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Predictive factors for metabolic syndrome in patients with metabolic dysfunction-associated steatotic liver disease (MASLD)

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Abstract

Background Metabolic dysfunction-associated steatotic liver disease (MASLD) is the leading cause of liver disease globally, closely associated with metabolic syndrome.

Objectives This study aimed to identify significant predictors of metabolic syndrome in patients with MASLD.

Methods A retrospective cross-sectional study was conducted on adult type 2 diabetes mellitus (T2DM) patients between January 2018 and April 2022. Of 314 initially collected patients, those without MASLD or with other liver diseases were excluded, leaving 240 MASLD patients for analysis. Metabolic syndrome was assessed using the NCEP ATP III criteria, and data analysis was performed using Stata17.

Results Higher systolic blood pressure (adjusted OR = 1.000427, $p < 0.0001$) and larger waist circumference (adjusted OR = 1.001517, $p < 0.0001$) were independently associated with increased odds of metabolic syndrome. Additionally, higher triglyceride levels (adjusted OR = 1.064834, $p < 0.0001$) and lower HDL cholesterol levels (adjusted OR = 0.998595, $p = 0.003$) were significant predictors. Other variables, including age, HbA1c, BMI, LDL, and hepatic steatosis index, were not significantly associated with metabolic syndrome after adjusting for confounders.

Conclusion Higher systolic blood pressure, larger waist circumference, elevated triglyceride levels, and lower HDL cholesterol levels are significant predictors of metabolic syndrome in MASLD patients.

Keywords Metabolic dysfunction-associated steatotic liver disease, MASLD, Metabolic syndrome, Waist circumference, Systolic hypertension, Triglyceride, High-density lipoprotein

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Introduction

Metabolic dysfunction–associated steatotic liver disease (MASLD), formerly known as non-alcoholic fatty liver disease (NAFLD), has emerged as the most common chronic liver disease worldwide [1]. MASLD is defined by evidence of hepatic steatosis in the presence of metabolic risk factors such as obesity, type 2 diabetes, or dyslipidemia [2]. Its global prevalence is high, affecting roughly 25% of the general adult population and up to 60% of high-risk groups (e.g. individuals with obesity or diabetes) [2]. This renaming of NAFLD to MASLD in 2023 emphasizes the key role of metabolic dysfunction in fatty liver disease. Indeed, MASLD is now recognized as a multisystem metabolic disorder with important extrahepatic implications, including substantial cardiovascular risk [1].

The interrelationship between MASLD and metabolic syndrome (MetS) is increasingly recognized as an area of significant clinical interest and research. MetS encompasses various metabolic abnormalities, including central obesity, hypertension, hyperglycemia, dyslipidemia, and insulin resistance, which markedly elevate the risk for cardiovascular disease and type 2 diabetes mellitus (T2DM) [3, 4]. Emerging evidence suggests that MASLD serves as a hepatic manifestation of MetS, with many patients satisfying the criteria for both diagnoses [3, 5, 6].

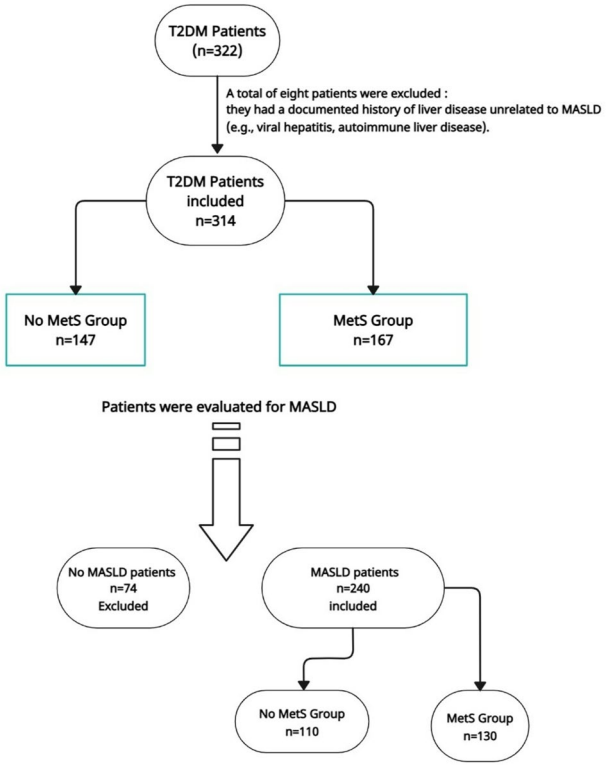

Fig. 1 Flowchart (MetS: Metabolic Syndrome;MASLD: Metabolic Dysfunction–Associated Steatotic Liver Disease; T2DM: Type 2 Diabetes Mellitus)

Cross-sectional studies have consistently demonstrated robust associations between (fig. 1) MASLD and MetS. One notable population-based study indicated that the presence of MetS significantly increased the odds of developing MASLD by nearly threefold (OR ≈ 2.95) [3]. Additionally, longitudinal research has highlighted that individuals diagnosed with NAFLD (the predecessor of MASLD terminology) experience a markedly increased incidence of MetS over time, further reinforcing the bidirectional nature of this relationship [3, 5].

However, it is essential to note that not all MASLD patients meet the full criteria for MetS. A considerable number present with hepatic steatosis but fewer metabolic risk factors, complicating the recognition of this bidirectional relationship [7]. This clinical heterogeneity suggests a need for further investigation into distinguishing features among MASLD patients with versus without MetS. Understanding these nuances is critical, as those with coexisting MASLD and MetS are at heightened risk for adverse health outcomes, including advanced liver fibrosis and cardiovascular complications [8]. For instance, a significant portion of NAFLD patients in specialized care settings meet MetS criteria, and the association of MetS with increased liver stiffness indicates a correlation with more severe forms of liver disease [3]. In the current study, we investigate the prevalence of MetS and the role of demographic, socioeconomic, clinical factors as predictors of MetS in patients previously diagnosed with MASLD.

