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Original Research Article

A Study of Prevalence of Non-Alcoholic Fatty Liver Disease in Chronic Diabetes Mellitus Type 2 Patients

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Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is a prevalent condition among those suffering from type 2 diabetes. It has been shown that up to 75% of these patients exhibit signs of liver fat when assessed through ultrasound imaging. This correlation underscores the intricate relationship between type 2 diabetes and liver health. The present study was conducted to determine the prevalence of NAFLD in cases of chronic diabetes mellitus.

Methods: We analyzed 80 patients with type 2 diabetes at Govt Medical College and Hospital, Jagtial, Telangana excluding those with pre-existing liver disease or alcohol intake. Using ultrasound, we identified those with NAFLD and categorized them into "fatty liver" and "non-fatty liver" groups. Further evaluation included body mass index, central obesity, HbA1c, and lipid profile and the correlation between NAFLD existence and duration of diabetes mellitus was analyzed. Data analysis was performed using SPSS version 20.0.

Results: The present study shows 63.75% of T2DM patients in the study had NAFLD, highlighting its significant presence in this population. While younger age groups (30-39 and ≥70) showed lower prevalence, the highest was observed in the 50-59 age group. BMI and waist circumference: Both were significantly higher in patients with NAFLD, suggesting a strong association with obesity and central adiposity. Glycemic control: Patients with NAFLD had significantly higher fasting and post-prandial blood sugar levels, as well as HbA1c, indicating poorer glycemic control. Liver enzymes: Elevated AST, ALT, and GGT levels in NAFLD patients suggested liver injury, while the AST/ALT ratio pointed towards predominant fatty liver disease.

Conclusions: This study found Poorer glycemic control, as indicated by higher blood sugar and HbA1c, was associated with NAFLD presence. Elevated liver enzymes (AST, ALT, GGT) suggested liver injury in NAFLD patients, with the pattern pointing towards predominant fatty liver disease. NAFLD patients exhibited an unfavorable lipid profile characterized by high triglycerides, low HDL-C, and slightly elevated total and LDL cholesterol, increasing their cardiovascular risk. A positive correlation was observed between the duration of T2DM and NAFLD prevalence, suggesting longer diabetes duration increases NAFLD risk.

Keywords: Diabetes Mellitus type 2, Non-Alcoholic Fatty Liver Disease, Liver enzymes.

Introduction

Non-alcoholic fatty liver disease (NAFLD) refers to the accumulation of fat in the liver, progressing from simple steatosis to steatohepatitis, cirrhosis, and even hepatocellular carcinoma (HCC) in the absence of excessive alcohol consumption [1]. NAFLD is characterized by macrovesicular steatosis, with more than 5% of hepatocytes affected, in the absence of inflammation. The global prevalence of diabetes is on the rise and is projected to affect approximately 57 million adults in India by 2025 [2]. NAFLD has emerged as the leading cause of chronic liver disease and abnormal liver enzymes worldwide, affecting both adults and children across developed and developing nations [3]. It manifests as excessive fat accumulation in the liver parenchyma among individuals with no history of

alcohol abuse (defined as <20 g per day in men and <10 g per day in women) and in the absence of other identifiable causes of fat accumulation, such as viral hepatitis, autoimmune hepatitis, alpha-1 antitrypsin deficiency, or certain medications like corticosteroids and anti-tuberculosis therapy. NAFLD is closely associated with metabolic syndrome and is frequently observed in patients with impaired fasting glycemia and diabetes mellitus, indicating a bidirectional relationship between liver disease and diabetes [4].

