



## PREVALENCE OF NON-ALCOHOLIC FATTY LIVER DISEASE IN NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS

### Diabetology

**Dr. Mohsin Aslam\*** Consultant Physician, Asian Institute of Gastroenterology, Somajiguda, Hyderabad – 500082, Telangana. \*Corresponding Author

**Dr. Niharika Chandra** Senior Resident, Department of Gastroenterology, Asian Institute of Somajiguda, Hyderabad – 500082, Telangana.

### ABSTRACT

Type 2 diabetes mellitus (T2DM) and Non-alcoholic fatty liver disease (NAFLD) are common conditions that often co-exist and can act synergistically to drive adverse outcomes.

**Aim:** To study the prevalence of NAFLD in newly diagnosed type 2 diabetes mellitus patients, correlate with anthropometry and biochemical parameters.

**Methodology:** 60 cases of newly diagnosed T2DM patients, evaluated clinically, biochemically and on ultrasound for NAFLD and its complications. Anthropometric measurements were taken, and laboratory parameters measured. Ultrasonography was done by the same observer using the same ultrasound machine. Relevant statistical tests were performed.

**Results:** The mean age of the patients was 48.9 years with a mean BMI of 29.6 kg/m<sup>2</sup>. Mean HbA1c was 9.8%. None of the patients had micro and macrovascular complications of diabetes mellitus. NAFLD was seen in 70% of patient on ultrasound abdomen. There was a significant correlation between weight and NAFLD ( $p = 0.009$ ), BMI and NAFLD ( $p = 0.04$ ), waist circumference and NAFLD ( $p = 0.01$ ), AST and NAFLD ( $p = 0.007$ ) and ALT and NAFLD ( $p = 0.006$ ).

**Conclusion:** NAFLD is more common in patients with T2DM and obesity. All the patients diagnosed to have T2DM recently should be screened for fatty liver disease.

### KEYWORDS

Type 2 Diabetes Mellitus, Non-alcoholic Fatty Liver Disease, Non-alcoholic Steatohepatitis, Obesity

### INTRODUCTION

Type 2 diabetes mellitus (T2DM) and non-alcoholic fatty liver disease (NAFLD) are closely related. It has been shown that NAFLD may be present in up to 70% of patients with diabetes<sup>1,2</sup> and biopsy proven NASH (non-alcoholic steatohepatitis) in upto 20% of patients with asymptomatic type 2 diabetics and normal liver function tests (LFTs)<sup>3</sup>. There is a significant burden of advanced fibrosis in asymptomatic individuals with T2DM ranging from 5% to 7%<sup>4,5</sup>. Obesity and physical inactivity are interlinked risk factors for the development of both diabetes and NAFLD. There is a relationship among T2DM, insulin resistance (IR) and NAFLD as insulin is delivered directly to the portal vein after secretion, taking the same route as the absorbed glucose, and the liver eliminates a large portion of portal insulin at the first pass. Obesity in NAFLD is associated with dysfunctional adipose tissue, and lipotoxicity promotes insulin resistance and pancreatic  $\beta$ -cell dysfunction<sup>6</sup>.

There is a strong association between NAFLD and diabetes risk. Individuals with NAFLD have approximately 5-fold increased risk of developing diabetes<sup>7</sup>. Whether type 2 diabetes increases an individual's risk of developing NAFLD is unclear and difficult to study as a large proportion of patients with type 2 diabetes are diagnosed long after the onset of their diabetes. Given the insidious nature of type 2 diabetes, it is not surprising that those with established diabetes have markedly more liver fat when compared to age, BMI and gender matched controls<sup>8</sup>. In a cross-sectional study, there was an increased risk of NAFLD with increasing levels of HbA1c and insulin resistance, independent of obesity introducing the concept of 'pre-diabetes' as a possible precursor for NAFLD and its subsequent progression<sup>9</sup>.

