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Association Between Liver Stiffness Severity and Atherosclerotic Cardiovascular Disease Risk Among Diabetic and Non-Diabetic Patients with Metabolic Dysfunction-Associated Fatty Liver Disease.

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Abstract

Background: Metabolic dysfunction-associated fatty liver disease (MAFLD) is closely linked to type 2 diabetes mellitus (T2DM) and heightened cardiovascular risk. Liver fibrosis, a marker of disease progression, has also been associated with adverse cardiovascular outcomes. This study compared liver stiffness, hepatic steatosis, and atherosclerotic cardiovascular disease (ASCVD) risk between diabetic and non-diabetic MAFLD patients and identified factors independently associated with elevated ASCVD risk.

Methodology: A hospital-based comparative cross-sectional study was conducted at Liaquat National Hospital, Karachi, Pakistan. A total of 240 adults with MAFLD confirmed by transient elastography (FibroScan®) were enrolled, including 120 diabetic and 120 non-diabetic participants. Hepatic steatosis was assessed using the controlled attenuation parameter (CAP), while liver fibrosis was measured by liver stiffness measurement (LSM). Demographic, anthropometric, biochemical, and cardiometabolic characteristics were compared. ASCVD risk was estimated using the PREVENT risk calculator.

Results: Diabetic participants were older and had higher HbA1c, ALT, total cholesterol, LDL/HDL ratio, serum creatinine, and ASCVD scores (all $p<0.05$). Advanced fibrosis was more frequent among diabetics (10.0% vs. 1.7%; $p=0.015$). Participants with high ASCVD risk exhibited higher total cholesterol, LDL/HDL ratio, CAP values, and fibrosis severity. Multivariable analysis identified age (OR=1.22; 95% CI: 1.13–1.32; $p<0.001$) and LDL/HDL ratio (OR=2.41; 95% CI: 1.47–3.97; $p=0.001$) as independent predictors. Diabetes, BMI, ALT, and LSM were not independently associated.

Conclusion: MAFLD patients with diabetes have worse metabolic profiles and greater fibrosis, but elevated ASCVD risk is primarily driven by age and atherogenic dyslipidemia rather than diabetes or liver stiffness, highlighting the need for comprehensive cardiometabolic risk assessment.

Keywords

Metabolic Dysfunction-Associated Fatty Liver Disease, Type 2 Diabetes Mellitus, Liver Fibrosis, Transient Elastography, Cardiovascular Risk, ASCVD

Introduction

Metabolic dysfunction-associated fatty liver disease (MAFLD) has emerged as one of the most prevalent chronic liver disorders worldwide and represents a major public health challenge. Recent meta-analyses estimate the global prevalence of MAFLD to range between 30% and 32%, affecting nearly one-third of the adult population[1,2]. The burden of disease varies considerably across regions, with prevalence exceeding 40% in several parts of the Americas and Asia. Furthermore, MAFLD is more common among men than women and continues to increase in parallel with the global epidemics of obesity, insulin resistance, and type 2 diabetes mellitus (T2DM)[1-3]. Beyond its hepatic manifestations, MAFLD is increasingly recognized as a multisystem metabolic disorder associated with substantial cardiovascular, endocrine, and renal morbidity[4].

Among the metabolic abnormalities associated with MAFLD, T2DM is considered one of the strongest predictors of disease progression. The relationship between MAFLD and diabetes is bidirectional and synergistic. Patients with T2DM are at significantly increased risk of developing hepatic steatosis, steatohepatitis, advanced fibrosis, cirrhosis, and hepatocellular carcinoma, while individuals with MAFLD have a higher likelihood of developing diabetes and its associated complications[5-7]. Evidence suggests that diabetes accelerates hepatic fibrogenesis through mechanisms involving insulin resistance, chronic low-grade inflammation, oxidative stress, and altered lipid metabolism[6].

Cardiovascular disease remains the leading cause of morbidity and mortality among patients with MAFLD. Increasing evidence indicates that the severity of liver fibrosis is associated with a higher risk of atherosclerotic cardiovascular disease (ASCVD), independent of traditional metabolic risk factors[8]. Park et al. demonstrated that advanced liver fibrosis was associated with an eight-fold increase in estimated ASCVD risk after adjustment for conventional cardiovascular risk factors[9]. Similarly, recent studies have suggested that increased liver stiffness may serve as a clinically useful marker of systemic metabolic dysfunction and cardiovascular vulnerability[10].

Although liver biopsy remains the reference standard for diagnosing and staging MAFLD, its invasive nature, sampling variability, and limited feasibility in routine clinical practice have encouraged the adoption of non-invasive diagnostic approaches[11]. Transient elastography (FibroScan®) is a validated, non-invasive technique that simultaneously quantifies hepatic steatosis through the controlled attenuation parameter (CAP) and hepatic fibrosis through liver stiffness measurement (LSM)[12]. Consequently, major international guidelines, including those from the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL), recommend transient elastography as a first-line tool for fibrosis assessment in patients with MAFLD[13]. Nevertheless, the clinical significance of FibroScan-derived fibrosis measurements in predicting cardiovascular risk, particularly among diabetic and non-diabetic MAFLD populations, remains incompletely understood[14].

