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Original Research Article

Prevalence of nonalcoholic fatty liver disease in type 2 diabetes mellitus

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Abstract

Background and objectives: Microvascular and macrovascular complications of Type 2 DM are well studied, but association of T2DM with Non alcoholic fatty liver disease (NAFLD) has been recognized recently. The prevalence of NAFLD amongst T2DM is higher compared to non diabetics. There is evidence that T2DM patients with NAFLD are at higher risk of developing cirrhosis compared to non diabetics. Recent data suggest that the prevalence of NAFLD may also be linked to increased coronary artery disease risk, independent of risk conferred by the elements of metabolic syndrome. Indentifying people with NAFLD would also highlight a subgroup of diabetic patients who would be targeted to decrease their risk of future CAD events.

Methods: This study was carried out in B.L.D.E.U's Shri B.M. Patil Medical College Hospital and Research Centre, Vijayapur, Karnataka; during the period from November 2013 to June 2015. A total of 122 patients who were known case of Type 2 diabetes mellitus and who satisfied inclusion criteria were included in the study.

Results: Out of 122 patients included in study 58(47.5%) had NAFLD, the most common sonographic grade of NAFLD was mild fatty liver (62%), followed by moderate (36%), then severe fatty liver (2%). The mean SGOT, SGPT and ALP levels were 31±14.4 IU/L, 25±14.2 IU/L and 104±47.6 respectively. An elevated level of ALP was found to be significantly higher in patients with NAFLD compared patients without NAFLD. 58.6% patients with NAFLD had BMI above normal compared to 36.2% of patients without NAFLD who had elevated BMI which is statistically significant p=0.0001

Conclusion: Prevalence of NAFLD was 47.5% in T2DM patients was significantly associated with overweight, obesity, raised levels of TG, VLDL, ALP. Microvascular complications of T2DM were found to be significantly higher in patients with NAFLD. Macrovascular complication of T2DM Coronary artery disease was found to be significantly higher in patients with NAFLD.

Keywords: NAFLD, Type 2 Diabetes mellitus.

1. Introduction

Fatty liver is defined as fat, largely triglyceride, exceeding 5% of liver weight. It is caused by failure of normal hepatic fat metabolism, either due to a defect within the hepatocyte or to deliver excess fat, fatty acid or carbohydrate beyond the secretory capacity for lipid of liver cell.

Nonalcoholic fatty liver disease (NAFLD) which develops in absence of alcohol abuse includes a spectrum of hepatic changes from steatosis alone to nonalcoholic steatohepatitis, fibrosis and cirrhosis.

The clinical implications of NAFLD are derived mostly from its common occurrence in general population and its potential to progress to cirrhosis and liver cell failure [1]**.** Estimates suggest that about 20-30% of adults in developed countries have excess fat accumulation in liver[2], 44-70% among people with diabetes about 80% in the obese and morbidly obese[3].

Metabolic syndrome and associated co morbidities like type 2 diabetes mellitus (T2DM) and dyslipedemia are predisposing factors of NAFLD, and prevalence of NAFLD has increased parallel to these epidemics [4]. The association of T2DM with microvascular and macrovascular complications is well established, but association of T2DM with NAFLD as a major complication has been recently recognized.

The prevalence of NAFLD amongst T2DM patients is described to be higher than non diabetic patients. Approximately 70% of T2DM patients have a fatty liver and they also appear to have more severe forms of disease

including non alcoholic steatohepatitis (NASH) and fibrosis [5].

Chronic liver disease is often identified by asymptomatic elevation of two serum transaminase; alanine transaminase (ALT) and aspartate transaminase (AST) during routine serum chemistry, but more often slight increase in levels are over looked. Nonetheless there is evidence to suggest that apparently mild elevation in levels of these enzymes may be marker for significant liver disease (i.e. bridging fibrosis and cirrhosis) [6]**.** Elevation of levels of any of two enzymes has been found to be in the range of 2.8%-13.3% in general population [7]**,** and 7.8%-31.5% in T2DM patients [8-13]. The studies have found that liver enzyme abnormalities plus T2DM constitutes a greater risk of CVD [14-16] and renal diseases [17]. This makes diagnosis of NAFLD in T2DM patients, not only essential for prevention of hepatic complications but also important for the prevention of CVD and renal impairment.

2. Material and Methods

This study was conducted in the Department of Medicine, BLDE University, Shri B.M. Patil Medical College Hospital and Research Centre, Vijayapur on patients with Type 2 diabetes mellitus during the period of December 2013-July 2015.

2.1 Sample Size

With prevalence of Nonalcoholic fatty liver disease is 9% in type 2 diabetes mellitus at confidence interval 95% at ±5 margin of error the sample size is 125.

