



A Study Of Non-Alcoholic Fatty Liver Disease In Type II Diabetes

¹Dr. A. Valarmathi, ²Dr. B. Shobana, ³Dr. R.Aravind Kumar

¹Professor & Head, ^{2,3}Assistant Profesor,

Department Of Physiology,

²Karpagam Institute Of Medical Sciences, Coimbatore

^{1,3}Rajah Muthiah Medical College & Hospital, Annamalai University, Chidambaram

***Corresponding Author:**

Dr. B. Shobana

Assistant Profesor, Department Of Physiology, Karpagam Institute Of Medical Sciences, Coimbatore.

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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. 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.

Aim Of The Study: To find out the Prevalence and General characteristics of Non-Alcoholic Fatty Liver Disease in persons with Type 2 Diabetes Mellitus. To correlate relationship between Body Mass Index and Non-Alcoholic Liver Disease in Type 2 Diabetes Mellitus.

Materials And Methods: This case-control study was conducted in the year august 2020- February 2021 at Shanthi Social Service, Singanallur, Coimbatore. 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 Patients with a history of Ketoacidosis or with a history of prolonged treatment with insulin were excluded. A detailed history was taken regarding the Duration of Diabetes, Symptoms of the Hepatobiliary System. A detailed Clinical Examination of all systems was made and signs of Liver Cell Failure, Organomegaly, Ascites were looked for. The patient's Height & Weight were recorded & Body Mass Index was calculated. BMI is defined as weight in kilograms divided by height in meters squared.

Results. Out of the total 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. There were 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. 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.

Conclusion: The persons with a higher body mass index are at a greater risk of developing nonalcoholic fatty liver disease (78.94 % diabetics with a BMI > 25 kg/m² had ultrasonographically proven fatty liver) Most of

the patients with 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.

Keywords: Diabetes Mellitus, Non-Alcoholic Fatty Liver Disease, Radiological Evaluation, Liver Enzymes

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 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.[4] 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.[5] 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.[6]

Materials And Methods: This case-control study was conducted in the year August 2020- February 2021 at Shanthi Social Service, Singanallur, Coimbatore. 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. **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 were included in the study. **EXCLUSION CRITERIA:** Patients with a history of alcohol consumption for any duration of time were excluded. Persons with a 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. Patients with a history of Ketoacidosis or with a history of prolonged treatment with insulin were excluded. A detailed history was taken regarding the Duration of Diabetes, Symptoms of the Hepatobiliary System. A detailed Clinical Examination of all systems was made and signs of Liver Cell Failure, Organomegaly, Ascites were looked for. The patient's Height & Weight were recorded & Body Mass Index was calculated. BMI is defined as weight in kilograms divided by height in meters squared. Patients were classified according to BMI. Symptoms of diabetes, plus Random Blood concentration more than 200 mg/dl. Fasting plasma glucose more than 126 mg/dl. (Fasting is defined as no caloric intake for at least 8 hours) Two-hour plasma glucose more than 200 mg/dl during an Oral Glucose Tolerance Test. (This test should be done using a glucose load containing the equivalent of 75 gm of anhydrous glucose dissolved in water). Type 2 DM subjects were defined as those with previous physician-diagnosed diabetes in whom hyperglycemia had been controlled for one year or

more with oral hypoglycemic agents and diet, with the absence of a history of ketoacidosis initially, or during the disease. Steatosis was defined as the presence of an Ultrasonographic pattern consistent with “BRIGHT LIVER,” with evident Ultrasonographic contrast between hepatic and renal parenchyma, vessel blurring, focal sparing, and narrowing of the lumen of the hepatic veins, according to international guidelines.³¹ The upper limit of normal liver size was 15 cm in the longitudinal plane, any measurement above this was considered hepatomegaly. Mild hepatomegaly was defined as liver size > 15 – 18 cm in the longitudinal plane. The presence of steatosis was graded from mild to severe and for calculation purposes, all grades were taken as positive fatty liver. All the images were reviewed by another radiologist to minimize observer errors. The L&T Ultrasound machine used had a 3.5 MHz probe.

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).

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 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. 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). Most of the persons with fatty liver were asymptomatic, i.e. 28 out of a total of 53. The next common symptom was right upper quadrant discomfort, which was present in 11 out of 53 patients, 2 persons in the fatty liver group had a complaint of abdominal distension, and no patient had the complaint of jaundice, 16 persons had a feeling of generalized weakness and malaise. Clinical examination of the abdomen revealed hepatomegaly in 6 patients with fatty liver and 1 patient in the normal group. No patient in both groups had splenomegaly or ascites. Ultrasonography showed hepatomegaly in 9 out of 53 persons with fatty liver compared to 1 out of 56 persons in the normal liver group.

