

Systematic Review

THE ASSOCIATION BETWEEN METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE AND DIABETES MELLITUS: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease worldwide and is closely associated with type 2 diabetes mellitus (T2DM). The coexistence of these conditions increases the risk of metabolic dysfunction-associated steatohepatitis (MASH), advanced fibrosis, cirrhosis, hepatocellular carcinoma, cardiovascular disease, and chronic kidney disease. This systematic review aimed to synthesize the current evidence on the association between MASLD and diabetes mellitus. **Materials and Methods:** A systematic literature search was conducted in PubMed/MEDLINE, Scopus, Web of Science, Embase, and the Cochrane Library for studies published in English. Eligible studies included observational studies, randomized controlled trials, and systematic reviews reporting the prevalence, risk factors, clinical outcomes, diagnostic approaches, and management of MASLD in individuals with diabetes mellitus. Data were extracted using standardized methods, and study quality was assessed using validated risk-of-bias tools.

Results: Published evidence consistently demonstrated a high prevalence of MASLD among individuals with T2DM. Global meta-analyses reported a pooled MASLD prevalence of approximately 65%, while MASH was present in approximately 32% of affected individuals. Advanced fibrosis was reported in 15–20% of patients, with significant fibrosis observed in 10–18%. Diabetes mellitus was consistently identified as a major predictor of fibrosis progression, cirrhosis, and hepatocellular carcinoma. Ultrasonography remained the most frequently used diagnostic modality, whereas transient elastography and non-invasive fibrosis scores, including the Fibrosis-4 Index (FIB-4), were increasingly used for risk stratification.

Conclusion: MASLD is highly prevalent among individuals with T2DM and is associated with significant liver-related and extrahepatic complications. Routine screening for MASLD and advanced fibrosis using non-invasive assessment tools should be integrated into diabetes care. Early diagnosis and multidisciplinary management may reduce disease progression and improve long-term clinical outcomes.

Keywords: Metabolic dysfunction-associated steatotic liver disease (MASLD), Type 2 diabetes mellitus (T2DM), Metabolic dysfunction-associated steatohepatitis (MASH), Insulin resistance, Liver fibrosis.

INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver

disease worldwide and represents the hepatic manifestation of metabolic dysfunction. The term MASLD, introduced in 2023, replaces non-alcoholic fatty liver disease (NAFLD) to better reflect the

underlying metabolic abnormalities associated with hepatic steatosis. MASLD is diagnosed in individuals with hepatic steatosis and at least one cardiometabolic risk factor, including overweight or obesity, type 2 diabetes mellitus (T2DM), hypertension, dyslipidemia, or other features of metabolic dysfunction. This updated nomenclature emphasizes the close relationship between liver disease and systemic metabolic disorders, particularly diabetes mellitus.^[1]

Diabetes mellitus, especially T2DM, has emerged as one of the strongest risk factors for the development and progression of MASLD. Insulin resistance, a central feature of T2DM, plays a pivotal role in the accumulation of hepatic fat through increased lipolysis, enhanced free fatty acid flux to the liver, de novo lipogenesis, and impaired lipid oxidation. Persistent hyperglycemia, chronic low-grade inflammation, oxidative stress, and mitochondrial dysfunction further contribute to hepatocellular injury, fibrosis, and disease progression. Conversely, MASLD exacerbates insulin resistance, thereby increasing the risk of incident T2DM and worsening glycemic control. This bidirectional relationship creates a vicious cycle that significantly increases both hepatic and extrahepatic complications.^[2]

The global prevalence of MASLD is estimated to exceed 30% among adults, with substantially higher rates reported in individuals with T2DM, ranging from 55% to 75%. Furthermore, patients with diabetes are at increased risk of developing progressive forms of MASLD, including metabolic dysfunction-associated steatohepatitis (MASH), advanced fibrosis, cirrhosis, hepatocellular carcinoma, and liver-related mortality. Beyond liver-specific outcomes, the coexistence of MASLD and diabetes is associated with an increased risk of cardiovascular disease, chronic kidney disease, and all-cause mortality, highlighting its significance as a major public health concern.^[3]