Materials and methods

Data source and study population

We conducted a retrospective cross-sectional study on adult patients diagnosed with type 2 diabetes mellitus (T2DM) who were receiving routine follow-up care at primary health care centers operated by the Palestinian Ministry of Health in the northern region of the West Bank. The data was retrospectively gathered from January 2018 to April 2022. A total of 314 diabetic patients were initially collected, and patients who were not diagnosed with Metabolic dysfunction-associated steatotic liver disease (MASLD) were excluded from the advanced analysis, as shown in Fig. 3. Ultimately, 240 patients were diagnosed with MASLD through abdominal ultrasound examinations performed at four radiology centers in Nablus city, West Bank (Alrahmma clinic, Rafidia Hospital, and Specialized Arab Hospital). These 240 MASLD patients then underwent assessments for metabolic syndrome during their clinical visits.

Participants and sample characteristics

Every other T2DM patient who met the inclusion criteria was invited to participate in the study. Patients were excluded if they had a personal history of any liver

disease other than MASLD, such as three autoimmune hepatitis, four genetic liver diseases, or one alcoholic fatty liver disease. Patients were also excluded if they had a family history of genetic liver disease or reported alcohol consumption. All cases were personally interviewed by the researcher. This selection process resulted in a final study population of 240 T2DM patients diagnosed with MASLD, who were then assessed for metabolic syndrome. The exclusion of patients with other known liver conditions or significant alcohol use helped ensure the study population was representative of the target MASLD patient population. Only glimepiride (among sulfonylureas), sitagliptin (among DPP-4 inhibitors), and dapagliflozin (among SGLT-2 inhibitors) were prescribed among our study population. No other agents within these drug classes, such as gliclazide, empagliflozin, or GLP-1 receptor agonists, were found in the medication histories of included patients.

Measurements and definition

The study used abdominal ultrasound examinations and the Hepatic Steatosis Index to diagnose MASLD, and defined metabolic syndrome according to the NCEP ATP III criteria. Abdominal ultrasonography has moderate sensitivity and specificity overall (65% and 81%, respectively), but these rise to 84.8% and 93.6% for moderate to severe steatosis; its accuracy is limited for detecting mild steatosis [9, 10]. Fatty infiltration is indicated by increased liver echogenicity due to diffuse fat accumulation, which may obscure visualization of the posterior right hepatic lobe, diaphragm, and intrahepatic vessels. A qualitative grading scale—absent, mild, moderate, or severe—is used to classify the extent of steatosis. Absent (Grade 0) when the echotexture of the liver is normal. Mild (Grade 1) has a diffuse slight increase in fine echoes with normal visualization of the diaphragm and intrahepatic vessels borders. Moderate (Grade 2) has a moderate diffuse increase in fine echoes with slightly impaired visualization of the intrahepatic vessels and diaphragm. Marked (Grade 3) is represented by a marked increase in fine echoes with poor or no visualization of the intrahepatic vessel borders, diaphragm, and posterior portion of the right lobe of the liver [11, 12].

The Hepatic Steatosis Index (HSI) is a non-invasive tool used for detecting and monitoring MASLD. It relies on readily available clinical and biochemical markers, making it especially valuable in settings where advanced imaging or liver biopsy is not accessible. The HSI incorporates body mass index (BMI), the ALT/AST ratio, and the presence of female gender or diabetes to estimate the likelihood of MASLD, using the following formula: [13]

HSI = 8 alanine aminotransferase/aspartate aminotransferase ratio + body mass index (BMI) + 2 if diabetes + 2 if female. (with values < 30 ruling out and values > 36 ruling in steatosis) [13, 14].

A definition of metabolic syndrome was developed by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) in 2001. The NCEP ATP III definition states that metabolic syndrome is present if three or more of the following five criteria come together: blood pressure over 130/85 mmHg, waist circumference over 40 inches for men or 35 inches for women, fasting TG level over 150 mg/dl, fasting HDL cholesterol level less than 40 mg/dl (men) or 50 mg/dl (women), and fasting blood sugar level over 100 mg/dl [15, 16]. NCEP ATP III definition is one of the most popular definitions of the metabolic syndrome. Its implementation in clinical and epidemiological settings is facilitated by using measures and laboratory findings that are easily accessible to medical professionals. It is straightforward to recall; it just requires that three out of the five conditions be met [15].

Variable Estimation

The potential association of sociodemographic, clinical, metabolic, lipid, and blood pressure factors with metabolic syndrome was examined. Metabolic syndrome status was categorized as present or absent based on established diagnostic criteria. After an overnight fast of 8–10 h, a venous blood sample was collected for laboratory investigations, including fasting blood glucose (FBS), high-density lipoprotein (HDL), triglycerides (TG), total cholesterol, aspartate aminotransferase (AST), alanine transaminase (ALT), glycated hemoglobin (HbA1c), and thyroid-stimulating hormone (TSH). Blood pressure was measured once after 5 min of rest using a Dinamap automated device.

Statistical analysis

Univariate analysis was conducted to compare participants based on the presence or absence of metabolic syndrome. Continuous variables were expressed as mean ± standard deviation and compared using either the student's t-test or the Mann–Whitney U test, depending on the normality of distribution. Categorical variables were presented as frequencies and percentages and compared using the Chi-squared test or Fisher's exact test, as appropriate based on expected cell counts. We developed a multivariable logistic regression model to predict metabolic syndrome in patients with MASLD, incorporating both demographic and clinical variables. Variable selection was based on a "thumb rule" statistical approach (retaining variables with a univariate p-value < 0.25), supplemented by clinical judgment and evidence from prior studies [2, 3, 17–21]. An inter-method strategy was applied to ensure relevance and model parsimony.

The final prediction model included the following variables: age, diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, dyslipidemia, Hepatic Steatosis Index (HSI), HbA1c, systolic blood pressure, diastolic blood pressure, waist circumference, body mass index (BMI), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, total cholesterol, years since MASLD diagnosis (YSD), and years with complications (YWC). Model development adhered to the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) guidelines [22].

To ensure the robustness of the model, multicollinearity was assessed using variance inflation factors (VIFs), and model calibration was evaluated via the Hosmer–Lemeshow goodness-of-fit test. We assessed potential nonlinear relationships between key continuous predictors (waist circumference, HDL, systolic BP, and diastolic BP) and the outcome using generalized additive models (GAM). Model discrimination was evaluated using receiver operating characteristic (ROC) curve analysis. All statistical analyses were conducted using Stata version 17 (StataCorp LLC, College Station, TX, USA).

