ORIGINAL ARTICLE

Evaluating Non-Alcoholic Fatty Liver Disease in Individuals with and without Type 2 Diabetes Comparative Cross-Sectional Study using Ultrasound Imaging

Muhammad Zaid Iqbal[1*], Ayesha Irfan[2], Mohsin Ejaz[3], Aamena Gardazi[4], Hamd Binte Shahab Syed[5], Amad Ali[6]

ABSTRACT

Objective: Non-Alcoholic Fatty Liver Disease (NAFLD) is a significant health concern globally, particularly in individuals with Type 2 Diabetes Mellitus (T2DM). This study aims to evaluate the frequency and severity of NAFLD among diabetic and non-diabetic populations using ultrasound imaging, focusing on its implications in Pakistan.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: The study was conducted at the Department of Medicine, Ibn-e-Siena Hospital & Research Institute, Multan, Pakistan from 17th September 2018 to 16th March 2019.

Methods: A total of 324 participants were enrolled, including 162 patients diagnosed with type 2 diabetes mellitus and 162 age- and gender-matched non-diabetic controls. The study included male and female patients aged 30-60 years, diagnosed with type 2 diabetes and on oral hypoglycemic agents or insulin for at least one year. Patients with suspected autoimmune hepatitis, viral hepatitis, chronic liver disease, excessive alcohol consumption, or those unwilling to participate were excluded. Abdominal ultrasonography was employed to assess liver echogenicity and grade hepatic steatosis. Statistical analysis was carried out using SPSS version 26.0. Categorical variables were analyzed using the chi-square test, while continuous variables were assessed using the independent t-test. A *P*-value <0.05 was considered statistically significant.

Results: The frequency of NAFLD was significantly higher in the diabetic group (76%) compared to non-diabetics (48%) ($P < 0.001$). Moreover, moderate to severe NAFLD was more frequent in diabetics (54%) than in non-diabetics (20%). NAFLD severity showed a significant correlation with increasing age (≥50 years), obesity (BMI ≥30 kg/m²), and poor glycemic control (HbA1c ≥7%).

Conclusion: Non-alcoholic fatty liver disease (NAFLD) is more prevalent and severe in type 2 diabetics compared to non-diabetics, as assessed through ultrasound imaging anatomy.

Keywords: *Dyslipidemia, Metabolic Syndrome, Non-Alcoholic Fatty Liver Disease (NAFLD), Type 2 Diabetes Mellitus, Ultrasonography.*

How to cite this: *Iqbal MZ, Irfan A, Ejaz M, Gardazi A, HBS Syed, Ali A. Evaluating Non-Alcoholic Fatty Liver Disease in Individuals with and without Type 2 Diabetes Comparative Cross-Sectional Study using Ultrasound Imaging. Life and Science. 2025; 6(3): 344-349. doi: http://doi.org/10.37185/LnS.1.1.772*

[1]*Department of Medicine*
Nishtar Medical University, Multan, Pakistan
[2]*Department of Anatomy*
Multan Medical & Dental College, Multan, Pakistan
[3]*District Headquarter Hospital South City, Multan, Pakistan*
[4]*Department of Medicine/Anatomy*[6]
Bakhtawar Amin Medical and Dental College, Multan, Pakistan
[5]*Department of Anatomy*
D. G. Khan Medical College, Dera Ghazi Khan, Pakistan
Correspondence:
Dr. Muhammad Zaid Iqbal
Department of Medicine
Nishtar Medical University, Multan, Pakistan
E-mail: zaidiqbal6774@gmail.com

Introduction

Non-alcoholic fatty liver disease (NAFLD) encompasses a spectrum of hepatic lesions, ranging from simple steatosis without significant necroinflammatory damage to non-alcoholic steatohepatitis (NASH), characterized by hepatocyte injury, apoptosis, cell death, and inflammation in the absence of alcohol consumption.[1] NAFLD is closely associated with obesity, insulin resistance, type 2 diabetes mellitus (T2DM), and other metabolic abnormalities such as dyslipidemia and