Recent clinical practice guidelines from international organizations advocate routine assessment of liver disease in individuals with T2DM due to the high prevalence of undiagnosed MASLD and advanced fibrosis. Several non-invasive diagnostic tools, including serum fibrosis scores and elastography, have been incorporated into clinical algorithms to facilitate early detection and risk stratification. In parallel, lifestyle modification remains the cornerstone of management, while newer antidiabetic agents such as glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and sodium-glucose cotransporter-2 (SGLT2) inhibitors have demonstrated promising benefits in improving hepatic steatosis and metabolic outcomes.

Despite the growing body of evidence linking MASLD and diabetes mellitus, the literature remains heterogeneous with respect to epidemiology, pathophysiological mechanisms, diagnostic strategies, disease progression, and therapeutic interventions. Differences in study populations, diagnostic criteria, and outcome measures have

contributed to variations in reported findings, making it challenging to draw comprehensive conclusions. Moreover, the transition from the NAFLD to MASLD nomenclature necessitates an updated synthesis of evidence that reflects current diagnostic definitions and clinical practice.^[4,5]

Therefore, this systematic review aims to comprehensively evaluate the association between metabolic dysfunction-associated steatotic liver disease and diabetes mellitus. Specifically, it seeks to summarize the available evidence regarding the epidemiology, pathophysiological mechanisms, clinical characteristics, disease progression, diagnostic approaches, and management strategies of MASLD in individuals with diabetes.^[6,7] By synthesizing current evidence, this review intends to provide clinicians, researchers, and policymakers with an updated understanding of the complex interplay between these two highly prevalent metabolic disorders and identify gaps that warrant future research.

MATERIALS AND METHODS

Study Design: This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. The review aimed to systematically identify, evaluate, and synthesize published evidence on the association between metabolic dysfunction-associated steatotic liver disease (MASLD) and diabetes mellitus, including epidemiology, pathophysiology, clinical characteristics, disease progression, diagnostic approaches, and management.

Studies were selected based on the following inclusion and exclusion criteria.

Inclusion Criteria

- Original research articles published in peer-reviewed journals.
- Observational studies (cross-sectional, case-control, and cohort studies).
- Randomized controlled trials (RCTs) and non-randomized interventional studies reporting outcomes related to MASLD and diabetes.
- Studies involving adults (≥ 18 years) diagnosed with MASLD or type 2 diabetes mellitus (T2DM).
- Studies reporting the prevalence, incidence, risk factors, pathophysiology, clinical outcomes, diagnosis, treatment, or prognosis of MASLD in patients with diabetes or the association between MASLD and diabetes.
- Articles published in English.
- Studies published between January 2015 and December 2026 (modify according to the actual search period).

Exclusion Criteria

- Case reports and case series involving fewer than 10 participants.

- Editorials, letters to the editor, commentaries, conference abstracts, protocols, and narrative reviews.
- Animal studies and in vitro studies.
- Pediatric studies (<18 years).
- Studies lacking sufficient data relevant to the review objectives.
- Duplicate publications.

Information Sources: A comprehensive literature search was performed in the following electronic databases as PubMed/MEDLINE, Scopus, Web of Science, Embase and Cochrane Library. Additionally, the reference lists of eligible studies and relevant review articles were manually screened to identify any additional studies that met the inclusion criteria.

Study Selection: All retrieved articles were imported into a reference management software (e.g., EndNote, Zotero, or Mendeley) for duplicate removal.

Two independent reviewers screened titles and abstracts for eligibility. Full-text articles of potentially relevant studies were then assessed against the predefined inclusion and exclusion criteria. Disagreements between reviewers were resolved through discussion, and where necessary, consultation with a third reviewer.

The study selection process was documented using a PRISMA 2020 flow diagram.

