DOI: https://doi.org/10.53350/pjmhs20221612909

ORIGINAL ARTICLE

Prevalence and Risk Factors of Non-Alcoholic Fatty Liver Disease in Patients with Type 2 Diabetes Mellitus: A Cross-Sectional Study at a Tertiary Care Center

SEHRISH SHERAZ[1], ZEESHAN GHIAS KHAN[2], SHUJA ANWAR KAZI[3], FATIMA HASAN KAZMI[4], NEHAL SHAIKH[5], ANIQA SALEEM[6]
[1]*Instructor, BS surgical technology, MSPH public health, Dow institute of medical technology, Dow university of health sciences, SZABIST*
[2]*Consultant Radiologist, MBBS FCPS, DHQ Hospital Gahkuch Gilgit*
[3]*King Faisal University Al-Ahsa, Kingdom of Saudi Arabia*
[4]*MBBS, Liaquat National Medical College & Hospital*
[5]*Department of Medicine, Ghulam Muhammad Mahar Medical College Sukkur, Sindh, Pakistan*
[6]*Lecturer, Physiology, Sindh Institute of Physical Medicine and Rehabilitation*
Corresponding author: Sehrish Sheraz, Email: sehrish.sheraz@ duhs.edu.pk

ABSTRACT

Background: Non-Alcoholic Fatty Liver Disease (NAFLD) is an emerging concern among patients with Type 2 Diabetes Mellitus (DM). This study was designed to evaluate the prevalence of NAFLD in Type 2 DM patients and to identify associated factors that may contribute to its occurrence.

Methodology: Conducted in a tertiary care center's general medicine department from May 2020 to June 2021, this cross-sectional study enrolled 400 type-II diabetic patients, aged 35 years and above. Comprehensive interviews were performed to determine disease duration and medication usage and to exclude alternative causes of NAFLD. Physical examinations, including measurements of BMI and waist-hip circumference, along with abdominal ultrasonography, were utilized to detect and grade fatty liver.

Results: The sample consisted of 217 females (59.8%) and 146 males (40.2%), with 67.2% having a diabetes diagnosis for over 10 years. NAFLD was identified in 69.1% of patients, more frequently in females (69%). A significant relationship was established between NAFLD occurrence and the duration of DM, BMI, and waist-hip ratio ($p < 0.05$).

Conclusion: NAFLD was found in a striking majority of the diabetic population studied, approximately 70%, with a higher prevalence in females. Factors significantly linked to NAFLD incidence included the duration of diabetes and elevated measures of obesity and waist circumference. These findings underscore the need for heightened awareness and targeted interventions for this patient population.

Keywords: Non-Alcoholic Fatty Liver Disease (NAFLD), Type-II Diabetes Mellitus (DM), prevalence, risk factors.

INTRODUCTION

Diabetes Mellitus (DM) is a chronic metabolic disorder affecting about 200 million people in the world today.[1] Over the last few decades, diabetes and its associated complications have become one of the leading causes of morbidity and mortality in the developed world.[2]

Diabetes is characterized by abnormally high blood glucose levels due to the inefficiency of the body's cells to metabolize glucose. The underlying mechanism is either a decrease in the production of the glucose lowering hormone called insulin, by the pancreas (Type-I DM), or an inability of cells in the body to respond to otherwise normal or even higher levels of insulin which is termed as insulin resistance (Type-II DM).[3-5] Of the two, Type-II DM is more prevalent and has a strong correlation with deranged lipids in the blood due to obesity, diet and physical inactivity.[6] Diabetes together with obesity and dyslipidemia is placed under the umbrella of the term "metabolic syndrome" to highlight the fact that it acts synergistically with these conditions in causing long-term and damaging effects on body tissues that result in a wide spectrum of disorders.[7] One of such subsequent disorders that is the key focus of our study, is Non-Alcoholic Fatty Liver Disease.