Received: July 21, 2024; 1st Revision Received: Jan 23, 2025
2nd Revision Received: May 10, 2025; Accepted: May 16, 2025

hypertension, collectively termed metabolic syndrome.[2] Additionally, NAFLD is linked with cardiovascular disease, which manifests as increased thickness of the tunica intima and media and the presence of carotid plaques, indicative of progressive atherosclerosis.[3]

The pathophysiology of NAFLD encompasses various mechanisms, such as reduced mitochondrial fatty acid beta-oxidation, heightened endogenous fatty acid synthesis, increased delivery of fatty acids to the liver, and impaired incorporation or export of triglycerides as very low-density lipoprotein (VLDL).[4] Numerous genes have been identified as potential contributors to the onset and progression of NAFLD.[5] Dietary factors, such as high intake of sugar-sweetened foods and beverages, particularly those high in fructose, also play a significant role in NAFLD pathogenesis.

Type 2 diabetes mellitus is marked by hyperglycemia due to a combination of insulin resistance, insufficient insulin secretion, and excessive or inappropriate glucagon secretion. Although many patients with T2DM are asymptomatic, classic symptoms can include polyuria, polydipsia, polyphagia, weight loss, soft tissue infections, blurred vision, and lower limb paresthesias.[6]

Epidemiological studies indicate a high frequency of NAFLD among individuals with T2DM. For instance, research in Iran reported an 86.66% frequency of NAFLD in T2DM patients, while a study in Korea found a frequency of 63.3%.[7,8] In Pakistan, a study by Alavi N. revealed that 69% of T2DM patients had NAFLD.[9]

The frequency of NAFLD varies widely across different populations, influenced by racial and genetic factors. However, there is a notable gap in comprehensive data on NAFLD frequency in the Pakistani population, particularly when comparing T2DM and non-diabetic groups. This study aims to bridge this gap by evaluating the burden of NAFLD in both T2DM and non-diabetic populations using ultrasound anatomy imaging.

Understanding NAFLD frequency and characteristics in the Pakistani population, particularly between T2DM and non-diabetic groups, is crucial due to the rising incidence of T2DM and metabolic syndrome in Pakistan. This study leverages non-invasive ultrasound imaging to provide accurate data on NAFLD, facilitating early diagnosis and management. By systematically comparing these populations, we aim to elucidate the specific impact of T2DM on liver health, contributing to global knowledge and informing targeted public health interventions.

Methods

The study was conducted at the Department of Medicine, Ibn-e-Siena Hospital & Research Institute, Multan, Pakistan. The research spanned six months from 17th September 2018 to 16th March 2019 after taking approval from the Ethical Review Board of the institute vide letter no: A-8-817, held on 30th August 2018. Initially, a sample size of 324 patients was planned. After excluding 5 patients, 324 patients were included in the final analysis. These 324 patients were divided into two groups: 162 type 2 diabetic patients and 162 non-diabetic individuals.

The sampling technique used was consecutive non-probability sampling. Inclusion criteria for both groups were: male and female patients aged between 30 and 60 years. The type 2 diabetic group consisted of individuals diagnosed with type 2 diabetes mellitus and on oral hypoglycemic agents or insulin for at least one year. The non-diabetic group included individuals without a diagnosis of diabetes. Exclusion criteria for both groups included patients with suspected autoimmune hepatitis (indicated by ANA, ASMA, or liver biopsy), viral hepatitis B and C (detected by ELISA), chronic liver disease (confirmed by abdominal ultrasound), patients consuming more than 30 grams of ethanol per day, and those unwilling to participate in the study.

To assess the presence and severity of non-alcoholic fatty liver disease (NAFLD), all participants underwent abdominal ultrasound imaging. The ultrasound examinations were performed using a high-resolution ultrasound machine with a curvilinear transducer.

The procedure was conducted by trained radiologists who followed standardized protocols to ensure consistency and accuracy. The imaging focused on evaluating liver echogenicity and detecting signs of fatty infiltration.

