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CORRELATION BETWEEN FIB-4 INDEX AND HBA1C IN ASSESSING LIVER FIBROSIS RISK AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS: A HOSPITAL-BASED CROSS-SECTIONAL ANALYTICAL STUDY

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is closely associated with metabolic-associated steatotic liver disease and progression to liver fibrosis. Liver fibrosis is an important predictor of long-term hepatic and systemic outcomes. The Fibrosis-4 (FIB-4) index is a simple, non-invasive and cost-effective marker calculated from age, AST, ALT and platelet count. HbA1c reflects long-term glycemic control and may be associated with the risk of liver fibrosis in patients with T2DM. The aim is to study the correlation between FIB-4 index and HbA1c in assessing liver fibrosis in patients with type 2 diabetes mellitus.

Materials and Methods: This hospital-based cross-sectional analytical study was conducted among 170 patients with T2DM attending Government General Hospital, Guntur. The study was carried out over a period of 18 months. The study population included male and female patients aged 20–60 years. Clinical, demographic and anthropometric details were recorded. Biochemical parameters including HbA1c, fasting blood glucose, post-prandial blood glucose, lipid profile, AST, ALT, serum total bilirubin and platelet count were analysed. Ultrasonography abdomen was performed to assess fatty liver changes. FIB-4 score was calculated using age, AST, ALT and platelet count. Data were analysed using SPSS version 25.0. Since the study variables were not normally distributed, median and interquartile range were used, and non-parametric tests were applied.

Results: A total of 170 patients were included, comprising 88 males and 82 females. The median HbA1c was 7.4 and the median FIB-4 score was 1.3. Based on FIB-4 categories, 85 patients were classified as no/low risk fibrosis, 79 as mild/moderate fibrosis and 6 as advanced fibrosis. HbA1c showed a weak but statistically significant positive correlation with FIB-4 score (rho = 0.157, p = 0.041). FIB-4 showed a moderate positive correlation with ultrasonographic fatty liver grade (rho = 0.497, p <0.001). Age showed a statistically significant positive correlation with FIB-4 score (rho = 0.454, p <0.0001). LDL showed a statistically significant weak negative correlation with FIB-4 score (rho = -0.158, p = 0.040), while VLDL, HDL and triglycerides showed no statistically significant correlation.

Conclusion: The present study showed that HbA1c had a weak but statistically significant positive correlation with FIB-4 index in patients with T2DM. FIB-4 also showed a moderate positive correlation with ultrasonographic fatty liver grade and a significant positive association with age. These findings support the use of FIB-4 as a simple, non-invasive and cost-effective screening tool for liver fibrosis risk assessment in patients with

T2DM, particularly when interpreted along with HbA1c and ultrasonographic fatty liver grading.
Keywords: Type 2 diabetes mellitus, HbA1c, FIB-4 index, liver fibrosis, fatty liver, MASLD, NAFLD, non-invasive fibrosis marker.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a major global public health problem, affecting an increasing proportion of the adult population and contributing significantly to morbidity and mortality. It is well established as a leading cause of cardiovascular disease, chronic kidney disease and microvascular complications. In recent years, T2DM has also been increasingly linked with metabolic-associated steatotic liver disease (MASLD), previously known as non-alcoholic fatty liver disease (NAFLD), which has emerged as one of the most common chronic liver diseases worldwide.[1,2]

MASLD encompasses a spectrum of liver pathology ranging from simple steatosis to steatohepatitis, progressive fibrosis, cirrhosis and hepatocellular carcinoma. Among these, liver fibrosis is the most important determinant of long-term outcomes and overall mortality.[3] Individuals with T2DM are at significantly higher risk of developing advanced fibrosis compared with non-diabetic individuals, even in the absence of alcohol consumption or viral hepatitis.[4] Furthermore, fibrosis in diabetic patients is associated not only with liver-related complications but also with increased cardiovascular events and all-cause mortality.[5]

Assessment of liver fibrosis remains challenging. Although liver biopsy is considered the gold standard for evaluating fibrosis, it is invasive, costly and associated with potential complications and sampling variability, limiting its use for routine screening.[6] Therefore, there is an increasing need for non-invasive, cost-effective and easily reproducible biomarkers for the assessment of liver fibrosis in routine clinical practice.

The Fibrosis-4 (FIB-4) index is one of the most widely used non-invasive scoring systems for evaluating liver fibrosis. It is calculated using simple clinical and biochemical parameters including age, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and platelet count. It has been validated across various liver diseases, including MASLD.[7] The European Association for the Study of the Liver recommends FIB-4 as an initial screening tool to identify patients at risk of advanced fibrosis.[8] Based on established cut-off values, patients are commonly categorized into low risk (<1.3), intermediate risk (1.3–2.67) and high risk (>2.67). Owing to its simplicity, wide availability and cost-effectiveness, FIB-4 is especially valuable in resource-limited settings.

