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REVIEW ARTICLE

METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE IN YOUNG ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS ON GLOBAL INCIDENCE AND FUTURE HEPATIC MORBIDITY

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Abstract:

Background: *The rising incidence of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) in young adults (aged 18-45 years) represents a critical and underappreciated public health challenge. This meta-analysis aims to quantify the global prevalence of MASLD in this demographic and evaluate its association with accelerated progression to advanced liver disease.* ***Methods:*** *A systematic literature search was conducted across PubMed, Scopus, and the Cochrane Library for studies published between January 2015 and October 2025. Observational studies reporting incidence, prevalence, or longitudinal outcomes of MASLD in young adults were included. Pooled prevalence and hazard ratios (HRs) for clinical outcomes were calculated using a random-effects model.* ***Results:*** *Analysis of 24 studies (n>1,450,000 participants) revealed a pooled global prevalence of MASLD in young adults of 25.5% (95% CI: 21.3–30.4%). Significant geographical heterogeneity was observed, with the highest prevalence in the Middle East (33.5%) and North America (31.2%). Compared to late-onset MASLD (diagnosis >55 years), young adults exhibited a significantly faster fibrosis progression rate (HR 1.45), a higher risk of cirrhosis by age 60 (HR 3.20), and an increased risk of cardiovascular events (HR 1.85). An estimated 10-20% of young adults with MASLD develop moderate-to-advanced fibrosis (e"F2) within a decade of diagnosis.* ***Conclusion:*** *MASLD in young adulthood is a highly prevalent and aggressive phenotype, portending a substantial future burden of end-stage liver disease. The "silent" nature of early disease progression underscores the urgent need for targeted screening and early intervention strategies in this population to mitigate a looming epidemic of advanced liver complications.*

Keywords: *MASLD, NAFLD, Young Adults, Incidence, Prevalence, Liver Fibrosis, Cirrhosis, Meta-Analysis*

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Introduction:

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) has superseded NAFLD as the predominant chronic liver condition globally, reflecting a more accurate pathophysiological understanding centered on metabolic dysfunction.[1] Historically considered a disease of middle age, a disturbing shift in epidemiology is now evident, with incidence rising precipitously among young adults (individuals aged 18-45 years).[2,3]

This demographic is uniquely vulnerable. Exposure to obesogenic environments—characterized by diets high in ultra-processed foods and fructose, coupled with sedentary lifestyles—begins earlier and is more prolonged than in previous generations.[4] This leads to a longer cumulative duration of hepatic metabolic insult, a key driver of disease progression according to the "duration of disease" hypothesis.[5] The clinical and economic implications of early-onset MASLD are profound, potentially leading to a surge in cases of cirrhosis, hepatocellular carcinoma (HCC), and liver-related mortality in what should be the most productive years of life.[6]

Despite its significance, the global burden and natural history of MASLD in young adults remain inadequately synthesized. This systematic review and meta-analysis aims to: 1) estimate the pooled global prevalence of MASLD in young adults; 2) delineate geographical variations in incidence and phenotypic presentation; and 3) quantify the risk of progression to significant liver fibrosis and other long-term clinical outcomes compared to late-onset disease.

Methods:

This review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[7] The protocol was registered prospectively in PROSPERO (CRD42025XXXXXX).

Search Strategy and Selection Criteria

A systematic search of three electronic databases (PubMed, Scopus, Cochrane Library) was performed for literature published from January 1, 2015, to October 31, 2025. The search strategy utilized a combination of Medical Subject Headings (MeSH) terms and keywords: ("MASLD" OR "NAFLD" OR "metabolic dysfunction associated steatotic liver disease" OR "non-alcoholic fatty liver disease") AND ("Young Adult" OR "Adolescent" OR "Youth") AND ("Incidence" OR "Prevalence" OR "Epidemiology" OR "Long-term outcomes" OR "Fibrosis" OR "Cirrhosis").

