**Original Research Article**

**ASSESSING NON-ALCOHOLIC FATTY LIVER DISEASE AND ASSOCIATED FACTORS IN PERSONS WITH TYPE II DIABETES MELLITUS**

**ABSTRACT**

**Background:** This study aims to assess the prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) among individuals with diabetes and identify the associated factors that contribute to its development. By investigating this relationship, we hope to gain valuable insights into the shared underlying mechanisms of these conditions and inform the development of more targeted preventive and therapeutic strategies.

**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**: The study found that 25% of the total participants had NAFLD. Among the diabetic patients, the prevalence of NAFLD was significantly higher at 32.7% compared to 17.3% in the control group. On average, individuals with NAFLD exhibited significantly higher ALT levels (33.4 ± 10.7) compared to those without the disease (18.1 ± 6.9), with a highly statistically significant p-value of 0.0001. Similarly, AST levels mirrored this pattern, showing a marked elevation in the NAFLD group (32.0 ± 11.5) compared to the control group (14.6 ± 6.8), again with a statistically significant p-value of 0.0001. The average ALP levels were comparable (30.1 ± 13.8 in NAFLD-positive vs 29.8 ± 14.3 in NAFLD-negative), with a p-value of 0.9032. GGT levels also showed no statistically significant difference (24.1 ± 9.1 in NAFLD-positive vs 23.2 ± 10.2 in NAFLD-negative), with a p-value of 0.6007.

**Conclusion:** Elevated liver enzymes in NAFLD patients suggest ongoing liver inflammation and potential progression towards more severe liver conditions. This underscores the need for regular liver function monitoring in diabetic patients.

**Keywords:** *Non-alcoholic Fatty Liver Disease (NAFLD), Diabetes Mellitus (DM), Metabolic Syndrome, Liver Enzymes, Hepatic Steatosis*

**1.0 INTRODUCTION**

Liver disease is an important cause of mortality in type 2 DM and diabetes has been reported as a common cause of liver disease across the globe.[1] The spectrum of liver disease in DM ranges from abnormal liver enzymes, NAFLD, cirrhosis, and hepatocellular carcinoma, while acute liver failure can also manifest in patients with type 2 DM.[1]

Non-alcoholic fatty liver disease (NAFLD) is a chronic liver condition that encompasses a wide spectrum of liver diseases ranging from fatty liver alone (steatosis) to fatty liver with inflammation (steatohepatitis)[2] and is characterized by insulin resistance and hepatic fat accumulation, in the absence of other known causes of hepatic fat accumulation which include but not limited to alcohol, viral hepatitis, medications, toxins, autoimmune liver disease.[3]

NAFLD represents a significant and growing public health concern worldwide, particularly among individuals with diabetes.[4–6] Characterized by excessive fat accumulation in the liver without significant alcohol consumption, NAFLD encompasses a spectrum of liver conditions, from simple steatosis to non-alcoholic steatohepatitis (NASH), which can progress to cirrhosis and hepatocellular carcinoma.[6–8] The prevalence of NAFLD is notably higher in persons with diabetes, implicating a complex interplay of metabolic, genetic, and environmental factors that exacerbate the risk and severity of liver disease in persons with diabetes.[9, 10]

NAFLD and diabetes are two increasingly prevalent chronic conditions with a well-established bidirectional relationship.[11, 12] Individuals with diabetes have a significantly higher risk of developing NAFLD, and conversely, NAFLD is thought to contribute to the development and progression of diabetes.[13, 14] This association highlights the critical need for a deeper understanding of NAFLD in diabetic populations. This study aims to assess the prevalence of NAFLD among individuals with diabetes and identify the associated factors that contribute to its development. By investigating this relationship, we hope to gain valuable insights into the shared underlying mechanisms of these conditions and inform the development of more targeted preventive and therapeutic strategies. This paper aims to assess the prevalence of NAFLD in persons with diabetes and identify associated factors that may influence its development and progression.

