

Evaluation of Biochemical Parameters in Type 2 Diabetes Mellitus Patients with Non-Alcoholic Fatty Liver Disease at a Tertiary Care Hospital in Bhopal

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is a leading cause of chronic liver disease worldwide and can progress to fibrosis and cirrhosis. NAFLD is increasingly prevalent, particularly in individuals with central obesity, type 2 diabetes mellitus (T2DM), dyslipidemia, and metabolic syndrome.

Objective: To assess biochemical parameters in patients with T2DM and NAFLD at a tertiary care hospital in Bhopal.

Methods: This study was conducted in the Department of Biochemistry at L.N. Medical College and J.K. Hospital, involving 70 subjects diagnosed with T2DM and NAFLD. NAFLD severity was classified into three grades (1–3) based on abdominal ultrasonography findings. Biochemical parameters analyzed included HbA1c, serum cholesterol, triglycerides, low-density lipoprotein (LDL), and high-density lipoprotein (HDL).

Results: Among 70 participants, those with NAFLD Grade 3 had the highest total cholesterol levels (Mean TC = 266 mg/dL). Grade 3 participants (n=17) exhibited elevated triglyceride levels (Mean TG = 246 mg/dL), while Grade 2 participants (n=25) had increased LDL levels. Grade 1 participants had the lowest HDL levels (Mean HDL = 35 mg/dL). Dyslipidemia, characterized by elevated triglycerides or LDL with reduced HDL, was the most common abnormality. Total cholesterol, LDL, and HDL levels were significantly associated with NAFLD severity, whereas triglyceride variations across NAFLD grades were not statistically significant.

Conclusion: This study highlights the importance of recognizing fatty liver as a component of metabolic syndrome in individuals with diabetes mellitus. Regular monitoring of lipid profiles in T2DM patients with NAFLD is essential for early intervention and management.

Keywords: Type 2 diabetes mellitus, Non-alcoholic fatty liver disease, Total cholesterol, Triglycerides, Low-density lipoprotein, High-density lipoprotein, HbA1c.

1. INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a leading cause of chronic liver disease in developed countries, affecting a significant proportion of the adult population.¹ It represents a spectrum of liver disorders, ranging from simple hepatic steatosis to more severe conditions such as non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma (HCC).² Due to the complex and heterogeneous pathogenesis of NAFLD, an international panel of experts in 2020 recommended renaming it as Metabolic Associated Fatty Liver Disease (MAFLD).³

NAFLD has become the most prevalent liver disease in Western countries,⁴ with a global prevalence of approximately 25.4%. The highest rates are reported in the Middle East and South America (~30%), while the lowest prevalence is seen in Africa (~13%).⁵⁻⁷ In India, the prevalence of NAFLD varies widely, ranging from 9% to 53%.⁸⁻¹⁰

The presence of NAFLD significantly increases the risk of type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD),^{11,12} with studies indicating that individuals with NAFLD have at least twice the risk of developing these conditions. Approximately 12–20% of individuals with T2DM are believed to have clinically significant liver fibrosis.¹³

T2DM is a major risk factor for CVD^{14,15} and is strongly associated with both the prevalence and severity of NAFLD.¹⁶ Studies suggest a complex bidirectional relationship between NAFLD and T2DM, with 60–70% of patients with T2DM also having NAFLD.¹⁷ This association may contribute to an increased cardiovascular risk in affected individuals.¹⁸ However, while some studies have demonstrated a strong link between NAFLD and CVD in T2DM patients,^{19,20,21,22} others have reported mixed results.¹⁹ A meta-analysis of 11 studies indicated that individuals with both T2DM and NAFLD have double the risk of developing cardiovascular disease compared to those with T2DM alone.²⁰

This study aims to assess the biochemical parameters in patients with T2DM and NAFLD to better understand their metabolic profile and the potential implications for disease progression and cardiovascular risk.

2. MATERIALS AND METHODS:

Study Population

This study included patients diagnosed with Type 2 Diabetes Mellitus (T2DM) who were above 18 years of age and attending JK Hospital, Bhopal. Patients were screened for the presence of Non-Alcoholic Fatty Liver Disease (NAFLD) using abdominal ultrasonography.

