

# Trend of Non-Alcoholic Fatty Liver Disease in Type II Diabetes Mellitus

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## ABSTRACT

**Background:** Non-alcoholic fatty liver disease (NAFLD) is becoming quite common in Type II Diabetes Mellitus (TIIDM) as obesity and insulin resistance are common within TIIDM and it is becoming a widespread liver condition globally. This study evaluated the prevalence of NAFLD patients who also had type II diabetes.

**Methods:** The demographic data (name, age, body mass index (BMI), gender, occupation, duration of TIIDM, and treatment taking for TIIDM), as well as the results of the tests for these enzymes, were also recorded. Alanine transaminase (ALT) and Aspartate transaminase (AST) levels, as well as abdominal ultrasound findings of the liver, were recorded in a proforma after informed consent for a total of 200 Type II diabetic patients. Using SPSS, the data were analyzed, and stratified groups were subjected to the Chi-square tests.

**Results:** There was a significant difference ( $p < 0.05$ ) observed in NAFLD patients of TIIDM concerning age, gender, BMI, treatment, occupation, and duration of diabetes. The sample size consisted of 200 patients of which 111 (55.5%) were men and 89 (44.5%) were women. Patients ranged in the age range of 40-70 years old, with a mean age of  $55.08 \pm 8.98$  years and a mean BMI of  $29.69 \pm 4.04$ , respectively. It was concluded that 64% of cases with diabetes mellitus had NAFLD.

**Conclusion:** TIIDM is an independent risk factor for NAFLD so early screening, diagnosis, and appropriate treatment are mandatory to reduce the risk of NAFLD and its related complications.

**Keywords:** Type II diabetes, Liver disease, NAFLD, Complications, Mortality.

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## INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) is quite common in Type II Diabetes mellitus (TIIDM) as obesity and insulin resistance are major causes of TIIDM<sup>1</sup>. The hepatic component of metabolic syndrome is thought of as NAFLD. With a median frequency of roughly 20% in the general population and 42%-70% in those with TIIDM, it is becoming a widespread liver condition globally<sup>2</sup>. NAFLD is defined as hepatic steatosis with no secondary cause in steatosis and either proton density or fat fraction of more than  $\geq 5.6\%$  determined with quantitative fat/water selective proton magnetic resonance spectroscopy (MRS) or magnetic resonance imaging (MRI), or with histology and macrovesicular steatosis imaging with  $\geq 5\%$  of hepatocytes<sup>3</sup>. Simple steatosis and non-alcoholic steatohepatitis that cause cirrhosis and such consequences make up NAFLD<sup>4</sup>.

Clinical, laboratory, and imaging investigations are used to identify non-alcoholic fatty liver disease. MRS is now the most trustworthy imaging method for hepatic fat steatosis<sup>5</sup>. The American Diabetes Association (ADA) recommended performing an ultrasonography (US) examination on patients with type II pre-diabetes or diabetes who showed increased NAFL or alanine aminotransferase (ALT) to check liver fibrosis and NASH. The ADA recommendations advise employing noninvasive biomarkers and vibration-controlled transient elastography (VCTE) in risk classification<sup>6</sup>. Insulin resistance is closely associated with the condition. The primary causes of hepatic insulin resistance in NAFLD are thought to be hepatic inflammation and fat buildup<sup>7</sup>. NAFLD is regarded as a separate risk factor in TIIDM, severe liver disease, and cardiovascular disease. It is crucial to spot early metabolic changes to stop these diseases and their progression<sup>8</sup>.

In a Pakistani study, patients with TIIDM reported a 51% frequency of hepatobiliary dysfunction<sup>9</sup>. NAFLD was reported with 60.8% occurrence with the time in diabetic individuals in a study and 55% of the time in TIIDM from Saudi Arabia<sup>10</sup>.

Foremost, we can initiate early proper management and prevent the patients from hazardous consequences of liver dysfunction or hepatic failure. It has been noticed that among patients of TIIDM, the frequency of NAFLD varies in different populations. Moreover, the variability was also observed in local studies. This study was conducted to estimate the prevalence of NAFLD in TIIDM patients in the local population.

