

Prevalence of Metabolic Dysfunction-associated Steatotic Liver Disease (MASLD) in Persons with Obesity and Type 2 Diabetes Mellitus: A Cross-sectional Study

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ABSTRACT

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is an important entity in patients with type-2 diabetes (T2D). Exploring the prevalence and related factors of MASLD is vital toward developing effective methods of diagnosis and treatment. The objective of this study was to determine the prevalence of MASLD in persons with obesity and T2D.

Materials and methods: This cross-sectional study was conducted at a private healthcare facility (Medicell Clinics) in Karachi, Pakistan, reviewing records from January to December 2022. Persons of either gender aged 18 or above with a diagnosis of T2D and/or obesity were analyzed.

Results: Of a total of 646 persons, 430 (66.6%) were females. The mean age was 48.58 ± 13.88 years, ranging between 18 and 85 years. T2D was noted in 351 (54.3%) patients, while obesity was observed in 593 (91.8%) persons, 396 (61.3%) had MASLD. Persons having MASLD had significantly higher body mass index (31.16 ± 5.13 vs 28.14 ± 4.76 kg/m², $p < 0.001$). Likewise, obesity was significantly associated with MASLD (94.9 vs 86.8% , $p < 0.001$). The odds ratios (OR) and 95% confidence intervals (CIs) are reported in multivariate logistic regression table. Persons with T2DM (OR = 1.519, $p = 0.009$), and obesity (OR = 2.651, $p = 0.001$) showed significantly increased odds of having MASLD. The analysis revealed that individuals in the age-group of 18–40 (OR = 1.627, $p = 0.014$) had increased odds of having MASLD.

Conclusion: The prevalence of MASLD was very high in persons with T2D, and obesity. Type-2 diabetes with or without obesity, or the other way around, significantly increases the risk of MASLD. Therefore, these persons should be screened for MASLD to improve clinical outcomes in the affected people.

Keywords: Body mass index, Diabetes mellitus, Obesity.

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INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD), previously termed nonalcoholic fatty liver disease (NAFLD), is a prevalent chronic liver condition affecting over 30% of the global population.^{1,2} Metabolic dysfunction-associated steatotic liver disease is acknowledged as the predominant type of hepatic condition linked to additional metabolic conditions like type-2 diabetes (T2D), hypertension, excessive weight, and heart diseases.^{3,4} South Asia and Asia Pacific regions have seen an increase in MASLD parallel to the increase in obesity and its associated diseases. Asian populations have relatively lower body mass index (BMI) than Caucasians but a higher prevalence of MASLD, which differences in the distribution of body fat or higher levels of insulin resistance could explain.^{2,5} The prevalence of MASLD is even more alarming among individuals with T2D or obesity, skyrocketing to ~ 70–80%.^{3,4} The heightened risk in those with T2D or obesity underscores the need for increased awareness and proactive measures toward prevention and management strategies for MASLD within vulnerable populations.^{6,7}

The progression of MASLD involves changes in glucose and lipid metabolism, insulin resistance, and secretion.⁸ Early detection of MASLD enables prevention or slowing down the condition developing into advanced liver damage.⁹ Liver biopsy is a benchmark for the diagnosis of MASLD but it is an invasive procedure that also incurs significant costs and has various drawbacks, such as patient apprehension, severe complications, and the possibility of inaccuracies in sample collection.¹

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In Pakistan, screening for MASLD is not routinely done in people with T2D and obesity as only limited studies are available mainly showing the association between MASLD and T2D. A local study from Peshawar showed that 47% of the general population had MASLD.¹⁰ In another study, the prevalence of MASLD in persons with T2D was found to be 72.4%, and nonalcoholic steatohepatitis (NASH) was present in 56.5% of T2D patients.⁹ This study seeks to determine the prevalence of MASLD in persons with obesity and T2D.

MATERIALS AND METHODS

This cross-sectional was conducted at Medicell Institute of Diabetes Endocrinology and Metabolism (MIDEM). The study duration period

was January to December 2022. Non-probability consecutive sampling technique was utilized. Inclusion criteria were persons of either gender, aged 18 or above with T2D and/or obesity. The study specifically excluded records of individuals with liver diseases attributable to viral infections (HBV, HCV), autoimmune diseases, other metabolic disturbances, or those who were on hepatotoxic medications or consumed alcohol. Persons with type 1 diabetes mellitus and pregnant women were also excluded.