Given the close interplay between diabetes mellitus, hepatic fibrosis, and cardiovascular disease, identifying reliable non-invasive markers that reflect both hepatic and cardiometabolic risk is of considerable clinical importance. While previous studies have investigated the relationship between liver fibrosis and cardiovascular risk, comparative data evaluating diabetic and non-diabetic MAFLD populations remain limited, particularly in South Asian populations. Therefore, this study aimed to compare liver stiffness severity, hepatic steatosis burden, and ASCVD risk among diabetic and non-diabetic patients with MAFLD and to determine the independent predictors of elevated ASCVD risk in this population.

Methodology

Study Design

This analytical comparative cross-sectional study was conducted to evaluate the association between liver stiffness severity and atherosclerotic cardiovascular disease (ASCVD) risk among diabetic and non-diabetic patients diagnosed with metabolic dysfunction-associated fatty liver disease (MAFLD). The study compared hepatic steatosis, fibrosis severity, cardiometabolic characteristics, and ASCVD

risk profiles between the two groups and further explored factors independently associated with high ASCVD risk. Data were collected prospectively over a six-month period from September 2023 to February 2024.

Ethics

Ethical approval for the study was obtained from the Ethical Review Committee of Liaquat National Hospital, Karachi, Pakistan (Ref No. App#1091-2024-ERC). Written informed consent was obtained from all participants before enrolment. Participation was voluntary, and participants were informed about the study objectives, procedures, potential risks, and benefits. Confidentiality was maintained by assigning unique identification codes to participants and removing personal identifiers from the analytical dataset. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki and subsequent amendments.

Setting

The study was conducted at the Department of Cardiology, Liaquat National Hospital, Karachi, Pakistan, a tertiary-care teaching hospital that receives referrals from both urban and rural regions of the country. Patients attending outpatient clinics or referred for metabolic and cardiovascular risk assessment were screened for eligibility. Clinical evaluations, laboratory investigations, and transient elastography examinations were performed within the hospital using standardized institutional protocols.

Participants

Eligible participants were adults aged more than 20 years with a diagnosis of MAFLD. MAFLD was defined according to contemporary consensus criteria as evidence of hepatic steatosis together with overweight/obesity, type 2 diabetes mellitus, or evidence of metabolic dysregulation [12,13]. Hepatic steatosis was confirmed using transient elastography with controlled attenuation parameter (CAP) assessment.

Patients were excluded if they had significant alcohol consumption (>20 g/day for women and >30 g/day for men), chronic hepatitis B or hepatitis C infection, radiological evidence of cirrhosis, previous splenectomy, pregnancy, malignant disease, or incomplete clinical or biochemical records, particularly missing lipid profile measurements. Alcohol intake and medical history were assessed through structured interviews and review of hospital records.

Participants were categorized into two groups. The diabetic group included patients with established or newly diagnosed type 2 diabetes mellitus according to American Diabetes Association (ADA) criteria documented in medical records. The non-diabetic group consisted of MAFLD patients without a history or laboratory evidence of diabetes who met all other eligibility criteria. Consecutive sampling was employed until the required sample size was achieved.

Variables

The primary exposure variable was diabetes mellitus status (diabetic versus non-diabetic). The primary outcome variables were liver stiffness severity, fibrosis stage, hepatic steatosis grade, and ASCVD risk category.

Secondary variables included age, sex, body mass index (BMI), waist circumference, hip circumference, waist-to-hip ratio, smoking status, hypertension, dyslipidemia, glycated hemoglobin (HbA1c), liver function parameters, renal function parameters, lipid profile components, and calculated LDL/HDL ratio. Fibrosis severity and steatosis grade derived from transient elastography were also evaluated as independent variables in regression analyses.

Data Sources / Measurement

Demographic information, medical history, and clinical characteristics were obtained through patient interviews and electronic medical records. Anthropometric measurements were performed by trained healthcare personnel using calibrated equipment. Body weight was measured to the nearest 0.1 kg and height to the nearest 0.1 cm, and BMI was calculated as weight (kg)/height² (m^2). Waist and hip circumferences were measured using non-stretchable measuring tape according to standardized protocols.

Venous blood samples were collected after a minimum fasting period of 8 hours. Biochemical analyses were performed in the hospital's central laboratory using the Roche Cobas® 8000 modular analyzer. Lipid parameters including total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol were measured using enzymatic colorimetric methods. Dyslipidemia was defined as triglycerides ≥200 mg/dL, LDL cholesterol ≥160 mg/dL, HDL cholesterol ≤40 mg/dL, or current treatment for dyslipidemia. Additional laboratory investigations included HbA1c, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, total bilirubin, serum creatinine, and blood urea.

