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**ORIGINAL ARTICLE**

# Nonalcoholic Fatty Liver Diseases in Newly Analyzed Diabetes Mellitus Patients with Risk Factors

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## ABSTRACT

**Aim:** NAFLD is becoming more common among Asians, as is type-II DM & obesity both of which are connected to fatty liver disease. The goal of the research was to govern the pervasiveness of NAFLD in T2DM patients, as well as their risk factors, in Pakistani population.

**Materials and Methods:** This cross-sectional study was held in the medicine department of Islam Medical and Dental College Sialkot for one-year duration from January 2021 to December 2021. This research included adult individuals who had been diagnosed with T2DM during the previous six months. Ultrasound of the liver was used to detect NAFLD. Measurements that were clinically and biochemically important were completed.

**Results:** NAFLD was detected in 124 T2DM individuals out of a total of 160. (77.5 percent). According to multivariable analysis, NAFLD is associated with dyslipidemia (95 percent, p = 0.035), higher LDL (OR 1.02, p = 0.003), HbA1c (OR1.27, p = 0.045), and diastolic blood pressure (OR 1.05, Hypertension, dyslipidemia, waist circumference, BMI, triglycerides, lack of physical activity, reduced LDL, HDL, ALT and HbA1c all had a combined risk of 11.2 for NAFLD.

**Conclusion:** Numerous lifestyle-related factors have been investigated in connection to a high incidence of NAFLD. It assesses risk factor values to demonstrate the need for NAFLD screening in newly diagnosed DM patients in Pakistan.

**Keywords:** diabetes, risk factors, non-alcoholic fatty liver disease and obesity

## INTRODUCTION

Nonalcoholic fatty liver disease, is growing progressively across the world, and particularly in Asia[1-2]. Several systemic diseases, including colorectal cancer, cardiovascular disease, and metabolic problems, have been linked to these pathological processes. Based on available statistics, it seems that around 5–20 percent of the population in Asia may be affected by NAFLD, however the prevalence varies significantly depending on region, gender, race, and age[3-4]. In addition, the absence of symptoms & health alarms in most NAFLD patients makes diagnosis and treatment more challenging[5-6].

Patients with NAFLD have been reported to have obesity, hypertension, and dyslipidemia, but type 2 diabetes (T2DM) is the most serious metabolic complication linked with this illness[7-8]. T2DM has been shown to be highly related with NAFLD, whether it is present in isolation or in conjunction with the metabolic syndrome. This is due to the emergence of insulin resistance. Furthermore, when T2DM and NAFLD are present together, greater rates of mortality due to liver disease, overall mortality and mortality linked to cardiovascular disease have all been described[9]. In Asian nations, the prevalence of these variables and co-factors is increasing. A genetic predisposition to insulin resistance even in the absence of obesity may be the cause of this disparity in body composition between Asians & Caucasians[10].

Although Pakistan has minimal information in this area, where frequent screening & monitoring of diabetes in individuals with nonalcoholic fatty liver disease is not widespread, other nations have some information. As a result, the vast majority of people with NAFLD do not get treatment. Pakistan's population would likely suffer from increased disease burden as a result of a lack of understanding about the illness, its accompanying disorders, and the danger of developing probable consequences from NAFLD[11]. The aim of this analysis is to find out the frequency of NAFLD disease among Pakistani people with type 2 diabetes. We also wanted to figure out what variables were related with NAFLD in the first place. Information regarding the disease burden among diabetics will be made available, and the idea of primary prevention and intervention at an early stage will be promoted. Furthermore, this may serve as a basis for future interventional initiatives in the treatment of NAFLD, with the goal of reducing the incidence of NAFLD-related comorbidities.

## METHOD AND MATERIALS

This cross-sectional study was held in the medicine department of Islam Medical and Dental College Sialkot for one-year duration from January 2021 to December 2021. After getting informed agreement, the study included consecutive adult patients who had been identified with type-II DDM during the last six-months. 160 total subjects were selected for the study.

To evaluate laboratory parameters, blood tests were conducted, and an ultrasound was achieved to govern the existence of fatty liver disease. The height and weight of the participants were assessed, and their BMI was computed as well. Persons with a BMI between 23 and 25 kg/m2 were classed as overweight, while those with a BMI more than 25 were classified as obese, according to WHO criteria for the Asian population. The waist-to-hip ratio was computed using the subjects' waist and hip circumferences. According to the WHO, diabetes is definite as having a fasting plasma glucose level of 126 mg/dL or a two-hour post-load plasma glucose level of 200 mg/dL.