Approval was obtained from the Institutional Review Board. Age, gender, height, weight, BMI, primary diagnosis, and comorbidities were noted. Laboratory examinations including alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (γ GT), uric acid, serum creatinine, total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), fasting blood glucose (FBG), and random blood glucose (RBG) were evaluated. A detailed inquiry into the person's medical history and a thorough physical assessment were conducted to confirm or rule out Wilson's disease or autoimmune hepatitis. These steps were crucial to accurately differentiate MASLD from other liver disorders.

Metabolic dysfunction-associated steatotic liver disease was defined as the existence of liver steatosis with at least one of five cardiometabolic criteria including impaired glucose regulation, T2D, overweight or obesity, hypertension, or dyslipidemia. Impaired glucose regulation was defined as an FBG level between 100 and 125 mg/dL, or HbA1c level ranging from 5.7 to 6.4%, or a known diagnosis of T2D, or receiving antidiabetic treatment. Dyslipidemia was characterized by abnormal lipid levels (elevated TG as plasma triglyceride levels >150 mg/dL, or receiving lipid-lowering treatment; low HDL cholesterol as HDL cholesterol levels below 40 mg/dL for men and below 50 mg/dL for women; or receiving lipid-lowering treatment). Hypertension was defined as systolic blood pressure >130 mm Hg or diastolic blood pressure >80 mm Hg, or receiving antihypertensive treatment. BMI more than 25 kg/m² was labeled as obesity as is the criteria for Asian Pacific population, with BMI 25–29.9 kg/m² subcategorized as obesity class 1 and BMI \geq 30 kg/m² as obesity class 2.¹¹ Skilled sonologists performed a liver examination on each individual to detect any manifestations of MASLD, thus providing visual evidence that supplemented the data from laboratory tests and other assessments.

Data were entered and analyzed into IBM-SPSS Statistics, version 26.0. The prevalence of association of MASLD with factors, such as age, BMI, T2D, duration of T2D, BP, ALT, AST, HbA1c, FBG, TC, LDL-C, and TG were determined using logistic regression analysis. Associations of categorical variables, such as gender, were ascertained through the Chi-square test of association along with their odds ratios. Correlation coefficients were calculated to understand the relationships among quantitative explanatory variables. Results were considered significant at a *p*-value of less than 0.05.

RESULTS

Of a total of 646 persons, 430 (66.6%) were females. The mean age was 48.58 ± 13.88 years, ranging between 18 and 85 years. T2D was noted in 351 (54.3%) persons, while obesity was observed in 593 (91.8%) persons. MASLD was found in 396 (61.3%) persons. Persons with MASLD had significantly higher BMI (31.16 ± 5.13 vs 28.14 ± 4.76 kg/m², *p* < 0.001). Likewise, obesity was significantly associated with MASLD (94.9 vs 86.8%, *p* < 0.001). Table 1 illustrates the

Table 1: Association of MASLD with demographic and clinical characteristics (*N* = 646)

Study variables	MASLD		<i>p</i> -value
	Yes (<i>n</i> = 396)	No (<i>n</i> = 250)	
Gender			
Male	133 (33.6%)	83 (33.2%)	0.919
Female	263 (64.4%)	167 (66.8%)	
Age (years)	53.72 ± 12.10	56.33 ± 11.55	0.050
Body mass index (kg/m ²)	31.16 ± 5.13	28.14 ± 4.76	<0.001
Smoking	41 (10.4%)	25 (10.0%)	0.802
Type-2 diabetes (T2D)	226 (57.1%)	125 (50.0%)	0.079
Obesity			
No	20 (5.1%)	33 (13.2%)	<0.001
Class-1	205 (51.8%)	141 (56.4%)	
Class-2	171 (43.2%)	76 (30.4%)	

association of MASLD with demographic and clinical characteristics of study participants.

Individuals with MASLD exhibited significantly higher levels of HbA1c ($7.19 \pm 2.29\%$ vs 6.51 ± 1.80 , *p* = 0.001), TC (185.89 ± 44.41 vs 174.51 ± 42.03 , *p* = 0.001), TG (213.51 ± 168.10 vs 153.60 ± 79.25 , *p* = 0.001), ALT (42.90 ± 27.90 vs 27.39 ± 18.69 , *p* = 0.001), and lower HDL (42.28 ± 13.41 vs 45.71 ± 14.76 , *p* = 0.002). Table 1 compares various laboratory parameters between persons with and without MASLD. Tables 2 and 3 present the comparison of characteristics of MASLD with respect to T2D and obesity.

