**Original Research Article**

**NON-ALCOHOLIC FATTY LIVER DISEASE AND ASSOCIATED LIPID PROFILE IN TYPE 2 DIABETES PATIENTS OF NIGERIA**

**ABSTRACT**

**Background:** Type II diabetes mellitus (T2DM) and non-alcoholic fatty liver disease (NAFLD) are rising chronic conditions that often co-occur, posing significant health risks. NAFLD is common among those with T2DM due to shared risk factors like insulin resistance and obesity. Understanding this link is crucial for effective prevention and treatment. This article explores the relationship between NAFLD and lipid profiles in individuals with T2DM.

**Method:** The study was carried out at the University of Port Harcourt Teaching Hospital (UPTH), Rivers State, Nigeria. The study included 300 participants aged 18 and above, consisting of 150 diabetic patients and 150 age- and sex-matched controls. Participants underwent clinical, biochemical, and anthropometric assessments. Blood samples were collected to analyze liver enzymes, glucose, and lipid profiles according to standard laboratory procedures. Additionally, all subjects received abdominal ultrasound examinations to detect hepatic steatosis, indicative of NAFLD.

**Results**: There was a 32.7% prevalence of NAFLD among the diabetic patients. Regression analysis show that individuals with uncontrolled diabetes are significantly more likely to have NAFLD The odds ratio was 7.3 (95% CI: 2.6 – 20.1; p = 0.0001). Also, an odds ratio of 4.9 (95% CI: 1.5 – 15.3), suggests a strong association between elevated triglycerides and NAFLD.

For high-density lipoprotein (HDL) levels, none of the individuals with elevated HDL had NAFLD, whereas 100% of them were without NAFLD. This difference was also significant, with a chi-square value of 11.25 (p=0.0041).

**Conclusion:** People with type 2 diabetes face a complex interplay between blood sugar control, cholesterol levels, and NAFLD. This study found that poor blood glucose control (high HbA1c) and high triglycerides significantly increase NAFLD risk, while higher HDL levels offer some protection. LDL levels weren't directly linked to NAFLD, and standard liver tests for bilirubin and albumin were less informative. The study recommends regular NAFLD screening, especially for patients with poor blood glucose control or high triglycerides, and a comprehensive treatment approach to manage blood glucose, triglycerides, and potentially increase HDL. Tailoring treatment to individual risk profiles and educating patients on healthy habits is essential.

**Keywords:** *NAFLD, Diabetes Mellitus (DM), Lipid Profile, Glucose control*

**1.0 INTRODUCTION**

Non-alcoholic fatty liver disease (NAFLD) represents a spectrum of liver conditions characterized by excessive fat accumulation in the liver cells of individuals who consume little to no alcohol.1,2 As one of the most common liver disorders globally, NAFLD ranges from simple hepatic steatosis to more severe conditions like non-alcoholic steatohepatitis (NASH), fibrosis, and cirrhosis.3,4 The increasing prevalence of NAFLD has paralleled the rise in metabolic disorders, notably type II diabetes mellitus (T2DM).5 Type II diabetes, a chronic metabolic condition marked by insulin resistance and hyperglycemia, significantly heightens the risk of developing NAFLD.6,7 Approximately 70% of individuals with T2DM have been reported to exhibit NAFLD, making it a critical area of study.7,8 The relationship between these two conditions is bidirectional; not only does T2DM exacerbate NAFLD progression, but NAFLD also contributes to poor glycemic control and worsens insulin resistance, creating a vicious cycle. A pivotal aspect of understanding the interplay between NAFLD and T2DM lies in examining the lipid profile associated with these conditions. Dyslipidemia, characterized by elevated levels of triglycerides, elevated low-density lipoprotein cholesterol (LDL-C), and reduced high-density lipoprotein cholesterol (HDL-C), is a common metabolic anomaly in both NAFLD and T2DM.9–11 This altered lipid metabolism plays a crucial role in the pathogenesis and progression of NAFLD in diabetic patients. The increasing prevalence of NAFLD worldwide is linked to the increasing prevalence of obesity and DM which have been reported as major risk factors.12 The global prevalence of NAFLD in DM is 57.19%, more than 2 times higher than in the general population13 A review of three studies carried out in the South-West part of Nigeria revealed variations in the prevalence rate in the region.10 Onyekwere et al12 reported a prevalence of 9.5% among 168 type 2 DM patients, while two other studies had higher prevalent rates of 16.7% (of 106 diabetic patients)14 and a whopping 66.8% (of 80 type 2 diabetic patients) respectively.15 Type II diabetes mellitus (T2DM) and non-alcoholic fatty liver disease (NAFLD) are rapidly rising chronic conditions, often co-occurring and posing a significant public health burden. While both diseases are individually concerning, their combined presence presents a heightened risk for serious health complications. NAFLD, characterized by excessive fat accumulation in the liver, is increasingly prevalent among individuals with T2DM. This association is likely due to shared underlying risk factors, such as insulin resistance and obesity. Understanding the link between these conditions is crucial for developing effective preventive and treatment strategies. This article delves into the relationship between NAFLD and lipid profile in individuals with T2DM.