All patients had their lipid profile, fasting blood sugar, hemoglobin A1c levels and alanine aminotransferase checked. Anti-HBsAg, anti-HCV, ceruloplasmin, antinuclear, anti-smooth muscle, and antimitochondrial antibodies were utilized to rule out other underlying liver illnesses (AMA). One expert sonographer did all ultrasounds, unaware of the other study participants' personal information. Hepatic echotexture was better as compared to renal echotexture. Vascular blurring and hepatic vein constriction were seen on ultrasonography. It was also evaluated for fine diffuse hyper-echogenicity (grade I mild steatosis) and moderate yet diffuse hyper-echogenicity (grade II mild steatosis) (moderate steatosis). The liver was classified as having grade III when the diaphragm and posterior right lobe were not visible (severe steatosis). 19

The data was analyzed with the use of SPSS 19.0. When dealing with quantitative data, the mean standard deviation was designed, and when dealing with categorical data, the proportions were calculated. For comparison analysis, the student t-test, the Fisher exact test and Pearson Chi-square test were employed

where it was acceptable. Researchers used multivariate and univariate logistic regression analysis to recognize risk variable quantity for NAFLD. With the use of binary logistic analysis, it was possible to evaluate the multiplicative impact of mixing a large number of risks.

## RESULTS

A total of 160 subjects were selected for the study. The patients clinical characteristics are summarized in Table 1. High fasting & random blood glucose levels, as well as a higher HBA1c & lower HDL, were seen in the majority of them.

Table 1: Clinicopathological and Demographic features of patients at baseline and patients comparison with and deprived of NAFLD

| | All patients (n = 160) | Comparison | | |
|---|---|---|---|---|
| | | Without NAFLD (n = 36) (group A) | With NAFLD (n = 124) (group B) | p value |
| Age (years) | 53.20 ± 8.66 | 51.68 ± 6.53 | 52.44 ± 9.63 | 0.89 |
| Gender<br>Male | 98 (61.3) | 22 (61.1) | 65 (52.4) | 0.62 |
| Female | 62 (38.7) | 14 (38.9) | 59 (47.6) | |
| Physical activity<br>Yes | 89 (55.6) | 26 (72.2) | 39 (31.5) | <0.0001 |
| No | 71 (44.4) | 10 (27.8) | 85 (68.5) | |
| HTN<br>No | 35 (21.9) | 20 (55.6) | 42 (33.9) | 0.01 |
| Yes | 125 (78.1) | 16 (44.4) | 82 (66.1) | |
| Dyslipidaemia<br>No | 33 (20.6) | 18 (50) | 29 (23.4) | 0.002 |
| Yes | 127 (79.4) | 18 (50) | 95 (76.6) | |
| Systolic BP (mm Hg) | 130.60 ± 15.10 | 124.87 ± 17.98 | 132.10 ± 15.1 | <0.0001 |
| Diastolic BP (mm Hg) | 82.15 ± 10.22 | 77.00 ± 8.66 | 82.98 ± 12.39 | <0.0001 |
| Waist circumference (cm) | 95.80 ± 16.40 | 90.99 ± 14.07 | 97.22 ± 14.88 | 0.001 |
| Hip circumference (cm) | 101.29 ± 15.49 | 94.89 ±11.96 | 102.99 ± 12.60 | <0.0001 |
| Waist to hip ratio | 0.95 ± 0.05 | 0.96 ± 0.04 | 0.93 ± 0.08 | 0.30 |
| BMI categories (kg/m$^2$)<br>18–22.9 | 10 (6.3) | 4 (11.1) | 10 (8.1) | <0.0001 |
| 23–24.9 | 20 (12.5) | 12 (33.3) | 23 (18.5) | |
| ≥25 | 130 (81.2) | 20 (55.6) | 91 (73.4) | |
| FBS (mg/dL) | 146.11 ± 50.11 | 132.11 ± 42.98 | 150.56 ± 52.29 | 0.01 |
| RBS (mg/dL) | 209.89 ± 80.20 | 189.40 ± 64.10 | 220.22 ± 81.20 | 0.008 |
| HBA1c | 7.90 ± 1.60 | 7.30 ± 1.30 | 8.17 ± 1.70 | 0.001 |
| Total cholesterol (mg/dL) | 170.89 ± 42.50 | 160.11 ± 41.64 | 175.14 ± 46.45 | 0.01 |
| Triglycerides (mg/dL) | 184.50 ± 98.19 | 150.99 ± 76.64 | 201.49 ± 105.10 | 0.001 |
| HDL (mg/dL) | 39.93 ± 8.90 | 41.91 ± 7.99 | 38.10 ± 8.66 | <0.0001 |
| LDL (mg/dL) | 115.66 ± 31.69 | 90.88 ± 31.99 | 118.22 ± 36.99 | <0.0001 |
| Alanine transaminase (IU/L) | 26 ± 16.55 (range 8–160) | 22.52 ± 14.60 | 29.71 ± 16.94 | 0.01 |
| ALT categories<br>Normal | 142 (88.8%) | 30 (83.3) | 98 (79.1) | 0.01 |
| Elevated | 18(11.2%) | 6 (16.7) | 26 (20.9) | |