Individuals with type 2 diabetes mellitus (T2DM) have a higher risk of developing NAFLD compared to non-diabetic individuals and are more prone to progressing to fibrosis and cirrhosis. The presence of NAFLD in T2DM patients may also contribute to an increased risk of cardiovascular disease [5]. T2DM significantly elevates the risk of liver-related mortality by up to 22-fold in individuals with NAFLD [6]. Diagnosis of NAFLD requires a high index of suspicion, especially in obese patients over the age of 45 with a history of diabetes mellitus, as they are at increased risk of developing cirrhosis [7]. Several studies have established NAFLD as a hepatic manifestation of metabolic syndrome, with peripheral insulin resistance, obesity, hypertension, hyperinsulinemia, and hypertriglyceridemia serving as predisposing factors [8]. The prevalence of NAFLD varies globally, ranging from 15% to 40% in Western countries and 9% to 40% in Asian countries. With the increasing incidence of diabetes mellitus, obesity, and insulin resistance in India over the past two decades, a corresponding rise in the prevalence of NAFLD is anticipated. However, data on the prevalence of NAFLD in India remains limited [1]. Several studies have reported a prevalence rate of NAFLD ranging from 9% to 32% in the general Indian population, with higher rates observed among obese and diabetic individuals [3-5]. The prevalence of NAFLD in T2DM is estimated to be between 12.5% and 87.5% in India [9]. This study aimed to determine the prevalence of NAFLD in T2DM and evaluate the associated risk factors for diabetic fatty liver.

Material and Methods

This cross-sectional study was conducted in the Department of General Medicine in co-ordination with the Departments of Radiology and Biochemistry. Institutional Ethical approval was obtained for the study. Written consent was obtained from all the participants in the study after explaining the nature of the study in the vernacular language. Those voluntarily willing to participate in the study were included. The sample selection was done by a convenient sampling method. During the duration of the study, a total of n=80 patients with type 2 diabetes mellitus aged between 30 – 70 years were included in the study.

Inclusion Criteria

1. Known Diabetics type 2
2. Aged 30 – 70 years
3. Males and females
4. Attending medical outpatient clinics
5. Voluntarily willing to participate in the study

Exclusion Criteria

1. Known hepatic diseases
2. Renal diseases
3. Undergone hepatic surgeries
4. Alcohol consumption
5. On hepatotoxic drugs

A structured questionnaire was administered to gather relevant information from the patients. Comprehensive history-taking and physical examinations were conducted for each patient. Anthropometric measurements including waist circumference, body mass index (BMI), and metabolic parameters such as fasting and postprandial blood sugar levels, glycosylated hemoglobin (HbA1c), serum uric acid, blood urea, serum creatinine, fasting lipid profile, serum bilirubin, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), and Alkaline phosphatase (ALP) were recorded. To assess fatty changes in the liver, all enrolled patients underwent ultrasonography, performed by a single experienced radiologist to minimize inter-observer variability, using a high-resolution B-mode ultrasonography system equipped with an electric linear transducer with a mid-frequency of 3-5 MHz. Fatty liver was diagnosed based on ultrasonographic findings consistent with a bright liver appearance, with blurring of the contrast between hepatic and renal parenchymal vessels and narrowing of the lumen of the hepatic vein, in the absence of features suggestive of chronic liver disease.

Obesity was defined as a BMI $\geq$ 25 kg/m^2, with a specific consideration for Asian populations due to differences in body fat distribution. Central obesity was determined based on waist circumference measurements (>80 cm in females and >90 cm in males). Patients were considered to have dyslipidemia if they met one of the following criteria: LDL-C >100 mg/dL, total cholesterol >200 mg/dL, triglycerides >150 mg/dL, or HDL-C <40 mg/dL in males and <50 mg/dL in females. Hypertension was diagnosed based on average systolic blood pressure ≥140 mmHg, average diastolic blood pressure ≥90 mmHg, or the use of antihypertensive medication. NAFLD was classified into three grades based on standard ultrasonographic criteria: Grade 1 (mild steatosis), Grade 2 (moderate steatosis), and Grade 3 (severe steatosis). The sensitivity and specificity of ultrasonography in detecting hepatic steatosis ranged from 60% to 94% and 84% to 95%, respectively. The hepatorenal sonographic index, calculated as the ratio of the

mean brightness level of the liver to that of the right kidney, was proposed as a measure of hepatic steatosis, with a cutoff value of 1.49 demonstrating high sensitivity (100%) and specificity (91%) for the diagnosis of steatosis > 5%.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), Pearson's Chi-Square Analysis test, and Fisher exact probability test. Mean and standard deviation were calculated for each variable, and comparisons were made between diabetic patients with and without fatty liver.

