

## Original Research Article

# Prevalence of non-alcoholic fatty liver disease in type-2 diabetes mellitus patients

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**Received:** 25 January 2018

**Accepted:** 26 February 2018

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### ABSTRACT

**Background:** Non-alcoholic fatty liver disease (NAFLD) is a common chronic condition of which diabetic fatty liver accounts for a large proportion, with 50 to 75% of the subjects demonstrating fat in the liver on ultrasound. As a result of epidemic increase in diabetes mellitus, hypertension, obesity and hyperlipidemia, the prevalence of NAFLD is increasing worldwide.

**Methods:** A study was conducted on a total 100 type-2 diabetes mellitus patients attending Geetanjali Medical College and Hospital, Udaipur, Rajasthan. Patients with known chronic liver disease and history of alcohol intake were excluded. These patients were evaluated by abdominal ultrasonography to determine the presence of fatty liver. They were divided into fatty liver group and non-fatty liver group; and were further evaluated by measurement of body mass index, Central obesity, HbA1c and lipid profile. The data obtained was analyzed using SPSS version 20.0.

**Results:** Of the 100 diabetic patients enrolled in this study, 64 (64%) presented with NAFLD. The highest prevalence of NAFLD was recorded in the age group of 50-59 years at 37.5%. The prevalence rate among males (65.62%) was higher than for females (34.38%). A comprised NAFLD patients (64%) and Non-NAFLD patients (34%).

**Conclusions:** This study revealed that the NAFLD is a vital part of cluster of abnormalities such as dysglycemia, dyslipidemia, hypertension and obesity. Age and duration of diabetes are also important contributing factors in occurrence of NAFLD.

**Keywords:** Hyperglycemia, Metabolic Syndrome, Non-alcoholic fatty liver disease, Type-2 diabetes mellitus

### INTRODUCTION

The term Non-alcoholic fatty liver disease (NAFLD) is a commonly categorized by accumulation of fat in liver which changes from simple steatosis to steatohepatitis, cirrhosis and hepatocellular carcinoma (HCC) in lack of excessive alcohol intake.<sup>1</sup>

NAFLD is distinct by macrovesicular steatosis of more than 5% hepatocytes in the absence of inflammation. Type 2 Diabetes Mellitus (T2DM) patients seem to have

an enlarged risk of developing NAFLD than non-diabetic subjects and certainly have higher risk of increasing fibrosis and cirrhosis. Existence of NAFLD in T2DM may also be accompanying to increased cardiovascular disease risk.<sup>2</sup> T2DM surges the risk of liver associated death by up to 22-fold in patients with NAFLD.<sup>3</sup> Diagnosis of NAFLD requires high index of suspicion, particularly in obese patient over the age of 45 years with history of diabetes mellitus, because these patients are at increased risk of developing cirrhosis.<sup>4</sup> Numerous studies have shown that NAFLD is the hepatic constituent of

metabolic syndrome. The central features of metabolic syndrome such as the peripheral insulin resistance, obesity, hypertension, hyperinsulinaemia, and hypertriglyceridemia are the predisposing factors for NAFLD.<sup>5</sup> The occurrence of NAFLD is 15 to 40% in western countries and 9 to 40% in Asian countries. Since last two decades, increasing the incidence of diabetes mellitus, obesity and insulin resistance in India, hence it is logical to expect increase in incidence of NAFLD. However, there is limited data on the prevalence of NAFLD in India.<sup>6</sup> Numerous studies leads to show the prevalence rate of NAFLD to be around 9-32% in the general Indian population, with a higher prevalence among the obese and diabetic entities. The prevalence rate of NAFLD in T2DM is predictable to be in the range of 12.5% to 87.5% in India.<sup>7</sup>

The present study was conducted to determine the prevalence of NAFLD in T2DM and also assess the risk factors associated with diabetic fatty liver.

## METHODS

In this prospective study, a total of 100 patients with T2DM study population was included the age group of 20-70 years, attending medical outpatient clinic from November 2015 to November 2017. Before initiating the study, we obtained the approval from the Institutional Ethics Committee and informed consent from the patients. The patients were interviewed by a designed questionnaire. A complete history taking and physical examination were performed. Anthropometric measurement such as waist circumference, body mass index and metabolic parameters such as fasting and postprandial blood sugar, glycosylated hemoglobin (HbA1c), serum uric acid, blood urea, serum creatinine, fasting lipid profile, serum bilirubin, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) and serum alkaline phosphatase (SAP) were measured.

The patients with criteria such as history of alcohol consumption, chronic liver disease of any cause and intake of hepatotoxic drugs were excluded. To detect fatty changes in the liver, all patients were enrolled experience ultrasonography, performed by single experienced radiologist (to prevent interpersonal variation), using a high-resolution B-mode ultrasonography system having an electric linear transducer mid frequency of 3-5MHZ.

Fatty liver was defined as the ultrasonographic features consistent with bright liver with ultrasonographic contrast between hepatic and renal parenchymal vessel blurring and narrow of the lumen of hepatic vein in the absence of findings suggestive of chronic liver disease.