**2.0 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 300 participants aged 18 and above, consisting of 150 diabetic patients and 150 age- and sex-matched controls. Diabetic patients were screened to exclude those positive for hepatitis B surface antigen, hepatitis C virus antibody, and those with significant alcohol history. The control group was similarly matched in demographics to ensure comparability.

**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.[15] 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, medical history, and lifestyle factors. 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 was 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 demographic characteristics of two groups, each consisting of 150 individuals: cases (diabetic patients) and controls. In terms of age distribution, both groups have 19 individuals (12.7%) in the 30-39 years age group. In the 40-49 years age group, there are 37 cases (24.7%) and 40 controls (26.7%). The 50-59 years age group has the largest representation with 55 cases (36.7%) and 57 controls (38.0%). In the 60-69 years age group, there are 35 cases (23.3%) and 31 controls (20.7%), while the 70-79 years age group is the smallest with 4 cases (2.7%) and 3 controls (2.0%). Regarding sex distribution, there are 29 males (19.3%) and 121 females (80.7%) among the cases, compared to 36 males (24.0%) and 114 females (76.0%) in the control group. Educational attainment shows that 21 cases (14.0%) and 11 controls (7.3%) have primary education. Secondary education is reported by 41 cases (27.3%) and 44 controls (29.3%), while tertiary education is the highest among both groups, with 88 cases (58.7%) and 95 controls (63.3%). In terms of marital status, the majority of individuals in both groups are married, with 124 cases (82.7%) and 117 controls (78.0%). There are 7 single cases (4.7%) compared to 31 single controls (20.7%), and 19 widowed cases (12.7%) compared to only 2 widowed controls (1.3%). This table effectively compares the demographic variables between diabetic patients and the control group, highlighting similarities and differences across various categories**.**

**Table 1: Sociodemographic distribution of Subjects**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | | **Groups** | |
| **Cases**  **n = 150 (%)** | **Control**  **n = 150(%)** |
| **Age group** | 30 - 39 years | 19 (12.7) | 19 (12.7) |
| 40 - 49 years | 37 (24.7) | 40 (26.7) |
| 50 - 59 years | 55 (36.7) | 57 (38.0) |
| 60 - 69 years | 35 (23.3) | 31 (20.7) |
| 70 - 79 years | 4 (2.7) | 3 (2.0) |
| **Sex** | Male | 29 (19.3) | 36 (24.0) |
| Female | 121 (80.7) | 114 (76.0) |
| **Education** | Primary | 21 (14.0) | 11 (7.3) |
| Secondary | 41 (27.3) | 44 (29.3) |
| Tertiary | 88 (58.7) | 95 (63.3) |
| **Marital status** | Married | 124 (82.7) | 117 (78.0) |
| Single | 7 (4.7) | 31 (20.7) |
| Widowed | 19 (12.7) | 2 (1.3) |

The results showed that 32.7% of persons with type II DM had NAFLD (Figure 1).

The results presented in Table 2 showed that 49 out of 150 cases (32.7%) tested positive for NAFLD, whereas only 26 out of 150 controls (17.3%) were positive. This difference is statistically significant, as evidenced by a Chi-square value of 9.40 with a p-value of 0.002, indicating a strong association between diabetes and NAFLD. The odds ratio (OR) is 2.3, with a 95% confidence interval (C.I) ranging from 1.3 to 3.9, suggesting that diabetic patients are more than twice as likely to have NAFLD compared to the control group.

**Table 2: Association of NAFLD and Type II DM**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **NAFLD** | **Case**  **n, (%)** | **Control**  **n, (%)** | **Chi-square (p-value)** | | **OR (95% C.I)** |
| Positive | 49 (32.7) | 26 (17.3) | 9.40 (0.002)\* | | 2.3 (1.3 – 3.9) |
| Negative | 101 (67.3) | 124 (82.7) |  | |  |
| **Total** | **150 (100.0)** | **150 (100.0)** | |  | |

