

Original Research Article

A study of non-alcoholic fatty liver disease in type -2 diabetes mellitus patients of Institute of Diabetology, Madras Medical College

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Abstract

Introduction: Non-alcoholic steatohepatitis (NASH) is a subset of non-alcoholic fatty liver disease (NAFLD). It is a disorder currently characterized by a constellation of histological abnormalities identified on liver biopsy that are similar to those seen in alcoholic liver disease but in patients who consume little or no alcohol. The prevalence of NASH is increasing in parallel with dramatic increases in obesity, sedentary lifestyle, and Type II Diabetes Mellitus. Diabetes is a common metabolic disorder that affects a large number of people worldwide, the diabetic population is ever-growing and it has now reached enormous proportions. Diabetes mellitus affects almost all systems in the body and it causes considerable morbidity and mortality. Diabetes mellitus, hyperlipidemia, and obesity have been implicated as potential causes for the development of NAFLD and now newer risk factors have been proposed.

Aim of this study: To find out the Prevalence and General characteristics of Non-Alcoholic Fatty Liver Disease in persons with Type 2 Diabetes Mellitus and the different clinical presentations of Non-Alcoholic Fatty Liver Disease in Type 2 Diabetes Mellitus patients.

Materials and methods: The Study Population was derived from the patients attending the Outpatient Department of Institute of Diabetology, Madras Medical College, in the year 2019. A detailed history was taken regarding the duration of Diabetes, and symptoms about the Hepatobiliary System. The history of previous and current medications was obtained in detail. History of alcohol consumption was recorded and any person with a history of alcohol use was excluded from the study population. Any history of previous abdominal surgeries such as Jejunio- Ileal Bypass, Gastrectomy was recorded. Women were enquired about oral contraceptive or hormonal use. A detailed Clinical Examination and ultra-sonogram of all organs was made and signs of Liver Cell Failure, Organomegaly, Ascites were looked for the study.

Results: A total of 109 patients diagnosed with type 2 Diabetes Mellitus for 3 years and more were included in this study after applying the selection criteria. Out of the 109 participants, 60 were females and 49 were males. Out of the total of 109 participants, 53 persons (48.62%) had ultrasonographically detected fatty liver. Most of them had moderate or severe steatosis ultrasonogram wise. They were called the NAFLD (Non-Alcoholic Fatty Liver Disease) group. Of these 53 persons, 36 were females and 17 were males. The duration of Diabetes varies from 3 to 20 years in the study group with a mean value of 5.48 ± 3.57 years. Most of the patients of nonalcoholic fatty liver disease are asymptomatic (52.8%). Right, Upper Quadrant discomfort and malaise are other symptoms. Hepatomegaly was the commonest physical finding in Nonalcoholic fatty liver disease (16.98%). It was found to be present in varying incidences in other studies. No significant relationship was observed between the age of the patient, duration of diabetes, fasting blood sugar levels and the presence of Nonalcoholic fatty liver disease by ultrasound. There was a significant difference in mean serum transaminase (SGOT, SGPT) levels between the normal and fatty liver groups with the fatty liver group having higher values. But the absolute elevation of transaminases above normal was not seen in many cases.

Conclusions: Management of patients with NAFLD should be aimed at fighting the metabolic risk factors such as visceral obesity, hyperglycemia, type II diabetes mellitus (DM) and hypertriglyceridemia. DM is a predictor of worsening of fibrosis. Successful lifestyle modification with increased exercise and decreased food intake can remove the accumulation of liver fat and can reverse insulin resistance. Unfortunately, there are no well-controlled, randomized trials of weight control as therapy for NAFLD. Some pharmacological pilot trials have been undertaken in NAFLD, but no proved treatment for all patients with NAFLD and/or NASH is available at the current time.

Key words

Fatty liver, Type-2 diabetes mellitus, Dyslipidemia, Ultrasonographically.

Introduction

Non-alcoholic steatohepatitis (NASH) is a subset of non-alcoholic fatty liver disease (NAFLD). It is a disorder currently characterized by a constellation of histological abnormalities identified on liver biopsy that are similar to those seen in alcoholic liver disease but in patients who consume little or no alcohol [1]. The prevalence of NASH is increasing in parallel with dramatic increases in obesity, sedentary lifestyle and Type II Diabetes Mellitus. Diabetes is a common metabolic disorder that affects a large number of

people worldwide, the diabetic population is ever-growing and it has now reached enormous proportions [2]. Diabetes mellitus affects almost all systems in the body and it causes considerable morbidity and mortality. Diabetes mellitus, hyperlipidemia, and obesity have been implicated as potential causes for the development of NAFLD and now newer risk factors have been proposed [3]. A plethora of case series of NAFLD have been reported over the past few years but whether this indicates a true increase in prevalence or simply an

increased awareness of this disorder is unclear. Many cases of Diabetes mellitus also have chronic liver disease; some of them do not have a history of significant alcohol consumption, so we thought that these cases might represent a sample of what is called cryptogenic cirrhosis [4]. A significant proportion of patients previously thought to have cryptogenic cirrhosis share many of the clinical and demographic features of nonalcoholic fatty liver disease, suggesting that the etiology of their cirrhosis may be unrecognized NAFLD [5].

