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FREQUENCY OF METABOLIC-ASSOCIATED FATTY LIVER DISEASE IN PATIENTS WITH DIABETES MELLITUS TYPE II

Dr Ammara Amjad[*1], Prof. Dr. Nayyer Yaqoob[2]

*[*1]MBBS Postgraduate Resident FCPS Medicine Fauji Foundation Hospital Rawalpindi*
[2]MBBS; FCPS Professor of Medicine Foundation University Medical College, Rawalpindi Fauji Foundation Hospital Rawalpindi

[*1]ammaraamjad9@live.com, [2]dranayyaryaqoob@yahoo.com

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Corresponding Author: *
Dr Ammara Amjad

Abstract

Background: *Type 2 diabetes mellitus (T2DM) and metabolic dysfunction-associated fatty liver disease (MAFLD) share a bidirectional relationship, yet the burden of MAFLD in our local diabetic population remains underexplored. This study aimed to determine the prevalence of MAFLD among T2DM patients and identify associated metabolic risk factors.*

Methodology: *This cross-sectional study was conducted at Fauji Foundation Hospital, Rawalpindi from September 2024–February 2025. 188 adults with age between 18–65 years and BMI ≥25 kg/m² were enrolled with T2DM. MAFLD was diagnosed via B-mode ultrasound (hepatic steatosis) plus ≥2 metabolic abnormalities: waist circumference ≥90/80 cm (men/women), BP ≥130/85 mmHg, triglycerides ≥150 mg/dL, HDL-C <40/50 mg/dL (men/women), HOMA-IR ≥2.5, or CRP >2 mg/L. Data were analyzed using SPSS.*

Results: *We identified 60.1% patients with MAFLD among 188 patients with T2DM. Significant correlations were seen with elevated prevalence in males, adults over 45 years of age and obese persons ($p<0.001$). Sedentary patients exhibited a 12.7-fold increased risk compared to their active counterparts (55.8% vs 4.4%, $p<0.001$), whilst a diabetic duration exceeding 10 years was associated with a prevalence of 50.4%, in contrast to 15% for those with a duration of 5 years or less ($p<0.001$). No significant correlation was seen between glycemic control and residential status ($p>0.05$).*

Conclusion: *MAFLD is highly prevalent in Pakistani T2DM patients, driven by obesity, insulin resistance, and inactivity. Routine screening and targeted interventions are urgently needed to mitigate hepatic and cardiometabolic risks.*

INTRODUCTION

Diabetes mellitus type II (DMT2) is a metabolic disorder that presents a considerable challenge to healthcare systems globally, especially in low- and middle-income nations. This disorder is defined by two main factors: impaired insulin secretion from pancreatic β-cells and the failure of insulin-sensitive tissues to respond adequately to insulin.[i] The International Diabetes Federation (IDF) reported that

around 415 million adults had Type 2 Diabetes Mellitus (DMT2) in 2015, with projections indicating an increase of an additional 200 million by 2040.[ii] The prevalence of Type 2 Diabetes Mellitus (T2DM) among adults in Pakistan exceeds one in four, at 26.7%, representing the highest national prevalence globally. [iii]

Insulin resistance, a primary contributor to type 2 diabetes mellitus (DMT2), significantly facilitates the buildup of free fatty acids in hepatic cells, leading to lipotoxicity, non-alcoholic fatty liver disease (NAFLD), and fibrosis.[iv] The key features of metabolic syndrome, such as peripheral insulin resistance, obesity, hypertension, hyperinsulinemia, and hypertriglyceridemia, function as predisposing factors for the onset of fatty liver disorders. The incidence of fatty liver disease in Asian nations varies between 9% and 40%.[v,vi] NAFLD refers to a medical condition identified by the buildup of fat in the liver, occurring without significant alcohol consumption.[vii] A panel of specialists has recently recommended replacing the term NAFLD with "metabolic dysfunction-associated fatty liver disease" (MAFLD). The notion of MAFLD was established to include the hepatic manifestation of a multisystem disorder marked by metabolic dysregulation. MAFLD is diagnosed using a specific set of positive criteria, does not necessitate the elimination of alternative causes of chronic liver disease, and distinctly associates the condition with its underlying etiology.[viii] In contrast to NAFLD, it is unnecessary to exclude alternative etiologies of liver disease, including chronic viral hepatitis, drugs that produce steatosis, other chronic liver conditions, and substantial alcohol intake.[ix,x]