A standardized data extraction form was developed prior to data collection. The following

The methodological quality of included studies was independently evaluated by two reviewers.

The following assessment tools were used according to study design:

- Newcastle–Ottawa Scale (NOS) for cohort and case-control studies.
- Joanna Briggs Institute (JBI) Critical Appraisal Checklist for cross-sectional studies.
- Cochrane Risk of Bias 2 (RoB 2) tool for randomized controlled trials.

Studies were categorized as having low, moderate, or high risk of bias based on the respective scoring systems.

A qualitative synthesis of the included studies was performed by summarizing findings according to the following themes Epidemiology and prevalence, Pathophysiological mechanisms, Risk factors, Clinical manifestations, Disease progression, Diagnostic modalities, Therapeutic interventions and Clinical outcomes

Where sufficient homogeneous data were available, quantitative synthesis (meta-analysis) was considered using pooled effect estimates.

Statistical Analysis: If a meta-analysis was feasible, pooled estimates of odds ratios (ORs), relative risks (RRs), or hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated using a random-effects model.

Statistical heterogeneity was assessed using Cochran's Q test and I² statistic

Heterogeneity was interpreted as:

- 0–25%: Low
- 26–50%: Moderate
- 51–75%: Substantial
- 75%: Considerable

Publication bias was evaluated using funnel plots and Egger's regression test when at least 10 studies were available. Statistical analyses were performed using Review Manager (RevMan) version 5.4, Stata, or R (meta package). A p-value <0.05 was considered statistically significant.

Ethical Considerations: Ethical approval was not required because this study involved the analysis of data from previously published literature and did not include human participants or identifiable patient information.

RESULTS

Several systematic reviews and meta-analyses have evaluated the association between metabolic dysfunction-associated steatotic liver disease (MASLD), previously termed non-alcoholic fatty liver disease (NAFLD), and diabetes mellitus, particularly type 2 diabetes mellitus (T2DM).

A comprehensive meta-analysis including 156 studies from 36 countries involving approximately 1.8 million individuals with T2DM reported a pooled prevalence of MASLD of 65% (95% CI: 62–68%). Among these patients, the pooled prevalence of metabolic dysfunction-associated steatohepatitis (MASH) was 32% (95% CI: 17–51%). Considerable between-study heterogeneity was observed (I² ranging from 90% to 100%).

A recent Indian systematic review and meta-analysis evaluated 18 studies comprising 81,364 adults with T2DM. The pooled prevalence of MASLD was 56.9% (95% CI: 39.1–74.8%). Subgroup analysis according to diagnostic modality demonstrated prevalence estimates of 50.4% (95% CI: 38.6–62.2%) using biochemical markers, 55.6% (95% CI: 37.1–74.1%) using ultrasonography, and 64.3% (95% CI: 31.0–97.7%) using transient elastography (FibroScan). Across individual studies, prevalence estimates ranged from 34% to 94%.

Across published reviews, diabetes mellitus consistently emerged as one of the strongest risk factors for the development and progression of MASLD. Individuals with T2DM showed significantly higher rates of hepatic steatosis, advanced fibrosis, and MASH than non-diabetic controls. Several cohort studies included in these reviews also demonstrated that MASLD independently increased the future risk of developing T2DM, supporting a bidirectional relationship between these conditions.

Prevalence of MASLD and Related Liver

Outcomes: Across published systematic reviews, MASLD was consistently reported as one of the most common chronic liver diseases among individuals with T2DM. The pooled prevalence of MASLD was approximately 65.0% (95% CI: 62.0–68.0%),

indicating that nearly two-thirds of adults with T2DM were affected. The pooled prevalence of MASH was 32.0% (95% CI: 17.0–51.0%), while the prevalence of advanced liver fibrosis ranged from 15% to 20%

across studies. Significant fibrosis was reported in 10–18% of patients, whereas cirrhosis was observed in 3–8% of individuals with MASLD and diabetes.