Results

Table 1 shows the distribution of patients with type 2 diabetes (T2D) across different age groups, categorized by the presence or absence of non-alcoholic fatty liver disease (NAFLD). *Overall prevalence:* 63.75% (51/80) of T2D patients in the study had NAFLD. 36.25% (29/80) of patients did not have NAFLD. *Age-specific prevalence:* The highest prevalence of NAFLD was observed in the 50-59 age group (47.5%), followed by 40-49 (18.75%) and 60-69 (18.75%) age groups. Younger age groups (30-39 and ≥70) had lower prevalence at 10.0% and 5.00%, respectively. *Distribution within age groups:* In most age groups, the number of patients with NAFLD was higher than those without NAFLD. The only exception was the ≥70 age group, where 3 patients had NAFLD, and 1 patient did not. The findings suggest a positive correlation between age and NAFLD prevalence in this T2D population. The highest prevalence occurred in middle-aged individuals (50-59 years). This aligns with existing research suggesting increased risk factors for NAFLD, such as declining metabolic function and body composition changes, with advancing age.

Table 1: Age distribution of NAFLD in T2D patients (N=80)

Age Group	*Frequency (%)*	*NAFLD Present*	*NAFLD Absent*
30- 39	8(10.0%)	2(2.5%)	6(7.5%)
40-49	15(18.75%)	9(11.25%)	6(7.5%)
50-59	38(47.5%)	21(26.25%)	17(21.25%)
60-69	15(18.75%)	10(12.5%)	5(6.25%)
≥70	4(5.00%)	3(3.75%)	1(12.5%)
Total	80(100%)	51(63.75)	29(36.25%)

Table 2 shows the distribution of patients with type 2 diabetes (T2DM) across genders, categorized by the presence or absence of non-alcoholic fatty liver disease (NAFLD). *Gender prevalence:* A slightly higher prevalence of NAFLD was observed in males (42.5%) compared to females (21.25%). However, the difference is not statistically significant based on the sample size provided. *Distribution within genders***:** More males had NAFLD (34) compared to females (17). Similarly, more males did not have NAFLD (19) compared to females (10). This data suggests that there is no significant gender difference in NAFLD prevalence within this T2DM population. Both genders show a similar overall susceptibility to NAFLD.

Table 2: Gender distribution of NAFLD in T2DM patients (N=80).

Sex	*NAFLD Present*	*NAFLD Absent*	*Total*
Male	34(42.5%)	19(23.75%)	53(66.25%)
Female	17(21.25%)	10(12.5%)	27(33.75%)
Total	51(63.75%)	29(36.25%)	80(100.0%)

Table 3 compares the characteristics of patients with and without non-alcoholic fatty liver disease (NAFLD) based on age, body mass index (BMI), and waist circumference. The average age of patients with NAFLD is lower than those without NAFLD (45.22 years vs. 56.19 years). However, the p-value (0.125) suggests this difference might not be statistically significant with this sample size. *BMI***:** Patients with NAFLD have a significantly higher average BMI (27.34 kg/m²) compared to those without NAFLD (23.91 kg/m²). The p-value (<0.021) indicates a statistically significant difference between the two groups, suggesting higher BMI is associated with NAFLD presence. *Waist circumference:* Similar to BMI, patients with NAFLD have a significantly larger average waist circumference (101.89 cm) compared to those without NAFLD (98.59 cm). The p-value (<0.014) again suggests a statistically significant difference, supporting the association between larger waist circumference and NAFLD presence. While age might not be a significant factor in this dataset, higher BMI and waist circumference are significantly associated with NAFLD presence.