In addition to its role in liver disease, FIB-4 has been shown to correlate with systemic metabolic dysfunction. Studies have demonstrated associations between elevated FIB-4 scores and chronic kidney disease, cardiovascular disease and increased mortality, suggesting that it may reflect a broader spectrum of metabolic injury.[9] This expands its clinical utility, especially in patients with T2DM, where multi-organ involvement is common.

Glycatedhemoglobin (HbA1c) is a well-established marker of long-term glycemic control and reflects average blood glucose levels over the preceding two to three months. It plays a central role in the management of diabetes and is widely used to guide treatment decisions and predict complications.[10] Emerging evidence suggests that poor glycemic control, as indicated by elevated HbA1c levels, may contribute to the progression of MASLD and liver fibrosis.[11]

Despite growing evidence, important gaps remain in the current literature. Population-specific data evaluating the relationship between HbA1c and FIB-4 are limited, particularly in South Asian and Indian populations where the burden of T2DM and MASLD is rapidly increasing. There is also insufficient data comparing FIB-4 values across different HbA1c categories such as <7%, 7–8% and >8%, which may provide clinically useful thresholds for risk stratification. In addition, since age is a component of the FIB-4 index, its influence on fibrosis severity and interaction with glycemic control requires further evaluation.

Given the rising prevalence of T2DM and MASLD, especially in developing countries, early detection of liver fibrosis using non-invasive and cost-effective tools is essential. The present study was therefore conducted to evaluate the correlation between HbA1c and FIB-4 index, assess FIB-4 as a practical screening tool, examine the influence of age and compare fibrosis risk across different HbA1c categories among patients with T2DM.

Aim and Objectives

Aim

To study the correlation between FIB-4 index and HbA1c in assessing liver fibrosis in type 2 diabetes mellitus patients.

Objectives

1. To assess FIB-4 as a non-invasive marker of liver fibrosis in type 2 diabetes mellitus patients.
2. To evaluate the relationship between FIB-4 index and HbA1c levels in type 2 diabetes mellitus patients.
3. To compare FIB-4 across different HbA1c categories in type 2 diabetes mellitus patients.
4. To correlate age with glycemic control and severity of fibrosis in type 2 diabetes mellitus patients.
5. To assess the correlation between lipid profile parameters and the FIB-4 index in patients with type 2 diabetes mellitus.

MATERIALS AND METHODS

Study design: The present study was conducted as a hospital-based cross-sectional analytical study aimed at assessing the risk of liver disease using the FIB-4 index and HbA1c levels among patients attending Government General Hospital, Guntur.

Study duration: The study was carried out over a period of 18 months.

Study setting: The study was conducted at Government General Hospital (GGH), Guntur and the Department of Biochemistry, Guntur Medical College, Guntur. All biochemical investigations were performed in the central laboratory of the Department of Biochemistry using standard laboratory procedures. For all patients included in the study, ultrasonography abdomen was performed in collaboration with the Department of Radiology to assess fatty changes in the liver.

Study population: The study population comprised 170 male and female patients aged between 20 and 60 years attending Government General Hospital, Guntur during the study period.

Sample size: A total of 170 patients were included in the study.

Sampling method: Patients who fulfilled the inclusion criteria and provided written informed consent were enrolled using a convenience sampling method.

Inclusion criteria:

Patients fulfilling the following criteria were included:

- Known type 2 diabetic patients.
- Age between 20 and 60 years.

Exclusion criteria:

Patients with the following conditions were excluded:

- Known cases of hepatocellular carcinoma.
- Known chronic liver disease.
- Known cases of jaundice.
- Alcoholic liver disease.
- Viral hepatitis.
- Smokers.

Data collection: After obtaining written informed consent, detailed clinical and demographic data were collected using a structured proforma. The following information was recorded:

- Age.
- Gender.
- Dietary habits.
- Occupational status.
- Alcohol consumption.

Anthropometric measurements: Anthropometric measurements were recorded using standardized methods. Body weight was measured using a calibrated weighing scale and height was measured using a stadiometer. Body mass index (BMI) was calculated using the formula:

BMI = weight (kg) / height (m^2)

Waist and hip circumferences were measured using a measuring tape, and waist–hip ratio was calculated.

Ultrasonography abdomen: Ultrasonography abdomen reports of all patients were noted to assess fatty changes in the liver. Fatty liver changes were categorized into four groups:

- Normal liver.
- Grade 1 fatty liver: mild steatosis, where fat accumulation is up to 5% to 33%.
- Grade 2 fatty liver: moderate steatosis, where fat accumulation is 34% to 66%.
- Grade 3 fatty liver: severe steatosis, where fat accumulation exceeds 66%.

