A Study on BMI as a Prognostic Marker for NAFLD (Non-Alcoholic Fatty Liver Disease) among Patients of Type 2 Diabetes - A Hospital Based Cross Sectional Observational Study

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ABSTRACT

BACKGROUND

Diabetes mellitus (DM) is one of the common non communicable diseases. A study was conducted to determine the prevalence of non-alcoholic fatty liver disease (NAFLD) with regard to the body mass index (BMI).

METHODS

This study was conducted in the Department of Internal Medicine, Thanjavur Medical College, for 10 months. Individuals with type 2 DM, newly diagnosed or on follow up cases were included in the study. Weight was measured, BMI was calculated. The participants were subjected for ultrasonographic examination, based on findings graded as 0, 1, 2 and grade 3 fatty liver (FL). $p<0.05$ was considered statistically significant.

RESULTS

A total of 224 patients were included, of which 66.1% were diagnosed to be NAFLD. Statistically there was no significant difference between the mean ages. NAFLD was maximum in 40-60 years age group followed by > 60 years. Gender wise, grade 1 FL was higher (52.7%) among female population. NAFLD with BMI ranged from 18.5 to 24.99.

CONCLUSIONS

Prevalence of NAFLD was high among T2DM patients. BMI can be used as a predictive and prognostic marker for NAFLD and obesity is the most important risk factor. Grade 1 FL was identified to be more common.

KEYWORDS

Fatty Liver, Diabetes Mellitus, Individuals, Report

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BACKGROUND

Diabetes mellitus (DM) is one of the common as well as major non-communicable diseases, more prevalent in men than women.[1] Due to the prevalence, Indian subcontinent is being considered as global capital for DM.[2,3] Studies mentioned that the DM population will reach 87 million by 2030.[3] The clinical condition, fatty liver (FL), occur among the non-alcoholic individuals is termed as non-alcoholic fatty liver disease (NAFLD) and type 2 DM individuals were reported to be at high risk in developing NAFLD.[4] NAFLD leads to a spectrum of liver disorders, causes lipid accumulation without inflammation to non-alcoholic steatohepatitis (NASH). This leads to fibrosis, cirrhosis and in some patients to hepatocellular carcinoma.[5] Obesity, hyperinsulinaemia, hypertension and hypertriglyceridemia were reported to the predisposing factors of NAFLD.[6] the incidence of NAFLD was reported to be 9 to 40% in Asian countries. The risks of liver associated deaths were reported to be 22 folds in patients with NAFLD especially type 2 Diabetes Mellitus (T2DM).[7] So the diagnosis of NAFLD is to be priory among diabetes with DM. Different techniques such as liver biopsy, CT, MRI and so on were reported in the literature for the diagnosis of NAFLD. These techniques had couple of disadvantages in spite of their sensitivity as well as specificity. With these a study was conducted to find the prevalence of NAFLD by considering the body mass index (BMI) as per the standard guidelines.

METHODS

This was cross sectional observational study, conducted among 308 type 2 diabetes mellitus patients (newly diagnosed or on followup) attending diabetology OPD clinic of the Department of Internal Medicine, Thanjavur Medical College, Thanjavur. An informed consent was obtained after approval by ethics committee of the institute. Study was conducted from November 2017-August 2018, over a period of 10 months. To the participants, routine blood investigation such as sugar was measured. Then weight was measured with light clothes, without shoes and then height was measured. BMI (Kg/m^2) was calculated for all subjects by dividing a person's weight in kilograms by the square of their height in meters. Patients were classified as normal weight (BMI <25.0 Kg/m^2), overweight (BMI ≥25.0 and ≤29.9 Kg/m^2), and obese (BMI ≥30.0 Kg/m.^{2}) the participants were subjected for ultrasonographic examination in the institute. The indication for ultrasound was to assess the liver parenchyma, liver size, gallbladder, biliary, and portal system and graded as grade 0-no FL, 1-grade 1 FL, 2-grade 2 FL, and 3-grade 3 FL. [8]

Exclusion Criteria

- H/O type 1 Diabetes Mellitus or Gestational DM.
- Known H/O Hypertension.
- Known H/O Cardiac, Renal, hepatic failure, stroke.
- Alcoholic (>30 g/day in men & >20 g/day in women)[8] and critically ill patient.
- Patients on drugs altering liver function except OHAs.