Table 3 Characteristics of Patients with and without NAFLD

	NAFLD Present	*NAFLD Absent*	*P value*
Age (years; Mean ± SD)	45.22 ± 8.54	56.19 ± 6.61	0.125
BMI (kg/m^2; Mean ± SD)	27.34 ± 1.91	23.91 ± 1.14	<0.021*
Waste circumference in cm; Mean ± SD)	101.89 ± 6.28	98.59 ± 6.43	<0.014*

Table 4 compares various laboratory parameters of patients with and without non-alcoholic fatty liver disease (NAFLD). *Glycemic control:* Both fasting and post-prandial blood sugar levels, as well as HbA1c (a long-term indicator of blood sugar control), are significantly higher in patients with NAFLD compared to those without. This suggests poorer glycemic control is associated with NAFLD presence. *Liver enzymes:* Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT), markers of liver damage, are elevated in patients with NAFLD compared to those without. This indicates potential liver injury due to NAFLD. Interestingly, the AST/ALT ratio is lower in patients with NAFLD, which might suggest predominant fatty liver disease rather than significant inflammation. Gamma-glutamyl transferase (GGT), another liver enzyme, is also significantly elevated in NAFLD patients, further supporting liver involvement. *Alkaline phosphatase (ALP):* While slightly elevated in NAFLD patients, the difference in ALP levels compared to the non-NAFLD group is statistically significant. This could indicate additional involvement of other organs or processes beyond the liver. These findings align with established knowledge that poor glycemic control and impaired liver function are associated with NAFLD. The specific patterns of enzyme elevation suggest potential mechanisms like fatty liver accumulation and less severe inflammation. Elevated ALP warrants further investigation to rule out the involvement of other organ systems.

Table 4 Laboratory profile of patients with and without NAFLD

Parameter	*NAFLD Present*	*NAFLD Absent*	*P value*
Fasting blood sugar (mg/dl)	162.55 ± 29.64	141.20 ± 19.54	0.001
Post Prandial blood sugar (mg/dl)	234.71 ± 25.18	195.54 ± 13.65	0.001
HbA1c (mg/dl)	8.27 ± 1.24	7.12 ±1.02	
AST (IU/L)	56.31 ± 19.56	36.54 ± 17.64	0.01
ALT (IU/L)	37.02 ± 11.37	21.65 ± 16.2	0.02
AST/ALT	0.81 ± 0.14	0.97 ± .12	0.01
GGT (IU/L)	48.82 ± 14.32	26.54 ± 11.37	0.03
ALP (IU/L)	110.24 ± ± 53.22	95.24 ± 9.75	0.032

Table 5 compares the lipid profiles of patients with and without non-alcoholic fatty liver disease (NAFLD). *Triglycerides:* Patients with NAFLD have significantly higher *Serum Triglycerides* compared to those without (198.22 mg/dL vs. 139.74 mg/dL, p=0.012). *HDL-C:* Patients with NAFLD have significantly lower *HDL cholesterol (HDL-C)* compared to those without (36.70 mg/dL vs. 41.24 mg/dL, p=0.020). *Total Cholesterol:* Patients with NAFLD have slightly higher *Total Cholesterol* compared to those without (246.33 mg/dL vs. 210.64 mg/dL, p=0.035). *LDL-C:* Patients with NAFLD have slightly higher *LDL cholesterol (LDL-C)* compared to those without (141.82 mg/dL vs. 129.04 mg/dL, p=0.011). *VLDL:*Patients with NAFLD have significantly higher *VLDL cholesterol* compared to those without (40.15 mg/dL vs. 33.15 mg/dL, p=0.067). The data suggests an unfavorable lipid profile in individuals with NAFLD compared to those without. Higher triglycerides and lower HDL-C are known risk factors for cardiovascular disease, and this table supports their association with NAFLD. Slightly elevated total cholesterol and LDL-C levels further contribute to the increased cardiovascular risk in NAFLD patients. The significant increase in VLDL, a cholesterol carrier produced by the liver, suggests altered lipid metabolism in NAFLD patients.

