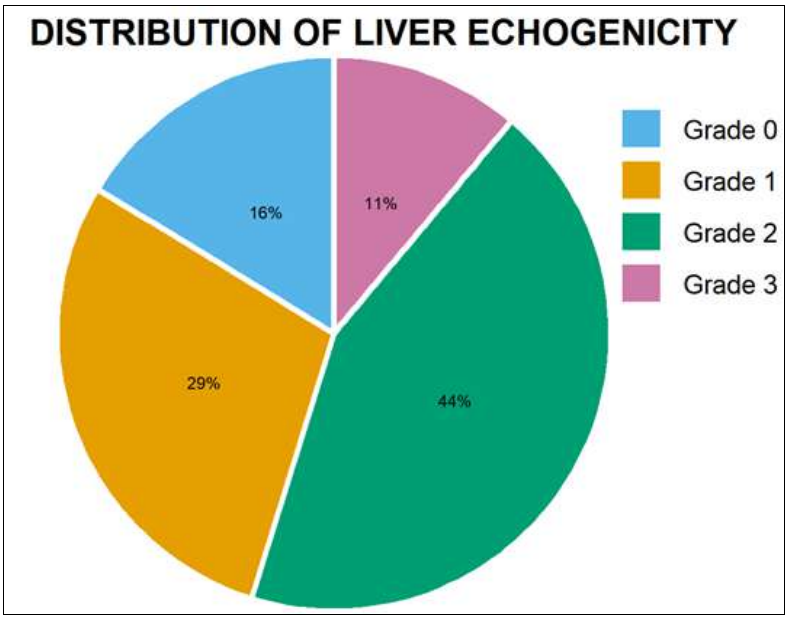

Fig 6: Graph showing percentage of distribution of liver echogenicity in cases

In diabetic patients the following parameters showed significant association with Non-alcoholic fatty liver disease (p value- <0.05) which included: Age (Years), BMI (kg/m2), Liver Echogenicity, Portal Vein Velocity (cm/s), paraumbilical mesenteric fat thickness and CIMT of bilateral carotid arteries.

At a cut-off of Portal Vein Velocity (cm/s) <28.5, it predicts Fatty Liver Disease with a sensitivity of 70%, specificity of 86%, PPV of 96%, NPV of 36% and diagnostic accuracy of 73% in our study. The relative risk (95% CI) for Fatty Liver Disease in patients with Portal Vein Velocity (cm/s)<28.5 was 1.5 (1.26-1.91).

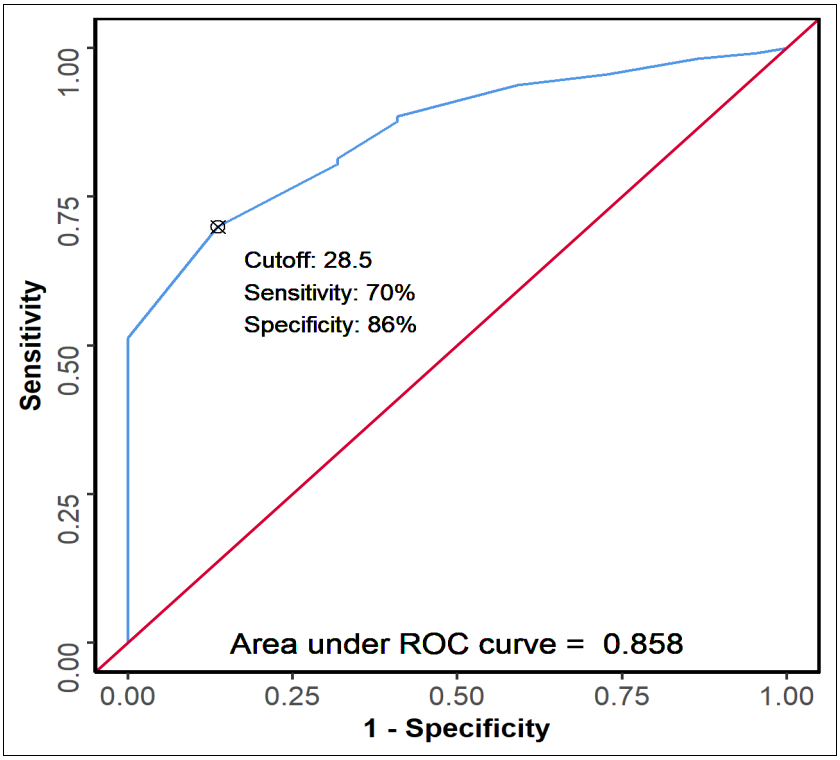

Fig 7: ROC Curve Analysis Showing Diagnostic Performance of Portal Vein Velocity (cm/s) in Predicting Fatty Liver Disease

At a cutoff of Paraumbilical Mesenteric Fat Thickness (mm) >11.5, it predicts Fatty Liver Disease with a sensitivity of 66%, specificity of 91%, PPV of 97%, NPV of 34% and diagnostic accuracy of 70% in our study. The relative risk (95% CI) for having Fatty Liver Disease in patients with Paraumbilical Mesenteric Fat Thickness (mm) >11.5 was 1.47 (1.26-1.83) times greater than controls.