ASCVD risk was estimated using the American Heart Association PREVENT risk calculator, which incorporates age, sex, body mass index, blood pressure, lipid profile, diabetes status, and other cardiovascular risk factors to estimate future cardiovascular risk. Participants were subsequently categorized into predefined ASCVD risk strata for comparative analyses.

Transient elastography (FibroScan®, Echosens, Paris, France) was performed by trained and certified operators who were blinded to participants' diabetic status. Hepatic steatosis was quantified using controlled attenuation parameter (CAP) values and categorized as S0 (<238 dB/m), S1 (238–259 dB/m), S2 (260–290 dB/m), and S3 (>290 dB/m). Liver fibrosis was assessed using liver stiffness measurement (LSM) values and categorized as F0–F1 (<7.0 kPa), F2 (7.0–8.6 kPa), F3 (8.7–10.2 kPa), and F4 (>10.3 kPa), based on validated transient elastography thresholds reported in previous studies[11,12].

Bias

Several measures were implemented to minimize potential bias. Selection bias was reduced by recruiting consecutive eligible patients during the study period. Measurement bias was minimized through the use of standardized clinical assessment procedures, calibrated equipment, validated laboratory assays, and certified FibroScan operators. Observer bias was reduced by ensuring that transient elastography technicians were blinded to participants' diabetes status. Information bias was minimized by obtaining clinical and laboratory data from hospital records and standardized assessment forms. Potential confounding variables including age, sex, BMI, diabetes status, liver stiffness measurements, and lipid parameters were controlled during multivariable regression analysis.

Study Size

Sample size was calculated using previously reported prevalence estimates of MAFLD among diabetic and non-diabetic populations. Assuming a prevalence of approximately 60% among diabetic individuals and 30% among non-diabetic individuals, a two-sided chi-square test with 80% statistical power and a 5% level of significance indicated a minimum requirement of 42 participants per group. To improve statistical precision, increase power for subgroup analyses, and account for potential exclusions and missing data, a total sample of 240 participants was recruited, comprising 120 diabetic and 120 non-diabetic MAFLD patients.

Quantitative Variables

Continuous variables including age, BMI, waist circumference, HbA1c, ALT, lipid profile measurements, CAP values, liver stiffness measurements, and ASCVD risk scores were analyzed as quantitative variables. For descriptive purposes and clinical interpretation, selected variables were categorized using clinically established thresholds. Age was categorized as ≤45 years and >45 years. Fibrosis and steatosis severity were categorized according to FibroScan cut-off values. ASCVD risk estimates were grouped into clinically meaningful risk categories as defined by the PREVENT risk assessment model.

Statistical Methods

Data were analyzed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using graphical methods and distributional characteristics. Normally distributed continuous variables were presented as mean ± standard deviation (SD) and compared using independent-samples t-tests. Non-normally distributed variables were compared using the

Mann–Whitney U test. Categorical variables were summarized as frequencies and percentages and compared using Pearson's chi-square test or Fisher's exact test where appropriate.

Comparisons across ASCVD risk groups were performed using one-way analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical variables. Unadjusted associations between demographic, clinical, and FibroScan-related variables and diabetes status were evaluated using binary logistic regression analysis, and results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). To identify independent predictors of high ASCVD risk, multivariable binary logistic regression analysis was performed. Variables with clinical relevance and those demonstrating significance in univariate analyses were entered into the regression model, including age, gender, diabetes mellitus, body mass index, ALT, LDL/HDL ratio, and FibroScan-derived fibrosis measurements. Adjusted odds ratios with corresponding 95% confidence intervals were reported. Model assumptions were assessed prior to analysis, and statistical significance was established at a two-tailed p-value ≤0.05.

Results

Participants

A total of 240 participants with metabolic dysfunction-associated fatty liver disease (MAFLD) were enrolled during the study period. The study population was equally distributed between diabetic (n = 120) and non-diabetic (n = 120) groups. All recruited participants fulfilled the eligibility criteria and had complete demographic, laboratory, transient elastography (FibroScan), and ASCVD risk assessment data available for analysis. No participants were excluded after enrolment due to missing outcome measures. The comparative analysis was therefore performed on the complete dataset of 240 participants.

