

Correlation of Glycemic Control with Liver Fibrosis Risk (FIB-4) in Patients with Type-2 Diabetes Mellitus

Aijaz Zeeshan K. Chachar¹,
Kinza Khan², Danish Khan³

ABSTRACT

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is highly prevalent among patients with type 2 diabetes mellitus (T2DM) and is a major risk factor for progressive liver fibrosis. Poor glycemic control may accelerate fibrogenesis, which can be assessed non-invasively using the Fibrosis-4 (FIB-4) index.

Objective: To evaluate the association between glycemic control, measured by glycated hemoglobin (HbA1c), and liver fibrosis risk as estimated by the FIB-4 score in patients with T2DM.

Methodology: This cross-sectional study included 60 adults with T2DM attending a tertiary care diabetes clinic between January 2023 and December 2024. Glycemic control was assessed using HbA1c. Liver fibrosis risk was estimated using the FIB-4 index and categorized as low (<1.3), intermediate (1.3-2.67), or high (>2.67). Differences in HbA1c across FIB-4 categories were analyzed using one-way ANOVA. Pearson correlation was used to assess the relationship between HbA1c and FIB-4 score.

Results: The mean age was 54.1 ± 9.3 years, and 55% of participants were male. Mean HbA1c was $8.4 \pm 1.6\%$. FIB-4 risk categories were low in 46.7%, intermediate in 36.7%, and high in 16.7% of patients. HbA1c increased significantly across fibrosis categories (low: $7.6 \pm 1.1\%$, intermediate: $8.6 \pm 1.3\%$, high: $9.7 \pm 1.4\%$; $p < 0.001$). A moderate to strong positive correlation was observed between HbA1c and FIB-4 score ($r = 0.61$, $p < 0.001$).

Conclusion: Poor glycemic control is significantly associated with higher FIB-4 scores, indicating increased risk of advanced fibrosis in patients with T2DM. Incorporation of FIB-4 assessment into routine diabetes care may facilitate early identification of patients at risk for progressive MASLD.

KEY WORDS: Type 2 Diabetes Mellitus; Metabolic Dysfunction-Associated Steatotic Liver Disease; Glycated Hemoglobin; Liver Fibrosis; FIB-4 Index.

INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD) is among the most common chronic liver disorders worldwide and is particularly prevalent in individuals with type 2 diabetes mellitus (T2DM).^{1,2} Chronic hyperglycemia promotes oxidative stress, inflammation, and lipid accumulation within

hepatocytes, contributing to fibrosis and progression to cirrhosis.³ Liver biopsy remains the gold standard for fibrosis evaluation but is invasive and impractical for routine clinical use. Noninvasive scoring systems, including the Fibrosis-4 (FIB-4) index, provide an effective alternative for stratifying fibrosis risk.⁴

Address for Correspondence: Kinza Khan
Department of Internal Medicine,
University of Pennsylvania,
Philadelphia, USA.
Email: Kinzak2040@gmail.com

Submitted: November 03, 2025 **Revision Received:** December 20, 2025

Accepted for Publication: December 26, 2025

This is an open access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Access this Article Online

URL:
<https://jpes.org.pk/index.php/jpes/article/view/72>

How to cite this: Chachar AZK, Khan K, Khan D. Correlation of Glycemic Control with Liver Fibrosis Risk (FIB-4) in Patients with Type-2 Diabetes Mellitus.. JPES. 2025;2(2):71-74.

Glycated hemoglobin (HbA1c) is the most widely used marker of long-term glycemic control and reflects the average plasma glucose over the preceding 3 months.⁵ Evidence suggests that poor glycemic control may exacerbate hepatic fat deposition, accelerate fibrogenesis, and increase MASLD severity.⁶ This study aimed to assess the relationship between HbA1c and fibrosis risk based on FIB-4 in a cohort of adults with T2DM.

