

# Frequency of Non-Alcoholic Fatty Liver Disease in Obese and Non-Obese Diabetics and Its Relation to Duration of Diabetes Mellitus

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## ABSTRACT

**Objective:** To find out the frequency of non-alcoholic fatty liver disease in obese and non-obese diabetics and its relation to duration of diabetes mellitus.

**Study Design:** Cross sectional study

**Place and Duration of Study:** This study was conducted at the Department of Medicine, Sheikh Khalifa Bin Zaid Al-Nahyan hospital Rawlakot from July 2017 to December 2017.

**Materials and Methods:** Patients with type 2 diabetes mellitus presenting to outpatient department were enrolled and their age, weight, height and duration of diabetes mellitus were noted. Body mass index (BMI) was calculated using formula  $BMI = (\text{weight in kilograms}) / (\text{height in meters})^2$ . Ultrasound abdomen was used to detect the presence and absence of fatty liver disease. SPSS version 20 was used for analysis of data. Chi-square test was applied to assess the significance of difference of fatty liver disease in normal weight, over weight, class I obese, class II obese and class III obese diabetics and relation of duration of diabetes mellitus with presence or absence of fatty liver disease.

**Results:** Out of 200 patients 10% were of normal weight, 44% were overweight and 41% had class I obesity while none had class II or class III obesity. Incidence of fatty liver was 50% in patients with normal weight, 76% of patient who were over-weight and 97% of patients with class I obesity. Also its incidence was 71% in patients with duration of disease between 1 to 4 years, 91% amongst patient with duration of diabetes between 5 to 8 years and 100% of patients with duration of diabetes between 9 to 12 years.

**Conclusion:** In type 2 diabetic patients Frequency of non-alcoholic fatty liver disease is high in patients who are obese as compared to patients who are non-obese and its incidence increases with increase in duration of diabetes

**Key Words:** Nonalcoholic fatty liver disease, Diabetes mellitus, Body mass index

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## INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is a major public health problem these days. It include steatosis, Nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis and ultimately hepatocellular carcinoma.<sup>1</sup>

About three decades ago Ludwig et al delineate liver lesions similar to alcohol associated lesions within liver in patients who did not take alcohol and called it NAFLD.<sup>2</sup>

Its definition needs (a) demonstration of steatosis in liver, either by ultrasonography or liver biopsy (b) other

causes for fat accumulation in liver are excluded e.g. alcohol consumption, use of steatogenic medication or hereditary disorders.<sup>3</sup>

In USA it is most common chronic liver disease and is increasing in Asia pacific region including South Asia.<sup>1,4</sup> Almost 15-40% of general population are affected by NAFLD and its prevalence is expanding worldwide.<sup>1,5</sup> The community prevalence of NAFLD in South Asia and South East Asia ranges from 5-30%. Recently a hospital based study in Pakistan had shown a frequency of approximately 14%.<sup>6</sup>

In most of patients, metabolic risk factors causing NAFLD are obesity, diabetes mellitus, and dyslipidemia.

Mostly patients with NAFLD do not develop symptoms and mostly recognized when routine laboratory assessment shows deranged liver function tests. Liver enzymes alanine aminotransferase and aspartate aminotransferase are increased. However, these enzymes may not be increased in all cases of NAFLD, and their level does not exactly foretell about inflammation and cirrhosis<sup>7</sup>

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**MATERIALS AND METHODS**

A cross-section study was carried out for six month at Sheikh Khalifa Bin Zaid Al-Nahyan Hospital Rawlakot (from July 2017 to December 2017). It includes all patients with type 2 diabetes mellitus presenting to outpatient department. Their age, weight, height and duration of diabetes mellitus was noted. Body mass index (BMI) was calculated using formula  $BMI = (\text{weight in kilograms}) / (\text{height in meters}^2)$ . Their liver function test (LFTS) and fasting lipid profile was performed.