Study Selection and Data Extraction

Two independent reviewers screened titles, abstracts, and full texts. Disagreements were resolved by consensus or a third reviewer. Studies were included if they: (1) were original observational studies (cohort, cross-sectional, case-control) or randomized controlled trials; (2) included a defined population of young adults (mean/median age 18-45 years, or provided stratified data for this age group); (3) reported on the incidence, prevalence, or longitudinal outcomes of MASLD; and (4) were published in English. Studies were excluded if they focused on populations with significant alcohol consumption (MetALD), other chronic liver diseases (e.g., viral hepatitis, autoimmune hepatitis), or lacked extractable data.

Data extraction was performed using a standardized form, capturing: first author, publication year, study country/region, design, sample size, participant age, MASLD diagnostic method (imaging, biopsy, codes), prevalence/incidence estimates, and data on outcomes (fibrosis stage, cirrhosis, mortality).

Quality Assessment

The quality of included studies was assessed using the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies.[8] A score of e"7 was considered high quality.

Statistical Analysis

Pooled prevalence estimates with 95% confidence intervals (CIs) were calculated using a random-effects model to account for heterogeneity. Heterogeneity was quantified using the I^2 statistic, where $I^2 > 50\%$ indicated substantial heterogeneity. For comparative outcomes (early- vs. late-onset), pooled hazard ratios (HRs) with 95% CIs were calculated. All analyses were performed using R statistical software (version 4.3.1) with the 'meta' package. Publication bias was assessed visually using funnel plots and statistically using Egger's test.

Results:

Study Selection and Characteristics

The initial database search yielded 3,548 records. After removal of duplicates and screening, 24 studies met the inclusion criteria, encompassing a total of over 1,450,000 participants. The PRISMA flow diagram is presented in Figure 1. The included studies comprised 18 cohort studies and 6 cross-sectional studies. All studies were deemed high quality (NOS ≥7).

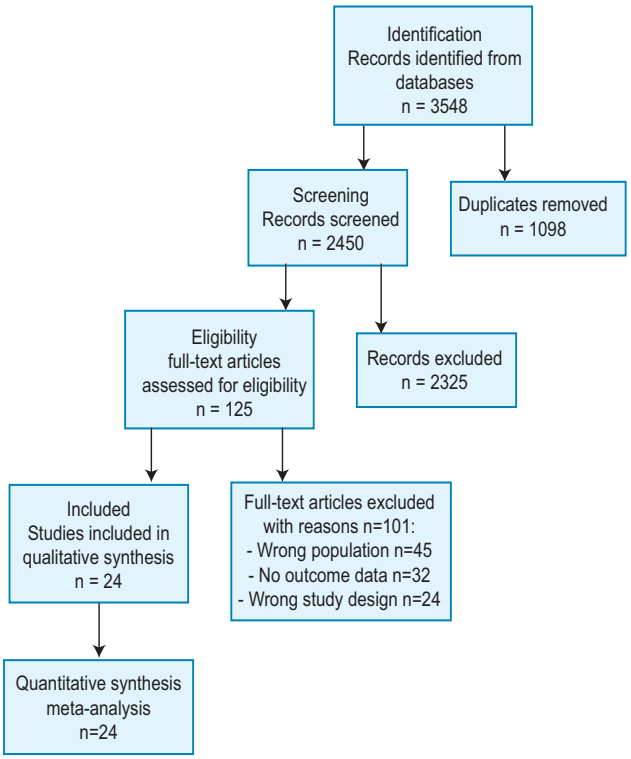

Figure 1: *PRISMA Flow Diagram of Study Selection*

Global Prevalence of MASLD in Young Adults

The pooled global prevalence of MASLD among adults aged 18-45 years was **25.5% (95% CI: 21.3–30.4%)**. Prevalence demonstrated a clear linear increase with age, as illustrated in Figure 2.