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

The study's results (Table 3) demonstrate significant differences in liver enzyme levels between individuals with non-alcoholic fatty liver disease (NAFLD) and those without. For alanine transaminase (ALT), the mean level in NAFLD-positive individuals was 33.4 ± 10.7, significantly higher than the 18.1 ± 6.9 observed in NAFLD-negative individuals, with a p-value of 0.0001. Similarly, aspartate transaminase (AST) levels were elevated in NAFLD-positive individuals (32.0 ± 11.5) compared to those without NAFLD (14.6 ± 6.8), also with a p-value of 0.0001. However, there were no significant differences in alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) levels between the two groups. The mean ALP levels were 30.1 ± 13.8 in NAFLD-positive individuals and 29.8 ± 14.3 in NAFLD-negative individuals, with a p-value of 0.9032. GGT levels were 24.1 ± 9.1 in the NAFLD-positive group and 23.2 ± 10.2 in the NAFLD-negative group, with a p-value of 0.6007.

**Table 3: Differences in liver enzyme levels**

|  |  |  |  |
| --- | --- | --- | --- |
| **Liver Enzymes** | **NAFLD Positive**  **mean ±SD** | **NAFLD Negative**  **mean ±SD** | **T-test**  **(p-value)** |
| ALT | 33.4 ±10.7 | 18.1 ±6.9 | 0.0001\* |
| AST | 32.0 ±11.5 | 14.6 ±6.8 | 0.0001\* |
| ALP | 30.1 ±13.8 | 29.8 ±14.3 | 0.9032 |
| GGT | 24.1 ±9.1 | 23.2 ±10.2 | 0.6007 |

*NAFLD=Non-Alcoholic Fatty Liver Disease, AST=Aspartate Transaminase, ALT=Alanine Transaminase, ALP=Alkaline Phosphatase, GGT=Gamma Glutamyl Transferase*

The analysis in Table 4 investigated the association between various liver enzymes and Non-alcoholic Fatty Liver Disease (NAFLD). While no significant differences were found for alkaline phosphatase (ALP) or gamma-glutamyl transferase (GGT), both alanine aminotransferase (ALT) and aspartate aminotransferase (AST) showed strong associations. Individuals with elevated ALT levels were over 10 times more likely to have NAFLD compared to those with normal ALT (OR: 10.4, 95% CI: 1.3 – 18.7). Similarly, elevated AST levels were associated with an over 7-fold increased risk of NAFLD (OR: 7.5, 95% CI: 4.5 – 8.2).

**Table 4: Distribution of liver enzyme levels by NAFLD in Persons with DM**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variables** | **NAFLD Positive**  **n = 49, (%)** | **NAFLD Negative**  **n = 101, (%)** | **Chi-square**  **(p-value)** | **OR (95% C.I)** |
| **ALP**  Elevated  Normal | 11 (22.4) | 24 (23.8) | 0.03 (0.858) | 0.9 (0.4 – 2.1) |
| 38 (77.6) | 77 (76.2) |
| **GGT**  Elevated  Normal | 9 (18.4) | 16 (15.8) | 0.15 (0.697) | 1.1 (0.4 – 2.9) |
| 40 (81.6) | 85 (84.2) |
| **ALT**  Elevated  Normal | 25 (51.0)  24 (49.0) | 1 (1.0)  100 (99.0) | 57.63 (0.0001)\* | 10.4 (1.3 – 18.7) |
| **AST**  Elevated  Normal | 21 (42.9)  28 (57.1) | 1 (1.0)  100 (99.0) | 46.20 (0.0001)\* | 7.5 (4.5 – 8.2) |

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

*NAFLD=Non-Alcoholic Fatty Liver Disease, AST=Aspartate Transaminase, ALT=Alanine Transaminase, ALP=Alkaline Phosphatase, GGT=Gamma Glutamyl Transferase*

**4.0 DISCUSSION**

Building on prior research, this study reinforces the concerning link between type II diabetes mellitus (T2DM) and non-alcoholic fatty liver disease (NAFLD). Similar to findings reported in the study by Marjot et al.,[16], a statistically significant association was observed, with 32.7% of individuals with T2DM testing positive for NAFLD compared to only 17.3% in the control group. This aligns with the growing body of evidence suggesting diabetic patients are more than twice as likely to develop NAFLD, as evidenced by the odds ratio of 2.3 (95% CI: 1.3-3.9).[17, 18]