NAFLD increases the risk of cardiovascular events in an individual with T2DM<sup>10</sup>. There is also increase risk of microvascular complications of diabetes including chronic kidney disease and retinopathy<sup>11</sup>. Individuals with co-existing diabetes and NAFLD have an additive detrimental liver outcome, making an individual more likely to have more severe NAFLD associated with complications of cirrhosis and mortality<sup>12,13</sup>. Overall, co-existent NAFLD and diabetes are associated with a more severe adverse outcome than either of the conditions in isolation.

NAFLD is becoming an important medical problem with the growing epidemic of obesity and diabetes mellitus. There is a need to recognise

at the earliest patient profiles, anthropometric and biochemical and non-invasive biomarkers which will guide clinicians.

### OBJECTIVES

To study the prevalence of NAFLD in newly diagnosed type 2 diabetes mellitus patients and to correlate with anthropometry and biochemical parameters.

### MATERIALS AND METHODS

This is an observational study. Between January 2017-June 2017, we enrolled a total of 60 cases of newly diagnosed T2DM patients, attending the diabetic clinic at our institution.

### Inclusion Criteria

Patients who were newly diagnosed as type 2 diabetes mellitus; having fasting blood sugar (FBS) > 126 mg/dl or random blood sugar (RBS) > or HbA1c > 6.5%.

Patients age > 35 years.

### Exclusion Criteria

Patients with a history of alcohol ingestion.

History of drugs like amiodarone, estrogen, steroids, herbal medicines and tamoxifen.

Known cases of hepatitis B/C, hemochromatosis, Wilson's disease, autoimmune hepatitis, primary biliary cirrhosis, sclerosing cholangitis, biliary obstruction or malignancy.

Known cases of acute pancreatitis, recurrent acute pancreatitis, chronic pancreatitis or pancreatic malignancy.

Patients with established T2DM and on Insulin or oral hypoglycemic agents.

### Data Collection

Anthropometric measurements: Measurement of height, weight, waist and hip circumference were taken. BMI was calculated as weight in Kg/height in metre square.

Laboratory Parameters: FBS, RBS, HbA1c, fasting lipid profile, liver function tests (LFT), renal function tests (RFT) were measured using an auto analyser.

Ultrasonography (USG): USG was done by the same observer using a curvilinear probe of frequency of 3.5-5 MHz and using the same ultrasound machine.

Criteria used to assess for steatosis included hepatorenal echo contrast, liver brightness (posterior beam) attenuation and vascular margin blurring.

**Grades of Fatty Liver**

Grade I: Slight diffuse increase in the fine echoes. Liver appears bright compared to the cortex of the kidney. Normal visualisation of the diaphragm and intrahepatic vessel margins.

Grade II: Moderate diffuse increase in fine echoes. Slightly impaired visualisation of the intrahepatic vessels and diaphragm.

Grade III: Marked increase in fine echoes. Poor or no visualisation of intrahepatic vessel borders, diaphragm and poor penetration of the posterior, segment of the right lobe of the liver.

**Statistical analysis**

All the continuous variables were expressed as mean ± SD. In addition, categorical variables were analysed by chi-square test. P value < 0.05 was considered significant. Statistical Package for Social Sciences version 21.0 (SPSS) was used for statistical analysis.

**RESULTS**

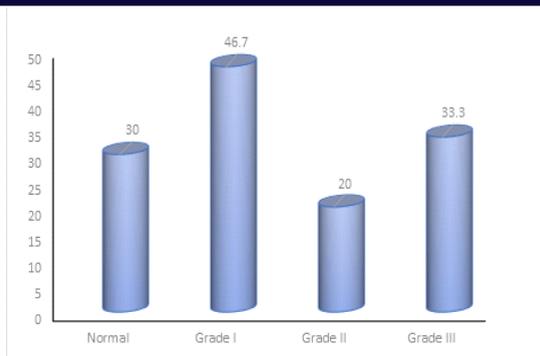
60 newly diagnosed T2DM patients were examined in detail and evaluated for fatty liver disease. The mean age of patients was 48.9 ± 10.4 years. There was a female preponderance in patients with newly diagnosed T2DM. Mean BMI of the patients was 29.6 ± 4.8 kg/m<sup>2</sup>. 32 out of 60 patients were known hypertensive and 13 were active smokers. Baseline characters of cases and controls are shown in table 1.