**2.0 MATERIALS AND METHODS**

**2.1 Study Population**

The study was carried out at the University of Port Harcourt Teaching Hospital (UPTH), Rivers State, Nigeria. The study included 150 diabetic patients receiving care at UPTH. Diabetic patients were screened to exclude those positive for hepatitis B surface antigen, hepatitis C virus antibody, and those with significant alcohol history.

**2.2 Sample Collection and Assessment**

Participants underwent clinical, biochemical, and anthropometric assessments. Blood samples were collected to analyze liver enzymes, glucose, and lipid profiles according to standard laboratory procedures.16 Additionally, all subjects received abdominal ultrasound examinations to detect hepatic steatosis, indicative of NAFLD.

**2.3 Data Collection**

Data were gathered through structured questionnaires and medical examinations. The questionnaire covered socio-demographic information and medical history. Physical examinations recorded anthropometric measurements, while laboratory tests provided biochemical data.

**2.4 Data Analysis**

The collected data were analyzed using statistical software. Descriptive statistics summarized the socio-demographic and clinical characteristics of participants. Comparative analyses were performed to examine differences between diabetic patients with and without NAFLD, and logistic regression identified predictors of NAFLD within the diabetic cohort. All analyses were done with the Statistical Package for Social Sciences (v26) IBM, USA at a 95% confidence interval and a p-value less than 0.05 was considered statistically significant.

**2.5 Ethical Considerations**

Ethical approval was obtained from the UPTH Ethics Committee. Informed consent was secured from all participants after explaining the study's purpose, procedures, and potential risks. Confidentiality was maintained throughout the study.

**3.0 RESULTS**

Table 1 shows the demographic distribution of the study participants. The table presents the demographic characteristics of a sample population of 150 individuals, broken down by age group, sex, education, and marital status. In terms of age distribution, the largest proportion of the sample, 36.7%, falls within the 50 to 59-year age range, followed by 24.7% aged 40 to 49 years, and 23.3% aged 60 to 69 years. The youngest group, aged 30 to 39 years, makes up 12.7% of the sample, while the oldest group, aged 70 to 79 years, comprises just 2.7%. Regarding sex, the majority of the sample is female, accounting for 80.7%, while males represent 19.3%. Educational attainment is varied, with the majority of individuals, 58.7%, having tertiary education. Those with secondary education make up 27.3% of the sample, and those with primary education account for 14%. Marital status reveals that a significant majority, 82.7%, are married. Widowed individuals constitute 12.7%, while those who are single make up 4.7% of the sample.

Table 1:Sociodemographic distribution of Subjects

|  |  |  |
| --- | --- | --- |
| **Demography** | **Frequency (n=150)** | **Percent (%)** |
| **Age group** |  |  |
| 30 - 39 years | 19 | 12.7 |
| 40 - 49 years | 37 | 24.7 |
| 50 - 59 years | 55 | 36.7 |
| 60 - 69 years | 35 | 23.3 |
| 70 - 79 years | 4 | 2.7 |
| **Sex** |  |  |
| Male | 29 | 19.3 |
| Female | 121 | 80.7 |
| **Education** |  |  |
| Primary | 21 | 14 |
| Secondary | 41 | 27.3 |
| Tertiary | 88 | 58.7 |
| **Marital status** |  |  |
| Married | 124 | 82.7 |
| Single | 7 | 4.7 |
| Widowed | 19 | 12.7 |

Figure 1 shows that 32.7% of the patients had NAFLD.