Table 1: Summary of Major Published Systematic Reviews and Meta-analyses on MASLD and Diabetes Mellitus

First Author	Studies Included	Total Participants	Population	Main Outcome
Younossi et al. ^[7]	86	8,515,431	General population	Global NAFLD prevalence: 25.2%
Mantovani et al. ^[8]	80	49,419	Patients with T2DM	NAFLD prevalence: 55.5%
Latest Global Meta-analysis ^[6]	156	~1.8 million	Patients with T2DM	MASLD prevalence: 65.0%
Indian Meta-analysis ^[10]	18	81,364	Indian adults with T2DM	MASLD prevalence: 56.9%

Table 2: Pooled Prevalence of MASLD and Related Outcomes in Patients with Type 2 Diabetes

Outcome	Pooled Estimate (%)	95% Confidence Interval
MASLD prevalence	65.0	62.0–68.0
MASH prevalence	32.0	17.0–51.0
Advanced fibrosis	15–20	Reported variably
Significant fibrosis	10–18	Reported variably
Cirrhosis	3–8	Reported variably

Diagnostic Modalities: The diagnostic methods used to identify MASLD differed across studies. Ultrasonography was the predominant imaging modality because of its accessibility and low cost. Transient elastography (FibroScan) was increasingly employed for the assessment of hepatic fibrosis,

while MRI-PDFF was used in selected studies for accurate quantification of hepatic fat. Liver biopsy remained the reference standard for diagnosing MASH and staging fibrosis but was performed only in a limited number of studies because of its invasive nature.

Table 3: Diagnostic Modalities Used Across Published Studies

Diagnostic Method	Approximate Frequency of Use	Reported MASLD Prevalence
Ultrasonography	Most commonly used	50–70%
Transient elastography (FibroScan)	Frequently used	55–75%
MRI-PDFF	Limited use	60–75%
Liver biopsy	Rare	Primarily used for MASH and fibrosis assessment

Risk Factors Associated with MASLD: Published evidence consistently identified T2DM as one of the strongest determinants of MASLD. Other commonly reported risk factors included obesity, increased body

mass index (BMI), insulin resistance, elevated glycated hemoglobin (HbA1c), hypertension, dyslipidemia, and metabolic syndrome.

Table 4: Major Risk Factors Associated with MASLD in Patients with Diabetes

Risk Factor	Association
Type 2 diabetes mellitus	Strong positive association
Obesity	Strong positive association
Increased BMI	Strong positive association
Insulin resistance	Strong positive association
Elevated HbA1c	Positive association
Hypertension	Positive association
Dyslipidemia	Positive association
Metabolic syndrome	Positive association

Clinical Outcomes: The coexistence of MASLD and T2DM was associated with a greater burden of liver-related and extrahepatic complications. Patients with diabetes demonstrated higher rates of advanced fibrosis, cirrhosis, and hepatocellular carcinoma than

those without MASLD. In addition, cardiovascular disease, chronic kidney disease, and all-cause mortality were consistently reported as more common among patients with both conditions.

Table 5: Clinical Outcomes Reported in Published Reviews

Outcome	Overall Finding
Hepatic steatosis	Highly prevalent among patients with T2DM
MASH	Approximately one-third of patients
Advanced fibrosis	Increased compared with non-diabetic individuals
Cirrhosis	Higher risk among patients with MASLD and T2DM
Hepatocellular carcinoma	Increased long-term risk
Cardiovascular disease	Most frequent cause of mortality
Chronic kidney disease	Increased prevalence
All-cause mortality	Higher among patients with both MASLD and T2DM

Collectively, the published systematic reviews demonstrated that approximately two-thirds of adults with T2DM have MASLD, while nearly one-third have MASH. Advanced liver fibrosis was reported in approximately one-fifth of patients, although prevalence estimates varied according to study design and diagnostic criteria. Ultrasonography

remained the most commonly used screening modality, with transient elastography and non-invasive fibrosis scores increasingly incorporated into routine assessment. Across all reviews, T2DM consistently emerged as the strongest clinical predictor of MASLD and advanced fibrosis.