Table 1: Comparison of the Diagnostic Performance of Various Predictors in Predicting Fatty Liver Disease

Predictor	AUROC	95% CI	P	Sn	Sp	PPV	NPV	DA
Portal Vein Velocity (cm/s)	0.858	0.789-0.927	<0.001	70%	86%	96%	36%	73%
Portal Vein Flow Phasic Varation	0.566	0.535-0.598	0.072	13%	100%	100%	18%	27%
Paraumbilical Mesenteric Fat Thickness (mm)	0.831	0.743-0.919	<0.001	66%	91%	97%	34%	70%

Table 2: Comparison of the Diagnostic Performance of Various Predictors in Predicting Cardiovascular Disease:

Predictor	AUROC	95% CI	P	Sn	Sp	PPV	NPV	DA
Right CCA CIMT (mm)	0.979	0.959-0.999	<0.001	90%	100%	100%	57%	91%
Left CCA CIMT (mm)	0.978	0.957-0.999	<0.001	92%	100%	100%	64%	93%
Atherosclerotic Plaque	0.697	0.653-0.742	0.002	40%	100%	100%	18%	47%
Par umbilical Mesenteric Fat Thickness (mm)	0.628	0.474-0.782	0.096	87%	38%	91%	27%	81%

In the diabetic patients the following parameters showed significant association with CARDIOVASCULAR DISEASE. (p value- <0.05) *Liver Echogenicity, Right and left CCA CIMT (mm).* At a cut-off of CCA CIMT (mm) >0.79, it predicts Cardiovascular Disease with a sensitivity of 90%, specificity of 100%, NPV of 57% and excellent diagnostic accuracy of 91%. The relative risk (95% CI) of having Cardiovascular Disease being Present in patients with CCA CIMT (mm)>0.79-0.8 was 2.33 times higher than healthy patients. In a study by Prashant *et al* the prevalence of NAFLD and NASH in our cohort of type 2 DM patients is high and increases with multiple components of metabolic syndrome [32]. Targher *et al*. concluded in their study that prevalence of NAFLD increased with age and NAFLD patients had remarkably (P < 0.001) higher age and sex-adjusted prevalences of coronary (26.6 vs. 18.3%), cerebrovascular (20.0 vs. 13.3%), and peripheral (15.4 vs. 10.0%) vascular disease than their counterparts without NAFLD [33].

5. Conclusion

Non-alcoholic fatty liver disease is fast reaching epidemic proportions worldwide and in the Indian subcontinent as well. Although alcohol related liver disease is the most common cause of liver disease related deaths, NAFLD is fast emerging as contender due to the rise of obesity and diabetes related diseases in India. Along with significant risk of morbidity and mortality secondary to progression to cirrhosis and hepatocellular carcinoma, NAFLD and diabetes are independently risk factors for cardiovascular accidents, in addition NAFLD is leading cause of donor rejection in living donor liver transplantation. In India which has already been named the diabetic capital of the world, this represents a significant burden to the existing medical infrastructure. This calls for early diagnosis and management of both non-alcoholic fatty liver disease and

cardiovascular disease before the advent of liver cirrhosis or major cardiovascular accident as this can prevent significant morbidity among the patients.

Both NAFLD and alcohol related liver disease are preventable by increasing public awareness on its effects, early diagnosis and management. The management is rather easy and convenient and might require both lifestyle modifications along with dietary changes and pharmacologic and surgical management in patients resistant to treatment. Regular aerobic exercise by promoting weight loss resulted in improvement in insulin resistance, aminotransferase levels, insulin resistance.[34] Ultrasonographic parameters as discussed in this study like the portal vein mean flow velocity and echogenicity of liver can be used to both diagnose and monitor diabetic and non-diabetic patients with NASH. The morbidity and mortality related to NAFLD is expected to rise with the upsurge of obesity and type 2 diabetes mellitus, so the need of the hour is to devise low cost, accurate, reproducible, and non-invasive techniques and means of estimating liver fat.

6. Abbreviations

NAFLD - Nonalcoholic fatty liver disease
NASH - Nonalcoholic steatohepatitis
CVD - Cardiovascular disease
DM - Diabetes mellitus
USG - Ultrasonography
BMI - Body mass index
HCC - Hepatocellular carcinoma
GLP - Glucagon like peptide
TNF - Tumor necrosis factor
ALT - Alanine amino transferase
HCV - Hepatitis C virus
hs-CRP - high-sensitivity C-reactive protein
CAD - Coronary artery disease
CIMT - Carotid Intima-media thickness
CAC - Coronary artery calcium score
MFV - Mean flow velocity

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