Biochemical investigations:

The following biochemical parameters were analysed using Beckman AU 480 fully automated clinical chemistry analyser:

- Glycatedhemoglobin (HbA1c).
- Fasting blood glucose.
- Post-prandial blood glucose.
- Fasting triglycerides.
- High-density lipoprotein (HDL) cholesterol.
- Low-density lipoprotein (LDL) cholesterol.
- Very low-density lipoprotein (VLDL) cholesterol.
- Aspartate aminotransferase (AST).
- Alanine aminotransferase (ALT).
- Serum total bilirubin.

Platelet count was measured using an automated hematologyanalyzer based on the electrical impedance principle.

Estimation methods: HbA1c was estimated by immunoturbidimetric method using the AU 480 automated clinical chemistry analyser. Fasting plasma glucose and 2-hour post-prandial glucose were measured using the hexokinase enzymatic method. Lipid profile parameters including HDL cholesterol, LDL cholesterol, triglycerides and VLDL cholesterol were estimated using enzymatic colorimetric methods with reagent kits compatible with the AU 480 analyser. AST and ALT activities were determined using enzymatic kinetic methods based on International Federation of Clinical Chemistry recommended procedures. Total bilirubin was estimated using the diazo reaction method. Platelet count was determined using an automated hematology analyser based on electrical impedance principle.

Calculation of FIB-4 index: The FIB-4 index was calculated using age, AST, ALT and platelet count. The formula used was:

FIB-4 = Age (years) × AST (U/L) / [Platelet count (10^9 /L) × √ALT (U/L)]

The calculated FIB-4 values were interpreted using established clinical cut-off values:

- FIB-4 <1.3: low probability of advanced liver fibrosis.
- FIB-4 1.3–2.67: indeterminate or intermediate risk.

- FIB-4 >2.67: high probability of advanced liver fibrosis.

Statistical analysis: The collected data were entered into Microsoft Excel and analysed using Statistical Package for Social Sciences (SPSS) software, version 25.0. Shapiro–Wilk test was used to assess normality of data. Since the study variables were not normally distributed, continuous variables were expressed as median and interquartile range. Categorical variables were expressed as frequencies and percentages.

Comparisons between males and females were performed using Mann–Whitney U test. Correlation between FIB-4 score and study variables was assessed using Spearman correlation. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total number of 170 individuals were selected as the study group for the present study. This study included 88 male and 82 female individuals. Blood samples of all study participants were taken and analysed for glycemic parameters, lipid profile parameters, platelet count, liver function parameters and FIB-4 score. Glycemic parameters included HbA1c, fasting blood sugar and post-prandial blood sugar. Lipid profile parameters included fasting triglycerides, HDL, LDL and VLDL. Blood count parameter included platelet count, and liver function parameters included AST, ALT and serum total bilirubin.

The FIB-4 score was calculated from age, ALT, AST and platelet count entered in the master chart. Anthropometric details including age, height, weight, BMI and waist–hip ratio were also recorded. Ultrasonography abdomen reports of all patients were noted to assess fatty changes in liver and categorized into normal liver, Grade 1 fatty liver, Grade 2 fatty liver and Grade 3 fatty liver.

The whole data was documented in Microsoft Excel sheet and statistical analysis was done using SPSS IBM software. Shapiro–Wilk test was performed for normality check of the data. Since the variables were not normally distributed, median and interquartile range were calculated, and non-parametric tests were performed for statistical interpretation. Mann–Whitney U test was used for comparison between males and females, and Spearman correlation was used to assess correlation among study variables.

Table 1: Descriptive statistics of the study participants (n=170)

Parameter / Variable	Minimum	Maximum	Median	IQR (Q1–Q3)
Age (years)	25	60	46	35.5–52.8
Weight (kg)	50.4	94.4	72.3	59.4–82.9
Height (m)	1.5	1.8	1.6	1.56–1.71
BMI (kg/m²)	16.76	40.88	25.7	22.3–31.7
Waist–hip ratio	0.75	1.05	0.9	0.82–0.98
HbA1c	5.1	10	7.4	6.2–9.2
FBS (mg/dL)	141	230	179	163.6–206.8
PPBS (mg/dL)	180	230	240	214.9–259.8
Platelet count (10^9 /L)	150	303.8	233.9	213.05–348
AST (U/L)	26.2	105.1	65.5	47.5–77.55
ALT (U/L)	22.3	117.8	69	50.45–84.45
Triglycerides (mg/dL)	101	295	197.6	146.2–249.8
HDL (mg/dL)	30	64	48.8	41.15–57.28
LDL (mg/dL)	81	190	136.3	104.03–164.33
VLDL (mg/dL)	20	59	39.5	29.2–49.93
FIB-4 score	0.4	4.9	1.3	0.88–1.72

The median age of the study participants was 46 years. The median HbA1c was 7.4, and the median FIB-4 score was 1.3. The median BMI was 25.7 kg/m². The median AST and ALT values were 65.5 U/L and 69 U/L, respectively.