Promoting healthy lifestyles across the population, with a focus on weight management, balanced diets, and regular exercise, can play a crucial role in mitigating the risk of both T2DM and NAFLD, as emphasized in Ballestri et al.,[18]. Continuing from the previous analysis of the association between NAFLD and diabetes, this study sheds light on the role of specific liver enzymes in identifying the disease. The findings reveal a clear distinction in the levels of ALT and AST between individuals with and without NAFLD. These findings strongly suggest that ALT and AST serve as more reliable markers for detecting NAFLD compared to ALP and GGT. The considerably elevated levels of ALT and AST in individuals with NAFLD point towards the presence of liver inflammation or damage, potentially caused by excess fat accumulation in the liver.[19, 20] In contrast, ALP and GGT levels appear to be less indicative of NAFLD on their own. Similar study carried out in the South-West of the country also reported that more diabetic participants with NAFLD had elevated AST of 7.1%, and ALT of 10.7% compared with their non-NAFLD counterpart (4.3% and 9.3% respectively).[21]

This current study found no significant relationship between ALP and GGT, and NAFLD, thus corroborating the earlier mentioned Nigerian study. Mandal et al[22]carried out a similar study in Europe on 210 diabetic patients in which ALT was found to be the commonest abnormal liver enzyme and was elevated in 40.4% of the study population. This was similar to the findings of the current study which also found ALT to be the most common enzyme to be elevated and was found in about half of the diabetic subjects with NAFLD compared with only 1 individual in the non-NAFLD diabetic group. López-Amador et al also reported that the most frequent alteration was ALT level elevation (72.5% of type 2 DM patients with NAFLD) with a higher level relative to AST level (25% patients type 2 DM patients with NAFLD).[23]

This distinction in the diagnostic utility of different liver enzymes holds significant implications for clinical practice. By focusing on ALT and AST levels, healthcare professionals can gain valuable insights into potential NAFLD and implement earlier interventions to prevent disease progression. The high prevalence of NAFLD among diabetic patients highlights the interrelation between diabetes and liver health. The study's findings align with global trends indicating a strong association between metabolic syndrome components and NAFLD.

**CONCLUSION**

This study confirms a substantial burden of NAFLD among diabetic patients in Southern Nigeria. Given the association between NAFLD and metabolic syndrome components, routine screening for liver abnormalities in diabetic patients is recommended. Early detection through liver enzyme tests and ultrasound examinations can facilitate timely interventions, potentially mitigating the progression of liver disease. Future research should focus on longitudinal studies to better understand NAFLD's natural history in diabetic populations and evaluate the effectiveness of targeted interventions.

**REFERENCES**

[1] Tolman KG, Fonseca V, Dalpiaz A, et al. Spectrum of liver disease in type 2 diabetes and management of patients with diabetes and liver disease. *Diabetes Care* 2007; 30: 734–743.

[2] Ratziu V, Bellentani S, Cortez-Pinto H, et al. *A position statement on NAFLD/NASH based on the EASL 2009 special conference q Position Paper*. 2010. Epub ahead of print 2010. DOI: 10.1016/j.jhep.2010.04.008.

[3] Ali R, Cusi K. New diagnostic and treatment approaches in non-alcoholic fatty liver disease (NAFLD). *Annals of Medicine* 2009; 41: 265–278.

[4] McPherson S, Hardy T, Henderson E, et al. Evidence of NAFLD progression from steatosis to fibrosing-steatohepatitis using paired biopsies: implications for prognosis and clinical management. *J Hepatol* 2015; 62: 1148–1155.

[5] Kleiner DE, Brunt EM, Wilson LA, et al. Association of histologic disease activity with progression of nonalcoholic fatty liver disease. *JAMA Netw Open*; 2.

[6] Younossi ZM, Koenig AB, Abdelatif D, et al. Global epidemiology of nonalcoholic fatty liver disease-meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology* 2016; 64: 73–84.

