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A Prospective Study of Ultrasonographic Assessment of Non-Alcoholic Fatty Liver Disease (Steatosis) Among Type 2 Diabetes Mellitus With Liver Function Test Correlation

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ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) emerging condition of liver disease. Prevalence of this disease is estimated to be around 9-32% among Indian population with increased incidence rate among obese and diabetes. Insulin resistance is strongly associated with NAFLD. The spectrum varies from simple steatosis (NAFL) to non-alcoholic steatohepatitis (NASH), finally to cirrhosis. It has been regarded as a manifestation of the metabolic syndrome. Ultrasonography (USG) is the simplest and cost-effective imaging technique for the identification of NAFLD. The Aminotransferase levels were also significantly elevated among T2DM. The results from the study reinforced the well established clinical association of NAFLD with higher Aminotransferase levels among T2DM. NAFLD may be considered as the hepatic hallmark of insulin resistance, and its correlation with liver enzymes, an excellent marker to predict disease outcome. This study is conducted to establish the prevalence of (NAFLD) among type 2 Diabetes mellitus (T2DM) along with Liver function test (Aminotransferase levels) correlation. The results from the study reinforced the well established clinical association of NAFLD with other co-morbidities like dyslipidemia, obesity, metabolic syndrome as the prevalence of NAFLD in these co-morbidities condition had a higher level rise in aminotransferases. The prevalence of NAFLD among T2DM in our study is higher when compared with other studies. NAFLD may be considered as a hepatic hallmark of insulin resistance and correlating it with alteration in liver enzymes will be an excellent marker to predict disease outcome.

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INTRODUCTION

NAFLD is one of the most common & emerging causes of liver cirrhosis worldwide. It has become a significant chronic liver disease which encompasses a spectrum of liver pathology with different clinical prognosis. NAFLD is characterized by abnormal fat accumulation in the hepatocyte, in the absence of excessive alcohol intake. NAFLD encloses wide range liver disease from isolated fatty liver (IFL), which is a form of hepatic macrovesicular steatosis having clinically benign extreme of the spectrum to non-alcoholic steatohepatitis (NASH) where steato-

sis becoming complicated with apparent hepatocyte death and inflammation with further progression leading on to decompensation, cirrhosis and hepatocellular carcinoma (HCC). Like Hepatitis B, it can directly lead on to liver malignancy without the clinical picture of cirrhosis. In the last two decade, the incidence and prevalence of NAFLD as been in the trend of increasing. NAFLD was found to be due to predisposing factors like-starvation, obesity, sedentary lifestyle, metabolic syndrome, insulin resistance. This study is done to show the prevalence of NAFLD among Type 2 Diabetes Mellitus with liver function test correlation. Since many studies were done before to show the correlation between these two conditions, the exact number of the association was not so precise. Studies show the insulin resistance promotes hyperglycemia, which in turn drives the pancreas to secrete more insulin to maintain glucose level. This hyperinsulinemia leads on to steatosis by increasing lipid uptake, fat synthesis and its storage at a hepatic level.

METHODOLOGY

IRB Approved Institution: Saveetha medical college and hospital institutional ethics committee (SMCH-IEC)

Approval date: Jan 2020-Jun 2020

After obtaining institutional ethical committee's approval, a Prospective study conducted at Saveetha Medical College and Hospital from Jan 2020 to Jun 2020. This study includes subjects with known Type 2 diabetes mellitus (T2DM) from 24-75 years of age. Alcoholics and any other significant liver conditions were excluded. Those with daily alcohol consumption of more than one drink per day (10g of ethanol) in female and two drinks per day in men, viral hepatitis and any significant liver conditions were excluded.

All 187 patient with Type 2 diabetes mellitus (T2DM) undergone Ultrasonography (USG) of liver and Liver function test (Aminotransferase levels) was done, and data were collected. The collection of venous blood samples evaluated the levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Internal quality control was maintained in the laboratory. The elevation of aminotransferase was compared with the standard reference value.
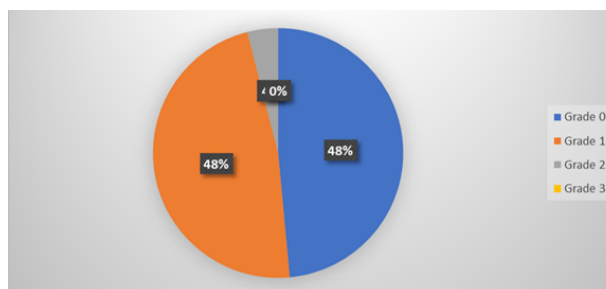
RESULTS