Descriptive Data

The baseline demographic, clinical, anthropometric, laboratory, and FibroScan characteristics of diabetic and non-diabetic MAFLD patients are summarized in Table 1. Diabetic participants were significantly older than non-diabetic participants (52.96 ± 8.36 vs. 50.55 ± 8.74 years, p = 0.030), and a greater proportion of diabetic patients were older than 45 years (83.3% vs. 66.7%, p = 0.003). No significant differences were observed regarding gender distribution, body mass index, waist circumference, waist-to-hip ratio, smoking status, or prevalence of hypertension between the two groups (Table 1). Regarding biochemical parameters, diabetic patients demonstrated significantly higher HbA1c levels (7.91 ± 0.76% vs. 5.20 ± 0.15%, p < 0.001), serum creatinine concentrations (p = 0.043), alanine aminotransferase (ALT) levels (p = 0.009), total cholesterol concentrations (p = 0.014), and LDL/HDL ratios (p < 0.001) compared with non-diabetic patients. Furthermore, diabetic participants had significantly higher calculated ASCVD risk scores than non-diabetic participants (12.04 ± 12.54% vs. 8.23 ± 8.55%, p = 0.006) (Table 1). FibroScan findings revealed no statistically significant differences in mean liver stiffness measurement (LSM) values or CAP scores between diabetic and non-diabetic groups. However, fibrosis severity differed significantly between groups (p = 0.015), with advanced fibrosis observed more frequently among diabetic patients (10.0%) than non-diabetic patients (1.7%). Although severe steatosis (S3) was more common among diabetic patients, differences in steatosis grades did not reach statistical significance (p = 0.348) (Table 1).

Outcome Data

The relationship between ASCVD risk status and clinical, biochemical, and FibroScan parameters among diabetic and non-diabetic MAFLD patients is presented in Table 2. Participants classified as having high ASCVD risk were significantly older than those with low ASCVD risk in both diabetic and non-diabetic groups (p < 0.001). High-risk participants also demonstrated significantly higher total cholesterol concentrations, LDL/HDL ratios, lifetime cardiovascular risk scores, and ALT levels compared with low-risk participants (all p < 0.05).

Gender distribution differed substantially across ASCVD risk categories, with males constituting the majority of high-risk individuals in both diabetic and non-diabetic groups (p < 0.001). Similarly,

participants older than 45 years were disproportionately represented in the high ASCVD risk category ($p < 0.001$). With respect to liver-related outcomes, CAP values were significantly higher among participants with elevated ASCVD risk ($p = 0.028$). Severe hepatic steatosis and overall steatosis prevalence were also significantly associated with higher ASCVD risk ($p = 0.010$ and $p = 0.041$, respectively). Fibrosis severity demonstrated a significant relationship with ASCVD risk status ($p < 0.001$), with advanced fibrosis being more frequently observed among diabetic patients classified as high ASCVD risk (Table 2). No statistically significant differences were observed across ASCVD risk categories for body mass index, waist circumference, waist-to-hip ratio, serum creatinine levels, hypertension status, smoking status, or overall presence of fibrosis (Table 2).

Main results

The association between demographic and clinical variables and diabetes status among MAFLD patients was evaluated using unadjusted binary logistic regression analysis (Table 3). Patients aged 45 years or younger had significantly lower odds of diabetes compared with older participants (OR = 0.40; 95% CI: 0.22–0.74; $p = 0.003$). Likewise, patients with no significant fibrosis (OR = 0.12; 95% CI: 0.03–0.59; $p = 0.008$) and those with mild fibrosis (OR = 0.15; 95% CI: 0.03–0.70; $p = 0.016$) had significantly lower odds of diabetes when compared with participants exhibiting advanced fibrosis.

No significant associations were identified for gender, hypertension, smoking status, steatosis grade, dyslipidemia patterns, or ASCVD risk categories (Table 3).

To determine independent predictors of high ASCVD risk, a multivariable binary logistic regression model was constructed incorporating age, gender, diabetes status, ALT, LDL/HDL ratio, FibroScan findings, and BMI (Table 4).

After adjustment for potential confounders, age remained a strong independent predictor of high ASCVD risk (adjusted OR = 1.22; 95% CI: 1.13–1.32; $p < 0.001$). Similarly, LDL/HDL ratio was independently associated with increased ASCVD risk (adjusted OR = 2.41; 95% CI: 1.47–3.97; $p = 0.001$). Gender also demonstrated a significant association with ASCVD risk (adjusted OR = 0.03; 95% CI: 0.008–0.102; $p < 0.001$).

In contrast, diabetes mellitus, ALT levels, body mass index, and FibroScan-derived liver stiffness measurements were not independently associated with high ASCVD risk after adjustment. These findings indicate that while diabetic MAFLD patients exhibit greater metabolic abnormalities and more advanced fibrosis, the principal determinants of elevated ASCVD risk are advancing age and atherogenic dyslipidemia rather than diabetes status or liver stiffness alone (Table 4).

Table 1: Comparison of Demographic, Clinical, and Laboratory Characteristics between Non-Diabetic and Diabetic MAFLD Patients (n = 240).