Materials and methods

The study population was derived from the patients attending the Diabetology Outpatient Department of Madras Medical College, in the year 2019. A detailed history was taken regarding the Duration of Diabetes, Symptoms about the Hepatobiliary System. The history of medications was obtained in detail. History of alcohol consumption was recorded and any person with a history of alcohol use was excluded from the study population. Any history of previous abdominal surgeries such as Jejunoleal Bypass, Gastrectomy was recorded. Women were enquired about oral contraceptive or hormonal use. A detailed Clinical Examination of all systems was made and signs of Liver Cell Failure, Organomegaly, Ascites were looked for the study.

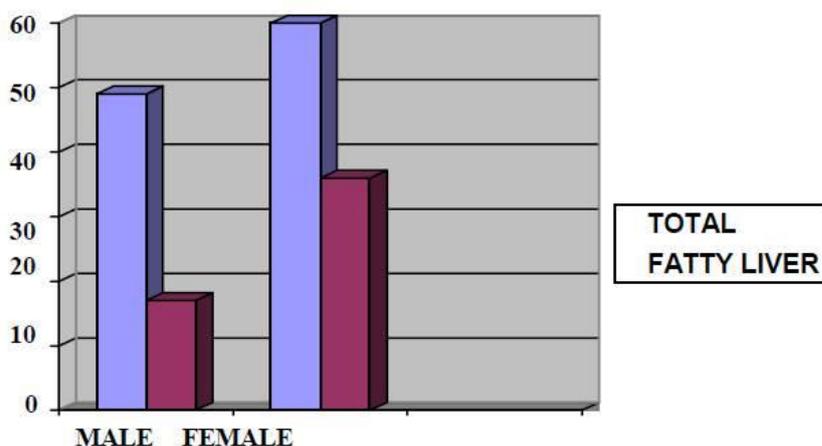
Inclusion criteria: Patients who were diagnosed to have Type 2 Diabetes Mellitus, for more than 3 years duration, belonging to both sexes and with the age of more than 40 years attending Diabetology Out-patient Department of Institute of Diabetology madras Medical College were included in the study.

Exclusion criteria: Patients with a history of alcohol consumption for any duration of the time were excluded. Persons with the previous history of jaundice, ascites, and signs of liver cell failure were excluded. Persons who tested positive for Hepatitis B serology by Elisa or by card test were excluded. Patients with a history of intake of Methotrexate, Amiodarone, Glucocorticoids, Synthetic Estrogens, Nucleoside Analogues (ddI, AZI) were excluded. Persons with a history of major abdominal surgeries were excluded. Persons with a history of Chronic Renal Failure and severe Ischemic Heart Disease were excluded from the study.

Statistical analysis

Statistical analysis of the data obtained from the study was done using the 'z' test or 'normal' test to compare the mean values of two groups of participants. The chi-square test was used to compare the prevalence between the two groups. The calculations were done for a 5% level of significance ($P = 0.05$).

Graph – 1: Sex-wise prevalence.



Results

A total of 109 patients diagnosed with type 2 Diabetes Mellitus for 3 years and more were included in this study after applying the selection criteria. Most of them belonged to the low and middle socioeconomic groups. Out of the 109 participants, 60 were females and 49 were males. The age of the participants varied from 40 to 75 years and the mean age was 52.45 ± 7.15 years.

Out of the total of 109 participants, 53 persons (48.62 %) had ultrasonographically detected fatty liver. Most of them had moderate or severe steatosis ultrasonogram wise. They were called the NAFLD (Non-Alcoholic Fatty Liver Disease) group. Of these 53 persons, 36 were females and 17 were males. The duration of Diabetes varies from 3 to 20 years in the study group with a mean value of 5.48 ± 3.57 years (**Graph – 1**).

Graph – 2: Age wise prevalence of cases categorized for fatty liver disease.