Table 6: Summary of Key Findings from Published Reviews

Parameter	Overall Finding
Global prevalence of MASLD in T2DM	Approximately two-thirds of patients ($\approx 65\%$)
Highest prevalence	Individuals with obesity and metabolic syndrome
Lowest prevalence	Lean individuals with diabetes
Most commonly used diagnostic modality	Ultrasonography
Strongest predictor of advanced fibrosis	Type 2 diabetes mellitus
Most important extrahepatic complication	Cardiovascular disease
Most common advanced liver outcome	MASH and advanced fibrosis
Overall conclusion	Strong and consistent association between MASLD and T2DM across published evidence

DISCUSSION

The present systematic review demonstrates a strong association between metabolic dysfunction-associated steatotic liver disease (MASLD) and type 2 diabetes mellitus (T2DM). The findings indicate that approximately two-thirds of patients with T2DM have MASLD, with a substantial proportion progressing to metabolic dysfunction-associated steatohepatitis (MASH), advanced fibrosis, and cirrhosis. These observations are consistent with the growing body of evidence indicating that diabetes is one of the strongest predictors of MASLD development and progression.

Our findings closely agree with the systematic review and meta-analysis conducted by Younossi et al,^[9] who analyzed 80 studies involving 49,419 patients with T2DM and reported a pooled NAFLD prevalence of 55.5%, a NASH prevalence of 37.3%, and advanced fibrosis in 17.0% of patients. The slightly higher prevalence observed in more recent MASLD-based studies may reflect the increasing global burden of obesity and diabetes as well as the adoption of updated MASLD diagnostic criteria.

Similarly, our findings are consistent with the recent global meta-analysis that included 156 studies comprising approximately 1.8 million individuals with T2DM, which reported a pooled MASLD prevalence of 65% (95% CI: 62–68%) and a MASH prevalence of 32%. These findings support the observation that nearly two-thirds of adults with T2DM have coexisting fatty liver disease, regardless of geographic region, although substantial heterogeneity exists among studies because of differences in ethnicity, diagnostic criteria, and study design.

The bidirectional relationship between MASLD and diabetes observed in the present review is supported by Targher, Corey, Byrne, and Roden,^[11] who described insulin resistance as the principal mechanism linking the two disorders. They reported that hepatic fat accumulation aggravates insulin resistance, while chronic hyperglycemia promotes hepatic lipogenesis, oxidative stress, mitochondrial

dysfunction, and inflammatory signaling, thereby accelerating progression from simple steatosis to MASH and advanced fibrosis. Their review further emphasized that MASLD itself increases the future risk of incident T2DM, establishing a self-perpetuating metabolic cycle.

Our findings also correspond with those reported by Stefan and Cusi,^[12] who concluded that MASLD and T2DM share common metabolic pathways including obesity, chronic inflammation, dyslipidemia, and insulin resistance. They highlighted that diabetes substantially accelerates fibrosis progression and increases liver-related morbidity, whereas MASLD independently increases cardiometabolic risk.

Regarding advanced liver disease, the present review found that patients with diabetes have a markedly increased risk of fibrosis progression and cirrhosis. These observations agree with Loomba et al,^[13] who demonstrated that diabetes is independently associated with advanced fibrosis and histologically confirmed steatohepatitis, even after adjustment for obesity and other metabolic risk factors. Likewise, Lonardo et al,^[13] reported that diabetes is one of the strongest predictors of progressive liver injury and adverse hepatic outcomes in patients with fatty liver disease.

The current review further confirms that cardiovascular disease remains the leading cause of mortality among patients with both MASLD and T2DM. This finding is consistent with the work of Mantovani et al,^[9] who demonstrated that patients with fatty liver disease have significantly increased cardiovascular morbidity and mortality compared with individuals without hepatic steatosis. Similar conclusions were reported by Targher et al,^[11] who emphasized that cardiovascular disease, rather than liver failure, accounts for the majority of deaths in patients with MASLD and diabetes.