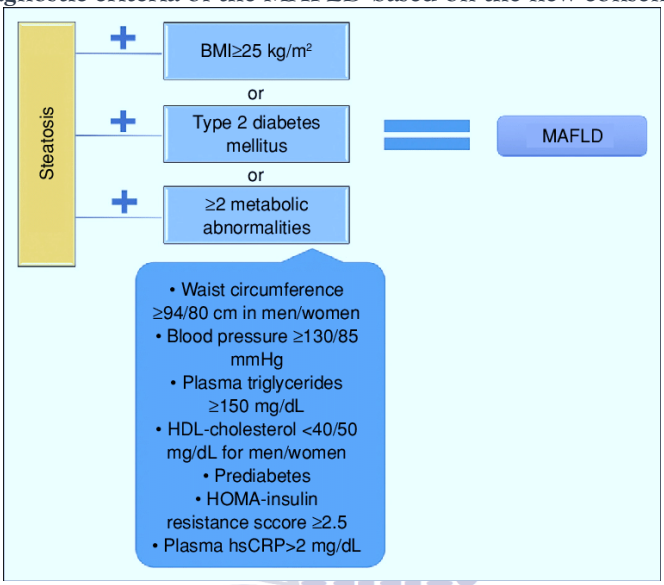
Due to the notable rise in the prevalence of DMT2 in Pakistan, it is rational to expect a concomitant rise in the prevalence of MAFLD. However, no study has done to date that estimated the burden of this disorder in our local population. So, present study is planned to fill this research gap. So, our study findings would help to estimate the burden of MAFLD among our local diabetic population. On the basis of our study findings future strategies would be devised for the systematic screening of MAFLD in our local population presenting with T2DM.

MATERIAL AND METHODS

This cross-sectional study was conducted in the Department of Medicine at Fauji Foundation Hospital, Rawalpindi, over a period of six months (from September 2024 to February 2025) following ethical approval. The study protocol was reviewed and approved by the hospital's ethics committee, ensuring adherence to ethical guidelines and the protection of participant rights. Confidentiality was maintained throughout the study, with all data anonymized during analysis to safeguard participant privacy. A total of 188 participants were enrolled using non-probability consecutive sampling, with the sample size calculated using the WHO sample size calculator. This calculation was based on a 95% confidence level, an anticipated MAFLD prevalence of 60.2% derived from existing literature, and a 7% margin of error to ensure robust and reliable results. The study included adults aged 18 to 65 years with a confirmed diagnosis of T2DM for at least one year and a BMI ≥25 kg/m². Both male and female participants were eligible. Exclusion criteria were designed to minimize confounding variables and included patients with renal failure, viral or drug-induced liver injury, any malignancy, autoimmune disorders, or those undergoing chemotherapy. Additionally, individuals who smoked more than 20 cigarettes per month or consumed more than 10 mL of alcohol per month were excluded, as were those taking hepatotoxic medications such as first-generation sulfonylureas, acarbose, anti-tuberculosis drugs, or anti-epileptic medications. Patients lacking complete medication or laboratory records were also excluded to ensure data integrity. Upon obtaining ethical approval and informed consent from all participants, a comprehensive clinical assessment was conducted. This included recording demographic details, medical history, and current medication use. Anthropometric measurements, such as weight, height, waist circumference, and blood pressure, were meticulously taken. BMI was calculated using the standard formula (weight in kilograms divided by height in meters squared). For laboratory investigations, 5 mL of venous blood was collected from each participant to analyze lipid profiles (including triglycerides and HDL-C), fasting insulin and glucose levels (for HOMA-IR calculation), and high-sensitivity CRP levels. Participants were then referred to the radiology