Out of 187 subjects with Type 2 diabetes mellitus (T2DM) who has been chosen, the prevalence rates of Type 2 diabetes mellitus (T2DM) in males (54%)
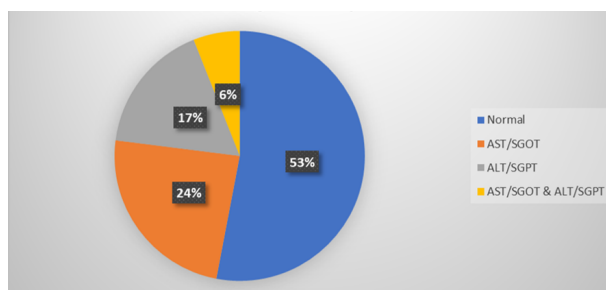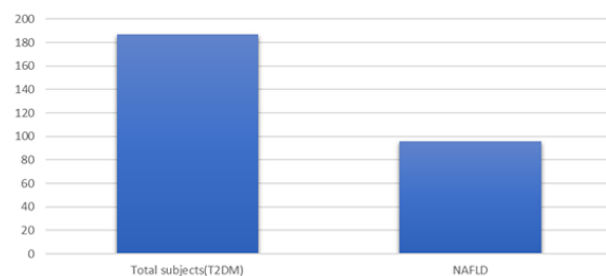
& females (46%) (Figure 1).
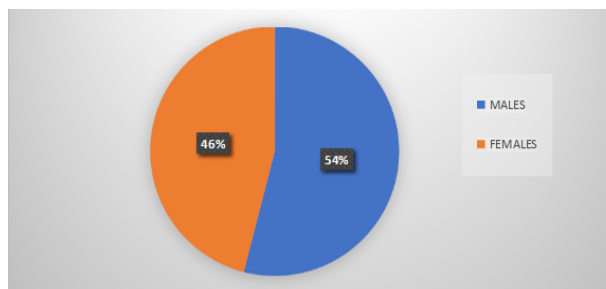
Figure 1: Shows rate of prevalence of T2DM among males and females

Figure 2: Shows prevalence rates of different grades fatty liver among T2DM

Figure 3: Shows liver function test outcome among NAFLD patients

Figure 4: Shows NAFLD among T2DM

Of that,96 of them where identified with Non-alcoholic fatty liver disease (Figure 2). The grading of the fatty liver showed 7 with grade 2 fatty liver disease(diffusely increased hepatic echogenicity obscuring periportal echogenicity but diaphragmatic echogenicity is still maintained) and rest 89 with grade 1 fatty liver(only diffusively increased

Table 1: Illustrates the Ultrasonographic (USG) assessment of NAFLD fatty liver grading among T2DM

Total subjects (T2DM)	Grade 0 normal	Grade 1 fatty liver	Grade 2 fatty liver	Grade 3 fatty liver
187	91	89	7	-

Table 2: Illustrates the Liver function test (Aminotransferase levels) among Type 2 diabetes mellitus (T2DM)

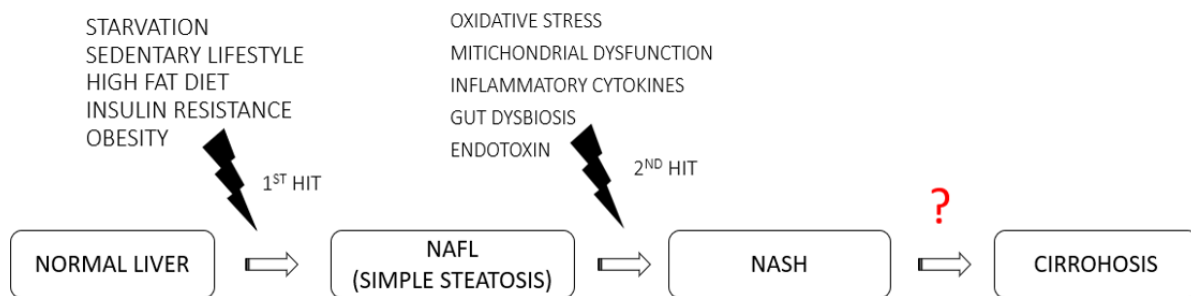| Total Subjects (T2DM)	Normal	AST/SGOT	ALT/SGPT	Both AST/SGOT & ALT/SGPT
187	100	45	31	11