Variable	Non-Diabetic (n = 120)	Diabetic (n = 120)	p-value
Age (years), Mean ± SD	50.55 ± 8.74	52.96 ± 8.36	0.030*
Age, n (%)			
≤ 45 years	40(33.3)	20(16.7)	0.003*
> 45 years	80 (66.7)	100 (83.3)	
Gender, n (%)			
Male	49 (40.8)	42 (35.0)	0.352
Female	71 (59.2)	78 (65.0)	
BMI (kg/m²), Mean ± SD	30.65 ± 3.65	30.88 ± 3.38	0.617
Waist Circumference (cm), Mean ± SD	102.19 ± 8.71	104.40 ± 9.03	0.055
Hip Circumference (cm), Mean ± SD	106.55 ± 8.98	109.06 ± 9.63	0.037*
Waist-to-Hip Ratio, Mean ± SD	0.95 ± 0.01	0.95 ± 0.02	0.629

Hemoglobin (g/dL), Mean ± SD	11.94 ± 1.56	11.91 ± 1.32	0.908
HbA1c (%),Mean ± SD	5.20 ± 0.15	7.91 ± 0.76	<0.001*
Serum Creatinine (mg/dL), Mean ± SD	0.99 ± 0.31	1.08 ± 0.34	0.043*
ALT (U/L)	48.25 ± 17.40	54.35 ± 18.61	0.009*
Total Cholesterol (mg/dL)	185.10 ± 47.85	202.19 ± 58.94	0.014*
LDL/HDL Ratio	3.08 ± 0.79	4.15 ± 1.58	<0.001*
Systolic Blood Pressure (mmHg)	131.67±19.05	131.65±18.28	0.994
ASCVD Risk Score (%)	8.23 ± 8.55	12.04 ± 12.54	0.006*
FibroScan LSM (kPa)	6.71 ± 2.08	7.10 ± 2.22	0.156
CAP (dB/m)	276.10 ± 68.24	282.30 ± 65.56	0.474
Fibrosis Severity, n (%)			
No significant fibrosis	50 (41.7)	37 (30.8)	0.015*
Mild fibrosis	42 (35.0)	37 (30.8)	
Significant fibrosis	26 (21.7)	34 (28.3)	
Advanced fibrosis	2 (1.7)	12 (10.0)	
Steatosis Grade (CAP category), n (%)			
S0 (<238 dB/m)	38 (31.7)	29 (24.2)	0.348
S1 (238–259 dB/m)	21 (17.5)	16 (13.3)	
S2 (260–290 dB/m)	3 (2.5)	4 (3.3)	
S3 (>290 dB/m)	58 (48.3)	71 (59.2)	
Hypertension, n (%)			
Yes	54(45)	58(48.3)	0.605
No	66(55)	62(51.7)	
Smoking, n (%)			
Smoker	31(25.8)	39(32.5)	0.256
Non-Smoker	89(74.2)	81(67.5)	
Dyslipidemia pattern, n (%)			
Normolipidemic	17 (14.2)	4 (3.3)	0.028*
Combined hyperlipidemia	5 (4.2)	5 (4.2)	
Hyperlipidemia	0 (0.0)	3 (2.5)	
Low HDL cholesterol	74 (61.7)	81 (67.5)	
Hypertriglyceridemia	2 (1.7)	2 (1.7)	
Dyslipidemia with MetS, n (%)			
Yes	22 (18.3)	25 (20.8)	0.626
No	98(81.7)	95(79.2)	

*p ≤ 0.05 is considered Significant

Independent t-test applied to continuous variables; Chi-square/Fisher's exact test to categorical variables.

Table 2: Clinical, Biochemical, and Demographic Characteristics of Diabetic and Non-Diabetic MAFLD Patients Stratified by ASCVD Risk Status.

Variables	Diabetic Low Risk (n = 61)	Diabetic High Risk (n = 59)	Non-Diabetic Low Risk (n = 75)	Non-Diabetic High Risk (n = 45)	p-value
Age (years)	48.13 ± 6.91	57.96 ± 6.62	48.20 ± 8.86	54.48 ± 7.03	<0.001*
Hemoglobin (g/dL)	11.65 ± 1.33	12.19 ± 1.27	11.36 ± 1.40	12.89 ± 1.34	<0.001*
HbA1c (%)	7.76 ± 0.73	8.06 ± 0.76	5.20 ± 0.17	5.21 ± 0.13	<0.001*