Study Design and Sample Size

- **Study Design:** Cross-sectional study
- **Sample Size:** 70 participants

Inclusion Criteria

- Adults (>18 years of age)
- Diagnosed cases of T2DM with NAFLD confirmed via ultrasonography

Exclusion Criteria

- Patients with Type 1 Diabetes Mellitus
- Individuals with a history of alcohol consumption
- Patients with pre-existing liver disease (e.g., viral hepatitis, autoimmune hepatitis, or cirrhosis)
- Pregnant and lactating women
- Patients with any other known chronic diseases (e.g., chronic kidney disease, malignancies)

Ethical Considerations

The study was conducted following ethical guidelines and was approved by the Institutional Ethics Committee. Informed written consent was obtained from all participants before enrollment. A detailed medical history was recorded, followed by a comprehensive physical examination.

Sample Collection and Laboratory Analysis

Venous blood samples were collected from all participants under aseptic conditions. Samples were centrifuged immediately to separate serum for biochemical analysis. The following parameters were measured using a semi-autoanalyzer:

- **Triglycerides (TG)** – Glycerol-3-phosphate oxidase (GPO-Trinder) method
- **Total Cholesterol (TC)** – Cholesterol oxidase-peroxidase (CHOD-PAP) method
- **High-Density Lipoprotein (HDL-C)** – Direct method
- **Low-Density Lipoprotein (LDL-C)** – Direct method
- **HbA1c** measured using high-performance liquid chromatography utilizing the D-100 system from Bio Rad.

3. STATISTICAL ANALYSIS

Data were analyzed using Graph Pad Instat software. Descriptive statistics were expressed as mean \pm Standard Error of Mean (SEM). Pearson's Chi-Square test was performed to compare biochemical parameters across different NAFLD grades. A p-value < 0.05 was considered statistically significant. Additionally, Spearman's correlation coefficient was calculated to assess the relationship between various biochemical parameters in T2DM patients with NAFLD.

Observation and Results

This study was conducted on Type 2 Diabetes Mellitus (T2DM) patients to assess the prevalence and biochemical characteristics of Non-Alcoholic Fatty Liver Disease (NAFLD). A total of **70** participants met the eligibility criteria and were included in the study.

Table 1: Distribution of Study Population According to Age Group

Age Group (Years)	Frequency (n)	Percentage (%)
19-29	16	22.86
30-39	23	32.86
40-49	19	27.14
≥50	12	17.14
Total	70	100

The table shows that the highest proportion (32.86%) of participants were in the 30-39 years age group, while the lowest proportion (17.14%) was in the ≥50 years age group.

Table 2: Gender Distribution in the Study Population

Gender	Frequency (n)	Percentage (%)
Male	46	65.7%
Female	24	34.3%
Total	70	100%

The table indicates a higher proportion of male participants (65.7%) compared to female participants (34.3%) in the study population.

Table 3: Association of Lipid Profile with Different Grades of NAFLD

S.No	Biochemical Parameter	Grade 1 (n=39) Mean ± SD	Grade 2 (n=19) Mean ± SD	Grade 3 (n=12) Mean ± SD	F-Test	P-Value
1	Triglycerides (TG)	162.62 ± 47.1	164.83 ± 45.63	171.33 ± 37.37	0.133 2	0.8755
2	Low-Density Lipoprotein (LDL)	116.6 ± 29.8	125.6 ± 20.98	147.33 ± 35.76	4.603 2	0.0134*
3	High-Density Lipoprotein (HDL)	35.0 ± 7.9	29.41 ± 6.08	28.22 ± 7.5	5.825 3	0.0047*
4	Total Cholesterol (TC)	200 ± 61.8	241.66 ± 53.62	266.6 ± 64.22	6.381 4	0.0029*
5	HbA1c	5.88 ± 0.34	5.76 ± 0.49	5.94 ± 0.46	0.827 9	0.4414

(P-value < 0.05 is considered statistically significant)

Interpretation of Results

- The most prevalent dyslipidemia pattern observed was a combination of high LDL and low HDL levels.
- Grade 3 NAFLD patients had the highest levels of Triglycerides (TG), LDL, and Total Cholesterol (TC), while HDL levels were significantly lower compared to other grades.
- The differences in LDL, HDL, and Total Cholesterol across different NAFLD grades were statistically significant ($p < 0.05$), indicating a strong association between dyslipidemia and NAFLD severity.
- HbA1c levels did not show significant variation across different NAFLD grades ($p = 0.4414$), suggesting that glycemic control was not significantly impacted by NAFLD severity in this study population.

This analysis highlights the strong link between NAFLD severity and dyslipidemia in T2DM patients, reinforcing the need for lipid profile monitoring in diabetic individuals with NAFLD.