Table 2: Distribution of males and females among different FIB-4 score categories (n=170)

FIB-4 score category	Males	Females	Total
<1.3 — No/low risk fibrosis	50	35	85
1.3–2.67 — Mild/moderate fibrosis	35	44	79
>2.67 — Advanced fibrosis	3	3	6
Total	88	82	170

Among 170 study participants, 85 were in the no/low risk fibrosis category, 79 were in the mild/moderate fibrosis category and 6 were in the advanced fibrosis category. Low-risk fibrosis category included 50 males and 35 females, while mild/moderate fibrosis category included 35 males and 44 females. Advanced fibrosis was observed in 3 males and 3 females.

Table 3: Comparison of study parameters among males and females (n=170)

Parameter	Male, Median (IQR)	Female, Median (IQR)	p-value
FIB-4 score	1.19 (0.84–1.62)	1.40 (0.91–1.81)	0.070
Waist–hip ratio	0.91 (0.82–0.99)	0.88 (0.82–0.96)	0.346
BMI	26.4 (23.22–32.64)	25.38 (21.56–30.48)	0.107

HbA1c	7.42 (6.32–8.85)	7.45 (6.06–9.38)	0.913
FBS	178.6 (162.9–201.2)	181.8 (164.4–210.4)	0.670
PPBS	232.8 (216.4–259.4)	238.4 (215–259.9)	0.841
Triglycerides	187.8 (147.2–253.6)	198.9 (148.2–243.7)	0.585
HDL	46.65 (40.23–55.1)	53.45 (41.73–58.45)	0.076
LDL	142.3 (96.95–168.2)	135.1 (109.8–156.9)	0.798
VLDL	37.55 (29.4–50.75)	39.8 (29.68–48.75)	0.570

The p-value was more than 0.05 for all parameters among males and females, indicating that there was no statistically significant difference in FIB-4 score, waist–hip ratio, BMI, HbA1c, FBS, PPBS, triglycerides, HDL, LDL and VLDL between males and females.

Table 4: Correlation between FIB-4 score and anthropometric parameters

Parameter	Median, IQR (n=170)	Spearman rho	p-value
Waist–hip ratio	0.9 (0.82–0.98)	-0.058	0.449
BMI	25.7 (22.3–31.7)	-0.039	0.611
Age	46 (35.5–52.8)	0.454	<0.0001

The correlation between FIB-4 and waist–hip ratio was not statistically significant, with slight negative correlation. The correlation between FIB-4 and BMI was also not statistically significant, with slight negative correlation. A statistically significant positive correlation was observed between FIB-4 index and age, indicating that FIB-4 values tend to increase as age advances.

Table 5: Correlation between FIB-4 score and lipid profile parameters

Parameter	Median, IQR (n=170)	Spearman rho	p-value
LDL	136.3 (104.03–164.33)	-0.158	0.040
VLDL	39.5 (29.2–49.93)	0.096	0.204
HDL	0.4 (0.29–0.46)	-0.001	0.993
Triglycerides	197.6 (146.2–249.8)	0.098	0.204

A statistically significant weak negative correlation was observed between FIB-4 index and LDL levels. In contrast, VLDL, HDL and triglycerides showed statistically non-significant correlations with FIB-4 score.

Table 6: Correlation between FIB-4 score and HbA1c

Parameter	Median, IQR (n=170)	Spearman rho	p-value
HbA1c	7.4 (6.2–9.2)	0.157	0.041
FIB-4 score	1.3 (0.88–1.72)	0.157	0.041

Spearman’s rank correlation analysis showed a weak positive correlation between HbA1c and FIB-4 score, which was statistically significant. This indicates that higher HbA1c levels were associated with a slight increase in FIB-4 scores.

Table 7: Distribution of HbA1c categories across FIB-4 categories

HbA1c	FIB-4 <1.3	FIB-4 1.3–2.67	FIB-4 >2.67	Total
<7	42	29	2	73
7–8	9	13	1	23
>8	34	37	3	74
Total	85	79	6	170

Spearman’s rho: 0.157
p-value: 0.041
N: 170
The distribution of HbA1c categories across FIB-4 categories showed that patients with higher HbA1c values were represented in the intermediate and advanced FIB-4 categories. Spearman’s rank correlation analysis showed a weak but statistically significant positive correlation between HbA1c and FIB-4 score.