Creatinine (mg/dL)	1.06 ± 0.36	1.09 ± 0.31	0.96 ± 0.24	1.04 ± 0.39	0.124
ALT (U/L)	50.52 ± 17.66	58.30 ± 18.89	48.04 ± 16.75	48.62 ± 18.62	0.006*
TC (mg/dL)	174.09 ± 27.93	231.23 ± 68.07	164.21 ± 33.24	219.91 ± 48.49	<0.001*
BMI (kg/m²)	30.82 ± 3.23	30.94 ± 3.55	30.31 ± 3.94	31.22 ± 3.07	0.540
Waist Circumference (cm)	104.37 ± 8.80	104.42 ± 9.34	101.22 ± 8.67	103.80 ± 8.64	0.110
Hip Circumference (cm)	109.26 ± 9.09	108.86 ± 10.24	105.57 ± 9.08	108.17 ± 8.67	0.087
LDL/HDL Ratio	3.41 ± 1.06	4.91 ± 1.68	2.80 ± 0.56	3.55 ± 0.89	<0.001*
FibroScan Score (kPa)	6.76 ± 2.34	7.46 ± 2.05	6.57 ± 2.00	6.94 ± 2.22	0.108
CAP (dB/m)	281.78 ± 64.51	282.83 ± 67.19	262.33 ± 64.65	299.04 ± 68.59	0.028*
ASCVD Risk Score (%)	3.33 ± 1.69	21.04 ± 12.57	2.96 ± 1.78	17.01 ± 8.15	<0.001*
Systolic BP (mmHg)	131.80 ± 18.69	131.50 ± 18.01	130.45 ± 19.54	133.71 ± 18.23	0.835
Lifetime Risk (%)	40.85 ± 7.40	62.90 ± 9.56	43.21 ± 11.46	66.69 ± 6.29	<0.001*
Waist-to-Hip Ratio	0.95 ± 0.02	0.96 ± 0.03	0.95 ± 0.01	0.95 ± 0.01	0.695
Gender, n (%)					
Male	6(9.6)	36(61)	9(12)	40(88.9)	<0.001*
Female	55(90.2)	23(39)	66(88)	5(11.1)	
Age, n (%)					
≤45 years	18(29.5)	2(3.4)	37(49.3)	3(6.7)	<0.001*
>45 years	43(70.5)	57(96.6)	38(50.7)	42(93.3)	
Hypertension, n (%)					
Yes	30(49.2)	28(47.5)	34(45.3)	20(44.4)	0.958
No	31(50.8)	31(52.5)	41(54.7)	25(55.6)	
Smoking Status, n (%)					
Smoker	24(39.3)	15(25.4)	23(30.7)	8(17.8)	0.095
Non-Smoker	37(60.7)	44(74.6)	52(69.3)	37(82.2)	
Fibrosis present, n (%)					
Present	41(67.2)	47(79.7)	54(72)	35(77.8)	0.406
Absent	20(32.8)	12(20.3)	21(28)	10(22.2)	
Hepatic Steatosis Grade (CAP)					
S0 (None)	17 (27.9)	12 (20.3)	31 (41.3)	7 (15.6)	0.010*
S1 (Mild)	5 (8.2)	11 (18.6)	7 (9.3)	14 (31.1)	
S2 (Moderate)	2 (3.3)	2 (3.4)	1 (1.3)	2 (4.4)	
S3 (Severe)	37 (60.7)	34 (57.6)	36 (48.0)	22 (48.9)	
Overall Steatosis Present n (%)					
Yes	35(57.4)	37(62.7)	39(52)	35(77.8)	0.041*
No	26(42.6)	22(37.3)	36(48)	10(22.2)	
Dyslipidemia pattern, n (%)					
Normolipidemic	0 (0.0)	4 (6.8)	7 (9.3)	10 (22.2)	<0.001*
Combined Hyperlipidemia	2 (3.3)	3 (5.1)	0 (0.0)	5 (11.1)	

Hyperlipidemia	2 (3.3)	1 (1.7)	0 (0.0)	0 (0.0)	
Dyslipidemia with MetS	7 (11.5)	18 (30.5)	7 (9.3)	15 (33.3)	
Low HDL-C	50 (82.0)	31 (52.5)	61 (81.3)	13 (28.9)	
CAP Severity, n (%)					
No Significance	27 (44.3)	22 (37.3)	38 (50.7)	12 (26.7)	0.016*
Mild	2 (3.3)	6 (10.2)	10 (13.3)	5 (11.1)	
Moderate	3 (4.9)	2 (3.4)	0 (0.0)	0 (0.0)	
Severe	29 (47.5)	29 (49.2)	27 (36.0)	28 (62.2)	
Fibrosis Severity, n (%)					
No significant	21 (34.4)	16 (27.1)	34 (45.3)	16 (35.6)	<0.001*
Mild	20 (32.8)	17 (28.8)	31 (41.3)	11 (24.4)	
Significant	18 (29.5)	16 (27.1)	10 (13.3)	16 (35.6)	
Advanced	2 (3.3)	10 (16.9)	0 (0.0)	2 (4.4)	

*p ≤ 0.05 is considered Significant

Continuous variables compared by one-way ANOVA; categorical variables by Chi-square or Fisher's exact test.

Table 3: Unadjusted Odds Ratios (95% CI) for Demographic and Clinical Variables Associated with Diabetes among MAFLD Patients.