Total number of patients to be studied: 125±5

It is calculated using formula: $n = Z\alpha^2 \times p \times q / d^2$

q=100-p

d=clinically expected variation

Z = standardized normal deviate

2.2 Statistical Analysis

Data will be analysed using chi square test or Fishers exact test. Data will be represented diagrammatically and by Mean ± standard deviation.

2.3 Method of collection of data

Patient enrolled in the study will undergo complete medical examination at the time of enrolment.

2.4 Inclusion Criteria

Type 2 Diabetes Mellitus patients.

2.5 Exclusion Criteria

1. All Type 2 diabetic patients with alcohol consumption of >30 gm/day for 3years
2. Type 2 diabetic patients

a) Suffering from acute and chronic hepatitis.
b) On hepatotoxic drugs and other hepatic diseases
c) Other hepatic diseases.

2.6 Data collection

Demographic data like gender and age were collected along with relevant history and recorded on predesigned and pretested proforma. A thorough clinical examination was conducted and the findings were also recorded required investigations were performed.

3. Observations and results

Careful statistical analysis was performed on the obtained raw data, and following explanatory tables and charts were constructed for better insight into the topic. In our study 122 patients with Type 2 Diabetes Mellitus were enrolled, 77(63%) were males and 45(37%) were females. Out of 122 patients included in study 37 patients were aged between 56-65 years, 36 were aged >=66 years, 30 patients between 46-55 years, 15 between 36-45 years and 4 were <= 35 years. For female patients with NAFLD, 59.2 %(n=16),37% (n=10) and 1(0.8%) had grade 1, grade2 and grade 3 NAFLD respectively. For males with NAFLD 64.5 %(n=20), 35.5(n=11), 0 had grade 1, grade2 and grade 3 NAFLD respectively (Table 1). In our study presence of obesity and overweight were significant (Table 3), presence of chronic kidney disease, non proliferative diabetic retinopathy and coronary artery disease were significant in patients with NAFLD (Table 4).

Table 1: Percentage distribution of Fatty Liver disease

USG Liver	Male		Female		Total	
	N	Percent	N	Percent	N	Percent (%)
Normal liver	46	59.7	18	40	64	52.5
Fatty liver Grade1	20	26	16	35.6	36	29.5
Fatty liver Grade2	11	14.3	10	22.2	21	17.2
Fatty liver Grade3	0	0	1	2.2	1	0.8
Total	77	100	45	100	122	100

Table 2: Comparison of means of parameters by presence and absence of NAFLD

Parameters	With NAFLD (N=58)		Without NAFLD (N=64)		p value
	Mean	SD	Mean	SD	
AGE	58.9	11.8	60.5	12.2	0.481
T2DM (YRS)	6.0	3.2	7.6	5.3	0.044*
HTN(YRS)	2.8	4.1	2.9	5.1	0.924
IHD(YRS)	0.3	1.0	0.9	3.9	0.233
BMI	27.3	4.8	24.0	3.1	0.000*
T Bilirubin	0.8	0.6	0.7	0.2	0.182
SGOT	31.0	14.4	29.5	16.4	0.582
SGPT	25.0	14.2	24.0	14.0	0.709
ALP	104.0	47.6	92.4	37.2	0.134
FBS	194.8	78.1	174.5	71.5	0.136
PPBS	247.8	72.3	233.1	77.1	0.281
HbA1C%	9.2	2.0	8.5	2.1	0.067
T CHOL	180.7	47.8	170.7	43.3	0.226
TG	167.2	92.3	128.1	45.1	0.003*
HDL	39.3	24.3	34.1	9.1	0.115
LDL	111.9	39.0	108.7	37.7	0.652
VLDL	34.0	19.0	26.4	9.6	0.005*
SR CREAT	1.2	0.9	2.0	2.5	0.014
B UREA	34.8	28.4	44.8	35.6	0.091
HB	11.9	2.2	11.6	2.4	0.385
TC	12766.0	5264.4	11766.0	5730.6	0.319
ESR	51.7	32.8	66.8	136.8	0.414

Table 3: Comparison of presence of HTN, Obesity, over weight in patients with and without NAFLD

	NAFLD	Non NAFLD	Total	P value
HTN	29	26	53	0.22
Obese	14	7	21	0.00*
Over Weight	20	14	34	0.00*

Table 4: Comparison of presence or absence of complications of T2DM in patients with and without NAFLD

		NAFLD	Non NAFLD	Total	OR	P Value
CAD	YES	30	21	31	2.19	0.03*
CKD	YES	13	4	23	4.33	0.01*
Retinopathy	YES	22	5	11	2.94	0.01*
CVA	YES	8	5	13	1.8	0.28

4. Discussion

Nonalcoholic fatty liver disease is defined as having hepatic steatosis either by imaging or by histology in absence of secondary hepatic steatosis like alcohol consumption, use of steatogenic drugs or hereditary disorder. This study is first cross sectional study to report on prevalence of NAFLD in Type 2 diabetes mellitus in this part of country.