Ethical approval

Ethical approval was taken from the *institutional review board (IRB) of An-Najah National University*. all methods were performed in accordance with the relevant guidelines and regulations.approval

Informed consent

Participants were informed about the purpose, technique, risks, and benefits of the study, and informed-consent was obtained from all participants prior to their involvement.

Discussion

The rise of MASLD and Metabolic Syndrome poses a significant health challenge. Understanding the interplay of sociodemographic, clinical, metabolic, lipid and blood pressure factors in predicting Metabolic Syndrome among MASLD patients is crucial for effective interventions. Our study confirms previous findings and identifies new correlates, indicating the need for continued investigation.(Fig. 2)

Sociodemographic characteristics and metabolic syndrome in participants

There were no differences between gender in case of metabolic syndrome, however Patients with metabolic syndrome had a significantly higher mean age of years compared to those without metabolic syndrome in which the older age is associated with an increased risk of developing metabolic syndrome in this MASLD whereas other cross-sectional study showed no difference according to age [23]. Dyslipidemia was significantly more prevalent among individuals with metabolic syndrome, consistent with findings from a 2021 study conducted in Southwest Ethiopia [24]. There is a higher rate of diabetic retinopathy complications in metabolic syndrome patients compared to those without. This suggests that in patients with Metabolic dysfunction-associated steatotic liver disease (MASLD), the presence of diabetic retinopathy is associated with an increased risk of having metabolic syndrome, however, comparing with other studies there were no significant difference in the prevalence of metabolic syndrome between diabetics with and without diabetic retinopathy [25, 26].Research from both basic and clinical studies indicates that obesity, hypertension, hyperglycemia, hyperlipidemia, and other components of metabolic syndrome are closely interconnected and play a significant role in the onset and progression of diabetic nephropathy [27].Our study confirms this finding in which diabetic nephropathy significantly higher in the metabolic syndrome group compared to the non-metabolic syndrome patients. Also, the presence of diabetic neuropathy is associated with an increased risk of having metabolic syndrome. Insulin use is significantly higher in those compared to the non-metabolic syndrome patients. This reflects the more advanced diabetic state and insulin resistance associated with metabolic syndrome in MASLD patients.

Similar to our study findings, previous Clinical Practice Guidelines have noted that ultrasound (US) has limited sensitivity and may not accurately detect steatosis when liver fat content is below 20%, or in patients with a high body mass index (BMI) [28].

Although dapagliflozin may have a modest influence on liver enzymes [29], our study didn't detect changes in liver enzyme levels among MS or non-MS. This suggests the therapy likely did not have any significant interference of liver enzyme markers among participants.

There is a high probability of MASLD per the HSI was seen in patients with metabolic syndrome in comparison to patients without metabolic syndrome. The HSI finding suggests that a higher degree of hepatic steatosis, is linked to an increased prevalence of metabolic syndrome in this population which also has been supported by other study [23]. On the other hand, 40.7% of non-metabolic syndrome (non-MS) patients had a high probability of MASLD based on the Hepatic Steatosis Index (HSI) due to steatosis, insulin resistance, and one or more non-MS risk factors including dyslipidemia and increased BMI. In these patients, formal diagnostic criteria for metabolic syndrome were not met, despite the presence of known components of metabolic risk. These metabolic risk factors are not unique to individuals with the diagnosis of metabolic syndrome, and contribute to the probability of having MASLD as indicated by HSI score [30].

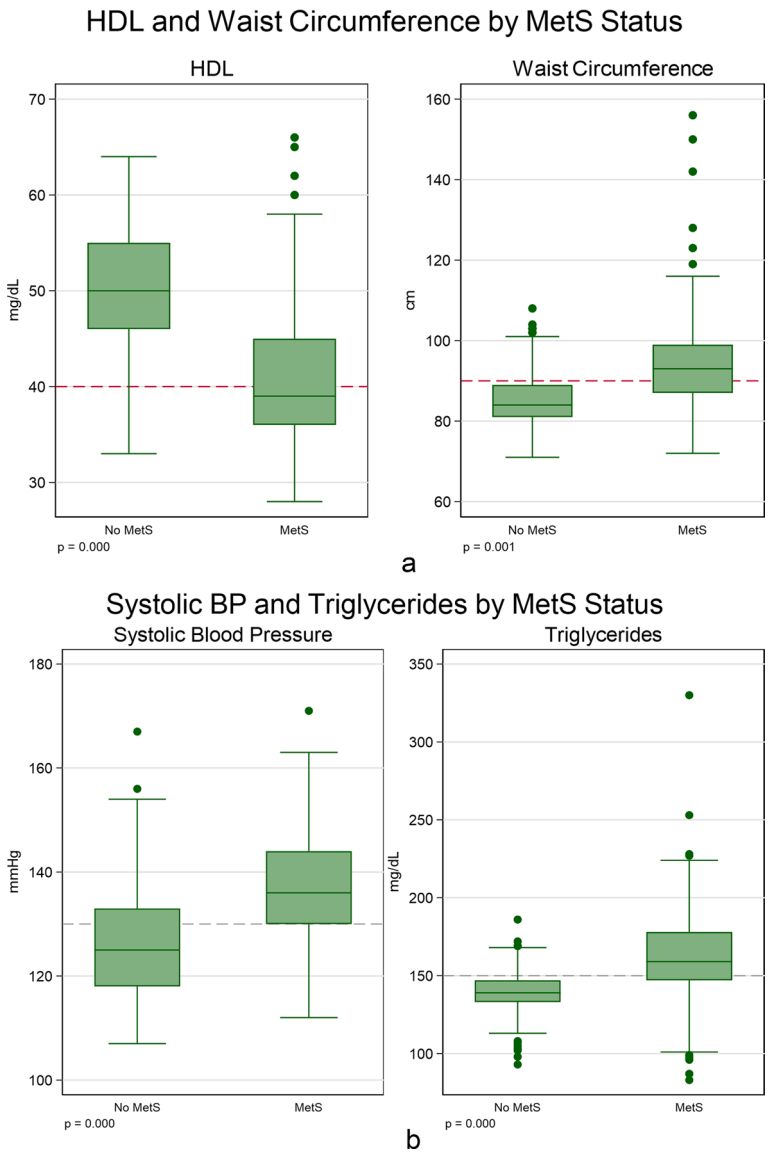

Fig. 2 (**A** and **B**): Box plots for HDL, Waist Circumference, Systolic BP, and Waist Circumference accordingly to the presence Metabolic Syndrome in Metabolic dysfunction-associated steatotic liver disease (MASLD).Box plots for HDL and Waist Circumference accordingly to the presence of Metabolic Syndrome in Metabolic dysfunction-associated steatotic liver disease (MASLD).