They were given appointment for ultrasound abdomen for presence and absence of fatty liver disease. They were grouped according to BMI as Normal Weight (BMI 18.5–24.9), Over Weight (BMI 25 -29.9), class I obesity (BMI 30 -35), class II obesity (BMI 35-40) and class III (BMI > 40). They were also grouped according to duration of diabetes into 3 groups. Group 1 included patients with duration of diabetes between 1 to 4 years, Group 2 duration of diabetes was from 5 to 8 years and in group 3 duration of diabetes was 9 to 12 years.

Data was entered in SPSS version 20. Chi-square test was applied to assess the significance of difference of fatty liver disease in normal weight, over weight class I obese, class II obese and class III obese diabetics and relation of duration of diabetes mellitus with presence or absence of fatty liver disease.

**RESULTS**

Out of 200 patients 65 (32.5%) were male and 135 (67.5%) were females. Mean age was 55 years. 10% of patients were normal weight, 44% were overweight and 41% had class I obesity while none had class II or class III obesity.

**Table No.1: Weight \* fatty liver Cross tabulation**

			Fatty liver		Total
			Present	Absent	
Weight	Normal weight	Count	11	11	22
		Expected Count	18.2	3.9	22.0
	Over weight	Count	70	22	92
		Expected Count	75.9	16.1	92.0
	Class I obesity	Count	84	2	86
		Expected Count	71.0	15.0	86.0
Total		Count	165	35	200
		Expected Count	165.0	35.0	200.0

Fatty liver disease was present in 165 patients and incidence of fatty liver was 50% in patients with normal weight, 76% of patient who were over-weight and 97% of patients with class I obesity and the difference in incidence was statistically significant. When duration of

diabetes was compared with presence or absence of fatty liver disease, it was found that Non-alcoholic fatty liver disease was present in 71% of patients with duration of disease between 1 to 4 years, 91% amongst patient with duration of diabetes between 5 to 8 years and 100% of patients with duration of diabetes between 9 to 12 years and results were statistically significant.

**Table No.2: No. of years\* fatty liver Cross tabulation**

			Fatty liver		Total
			Present	Absent	
No. of years	1 to 4 years	Count	69	28	97
		Expected Count	80.0	17.0	97.0
	5 to 8 years	Count	76	7	83
		Expected Count	68.5	14.5	83.0
	9 to 12 years	Count	20	0	20
		Expected Count	16.5	3.5	20.0
Total		Count	165	35	200
		Expected Count	165.0	35.0	200.0

**DISCUSSION**

Nonalcoholic fatty liver disease is a frequent disorder in which there is collection of fat in the liver cells in those who do not take much amount of alcohol. Injury to liver ranges from benign deposition of fat to steatohepatitis, advanced fibrosis and cirrhosis. It is more prevalent in patients who have insulin resistance due to overweight/obesity, type 2 diabetes mellitus (T2DM), dyslipidemia and the metabolic syndrome.<sup>8</sup> Insulin level in type 2 diabetes mellitus is either normal or increased but there is resistance to insulin action. This results in lipolysis, which result in fat deposition especially in patients in whom diabetes mellitus is not controlled. Free fatty acids are mobilized after lipolysis, which enter the liver cells and is, used for synthesis of triglycerides which results in deposition of fat in liver resulting in steatosis. Free fatty acids cause damage to cells and swelling of mitochondria, increase fragility of lysosomes, decrease in activity of enzymes, and integrity of membrane is impaired. The damage to cell resulting in inflammation ultimately causes cell death and fibrosis. Free fatty acids are increased in liver tissue of patients with obesity. so both diabetes mellitus and obesity cause increase in liver fibrosis through different mechanism however, their effect is increased when they both occur in the same person.<sup>9</sup> Our study has shown that frequency of nonalcoholic fatty liver disease was 82% in type II diabetes mellitus which was greater than the prevalence stated in normal population by shoba luxmi et al (60.8%)<sup>10</sup>, 55% in Saudi Arabia<sup>11</sup> and 49% in India<sup>12</sup>

Babusik P found that disparity in NAFLD prevalence among South Asians and Arabs residing in Kuwait was not significant. Factors predictive for developing liver steatosis are gender, history of diabetes mellitus and abdominal obesity delineate by waist circumference.<sup>13</sup> However, compared to non-Hispanics, subjects from Central American heritage were over three times as likely to have NAFLD compared to non-Hispanics.<sup>14</sup> Subjects with low physical activity levels were at increased risk for NAFLD (aOR = 4.52, 95% CI, 1.21-16.82) as compared to more active counterparts. When income was compared Families in whom income was low were twice as likely to have NAFLD then families with higher income<sup>15</sup>.