Statistical Analysis

Data were analysed using SPSS 21.0. Chi-square test, Fisher's exact test (sample with n<30) and t test were used to compare the proportions between the groups. p<0.05 was considered statistically significant.

RESULTS

Parameter	Patients without NAFLD n=76	Patients with NAFLD n=148	p	Statistical Test
Age in years	48.5±9.03	52.34±9.11	0.003	Unpaired t test

Table 1. Comparison between the Mean Age in Years with SD versus Individuals with and without NALFD

Sl. No.	Age in Years	Patients without NAFLD 76 (100)	Patients with NAFLD 148 (100)	P	Statistical Test
1.	< 40 years	12 (15.8)	12 (8.1)	0.108	Fisher's Exact test
2.	40-60 years	54 (71.1)	95 (64.2)	0.369	
3.	>60 years	10 (13.1)	41 (27.7)	0.0017	

Table 2. Age Distribution among Study Participants with and without NAFLD; n (%)

Parameter	Overall 224 (100)	Male 118 (100)	Female 106 (100)	P	Statistical Test
Normal liver	76 (33.9)	45 (38.1)	31 (29.3)	0.203 (NS)	Chi Square test
FL grade I	115 (51.4)	58 (49.1)	57 (52.7)	0.506 (NS)	
FL grade II	28 (12.5)	11 (9.4)	17 (16.1)	0.158 (NS)	Fisher's exact test
FL grade III	5 (2.2)	4 (3.4)	1 (0.9)	0.373 (NS)	

Table 3. Frequency Distribution of FL among the Study Participants; n (%)

BMI	Without NAFLD 76 (100)	With NAFLD 148 (100)	P	Statistical Test
Normal (18.5 – 24.99)	57 (75)	95 (64.2)	0.13 (NS)	Fisher's exact test
Overweight (25 – 29.99)	17 (22.4)	43 (29.1)	0.34 (NS)	
Obese (≥ 30)	2 (2.6)	10 (6.7)	0.346 (NS)	
Mean	23.2±2.85	24.5±3.31	0.003*	Unpaired t test

Table 4. Frequency Distribution of BMI among the Study Participants with and without NAFLD; N (%)

Sl. No.	Laboratory Investigation	Patients without NAFLD (N=76)	Patients with NAFLD (N=148)	p	(Statistical Test)
1.	Fasting blood glucose (mg/dL)	152.6 ± 60.1	177.23 ± 52.8	0.001*	Unpaired 't' Test
2.	Post prandial blood glucose (mg/dL)	196.3 ± 62.6	234.3 ± 54.1	<0.0001**	Unpaired 't' Test
3.	Plasma Cholesterol (mg/dL)	193.9 ± 34.9	217.5 ± 35.3	<0.0001**	Unpaired 't' Test
4.	Plasma triglycerides (mg/dL)	167.9 ± 34.1	183.2 ± 42.1	0.007*	Unpaired 't' test
5.	SGOT (IU/L)	42.2 ± 8.03	47.08 ± 8.84	<0.0001**	Unpaired 't' Test
6.	SGPT (IU/L)	42.9 ± 8.9	45.56 ± 8.74	0.035*	Unpaired 't' Test
7.	Serum Bilirubin (mg/dL)	0.74 ± 0.1	0.75 ± 0.1	0.728 (NS)	Unpaired 't' Test
8.	Serum Protein (g/dL)	6.63 ± 0.77	6.67 ± 0.36	0.62 (NS)	Unpaired 't' Test
9.	Alkaline phosphatase (IU/L)	77.5 ± 10.3	80.3 ± 10.7	0.063 (NS)	Unpaired 't' Test

Table 5. Comparison of Different Laboratory Parameters between Patients with and without NAFLD in the Study Population

Data are expressed as mean with standard deviation. *indicates p<0.05 and considered statistically significant. NS= Not significant.