The odds ratios (ORs) and 95% confidence intervals (CI) are reported in Table 4 applying multivariate logistic regression. Persons with T2D (OR = 1.519, *p* = 0.009), and obesity (OR = 2.651, *p* = 0.001) showed significantly increased odds of having MASLD. The analysis revealed that individuals in the age-group of 18–40 (OR = 1.627, *p* = 0.014) had increased odds of having MASLD (Table 5).

DISCUSSION

There is compelling evidence that highlights the worldwide burden of MASLD, which extends beyond liver-related complications and also increases the risk of metabolic diseases, such as T2D, dyslipidemia, metabolic syndrome, and cardiovascular disorders.^{12,13} Our study showed that persons with T2D had a 1.5 times higher likelihood of developing MASLD compared with persons without diabetes. A meta-analysis conducted by Younossi et al. aimed to assess the global prevalence of MASLD in individuals with T2D. The results revealed that 55.5% of persons suffering from T2D also reported MASLD, with the lowest prevalence of 30.4% reported in Africa.⁴ Other researchers have also shown a strong relationship between MASLD and T2D.¹⁴ The simultaneous existence of both these conditions in a person affects disease prognosis, with T2D at a much higher risk of developing hepatic cancer.¹⁵ The common feature between MASLD and T2D is obesity and insulin resistance, which explains why both these conditions can exist simultaneously.¹⁶ The association between T2D and MASLD can be further illustrated by the fact that the treatment of MASLD

Table 2: Comparison of laboratory parameters in persons with respect to MASLD (N = 646)

Laboratory parameters	MASLD		p-value
	Yes (n = 396)	No (n = 250)	
Systolic blood pressure (mm/Hg)	136.90 ± 16.98	134.79 ± 18.76	0.137
Diastolic blood pressure (mm/Hg)	84.60 ± 10.53	83.79 ± 11.89	0.363
Fasting blood glucose (mg/dL)	135.71 ± 21.29	135.12 ± 26.14	0.751
Random blood glucose (mg/dL)	163.01 ± 50.54	160.53 ± 51.48	0.541
HbA1c (%)	7.19 ± 2.29	6.51 ± 1.80	0.001
Total cholesterol (mg/dL)	185.89 ± 44.41	174.51 ± 42.03	0.001
Triglyceride (mg/dL)	213.51 ± 168.10	153.60 ± 79.25	0.001
High-density lipoprotein (HDL) (mg/dL)	42.28 ± 13.41	45.71 ± 14.76	0.002
Low-density lipoprotein (LDL) (mg/dL)	116.63 ± 42.29	112.02 ± 42.03	0.171
Uric acid (mg/dL)	6.36 ± 1.55	6.40 ± 1.57	0.748
Alanine transaminase (ALT) (IU/L)	42.90 ± 27.90	27.39 ± 18.69	0.001
Aspartate aminotransferase (AST) (IU/L)	11.44 ± 7.37	11.53 ± 4.97	0.850

Independent sample t-test applied

Table 3: Comparison of MASLD with respect to type-2 diabetes mellitus (N = 646)

T2D	Characteristics	MASLD		p-value
		Yes (n = 396)	No (n = 250)	
Yes (n = 351)	Age (years)	53.72 ± 12.10	56.33 ± 11.55	0.050
	Duration of T2D (years)	7.82 ± 7.45	8.15 ± 7.75	0.693
	Body mass index (kg/m ²)	31.16 ± 5.13	28.14 ± 4.76	0.000
	Gender			
	Male	92 (26.2%)	57 (16.2%)	0.375
	Female	134 (38.2%)	68 (19.4%)	
	Smoking status			
	Yes	23 (6.6%)	17 (4.8%)	0.334
	No	203 (57.8%)	108 (30.8%)	
No (n = 295)	Age (years)	41.26 ± 11.76	41.56 ± 13.38	0.841
	Duration of T2D (years)	4.83 ± 2.85	4.81 ± 3.01	0.950
	Body mass index (kg/m ²)	33.74 ± 4.99	30.51 ± 3.73	<0.001
	Gender			
	Male	41 (13.9%)	26 (8.8%)	0.502
	Female	129 (43.7%)	99 (33.6%)	
	Smoking status			
	Yes	18 (6.1%)	8 (2.7%)	0.210
	No	152 (51.5%)	117 (39.7%)	

Applied Chi-square test, independent t-test. BMI, body mass index; T2D, type 2 diabetes

that targets obesity and insulin resistance also reduces the risk of developing T2D.¹⁷ Lifestyle modifications such as dietary changes and increased physical activity improve liver injury in patients with MASLD, and at the same time, also prevent or delay the onset of T2D in high-risk patients.^{18,19}