Table 8: Correlation between FIB-4 and fatty changes in liver

FIB-4 score	Normal liver	Grade 1 fatty changes in liver	Grade 2 fatty changes in liver	Grade 3 fatty changes in liver	Total
<1.3 — No/low risk fibrosis	29	38	19	0	85
1.3–2.67 — Mild/moderate fibrosis	8	25	38	7	79
>2.67 — Advanced fibrosis	0	0	1	5	6
Total	37	63	58	12	170

Spearman's rho: 0.497
p-value:<0.001
N: 170
Spearman's rank correlation analysis showed a moderate positive correlation between FIB-4 score and fatty liver grade. This indicates that increasing fatty liver grade was associated with higher FIB-4 values. The correlation was statistically significant, suggesting a meaningful relationship between liver steatosis severity and fibrosis index.

Table 9: Comparison between FIB-4 score and HbA1c with age

Parameter	20–30 years	31–40 years	41–50 years	51–60 years	p-value
FIB-4 score, Median (IQR)	0.74 (0.53–1.21)	1.11 (0.83–1.31)	1.22 (0.88–1.57)	1.7 (1.33–2.1)	<0.0001
HbA1c, Median (IQR)	6.7 (5.8–8.1)	7.2 (6–8.3)	7.4 (6.2–9.5)	7.9 (6.6–9.5)	0.05

FIB-4 score and HbA1c levels showed a progressive increase with advancing age. FIB-4 demonstrated a highly significant association with age, while HbA1c showed borderline statistical significance. This suggests that older individuals with type 2 diabetes and poorer glycemic control are at a higher risk of liver fibrosis.

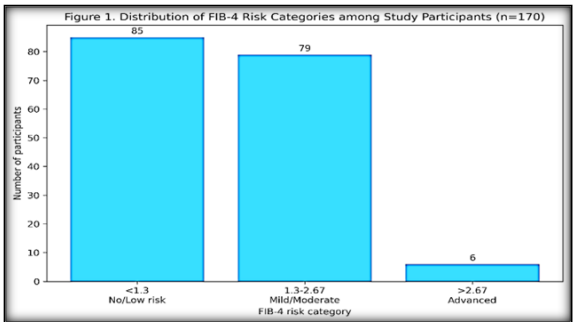

Figure 1: Distribution of FIB-4 Risk Categories among Study Participants

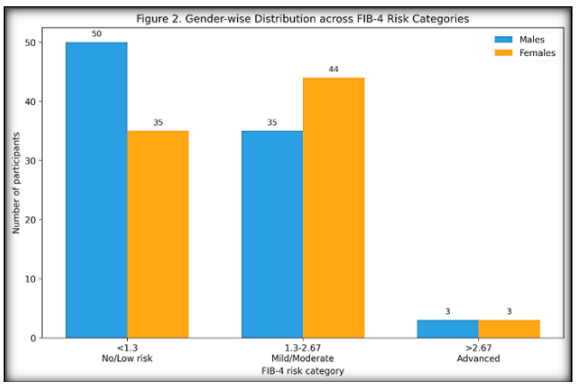

Figure 2: Gender-wise Distribution of Study Participants across FIB-4 Risk Categories

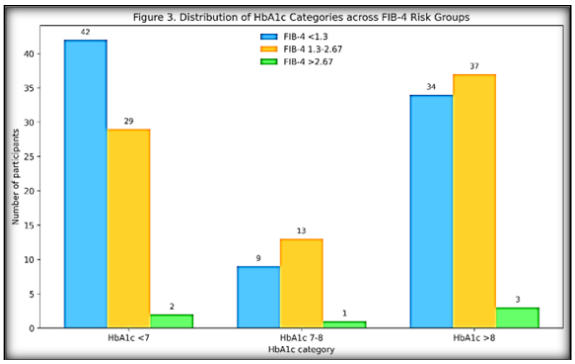

Figure 3: Distribution of HbA1c Categories across FIB-4 Risk Groups

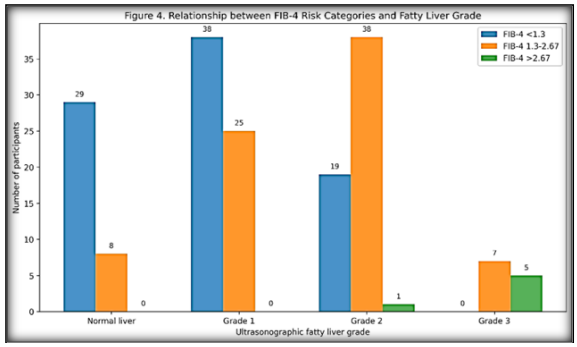

Figure 4: Relationship between FIB-4 Risk Categories and Ultrasonographic Fatty Liver