**Table 1: Baseline characters of cases**

Baseline Characteristics	Cases (60)
Age (Years)	48.9 ± 10.4
Sex (M: F)	24:36
BMI (Kg/m <sup>2</sup> )	29.6 ± 4.8
Hypertension	32 (53.3%)
Smoking	13 (21.67%)
Blood Pressure (mm/Hg)	136/92
S. Creatinine (mg/dl)	0.9 ± 0.2
Fasting blood sugar (mg/dl)	212.4 ± 90.1
HbA1c %	9.8 ± 2.3
Urine for albumin creatinine ratio (mg/mmol)	0.3 ± 0.1
Triglycerides (mg/dl)	164 ± 70.3
Total cholesterol (mg/dl)	190.6 ± 36.7
LDL-C (mg/dl)	121.9 ± 33.9
HDL-C (mg/dl)	40.1 ± 7.3
Aspartate transaminase (AST) (U/L)	20.6 ± 5.7
Alanine transaminase (ALT) (U/L)	26.2 ± 10.1

Fundus examination was normal in all the patients. None of the patients had abnormal electrocardiogram (ECG). All the patients had normal urine for albumin creatinine ratio suggesting that none of the patients had complications of T2DM.

70% of the patients were found to have NAFLD of which 46.7% of the patients had grade I fatty liver, 20% had grade II fatty liver and 3.3% had grade III fatty liver while 29.5% had a normal liver on ultrasound examination (figure 1).



**Figure 1:** USG findings in patients with newly diagnosed type 2 diabetes mellitus. Patients with advanced grades of fatty liver had significantly higher weight (p = 0.009), BMI (p = 0.04) and waist circumference (p = 0.01). There were no statistically significant differences in the age, height, hip circumference and waist hip ratio (table 2).

**Table 2: Comparison of Baseline & Anthropometry parameters with grades of fatty liver**

Variables	Grades of fatty liver			P value
	Normal	Grade I	Grade II/III	
Age (years)	46.5 ± 11.8	51.7 ± 10.4	46.3 ± 7.9	0.39
Weight (Kg)	69.6 ± 5.9	75.2 ± 13.1	90.4 ± 17.1	0.009
Height (cm)	160.8 ± 8.1	159.9 ± 10.9	165.1 ± 5.5	0.47
BMI (Kg/m <sup>2</sup> )	27.1 ± 3.8	29.4 ± 3.9	33.1 ± 5.9	0.04
Waist circumference	93.2 ± 7.6	95.2 ± 13.8	110.3 ± 11.7	0.01
Hip circumference	97.5 ± 5.3	96.3 ± 15.1	107.4 ± 16.3	0.2
Waist-hip ratio	0.96 ± 0.07	0.99 ± 0.1	1.03 ± 0.07	0.25

Patients with increased blood sugars at presentation had advanced fatty liver disease but the difference was not statistically significant (table 3).

**Table 3: Comparison of sugar parameters with grades of fatty liver**

Blood Sugars	Grades of fatty liver			P value
	Normal	Grade I	Grade II/III	
Fasting Blood Sugar	192.5 ± 66.5	189.8 ± 77.4	255 ± 126.5	0.26
Random Blood Sugar	274.9 ± 90.5	278.4 ± 128.9	362.4 ± 171.9	0.33
HbA1c (%)	9.7 ± 2.1	9.6 ± 2.1	10.1 ± 2.4	0.87

Aspartate transaminase and alanine transaminase were significantly higher in patients with newly detected T2DM with grade II/III fatty liver than those with grade I fatty liver and those with normal liver (table 4).