This study shows that people who were obese had 2.6 times higher risk of having MASLD when compared with persons who were not obese. Similar findings were also reported in a study where the impact of variables like obesity, insulin resistance, and MASLD, on the incidence of T2D were assessed over five years.¹⁸ Each of these three variables has been found to increase the risk of

developing T2D.¹⁸ Our study also shows that persons with MASLD had a significantly higher mean BMI. Studies have shown that higher BMI, as well as waist circumference, are associated with MASLD and impose an increased risk of disease progression.²⁰ This association may be due to MASLD being linked with the accumulation of visceral fat and not subcutaneous fat. Visceral fat is associated with higher lipolysis, greater insulin resistance, and the release of inflammatory and pro-fibrogenic mediators, thus resulting in the development of MASLD.²¹

Although there is a well-established correlation between MASLD, obesity, and metabolic syndrome, it has also been reported

Table 4: Comparison of characteristics of persons with respect to MASLD and obesity (N = 646)

Obesity	Characteristics	MASLD		p-value
		Yes (n = 396)	No (n = 250)	
Yes (n = 593)	Age (years)	47.84 ± 13.36	47.56 ± 14.37	0.813
	Duration of T2D (years)	6.29 ± 5.84	5.97 ± 5.28	0.510
	Body mass index (kg/m ²)	32.73 ± 4.93	30.29 ± 3.88	<0.001
	Gender			
	Male	127 (21.4%)	68 (11.5%)	0.542
	Female	249 (42.0%)	149 (25.1%)	
	Smoking status			
	Yes	40 (6.7%)	21 (3.5%)	0.711
	No	336 (56.7%)	196 (33.1%)	
	No (n = 53)	Age (years)	58.45 ± 10.99	58.06 ± 12.03
Duration of T2D (years)		11.15 ± 8.79	9.82 ± 9.38	0.611
Body mass index (kg/m ²)		23.50 ± 1.53	22.97 ± 11.81	0.280
Gender				
Male		6 (11.3%)	15 (28.3%)	0.265
Female		14 (26.4%)	18 (34.0%)	
Smoking status				
Yes		1 (1.9%)	4 (7.5%)	0.390
No		19 (35.8%)	29 (54.7%)	

Applied Chi-square test, Fisher's Exact test, independent t-test, BMI, body mass index; T2D, type 2 diabetes

Table 5: Multivariate logistic regression analysis for study variables associated with MASLD

Characteristics	Odds ratio	95% CI (lower-upper)	p-value
Age (years)			
18–40	Reference		0.344
>40	0.849	0.604–1.192	
Gender			
Male	Reference		0.470
Female	1.130	0.811–1.576	
T2DM			
Yes	1.519	1.109–2.080	0.009
No	Reference		
Smoking			
Yes	1.141	0.678–1.920	0.619
No	Reference		
Obesity			
Yes	2.651	1.477–4.757	0.001
No	Reference		

CI, confidence interval; T2D, type-2 diabetes

in non-obese persons. In the United States, ~ 7–10% of such cases have been documented, while the estimated prevalence in Asian countries is as high as 19%.²² A study conducted to investigate the relationship between BMI and MASLD revealed that 25.4% were classified as underweight, 33.2% as overweight, and 41.4%

as obese. Conversely, among persons without MASLD, 50.7% were underweight, 33.6% were overweight, and only 15.7% were considered obese.²³ The present study highlighted the relationship between BMI and MASLD and our findings are consistent with what has been documented in the literature.²⁴

A strong association between T2D and MASLD was found in our study, which makes it clinically imperative that patients who have T2D must be screened for MASLD and signs of liver fibrosis.²⁵ Furthermore, the findings in our study implicate the importance of weight management to overcome obesity and metabolic disease, which is a significant contributor to the development of MASLD. Data suggests that the loss of greater than 10% of body weight reduces the risk of liver diseases.²⁶

There were a few limitations to this research. The cross-sectional veracity of our study was a limiting factor, as this study was conducted at a single private healthcare center. Future research involving multiple centers on a much larger scale is warranted, employing a longitudinal approach. This would allow for the collection of vast data involving a larger cross-sectional sample size, which would help generalize the findings.

CONCLUSION

The prevalence of MASLD was very high in persons with T2D and obesity. T2D with or without obesity, or the other way around, significantly increases the risk of MASLD. Therefore, these persons should be screened for MASLD to improve clinical outcomes.

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