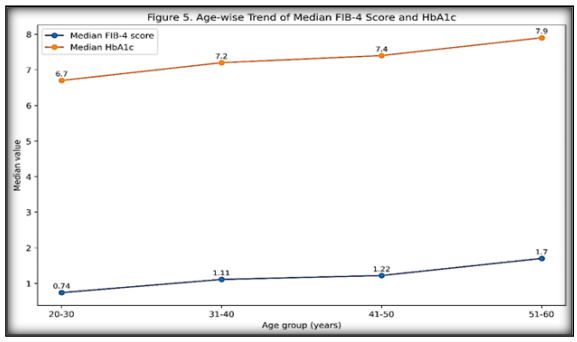

Figure 5: Age-wise Trend of Median FIB-4 Score and HbA1c Levels

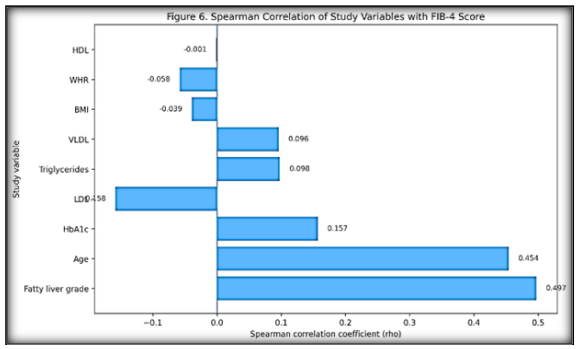

Figure 6: Spearman Correlation of Study Variables with FIB-4 Score

DISCUSSION

Type 2 diabetes mellitus (T2DM) is closely associated with metabolic liver disease, hepatic steatosis and progression to liver fibrosis. In diabetic patients, insulin resistance, chronic hyperglycemia, dyslipidemia and inflammatory activation contribute to hepatic fat accumulation, hepatocellular injury

and fibrogenesis. Previous studies have shown that T2DM is strongly linked with non-alcoholic fatty liver disease/metabolic dysfunction-associated steatotic liver disease and that diabetic patients are at increased risk of progressive liver fibrosis and adverse hepatic outcomes.[12,13] Therefore, early identification of liver fibrosis risk in patients with T2DM is clinically important.

In the present study, 170 patients with T2DM were evaluated. The study population included 88 males and 82 females. The median HbA1c was 7.4, and the median FIB-4 score was 1.3. Based on FIB-4 score, 85 patients were categorized as no/low risk fibrosis, 79 as mild/moderate fibrosis and 6 as advanced fibrosis. The key findings of the study were: a weak but statistically significant positive correlation between HbA1c and FIB-4 score, a moderate positive correlation between FIB-4 score and ultrasonographic fatty liver grade, a significant positive correlation between age and FIB-4 score, and a weak negative correlation between LDL and FIB-4 score.

The biological basis for the association between poor glycemic control and liver fibrosis is well supported. Chronic hyperglycemia and insulin resistance increase free fatty acid flux into the liver, promote de novo lipogenesis, increase oxidative stress and activate inflammatory pathways.[14,15] These mechanisms contribute to hepatocellular injury and activation of hepatic stellate cells, which are central to collagen deposition and hepatic fibrosis.[16,17] Thus, the observed association between higher HbA1c, increasing fatty liver grade and higher FIB-4 values in the present study is biologically plausible.

Correlation between FIB-4 index and HbA1c levels: The present study demonstrated a statistically significant positive correlation between HbA1c and FIB-4 index among patients with T2DM. Spearman correlation showed rho = 0.157 with p = 0.041. This indicates that higher HbA1c levels were associated with a slight increase in FIB-4 score. Although the correlation was weak, it was statistically significant, suggesting that poor glycemic control may be associated with increased liver fibrosis risk in diabetic patients.

This finding is consistent with previous studies that reported an association between glycemic control and liver fibrosis markers. Kim et al. reported an association between HbA1c and liver fibrosis.[18] Seka et al. described the relationship between glycemic control and fibrosis progression.[19] Williamson et al. also reported that HbA1c was related to liver disease outcomes in patients with diabetes.[20] Chachar et al. reported a positive correlation between glycemic control and FIB-4 index in patients with T2DM, with higher HbA1c levels being associated with greater fibrosis risk.[21] In the present study, the direction of association was similar, although the correlation was weak.

The weak strength of correlation in the present study may be due to the fact that FIB-4 is influenced by age, AST, ALT and platelet count. HbA1c alone cannot fully determine the FIB-4 score. Other factors such as duration of diabetes, obesity, liver enzyme levels, platelet count, medication use and degree of hepatic steatosis may modify the association between glycemic control and fibrosis risk. Therefore, HbA1c should be interpreted as an important metabolic risk marker rather than as an independent stand-alone marker of liver fibrosis.