department for abdominal ultrasound to assess hepatic steatosis. All data, including demographic information and diagnostic results, were recorded in a structured proforma to ensure consistency and accuracy. The diagnosis of T2DM was validated via clinical history and medication records, necessitating either documented administration of anti-diabetic drugs for a minimum of one year or laboratory proof of HbA1c values ≥6.5% recorded at least one year before the trial. MAFLD was identified by a combination of imaging and metabolic criteria. Participants underwent B-mode liver ultrasonography to identify hepatic steatosis, and MAFLD was confirmed in individuals with the following findings:

Diagnostic criteria of the MAFLD based on the new consensus



Reference: Demirtas CO, Yilmaz Y. Metabolic-associated Fatty Liver Disease: Time to integrate ground-breaking new terminology to our clinical practice? Hepatology Forum 2020; 1(3):79–81.

Data were analyzed using SPSS version 23.0. Quantitative variables, such as age and BMI, were presented as mean ± standard deviation (SD), while qualitative variables, including gender, duration of diabetes, residential status, diabetic control status, daily activity levels, and individual MAFLD components, were expressed as frequencies and percentages. To control for potential confounding factors, the data were stratified by age, gender, BMI, duration of diabetes, glycemic control status, and physical activity levels. Associations between these variables and MAFLD prevalence were assessed using the chi-square test, with a p-value of ≤0.05 considered statistically significant.

RESULTS

The study comprised 188 individuals diagnosed with T2DM, with a mean age of 48.35±10.08 years (ranging from 20 to 65 years). The average BMI was 29.28±3.12 kg/m², signifying that most participants were classified as overweight or obese (BMI ≥25 kg/m²). The study population exhibits a nearly equal distribution of genders, with 46.8% female and 53.2% male participants. Most patients were over 45 years old (62.2%), indicative of the standard age distribution for T2DM. 48.9% were classified as obese (BMI >29 kg/m²), reflecting a substantial prevalence of adiposity within this sample. A considerable percentage had chronic diabetes (41.0% for over 10 years; 28.7% for 5–10 years). Approximately 52.1% of the individuals exhibited managed diabetes. A comprehensive study of qualitative characteristics is presented in Table 1, Figure 1, and Figure 2.

MAFLD was widespread in the study cohort, impacting 60.1% (n=113) of participants, but 39.9% (n=75) did not satisfy the diagnostic criteria for MAFLD. This highlights the significant correlation between T2DM and hepatic metabolic impairment.

MAFLD was markedly more prevalent in males than in females (36.3%), with a *p*-value < 0.001. Individuals over 45 years exhibited a greater prevalence of MAFLD than their younger counterparts, with substantial statistical significance ($p<0.001$). Obesity shown a robust association with MAFLD. Patients with chronic diabetes exhibited a greater prevalence of MAFLD than those with a shorter duration, underscoring the increasing nature of metabolic problems ($p< 0.001$). A sedentary lifestyle was substantially correlated with MAFLD. This study found no significant difference between treated and uncontrolled diabetes ($p=0.144$) and residential status ($p=0.386$). Detailed stratification analysis is illustrated in table 2.