## METHODS

A cross-sectional study was done at Medical Unit 2 of Sir Ganga Ram Hospital in Lahore from January 29 to July 29, 2020, and ethical approval was obtained from the institution review board with reference number CPSP/REU/MED-2017-059-13448. A 200-sample size of patients was estimated with confidence

level (95%), margin of error (5%), and predicted percentage of NAFLD such as  $\geq 51\%$  in siblings of TIIDM patients using consecutive sampling technique and non-probability methods<sup>11</sup>. Patients in the age range of 40-70 were chosen who met the inclusion criteria and had type II diabetes (HbA1c $>6.5\%$  and/or on treatment for diabetes or symptoms of hyperglycemia and random blood sugar level (BSL) $>200\text{mg/dL}$  for more than 1 year). Patients with positive HBsAg, positive Anti-HCV antibodies, chronic liver disease before diabetes, or taking medicine for hepatic dysfunction including interferon therapy (on medical record), and those leading to hepatic dysfunction were omitted from the study.

After receiving informed consent, demographic information (name, occupation, gender, BMI, age, number of years with TIIDM, and medications used to treat it) was recorded. A 5cc disposable syringe was then used to draw blood, which was then forwarded to the hospital laboratory for AST and ALT testing. With the help of a researcher, a consultant radiologist with four years of residency experience performed ultrasonography on patients to assess fatty liver. NAFLD was labeled on the evidence of excessive fat on the liver on abdominal ultrasound with or without AST and ALT  $>40\text{IU}$  in the absence of alcohol intake. Patients with NAFLD were managed as per hospital protocol. All this information was recorded in a pre-designed performa<sup>12</sup>. The Statistical software (SPSS 20) was used to analyze the current data. The age, BMI, and length of patient TIIDM were quantitative factors that were provided as mean and standard deviation. Gender, occupation, and the frequency and proportion of TIIDM and hepatobiliary dysfunction therapy use were qualitative variables. The TIIDM was calculated using a two-stage, stratified, random sampling technique. The chi-square test was used as post-stratification to compare NAFLD in stratified groups, with significance consideration at  $p\text{-value}<0.05$ .

## RESULTS

The sample size consisted of 200 patients of which 111 (55.5%) were men and 89 (44.5%) were women. The mean age mentioned here was calculated with the mean of the age groups from 40 to 70 years and BMI was the mean of the age group between 40 to 70 years with their respective NAFLD presences. Thus, patients ranged in the age range of 40-70 years old, with a mean age of  $58.8 \pm 8.9$  years and a mean BMI of  $29.69 \pm 4.04$ , respectively. A significant difference was observed within each group concerning NAFLD (absent/present) ( $p<0.05$ ). Thus, results showed that the age group of 40-54 years showed NAFLD presence ( $58.8 \pm 8.9$ ), and thus the remaining NAFLD absent accounted for  $41.2 \pm 0.12$  population in the same age group while the age group of 55-70 years showed NAFLD presence of  $8.9 \pm 5.45$  and absent in  $31.1 \pm 0.14$  population and same results for all groups are shown in Table 1.

**Table 1: Basic characteristics of study groups depending on NAFLD.**

Parameters	Patients with NAFLD	Patients without NAFLD	p-value
Age (Mean±S.D)	58.8±8.9	41.2±0.12	0.402
Gender n (%)			
Male	49 (38%)	62 (62%)	0.415
Female	81 (62%)	8 (38%)	
BMI (kg/m <sup>2</sup> ) (Mean±S.D)			
Obese	29.69±4.04	34.8±0.23	0.000
Non-Obese	63.1±0.19	56.9±0.16	
Treatment (Mean±S.D)			
Oral	11.7±0.31	6.76±0.27	0.004
Insulin	9.95±0.33	8.13±0.24	
Occupation n (%)			
Office worker	45 (60.81%)	89 (70.63%)	0.003
Manual worker	17 (22.98%)	32 (25.40%)	
Other occupation	12 (16.21%)	5 (3.97%)	
TIIDM	19.42 (12.35-20.43)	8.67 (7.03-10.89)	<0.0001

Descriptive statistics implemented on different parameters; BMI= body mass index; TIIDM= Type II diabetes mellitus  
p-value <0.05 is considered significant.