METHODOLOGY

Study Design and Setting: This cross-sectional study was conducted at the Diabetes Clinic of Doctors Hospital, Lahore, from January 2023 to December 2024.

Study Population: A total of 60 adult patients (≥18 years) with a confirmed diagnosis of type 2 diabetes mellitus were enrolled through convenience sampling. Patients with known chronic liver disease other than MASLD, viral hepatitis, autoimmune hepatitis, significant alcohol intake (>20 g/day for women and >30 g/day for men), malignancy, or chronic systemic illness were excluded.

MASLD was defined based on the presence of metabolic risk factors (T2DM) with elevated liver enzymes and/or ultrasound evidence of hepatic steatosis, after exclusion of secondary causes of liver disease.

Clinical and Laboratory Assessment: Demographic data, body mass index (BMI), and duration of diabetes were recorded. Glycemic control was assessed using glycated hemoglobin (HbA1c). Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and platelet counts were obtained from fasting blood samples.

Liver fibrosis risk was estimated using the Fibrosis-4 (FIB-4) index:

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}$$

Participants were categorized as:

- Low risk: FIB-4 < 1.3
- Intermediate risk: FIB-4 1.3–2.67
- High risk: FIB-4 > 2.67

Ethical Considerations: The study was approved by the Institutional Review Board of FMH College of Medicine and Dentistry. Written informed consent was obtained from all participants.

Statistical Analysis: Data were analyzed using SPSS version 26.0. Continuous variables were assessed for normality using visual inspection of histograms and the Shapiro-Wilk test. Normally distributed continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Mean HbA1c levels across FIB-4 fibrosis risk categories (low, intermediate, high) were compared using one-way analysis of variance (ANOVA). When overall significance was observed, post-hoc Tukey's test was applied to identify pairwise differences between groups. The relationship between HbA1c and FIB-4 score was evaluated using the Pearson correlation coefficient, with correlation strength interpreted according to standard conventions. All tests were two-tailed, and a p-value <0.05 was considered statistically significant.

RESULTS

The study included 60 patients with type 2 diabetes mellitus, with a mean age of 54.1 ± 9.3 years; 33 (55%) were male. The mean BMI was 29.7 ± 3.8 kg/m², and

Table-I: Baseline clinical and biochemical characteristics of the study population.

Baseline Characteristics (n=60):

Variable	Mean ± SD / n (%)
Age (years)	54.1 ± 9.3
Male sex	33 (55%)
BMI (kg/m ²)	29.7 ± 3.8
HbA1c (%)	8.4 ± 1.6
AST (U/L)	38.2 ± 10.1
ALT (U/L)	42.5 ± 12.7
Platelets (10 ⁹ /L)	214 ± 58
FIB-4 score	1.68 ± 0.81

Table-II:

FIB-4 Risk Distribution:

FIB-4 Category	n (%)
Low (<1.3)	28 (46.7%)
Intermediate (1.3–2.67)	22 (36.7%)
High (>2.67)	10 (16.7%)

HbA1c Across FIB-4 Categories:

FIB-4 Category	Mean HbA1c (%) ± SD
Low	7.6 ± 1.1
Intermediate	8.6 ± 1.3
High	9.7 ± 1.4

ANOVA p-value <0.001.

Pearson correlation r = 0.61, p<0.001.

mean HbA1c was $8.4 \pm 1.6\%$. Baseline biochemical parameters showed mean AST of 38.2 ± 10.1 U/L, ALT of 42.5 ± 12.7 U/L, platelet count of $214 \pm 58 \times 10^9/L$, and mean FIB-4 score of 1.68 ± 0.81 (Table-I).

Based on FIB-4 categories, 28 patients (46.7%) were classified as low risk, 22 (36.7%) as intermediate risk, and 10 (16.7%) as high risk for advanced fibrosis.