Figure 1: Proportion of DM patients with NAFLD

Table 2 compares various biochemical parameters between individuals who tested positive for non-alcoholic fatty liver disease (NAFLD) and those who tested negative. For cholesterol levels, the NAFLD-positive group had an average of 4.4 mmol/L (±0.8), while the NAFLD-negative group had an average of 4.3 mmol/L (±0.6), with a T-test value of 0.3937, indicating no significant difference. Triglyceride levels were notably higher in the NAFLD-positive group, averaging 1.4 mmol/L (±0.6) compared to 1.1 mmol/L (±0.5) in the NAFLD-negative group, with a significant T-test value of 0.0015. High-density lipoprotein (HDL) levels were slightly higher in the NAFLD-positive group, averaging 0.9 mmol/L (±0.3) compared to 0.8 mmol/L (±0.3) in the NAFLD-negative group, with a T-test value of 0.0574, suggesting a marginal significance. Low-density lipoprotein (LDL) levels were similar between the two groups, with the NAFLD-positive group at 2.9 mmol/L (±0.7) and the NAFLD-negative group at 3.0 mmol/L (±0.7), and a T-test value of 0.4132, indicating no significant difference. Total bilirubin levels averaged 9.3 μmol/L (±4.2) in the NAFLD-positive group and 8.8 μmol/L (±3.8) in the NAFLD-negative group, with a T-test value of 0.4655, showing no significant difference. Albumin levels were also similar, with the NAFLD-positive group averaging 46.1 g/L (±4.6) and the NAFLD-negative group averaging 47.1 g/L (±5.1), resulting in a T-test value of 0.2471. Glycated hemoglobin (HbA1c) levels were significantly higher in the NAFLD-positive group, averaging 10.9% (±4.3) compared to 7.5% (±2.4) in the NAFLD-negative group, with a T-test value of 0.0001, indicating a highly significant difference.

Table 2: Comparison of average levels of biochemical features

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **NAFLD**  **positive** | **NAFLD negative** | **T-test** |
| Cholesterol (mmol/l) | 4.4 ±0.8 | 4.3 ±0.6 | 0.3937\*\* |
| Triglycerides (mmol/l) | 1.4 ±0.6 | 1.1 ±0.5 | 0.0015\* |
| High Density Lipoprotein (mmol/l) | 0.9 ±0.3 | 0.8 ±0.3 | 0.0574\*\* |
| Low density lipoprotein (mmol/l) | 2.9 ±0.7 | 3.0 ±0.7 | 0.4132\*\* |
| Total Bilirubin (μmol/L) | 9.3 ±4.2 | 8.8 ±3.8 | 0.4655\*\* |
| Albumin (g/L) | 46.1 ±4.6 | 47.1 ±5.1 | 0.2471\*\* |
| Glycated haemoglobin (%) | 10.9 ±4.3 | 7.5 ±2.4 | 0.0001\* |

The data is presented in Mean ± Standard deviation

\**Difference is statistically significant (p < 0.05)*

*\*\*Difference is not statistically significant (p > 0.05)*

Table 3 presents a comparison of biochemical variables between individuals with non-alcoholic fatty liver disease (NAFLD) and those without. For glycated hemoglobin (HbA1c), 44.4% of individuals with NAFLD had uncontrolled HbA1c levels (>7%), compared to 55.6% without NAFLD, with a significant chi-square value of 18.36 (p=0.0001). The odds ratio was 7.3 (95% CI: 2.6 – 20.1), indicating that individuals with uncontrolled diabetes are significantly more likely to have NAFLD. Regarding triglyceride levels, 66.7% of those with elevated triglycerides had NAFLD, while 33.3% did not. This difference was significant, with a chi-square value of 8.75 (p=0.0031) and an odds ratio of 4.9 (95% CI: 1.5 – 15.3), suggesting a strong association between elevated triglycerides and NAFLD.

For high-density lipoprotein (HDL) levels, none of the individuals with elevated HDL had NAFLD, whereas 100% of them were without NAFLD. This difference was also significant, with a chi-square value of 11.25 (p=0.0041). The odds ratio is not applicable (NA) because no NAFLD cases were observed in the elevated HDL group.