FIB-4 as a non-invasive marker of liver fibrosis risk: The FIB-4 index is a simple and widely used non-invasive fibrosis score calculated using age, AST, ALT and platelet count. Sterling et al. developed FIB-4 as a simple non-invasive index to predict significant fibrosis.[22] Vallet-Pichard et al. also supported the role of FIB-4 in fibrosis prediction.[23] The major advantage of FIB-4 is that it uses routinely available clinical and laboratory parameters, making it useful in outpatient and resource-limited clinical settings.

In the present study, standard FIB-4 categories were used: <1.3 for no/low risk fibrosis, 1.3–2.67 for mild/moderate fibrosis and >2.67 for advanced fibrosis. Among 170 patients, 85 were in the no/low risk category, 79 were in the mild/moderate category and 6 were in the advanced fibrosis category. This indicates that a considerable proportion of patients with T2DM had FIB-4 values falling into the intermediate or advanced fibrosis-risk categories.

The clinical role of FIB-4 should be interpreted as screening and risk stratification rather than definitive diagnosis. Shah et al. reported that non-invasive fibrosis markers, including FIB-4, are useful in identifying advanced fibrosis in NAFLD.[24] McPherson et al. demonstrated progression from steatosis to fibrosis using non-invasive markers, supporting the clinical relevance of fibrosis scoring in NAFLD.[25] Chalasani et al. also emphasized the importance of non-invasive assessment in the diagnosis and management of NAFLD (26). Thus, FIB-4 can help identify diabetic patients who may require further evaluation by repeat biochemical testing, ultrasonography, elastography or specialist referral.

Relationship between FIB-4 and ultrasonographic fatty liver grade: One of the strongest findings in the present study was the statistically significant moderate positive correlation between FIB-4 score and ultrasonographic fatty liver grade. Spearman correlation showed rho = 0.497 with p <0.001. This indicates that increasing fatty liver grade was associated with higher FIB-4 values.

In the retained results table, patients in the no/low risk FIB-4 category were distributed among normal liver, Grade 1 fatty liver and Grade 2 fatty liver, whereas patients in the advanced fibrosis category were concentrated mainly in Grade 3 fatty liver. This pattern suggests that increasing ultrasonographic fatty liver severity is associated with increasing FIB-4-based fibrosis risk.

This finding is clinically meaningful because fatty liver disease can progress from steatosis to steatohepatitis, fibrosis, cirrhosis and liver-related complications. Angulo et al. reported that liver fibrosis, rather than other histological features, is strongly associated with long-term outcomes in NAFLD.[27] Therefore, the moderate positive association between FIB-4 and fatty liver grade in the present study supports the use of FIB-4 as a practical non-invasive risk marker in diabetic patients with fatty liver changes.

Ultrasonography is widely available and useful for detecting hepatic steatosis, but it is limited in accurately staging fibrosis. Yang et al. discussed the applications and limitations of ultrasound imaging in non-alcoholic liver disease.[28] Damjanovska et al. reported that ultrasound elastography performed better than FIB-4 in ruling out cirrhosis in obese NAFLD patients, highlighting the importance of advanced imaging when available.[29] Therefore, the present study supports a two-step approach in clinical practice: initial FIB-4 calculation, followed by ultrasound or elastography in patients with intermediate or high-risk FIB-4 values.

FIB-4 across different HbA1c categories: The present study compared FIB-4 risk categories across HbA1c groups of <7, 7–8 and >8. Among patients with HbA1c <7, 42 were in the FIB-4 <1.3 category, 29 were in the FIB-4 1.3–2.67 category and 2 were in the FIB-4 >2.67 category. Among patients with HbA1c 7–8, 9 were in the FIB-4 <1.3 category, 13 were in the FIB-4 1.3–2.67 category and 1 was in the FIB-4 >2.67 category. Among patients with HbA1c >8, 34 were in the FIB-4 <1.3 category, 37 were in the FIB-4 1.3–2.67 category and 3 were in the FIB-4 >2.67 category.

These findings show that patients with higher HbA1c values were represented in the intermediate and advanced FIB-4 categories. However, the relationship was not completely linear, as several patients with HbA1c >8 remained in the low-risk FIB-4 category. This suggests that poor glycemic control is associated with fibrosis risk but does not alone determine fibrosis category. Age, AST, ALT, platelet count, duration of diabetes, obesity, medication use and background hepatic steatosis may all influence the FIB-4 score.

The findings are broadly consistent with studies suggesting that elevated HbA1c and metabolic dysfunction are associated with higher liver fibrosis risk. Xie et al. reported that HbA1c was associated with severity of liver steatosis and fibrosis measured by transient elastography.[30] Thus, HbA1c may be useful as part of a broader metabolic risk assessment, but it should not be used alone to predict liver fibrosis.