**Table 4: Comparison of liver function test with grades of fatty liver**

Liver function tests	Grades of fatty liver			P value
	Normal	Grade I	Grade II/III	
Total bilirubin (mg/dl)	0.52 ± 0.24	0.59 ± 0.21	0.52 ± 0.16	0.67
Direct bilirubin (mg/dl)	0.18 ± 0.09	0.18 ± 0.08	0.20 ± 0.04	0.86
Ind. bilirubin (mg/dl)	0.33 ± 0.17	0.41 ± 0.17	0.33 ± 0.12	0.39

AST (U/L)	17.3 ± 5.5	18.5 ± 3.8	26.1 ± 7.8	0.007
ALT (U/L)	19.3 ± 6.4	23.1 ± 7.1	36.1 ± 16.6	0.006
ALP (U/L)	88.4 ± 21.1	90.9 ± 25.8	102 ± 28.3	0.53
Serum Albumin (g/dl)	4.3 ± 0.2	4.4 ± 0.2	4.1 ± 0.3	0.98

There was no significant correlation between triglyceride, total cholesterol, LDL cholesterol, HDL cholesterol and NAFLD. However, there was some correlation between VLDL cholesterol and NAFLD (table 5).

**Table 5: Comparison of lipid profile with grades of fatty liver**

Lipid profile	Grades of fatty liver			P value
	Normal	Grade I	Grade II/III	
Triglyceride (mg/dl)	168.8 ± 82.6	133.1 ± 54	190.1 ± 74.3	0.18
T. cholesterol(mg/dl)	176.8 ± 33.2	189.9 ± 32.4	205 ± 44.4	0.31
LDL-C (mg/dl)	106.8 ± 36.4	125.8 ± 27.2	133.1 ± 38.2	0.25
HDL-C (U/L)	41.8 ± 11.2	39.5 ± 7.1	39 ± 3.5	0.74
VLDL-C (U/L)	27.6 ± 9.1	23.3 ± 9.5	36.5 ± 9.9	0.02

## DISCUSSION

NAFLD is a spectrum of disease ranging from mild fatty liver to NASH to cirrhosis. NAFLD is increasingly being diagnosed as the most common cause of liver disease. With the ever-increasing epidemic of obesity and diabetes, prevalence of NAFLD is only expected to increase in the years to come. Liver biopsy remains the gold standard in the diagnosis of NAFLD/NASH but comes with concomitant risks of an invasive procedure. It is therefore not suitable to evaluate all suspected cases of NAFLD with a liver biopsy. In the present study, we evaluated 60 newly diagnosed cases of T2DM for complications of diabetes, NAFLD and its complications. The mean age at the diagnosis was 48.9 years. 60% of them were females. Most of the patients were found to be obese with 43.35% of the study population in the 25-29.9 kg/m<sup>2</sup> BMI range and falling under grade I obesity. 21.67% were active smokers and 53.3% were hypertensive although no statistical significance was found between them and the prevalence of NAFLD. None of the patients had micro and macrovascular complications of diabetes mellitus. NAFLD was seen in 70% of patient on ultrasound abdomen. 2 patients had grade III fatty liver. And only 1 patient had transaminitis. There was a correlation between weight, BMI, waist circumference, liver enzymes (AST and ALT) and NAFLD.

In a study by Leite NC et al<sup>6</sup>, the prevalence of NAFLD on USG was 69.4% in 180 patients with T2DM. NAFLD was associated with obesity (abdominal), hypertriglyceridemia and high-normal ALT levels.

In an Indian study<sup>14</sup>, the prevalence of NAFLD on USG was 62.2% in 204 patients with known T2DM. NAFLD was confirmed by liver biopsy with subsequent histology in 87% of the patients, indicating a 54.11% histologically confirmed prevalence in T2DM. Steatohepatitis and fibrosis were found in 38.9% and 23.2%, respectively, of Indian patients with T2DM.

Leite et al<sup>15</sup> found a 78% NASH prevalence at the histological examination in nearly 100 patients with T2DM and US evidence of NAFLD. The presence of high triglyceride, low HDL-cholesterol and increased ALT levels were independently associated with a higher risk of histologically confirmed NASH. The presence of NASH was independently correlated with high serum GGT levels, older age and male gender.

## CONCLUSION

NAFLD is more common in patients with T2DM and obesity. All the patients diagnosed to have T2DM recently should be screened for fatty

liver disease. Patients with newly diagnosed T2DM found to have fatty liver on USG, should be advised to abstain from alcohol, control their weight and follow healthy lifestyle.

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