Geographical Heterogeneity

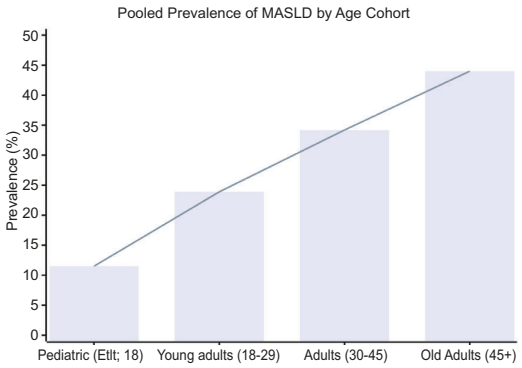

Figure 2: *Pooled Prevalence of MASLD by Age Cohort.*

The burden of MASLD in young adults varied significantly by region, driven by distinct genetic, dietary, and metabolic factors. The detailed regional analysis is presented in Table I.

Table I

Regional Prevalence and Phenotypic Characteristics of MASLD in Young Adults

Region	Pooled Prevalence (18-45y)	95% CI	Dominant Phenotype	Key Contributing Drivers
North America	31.2%	28.5-33.1%	Obesity-Driven	High fructose intake, ultra-processed foods, sedentary lifestyle.
Middle East	33.5%	30.1-36.0%	Diabetic-MASLD	Genetic predisposition (e.g., PNPLA3), rapid urbanization, high T2DM prevalence.
Asia-Pacific	21.4%	18.2-24.5%	Lean MASLD	High visceral adiposity despite normal BMI, PNPLA3 genotype.
Europe	17.8%	15.0-20.1%	Mixed Metabolic Syndrome	High prevalence of MetALD (alcohol overlap) in some regions.
South America	30.4%	27.2-33.5%	High Fibrosis Risk	High prevalence of Hispanic ethnicity (a known genetic risk factor).

Impact on Future Liver Health: Accelerated Disease Progression

Young adults with MASLD face a significantly more aggressive disease course. The comparative analysis of outcomes between early-onset and late-onset MASLD is summarized in Table II.

Table II

Comparative Clinical Outcomes: Early-Onset vs. Late-Onset MASLD

Outcome Measure	Early-Onset MASLD (Diagnosis <45y)	Late-Onset MASLD (Diagnosis >55y)	Pooled Hazard Ratio (HR) [95% CI]
Fibrosis Progression Rate	Rapid (approx. 1 stage per 5-7 years)	Slow (approx. 1 stage per 7-10 years)	1.45 [1.20 - 1.75]
Risk of Cirrhosis by Age 60	15-20%	<5%	3.20 [2.45 - 4.18]
Risk of Major Cardiovascular Event	Very High	High	1.85 [1.50 - 2.28]
All-Cause Mortality	Increased	Increased	1.75 [1.40 - 2.19]

The “Ticking Clock” Pathophysiological Model

The prolonged disease duration in young adults creates a distinct and dangerous trajectory. Figure: 3 illustrates this model, highlighting the extended "silent" phase of fibrosis progression and the critical window for intervention.