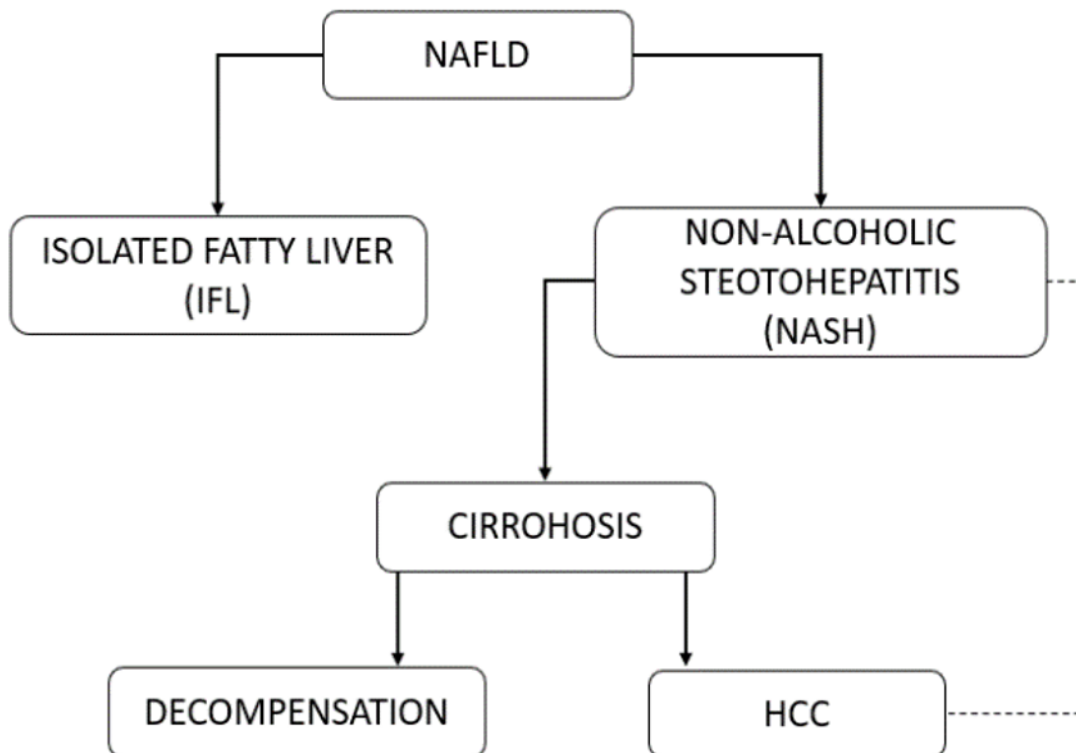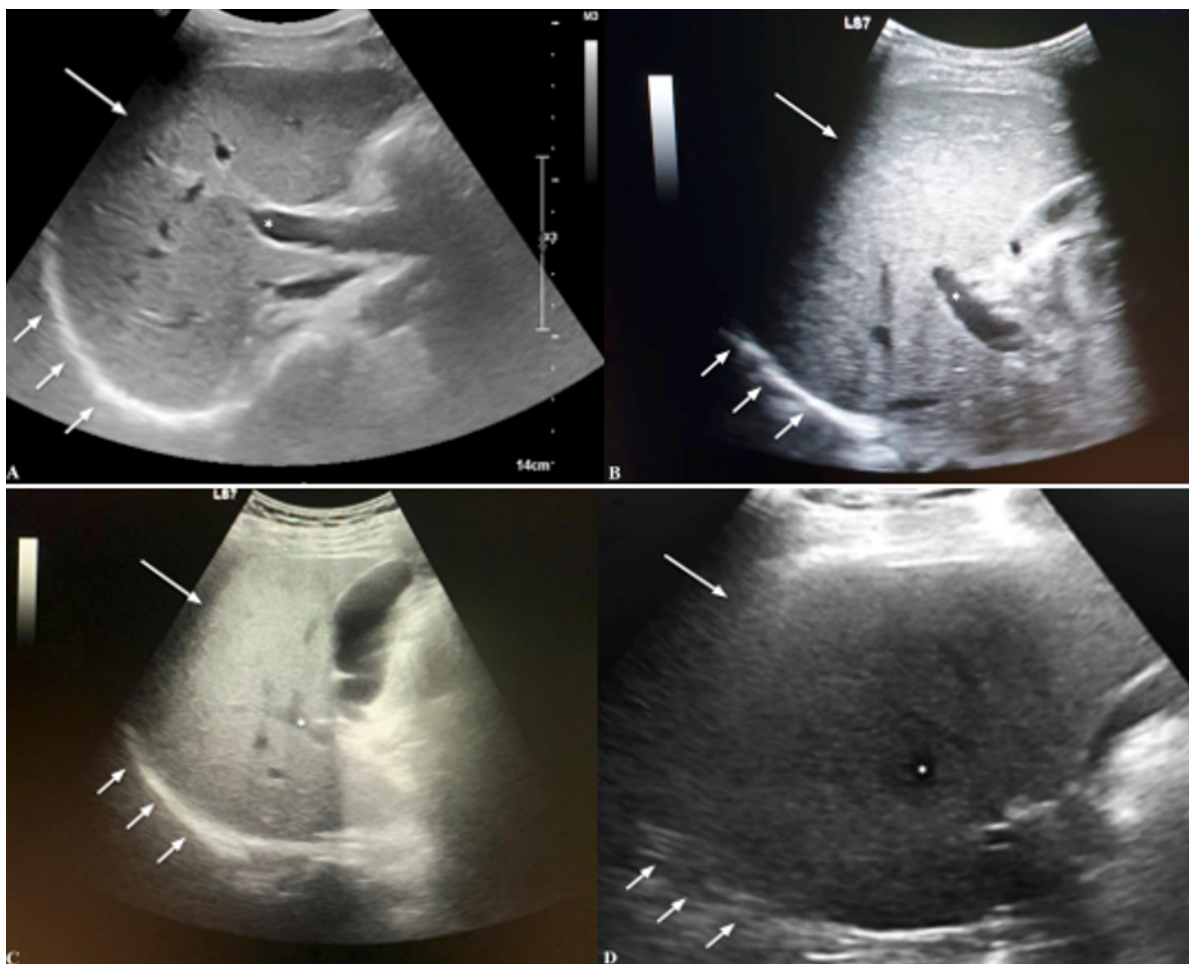Diagram 1: Sequence of progression of non-alcoholic fatty liver disease