NAFLD was discovered in 124 (77.5%) of the cases, with Grade I, II, and III NAFLD in 64 (51.6%), 43 (34.7%), and 17 (13.7%) of the patients, respectively. Only four patients accepted the offer of a liver biopsy to confirm the diagnosis. In three cases, the liver biopsy revealed Grade II NAFLD, and in one case, the biopsy revealed NASH. In addition, two groups of patients were compared: those who did not have NAFLD (group A) and those who did have NAFLD (group B) (group B).

The findings of the univariate analysis, which are shown in Table 2, indicate that there is a relationship between numerous lifestyle-related factors and NAFLD.

Table 2: Univariate analysis for factors related with NAFLD in in recently identified type-II DM patients

| | OR (95% CI) | p value |
|---|---|---|
| Age in years | 0.98 (0.95–1.01) | 0.98 |
| Gender<br>Female | 1.0 | |
| Male | 1.20 (0.61–2.19) | 0.56 |
| Physical activity<br>No | 1.0 | |
| Yes | 0.22 (2.09–7.90) | <0.0001 |
| Hypertension<br>No | 1.0 | |
| Yes | 2.30 (1.20–4.18) | 0.02 |
| Dyslipidaemia<br>No | 1.0 | |
| Yes | 2.84 (1.50–5.80) | 0.001 |
| Systolic Blood Pressure (mm Hg) | 1.10 (1.08–1.15) | 0.001 |
| Diastolic Blood Pressure (mm Hg) | 1.05 (1.01–1.09) | <0.0001 |
| Waist perimeter in cm | 1.05 (1.02–1.07) | 0.002 |
| Hip perimeter in cm | 1.04 (1.02–1.10) | <0.0001 |
| Waist to hip ratio | 0.05 (0.00–7.01) | 0.21 |
| BMI categories (kg/m$^2$)<br>18–22.9 | 1.0 | |
| 23–24.9 | 0.39 (0.09–1.70) | 0.22 |
| ≥25 | 2.24 (0.69–7.65) | 0.17 |
| Fasting blood sugar (mg/dL) | 1.03 (1.02–1.08) | 0.02 |
| Random blood sugar (mg/dL) | 1.02 (1.02–1.03) | 0.01 |
| HBA1c | 1.49 (1.20–1.88) | 0.001 |
| Total cholesterol (mg/dL) | 1.04 (1.02–1.09) | 0.01 |
| TGs (mg/dL) | 1.02 (1.01–1.06) | 0.001 |
| High density lipoprotein (mg/dL) | 0.91 (0.92–0.98) | <0.0001 |
| Low density lipoprotein (mg/dL) | 1.01 (1.00–1.02) | <0.0001 |
| ALT (IU/L) | 1.06 (1.07–1.09) | 0.01 |
| ALT categories<br>Regular | 1.0 | |
| Raised | 5.39 (1.18–22.70) | 0.02 |