Mean HbA1c levels increased progressively across fibrosis risk categories:

- Low risk: $7.6 \pm 1.1\%$
- Intermediate risk: $8.6 \pm 1.3\%$
- High risk: $9.7 \pm 1.4\%$

This difference was statistically significant on one-way ANOVA ($F = 12.4$, $p < 0.001$). Post-hoc analysis demonstrated that HbA1c was significantly higher in the high-risk group compared with both low and intermediate-risk groups ($p < 0.01$ for all comparisons) (Table-II).

Pearson correlation analysis demonstrated a moderate-to-strong positive association between HbA1c and FIB-4 score ($r = 0.61$, $p < 0.001$), indicating that poorer glycemic control was associated with higher estimated liver fibrosis risk.

DISCUSSION

This study demonstrates a significant positive correlation between HbA1c levels and FIB-4 scores in patients with T2DM; reinforcing the concept that poor glycemic control is closely associated with increased fibrosis risk in MASLD. Hyperglycemia induces hepatic lipid accumulation by promoting de novo lipogenesis and impairing fatty acid oxidation, resulting in triglyceride deposition within hepatocytes.⁷

This steatotic environment triggers oxidative stress, mitochondrial dysfunction, and activation of inflammatory cascades, ultimately stimulating hepatic stellate cells to produce extracellular matrix and drive fibrosis. Advanced glycation end-products (AGEs) further amplify chronic inflammation through receptor-mediated pathways, exacerbating hepatocellular injury.⁸

These mechanisms collectively provide a biological rationale for the observed association between elevated HbA1c and higher FIB-4 categories. Epidemiological evidence indicates that MASLD is not only a hepatic condition but also a major cardiometabolic risk factor, closely linked to cardiovascular morbidity and mortality, particularly in patients with T2DM.^{9,10} This underscores the clinical relevance of identifying fibrosis risk early in this population.

The stepwise increase in HbA1c across rising fibrosis categories emphasizes glycemic control as a modifiable risk factor with potential implications for disease progression. The adoption of metabolic-based disease definitions highlights the importance of integrating glycemic status into MASLD risk stratification frameworks.¹² Clinically, these findings support the incorporation of simple noninvasive tools such as FIB-

4 and other validated indices into routine diabetes care to identify individuals at higher risk for advanced liver disease.¹¹

Lifestyle interventions, including weight reduction, dietary optimization, and increased physical activity, improve insulin sensitivity and reduce hepatic steatosis. Nutritional modulation plays a pivotal role in reducing liver fat content and mitigating disease progression, particularly when combined with improved glycemic control.¹³ Pharmacologic strategies aimed at improving glycemic control, such as metformin, GLP-1 receptor agonists, and SGLT2 inhibitors, have been associated with reductions in liver fat, inflammation, and even fibrosis regression in early disease.¹³⁻¹⁵ Addressing hyperglycemia alongside other metabolic risk factors – including obesity, dyslipidemia, and hypertension – may synergistically reduce the risk of fibrosis progression and cardiovascular complications.

Limitations: The cross-sectional design precludes causal inference between glycemic control and fibrosis progression. The relatively small sample size and single-center setting limit generalizability of the findings. Liver fibrosis was assessed using the FIB-4 index rather than histopathology or elastography, and misclassification is possible, particularly in older patients in whom age may inflate FIB-4 values. Potential confounders such as lipid profile, insulin resistance indices, and use of antidiabetic medications were not analyzed. Larger prospective studies incorporating imaging-based or histological assessment of fibrosis are warranted to validate these findings.

CONCLUSION

Poor glycemic control, as reflected by elevated HbA1c, is strongly associated with increased fibrosis risk based on FIB-4 scores in T2DM patients. Routine FIB-4 screening combined with optimized glycemic management may facilitate early identification and management of MASLD, potentially reducing progression to advanced liver disease and related complications.