Biomarker level and metabolic syndrome in participants

Patients with metabolic syndrome tend to have an Increased levels of systolic and diastolic pressure in comparison with others without metabolic syndrome. A study was published in 2021 Explained that MetS Patients has insulin resistance as its main component. in which insulin has an anti-natriuretic effect, and this effect can be increased n MetS Patients, which in turn can lead to hypertension within the metabolic syndrome [31]. Patients with metabolic syndrome had significantly higher mean HbA1c levels compared to those without metabolic syndrome indicating poorer glycemic control in the metabolic syndrome group. In the other hand another study revealed that higher levels of HbA1c are associated with Increased prevalence of MetS [32]. Metabolic syndrome Patients has worst lipid profile and higher levels of TG, LDL, Cholesterol and lower HDL levels, participants with MetS Patients in another study also had increased TG and decreased HDL-C which suggests that the lipid disorder had a crucial role in the development of MetS in these patients [33]. Waist circumference and BMI were significantly higher in the metabolic syndrome patients. Stolzman's study found that adolescents with higher BMI Levels had a greater incidence of MetS than those with normal BMI [34]. In our study, we identified two novel variables, years with complication (YWC) and years since diagnosis (YSD), as significant predictors. Statistical analysis revealed that both YWC and YSD were

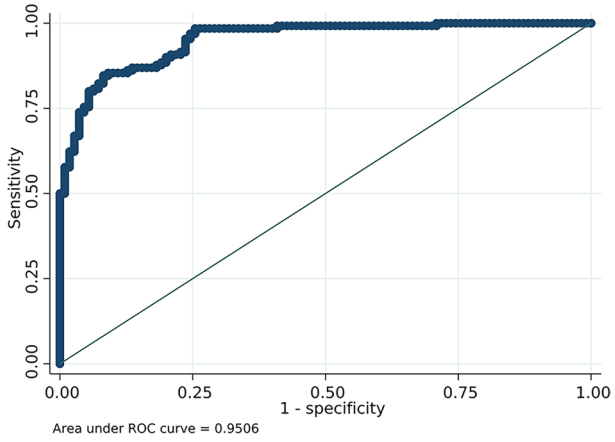

Fig. 3 Receiver Operating Characteristic (ROC) Curve for the Performance of Predictors of Metabolic Syndrome in Metabolic dysfunction-associated steatotic liver disease (MASLD).in MASLD Model

significantly associated with biomarker levels indicative of metabolic syndrome in participants, the duration of complications and the time since diagnosis are critical factors in predicting the likelihood of metabolic syndrome in MASLD patients.

Filling a gap in the existing literature where these variables had not been previously examined.

Multivariable analysis and MASLD model

Several studies discussed the relationship between MASLD and metabolic syndrome, Yongyuan Zhang et al. confirmed the bidirectional association between MASLD and metabolic syndrome [35]. Multiple studies establish the risk of having MASLD in patient with MetS, a study published in 2022 discovered that the odds of having any level of steatosis were higher in patients with MetS [36]. Indicating that Mets increases the risk of having MASLD. Whereas a few studies focused on the Mets risk in MASLD patients, which still not fully discussed. So, we conducted a comprehensive analysis to identify significant predictors for metabolic syndrome MASLD patients. Using advanced multivariable logistic regression analysis models, the results of the analysis showed that several demographics, clinical, and metabolic factors are associated with the risk of Metabolic Syndrome in the in MASLD patients. In MASLD there is a significantly higher level of blood pressure [37], it also has been found that.

hypertension consistently exhibited the strongest link with the development of major adverse liver outcomes [38]. However, our study has found that Elevated systolic blood pressure in patients with Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) has been linked to an increased risk of developing metabolic syndrome. Also, the increased waist circumference, will increase the risk for MetS. A study published in 2019 discovered that an increased WC is attributed to increased risk of developing DM in prediabetes with MASLD [39].

Regarding lipid profile our study pointed that higher triglycerides, and lower HDL levels were significantly linked with the metabolic syndrome outcome in MASLD patients. Anna Boulouta et al., also found that higher triglyceride and, lower HDL levels are associated with Higher risk of metabolic unhealthiness in MASLD patients [40]. Our study states result after picking up all confounding factors and found that None of the other variable -age, diabetic complications, dyslipidemia, hepatic steatosis index, HbA1c, diastolic blood pressure, BMI, LDL, total cholesterol, years since diagnosis, and years with complications showed a significant association with the presence of metabolic syndrome following rigorous adjustment for confounding factors. However other study showed that Mets risk is much less common in younger patients [40].

Lack of association between HbA1c and metabolic syndrome

Our analysis showed that HbA1c was not significantly associated with the presence of metabolic syndrome (MetS) in patients with MASLD. This finding aligns with recent evidence by **Wisniewski et al. (2024)** [41], who demonstrated that while HbA1c correlates with MetS components in non-diabetic individuals, this relationship disappears once type 2 diabetes mellitus (T2DM) is established. In their cross-sectional study of over 8,000 adults, they found that none of the five classical MetS criteria, including waist circumference, blood pressure, HDL-C, triglycerides, or fasting glucose, remained significantly linked to HbA1c among diabetic participants. The authors attributed this to a **"glycemic ceiling effect,"** whereby sustained hyperglycemia in diabetic patients narrows HbA1c variability, thereby reducing its discriminatory power for detecting metabolic clustering. **In our cohort**, which included only patients with established T2DM, a similar ceiling phenomenon may have occurred. This suggests that while HbA1c is essential for monitoring glycemic control, it may not serve as a reliable independent predictor of MetS once chronic dysglycemia is already present.