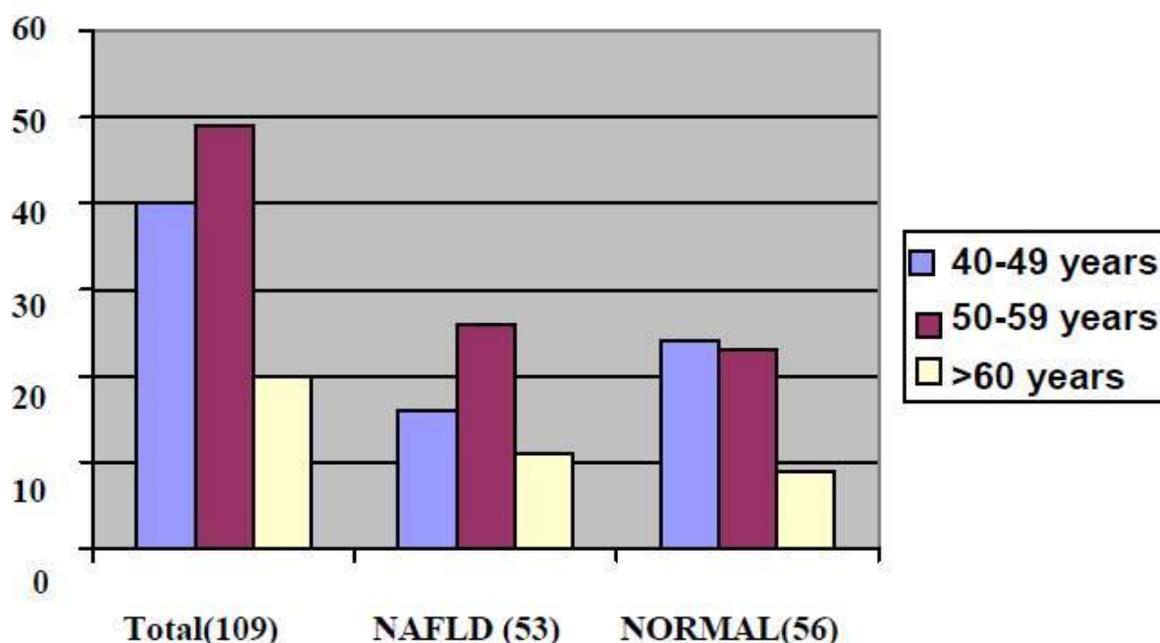


Table – 1: Blood sugar level in cases.

FBS (mg/dl)	Total	Fatty liver	Normal USG
< 125	19	6	13
125 TO 150	38	20	18
150 TO 175	30	15	15
> 175	22	12	10

The mean duration of Diabetes in the fatty liver group was 5.47 ± 3.19 years as compared to 5.48 ± 3.94 years in the normal liver group. There was no significant difference between the NAFLD group and the normal group duration wise (P-value >0.05). The age-wise distribution of patients with and without fatty liver in Ultrasonogram was as per **Graph - 2**.

All the patients had done random, fasting and postprandial blood sugar estimation. The number

of patients with and without fatty liver in the different fasting blood sugar was categorized as per **Table - 1**.

The liver function tests included the Serum Transaminases (SGOT and SGPT), Serum Alkaline Phosphatase, Serum Total Bilirubin, and Total Proteins. The normal value of serum transaminases is 5 to 35 IU/l. The normal value of Serum alkaline Phosphatase is up to 150 IU/l. The participants were categorized into a low

Transaminase level group of 25 IU/l or below and a high normal and increased Transaminase level group with a value of more than 25 IU/l. Out of the total of 53 persons who had Ultrasonographically proven fatty liver 26 persons had an SGPT value of more than 25 IU/L and 11

had an SGPT value of more than 35 IU/L. Out of 56 persons who had normal liver in Ultrasonography 11 persons had an SGPT value of more than 25 IU/L and 3 persons had an SGPT value of more than 35 IU/L (**Table – 2**).

Table – 2: Clinical enzymes correlation of fatty liver in type -2 diabetes.