4. DISCUSSION

This study highlights the significant prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) among Type 2 Diabetes Mellitus (T2DM) patients, with the highest proportion of affected individuals found in the 30-39 years age group (32.86%), followed by the 40-49 years age group (27.14%). These findings are consistent with previous research conducted by Xiang Hu et al., which also identified a peak prevalence of NAFLD among individuals aged 35-45 years.²³

Gender Distribution and NAFLD Prevalence: The percentage of females included in region wise [India] study to be only 20%, 10% and 30% in New Delhi, Chandigarh and Lucknow region respectively.²⁴

A male predominance (65.7%) was observed in this study, which aligns with the findings of Yang et al. (2014),²⁵ who also reported a higher prevalence of NAFLD in males. This gender-based difference could be attributed to hormonal influences, metabolic differences, and lifestyle factors such as dietary habits and physical activity levels.

Lipid Profile and Metabolic Abnormalities in NAFLD

Dyslipidemia was a common finding in NAFLD patients, with Grade 3 NAFLD showing the highest levels of total cholesterol (266.6 mg/dL), LDL (147.33 mg/dL), and triglycerides (171.33 mg/dL), while HDL was lowest (28.22 mg/dL). These findings are in agreement with Oikonomou et al., who identified dyslipidemia, particularly elevated LDL and reduced HDL, as key metabolic abnormalities in NAFLD.²⁶

The triglyceride levels did not show significant variation across different NAFLD grades, whereas total cholesterol, LDL, and HDL differences were statistically significant ($p < 0.05$). This suggests that LDL and HDL levels are better indicators of NAFLD severity in diabetic patients. The abnormal lipid metabolism observed in NAFLD is likely due to insulin resistance, increased hepatic triglyceride synthesis, and impaired clearance of atherogenic lipoproteins.

Association of HbA1c with NAFLD Severity

The mean **HbA1c** level among NAFLD patients was 5.8%, with Grade I, II, and III. NAFLD patients having mean HbA1c values of 5.88%, 5.76%, and 5.94%, respectively. These findings support the observation by Miwa Tatsuta et al. (2023) that HbA1c levels $\geq 5.8\%$ serve as a predictive marker for NAFLD, warranting abdominal ultrasonography in patients with borderline glycemic control.²⁷

Interestingly, despite the presence of NAFLD, HbA1c levels remained within the prediabetic range, suggesting that in early NAFLD, glycemic dysregulation may not be severe. However, as NAFLD progresses, insulin resistance worsens, potentially increasing the risk of developing full-blown diabetes.

The Bidirectional Relationship between NAFLD and T2DM

This study supports previous research indicating a bidirectional link between NAFLD and T2DM, wherein NAFLD increases the risk of diabetes, and diabetes, in turn, exacerbates liver disease. According to Xia et al. (2019), the prevalence of diabetes among NAFLD and NASH patients is 22.51% and 43.63%, respectively, significantly higher than the global diabetes prevalence of **8.5%**. This interaction increases the risk of hepatic fibrosis, cardiovascular disease, and overall mortality in patients with both conditions.²⁸

The findings of this study are in agreement with Puneem et al. (2023), who reported that T2DM-NAFLD patients exhibited significantly higher levels of total cholesterol, LDL, triglycerides, and HbA1c, with no significant difference in HDL levels ($p > 0.05$).²⁹

Similarly, Mala Darmalingam et al. (2018) emphasized the frequent coexistence of NAFLD and T2DM, with a 59.67% prevalence of NAFLD among diabetic patients, **and biopsy-proven** nonalcoholic steatohepatitis (NASH) found in 20% of asymptomatic T2DM patients with normal liver function tests. This underscores the need for early screening of NAFLD in T2DM patients, even in the absence of overt liver disease symptoms.³⁰

Clinical Implications

A study by Krishnakant Niranjana Bhatt et al. (2020) in Gujarat revealed a high prevalence of NAFLD in T2DM patients, reinforcing the importance of routine screening for NAFLD in diabetic populations. Early identification and management of NAFLD in T2DM patients can help prevent progression to cirrhosis, hepatocellular carcinoma, and cardiovascular complications.³¹

5. CONCLUSION

This study reinforces the strong association between NAFLD and dyslipidemia, insulin resistance, and Type 2 diabetes, with male gender and middle-aged adults being at the highest risk. The findings highlight the importance of lipid profile monitoring, glycemic control, and early screening for NAFLD in diabetic patients to mitigate the risk of hepatic and cardiovascular complications.

Conflict of interest: Nil

Source of funding: Nil

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