These cases had a mean duration of TIIDM ranging from 8.67 to 19.42 in most prevalence situations. There were 62(31.0%) working men and women, 72(36.0%) were Govt. Employed, 49 (24.5%) were doing their own business and 17(8.5%) cases had other work occupations. In 107 instances (53.5%), insulin therapy was used, while oral medication was used in 93 cases (46.5%). A total of 128(64%) cases had non-alcoholic fatty liver disease.

The mean patient age in the current study was 55.08±8.98 years. There were 89 (44.5% of the cases)

females and 111 (55.5%) males. In the TIIDM study, 130 instances comprised 81 (62%) females and 49 (38%) males. The patients were 52.31±5.96 years old on average. In the present study, there are differences in the distribution of gender and age. Out of 130 type II diabetes patients, results showed that 78 (60%) had fatty livers. NAFLD was evaluated according to its presence or absence within different age groups. The table shows the age at which NAFLD would be present or absent with the passage of age (Table 2).

**Table 2: Comparison of NAFLD within age groups concerning gender, BMI, treatment, occupation, and duration of TIIDM**

Gender	NAFLD	Age-groups		Total	p-value
		40 – 54	55 – 70		
Male	Present	52 (61.90%)	10 (37.03%)	62 (55.86%)	0.423
	Absent	32 (38.10%)	17 (62.97%)	49 (44.14%)	
	Total	84 (75.68%)	27 (24.32%)	111	
Female	Present	34 (64.15%)	17 (47.22%)	51 (57.30%)	0.404
	Absent	19 (35.85%)	19 (52.78%)	38 (42.70%)	
	Total	53 (59.55%)	36 (40.45%)	89	
BMI	NAFLD	Age-groups		Total	p-value
		40 – 54	55 – 70		
Obese	Present	44 (81.49%)	24 (80%)	68 (80.95%)	<0.0001
	Absent	10 (18.51%)	6 (20%)	16 (19.05%)	
	Total	54 (64.29%)	30 (35.71%)	84	
Non-obese	Present	17 (24.64%)	28 (59.58%)	45 (38.79%)	<0.0001
	Absent	52 (75.36%)	19 (40.42%)	71 (61.21%)	
	Total	69 (59.49%)	47 (40.51%)	116	

Treatment	NAFLD	Age- groups		Total	p-value	
		40 – 54	55 – 70			
Oral	Present	28 (40.58%)	17 (70.83%)	45 (48.39%)	0.004	
	Absent	41 (59.42%)	7 (29.17%)	48 (51.61%)		
	Total	69 (74.19%)	24 (25.81%)	93		
Insulin	Present	26 (44.83%)	22 (44.90%)	48 (44.86%)	0.002	
	Absent	32 (55.17%)	27 (55.10%)	59 (55.14%)		
	Total	58 (54.20%)	49 (45.80%)	107		
Occupation	NAFLD	Age- groups		Total	p-value	
Office worker	Present	40 – 54	40 – 54	45 (33.58%)	0.001	
		34 (43.04%)	11 (20%)			
		Absent	44 (80%)			89 (66.42%)
Manual worker	Present	79 (58.95%)	55 (41.05%)	134	0.005	
		Absent	7 (46.67%)	17 (34.70%)		
		24 (70.59%)	8 (53.33%)	32 (65.30%)		
Other Occupation	Present	34 (69.39%)	15 (30.61%)	49	0.046	
		Absent	4 (66.67%)	12 (70.59%)		
		3 (27.28%)	2 (33.33%)	5 (29.41%)		
TIIDM duration	NAFLD	Age- groups		Total	p-value	
		40 – 54	40 – 54			
		44 (53.01%)	34 (72.34%)			78 (60%)
TIIDM	Absent	39 (46.99%)	13 (27.66%)	52 (40%)		
		Total	83 (63.85%)	47 (36.15%)		130

Descriptive statistics was implemented on different parameters concerning frequency and %age [n (%)].

BMI= body mass index; TIIDM= Type II diabetes mellitus

## DISCUSSION

The most prevalent NAFLD and liver illnesses are becoming global public health concern<sup>13</sup>. The NAFLD (steatosis hepatic and NAFL) and steatohepatitis (NASH), which are both characterized by fibrosis, hepatocyte lobular inflammation, and ballooning may proceed with cirrhosis and, in rare cases, hepatocellular carcinoma<sup>14</sup>.