Sl. No.	Parameter	Patients without NAFLD (N=76)	Patients with NAFLD (N=148)	p	(Statistical Test)
1.	Height in cm	155.2±8.9	156.5±8.34	0.293 (NS)	Unpaired 't' test
2.	Weight in KG	55.7±9.92	60.02±9.1	0.001*	Unpaired 't' test
3.	BMI	23.2±2.85	24.5±3.31	0.003*	Unpaired 't' test
4.	Waist circumference in cm	82.9±10.1	87.5±9.38	0.0008*	Unpaired 't' test

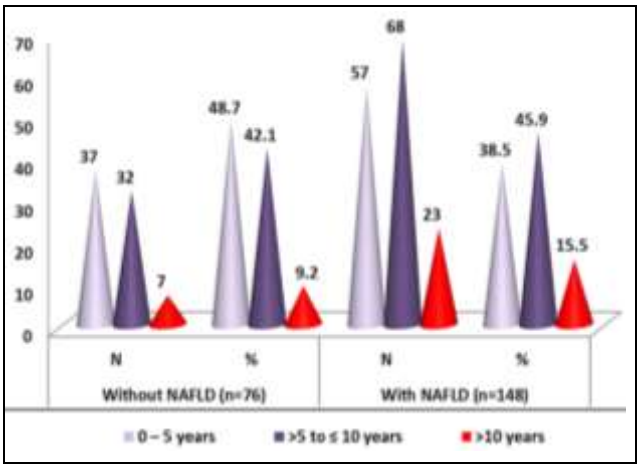
Table 6. Comparison of Different Parameters between Patients with and without NAFLD in the Study Population

Data are expressed as mean with standard deviation. *indicates p<0.05 and considered statistically significant. NS= Not significant.

Sl. No.	Duration of Diabetes Mellitus	Patients without NAFLD (N=76)	Patients with NAFLD (N=148)	p	(Statistical Test)
1.	0 – 5 years	37 (48.7)	57 (38.5)	0.155 (NS)	Chi Square Test
2.	>5 to ≤ 10 years	32 (42.1)	68 (45.9)	0.67 (NS)	Chi Square Test
3.	>10 years	7 (9.2)	23 (15.5)	0.218 (NS)	Fisher's exact Test
4.	Overall (mean duration)	5.87±3.49	6.67±3.79	0.108 (NS)	Mann Whitney U Test

Table 7. Comparison of Duration of Diabetes Mellitus between Patients with and without NAFLD in the Study Population

Data are expressed as n (%) except for overall duration wherein data are expressed as mean with SD. NS = Not significant.



Graph 1. Distribution of Duration of Diabetes Mellitus in the Study Population

Graph 1: Distribution of duration of diabetes mellitus in the NAFLD and Non-NAFLD patients in the study population represented as vertical cone diagram. NAFLD = Nonalcoholic fatty liver disease. N= frequency and% = proportion.

Figure 1. Ultrasonographic Grading of Fatty Liver. A- Fatty Liver Grade 1, B- Fatty Liver Grade 2, C- Fatty Liver Grade 3

In this study, a total of 224 patients was included. In this, using ultrasonogram, 66.1% (148) were diagnosed to be NAFLD and 33.9% (76) were identified to be normal liver. The mean ages were respectively, 52.34±9.11 years, 48.5±9.03 years for individuals with and without NAFLD, this was statistically significant (p= 0.003). This showed that the mean age of patients with NAFLD was significantly higher than patients without NAFLD (table 1) When the age was divided into 3 different age groups of <40 years, 40-60 years, >60 years, patients with NAFLD was maximum in 40-60 years group (64.2%) followed by >60 years group (27.7%) and <40 years group (13.1%), this was statistically significant p= 0.0017 (table 2). Gender wise, 118 were male patients and 106 female patients. Among 118 male patients, 61.9% had FL, in this 49.1% were detected to be grade 1 FL. Among 106 female patients, 69.7% had FL with 52.7% were identified to be grade 1 FL. Grade 1 FL was higher (52.7%) among female population than males. Statistically there was no significant difference (table 3). In this study, 64.2% patients were in the group of NAFLD with BMI range of 18.5-24.99. While there was no statistical significance among the patients with or without NAFLD in the same BMI range.

USG Grading of Fatty Liver

Grade 1: A slight diffuse increase in fine echoes in the hepatic parenchyma with normal visualization of the diaphragm and intrahepatic vessel borders.