Obesity is defined if body mass index (BMI)  $25\text{kg}/\text{m}^2$ .<sup>8</sup> For given age, sex and body fat level Caucasians have higher BMI than Asians. It is generally recommended to

consider Asians as obese if their BMI is  $25\text{kg}/\text{m}^2$ . Patients were considered centrally obese if the waist circumference was  $>80\text{cm}$  in females and  $>90\text{cm}$  in males.<sup>9</sup> Patients with one of the criteria: LDL-C  $>100\text{mg}/\text{dL}$ , total cholesterol  $>200\text{mg}/\text{dL}$ , triglycerides  $>150\text{mg}/\text{dL}$ , or HDL-C  $<40\text{mg}/\text{dL}$  in males and  $<50\text{mg}/\text{dL}$  in females were considered to have dyslipidemia. Metabolic syndrome was defined according to guidelines of IDF.<sup>10</sup> The diagnosis of hypertension was done when average systolic BP  $140\text{mmHg}$ , or average diastolic BP  $90\text{mmHg}$ , or use of antihypertensive medication was established.<sup>11</sup>

## NAFLD was classified based on the standard ultrasonographic criteria

- Grade 1 - (Mild steatosis) slightly increased liver echogenicity with normal vessels and absent posterior attenuation.
- Grade 2 - (Moderate steatosis) moderate increase in liver echogenicity with partial dimming of vessels and early posterior attenuation.
- Grade 3 - (severe steatosis) diffuse increase in liver echogenicity with absence of visible vessels and heavy posterior attenuation.

Sensitivity of ultrasonogram in detection of hepatic steatosis ranges from 60 to 94% and specificity 84 to 95%. Hepatorenal sonographic index which is the ratio between mean brightness level of liver and right kidney, has also been proposed as a measure of hepatic steatosis with a cutoff value of 1.49, yielding a very high sensitivity (100%) and specificity (91%) for diagnosis of steatosis  $>5\%$ .<sup>12</sup>

## Statistical analysis

Data documented and analyzed using Statistical Package for Social Sciences [SPSS], Pearson's Chi Square Analysis test and Fisher exact probability test. Mean and standard deviation were calculated for each variable. The diabetic patients with fatty liver were compared with the diabetic patients without fatty liver.

## RESULTS

A total of 100 subjects were recruited of which 106 subjects with T2DM were included in data analysis. 6 subjects were excluded due to incomplete laboratory evaluation. The present study observed a higher frequency of NAFLD in the diabetic female population (22/100) compared with the male population (42/100) (Table 1) with a Female to Male ratio of 1:1.8. Statistically, there is no significant difference between male and female subjects. The mean age of the patients with T2DM was  $51.81\pm 9.87$  years. The age distribution of NAFLD patients was given in the Table 2. The frequency of patients with NAFLD was more in the age group of 50-59years. No significant difference was found between age and disease by statistical analysis (Table 3).

The prevalence of NAFLD to be 10.51% which increased with advancing age (38%) and longer duration of diabetes (49%). Results were statistically significant.

**Table 1: Gender distribution of NAFLD in T2DM patients (N=100).**

Sex	NAFLD	Non- NAFLD
Male	42 (65.62%)	24 (66.66%)
Female	22 (34.38%)	12 (33.33%)
Total	64 (100%)	36 (100%)

**Table 2: Age distribution of NAFLD in T2D patients (N=100).**

Age (Years)	NAFLD	
	Present	Absent
30- 39	08 (12.50%)	03 (08.33%)
40-49	16 (25.0 0%)	13(36.11%)
50-59	24 (37.50%)	11(30.55%)
60-69	14 (21.87%)	9 (25.00%)
≥70	2 (03.12%)	0
Total	64	36

**Table 3: Comparison of the demographic and laboratory variables in diabetic patients with and without fatty liver.**

Characteristics	Fatty liver group (n = 64)	Non-fatty liver group (n=36)	P value
Age (years; Mean±S)	51.81±9.87	50.93±8.51	NS
BMI (kg/m <sup>2</sup> ; Mean±SD)	27.79±2.31	24.28±3.14	<0.0001
WC (cm; Mean±SD)	101.89±6.28	98.59±6.43	0.0141
FBS (mg/dl; Mean±SD)	158.61±52.89	129.47±44.26	0.006
HbA1c (mg/dl; Mean±SD)	8.96±1.12	7.87±1.31	<0.0001
DM (duration in yrs; Mean±SD)	7.23±2.38	3.23±1.19	<0.0001
Cholesterol (mg/dl; Mean±SD)	171.69±27.54	169.74±25.63	NS
TGL (mg/dl; Mean±SD)	137.43±47.31	117.93±42.98	0.042
LDL (mg/dl; Mean±SD)	101.81±30.84	87.88±31.09	0.033
HDL (mg/dl; Mean±SD)	42.36±4.97	44.89±4.18	0.011
Prevalence of CAD (n;%)	37 (57.81%)	16 (33.33%)	0.032
Prevalence of metabolic Syndrome(n,%)	56 (87.5%)	23 (63.88%)	0.011

A large proportion of the study population was obese and dyslipidaemic, as almost 90% and 36% had BMI >25kg/m<sup>2</sup> and serum triglycerides >150mg/dl,

respectively. The prevalence of obesity (BMI >25kg/m<sup>2</sup>) in patients with NAFLD was 92.2%, as compared to 86.11% in non-NAFLD patients.

