RESEARCH ARTICLE

Lean and Non-obese Metabolic Dysfunction Associated Steatotic Liver Disease in Diabetics and Gender-wise association in a Low-income country

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Abstract

Objective: To assess the prevalence of lean, non-obese and obese metabolic dysfunction-associated steatotic liver disease in diabetics, and to explore gender-wise correlation of lifestyle, hypertension and dyslipidaemia with body mass index categories.

Method: The descriptive study was conducted at the Diabetes Clinic of Jinnah Postgraduate Medical Centre, Karachi, from March 1 to August 25, 2023, and comprised adult patients of either gender having fatty liver. Data regarding patients' demographics, baseline characteristics and history of hypertension, dyslipidaemia and duration of diabetes was collected using a predesigned proforma. Data was analysed using SPSS 21.

Results: Of the 229 patients with mean age 53.12±9.82 years, 151(65.93%) were females. Overall mean body mass index was 27.41±4.80kg/m2. Triglycerides, low-density lipoprotein, body mass index and waist circumference values were significantly raised in obese patients (p<0.05). Overall, 153(66.8%) patients had obese metabolic dysfunction-associated steatotic liver disease, and, of them, 111(72.5%) were females (p<0.05). Sedentary lifestyle was more prevalent in females than in males (p<0.05).

Conclusion: A significant number of diabetics were found to have obese metabolic dysfunction-associated steatotic liver disease, and it was significantly more common among females. Sedentary lifestyle was also significantly more prevalent in female diabetics.

Keywords: MASLD, Lean, Non-obese, Diabetics, BMI. (JPMA 76: 530; 2026) **DOI: https://doi.org/10.47391/JPMA.22571**

Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD), previously known as non-alcoholic fatty liver disease (NAFLD), is an emerging contributor to liver disease in both developing and developed countries.[1] Its prevalence is increasing globally, and correlates with obesity, but now it is increasingly seen in lean or non-obese cases as well. Lean/non-obese MASLD can progress to metabolic dysfunction-associated steatohepatitis(MASH) and cirrhosis.[2] The new nomenclature MASLD can be applied to NAFLD population as only one metabolic risk factor is required in MASLD population, hence confirmatory studies are not needed when transitioning from NAFLD to MASLD.[3] Therefore, contrary to NAFLD, MASLD diagnosis does not require other liver diseases to be excluded.[4]

MASLD is defined as any hepatic steatosis on liver imaging along with any one of the cardiometabolic risk factors: obesity, diabetes mellitus (DM) or pre-diabetes, hypertension (HTN), triglyceride (TG) and high-density lipoprotein (HDL). Cryptogenic SLD is assumed to be the condition in those without metabolic characteristics and having an unknown origin. A new category called metabolic dysfunction and alcohol-related liver disease (MetALD) characterises MASLD patients consuming excessive alcohol on a weekly basis (140-350g for males and 210-420g for females) due to the frequent conjunction of the two conditions.[5]

In a meta-analysis from 24 countries, the global prevalence of non-obese MASLD was found to be 40% compared to 19.2% lean MASLD.[6] In a study, the prevalence of NAFLD was 49.3% among whom 60% were obese and 34% were non-obese.[7] The prevalence of lean and non-obese MASLD ranges from 8% to 19% in Asian population.[8] In men, NAFLD was found to be more prevalent than in women (39·7% vs 25·6%; p<0·0001).[9] A study in Karachi showed prevalence of MASLD to be 40.8% which was more among those aged 45-55 years.[10]

Sexual dimorphism has been observed in MASLD patients, and sex hormones seem to play a role in its progression, with oestrogen being protective against it, and androgens promoting its progression.[11]

There is a bi-directional relationship between MASLD and type 2 DM (T2DM), suggesting that pre-diabetes and DM can increase the risk of MASLD and vice versa.[12] There is a synergistic increase in cardiovascular disease (CVD) risk in

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Submission complete: 12-11-2024 **1st Revision received:** 22-04-2025

Acceptance: 17-12-2025 **Last Revision received:** 16-12-2025

T2DM patients who have developed MASLD.[13] It mostly occurs in patients who are obese, but recent studies have shown increasing number of MASLD cases in lean and non-obese populations. Since MASLD goes unnoticed in lean subjects until advance fibrosis has occurred in a majority of affected subjects, it may have compromised prognosis.[14] As such, early screening is essential in lean and non-obese diabetics for better outcomes.