Grade 2: A moderate diffuse increase in fine echoes with slightly impaired visualization of the intrahepatic vessels and diaphragm.

Grade 3: A marked increase in fine echoes with poor or no visualization of the intrahepatic vessel borders, diaphragm and posterior portion of the right lobe of the liver.

DISCUSSION

Due to the clinical significance, it is very important and essential to diagnose NAFLD especially among the overweight individuals due to its association with severe liver disorder.[9] in this study, mainly, the parameters such as BMI, ultrasound were correlated to detect the NAFLD. We included 224 DM patients in this study on outpatient basis and all were screened for NAFLD using USG. The clinical symptoms of FL are nonspecific or silent this study does not attempt to define the clinical symptoms of FL. In this study hepatic steatosis was detected by ultrasonography which had a sensitivity and specificity of 83% and 100%, respectively, as compared with histological finding as the gold standard method. In our report, the prevalence of NAFLD in DM was 66.1% and in normal patients was 33.9%. This was comparable to Arun J ET al.[10] and S Kalra ET al.[11] studies, which were reported to be 56.5% each, respectively among the DM patients who were identified to be having NAFLD.

There was significant statistical difference in the mean ages of patients with FL as compared to those with normal liver. The prevalence of ultrasonographic NAFLD among T2DM was reported to be 64.2% in this study. The majority were in the age group of 40-60 years, followed by >60 years age group. An Indian report by Kalra S ET al.[11] reported that prevalence of the disease was found to be higher with increasing age and commonest in the fifth decade. In another Indian study in Chennai by Vishwanathan V ET al.[12] also found and reported predominant incidence of FL with

DM in the sixth decade of life. Gender wise, 69.7% patients with FL in this study were female participants and statistically there was no significant difference ($p > 0.05$) in proportion based on gender was found in those with FL compared to those without evidence of FL. These finding were comparable to that of Ludwig et al., [13] who also reported that there was no statistically significant association between NAFLD and gender. These authors reported that the incidence of NAFLD was similar among the gender. The most common sonographic grade of NAFLD in this report was mild FL (51.4%), followed by moderate FL (12.5%) and severe FL (2.2%). Another report by Gupte et al., [14] observed that the prevalence of NAFLD was 65.5%, 12.5%, and 9.35% respectively among the mild, moderate, and severe FL in T2DMs, respectively. In this study, 64.2% patients were in the group of NAFLD with BMI range of18.5-24.99 while there was no statistical significance among the patients with or without NAFLD in the same BMI range. In a study conducted in Kalra S et al.,[11] 53.6% of patients with obesity were enrolled in the study were found to be associated with FL. In another study by Viswanathan ET al.[12] reported that 27.6% of the patients with BMI >25% enrolled were found to be associated with NAFLD. The effect of BMI was reported to be similar in Rocha ET al.[15] and Fassio ET al.[16] reports, and the authors suggested that BMI measurement is helpful for evaluation of NAFLD. And BMI was identified to be the predictor of NAFLD severity or significantly higher in the patients with FL.

CONCLUSIONS

In our study, it was found that that the prevalence of NAFLD was high among T2DM patients. BMI can be used as a predictive and prognostic marker for NAFLD and obesity is the most important risk factor. Grade I FL was identified to be the more common.

Limitations

A large trail of a longer follow up period is necessary to establish the prognosis of liver disease caused by diabetes mellitus. Non availability of data regarding HbA1c to assess diabetic control more precisely. Most important defects of ultrasonography are, overlap between close grades because ultrasonography is a visual rating system, and highly operator dependent. To obtain more and better data, we used an expert radiologist and repeated suspicious ultrasonographs. Improved imaging modality like MRI spectroscopy was not used in the diagnosis of NAFLD in this study. Histological evidence for NAFLD using biopsy does not affect the treatment course, and according to the Sleisenger and Fordtran's Gastrointestinal and Liver Disease Textbook, for defining NAFLD, liver biopsy is controversial and not necessary, so we did not perform liver biopsy. The golden standard to diagnose NAFLD is liver biopsy, but it not necessary in all patients or in mild form of disease.

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