Key parameters assessed included the following:

Increased liver echogenicity compared to the renal cortex was used to indicate fatty infiltration.

The size and contour of the liver were evaluated to identify any abnormal enlargement or irregularities.

The degree of steatosis was categorized as mild, moderate, or severe based on the echogenicity and the liver-to-kidney echogenicity ratio.

Data analysis was conducted using SPSS version 26.0. Categorical data were represented as frequencies and percentages, while continuous data were presented as means and standard deviations. A t-test was utilized to compare continuous variables, and the chi-square test was employed for categorical data analysis. A *P*-value of less than 0.05 was considered statistically significant.

Results

The mean age of participants was 46.03 ± 8.92 years, with no significant difference between diabetics and non-diabetics. The diabetic group had a higher BMI (≥30 kg/m²) and HbA1c levels (≥7%) compared to the non-diabetic group ($P < 0.001$).

Overall, NAFLD frequency was 62%, with a significantly higher frequency in diabetics (76%) than non-diabetics (48%) ($P < 0.001$). Moderate to severe NAFLD was more frequent in diabetics (54%) compared to non-diabetics (20%) ($P < 0.001$).

Age ≥50 years, BMI ≥30 kg/m², and HbA1c ≥7% were independently associated with higher NAFLD severity. Gender differences were not statistically significant. Key findings underscore a higher frequency and greater severity of NAFLD among diabetic patients, with age, obesity, and glycemic control emerging as substantial contributors. These results align with the hypothesis that metabolic disturbances in diabetics exacerbate NAFLD progression. (Table 1).

Table 1: Participant characteristics of the study between the Groups

Continuous Characteristics	Type II Diabetics (N = 162)		Non- diabetics (N = 162)	
	Mean	SD	Mean	SD
Age (Years)	46.20	8.86	45.86	8.96
Categorical Characteristics	Male N (%)		Female N (%)	
Type II Diabetics (N = 162)	61 (38%)		101 (62%)	
Non- diabetics (N = 162)	59 (36%)		103 (64%)	

Table 2: Ultrasound Findings of Liver Characteristics in Type II Diabetics and Non-diabetics

Groups	Liver echogenicity		Liver size		Presence of Steatosis	
	Increased	Normal	Enlargement	Normal Size and Contour	Yes	No
Type II Diabetics	118 (73%)	44 (27%)	112 (69%)	50 (31%)	104 (64%)	58 (36%)
Non- diabetics	80 (49%)	82 (51%)	73 (45%)	89 (55%)	59 (36%)	103 (64%)
t-test value	18.753		19.164		25.001	
P- value	.000*		.000*		.000*	

Table 3: Biochemical Markers in Type II Diabetics and Non-diabetics

Biochemical markers	Type II Diabetics (N = 162)		Non- diabetics (N = 162)			
	Mean	SD	Mean	SD	*t-test* value	*P*-value
Serum ALT (U/L)	57.06	25.07	47.51	22.84	0.399	0.000*
Serum AST (U/L)	41.74	19.81	37.52	16.64	-0.402	0.039*
HbA1c	8.44	1.98	5.13	1.11	18.530	0.000*

Discussion

The comparison of the assessment of NAFLD to T2DM patients and non-diabetic populations is important as both conditions are becoming more common around the world. This cross-sectional study, performed at Ibn-e-Siena Hospital, Multan, Pakistan, with the help of Ultrasonography for detecting liver echogenicity and steatosis in 324

participants, showed highly effective results, with elevated rates and greater severity of NAFLD in the diabetic group (76%) compared to the non-diabetic group (48%).[10] We have established that some form of imaging should be the approach to diagnosing moderate to severe fatty liver diseases using non-invasive techniques including the use of ultrasonic technology, which has revealed good sensitivity and specificity in diagnosing FLD.[11]