Diabetes and NAFLD development are both correlated risk factors for obesity and physical inactivity. According to several studies, the prevalence of NAFLD in people with TIIDM ranges roughly between 34 and 94%<sup>15</sup>. If a person has NAFLD, their chance of acquiring diabetes is about five times higher. The insulin resistance, hepatic triglyceride (TG) dyslipidemia factors buildup in NAFLD and a faulty B-cell in TIIDM may all contribute to the link between NAFLD and type II diabetes<sup>16</sup>. Patients with TIIDM showed a higher chance of advanced liver disease development, such as hepatocellular carcinoma, fibrosis, and cirrhosis as compared to healthy

people<sup>17</sup>. The role of diabetologists is crucial in identifying type II diabetes patients with higher NAFLD complications. But, thanks to recent advancements in the diagnosis of NAFLD and various phase III trials for NASH-specific therapies, an evolved caring plan is initiated for integrated multi-disciplinary controls in such matters<sup>18</sup>.

The NAFLD prevalence in type II diabetes patients and its relationship to the resistance of insulin were assessed in 2017, and it was found that 45% of patients with NAFLD showed higher rates leading to central obesity (as determined by waist-hip ratio, BMI, and waist circumference), higher triglyceride and HbA1c levels<sup>19</sup>. As a result, among TIIDM patients, insulin resistance and the occurrence of NAFLD appear to be associated<sup>20</sup>. Higher NAFLD statistics were discovered in the current investigation, however, BMI had no significant effect.

This study compromised the results in agreement with a cross-sectional study that evaluated NAFLD

prevalence and identified predictive factors related to NAFLD among South Asian Pakistani patients with Metabolic Syndrome (MS) and type II DM. The prevalence of NAFLD overall was 72.4%, and it was greater in patients with dyslipidemia, obesity, and HTN<sup>21</sup>. While higher values were observed among males than females. In this group, people with type II diabetes and metabolic syndrome, NAFLD prevalence was higher. Additionally, it was discovered that the growing MS components were linked with larger NAFLD risks, in addition to the fact that NAFLD was highly connected with MS<sup>22</sup>.

Similar to one previous study, this study established NAFLD prevalence and pinpointed risk factors in type II DM patients with NAFLD. In NAFLD individuals with Type II DM, obesity and high liver enzymes, triglycerides, and cholesterol are considerably elevated. It emphasizes the significance of routine lipid profiles and liver function testing in individuals with type II diabetes, who must be closely monitored for liver consequences and NAFLD<sup>23</sup>.

Another local study was utilized to ascertain NAFLD prevalence in type II diabetes patients present at Jinnah Postgraduate Medical Centre, Karachi, Pakistan. The study had 120 participants with type II diabetes in total. They were split into two groups, one with fatty livers and the other without, and further assessed using measurements of liver function tests, body mass index, lipid profile, and HbA1c. On ultrasonography, 73 (60.8%) of the 120 patients had fatty liver<sup>24</sup>. While, in comparison with non-fatty liver groups, the fatty liver group showed higher levels of HbA1c, BMI, AST, GGT, alkaline phosphatase, LDL, ALT, triglycerides, total cholesterol, and decline of HDL levels<sup>25</sup>.

Although this study showed a higher NAFLD prevalence in type II DM patients, lack of early screening, available resources for non-invasive investigations, and the cost of diagnostic scanning are the main limitations for proper diagnosis and management of these patients. Therefore, the author would recommend carrying out a multicenter study with a large sample size for more accurate results.

### CONCLUSION

NAFLD was present in 64% of cases with type II diabetes mellitus. Early detection, diagnosis, and treatment are essential to lower the risk of NAFLD and the consequences linked to it. Mortality and morbidity among type II diabetic individuals can be greatly decreased by lowering NAFLD. Future research advancements in the diagnosis of NAFLD and various phase III trials for NASH-specific therapies will evolve the caring plan with initiation for integrated multidisciplinary controls in diabetes mellitus.

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### CONFLICT OF INTEREST

The author declares that there is no conflict of interest for the publication of this manuscript.

### ETHICAL APPROVAL

Ethical Approval was obtained from the institution review board with reference number CPSP/REU/MED-2017-059-13448.

### PATIENT CONSENT

Informed consent was taken from the patients for the collection of data and publication of results.

### AUTHORS CONTRIBUTION

Each other has contributed to the manuscript equally and approved for submission of the manuscript.

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