Table 5 Lipid Profile of Patients with and without NAFLD

	NAFLD Present	*NAFLD Absent*	*P value*
Serum Triglycerides	198.22 ± 38.95	139.74 ± 39.81	0.012
HDL-C	36.70 ± 3.15	41.24 ± 2.90	0.020
Total Cholesterol	246.33 ± 39.24	210.64 ± 32.71	0.035
LDL-C	141.82 ± 29.44	129.04 ± 19.88	0.011
VLDL	40.15 ± 15.42	33.15 ± 10.34	0.067

Table 6 shows the relationship between the duration of type 2 diabetes mellitus (T2DM) and the presence of non-alcoholic fatty liver disease (NAFLD) in patients. It displays the frequency and percentage of patients with and without NAFLD for each duration category, along with the coefficient correlation "r" value. ***NAFLD prevalence increases with diabetes duration:*** The highest percentage of patients with NAFLD (27.5%) is observed in the 5-10 year duration category, followed by 15.0% for 3-5 years and 12.5% for >10 years. The lowest prevalence (8.75%) is seen in the 1-3 year category. ***Positive correlation between duration and NAFLD:***The coefficient correlation "r" values are all positive, ranging from 0.253 to 0.657. This indicates a positive correlation between the duration of diabetes and the presence of NAFLD, meaning longer diabetes duration is associated with a higher likelihood of having NAFLD.

Table 6: Duration of Diabetes Mellitus and NAFLD Prevalence

Duration of Diabetes Mellitus in years	*NAFLD Present*		*NAFLD Absent*		Coefficient correlation 'r' value
	Frequency	%	Frequency	%	
1 – 3	7	8.75	11	13.75	+ 0.253
3 – 5	12	15.0	9	11.25	+ 0.337
5 – 10	22	27.5	6	7.5	+ 0.657
> 10	10	12.5	3	3.75	+ 0.519

These findings suggest that the longer someone has type 2 diabetes, the more likely they are to develop NAFLD. This aligns with existing research linking chronic hyperglycemia and metabolic disturbances in diabetes to NAFLD development. The highest NAFLD prevalence in the 5-10-year category might suggest a critical timeframe for intervention or accelerated risk factors during this period.

Discussion

Non-alcoholic fatty liver disease (NAFLD) encompasses a spectrum of conditions distinguished histologically by excessive accumulation of fat in the liver, occurring in the absence of substantial alcohol intake, and may manifest with or without inflammation, varying levels of fibrosis, and cirrhosis. [10] The important findings of the present study show that 63.75% of T2DM patients in the study had NAFLD, highlighting its significant presence in this population. While younger age groups (30-39 years and ≥70 years) showed lower prevalence, the highest was observed in the 50-59 age group. No significant gender difference was found. BMI and waist circumference: Both were significantly higher in patients with NAFLD, suggesting a strong association with obesity and central adiposity. Glycemic control: Patients with NAFLD had significantly higher fasting and postprandial blood sugar levels, as well as HbA1c, indicating poorer glycemic control. Liver enzymes: Elevated AST, ALT, and GGT levels in NAFLD patients suggested liver injury, while the AST/ALT ratio pointed towards predominant fatty liver disease. Alkaline phosphatase (ALP): Slightly elevated in NAFLD, potentially implying involvement of other organs or processes beyond the liver. Dyslipidemia: Patients with NAFLD had an unfavorable lipid profile characterized by high triglycerides, low HDL-C, and slightly elevated total and LDL cholesterol.