Diagram 2: Events of non-alcoholic fatty liver disease

Figure 6 (A, B, C, D): Ultrasonography (USG) Grading Of Fatty Liver

A. Grade 0: normal.

B. Grade 1: hepatic echogenicity diffusely increased but periportal and diaphragmatic echogenicity is still appreciable.

C. Grade 2: hepatic echogenicity diffusely increased obscuring periportal echogenicity but diaphragmatic echogenicity is still appreciable.

D. Grade 3: hepatic echogenicity diffusely increased obscuring periportal as well as diaphragmatic echogenicity.

Note: Hepatic echogenicity (large white arrow), Periportal echogenicity (white asterisk) and Diaphragmatic echogenicity (small white arrows).

Figure 6: Showing ultrasonographic images of different gradings of fatty liver
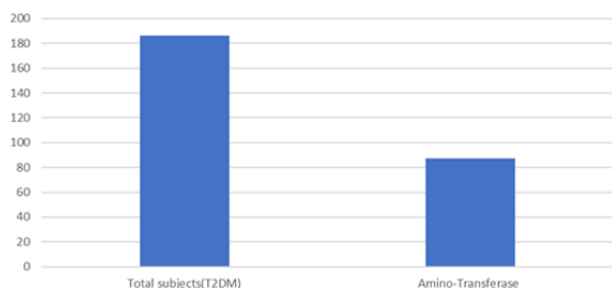
Figure 5: Shows patients with elevated amino-transferase level among NAFLD

hepatic echogenicity) & no one shows grade 3 fatty liver (Table 1).