Relationship between age, HbA1c and FIB-4 index: Age showed a statistically significant positive correlation with FIB-4 score in the present study, with rho = 0.454 and p <0.0001. Age-wise comparison also showed progressive increase in median FIB-4 score across age groups: 0.74 in 20–30 years, 1.11 in 31–40 years, 1.22 in 41–50 years and 1.7 in 51–60 years. HbA1c also showed a gradual increase with age, from 6.7 in the 20–30-year group to 7.9 in the 51–60-year group, with borderline statistical significance.

The increase in FIB-4 with age is expected because age is a direct component of the FIB-4 formula. However, the finding is also clinically relevant. Older patients with T2DM may have longer cumulative exposure to hyperglycemia, insulin resistance, dyslipidemia and metabolic inflammation. These factors can contribute to progressive liver injury and fibrosis over time. Therefore, older diabetic patients with elevated FIB-4 scores may require closer clinical evaluation.

At the same time, age-related increases in FIB-4 should be interpreted carefully. Since age is part of the formula, higher scores in older individuals may partly reflect age itself rather than fibrosis alone. Therefore, FIB-4 should be interpreted along with liver enzymes, platelet count, glycemic status, ultrasound findings and, where available, elastography.

Correlation between lipid profile and FIB-4 index: In the present study, LDL showed a statistically significant weak negative correlation with FIB-4 score, with rho = -0.158 and p = 0.040. In contrast, VLDL, HDL and triglycerides showed statistically non-significant correlations with FIB-4.

The negative association between LDL and FIB-4 may appear paradoxical because LDL is traditionally considered a cardiometabolic risk marker. However, in progressive liver disease, lipid metabolism may be altered because the liver plays a central role in lipoprotein synthesis and secretion. Lower LDL values in patients with higher FIB-4 may reflect altered hepatic lipid handling, reduced lipoprotein synthesis or treatment-related effects such as statin use. Since the observed correlation was weak, LDL should not be interpreted as an independent fibrosis marker. Instead, lipid profile should be considered as part of the overall cardiometabolic evaluation of patients with T2DM.

CONCLUSION

The present study demonstrated a weak but statistically significant positive correlation between HbA1c and FIB-4 index in patients with type 2 diabetes mellitus, indicating that poorer glycemic control was associated with higher fibrosis risk. FIB-4 also showed a moderate positive correlation with ultrasonographic fatty liver grade, supporting its usefulness as a non-invasive fibrosis-risk marker. Age showed a significant positive correlation with FIB-4 score, while LDL showed a weak negative correlation. VLDL, HDL and triglycerides did not show statistically significant correlations with FIB-4.

Overall, the findings support the use of FIB-4 as a simple, non-invasive and cost-effective screening

tool for liver fibrosis risk assessment in patients with type 2 diabetes mellitus, particularly when interpreted along with HbA1c and ultrasonographic fatty liver grading. Patients with poor glycemic control, advancing age and higher fatty liver grade may require closer metabolic monitoring and further liver-related evaluation.

Strengths of the Study:

1. The study was conducted in patients with type 2 diabetes mellitus, a population at increased risk for metabolic liver disease and fibrosis.
2. The study used FIB-4, a simple, non-invasive and cost-effective marker calculated from routinely available laboratory parameters.
3. The study correlated FIB-4 not only with HbA1c but also with ultrasonographic fatty liver grade, age, anthropometric variables and lipid profile.
4. Standard FIB-4 categories and predefined HbA1c groups were used, providing a clinically interpretable framework for fibrosis-risk assessment.
5. The study provides hospital-based regional data from an Indian population, where data on HbA1c and FIB-4 relationship are relatively limited.

Limitations:

1. The study was cross-sectional in design, so causal relationship between poor glycemic control and liver fibrosis risk cannot be established.
2. Liver fibrosis was assessed using FIB-4 and ultrasonography, but elastography, magnetic resonance elastography or liver biopsy was not used for confirmation.
3. Ultrasonography is useful for detecting fatty liver but has limited accuracy for staging fibrosis.
4. The influence of duration of diabetes, antidiabetic medications, statin use and other metabolic drugs was not fully evaluated.
5. Being a hospital-based study, the findings may not be generalizable to all community-based type 2 diabetes mellitus populations.

Recommendations:

1. Longitudinal follow-up studies are required to determine whether improvement in HbA1c is associated with stabilization or reduction of FIB-4 score.
2. Larger multicentric Indian studies are needed to validate population-specific FIB-4 cut-offs among patients with type 2 diabetes mellitus.
3. Future studies should include elastography or magnetic resonance-based methods to improve diagnostic accuracy and validate FIB-4 against liver stiffness.
4. The role of newer glucose-lowering agents such as SGLT2 inhibitors, GLP-1 receptor agonists and pioglitazone on liver enzymes, steatosis, FIB-4 score and fibrosis progression should be evaluated.
5. A combined screening approach using HbA1c, FIB-4, liver enzymes, platelet count and ultrasonographic fatty liver grading may be considered in routine diabetes care.

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