Non-Alcoholic Fatty Liver disease (NAFLD) is a disorder of fat metabolism that affects 24% to 30% of the general population in most countries. It has become a prevalent cause of referrals to hepatobiliary clinics and the burden is growing alongside a rise in diabetes, obesity and metabolic diseases.[8] The pathophysiology of NAFLD is similar to that of Alcoholic Liver disease (ALD) but unlike the latter it is not due to alcohol induced liver damage and therefore occurs in patients without any history of alcohol consumption. NAFLD involves the accumulation of fat(steatosis) in the Liver parenchymal cells. This starts manifesting first as microvesicular steatosis and later as macrovesicular steatosis, which may or may not be accompanied by inflammation of hepatocytes (steatohepatitis).[8] Over time there is widespread injury and necrosis of hepatocytes with the dead cells being replaced by fibrosis. Therefore NAFLD eventually progresses to cirrhosis and end stage liver disease.[9] The clinical course of the disease is often insidious with an asymptomatic elevation of the liver aminotransferase levels (43). It can, however, be picked up and adequately graded on ultrasonography which has high sensitivity and specificity for fatty liver diseases.[9-10] On an ultrasound, NAFLD would show up as increased liver echogenicity and vascular blurring especially involving the hepatic veins.[10]

It is now believed that the presence of Type-II Diabetes (insulin insensitivity) increases both the risk and the severity of NAFLD.[11] This implies that NAFLD may respond to treatments originally developed for insulin resistance such as weight loss, metformin and thiazolidinediones.[12] Studies therefore need to be conducted to better understand and establish the extent of the relationship between these two entities. The purpose of our study is to determine the frequency of NAFLD in Type-II diabetic patients in our population and furthermore to examine how various factors such as age, gender and BMI of these patients would individually correlate with this frequency.

METHODS AND MATERIALS

Study Design and Setting: A cross-sectional study was conducted in the Department of General Medicine at a tertiary care center in Pakistan from May 2020 to June 2021. The study adhered to WHO guidelines.

Participants: The study population comprised Type-II diabetic patients of both genders aged 35 years and above, not consuming alcohol.

Inclusion Criteria:

Type-II diabetic patients
Both genders
Age 35 years and above
No alcohol consumption

Exclusion Criteria: Patients with other chronic liver diseases (e.g., Hepatitis B and C, hemochromatosis, primary biliary cirrhosis, Wilson's disease, autoimmune liver disease)

Decompensated liver disease

Patients on drugs known to cause fatty liver disease (e.g., amiodarone, tamoxifen, glucocorticoids, tetracycline, estrogen, methotrexate, thallium)

Patients with surgical procedures causing fatty liver disease (e.g., gastric bypass or jejuno-ileal bypass for obesity)

Pregnancy

Data Collection: Data was collected through a performa after receiving permission from the hospital's ethical committee. Informed written consent was obtained from the patients. The performa contained the personal profile, detailed history including diabetes duration, medication compliance, and medication type. Physical examination was conducted to determine BMI and waist-hip ratio. Weight and height were recorded for BMI calculation, and the waist circumference was measured using conventional measuring tape. The waist-hip ratio was calculated as per international guidelines. Abdominal ultrasonography for the liver was performed by a senior radiologist to assess NAFLD and grade it as mild, moderate, or severe if present.

Data Analysis: Analysis was performed using SPSS version 23. Frequencies and percentages were estimated for qualitative characteristics such as gender, NAFLD, and therapy. Chi-square testing was used to examine variations in proportions between waist-hip ratio (normal or increased), BMI (normal or elevated), and diabetes mellitus (DM) duration. Results were translated into categorical information, with significance set at a p-value less than 0.05.

RESULTS

Out of the 400 Type-II diabetic patients enrolled in our study, most fell in the old age group of 50 years and above (Table 1). These patients had diabetes for many years and the majority of them were using oral hypoglycemics. Our study found that a total of 277 of our diabetic patients had NAFLD which translates to a frequency of 69.3%. Table 2 illustrates the severity of fatty liver in these patients showing that only a small percentage of these patients had features of severe NAFLD. Furthermore, the results for association of incidence of NAFLD with age, gender and the duration of diabetes were also statistically significant (as shown in table 3). To summarize, most patients in our study who had NAFLD were found to be females (69%), most were aged above 55 years (65.3%) and the majority (88.09%) were living with Type-II diabetes for more than ten years.