To our knowledge, data of lean and non-obese MASLD prevalence in Pakistan is scarce. The current study was planned to fill the gap in literature by assessing the prevalence of lean and non-obese MASLD in DM patients, and exploring the gender-wise correlation of lifestyle, HTN and dyslipidaemia with body mass index (BMI) categories.

Patients and Methods

The descriptive, cross-sectional study was conducted at the Diabetes Clinic of Jinnah Postgraduate Medical Centre (JPMC), Karachi, from March 1 to August 25, 2023. Approval was obtained from the institutional ethics review board, and written informed consent was taken from all the participants.

The sample size was calculated with 90% confidence interval (CI) and 10% margin of error, using OpenEpi version 3 calculator on the basis of the formula.[15]

$$n = [DEFF*Np(1-p)]/ [(d^2/Z^2_{1-\alpha/2}*(N-1)+p*(1-p)].$$

For the purpose of this calculation, MASLD prevalence was taken as 29.6%.[16]

The sample was raised using non-purposive, convenience sampling technique. Those included were adult patients of either gender having fatty liver. Those excluded were patients with cirrhosis and malignancy, like hepatocellular carcinoma, and those who took excessive alcohol based on WHO Alcohol Use Disorders Identification Test (AUDIT) and MetALD class.[17,18]

Data was collected regarding patients' demographics, baseline characteristics and history of HTN, dyslipidaemia and DM duration using a predesigned proforma.

For the purpose of standardisation, operational parameters were defined at the outset. NAFLD meant no history of current or past alcohol consumption (based on AUDIT test), hepatitis B and hepatitis C non-reactive status, with patients having no evidence of cirrhosis on ultrasound and on biochemical parameters. SLD) referred to hepatic steatosis shown on any liver imaging study, regardless of the underlying cause. MASLD was any SLD based on imaging data if any of the following five cardiometabolic risk factors were present: obesity BMI>25 kg/m^2 or waist circumference (WC) >90cm for males [M] and 80cm for females (F); DM or pre-diabetes defined as fasting blood sugar (FBS) >100mg/dl or post-prandial glucose (PPG) >140mg/dl or glycated haemoglobin (HbA1c) >5.7 or patients being on glucose-lowering agents; HTN >130/80mmHg or taking anti-HTN medications; TG >150mg/dl or on lipid-lowering medications; HDL <40mg/dl (M) and <50mg/dl (F) or on medications for deranged lipid.[18]

Using the Adult Treatment Panel (ATP) III cholesterol guidelines, dyslipidaemia was defined as TG ≥150mg/dl or low-density lipoprotein (LDL) >100mg/dl or total cholesterol (TC) >200mg/dl, or HDL ≤40mg/dl in males and ≤50mg/dl in females, or those on treatment for deranged lipids.[19] Lean MASLD was identified in patients with BMI 18.5-22.9 kg/m^2 (Asian cutoff), non-obese MASLD was identified in patients with BMI 23-24.9kg/m^2 (Asian cutoff), and obese MASLD was identified in patients having BMI ≥25kg/m^2 (Asian cutoff), or WC >90cm (M), 80 cm (F).[20,21]

Data was analysed using SPSS 21. Demographic and clinical characteristics of MASLD patients were compared using independent sample *t*-test and cross-tab test. BMI categories and lifestyle were compared using partial correlation and univariant analysis, while correlation among DM duration, HTN, BMI categories, WC and dyslipidaemia was analysed using chi-square and partial correlation coefficient. P<0.05 was considered significant.

Results

Of the 229 patients with mean age 53.12±9.82 years, 151(65.93%) were females and 78(34.06%) were males. Overall mean BMI was 27.41±4.80kg/m^2, mean WC was 97.41±11.57cm and mean DM duration was 10.07±6.21 years. There were 171(74.67%) patients with a sedentary lifestyle and 58(25.32%) had a non-sedentary lifestyle. Overall, 133(58.07%) patients had HTN and 153(66.8%) were obese. Mean TG level was 182.38±24.71mg/dl, mean HDL was 41.48±5.42 and mean LDL was 83.32±9.16mg/dl. Age, BMI, DM duration, WC and dyslipidaemia had no significant gender-based differences (p>0.05), but sedentary lifestyle was more prevalent in females than in males (p<0.05) (Table 1).