Parameter	NAFLD group (n=63)	Normal USG group (n=66)	Statistical Significance at 5% level
Duration	5.57 ± 3.19	5.48 ± 3.94	No significant difference (P value=0.05)
BMI (kg/m²)	24.97 ± 3.54	2.29 ± 2.05	Significant difference present (P value<0.05)
SGOT (IU/L)	25.02 ± 20.64	18.41 ± 11.97	Significant difference present (P value<0.05)
SGPT (IU/L)	29.00 ± 28.35	17.47 ± 10.02	Significant difference present (P value<0.05)
ALP (IU/L)	123.97 ± 66.13	106.52 ± 68.75	No significant difference (P value=0.05)
Bilirubin (mg/dl)	1.10 ± 1.12	0.84 ± 0.36	No significant difference (P value=0.05)
Total cholesterol (mg/dl)	225.33 ± 43.95	192.67 ± 35.38	Significant difference present (P value<0.05)
TGL (mg/dl)	235.82 ± 105.18	155.81 ± 61.08	Significant difference present (P value<0.05)
HDL (mg/dl)	46.24 ± 8.03	49.21 ± 9.93	No significant difference (P value=0.05)
LDL (mg/dl)	125.82 ± 11.66	111.45 ± 27.80	Significant difference present (P value<0.05)

Out of the total of 53 persons who had Ultrasonographically proven fatty liver 19 (35.84%) persons had a Serum Alkaline Phosphatase value of more than 150 IU/L and 4 individuals had a value of more than 250 IU/l. Out of a total of 56 persons who had normal liver in Ultrasonography 17 (30.35%) persons had a Serum Alkaline Phosphatase value of more than 150 and 1 person had a Serum Alkaline Phosphatase value of more than 250 IU/l. The mean Serum Total Bilirubin in the NAFLD group was 1.10 mg/dl and the Serum Total Bilirubin in the normal group was 0.84 mg/dl. There was no statistical difference in levels of Serum Bilirubin between the two groups. The mean value of Total Protein in the NAFLD group was 6.43 gm and in the normal group, it was 6.48 gm. There was no statistical difference in levels of Total Protein between the NAFLD and normal liver groups. The lipid done after overnight fasting of 12 hours included Total Cholesterol, Serum Triglycerides (TGL), Serum High-Density Lipoprotein (HDL) and Low-Density Lipoprotein (LDL) value was calculated using the Friedwald formula. According to the ATP III

guidelines for the treatment of lipid disorders, the levels of lipoproteins were considered abnormal if total cholesterol was above 200 if serum triglyceride level was above 150 mg/dl, serum HDL level was below 50 and LDL levels were above 100. A total of 58 out of 109 had a high Total Cholesterol value. Among the NAFLD group out of the total 53 patients, 37 (69.81 %) had a Total Cholesterol value of more than 200 and among the normal liver group, 21 (37.5 %) out of the 56 had a Total Cholesterol value of more than 200. Out of the 53 patients in the NAFLD group, 31 (58.49 %) patients had a triglyceride level of more than 150 mg/dl. Of the 56 patients in the normal liver group, 23 (41.07 %) persons had a triglyceride level of more than 150 mg/dl. Out of the 53 patients in the NAFLD group, 30 (56.6 %) patients had an HDL level of less than 50 mg/dl. Of the 56 patients in the normal liver group, 23 persons had an HDL level of less than 50 mg/dl. The LDL levels varied from 52 to 273 mg/dl and a total of 74 patients had LDL levels above 100 mg/dl. In the fatty liver group, 39 out of the 53 persons had elevated LDL values above 100 mg/dl. In the normal liver

group, 35 out of the 66 persons had an elevated LDL level of more than 100 mg/dl. Statistically significant difference at 5 % level ($P=0.05$) between NAFLD and NORMAL USG groups was present for SGPT, Total Cholesterol and Triglyceride levels. Other parameters did not show any significant difference by comparing the two groups using the 'chi-square test'. But mean LDL levels in the NAFLD group were much higher than in that of the normal group (**Table – 2**).

Discussion

Non-alcoholic fatty liver disease (NAFLD) has been increasingly recognized as the most common pathological conditions affecting the liver. In concert with the increase in Body Mass Index in developed countries that have occurred during the last decades, more and more individuals referred for evaluation of abnormal liver tests are found to have NAFLD [6]. In most cases, the increase in fat within the liver is not associated with impaired liver structure or function in the long-term. However, liver steatosis should be considered to be a marker of the metabolic syndrome [7]. A minority of patients with NAFLD develops liver cirrhosis but NAFLD is probably the most common underlying cause of cryptogenic cirrhosis. Patients with NAFLD have increased cardiovascular mortality as well as an increase in liver-related complications compared with matched controls [8]. Of the 109 diabetics included in this study 53 (48.6 %) of them had an ultrasonographically detectable fatty liver, according to several reports the prevalence of fatty liver in Diabetes Mellitus is more than that of the general population, many studies have shown that the prevalence of NAFLD in type 2 Diabetes Mellitus was up to 70 %.The prevalence of fatty liver in this study group is similar to the prevalence observed in other studies [9]. The mean duration of diabetes in persons with NAFLD was 5.47 ± 3.19 years and the mean duration of diabetes in persons with Normal liver in USG was 5.47 ± 3.94 years. No statistically significant relationship was found