Table 1: Clinical and demographic parameters of study subjects (n=188)

Variable	Category	Frequency	Percent
Gender	Female	88	46.8%
	Male	100	53.2%
Age Groups	≤45 Years	71	37.8%
	>45 Years	117	62.2%
Diabetes Status	Controlled	98	52.1%
	Uncontrolled	90	47.9%
Residential Status	Rural	105	55.9%
	Urban	83	44.1%
Waist Circumference (≥90/80 cm)	No	66	35.1%
	Yes	122	64.9%
Blood Pressure (≥130/85 mmHg or on Rx)	No	53	28.2%
	Yes	135	71.8%
Plasma Triglycerides (≥150 mg/dL)	No	61	32.4%
	Yes	127	67.6%
Deranged HDL (<40 mg/dL men, <50 women)	No	65	34.6%
	Yes	123	65.4%

Variable	Category	Frequency	Percent
HOMA-IR (≥2.5)	No	63	33.5%
	Yes	125	66.5%
CRP Level (>2 mg/L)	No	61	32.4%
	Yes	127	67.6%

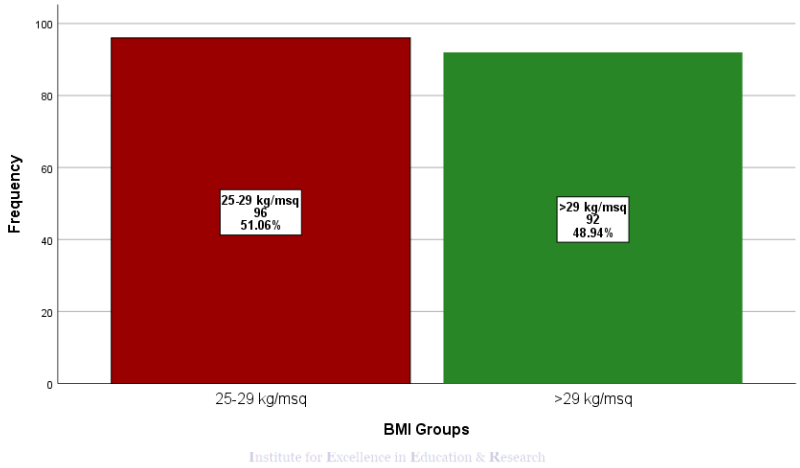


Figure 1: Distribution of patients in different BMI categories (n=188)

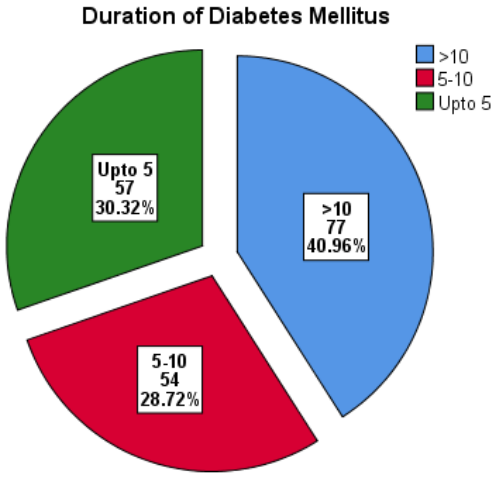


Figure 2: Distribution of patients in different groups on the basis of duration of diabetes (n=188)

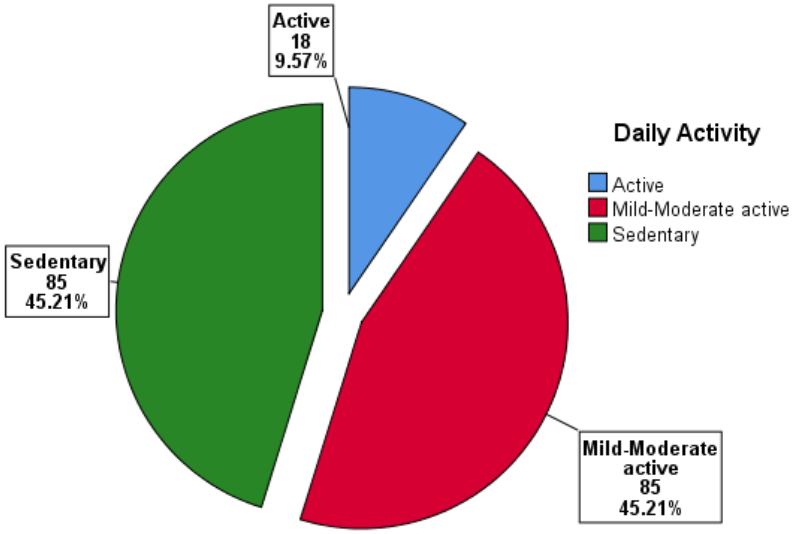


Figure 3: Distribution of patients in different groups on the basis of daily activity routine (n=188)