TG, LDL, BMI and WC values were significantly raised in obese MASLD patients (p<0.05). BMI categories were significantly correlated to with HTN, dyslipidaemia and MASLD (NAFLD) grading (Table 2 and 3).

Prevalence of obese MASLD was 153(66.8%), followed by non-obese 39(17.03%) and lean 37(16.15%). Among 78(34.06%) male MASLD patients, 14(17.94%) were lean, 22(28.20%) were non-obese and 42(54.84%) were obese.

Table-1: Gender-based comparison of MASLD patients.

Parameters	Total (n=229)[n(%)]	Male MASLD (n=78)[n(%)]	Female MASLD (n=151)[n(%)]	*p*-value
Mean Age (years)	53.12±9.82	51.84±17.23	54.40±15.76	>0.05
Mean BMI (kg/m^2)	27.41±4.89	27.35±14.71	28.81±18.02	>0.05
Life style				
Non-sedentary	58(25.32)	27(34.61)	27(17.88)	<0.05
Sedentary	171(74.67)	51(65.38)	120(79.47)	
Mean Duration of diabetes	10.07±6.21	9.47±5.98	10.37±6.34	>0.05
Hypertension				
Yes	133(58.07)	41(52.56)	93(61.58)	<0.05
No	96(41.92)	37(47.43)	58(38.41)	>0.05
Dyslipidaemia				
Triglyceride	182.43±24.71	175.83±21.2	181.96±44.6	>0.05
HDL	41.48±5.42	41.7±3.8	41.37±6.11	>0.05
LDL	83.32±39.16	77.83±48.97	86.22±32.8	>0.05
BMI categories				
Lean	37(16.15)	14(17.94)	23(15.23)	>0.05
Non-obese	39(17.03)	22(28.20)	17(11.25)	<0.05
Obese	153(66.81)	42(53.84)	111(73.50)	<0.05

MASLD: Metabolic dysfunction-associated steatotic liver disease, BMI: Body mass index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein.

Table-2: Correlation of lifestyle with dyslipidaemia and hypertension.

Parameters	Sedentary Life style	Non-sedentary Life style
Hypertension	0.063*	0.071
Triglycerides	-0.40*	-0.234
HDL	0.053	-0.42*
LDL	-0.016*	0.275

MASLD: Metabolic dysfunction-associated steatotic liver disease, HDL: High-density lipoprotein, LDL: Low-density lipoprotein; (**p*-value is significant upto<0.05).

Table-1: Impact of hypertension, dyslipidemia, NAFLD grading, duration of diabetes and waist circumference on BMI categories.

Parameters	Lean with MASLD	Non -Obese with MASLD	Obese with MASLD	*p*-value
Hypertension	1.59±0.48	1.62±0.49	1.33±0.37	>0.05
Triglycerides	165.95±26.44	174.63±27.40	187.74±33.74	<0.05
HDL	41.62±7.7	42.58±7.76	41.62±5.42	>0.05
LDL	78.68±37.96	78.29±26.42	85.7±42.01	<0.05
NAFLD grading	1.92±0.7	2.1±0.79	2.23±064	<0.05
Duration of diabetes	11.81±6.35	10.76±7.36	9.47±5,79	>0.05
BMI	20.84±1.71	23.92±0.63	26.35±3.9	<0.05
Waist circumference	86.68±9.49	92.12±10.26	104.35±13.54	<0.05

MASLD: Metabolic dysfunction-associated steatotic liver disease, NAFLD: Non-alcoholic fatty liver disease, HDL: High density lipoprotein, LDL: Low-density lipoprotein, BMI: Body mass index.

Among 151(65.93%) females, 23(15.23%) were lean, 17(11.25%) were non-obese and 111(73.50%) were obese. Non-obese MASLD was more prevalent in males (p<0.05), while obese MASLD was more prevalent in females (p<0.05).