NAFLD and T2DM are o, are associated with insulin resistance. Insulin resistance does not act merely as a risk factor for the accumulation of fat within the liver but also as a modulator that worsens the clinical manifestation of NAFLD.[12] These findings are consistent with earlier literature showing that NAFLD complicates metabolic syndrome, which encompasses T2DM.[10] In addition, the observed relationship between the progression of NAFLD and risk factors, including age, BMI, and HbA1c levels, suggests that metabolic disturbance is the most probable factor behind NAFLD in diabetics.[13] However, these conclusions are not confined to hepatic conditions only, as the chapter reveals above. NAFLD has been linked to cardiovascular disease in patients with T2DM.[14] The present investigation calls for early detection and intervention of NAFLD among the diabetic population to reduce its attendant cardiovascular risk and other features of metabolic syndrome.[15] Practice of using ultrasound imaging in primary care could also mean that opportunities to intervene early is created and therefore patient benefits would be realized.[16]

Table-2 compares the results of the study, showing differences in liver features in Type II diabetics compared to non-diabetics using ultrasonic examination. The results suggest that more Type II diabetes patients have higher liver echogenicity than the non-diabetes patients, that is, 118 out of 162, with a significant $P < 0.001$. This finding accords with other studies, which have reported that diabetes serves as a risk factor for hepatic steatosis, a defining feature of NAFLD. The higher echochencity seen in diabetics therefore relates to more fat in the liver, the cardinal feature of NAFLD in which excess tryglycerides accumulate in liver cells – Hepatocytes.[17] Again, the results were statistically significant: 112 out of Type II diabetics had an enlarged liver compared to 73 non-diabetic patients, $P < 0.001$. This enlargement of the liver in diabetics can be blamed on the metabolic derangement that characterizes insulin resistance, a common condition among diabetics.[18] The interaction between liver enlargement and diabetes is well understood since the liver is involved directly in the regulation of glucose and lipid metabolism, and IR is often aggravated by liver dysfunction.[18] The presence proved to be significantly higher in the Type II Diabetic group with 104 patients demonstrating steatosis as opposed to 59 non-diabetic patients ($P = 0.003$). This comes out clearly to show that NAFLD is strongly associated with diabetes. The existing literature explains that patients with T2DM face a higher likelihood of steatosis owing to obese societies, inactive living standards, and abnormal diets.

The biochemical characteristics listed in table-3 show differences between Type II diabetics and non-diabetics, mainly involving serum ALT, AST, and HbA1c. The mean serum ALT level in this group of Type II diabetics was 57.06 U/L, while in the non-diabetic control group, the value obtained was 47.51 U/L, $P < 0.001$. It was 41.74 U/L in diabetics and 37.52 U/L in non-diabetics with $P = 0.039$. These findings are consistent with the understanding that elevated liver enzymes are indicative of liver injury or dysfunction, commonly associated with Non-Alcoholic Fatty Liver Disease (NAFLD) and metabolic disorders.[18] Elevated serum ALT and AST in Type II diabetics can be a result of NAFLD, which is associated with hepatic steatosis and inflammation. Research works have highlighted the fact that patients with diabetes have been proven to have raised liver enzymes occasioned by fatty liver infiltration leading to hepatocellular damage.[19,20] Hypoxic stress impairs the liver's essential function regarding glucose homeostasis, and it only makes insulin resistance worse by increasing the challenge of diabetic regulation.[20] In addition, the mean HbA1c level in the Type II diabetics was significantly higher at 8.44±5.44% compared to non-diabetics whose mean HbA1c level was 5.13±1.07% ($P < 0.001$). This variation highlights the failures to obtain good glycemic control seen in diabetic patients, which can be contributing factors for NAFLD development and

manifestation.[21,22] Multiple studies have established a connection between elevated HbA1c and NAFLD, as chronic hyperglycemia predisposes individuals to lipogenesis, leading to increased fat accumulation in the liver.[19,23]

This study offers a novel contribution by providing one of the few comparative assessments of NAFLD in diabetic and non-diabetic individuals within the Pakistani population. It uniquely highlights the statistically significant link between NAFLD severity and metabolic risk factors sucha as age, obesity, and poor glycemic control. Using age- and gender-matched groups to ensure robust comparison. The use of ultrasound as a practical, non-invasive screening tool further strengthens its clinical relevance.