Liver function test (Amino-transferase levels) was done showed 87 subjects with elevated Amino-transferase levels (45 subjects shows elevated AST/SGOT, 31 subjects shows elevated ALT/SGPT and 11 subjects shows elevated both AST/SGOT & ALT/SGPT) (Table 2) and prevalence rates (elevated AST/SGOT - 24%, elevated ALT/SGPT - 17% and elevated both AST/SGOT & ALT/SGPT - 6%) (Figure 3)

This study demonstrates the correlation of NAFLD with Liver function test (Aminotransferase levels) among T2DM. In this study, out of a total of 187 subjects with Type 2 Diabetes mellitus,96 subjects shows non-alcoholic fatty liver (Figure 4) & 87 subjects shows elevated Aminotransferase levels (Figure 5). Prevalence rates of NAFLD and elevated Aminotransferase levels among Type 2 Diabetes mellitus was found to be 51.3% and 46.5% respectively showing its significant association.

NAFLD is the most common liver entity and the fastest rising condition liver problem worldwide. Since the majority of them with NAFLD are asymptomatic, the diagnosis often made when abnormal aminotransferase levels or features of fatty liver on radiological intervention are noted during an evaluation performed for other reasons. Few studies also show that there is a risk of progression of NAFLD to cirrhosis, HCC and even some directly to HCC, but the cause behind these progressions is still unknown. In our study, the elevation of AST and ALT or both to mild and moderate levels is a very common finding in NAFLD, thus emphasizing the usage of liver enzymes as a useful marker in NAFLD.

DISCUSSION

Non-alcoholic fatty liver disease (NAFLD) is one of the emerging condition of clinical importance with increasing prevalence, pathophysiology, and therapeutics (Williams *et al.*, 2011). It has become the major chronic liver entity which encompasses a spectrum of liver pathology with different clinical prognosis. NAFLD found to be associated with obesity, dyslipidemia insulin resistance, hypertension and hepatic outcome of the metabolic syndrome (de Alwis and Day, 2008; Juurinen *et al.*, 2007; Korenblat *et al.*, 2008). NAFLD is characterized by excessive fat accumulation in hepatocyte on a background of absence of excessive alcohol intake. The manifestation of NAFLD starts with simple steatosis followed by non-alcoholic steatohepatitis (NASH) then to liver cirrhosis (Farrell and Larter, 2006). Isolated fatty liver, which is a form of hepatic macrovesicular steatosis having clinically benign extreme of the spectrum to Non-alcoholic steatohepatitis which is steatosis becoming complicated with apparent hepatocyte death and inflammation with further progression leading on to decompensation, cirrhosis and hepatocellular carcinoma (HCC). Other predisposing factors are genetic disorders obesity, sedentary lifestyle, viral hepatitis, use of certain drugs, dietary and nutritional abnormalities. The prevalence rate is higher among obese (70%) and diabetic (90%) individuals (Hannah and Harrison, 2016).

Few studies also show that there is a risk of progression of NAFLD to cirrhosis, hcc and even some directly to hcc, but the cause behind these progressions is still unknown. In our study, mean AST levels were found to be higher than ALT levels is identified. The elevation of ALT and AST or both to mild and moderate levels is a very common finding in NAFLD, thus emphasizing the usage of liver enzymes as a useful marker in NAFLD patients. Similarly, in T2DM patients, chronic mild elevation of liver enzymes are frequently encountered, so the only significant rise in aminotransferase should only be considered. Diagrams 1 and 2 shows the pathophysiology of NAFLD and its stage of progression.

Imaging Modality

Ultrasonography

Conventional Ultrasonography (USG) has been considered as initial imaging technique used to evaluate fatty liver clinically (Chen *et al.*, 2014),mainly for those at higher risk of Non-alcoholic fatty liver disease, due to its wide availability, non-invasive and cost-effectiveness (Das *et al.*, 2013). Ultrasonography detects steatosis with a reported sensitivity of 79.7% and specificity of 86.2% (Shannon *et al.*, 2011).

The limitations of conventional Ultrasonography (USG) for NAFLD evaluation: (1) Its qualitative & subjective, (2) Sensitivity is limited (Shannon *et al.*, 2011);(3) Increased body mass index decrease the value of imaging. Figure 6 shows ultrasonographic

images of various grades of fatty liver.

CONCLUSION

This study has established a significant association and prevalence of Ultrasonographic (USG) assessment of NAFLD with Liver function test (Aminotransferase levels) among non-insulin-dependent diabetes mellitus. NAFLD may be considered as a hepatic hallmark of insulin resistance. The appropriate management of NAFLD is lifestyle changes, control over insulin resistance and diet modification.

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