Table 2: Stratification of MAFLD in patients with T2DM on the basis of various clinical and demographic variables

Variable	Category	No MAFLD (n=75)	MAFLD (n=113)	Chi-Square Test *p*-value
Gender	Female	47 (62.7%)	41 (36.3%)	<0.001
	Male	28 (37.3%)	72 (63.7%)	
Age Groups	≤45 Years	44 (58.7%)	27 (23.9%)	<0.001
	>45 Years	31 (41.3%)	86 (76.1%)	
BMI Groups	25–29 kg/m²	61 (81.3%)	35 (31.0%)	<0.001
	>29 kg/m²	14 (18.7%)	78 (69.0%)	
Duration of Diabetes	>10 Years	20 (26.7%)	57 (50.4%)	<0.001
	5–10 Years	15 (20.0%)	39 (34.5%)	
	≤5 Years	40 (53.3%)	17 (15.0%)	

Variable	Category	No MAFLD (n=75)	MAFLD (n=113)	Chi-Square Test *p*-value
Diabetes Status	Controlled	44 (58.7%)	54 (47.8%)	0.144
	Uncontrolled	31 (41.3%)	59 (52.2%)	
Residential Status	Rural	39 (52.0%)	66 (58.4%)	0.386
	Urban	36 (48.0%)	47 (41.6%)	
Daily Activity	Active	13 (17.3%)	5 (4.4%)	<0.001
	Mild-Moderate Active	40 (53.3%)	45 (39.8%)	
	Sedentary	22 (29.3%)	63 (55.8%)	

DISCUSSION

Findings of our study reveal a notably high prevalence of MAFLD (60.1%) in patients with type 2 diabetes mellitus, underscoring the documented metabolic relationship between both diseaese. This incidence corresponds with global epidemiological statistics indicating that MAFLD impacts 50-70% of diabetic populations, highlighting the therapeutic importance of hepatic steatosis in diabetes therapy.[7-10] The pathophysiological connections are multifaceted, with insulin resistance identified as a primary contributor, as demonstrated by 66.5% of our group exhibiting HOMA-IR ≥2.5. This metabolic disorder enhances lipolysis and elevates free fatty acid transport to the liver, while persistent hyperglycemia hastens de novo lipogenesis, resulting in optimal conditions for hepatic fat storage. Additionally, we identified considerable dyslipidemia, with 67.6% exhibiting hypertriglyceridemia and 65.4% presenting low HDL, which further exacerbates MAFLD pathogenesis via disrupted lipid metabolism. Recent studies reported a debatable association of DMT2 with MAFLD as results are conflicting. On the other hand, a study conducted in China on 5,594 patients from July 2020 to June 2021, reported a prevalence of 13.10% of MAFLD in DMT2 patients.[xi] Our observed MAFLD prevalence of 60.1% is consistent with studies from diverse populations, such as Yilmaz Y et al, who conducted a multicenter study in Turkey and they found that 60.2% of the patient with DMT2 had MAFLD.[xii] Similarly, Guan et al,[xiii] reported that 63.2% of T2DM patients had MAFLD, with obesity and insulin resistance as key drivers. A study from Pakistan[xiv] reported 58.6% of T2DM patients had fatty liver, linked to poor glycemic control and longer diabetes duration. Butt et al[xv] from Australia, found 38.7% of FibroScan-assessed patients met MAFLD criteria, with T2DM increasing odds 4.8-fold. These parallels suggest that MAFLD is a pervasive comorbidity in T2DM worldwide, though prevalence varies by diagnostic method.