between the presence of NAFLD and the duration of Diabetes [10]. The result was similar to the study conducted in Saudi Arabia Dixon JB et.al The mean Body Mass Index in the NAFLD group was significantly higher than that of the normal group [11]. 38 persons had a BMI of more than 25 kg/m^2 and out of the 30 (78.94 %) had NAFLD. In the study done by Falck-Ytter Y, et al. in Saudi Arabia, Obesity was identified as an independent factor for the development of NAFLD. The number of persons with a BMI of more than 30 kg/m^2 was less compared to studies done in other countries. This is probably due to the low and middle socioeconomic status of the study group [12]. Upper abdominal pain was a common reason for presentation. Many studies have shown a high proportion of patients (48 % to 100 %) have no symptoms of liver disease, and a small percentage (especially children have vague abdominal discomfort or pain in the right upper quadrant or fatigue and malaise [13]. There were gross variations in the incidence of hepatomegaly between many groups. None of the patients in the NAFLD group had splenomegaly of ascites. Many studies have shown that the most common finding at the initial presentation is asymptomatic hepatomegaly [14]. The prevalence of NAFLD was not significantly different among different levels of fasting sugar levels in our study. There was no statistical difference between the two groups in terms of SGOT and Alkaline Phosphatase elevation in terms of the number of persons showing enzyme elevation. But when the mean enzyme values were compared the NAFLD group had a statistically significantly higher value than the normal group [15]. Asymptomatic elevation of transaminases is one of the commonest reported and studied abnormality in NAFLD. The most frequently noted abnormality is the two to the threefold elevation of levels of ALT and AST in plasma. Lee RG et.al found that 19 % of patients (17 of 90) who had a liver biopsy for evaluation of chronically elevated plasma levels of ALT and AST in contrast to 7% to 9% of all patients who had liver biopsies for other reasons, nonalcoholic steatosis or steatonecrosis [16]. Some studies have mentioned that Liver enzyme levels in

NAFLD patients fluctuate, normal values being present in up to 78% of patients at any one time. When levels are elevated, the increase is mild and often restricted to one or both of alanine aminotransferase (ALT) and aspartate aminotransferase (AST). The AST: ALT ratio is usually less than 1, although it may reverse in the presence of cirrhosis [17]. The SGOT: SGPT ratio in the NAFLD group in this study was 0.8. In cases with NAFLD the SGOT: SGPT ratio is less than 1 according to literature. In two major studies, levels of ALT were noted to be higher than levels of AST, a pattern that contrasts with that seen in alcoholic hepatitis [18]. Although values < 1 suggest NAFLD, a ratio of ≥ 2 is strongly suggestive of alcoholic liver disease. There was no statistically significant difference in the levels of bilirubin and total proteins between the two groups which were similar to the observations done elsewhere [19]. Traditionally Total Cholesterol and Triglyceride values were found to be elevated in persons with NAFLD. Our study population consisted of type 2 diabetics and atherogenic dyslipidemias are common among diabetics. The total Cholesterol, TGL values were significantly higher in terms of several persons showing elevation and also in terms of the mean values in the NAFLD group. The number of persons showing elevated LDL was similar in both groups but the mean LDL was much higher in the NAFLD group. The HDL values were similar in both groups with mean values being marginally lower in the NAFLD group [20].

Conclusions

Nonalcoholic fatty liver disease is common among the type 2 diabetic population of this region (Prevalence of 48.6% in type 2 diabetics). The persons with a higher body mass index are at a greater risk of developing the nonalcoholic fatty liver disease (78.94 % diabetics with a BMI > 25 kg/m² had ultrasonographically proven fatty liver) Most of the patients of nonalcoholic fatty liver disease are asymptomatic (52.8%). Right, Upper Quadrant discomfort and malaise are other symptoms. Hepatomegaly was the commonest

physical finding in Nonalcoholic fatty liver disease (16.98%). It was found to be present in varying incidences in other studies. There was no significant relationship observed between Serum Alkaline Phosphatase, Total Bilirubin, and Total Proteins and the prevalence of fatty liver by ultrasound. Significantly high Serum Total Cholesterol, Triglycerides, and Low-Density Lipoproteins were present in persons with fatty liver. No significant correlation was observed between Low-Density Lipoprotein levels and the presence of fatty liver in Ultrasound but marginally low mean HDL values were present in the fatty liver group.

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