The use of GAM allowed us to detect potential non-linear relationships between continuous predictors and MetS. Notably, GAM revealed non-linear associations for waist circumference, HDL, systolic blood pressure, and diastolic blood pressure. These patterns were further evaluated using a multivariable logistic regression model, and the direction of associations remained consistent. This confirms that the non-linear trends captured by the GAM were not spurious and supports the robustness of the findings.

However, it is important to interpret these results with caution. Due to the cross-sectional design of this study, causal inferences cannot be made. While the identified variables show strong statistical associations with MetS, temporality and directionality cannot be determined. Thus, the findings should be viewed as correlational, highlighting variables that may warrant further investigation as potential predictors in future longitudinal or interventional studies. The model was developed in accordance with the TRIPOD (Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis) guidelines and demonstrated good discrimination and calibration (Hosmer–Lemeshow). The use of variance inflation factors (VIFs) also confirmed no significant multicollinearity between included predictors.

Our findings contribute to the growing body of literature on the metabolic burden in MASLD and offer a clinically relevant set of variables that may inform risk stratification strategies. Early identification of patients at risk of developing MetS within the MASLD population is essential, given its association with cardiovascular events, disease progression, and poor outcomes. ROC Curve for the Performance of Predictors of Metabolic Syndrome in Metabolic dysfunction-associated steatotic liver disease (MASLD) showed an Area Under the Curve (AUC) of 0.9506, which is very close to 1.0, indicating an outstanding excellent discriminative ability of systolic blood pressure, WC, TG, and HDL to predict the risk of Mets in MASLD patients, and they can very accurately distinguish between MASLD patients with and without the MetS condition.

Limitations

Several limitations merit consideration. First, the cross-sectional nature of the study limits our ability to infer temporal or causal relationships between predictors and metabolic syndrome. Second, despite incorporating a broad spectrum of clinical and biochemical variables, the possibility of residual confounding from unmeasured factors cannot be excluded. Third, as all participants were drawn from a single regional population, the generalizability of our findings to other settings or ethnic groups may be restricted. Fourth, although cardiovascular complications are of high clinical relevance in individuals with T2DM and are mechanistically intertwined with both MASLD and MetS, these could not be analyzed in our study due to non-standardized or incomplete cardiology documentation across the medical records reviewed. We therefore acknowledge this as a limitation and recommend that future prospective research include structured cardiovascular assessment to better characterize this relationship.

Conclusion and future directions

our study stated the significant predictors for metabolic syndrome using advanced statistical methods. It shows that higher systolic blood pressure, larger waist circumference, elevated triglycerides, and lower HDL cholesterol levels are independently associated with metabolic syndrome in MASLD patients. These associations were confirmed through multivariable logistic regression analysis, which accounted for potential confounding factors.

Future research should validate these findings in larger and more diverse populations and explore the underlying mechanisms of these predictors. Longitudinal studies could offer insights into causal relationships. Given the high accuracy of the GAM analysis, future studies should utilize similar advanced models to uncover nonlinear relationships in clinical data, improving risk assessment tools and patient outcomes in MASLD and related conditions.

The results of the multivariate logistic regression analysis in Table 5 show that several demographics, clinical, and metabolic factors are associated with the risk of Metabolic Syndrome in the study population. The results showed that higher systolic blood pressure (adjusted OR = 1.000427, $p < 0.0001$) and larger waist circumference (adjusted OR = 1.001517, $p < 0.0001$) were both independently associated with an increased odds of having metabolic syndrome. Additionally, higher triglyceride levels (adjusted OR = 1.064834, $p < 0.0001$) were linked to greater odds of metabolic syndrome, while lower HDL cholesterol levels (adjusted OR = 0.998595, $p = 0.003$) were associated with increased odds.

The other variables, including age, diabetic complications, dyslipidemia, hepatic steatosis index, HbA1c, diastolic blood pressure, BMI, LDL, total cholesterol, years since diagnosis, and years with complications, were not significantly associated with the outcome of metabolic syndrome after adjusting for confounding factors. The Hosmer-Lemeshow test, with a chi-square statistic of 4.40 and a p-value of 0.8192, suggests that the logistic regression model fits the data well and provides an adequate representation of the observed and expected outcomes. The variance inflation factor (VIF) of 2.18 indicates that multicollinearity is not a severe issue in the regression model.

The generalized additive model analysis indicates that nonlinearity in the model is statistically significant, with a total gain (nonlinearity chi-square) of 116.313 and a p-value of 0.0000.

The generalized additive model (GAM) analysis revealed that four variables were statistically significant predictors of the binary outcome variable: waist circumference ($p < 0.0001$), HDL cholesterol ($p < 0.0001$), systolic blood pressure ($p = 0.0003$), and diastolic blood pressure ($p < 0.0001$). To further examine the potential non-linear

relationships between these predictors and the outcome, we squared the values of these four variables and included them in a logistic regression model.

The results of the logistic regression confirmed that the direction of the relationships between the linear and non-linear terms for each of these four variables was consistent. This suggests that the non-linear effects of waist circumference, HDL, systolic blood pressure, and diastolic blood pressure were adequately captured in the original GAM analysis. By verifying the consistent directionality of the linear and non-linear relationships, we can have confidence that the GAM results provide an accurate representation of the underlying associations.

This approach allowed us to control for potential non-linear effects and obtain reliable estimates of the influences of these waist circumference, HDL, systolic blood pressure, and diastolic blood pressure factors on the binary outcome of interest in this population of patients with Metabolic Dysfunction-Associated Fatty Liver Disease.