Variables	OR (95% CI)	p-value
Gender		
Male	0.78 (0.46 – 1.32)	0.352
Female	1.00	
Age group		
≤ 45 years	0.40 (0.22 – 0.74)	0.003*
> 45 years	1.00	
Hypertension		
Yes	1.14 (0.69 – 1.90)	0.605
No	1.00	
Smoking status		
Smoker	1.38 (0.79 – 2.42)	0.257
Non-smoker	1.00	
Fibrosis (overall)		
Present	0.96 (0.54 – 1.70)	0.883
Absent	1.00	
Hepatic steatosis grade (CAP)		
S0	0.62 (0.34 – 1.13)	0.120
S1	0.62 (0.30 – 1.30)	0.207
S2	1.09 (0.23 – 5.06)	0.913
S3	1.00	
Steatosis (present vs. absent)	1.07 (0.64 – 1.80)	0.791
Dyslipidemia category		
Normolipidemic	0.24 (0.03 – 2.22)	0.206
Combined hyperlipidemia	1.00 (0.10 – 10.17)	1.000
Hyperlipidemia	—	0.999
Dyslipidemia with MetS	1.14 (0.15 – 8.76)	0.902

Low HDL-C	1.10 (0.15 – 7.97)	0.929
Hypertriglyceridemia	1.00	
Metabolic syndrome–related dyslipidemia		
Absent	0.85 (0.45 – 1.62)	0.626
Present	1.00	
CAP category		
No significance	0.93 (0.54 – 1.59)	0.790
Mild	0.51 (0.20 – 1.29)	0.153
Moderate	—	0.999
Severe	1.00	
FibroScan fibrosis severity		
No significant fibrosis	0.12 (0.03 – 0.59)	0.008*
Mild fibrosis	0.15 (0.03 – 0.70)	0.016*
Significant fibrosis	0.22 (0.05 – 1.06)	0.059
Advanced fibrosis	1.00	
ASCVD risk category		
Low risk	0.49 (0.22 – 1.07)	0.073
Intermediate risk	0.58 (0.21 – 1.58)	0.284
Moderate risk	0.74 (0.32 – 1.70)	0.471
High risk	1.00	

Binary logistic regression applied. Odds ratios < 1.0 indicate reduced odds of diabetes relative to the reference category.
*p ≤ 0.05 is considered significant

Table 4: Multivariate Logistic Regression Analysis for High ASCVD Risk.

Variables	Adjusted OR	95% CI	p-value
Age (years)	1.222	1.128 – 1.324	<0.001*
Gender	0.029	0.008 – 0.102	<0.001*
Diabetes mellitus	0.642	0.235 – 1.756	0.388
ALT (U/L)	0.988	0.962 – 1.015	0.368
LDL/HDL ratio	2.412	1.465 – 3.972	0.001*
FibroScan finding	1.026	0.788 – 1.335	0.851
BMI (kg/m²)	1.076	0.920 – 1.257	0.360

OR: odds ratio; CI: confidence interval. Regression analysis based on all variables mentioned.
*p ≤ 0.05 is considered Significant

Discussion

This comparative cross-sectional study evaluated the association between liver stiffness severity and atherosclerotic cardiovascular disease (ASCVD) risk among diabetic and non-diabetic patients with metabolic dysfunction-associated fatty liver disease (MAFLD). The findings demonstrate that diabetic patients with MAFLD exhibit a substantially more adverse cardiometabolic profile, characterized by higher levels of glycated hemoglobin, total cholesterol, LDL/HDL ratio, alanine aminotransferase (ALT), serum creatinine, and estimated ASCVD risk. In addition, advanced liver fibrosis was significantly more prevalent among diabetic patients than non-diabetic individuals. However, after adjustment for potential confounders, only age and LDL/HDL ratio remained independent predictors of elevated ASCVD risk, whereas diabetes status and FibroScan-derived liver stiffness measurements were not independently associated with cardiovascular risk.

The higher prevalence of advanced fibrosis among diabetic participants observed in the present study is consistent with the well-established bidirectional relationship between MAFLD and type 2 diabetes mellitus (T2DM)[5-7]. Diabetes contributes to hepatic fibrogenesis through multiple interconnected mechanisms, including insulin resistance, chronic inflammation, oxidative stress, mitochondrial dysfunction, and altered lipid metabolism[6]. Previous studies have shown that patients with T2DM are more likely to develop progressive liver disease and advanced fibrosis than non-diabetic individuals with MAFLD[5,14]. Our findings further support the growing body of evidence that diabetes is associated with greater hepatic disease severity and should be considered a major risk factor for fibrosis progression in patients with MAFLD.

A notable finding of this study was the significantly higher ASCVD risk observed among diabetic participants. This observation is biologically plausible because diabetes and MAFLD share several common pathophysiological pathways, including insulin resistance, endothelial dysfunction, systemic inflammation, and atherogenic dyslipidemia[4,6]. Cardiovascular disease is the leading cause of mortality in patients with MAFLD, often exceeding liver-related mortality[8]. Therefore, identifying patients with both metabolic and hepatic abnormalities remains clinically important for comprehensive risk stratification.

Although liver stiffness and fibrosis severity demonstrated significant associations with ASCVD risk in unadjusted analyses, these relationships lost statistical significance in the multivariable model. This finding suggests that liver fibrosis may reflect the cumulative burden of metabolic dysfunction rather than acting as an independent driver of cardiovascular risk. Similar observations have been reported in previous studies indicating that the association between hepatic fibrosis and cardiovascular disease is substantially influenced by age, obesity, diabetes, hypertension, and dyslipidemia[8-10]. Consequently, liver fibrosis may serve as an important clinical marker of systemic metabolic injury rather than an independent determinant of cardiovascular outcomes.