Limitations

There are certain limitations to this study. Ultrasound-based diagnosis, although it is practical but it lacks the precision of histological confirmation (e.g., liver biopsy). The study does not track NAFLD progression or response to treatment over time.

Conclusion

In conclusion, non-alcoholic fatty liver disease (NAFLD) is more prevalent and severe in type 2 diabetics compared to non-diabetics, as assessed through ultrasound imaging anatomy.

Acknowledgement: None

Conflict of Interest: The authors declare no conflict of interest

Grant Support and Financial Disclosure: None

REFERENCES

1. Ye Q, Zou B, Yeo YH, Li J, Huang DQ, Wu Y, et al. Global prevalence, incidence, and outcomes of non-obese or lean non-alcoholic fatty liver disease: a systematic review and meta-analysis. The lancet Gastroenterology & Hepatology. 2020; 5: 739-52. doi: 10.1016/S2468-1253(20)30077-7
2. Qureshi K, Neuschwander-Tetri BA. The molecular basis for current targets of NASH therapies. Expert opinion on investigational drugs. 2020; 29: 151-61. doi: 10.1080/13543784.2020.1703949
3. Kasper P, Martin A, Lang S, Kuetting F, Goeser T, Demir M, et al. NAFLD and cardiovascular diseases: a clinical review. Clinical research in cardiology. 2021; 110: 921-37. doi: 10.1007/s00392-020-01709-7
4. Acierno C, Caturano A, Pafundi PC, Nevola R, Adinolfi LE, Sasso FC. Nonalcoholic fatty liver disease and type 2 diabetes: Pathophysiological mechanisms shared between the two faces of the same coin. Exploration of Medicine. 2020; 1: 287-306. doi: 10.37349/emed.2020.00019
5. Di Rosa M, Malaguarnera L. Genetic variants in candidate genes influencing NAFLD progression. Journal of molecular medicine. 2012; 90: 105-18. doi: 10.1007/s00109-011-0803-x
6. Rossboth S, Lechleitner M, Oberaigner W. Risk factors for diabetic foot complications in type 2 diabetes—a systematic review. Endocrinology, Diabetes & Metabolism. 2021; 4: e00175. doi: 10.1002/edm2.175
7. Heidari Z, Gharebaghi A. Frequency of non alcoholic fatty liver disease and its association with diabetic nephropathy in patients with type 2 diabetes mellitus. Journal of clinical and diagnostic research. 2017; 11: OC04-7. doi: 10.7860/JCDR/2017/25931.9823
8. Kim BY, Jung CH, Mok JO, Kang SK, Kim CH. Prevalences of diabetic retinopathy and nephropathy are lower in K orean type 2 diabetic patients with non-alcoholic fatty liver disease. Journal of diabetes investigation. 2014; 5: 170-5. doi: 10.1111/jdi.12139
9. Alavi N, Amin S, Mumtaz M. Non-alcoholic fatty liver disease (NAFLD): frequency in diabetes mellitus (type II) patients and non-diabetic group at Shalamar Medical and Dental College, Lahore. The Professional Medical Journal. 2016; 23: 029-033. doi: 10.17957/TPMJ/16.3110
10. Lee BW, Lee YH, Park CY, Rhee EJ, Lee WY, Kim NH, et al. Non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus: a position statement of the Fatty Liver Research Group of the Korean Diabetes Association. Diabetes & metabolism journal. 2020; 44: 382-401. doi: 10.4093/dmj.2020.0010
11. Hung WC, Yu TH, Wu CC, Lee TL, Tang WH, Chen CC, et al. Nonalcoholic fatty liver disease is related to abnormal corrected QT interval and left ventricular hypertrophy in Chinese male steelworkers. International Journal of Environmental Research and Public Health. 2022; 19: 14555. doi: 10.3390/ijerph192114555
12. Araki N, Takahashi H, Takamori A, Kitajima Y, Hyogo H, Sumida Y, et al. Decrease in fasting insulin secretory function correlates with significant liver fibrosis in Japanese non-alcoholic fatty liver disease patients. JGH Open. 2020; 4: 929-36. doi: 10.1002/jgh3.12367
13. Aimuzi R, Xie Z, Qu Y, Jiang Y. Air pollution, life's essential 8, and risk of severe non-alcoholic fatty liver disease among individuals with type 2 diabetes. BMC Public Health. 2024; 24: 1350. doi: 10.1186/s12889-024-18641-4
14. Fiorentino TV, Succurro E, Sciacqua A, Andreozzi F, Perticone F, Sesti G. Non-alcoholic fatty liver disease is associated with cardiovascular disease in subjects with different glucose tolerance. Diabetes/metabolism research and reviews. 2020; 36: e3333. doi: 10.1002/dmrr.3333
15. Shi R, Li X, Sun K, Liu F, Kang B, Wang Y, et al. Association between severity of nonalcoholic fatty liver disease and major adverse cardiovascular events in patients assessed by coronary computed tomography angiography. BMC Cardiovascular Disorders. 2024; 24: 267. doi: 10.1186/s12872-024-03880-5
16. Hayward KL, McKillen BJ, Horsfall LU, McIvor C, Liew K, Sexton J, et al. Towards collaborative management of non-alcoholic fatty liver disease: a 'real-world' pathway for fibrosis risk assessment in primary care. Internal Medicine Journal. 2022; 52: 1749-58. doi: 10.1111/imj.15422