Shoba luxmi et al also showed that BMI was 30 in patients who have fatty liver disease and 23 in patients without fatty liver. Also level of HBA1c, liver enzymes, total cholesterol, triglycerides (TG), low-density lipoprotein (LDL) were high and HDL was low in patients with fatty liver disease as compared to patient without fatty liver disease<sup>10</sup>.

In our study 10% of patients with diabetes mellitus have normal BMI, 44% were overweight and 41% have class I obesity while none have class II or class III obesity. Incidence of fatty liver was 50% in patients with normal weight, 76% in patient who were overweight and 97% in patients with class I obesity.

Cazzo E, et al compared the histological changes in patients with obesity who are either diabetic or non-diabetic who had Roux-en-Y gastric bypass. Obese Non-diabetics have less histological abnormalities, regarding steatosis, fibrosis as compared to obese diabetics who have increased frequency of moderate forms of steatosis and fibrosis.<sup>15</sup>

Ostovaneh MR, et al found that NAFLD is strongly related to central obesity as compared to increase BMI. 22.1% of patients with BMI < 30 had NAFLD<sup>16</sup> which is less than our patients with Diabetes mellitus in whom incidence of fatty liver was 50% in patients with normal weight, 76% in patient who were over-weight.

BMI and waist circumference was low in patients with lean-NAFLD but visceral adiposity index was high as compared to overweight-obese controls. Level of TG, total cholesterol and LDL was high in Lean-NAFLD, a finding similar to overweight-obese NAFLD patients.<sup>17</sup> Factors associated with NAFLD in non-obese but overweight Asia-Pacific subjects are differential distribution of visceral adipose tissue, recent weight gain, diet high in cholesterol and genetic susceptibility. Also resistance to insulin may be an important mechanism. Since NAFLD is the manifestation of metabolic syndrome in liver, it predicts the future development of type 2 diabetes, metabolic syndrome and cardiovascular disease.<sup>18</sup>

Similarly Du T et al found that presence of NAFLD may prone the study population to develop diabetes without other metabolic risk factors. These features like

obesity, hypertension, hyperlipidemia and NAFLD are common in diabetic population and significantly increase the risk of developing diabetes,<sup>19</sup> While transient remission of NAFLD significantly decreased the risk of developing T2DM.<sup>20,21</sup>

When relation of duration of diabetes was compared with development of fatty liver disease, it was found that fatty liver disease was present in 71% of patients with duration of disease between 1 to 4 years, 91% amongst patient with duration of diabetes between 5 to 8 years and 100 % of patients with duration of diabetes between 9 to 12 years.

One of limitation of our study was that the ultrasonography was used for the diagnosis of NAFLD but it could not be confirmed by liver biopsy. However, in clinical practice ultrasonography is commonly used for diagnosis of NAFLD and can identify steatosis

## CONCLUSION

Frequency of NAFLD is high in type 2 diabetic patients who are obese as compared to patients who are non-obese weight reduction will result in decrease in incidence of fatty liver disease in diabetes mellitus. Also its frequency increases with increase in duration of diabetes mellitus.

### Author's Contribution:

Concept & Design of Study:	Kausar Malik, Shazia Siddiq
Drafting:	Shazia Siddiq, Faiza Batool
Data Analysis:	Kausar Malik
Revisiting Critically:	Faiza Btool, Shazia Siddiq
Final Approval of version:	Faiza Batool

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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