Our investigation identified numerous significant demographic and clinical correlations with MAFLD. Notably, we identified considerable gender inequalities, with males demonstrating a much greater frequency of MAFLD (63.7%) than females (36.3%). This disparity presumably signifies both biological factors, especially the protective effects of estrogen in premenopausal women, and behavioral impacts. Age proved to be a significant determinant, as patients over 45 years exhibited a 3.2-fold greater prevalence of MAFLD compared to their younger counterparts, likely attributable to age-related reductions in mitochondrial function and escalating sarcopenia that intensify insulin resistance.

Our finding that 66.5% of patients had HOMA-IR ≥2.5 aligns with Guan et al[13] who described that higher HOMA-IR values confirms insulin resistance as a central mechanism. The most significant correlation was observed with obesity, as 69% of patients with a BMI exceeding 29 kg/m² exhibited MAFLD, underscoring visceral adiposity as a principal contributor to hepatic steatosis via inflammatory adipokine dysregulation. Kolluru et al. noticed that pre-diabetics with MAFLD showed worse anthropometric indices (e.g., waist-hip ratio), suggesting early metabolic derangements precede T2DM diagnosis.[xvi]

Lifestyle factors were equally significant, with sedentary behavior linked to a 12.7-fold heightened risk of MAFLD compared to active individuals. This significant disparity highlights the essential significance of physical activity in preserving liver metabolic health, presumably via AMPK activation and enhanced mitochondrial function. The duration of diabetes exhibited a robust connection, with individuals having diabetes for over 10 years demonstrating a considerably elevated prevalence of MAFLD, indicating cumulative metabolic damage over time. Sedentary patients in our cohort had 12.7× higher MAFLD risk, a finding supported by Egyptian study in which MAFLD prevalence was 55% in diabetic kidney disease patients, with inactivity exacerbating cardiometabolic risks.[xvii] Notably, we observed no substantial variations related to diabetes control status or residential environment, suggesting that the risk of MAFLD is consistent in well-managed diabetes and impacts both urban and rural people equally. Korean Diabetes Association highlights the shift from NAFLD (exclusion-based) to MAFLD/MASLD (inclusion-based), capturing more high-risk patients.[xviii] NHANES Study alarmed that MAFLD criteria increased fatty liver diagnosis by 68.89%, but may overestimate morbidity in T2DM.[xix] These findings possess significant clinical ramifications. The elevated prevalence of MAFLD indicates that routine screening via ultrasonography or elastography should be implemented for all T2DM patients, especially those with supplementary risk factors such as obesity or a sedentary lifestyle. Therapeutic interventions must prioritize weight reduction (aiming for a 7-10% decrease in body weight), enhancement of physical activity (minimum of 150 minutes per week of moderate exercise), and optimization of metabolic parameters. Pharmacological interventions such as GLP-1 agonists and pioglitazone may be especially advantageous for high-risk patients. The absence of correlation with glycemic control indicates that addressing MAFLD necessitates a more comprehensive metabolic strategy beyond mere glucose regulation.

This study offers useful information, although several limitations must be recognized. The cross-sectional design prevents causal inference, and the lack of liver biopsy data may have led to an underestimation of more advanced disease. Future longitudinal investigations utilizing improved imaging and histological evaluation would elucidate the natural evolution of MAFLD in diabetes. Examining genetic variants that affect hepatic fat metabolism may enhance risk stratification.

CONCLUSION

Our study findings validated MAFLD as a frequent and clinically relevant comorbidity in T2DM patients, notably impacting older, obese, sedentary guys with a prolonged history of diabetes. The significant correlations with alterable metabolic and lifestyle parameters provide evident options for intervention. A multimodal strategy focusing on weight management, physical exercise, and thorough metabolic regulation is crucial to alleviate the increasing prevalence of MAFLD in individuals with diabetes and avert its advancement to more severe hepatic conditions. These findings highlight the necessity for further incorporation of hepatology evaluations into standard diabetes management strategies.

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