Age emerged as the strongest independent predictor of high ASCVD risk in the present study. Each incremental increase in age was associated with a significant rise in the likelihood of elevated cardiovascular risk. This finding is consistent with established cardiovascular epidemiology and current ASCVD prediction models, in which age remains one of the most influential non-modifiable risk factors[15,16,18]. The clustering of diabetes, dyslipidemia, hepatic fibrosis, and elevated ASCVD risk among older participants highlights the cumulative effects of prolonged metabolic exposure and vascular aging. Given increasing life expectancy and the rising prevalence of metabolic disorders globally, these findings emphasize the need for earlier identification and management of cardiometabolic risk factors.

Among all metabolic parameters examined, the LDL/HDL ratio demonstrated the strongest independent association with ASCVD risk. This finding is clinically relevant because the LDL/HDL ratio reflects the balance between atherogenic and protective lipoproteins and may provide a more comprehensive assessment of cardiovascular risk than individual lipid parameters alone[19]. Insulin resistance and hepatic steatosis are known to promote increased production of very-low-density lipoproteins, reduced HDL concentrations, and the formation of small dense LDL particles, all of which contribute to accelerated atherosclerosis[20]. The present findings reinforce the importance of atherogenic dyslipidemia as a central mechanism linking MAFLD and cardiovascular disease.

Interestingly, diabetes status was not an independent predictor of high ASCVD risk after adjustment for age, lipid abnormalities, and other covariates. This observation suggests that the cardiovascular burden associated with diabetes in MAFLD may be mediated largely through associated metabolic abnormalities rather than the diagnosis of diabetes alone[21,22]. Similarly, body mass index and liver stiffness measurements were not independently associated with ASCVD risk, supporting emerging evidence that metabolic health and lipid abnormalities may be more important determinants of cardiovascular outcomes than obesity or hepatic fibrosis alone[23].

Gender differences were also observed, with males demonstrating a higher prevalence of elevated ASCVD risk. This finding is consistent with previous epidemiological studies reporting a greater burden of cardiovascular disease among men, likely attributable to differences in hormonal regulation, visceral adiposity, lifestyle factors, and lipid metabolism[24]. These observations highlight the importance of incorporating sex-specific considerations into cardiovascular risk assessment strategies for patients with MAFLD.

The findings of this study support the concept that MAFLD is a multisystem cardiometabolic disorder rather than a disease confined to the liver. While diabetic patients exhibit greater fibrosis severity and metabolic derangements, cardiovascular risk appears to be driven predominantly by advancing age and atherogenic dyslipidemia. These findings underscore the importance of integrated cardiovascular and hepatic risk assessment in patients with MAFLD and support the routine evaluation of lipid abnormalities and cardiovascular risk factors alongside liver disease severity.

Limitations

Several limitations should be considered when interpreting the findings of this study. First, the cross-sectional design precludes the establishment of temporal or causal relationships between diabetes, liver fibrosis, and ASCVD risk. Therefore, the observed associations should not be interpreted as evidence of causality. Prospective longitudinal studies are required to determine whether progressive liver fibrosis contributes directly to future cardiovascular events. Second, the study was conducted at a single tertiary-care center, which may limit the generalizability of the findings to broader populations or community-based settings. Referral bias may have resulted in the inclusion of patients with more severe metabolic disease than those typically encountered in primary care. Third, although transient elastography is a validated and widely accepted non-invasive tool for assessing hepatic steatosis and fibrosis, it does not provide the histopathological information obtainable through liver biopsy, which remains the reference standard for fibrosis staging [11]. Furthermore, FibroScan measurements can be influenced by obesity, hepatic inflammation, operator variability, and technical factors. Fourth, ASCVD risk was estimated using a validated risk prediction model rather than actual cardiovascular events. Consequently, the study evaluated predicted cardiovascular risk rather than incident cardiovascular outcomes. Longitudinal studies incorporating hard cardiovascular endpoints such as myocardial infarction, stroke, and cardiovascular mortality would provide more definitive evidence regarding the relationship between liver fibrosis and cardiovascular disease. Finally, residual confounding cannot be completely excluded despite multivariable adjustment. Information regarding medication use, duration of diabetes, dietary habits, physical activity levels, socioeconomic status, inflammatory biomarkers, and genetic predisposition was not comprehensively evaluated and may have influenced the observed associations.

Conclusion

In conclusion, diabetic patients with MAFLD demonstrated significantly greater fibrosis severity, higher liver enzyme levels, more pronounced dyslipidemia, and increased estimated ASCVD risk compared with non-diabetic patients. Although liver fibrosis and liver stiffness were associated with ASCVD risk in unadjusted analyses, they did not independently predict elevated cardiovascular risk after adjustment for metabolic and demographic factors. Instead, advancing age and an increased LDL/HDL ratio emerged as the principal independent determinants of high ASCVD risk.

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