Discussion

MASLD(Metabolic Dysfunction Associated Steatotic Liver Disease), previously known as NAFLD(Non-Alcoholic Fatty Liver Disease), has gained attention due to its increasing prevalence worldwide, with risk factors including obesity, diabetes mellitus(DM) and metabolic syndrome (MS).[18]

The prevalence of MASLD in T2DM is significantly higher compared to individuals without diabetes mellitus. The current study showed the prevalence of lean MASLD in diabetic subjects to be 16.15%, while 17.03% had non-obese MASLD. In a meta-analysis comprising 85 studies, 13.11% subjects had lean MASLD globally and 14.55% in Asia, while among the diabetics, the prevalence was 19.56%.[22] It was found to be 28.3% in those with Type 2 DM in a study conducted in Pakistan.[23] It can be seen that the prevalence of lean and non-obese MASLD in Pakistan is surprisingly high, suggesting that metabolic dysfunction can contribute to liver disease even in individuals who are not overweight, and this highlights the importance of early detection for metabolic dysfunction to prevent the development of SLD.

In the current study, a significant association of MASLD with gender was also observed, with a higher prevalence of obese MASLD in diabetic females compared to males (p<0.05), while non-obese MASLD was more prevalent in males(p<0.05). This gender difference may have implications for targetted screening and treatment strategies for MASLD in T2DM.

A study in Pakistan showed that female gender was associated with dyslipidaemia. with low HDL levels being more prevalent in female compared to males with diabetes (p<0.05), and raised LDL levels being more common in male compared to females with diabetes (p>0.05).[24] The current study shows the possibility of females with diabetes being more prone to dyslipidaemia than the males, thus exposing the females to increased risk of coronary heart disease.

In a study, multivariate Cox regression analyses showed high levels of TG-related indices, particularly in relation to BMI (TG-BMI) and WC (TG-WC), being significantly associated with all-cause mortality, cardiovascular mortality, and DM mortality in either NAFLD or MASLD.[25] Although, both males and females alike are exposed to MS, the female diabetic is especially prone to this syndrome.[26] Further research is needed to explore the underlying mechanisms behind the gender differences in MASLD prevalence among type 2 diabetics. Understanding these differences could lead to more personalised and effective interventions for both male and female diabetics at risk of liver disease.

Gender differences exist in the prevalence of obesity and

its associated diseases, with women being more prone to obesity.[27] Research suggests lean and non-obese MASLD as a metabolically unhealthy status with high incidence in Asian population and closely linked with metabolic diseases, including DM. The combined prevalence of lean and non-obese MASLD in the current diabetic MASLD patients was 33%, which was high. Subgroup analysis suggests female gender and sedentary lifestyle were risk factors in the development of obese MASLD, while lean and non-obese NAFLD were more prevalent in males. The result seems to be an indication that obese MASLD is a gender-specific phenotype. These factors suggest targetted interventions for female patients to manage and mitigate MASLD complications.

A sedentary lifestyle significantly impacts HTN and dyslipidaemia, especially TG and HDL, in MASLD patients. Specifically, sedentary behaviour is associated with higher TG and lower HDL levels, contributing to cardiovascular risks. Active leisure time physical activity has an inverse relation with MASLD, and a negative correlation with hepatic fibrosis.[28]

Understanding the mechanisms underlying MASLD, and developing effective prevention and treatment strategies are crucial to the task of addressing this growing public health concern.

The current study has limitations. Further studies and larger sample sizes are needed to study gender differences in detail. Besides, the lack of a standardised selection process in the study means further studies are needed to validate the current findings. Finally, the sample was not representative of the general population which many have limited the generalizability of the findings.

Conclusion

A significant number of diabetics were found to have obese MASLD, and it was significantly more common among females. Sedentary lifestyle was also significantly more prevalent in female diabetics. While it is important to address the prevalence of MASLD, it is also essential to consider other factors, such as genetic predisposition and influence of lifestyle, in the development of the disease.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

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Author Contribution:

FNM: Concept, data analysis, interpretation, drafting and final approval.
SN: Concept, data analysis, revision and final approval.
SMA: Design, critical revision and final approval.
ZA: Concept, revision and final approval.
MFW: Design, revision and final approval.