Table 1: Demographics of the study participants

Characteristics	N (%)
Age	
35-45 years	106 (26.5%)
46-55 years	97 (24.3%)
older than 55 years	197 (49.3%)
Gender	
Male	161 (40.3%)
Female	239 (59.8%)
Duration of the DMT2	
less than ten years	131 (32.8%)
greater than ten years	269 (67.3%)
Treatment	
OHGA	320 (80%)
INSULIN	44 (11%)
COMBINATION	36 (9%)
Compliance	
Yes	240 (60%)
No	160 (40%)
NAFLD	
Yes	277 (69.3%)
No	123 (30.8%)

Table 2: Incidence of fatty liver in NAFLD positive

Severity of fatty liver	N (%)
Mild	149 (53.8%)
Moderate	98 (35.4%)
Severe	30 (10.8%)

Table 3: Association of factors with incidence of NAFLD

	NAFLD		
	Yes	No	P-value
Age			
35-45 years	30 (10.8%)	76 (61.8%)	
46-55 years	66 (23.8%)	31 (25.2%)	
older than 55 years	181 (65.3%)	16 (13%)	<0.0001
Gender			
Male	86 (31%)	75 (61%)	
Female	191 (69%)	48 (39%)	<0.0001
Duration of the DMT2			
less than ten years	33 (11.91%)	98 (79.67%)	
greater than ten years	244 (88.09%)	25 (20.33%)	<0.0001

DISCUSSION

The increasing prevalence and significant clinical implications of non-alcoholic fatty liver disease (NAFLD) in various populations, particularly among those with type 2 diabetes mellitus (T2DM), have been highlighted in recent years. In a cross-sectional study conducted at Nishtar Hospital and PMRC Research Centre in Multan, the frequency of NAFLD among 100 type-2 diabetic patients was 51%, with the majority being female[13]. Besides, it was observed that 92.15% of NAFLD patients had serum triglyceride levels higher than 160 mg/dl, and 47.05% had serum cholesterol levels surpassing 200 mg/dl. Notably, liver enzymes, AST and ALT, were not prominently raised in most NAFLD patients, pointing towards the importance of monitoring serum triglycerides and cholesterol in diabetics for early identification of NAFLD.[13]

The worldwide prevalence of NAFLD has shown a disturbing increase over the years. In a comprehensive meta-analysis, the global prevalence of NAFLD was estimated at 32.4%. The period from 2005 saw a significant jump in NAFLD cases, from 25.5% to 37.8% by 2016. The prevalence was notably higher in men compared to women, which could be attributed to different metabolic or hormonal factors among genders.[14]

Conversely, it's anticipated that the incidence of nonalcoholic steatohepatitis (NASH) could surge by up to 56% within the next decade.[15] With the looming obesity epidemic, NAFLD-related hepatocellular carcinoma (HCC) is expected to rise as well. In fact, NAFLD is now the primary cause of HCC in several countries, including the USA, France, and the UK. As such, measures to enhance global awareness and address the associated metabolic risk factors become paramount.[15]

In the context of the U.S., the Veterans Administration database was analyzed between 2003 and 2011, revealing a 2.8-fold increase in NAFLD prevalence from 6.3% in 2003 to 17.6% in 2011. While the annual incidence of NAFLD remained stable (ranging from 2% to 3%), there was a marked rise in the younger population, signifying a potential shift in disease dynamics.[16]

Understanding the molecular basis of NAFLD and related disorders is crucial for its prevention and treatment. Nuclear receptors are transcription factors playing a pivotal role in regulating metabolic pathways, including lipid and glucose metabolism. Their interaction with lipases, such as adipose triglyceride lipase (ATGL), underscores the intricate balance of metabolic processes and the potential therapeutic interventions in conditions like obesity, diabetes, and NAFLD.[17]

Interestingly, not all NAFLD cases are associated with obesity. There's a subtype, NAFLD in lean, which occurs in the absence of obesity. A meta-analysis revealed that globally, NAFLD in lean accounted for 13.11% of the population, and this figure was slightly higher in Asia at 14.55%. It's crucial to note that lean subjects with NAFLD exhibited significantly fewer metabolic abnormalities than their overweight or obese counterparts. For instance, only 19.56% of lean NAFLD patients were diabetic, in contrast to 45.70% in the obese subgroup.[18]

In summary, the global burden of NAFLD is undeniable, and its association with type-2 diabetes, obesity, and metabolic dysfunction needs robust strategies for early detection, prevention, and management.

CONCLUSION

The findings of our study reveal that approximately 68% of Type-II diabetic patients within our population exhibit a prevalence of NAFLD. This figure aligns with prior research conducted both in Pakistan and globally. We observed that the majority of NAFLD patients in our study were over the age of 55, with incidence rates escalating alongside the increasing age of the population. Additionally, we discerned a higher prevalence of NAFLD among females, with an upward trend corresponding to the length of time a patient has had diabetes. In light of the growing global prevalence of obesity and diabetes mellitus (DM), we anticipate a substantial increase in the number of patients suffering from chronic liver disease in the form of NAFLD. Consequently, it's expected that the risk associated with cardiovascular diseases (CVD) will also see a rise in the near future.