The study population was mostly urban and from diverse occupational backgrounds. The age range of study subject was 32- 80 years, with mean age of 59.7±12 years. The majority of all subjects studied were in age group of 56-65 years.

The prevalence of ultrasonographic NAFLD among type 2 diabetic subjects in this study was 47.5%, the majority being in the age group 45-49 years, followed by the age group 40-44 years. Our findings were comparable with those of a study carried out by Matteoni *et al* that found the highest prevalence of NAFLD in a similar age group [18]. The most common sonographic grade of NAFLD was mild fatty liver (62%), followed by moderate (36%) and then severe fatty liver (2%). A similar Italian study by Giovanni *et al*, also employing U/S as a screening tool, found a much higher prevalence of 69.5%. 38% (n=64) of the female study subjects had NAFLD, while 30% (n=48) of male study subjects had NAFLD. There was no statistically significant association of gender with NAFLD. This finding was comparable to that of Ludwig *et al*[19], who found no statistically significant association between NAFLD and gender, with the disease occurring in similar proportion among males and females.

The mean SGOT, SGPT and ALP levels were 31±14.4 IU/L and 25±14.2 IU/L and 104 ±47.6 respectively in NAFLD population. Elevated levels of SGOT, SGPT and ALP were seen in 14, 8 and 21 patients with NAFLD respectively. A level of ALP was found to be significantly higher in patients with NAFLD compared to patients without NAFLD. There was no significant difference in levels of SGOT and SGPT, this is similar to study by Jali MV *et al*, in which they found 30% had abnormal SGOT and 22% had abnormal SGPT [20]. It is evident that the level of liver enzymes will provide little diagnostic or prognostic value when assessing NAFLD patients.

In our study 58.6% patients with NAFLD had a BMI that was above normal (27.3± 4.8), compared to 36.2% of patients without NAFLD (24±3.1) that had an elevated BMI. This was statistically significant with a p value of 0.0001, making obesity an important association. Though in our study only BMI was taken as a marker for obesity, raised BMI showed strong correlation with presence of fatty liver. This finding is similar to Shobhaluxmi *et al*[21] where BMI was 30.17±3.92 in patients with NAFLD and 23.7±2.55 in patients without NAFLD which was statistically significant with p value of 0.03.

Our study showed triglyceride level of 167.2±92.3 in patients with NAFLD compared to 128.1 ±45 in patients without NAFLD and VLDL level of 34±19 in patients with NAFLD and 26.4±9.6 in patients without NAFLD both were significant with P value of 0.003 and 0.005 for triglyceride and VLDL respectively. Total cholesterol levels were 180±47.8 and 170.7±40.3 in patients with and without NAFLD respectively and were not significant, these are similar to Jin HB *et al* which showed increased TG (p<0.01), total cholesterol (P=0.88)[22].

In our study NAFLD patients had higher prevalence of retinopathy (P= 0.01), nephropathy (P=0.01) and Coronary artery disease (P=0.03), which were significant and prevalence and prevalence of cerebrovascular accident (P=0.28) was not significant. It is similar to study by Somalwar AM *et al* who found significantly higher prevalence of retinopathy (P=<0.001), nephropathy (P=<0.05) and coronary artery disease (P= <0.001)[23].

5. Conclusion

1) In our study we found the prevalence of NAFLD in Type 2 diabetes mellitus patients being 47.5%.
2) NAFLD was significantly associated with overweight and obesity.
3) NAFLD was significantly associated with biochemical abnormalities of hyper-triglyceridemia and raised VLDL levels.
4) Raised levels of Alkaline phosphatase was found significant in patients with NAFLD.
5) There were no significant changes in SGOT and SGPT levels compared to non NAFLD patients.
6) Microvascular complications of Type 2 Diabetes mellitus, nephropathy and retinopathy were found to be significantly higher in patients with NAFLD.
7) Macrovascular complication of Type 2 Diabetes mellitus coronary artery disease was found significantly higher in patients with NAFLD.

Early detection of NAFLD and its early treatment is necessary as these patients are at risk of developing cirrhosis, end stage liver failure and hepatocellular carcinoma. Furthermore, diabetic patients with NAFLD are at increased risk of developing cardiovascular disease, retinopathy and nephropathy.

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