Table :1 Mean BMI values:

BMI (kg/ m ²)	NAFLD GROUP (53)	NORMAL USG (56)
<25 (71)	23 (32.39 %))	48 (67.61 %)
>25 (38)	30 (78.94 %)	8 (21.06 %)

Table :1 shows The Body Mass Index varied (BMI) from 17 to 37 kg/m2 with a mean Body Mass Index of 23.60 ± 3.17 kg/m2. A BMI of 25 kg/m2 was taken as a cut-off between overweight and obese, 71 persons had a BMI below 25 kg/ m2 and 38 persons had a BMI of above 25 kg/m2. Only 4 persons had a BMI of more than 30 kg/m2 and all of them had fatty liver. Out of the patients with a BMI of more than 25 kg/m2 (total 38) 30 persons had fatty liver detected in ultrasonogram. In the low BMI group (total 71) 27 persons had Ultrasonographically detected fatty liver.

TABLE :2 PARAMETERS ANALYZED IN GROUPS

PARAMETER	NAFLD GROUP (n=63)	NORMAL USG GROUP (n=66)	STATISTICAL SIGNIFICANCE
DURATION OF DIABETES (yrs)	5.57 ± 3.19	5.48 ± 3.94	No significant difference (P value=0.05)
BMI (kg/m ²)	24.97 ± 3.54	22.29 ± 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)

Table:2 The liver function tests are done included the Serum Transaminases, 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. 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 the 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. MEAN LDL. A 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.

Discussion

In other studies conducted among type 2 diabetics, the prevalence was found to be more among females. There was no significant variation in the mean age between the NAFLD group and the normal liver group. The mean age of the study population was higher because only persons above the age of 40 years were recruited into the study. 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. The mean Body Mass Index in the NAFLD group was significantly higher than that of the normal group. 38 persons had a BMI of more than 25 kg/m^2 and out of the 30 (78.94 %) had NAFLD [7]. In the study done by Chalasani N, 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. In our study group, the persons with high BMI had a prevalence of fatty liver equal to that observed elsewhere. [8] The prevalence of NAFLD was not significantly different among different levels of fasting sugar levels in our study. Many studies have shown that the levels of blood sugar did not have any correlation with the development of NAFLD. Moreover, HbA1c estimation was done by Cortez-Pinto et al stated that was no significant relationship between glycemic control and NAFLD. There was no statistical difference between the two groups in terms of SGOT and Alkaline Phosphatase elevation in terms of several 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. Asymptomatic elevation of transaminases is one of the commonest reported and studied abnormalities in NAFLD. [9] Alkaline phosphatase levels are abnormal in fewer than half of

patients. Another article has stated that Liver transaminases may be normal, or only marginally elevated Curzio M, et. al There is a poor correlation between biochemistry, ultrasonography, and histology, and the entire histological spectrum of NAFLD can be seen in individuals with normal transaminase values. 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[10]. 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 the number of 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.[11]The HDL values were similar in both groups with mean values being marginally lower in the NAFLD group. The values observed in other studies were as follows. Hyperlipidemia (hypertriglyceridemia, hypercholesterolemia, or both) is another common abnormality and has been reported in 20% to 81% of patients with NAFLD. [12]Dyslipidemia was present in 65% of cases of NAFLD. In another study, Hypertriglyceridemia and fatty liver: clinical diagnosis of fatty liver and lipoprotein profiles in hypertriglyceridemic patients with fatty liver. Most of these patients with fatty liver had hypertriglyceridemia. [13]Ongoing research has shown that Nonalcoholic fatty liver disease has a broad clinical spectrum, different presentations, most of the research has shown that NAFLD has a stable course, some subsets of the NAFLD population might have a progression to severe forms of the disease with inflammation termed steatohepatitis and a minority may end up in having cirrhosis. A significant proportion of patients previously thought to have cryptogenic cirrhosis share many of the clinical and demographic features of NAFLD, suggesting that the etiology of their cirrhosis may be

unrecognized NAFLD. [14]Outcomes of NAFLD are different among different groups and other studies that looked at the outcome of people with NAFLD and Diabetes also report a more aggressive form of the disease and higher overall mortality and mortality related to liver disease Older age, increasing obesity, type 2 diabetes, and hypertriglyceridemia appear to be the strongest independent predictors of more advanced disease.[15]

Conclusions

Hepatomegaly was the commonest physical finding in Nonalcoholic fatty liver disease. 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 were 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. 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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