REFERENCES

1. Hasnain S, Sheikh NH. Knowledge and practices regarding foot care in diabetic patients visiting diabetic clinic in Jinnah Hospital, Lahore. J Pak Med Assoc. 2009;59:687-90.
2. Fan JG. Impact of non-alcoholic fatty liver disease on accelerated metabolic complications. Journal of digestive diseases. 2008 May;9(2):63-7.
3. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030.Diabetes Care.2004; 27:1047-53.
4. Rother KI. Diabetes treatment--bridging the divide. N Engl J Med. 2007;356:1499-501
5. Cnop M, Welsh N, Jonas JC, Jörns A, Lenzen S, Eizirik DL. Mechanisms of pancreatic beta-cell death in type I and type II diabetes: many differences, few similarities. Diabetes. 2005;54:97-107
6. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med. 2001; 345:790-7
7. Vakili O, Borji M, Saffari-Chaleshtori J, Shafiee SM. Ameliorative effects of bilirubin on cell culture model of non-alcoholic fatty liver disease. Molecular Biology Reports. 2023 May;50(5):4411-22.
8. Safari Z, Gérard P. The links between the gut microbiome and non-alcoholic fatty liver disease (NAFLD). Cellular and Molecular Life Sciences. 2019 Apr 3;76:1541-58.
9. Golabi P, Otgonsuren M, Cable R, Felix S, Koenig A, Sayiner M, Younossi ZM. Non-alcoholic fatty liver disease (NAFLD) is associated with impairment of health related quality of life (HRQOL). Health and quality of life outcomes. 2016 Dec;14(1):1-7.
10. Popa SL, Ismaiel A, Cristina P, Cristina M, Chiarioni G, David L, Dumitrascu DL. Non-alcoholic fatty liver disease: implementing complete automated diagnosis and staging. a systematic review. Diagnostics. 2021 Jun 12;11(6):1078.
11. Marušić M, Paić M, Knobloch M, Liberati Pršo AM. NAFLD, insulin resistance, and diabetes mellitus type 2. Canadian Journal of Gastroenterology and Hepatology. 2021 Feb 17;2021.
12. Cariou B, Byrne CD, Loomba R, Sanyal AJ. Nonalcoholic fatty liver disease as a metabolic disease in humans: A literature review. Diabetes, Obesity and Metabolism. 2021 May;23(5):1069-83.
13. Taseer IH, Hussain L, Safdar S, Mirbahar AM, Ahmad I. Frequency of non alcoholic fatty liver disease (NAFLD) & its biochemical derangements in Type-2 diabetic patients. Pak J Med Sci 2009;25(5):817-820.
14. Paik JM, Henry L, De Avila L, Younossi E, Racila A, Younossi ZM. Mortality related to nonalcoholic fatty liver disease is increasing in the United States. Hepatology Communications. 2019 Nov;3(11):1459-71.
15. Huang DQ, El-Serag HB, Loomba R. Global epidemiology of NAFLD-related HCC: trends, predictions, risk factors and prevention. Nature Reviews Gastroenterology & Hepatology. 2021 Apr;18(4):223-38.
16. Kanwal F, Kramer JR, Duan Z, Yu X, White D, El-Serag HB. Trends in the burden of nonalcoholic fatty liver disease in a United States cohort of veterans. Clinical Gastroenterology and Hepatology. 2016 Feb 1;14(2):301-8.
17. Tang A, Ng CH, Phang PH, Chan KE, Chin YH, Fu CE, Zeng RW, Xiao J, Tan DJ, Quek J, Lim WH. Comparative burden of metabolic dysfunction in lean NAFLD vs non-lean NAFLD-a systematic review and meta-analysis. Clinical Gastroenterology and Hepatology. 2023 Jul 1;21(7):1750-60.
18. Liu Z, Zhang Y, Graham S, Wang X, Cai D, Huang M, Pique-Regi R, Dong XC, Chen YE, Willer C, Liu W. Causal relationships between NAFLD, T2D and obesity have implications for disease subphenotyping. Journal of hepatology. 2020 Aug 1;73(2):263-76.