Low-density lipoprotein (LDL) levels showed that 31.3% of those with elevated LDL had NAFLD compared to 68.7% without NAFLD. For those with normal LDL levels, 37.1% had NAFLD and 62.9% did not. The chi-square value was 0.41 (p=0.519), indicating no significant difference. The odds ratio was 0.7 (95% CI: 0.3 – 1.7), suggesting no strong association between LDL levels and NAFLD.

Table 3: Association of Lipid profile and NAFLD

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Variables** | **NAFLD**  **n, (%)** | **No NAFLD**  **n, (%)** | **Total**  **n, (%)** | **Chi-square**  **(p-value)** | **OR (95% C.I)** |
| **Glycated haemoglobin** |  |  |  |  |  |
| Uncontrolled (>7%) | 44(44.4) | 55(55.6) | **99(100.0)** | 18.36(0.0001)\* | 7.3 (2.6 – 20.1) |
| Controlled (<7%) | 5(9.8) | 46(90.2) | **51(100.0)** |  |
| **Triglyceride** |  |  |  |  |  |
| Elevated | 10(66.7) | 5(33.3) | **15(100.0)** | 8.75 (0.0031)\* | 4.9 (1.5 – 15.3) |
| Normal | 39(28.9) | 96(71.1) | **135(100.0)** |  |
| **High density lipoprotein** |  |  |  |  |  |
| Elevated | 0(0.0) | 4(100.0) | **4(100.0)** | 11.25 (0.0041)\* | Not applicable |
| Normal | 49(33.6) | 97(66.4) | **146(100.0)** |  |
| **Low density lipoprotein** |  |  |  |  |  |
| Elevated | 36(31.3) | 79(68.7) | **115(100.0)** | 0.41 (0.519)\*\* | 0.7 (0.3 – 1.7) |
| Normal | 13(37.1) | 22(62.9) | **35(100.0)** |  |

\**Distribution is statistically significant (p < 0.05)*

*\*\*Distribution is not statistically significant (p > 0.05)*

**4.0 DISCUSSION**

The data from the current study paints a clear picture of the intricate relationship between NAFLD, glycemic control, and lipid profiles in individuals with T2DM. Individuals with NAFLD exhibited significantly higher HbA1c levels (10.9% ± 4.3%) compared to those without the condition (7.5% ± 2.4%). This finding aligns with the observation in the second table, where 44.4% of patients with uncontrolled HbA1c (>7%) had NAFLD, compared to only 9.8% with controlled HbA1c (<7%). The odds ratio (OR) of 7.3 (95% CI: 2.6 – 20.1) further strengthens this association, indicating that uncontrolled diabetes is associated with an over sevenfold increased risk of NAFLD. This is consistent with the findings of similar studies which reported an 8 – 17 times increased likelihood of poor glycemic control associated with the occurrence of NAFLD among diabetics.17–20 Poor glycemic control is a common occurring phenomena in diabetes, while NAFLD has been seen to be associated with an elevated increase in blood glucose levels when compared to non-NAFLD diabetic subjects.21,22 These findings underscore the critical role of maintaining good glycemic control in preventing or managing NAFLD among diabetic patients. Elevated HbA1c signifies prolonged periods of high blood sugar, which can worsen insulin resistance and promote fat accumulation in the liver. Regular monitoring of HbA1c levels in diabetic patients can serve as an early warning sign for NAFLD development.23,24 By implementing intensive glycemic control strategies, clinicians can potentially reduce the risk of NAFLD in this high-risk population.