Table 5 Association between predictor factors for metabolic syndrome outcome in metabolic dysfunction-associated steatotic liver disease (MASLD): A MASLD model The results of the multivariate logistic regression analysis in Table 5 show that several demographics, clinical, and metabolic factors are associated with the risk of Metabolic Syndrome in the study population. The results showed that higher systolic blood pressure (adjusted OR = 1.000427, $p < 0.0001$) and larger waist circumference (adjusted OR = 1.001517, $p < 0.0001$) were both independently associated with an increased odds of having metabolic syndrome. Additionally, higher triglyceride levels (adjusted OR = 1.064834, $p < 0.0001$) were linked to greater odds of metabolic syndrome, while lower HDL cholesterol levels (adjusted OR = 0.998595, $p = 0.003$) were associated with increased odds

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Table 1 presents that the study included 314 participants, with 56.4% male and 43.6% female. Most resided in cities (57.3%), followed by villages (40.1%) and camps (2.5%). MASLD was detected in 76.4% by ultrasound, with 32.8% mild, 40.1% moderate, and 3.5% severe cases. Diabetic complications included retinopathy (26.8%), nephropathy (15.0%), and neuropathy (26.1%). Dyslipidemia was present in 41.1%, and 31.2% were current smokers. Alcohol use was rare (0.3%), and no participants reported a family history of liver disease. HSI indicated a high probability of MASLD in 91.7%. Regarding treatment, 24.8% used insulin, 27.1% glimepiride, 8.9% sitagliptin, 6.4% dapagliflozin, and 82.2% were on metformin.

Table 2 show Patients with metabolic syndrome had a significantly higher mean age of 57.25 ± 10.08 years compared to those without metabolic syndrome at 53.35 ± 10.24 years ($p = 0.001$), suggesting that older age is associated with an increased risk of developing metabolic syndrome in this MASLD population. The prevalence of diabetic retinopathy (34.7% vs. 38.5%, $p = 0.001$), diabetic nephropathy (10.2% vs. 4.8%, $p = 0.027$), and diabetic neuropathy (17.2% vs. 8.9%, $p = 0.010$) was significantly higher in the metabolic syndrome group compared to the non-metabolic syndrome group, indicating that the presence of diabetic microvascular complications is linked to a higher likelihood of also having metabolic syndrome in MASLD patients. Dyslipidemia was much more common in the metabolic syndrome group, with 34.4%

Table 1 Baseline characteristics

Variable	Category	Frequency (*n*)	Percent (%)
Gender	Male	177	56.4
	Female	137	43.6
Residency	City	180	57.3
	Village	126	40.1
	Camp	8	2.5
Ultrasound	**No** MASLD	74	23.6
	Mild MASLD	103	32.8
	Moderate MASLD	126	40.1
	Severe MASLD	11	3.5
Age (y)	Mean ± SD		
Diabetic retinopathy	YES	84	26.8
	No	230	73.2
Diabetic nephropathy	Yes	47	15.0
	No	267	85.0
Diabetic neuropathy	Yes	82	26.1
	No	232	73.9
Dyslipidemia	Yes	129	41.1
	No	185	58.9
Smoking	Yes	98	31.2
	No	209	66.6
	Ex-smoker	7	2.2
HSI (Hepatic Steatosis Index)	High probability of MASLD	288	91.7
	Indeterminate risk of MASLD	26	8.3
insulin	Yes	78	24.8
	No	236	75.2
glimepiride	Yes	85	27.1
	No	229	72.9
Sitagliptin	Yes	28	8.9
	No	286	91.1
dapagliflozin	Yes	20	6.4
	No	294	93.6
metformin	Yes	258	82.2
	No	56	17.8

having dyslipidemia compared to only 6.7% in the non-metabolic syndrome group ($p = 0.001$), a strong association that aligns with the known components of metabolic syndrome, including atherogenic dyslipidemia. A high probability of MASLD per the HSI was seen in 50.96% of the metabolic syndrome group compared to 40.76% in the non-metabolic syndrome group ($p = 0.007$), suggesting that a higher degree of hepatic steatosis, as indicated by a high HSI, is linked to an increased prevalence of metabolic syndrome in this population. Insulin use was significantly higher in the metabolic syndrome group at 18.2% versus 6.7% in the non-metabolic syndrome group ($p < 0.001$), likely reflecting the more advanced diabetic state and insulin resistance associated with metabolic syndrome in MASLD patients.

Table 3 show Patients with metabolic syndrome had significantly higher mean HbA1c levels of 8.34% ± 1.32% compared to 7.92% ± 1.22% in those without metabolic syndrome ($p = 0.004$), indicating poorer glycemic control in the metabolic syndrome group. Systolic and diastolic blood pressure were also significantly elevated in the metabolic syndrome group, with median systolic BP of 136 mmHg (IQR: 130–144 mmHg) versus 125 mmHg (IQR: 118–133 mmHg) in the non-metabolic syndrome group ($p < 0.001$), and median diastolic BP of 86 mmHg (IQR: 82–92 mmHg) versus 82 mmHg (IQR: 76–85 mmHg) ($p < 0.001$). Waist circumference and BMI were significantly higher in the metabolic syndrome group, with mean values of 94.13 ± 12.10 cm and 31.17 ± 5.29, respectively, compared to 85.20 ± 6.83 cm and 27.83 ± 3.45 in the non-metabolic syndrome group ($p = 0.001$ for both). Lipid profiles were worse in the metabolic syndrome cohort, with higher mean LDL (129.62 ± 22.97 mg/dL vs. 105.69 ± 15.21 mg/dL, $p = 0.001$), lower HDL (40.69 ± 7.68 mg/dL vs. 49.76 ± 5.91 mg/dL, $p < 0.001$), and higher triglycerides (161.71 ± 32.83 mg/dL vs. 138.58 ± 14.33 mg/dL, $p < 0.001$).

Table 4 presents a comparison of clinical and biochemical characteristics between MASLD patients with and without metabolic syndrome based on the NCEP ATP III criteria. Patients with MetS were significantly older (57.6 ± 10.1 vs. 54.5 ± 9.5 years, $p = 0.016$). The prevalence of diabetic retinopathy and dyslipidemia was significantly higher in the MetS group ($p = 0.002$ and $p < 0.001$, respectively). A greater proportion of patients in the MetS group had a high probability of MASLD according to the Hepatic Steatosis Index (HSI) ($p = 0.014$). MetS patients also demonstrated significantly higher values in several cardiometabolic indicators, including systolic and diastolic blood pressure, waist circumference, BMI, LDL, triglycerides, total cholesterol, and HbA1c. In contrast, HDL levels were significantly lower among MetS patients ($p < 0.001$ for most comparisons). Furthermore, the MetS group had longer disease duration (YSD) and more years with complications (YWC) ($p < 0.001$ for both), suggesting more advanced disease and comorbidity burden.