Table 3: Multivariate analysis for factors related with NAFLD in recently identified type-II DM patients

| | OR (95% CI) | p value |
|---|---|---|
| Physical activity | 0.21 (0.11–0.49) | <0.0001 |
| Low density lipoprotein (mg/dL) | 1.10 (1.12–1.15) | 0.004 |
| High density lipoprotein (mg/dL) | 0.89 (0.90–0.97) | <0.0001 |
| Dyslipidaemia | 2.40 (1.15–6.14) | 0.034 |
| Diastolic Blood Pressure (mm Hg) | 1.02 (1.03–1.12) | 0.008 |
| HbA1c | 1.30 (0.98–1.70) | 0.044 |

According to a univariate research, physical activity and raised High density lipoprotein cholesterol levels were shown to be shielding factors against NAFLD. The outcomes of multivariate

analysis revealed that dyslipidemia, increased LDL HbA1c, and diastolic blood pressure are all variables that are significantly linked with NAFLD, as indicated in Table 3.

Physical exercise and a greater level of it were shown to be defending factors against NAFLD. With an growing numeral of risk variables, a growing trend in the probabilities of developing NAFLD was identified.

## DISCUSSION

According to ultrasonography criteria, about 77.5 percent of our diabetic patients had NAFLD at the time of their first diabetes diagnosis[11-12]. According to this article, a high pervasiveness of NAFLD in individuals with recently identified diabetes has been documented; however, a decisive statement cannot be made at this time since the frequency of NAFLD may vary significantly based on a variety of factors such as age and gender. Among the general population in South-East Asia, the total prevalence of NAFLD ranges from 9 percent to 45 percent, and among diabetic patients, it ranges from 6–62 percent[13]. Even greater incidence of NAFLD has been documented in individuals with diabetes in South Asian nations (India 31–92 percent and Sri Lanka 56 percent). Though, this is the first research from Pakistan to address this problem in a systematic manner, and it is the first of its kind in the world[14]. This research employed ultrasonography to identify NAFLD, which is regarded a reasonable first-line screening tool for NAFLD in a larger population of patients when the acceptance rate for liver biopsy would be low, as shown in previous studies[15-16]. Despite the fact that it is a cost-efficient and readily accessible diagnostic technique that is regularly employed in clinical practice, its vintage is inferior in CLD and obese patients, and it is less effective overall.

However, liver biopsy might offer more solid information on NAFLD, and owing to the invasive nature of this procedure, it was not possible to do one in this research. It is mostly used when it is necessary to stage fibrosis, monitor disease progression, and assess the effectiveness of treatment[17]. The patient's percentage with NAFLD who had hypertension, obesity, a larger waist circumference, and a larger hip circumference was considerably greater than the proportion of patients without NAFLD. Kalra et al. from India have reported results that are similar to theirs. In our research, we discovered that those with NAFLD had higher levels of fasting and random blood glucose, as well as LDL and HbA1c[18]. This was consistent with the relationship between parameters associated with metabolic syndrome and diabetes. Since HbA1c is a well-established biomarker for uncontrolled diabetes, it is possible to explain the relationship between HbA1c and NAFLD. A number of biochemical indicators were found to be higher in diabetic individuals with NAFLD (levels of ALT)[19]. If the ALT level is increased, it is regarded as a surrogate/marker for hepatic inflammation and, as a result, as an indirect indicator of NASH[20-21].

These conclusions were in agreement with information gathered from Indian sources. Several blood parameters were shown to be strongly linked with NAFLD in our investigation, which was conducted using multivariate analysis. Recent research from Sri Lanka found a similar link between NAFLD and diastolic blood pressure, as well as the association between NAFLD and obesity. In accordance with earlier research, daily exercise was shown to be a protective factor[22-23]. In our investigation, we discovered a significant discovery linked to the combined impact of numerous risk variables, which had not been assessed in the majority of previous studies.

## CONCLUSION

It has become more important to screen for NAFLD in diabetic patients since the majority of them are treated by endocrinologists or medical physicians, and it has been discovered that these specialists only check for diabetic retinopathy, neuropathy, and nephropathy in diabetic patients. The significant prevalence of NAFLD in individuals with diabetes was shown in our investigation. In order to raise knowledge of the link between NAFLD and diabetes among doctors and internists, it would be necessary to educate them on the subject. Early identification and good counselling of patients will aid in the prevention of long-term consequences related with NAFLD, as well as the reduction of the disease's burden.

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