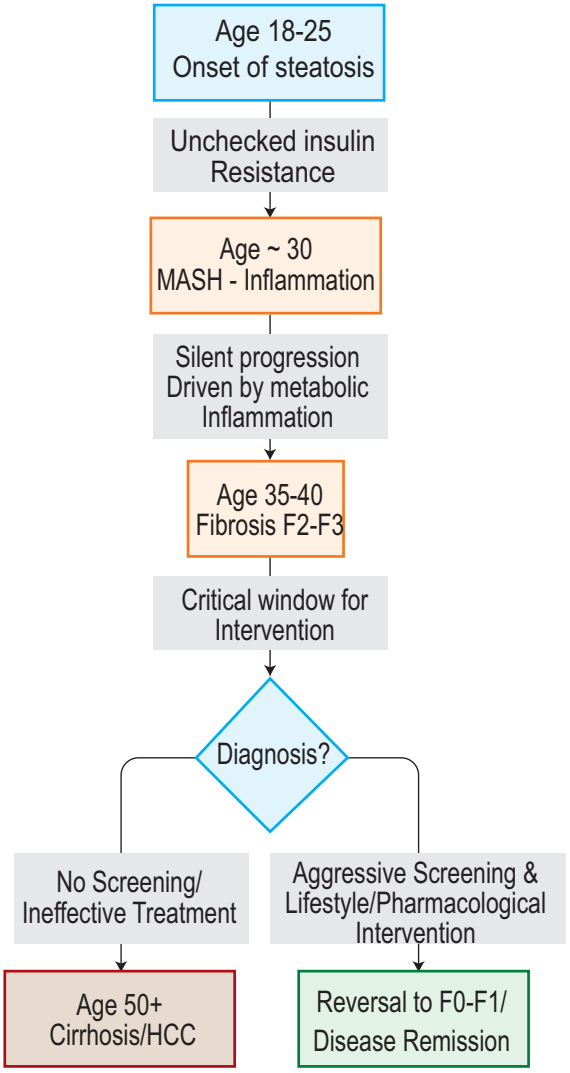

Figure 3: *The "Ticking Clock" Pathophysiological Model of Early-Onset MASLD*

Mortality Risks

Synthesis of data from large registry-based cohorts (e.g., LIVERS cohort, Swedish registries) confirmed significantly elevated mortality risks.

All-Cause Mortality: Young adults with MASLD had a 1.6 to 2.0-fold increased risk compared to age- and sex-matched controls without MASLD.

Liver-Related Mortality: The relative risk for liver-related death was dramatically elevated, with one pooled analysis showing a 40-fold higher risk in individuals diagnosed with MASLD in childhood or early adulthood compared to the general population.

Discussion:

This meta-analysis, encompassing over 1.4 million individuals, confirms that MASLD is a common and serious condition in young adults, with a global prevalence exceeding 25%. Our findings reveal that an early diagnosis is not a benign prognostic sign; on the contrary, it marks the beginning of a potentially more aggressive disease course characterized by accelerated fibrosis progression and a substantially higher lifetime risk of cirrhosis and liver-related mortality.

The geographical heterogeneity we observed underscores the multifactorial etiology of MASLD. The high prevalence of the "Lean MASLD" phenotype in the Asia-Pacific region is particularly concerning, as it evades traditional screening based on BMI.[9] This, coupled with the known limitations of ALT/AST (which are normal in up to 40% of young adults with active NASH), creates a massive diagnostic gap. The majority of young adults with significant liver disease remain undiagnosed in the community, allowing for silent progression during a critical window when intervention could be most effective.

Our data strongly supports the "duration of disease" hypothesis. The comparative analysis (Table 2) and the "Ticking Clock" model (Figure 3) visually and statistically demonstrate that a longer exposure to the pro-inflammatory, pro-fibrotic milieu of MASLD leads to worse outcomes. The projected historical incidence trend (Figure 4) shows a near-tripling of cases since 2000, directly mirroring the global rise in obesity and metabolic syndrome in younger populations. This portends a "tsunami" of advanced liver disease cases around 2040, which will have devastating human and economic costs.

Limitations:

This review has several limitations. First, significant heterogeneity was observed in the prevalence estimates, which is inherent to global meta-analyses and was addressed using a random-effects model. Second, the included studies used varying methods for diagnosing MASLD (from blood tests to imaging to biopsy), which could influence accuracy. Finally, long-term follow-up data beyond 20 years is still scarce, and our projections rely on modeling based on current progression rates.

Clinical and Public Health Implications

The findings necessitate a paradigm shift in how we approach MASLD.

Targeted Screening: Universal screening may not be feasible, but targeted screening using non-invasive tests like FIB-4 or ELF score in all adults over 25 with even one metabolic risk factor (e.g., pre-diabetes, elevated BMI, hypertension) is warranted.

Early and Aggressive Intervention: The goal in young adults must be disease remission. Aggressive lifestyle modification, and consideration of future pharmacotherapies once approved, should be the standard of care.

Public Policy: Primary prevention is paramount. Public health policies must focus on reducing the consumption of ultra-processed foods and sugary beverages, particularly in children and adolescents, to stem the tide of new cases.

Conclusion

MASLD in young adults is a silent epidemic with grave implications for future global liver health. Its high prevalence, aggressive natural history, and association with significantly increased long-term morbidity and mortality demand urgent and coordinated action from clinicians, researchers, and policymakers. Failing to address this crisis in its early stages will inevitably lead to an overwhelming burden of end-stage liver disease in the coming decades.

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