Table 2 Association between sociodemographic characteristics and metabolic syndrome in participants

Variable	Category	Non-metabolic syndrome according to the NCEP ATP III criteria *n* (147)	Metabolic syndrome according to the NCEP ATP III criteria *n* (167)	*P*-value
Gender	Male	82 26.1%	95 30.3%	0.844[b]
	Female	65 20.7%	72 22.9%	
Residency	City	90 28.7%	90 28.7%	.091[a]
	Village	56 17.8%	70 22.3%	
	Camp	1 0.3%	7 2.2%	
Ultrasound	**No** MASLD	37 11.8%	37 11.8%	0.524 [a]
	Mild MASLD	50 15.9%	53 16.9%	
	Moderate MASLD	57 18.2%	69 22.0%	
	Severe MASLD	3 1.0%	8 2.5%	
Age (y)	Mean ± SD	53.35 ± 10.24	57.25 ± 10.08	0.001[C*]
Diabetic retinopathy	YES	26 8.3%	58 18.5%	0.001[b*]
	No	121 38.5%	109 34.7%	
Diabetic nephropathy	Yes	15 4.8%	32 10.2%	0.027[b*]
	No	132 42.5%	135 50.6%	
Diabetic neuropathy	Yes	28 8.9%	54 17.2%	0.010[b*]
	No	119 37.9%	113 36.0%	
Dyslipidemia	Yes	21 6.7%	108 34.4%	0.001[b*]
	No	126 40.1%	59 18.8%	
Smoking	Yes	48 15.3%	50 15.9%	0.567[b]
	No	97 30.9%	112 35.7%	
	Ex-smoker	2 0.6%	5 1.6%	
HSI (Hepatic Steatosis Index)	High probability of MASLD	128 40.76%	160 50.96%	0.007[a*]
	Indeterminate risk of MASLD	19 6.05%	7 2.23%	
insulin	Yes	21 6.7%	57 18.2%	0.00[b]
	No	126 40.1%	110 35.0%	
glimepiride	Yes	33 10.5%	52 16.6%	0.098[b]
	No	114 36.3%	115 36.6%	

Table 2 (continued)

Variable	Category	Non-metabolic syndrome according to the NCEP ATP III criteria *n* (147)	Metabolic syndrome according to the NCEP ATP III criteria *n* (167)	*P*-value
Sitagliptin	Yes	13 4.1%	15 4.8%	1.00[a]
	No	134 42.7%	152 48.4%	
dapagliflozin	Yes	7 2.2%	13 4.1%	0.365[a]
	No	140 44.6%	154 49.0%	
metformin	Yes	118 37.6%	140 44.6%	0.412[a]
	No	29 9.2%	27 8.6%	

a; Fisher's exact test, b; chi square test, C; Independent T test, *; Statistically significant, N/A; not available, MASLD; Metabolic dysfunction-associated steatotic liver disease.

Table 3 Association between clinical and biochemical variables and metabolic syndrome in participants

Variable		Non-metabolic syndrome according to the NCEP ATP III criteria *n* (147)	Metabolic syndrome according to the NCEP ATP III criteria *n* (167)	*P* value
HbA1c	Mean ± SD	7.9204 ± 1.21728	8.3383 ± 1.31702	0.004 [a*]
Systolic blood pressure	Median(Q1-Q3) Mean	125(118–133) 126.34	136(130–144) 136.58	0.0000[b*]
Diastolic blood pressure	Median(Q1-Q3) Mean	82(76–85) 81.51	86(82–92) 86.02	0.0000[b*]
Pack year	Median(Q1-Q3) Mean	0 (0–20) 13.05	0(0–25) 14.98	0.995 [b]
Waist Circumference (cm)	Mean ± SD	85.20 ± 6.827	94.13 ± 12.099	0.001[a*]
BMI	Mean ± SD	27.834145+- 3.454334	31.1682+- 5.293561	0.001 [a*]
LDL (mg/dL)	Mean ± SD	105.69 ± 15.213	129.62 ± 22.965	0.001[a*]
HDL (mg/dL)	Mean ± SD	49.76 ± 5.91	40.69 ± 7.68	0.000[a*]
Cholesterol (mg/dL)	Mean ± SD	168.64 ± 16.638	187.10 ± 25.385	0.003 [a*]
Triglycerides(mg/dL)	Mean ± SD	138.58 ± 14.33	161.71 ± 32.83	0.0000[a*]
AST (U/L)	Mean ± SD	17.4558 ± 6.87783	19.2293 ± 7.47716	0.648 [a]
ALT (U/L)	Mean ± SD	20.1633 ± 7.67226	21.8102 ± 8.12481	0.723 [a]
YWC	Median(Q1-Q3) Mean	0(0–2) 1.20	8(3–13) 9.46	0.0004[b*]
YSD	Median(Q1-Q3) Mean	5(2–10) 6.76	1(0–3) 1.95	0.0003[b*]

BMI: Body Mass Index, LDL: Low Density Lipoprotein, AST: Aspartate aminotransferase, ALT: Alanine transaminase, YSD: years since diagnosis in Metabolic dysfunction-associated steatotic liver disease (MASLD), YWC: years with complications, HDL: high-density lipoprotein. a: Independent T test *: Statistically significant b: Mann Whitney test