CAD was more prevalent in the NAFLD subgroup (57.1%) as compared to the non-NAFLD subgroup (44.4%). On analyzing the risk factors for CAD, the NAFLD subgroup had a higher prevalence of hypertension, smoking, obesity (measured by BMI), central obesity (measured by waist circumference and WHR), higher HbA1c and triglyceride levels, lower HDL level. Using a cut off level of HbA1c >7% as a measure for poor control, 86.1% in the non-NAFLD subgroup and 95.3% in the NAFLD group had poor glycemic control (Table 3).

Metabolic syndrome, as defined by ATP III criteria, was present in 79% of the study group. Prevalence of the metabolic syndrome was significantly higher in the NAFLD subgroup, as compared to those who did not have NAFLD (87.5% vs. 63.88%) (p=0.011). Patients with NAFLD were further subcategorized, according to USG grading of NAFLD, into 3 grades - grade 1 to grade 3. From only 2 patients had grade 3 NAFLD, analysis was limited to grade 1 and grade 2 patients. CAD was prevalent in grade 2 than in grade 1 NAFLD patients. Patients with grade 2 disease had poorer glycemic control and greater derangements in lipid profile than grade 1 patients.

**DISCUSSION**

Non-alcoholic fatty liver disease (NAFLD) characterizes a variety of disease, characterized histologically by extreme growth of hepatic fat in the absence of significant alcohol consumption; with or without swelling, varying degree of fibrosis, and cirrhosis. A number of studies have found a positive relationship between hyperinsulinaemia, abnormal glucose tolerance, and NAFLD. Mishra et al, found the prevalence of metabolic syndrome and NAFLD to be 24% and 14.8%, respectively, in nonalcoholic North Indian men.<sup>13</sup> Gupte et al, observed that NAFLD such as mild, moderate, and severe was existing in 65.5%, 12.5%, and 9.35% of otherwise asymptomatic type 2 diabetics, respectively.<sup>14</sup> A multiple components of the metabolic syndrome which increased in type 2 diabetics with a high prevalence of NAFLD and NASH found by Prashanth et al.<sup>7</sup> On histologically, Banerjee et al, found that only fatty change was contemporary in 43%, NASH in 40% and more advanced disease in 23%.<sup>15</sup>

The prevalence rate of NAFLD was highest in the 50 to 59 years age group (24/100), subsequently followed by 40-49 years (16/100), 60-69 years (14/100) and less than 40 years age groups (8/100). The study also revealed a higher prevalence of NAFLD in male patients (42/100) with T2DM compared with the female community (22/100). The larger number of male subjects included in the study population may account for the male fondness

seen in this study. Controversially trend was reported by S Kalra et al, in which the frequency of the disease was more in female patients.<sup>16</sup>

In our study, 59% patients with NAFLD had a BMI that was above normal ( $27.79 \pm 2.31$ ), compared to 35% of patients without NAFLD ( $24.28 \pm 3.14$ ) that had higher BMI which is statistically significant ( $p < 0.0001$ ). BMI was associated as marker of obesity which is strongly correlation with presence of fatty liver disease. Moreover, Similar to Shobhaluxmi et al, studies where BMI was  $30.17 \pm 3.92$  in patients with NAFLD and  $23.7 \pm 2.55$  in patients without NAFLD which was statistically significant with p value of 0.03.<sup>17</sup>

In a study among severely obese patients with diabetes, 100% were found to have at least mild steatosis, 15% steatohepatitis and 21% cirrhosis.<sup>18</sup> In our study, 65% patients were obese with NAFLD. Hypertension has also been reported frequently in patients with NAFLD but it is not an independent risk factor as is also found in this study.<sup>19-20</sup> In this study, 34% HTN patients had NAFLD. Dyslipidemia has been reported in 20 to 90% of patients with NAFLD.<sup>21</sup> We found that Hypertriglyceridemia-37%, High LDL- 54% and Low HDL- 42%) were significantly higher among subjects with NAFLD-Group. In a hospital based study from North India Prashanth et al, found almost similar findings.<sup>7</sup>

The finding of NAFLD in our study was based on standard ultrasonography, which is by for the commonest way of diagnosing this increasingly recognized liver disorder in clinical practice. Radiologic imaging such as sonography has an adequate threshold for diagnosing fatty liver.<sup>17</sup>

## CONCLUSION

NAFLD is a common chronic hepatic disorder globally. T2DM and NAFLD are rapidly increasing, reaching levels of a pandemic in countries like India. Prevalence of NAFLD has increased along with the multiple components of metabolic syndrome. The results from this study have established a prevalence design of NAFLD in T2DM patients, highlighting the need to formulate preventive strategies.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Patel H, Verma YN. Prevalence of non-alcoholic fatty liver disease in type-2 diabetes mellitus patients. *Int J Res Med Sci* 2018;6:1322-6.