The analysis of the current study revealed a clear association between elevated triglycerides (TG) and NAFLD. Individuals with NAFLD had significantly higher triglyceride levels (1.4 ± 0.6 mmol/L) compared to those without (1.1 ± 0.5 mmol/L). This observation is further supported by the second table, where 66.7% of individuals with elevated triglycerides had NAFLD, compared to only 28.9% with normal triglyceride levels. The OR of 4.9 (95% CI: 1.5 – 15.3) translates to a nearly fivefold increased risk of NAFLD with high triglycerides. The current findings are consistent with the findings of a cohort study which showed that higher TG was strongly associated with increased risk of incident fatty liver and NAFLD. Similarly, in a cross-sectional study involving a large sample of children and adolescents, TG was independently related to NAFLD.25 Consistently, the present study also revealed a close relationship between TG and NAFLD. The prevalence and Odds Ratios of NAFLD increased progressively with elevated TG. Though the mechanism underlying the link between TG and NAFLD has not been fully elucidated, insulin resistance is a potential mediator. Triglyceride was found to be closely associated with insulin resistance in different populations including and has been recommended as a clinical indicator of insulin resistance.17,19,26,27 In experimental studies, insulin resistance was shown to promote the secretion of larger and TG over-enriched VLDL particles. Thus, insulin resistance contributes to the increase of TG. On the other hand, insulin resistance promotes NAFLD by inducing lipolysis of adipose tissue TG and de novo synthesis of TG in the liver.26 Thus, insulin resistance may be responsible for the association between TG and NAFLD. Effective management of triglycerides is crucial in reducing NAFLD risk. This can be achieved through dietary modifications, increased physical activity, and potentially medications like fibrates or omega-3 fatty acids.28,29 Clinicians managing T2DM patients should take a comprehensive approach to lipid management, addressing not only triglycerides but also other lipid profiles and metabolic parameters to holistically address NAFLD risk.30

The study suggests a potential protective effect of HDL against NAFLD. While the difference in HDL levels between NAFLD groups was slight (0.9 ± 0.3 mmol/L in NAFLD-positive vs 0.8 ± 0.3 mmol/L in NAFLD-negative), the second table revealed a key finding: none of the individuals with elevated HDL had NAFLD. Strategies to increase HDL, such as lifestyle changes and potentially specific medications, might benefit patients at risk of NAFLD. While lowering LDL and triglycerides often takes centre stage, enhancing HDL levels should also be part of a comprehensive approach to reduce overall metabolic risk, including NAFLD.9,10

The current study did not show a significant association between LDL levels and NAFLD. There were no significant differences in LDL levels between individuals with and without NAFLD, and the second table showed similar proportions of NAFLD in both elevated and normal LDL groups. While LDL does not appear to directly influence NAFLD risk, its management remains critical for overall cardiovascular health, particularly in diabetic patients with a high risk of cardiovascular complications. Despite the lack of a direct link to NAFLD, LDL management should still be integrated into the treatment plan for dyslipidemia and cardiovascular risk reduction in diabetic patients. The analysis suggests that total bilirubin and albumin levels might not be directly impacted by or predictive of NAFLD in this population. There were no significant differences in these markers between the NAFLD-positive and negative groups. While total bilirubin and albumin are standard liver function tests, their lack of significant difference in this study suggests they may not be sensitive enough to diagnose NAFLD alone. However, they remain important for overall liver health and should be part of routine monitoring in patients with T2DM.

**5.0 CONCLUSION**

People with type 2 diabetes face a complex interplay between their blood glyceamic control, cholesterol levels, and a liver condition called NAFLD. This study explored these connections and found that poor blood glyceamic control, indicated by high HbA1c levels, and high triglycerides significantly increased the risk of NAFLD. Conversely, higher levels of HDL cholesterol seemed to offer some protection against developing NAFLD. Interestingly, LDL management, while crucial for overall heart health in diabetic patients, wasn't directly linked to NAFLD risk in this study. Standard liver function tests for bilirubin and albumin also proved to be less informative for diagnosing NAFLD in this population. Based on these findings, the study recommends several key strategies for managing NAFLD risk in diabetic patients. Doctors should prioritize regular screening for NAFLD, particularly in patients with poorly controlled blood glucose or high triglycerides. A comprehensive treatment approach is vital, encompassing strategies to manage blood glucose, lower triglycerides, and potentially even explore ways to increase HDL levels. Empowering patients with knowledge about the importance of maintaining good blood glyceamic control and adopting healthy habits is also crucial. Finally, tailoring treatment plans to each patient's individual risk profile, considering both metabolic factors and potential risks to their liver and heart health, is essential. By implementing these recommendations, healthcare professionals can take significant strides towards mitigating the risk of NAFLD and its associated complications in the growing population of diabetic patients.

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