17. Bahnasawy SA, El Gammal NE, El Attar NI, El-Gebaly AM. Liver Fatty Acid-binding Protein (L-FABP) as a Diagnostic Marker for Non-alcoholic Fatty Liver Disease. The Egyptian Journal of Hospital Medicine. 2023; 91: 5345-52. doi: 10.21608/ejhm.2023.305534
18. Olteanu VA, Balan GG, Timofte O, Dascalu CG, Gologan E, Gilca-Blanariu GE, et al. Risk predictors of advanced fibrosis in non-alcoholic fatty liver disease. Diagnostics. 2022; 12: 2136. doi: 10.3390/diagnostics12092136
19. Adhikari P, Oli K, Shrestha S. Diabetes Mellitus among Patients with Non-alcoholic Fatty Liver Disease Visiting the Outpatient Department of Internal Medicine in a Tertiary Care Centre. Journal of the Nepal Medical Association. 2023; 61: 871. doi: 10.31729/jnma.8324
20. Yan C, Bao J, Jin J. Exploring the interplay of gut microbiota, inflammation, and LDL-cholesterol: a multiomics Mendelian randomization analysis of their causal relationship in acute pancreatitis and non-alcoholic fatty liver disease. Journal of Translational Medicine. 2024; 22: 179. doi: 10.1186/s12967-024-04996-0
21. Kuwashiro T, Takahashi H, Hyogo H, Ogawa Y, Imajo K, Yoneda M, et al. Discordant pathological diagnosis of non-alcoholic fatty liver disease: a prospective multicenter study. JGH Open. 2020; 4: 497-502. doi: 10.1002/jgh3.12289
22. Majid Z, Somoro GB, Haque MM, Yaseen RT, Khan SA, Achakzai IK, et al. Non alcoholic fatty liver disease in a young male with celiac disease. Pan African Medical Journal. 2019; 32: 25. doi: 10.11604/pamj.2019.32.25.16345
23. Salari N, Darvishi N, Mansouri K, Ghasemi H, Hosseinian-Far M, Darvishi F, et al. Association between PNPLA3 rs738409 polymorphism and nonalcoholic fatty liver disease: a systematic review and meta-analysis. BMC endocrine disorders. 2021; 21: 125. doi: 10.1186/s12902-021-00789-4

Author Contributions

MZI: Conception and design of the work
AI: Manuscript writing for methodology design and investigation
MI: Validation of data, interpretation, and write-up of results
AG: Data acquisition, curation, and statistical analysis
HBSS: Writing the original draft, proofreading, and approval for final submission
AA: Revising, editing, and supervising for intellectual content