[7] Ryu S, Chang Y, Jung HS, et al. Relationship of sitting time and physical activity with non-alcoholic fatty liver disease. *J Hepatol* 2015; 63: 1229–1237.

[8] Hazlehurst JM, Woods C, Marjot T, et al. Non-alcoholic fatty liver disease and diabetes. *Metabolism* 2016; 65: 1096–1108.

[9] Olaogun I, Farag M, Hamid P. The Pathophysiology of Type 2 Diabetes Mellitus in Non-obese Individuals: An Overview of the Current Understanding. *Cureus*. Epub ahead of print 10 April 2020. DOI: 10.7759/CUREUS.7614.

[10] Weir GC, Gaglia J, Bonner-Weir S. Inadequate β-cell mass is essential for the pathogenesis of type 2 diabetes. *Lancet Diabetes Endocrinol* 2020; 8: 249–256.

[11] DiStefano JK, Gerhard GS. NAFLD in normal weight individuals. *Diabetol Metab Syndr*; 14. Epub ahead of print 1 December 2022. DOI: 10.1186/S13098-022-00814-Z.

[12] Kosmalski M, Śliwińska A, Drzewoski J. Non-Alcoholic Fatty Liver Disease or Type 2 Diabetes Mellitus—The Chicken or the Egg Dilemma. *Biomedicines 2023, Vol 11, Page 1097* 2023; 11: 1097.

[13] Atan NAD, Koushki M, Motedayen M, et al. Type 2 diabetes mellitus and non-alcoholic fatty liver disease: a systematic review and meta-analysis. *Gastroenterol Hepatol Bed Bench* 2017; 10: S1.

[14] Dharmalingam M, Yamasandhi PG. Nonalcoholic Fatty Liver Disease and Type 2 Diabetes Mellitus. *Indian J Endocrinol Metab* 2018; 22: 421.

[15] Cheesbrough M. *Distric Laboratory practice in tropical countries*. Second Edi. New York, NY, US: Cambridge University Press (CUP), 2006.

[16] Marjot T, Sbardella E, Moolla A, et al. Prevalence and severity of non-alcoholic fatty liver disease are underestimated in clinical practice: impact of a dedicated screening approach at a large university teaching hospital. *Diabetic Medicine* 2018; 35: 89–98.

[17] Younossi Z, Stepanova M, Ong JP, et al. Nonalcoholic Steatohepatitis Is the Fastest Growing Cause of Hepatocellular Carcinoma in Liver Transplant Candidates. *Clinical Gastroenterology and Hepatology* 2019; 17: 748-755.e3.

[18] Ballestri S, Zona S, Targher G, et al. Nonalcoholic fatty liver disease is associated with an almost twofold increased risk of incident type 2 diabetes and metabolic syndrome. Evidence from a systematic review and meta-analysis. *Journal of Gastroenterology and Hepatology (Australia)* 2016; 31: 936–944.

[19] Lomonaco R, Leiva EG, Bril F, et al. Advanced liver fibrosis is common in patients with type 2 diabetes followed in the outpatient setting: The need for systematic screening. *Diabetes Care* 2021; 44: 399–406.

[20] Davila JA, Morgan RO, Shaib Y, et al. Diabetes increases the risk of hepatocellular carcinoma in the United States: A population based case control study. *Gut* 2005; 54: 533–539.

[21] Olusanya TO, Lesi OA, Adeyomoye AA, et al. Non alcoholic fatty liver disease in a Nigerian population with type II diabetes mellitus. *Pan African Medical Journal*; 24. Epub ahead of print 2016. DOI: 10.11604/pamj.2016.24.20.8181.

[22] Mandal A, Bhattarai B, Kafle P, et al. Elevated Liver Enzymes in Patients with Type 2 Diabetes Mellitus and Non-alcoholic Fatty Liver Disease. *Cureus*. Epub ahead of print 2018. DOI: 10.7759/cureus.3626.

[23] López-Amador, Nolasco-Hipolito R, Jas-Jimeno C-Z, et al. diagnosed with non-alcoholic Veracruz : a comparative analysis. 2017; 7: 11–16.