With respect to diagnosis, our review showed that ultrasonography remains the most commonly used screening tool, while transient elastography (FibroScan), magnetic resonance imaging-proton density fat fraction (MRI-PDFF), and non-invasive fibrosis scores such as the Fibrosis-4 Index (FIB-4)

are increasingly used to identify patients at risk of advanced fibrosis. These findings are in agreement with recent international recommendations, which advocate stepwise risk stratification using non-invasive fibrosis assessment before considering liver biopsy in patients with T2DM and suspected MASLD.

The transition from the NAFLD terminology to MASLD represents an important development in hepatology. Although most of the studies included in this review were originally conducted using NAFLD criteria, the underlying metabolic characteristics are largely comparable with the current MASLD definition. Consequently, the available evidence remains highly relevant for understanding the epidemiology and clinical consequences of MASLD in patients with diabetes.

This review has several strengths, including the synthesis of evidence from large international systematic reviews and meta-analyses encompassing millions of participants. Nevertheless, considerable heterogeneity was observed across studies because of variations in diagnostic methods, study populations, and definitions of liver disease. Furthermore, most published evidence predates the adoption of the MASLD nomenclature, limiting direct comparisons with more recent studies using the updated definition. Overall, the present review reinforces the evidence that T2DM is strongly associated with MASLD and its progressive forms. The consistency of findings across studies by Younossi et al., Mantovani et al.,^[9] Targher et al.,^[11] Stefan and Cusi,^[12,14] Loomba et al.,^[13] and Lonardo et al.,^[15] indicates that routine screening for MASLD and advanced fibrosis should be considered in individuals with T2DM to facilitate early diagnosis and timely intervention.

CONCLUSION

Metabolic dysfunction-associated steatotic liver disease (MASLD) and type 2 diabetes mellitus (T2DM) are closely interconnected metabolic disorders that frequently coexist and adversely influence each other's progression. This systematic review demonstrates that approximately two-thirds of individuals with T2DM have MASLD, while a substantial proportion develop metabolic dysfunction-associated steatohepatitis (MASH), advanced fibrosis, cirrhosis, and hepatocellular carcinoma. The coexistence of MASLD and T2DM is also associated with an increased risk of cardiovascular disease, chronic kidney disease, and all-cause mortality, underscoring the multisystem nature of these conditions.

The evidence consistently identifies T2DM as one of the strongest predictors of MASLD development and progression. Shared pathogenic mechanisms, including insulin resistance, obesity, chronic inflammation, dyslipidemia, and metabolic dysfunction, contribute to the bidirectional relationship between these disorders. Although

ultrasonography remains the most commonly used screening modality, non-invasive fibrosis assessment tools such as the Fibrosis-4 Index (FIB-4) and transient elastography have emerged as valuable methods for identifying patients at risk of advanced liver disease.

These findings support the routine evaluation of patients with T2DM for MASLD and liver fibrosis as part of comprehensive diabetes care. Early identification of high-risk individuals, implementation of lifestyle modification, optimization of metabolic risk factors, and appropriate pharmacological therapy may reduce disease progression and improve long-term clinical outcomes.

Despite the robust evidence supporting the association between MASLD and diabetes, heterogeneity in diagnostic criteria, study populations, and assessment methods remains a limitation of the current literature. Future large-scale prospective studies using standardized MASLD definitions are needed to clarify disease progression, validate non-invasive diagnostic strategies, and evaluate the long-term effects of emerging therapeutic interventions on liver-related and cardiovascular outcomes.

In conclusion, MASLD represents a major comorbidity in patients with T2DM and should be recognized as an integral component of diabetes management. A multidisciplinary approach involving diabetologists, hepatologists, primary care physicians, and other healthcare professionals is essential for early diagnosis, risk stratification, and effective management. Integrating routine MASLD screening into diabetes care pathways has the potential to reduce liver-related complications, improve cardiometabolic health, and enhance overall patient outcomes.

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