Several studies have demonstrated a positive correlation between hyperinsulinemia, impaired glucose tolerance, and NAFLD. Mishra et al. [11] reported a prevalence of 24% for metabolic syndrome and 14.8% for NAFLD among non-alcoholic North Indian men. Gupte et al. [12] observed NAFLD in 65.5%, 12.5%, and 9.35% of asymptomatic type 2 diabetics, categorized as mild, moderate, and severe, respectively.Prashanth et al. [9] identified multiple components of metabolic syndrome in type 2 diabetics, which were associated with a high prevalence of NAFLD and NASH. Histologically, Banerjee et al. [13] found that 43% exhibited fatty changes, 40% had NASH, and 23% had more advanced disease. NAFLD is strongly linked to overweight/obesity and insulin resistance. The risk of advanced liver fibrosis is highest among individuals with NASH who are older than 40–45 years and overweight/obese or affected by T2DM. [5] This association between T2DM, insulin resistance (IR), and NAFLD is expected due to insulin being transported directly to the portal vein after secretion, following the same pathway as absorbed glucose, and the liver removing a significant portion of portal insulin during the initial passage. Similar observations were made by Arun J et al. [14] (56.5%) and S Kalra et al. [15] (56.5%) in identifying diabetes mellitus patients with NAFLD. Additionally, an increased duration of diabetes was significantly linked to NAFLD. The mean duration of DM was 10.3 years in the NAFLD group compared to 6.6 years in the non-NAFLD group, as reported by Viswanathan et al. [16] Our findings suggest that worsening glycemic control is associated with an increased risk of developing NAFLD. In our study, elevated levels of fasting blood sugar (FBS), postprandial blood sugar

(PPBS), and HbA1c were significantly correlated with the incidence of NAFLD, with p-values <0.05, respectively. These results are consistent with findings from other studies such as G Bedogni et al. [17] (p-value 0.007) and Giovanni et al (p-value <0.0001). Among DM-2 patients with NAFLD, serum AST was >ULN in 33.9%, ALT in 36.8%, GGT in 27.1%, ALP in 38%, and serum bilirubin (>2mg%) in 16% of patients. Jayarama N et al. [18] observed that the mean level of ALT in cases and controls was 66.68 IU/L and 32.58 IU/L, respectively, which was statistically significant. Salmela et al. [19] found that the prevalence of elevated ALT levels among type 2 DM patients was 22.9%.

In a study involving severely obese patients with diabetes, it was found that 100% exhibited at least mild steatosis, 15% had steatohepatitis, and 21% had cirrhosis. [20] In our study, 65% of patients with NAFLD were obese. Hypertension has also been commonly observed in NAFLD patients, although it is not deemed an independent risk factor, as indicated in this study. Dyslipidemia has been reported in 20% to 90% of NAFLD patients. We observed significantly higher rates of hypertriglyceridemia, high LDL, and low HDL among subjects in the NAFLD group. Similar findings were reported in a hospital-based study from North India by Prashanth et al. [9] The diagnosis of NAFLD in our study relied on standard ultrasonography, which remains the most common method for diagnosing this increasingly recognized liver disorder in clinical practice. Radiologic imaging techniques such as sonography have shown sufficient sensitivity for diagnosing fatty liver.

Conclusion

This study, though limited by sample size, found a strong association between several factors and non-alcoholic fatty liver disease (NAFLD) in patients with type 2 diabetes mellitus (T2DM). 63.75% of T2DM patients had NAFLD, highlighting its significant burden in this population. While no significant gender difference was observed, NAFLD prevalence peaked in the 50-59 age group. Poorer glycemic control, as indicated by higher blood sugar and HbA1c, was associated with NAFLD presence. Elevated liver enzymes (AST, ALT, GGT) suggested liver injury in NAFLD patients, with the pattern pointing towards predominant fatty liver disease. NAFLD patients exhibited an unfavorable lipid profile characterized by high triglycerides, low HDL-C, and slightly elevated total and LDL cholesterol, increasing their cardiovascular risk. A positive correlation was observed between the duration of T2DM and NAFLD prevalence, suggesting longer diabetes duration increases NAFLD risk. Overall, this study highlights the complex interplay of factors contributing to NAFLD in T2DM patients. Addressing obesity, improving glycemic control, and managing dyslipidemia may be crucial strategies for preventing and managing this prevalent liver condition in this population.

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