REFERENCES

1. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease—meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology*. 2016;64(1):73–84.
2. Mantovani A, Byrne CD, Bonora E, Targher G. Nonalcoholic fatty liver disease and risk of incident type 2 diabetes: a meta-analysis. *Diabetes Care*. 2018;41(2):372–82.
3. Ntikoudi A, Papachristou A, Tsalkitzi A, Margari N, Manolakopoulos S. Liver fibrosis in type 2 diabetes mellitus: pathophysiology, diagnostic approaches, and therapeutic interventions. *Diabetology*. 2022;6(4):23.
4. Xiao G, Zhu S, Xiao X, Yan L, Yang J, Wu G. Comparison of laboratory tests, ultrasound, or transient elastography to detect fibrosis in patients with nonalcoholic fatty liver disease: a meta-analysis. *Hepatology*. 2017;66(5):1486–501.
5. Yazdanpanah S, Rabiee M, Tahriri M, Abdolrahim M, Rajab A, Jazayeri HE, et al. Evaluation of glycated albumin (GA) and HbA1c in diabetic patients: a review. *Crit Rev Clin Lab Sci*. 2017;54(4):219–32.

6. Targher G, Bertolini L, Rodella S, Zoppini G, Lippi G, Day C, et al. Non-alcoholic fatty liver disease is independently associated with chronic kidney disease and cardiovascular disease in type 2 diabetes. *Diabetologia*. 2008;51(3):444-50.
7. Santos JCDF, Valentim IB, de Araújo OR, Ataíde TR, Goulart MOF. Development of nonalcoholic hepatopathy: contributions of oxidative stress and advanced glycation end products. *Int J Mol Sci*. 2013;14(10):19846-66.
8. Adams LA, Anstee QM, Tilg H, Targher G. Non-alcoholic fatty liver disease and its relationship with cardiovascular disease and other extrahepatic diseases. *Gut*. 2017;66(6):1138-53.
9. Ballestri S, Lonardo A, Bonapace S, Byrne CD, Loria P, Targher G. Risk of cardiovascular, cardiac and arrhythmic complications in patients with non-alcoholic fatty liver disease. *World J Gastroenterol*. 2014;20(7):1724-45.
10. Patel K, Asrani SK, Fiel MI, Levine D, Leung DH, Thung SN, et al. AASLD practice guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology*. 2023;81(1):358-79.
11. Eslam M, Sanyal AJ, George J; International Consensus Panel. MAFLD: a consensus-driven proposed nomenclature for metabolic associated fatty liver disease. *Gastroenterology*. 2020;158(7):1999-2014.
12. Romero-Gómez M, Aller R, Martín-Bermudo F. NAFLD and metabolic syndrome. *Horm Metab Res*. 2022;42(4):434-45.
13. Lee, H.A.; Kim, H.Y. Therapeutic Mechanisms and Clinical Effects of Glucagon-like Peptide 1 Receptor Agonists in Nonalcoholic Fatty Liver Disease. *Int. J. Mol. Sci*. 2023, 24, 9324.
14. Yabut, J.M.; Drucker, D.J. Glucagon-like Peptide-1 Receptor-Based Therapeutics for Metabolic Liver Disease. *Endocr. Rev*. 2023, 44, 14-32.
15. Drygalski K. Pharmacological treatment of MASLD: contemporary treatment and future perspectives. *International journal of molecular sciences*. 2025 Jul 7;26(13):6518.

Author's Contribution:

AZKC: Study conception, clinical data acquisition, and manuscript review.

KK: Data analysis, manuscript writing, and editing.

DK: Data collection and literature review.

All authors approved the final manuscript.

AUTHORS:

1. Aijaz Zeeshan K. Chachar,
Department of Internal Medicine,
FMH College of Medicine and Dentistry,
Lahore, Pakistan.
2. Kinza Khan,
Department of Internal Medicine,
University of Pennsylvania,
Philadelphia, USA.
3. Danish Khan
Medical Student,
Central Park Medical College,
Lahore, Pakistan.