Table 4 Predictors variables to metabolic syndrome in MASLD patients

Variable	Category	Non-metabolic syndrome according to the NCEP ATP III criteria *n* (110)	Metabolic syndrome according to the NCEP ATP III criteria *n* (130)	*P*-value
Age (y)	Mean ± SD	54.518 ± 9.487	57.592 ± 10.08	0.016[a]
Diabetic retinopathy	YES	20(8.33)	48(20.00)	0.002[b]
	No	90(37.50)	82(34.17)	
Diabetic nephropathy	Yes	12(5.00)	25(10.42)	0.106[b]
	No	98(40.83)	105(43.75)	
Diabetic neuropathy	Yes	25(10.42)	42(17.50)	0.113[b]
	No	85(35.42)	88(36.67)	
Dyslipidemia	Yes	17(7.08)	79(32.92)	0.000[b]
	No	93(38.75)	51(21.25)	
HSI (Hepatic Steatosis Index)	High probability of MASLD	100(41.67)	128(53.33)	0.014[b]
	Indeterminate risk of MASLD	10(4.17)	2(0.83)	
HbA1c	Mean ± SD	8.075 ± 1.282	8.37 ± 1.372	0.089[a]
Systolic blood pressure	Median(Q1-Q3)	125.5(119–133)	135.5(130–144)	0.000[c]
Diastolic blood pressure	Median(Q1-Q3)	82(77–85)	86(82–91)	0.000[c]
Waist Circumference (cm)	Mean ± SD	85.709 ± 6.759	94.969 ± 12.603	0.000[a]
BMI	Mean ± SD	28.395 ± 3.407	31.701 ± 5.019	0.000[a]
LDL	Mean ± SD	106.609 ± 15.069	128.4 ± 23.877	0.000[a]
HDL	Mean ± SD	49.318 ± 5.765	40.915 ± 7.824	0.000[a]
Triglycerides	Mean ± SD	138.763 ± 15.080	161.530 ± 33.055	0.000[a]
cholesterol	Mean ± SD	169.636 ± 17.585	188.107 ± 25.879	0.000[a]
YSD	Median(Q1-Q3) Mean	5.5(3–10)	8(4–12)	0.0003[c]
YWC	Median(Q1-Q3) Mean	0(0–2)	1(0–3)	0.0004[c]

BMI: Body Mass Index, LDL: Low Density Lipoprotein, AST: Aspartate aminotransferase, ALT: Alanine transaminase, YSD: years since diagnosis in Metabolic dysfunction-associated steatotic liver disease (MASLD), YWC: years with complications, HDL: high-density lipoprotein. a independent t test; b Fisher's exact; c Mann–Whitney test

Table 5 Association between predictor factors for metabolic syndrome outcome in metabolic dysfunction-associated steatotic liver disease (MASLD): A MASLD model

Metabolic Syndrome *N* (240)	Odds ratio	Std. errs.	z	*P* value	[95% conf. interval]	
Age	0.978285	0.030411	−0.71	0.48	0.92046	1.039744
Diabetic retinopathy	2.273867	1.450227	1.29	0.198	0.651457	7.936784
Diabetic nephropathy	1.458246	1.192451	0.46	0.645	0.293615	7.242417
Diabetic neuropathy	0.711304	0.422068	−0.57	0.566	0.222319	2.275804
Dyslipidemia	2.561892	1.560877	1.54	0.123	0.776161	8.456101
HSI (Hepatic Steatosis Index)	0.369781	0.406455	−0.91	0.365	0.042887	3.18836
HbA1c	0.92724	0.161538	−0.43	0.665	0.659024	1.304618
Systolic blood pressure	1.000427	0.000114	3.75	0.0001	1.000204	1.000651
Diastolic blood pressure	1.000271	0.000186	1.46	0.144	0.999907	1.000635
Waist Circumference (cm)	1.001517	0.000303	5.01	0.0001	1.000923	1.002112
BMI	0.886091	0.083335	−1.29	0.198	0.736927	1.065448
LDL	1.017434	0.017711	0.99	0.321	0.983307	1.052745
HDL	0.998595	0.00047	−2.99	0.003	0.997674	0.999517
Triglycerides	1.064834	0.018139	3.69	0.0001	1.02987	1.100985
cholesterol	0.992493	0.015306	−0.49	0.625	0.962943	1.02295
YSD	1.025627	0.063569	0.41	0.683	0.908305	1.158104
YWC	0.980986	0.153879	−0.12	0.903	0.721344	1.334086

BMI: Body Mass Index, LDL: Low Density Lipoprotein, AST: Aspartate aminotransferase, ALT: Alanine transaminase, YSD: years since diagnosis in Metabolic dysfunction-associated steatotic liver disease (MASLD), YWC: years with complications, HDL: high-density lipoprotein

Abbreviations

MASLD	Metabolic Dysfunction-Associated Steatotic Liver Disease
NAFLD	Non-Alcoholic Fatty Liver Disease
MetS	Metabolic Syndrome
BMI	Body Mass Index
HDL	High-Density Lipoprotein
LDL	Low-Density Lipoprotein
TG	Triglycerides
HSI	Hepatic Steatosis Index
AST	Aspartate Aminotransferase
ALT	Alanine Aminotransferase
YSD	Years Since Diagnosis
YWC	Years With Complications
NCEP ATP III	National Cholesterol Education Program Adult Treatment Panel III
ROC	Receiver Operating Characteristic
AUC	Area Under the Curve
IRB	Institutional Review Board
US	Ultrasound
GAM	Generalized Additive Model
BP	Blood Pressure
OR	Odds Ratio
IQR	Interquartile Range
TRIPOD	Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis

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Author contributions
N.A.H. and M.A.: Conceptualized and designed the study, led data collection, and drafted the manuscript. M.A.: Provided statistical expertise, performed the statistical analysis, and assisted in the interpretation of data. M.A., D.N., A.D., O.H.: Assisted in data collection, performed literature review, and contributed to the writing of the manuscript. M.A.,A.A.T.A., J.A., K.J.: Contributed to data analysis, interpretation of the results, and manuscript revisions. A.A., O.S., Q.A., H.A.K.: Contributed to the study's design, manuscript editing, filled the tables and graphs, and provided critical revisions for important intellectual content. All authors have read and approved the final manuscript.

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Data availability
The data sets supporting the current research results are available from the corresponding authors upon request.

Declarations

Ethics approval and consent to participate
Ethical approval for this study was obtained from the Institutional Review Board (IRB) at An-Najah University, West Bank– Palestine. Participants were informed about the purpose, technique, risks, and benefits of the study, and consent was obtained from all participants prior to their involvement. Confidentiality and privacy of participants and their data was strictly maintained throughout the study as only the researchers and supervisors are able to access them. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Consent for publication
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Competing interests
The authors declare no competing interests.

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