AMERICAN JOURNAL OF APPLIED MEDICAL SCIENCE
ISSN: 2996-5101 (online) | ResearchBib (IF) = 10.81 IMPACT FACTOR
Volume-3| Issue-11| 2025 Published: |30-12-2025|

METABOLIC DYSFUNCTION–ASSOCIATED FATTY LIVER DISEASE: PATHOGENESIS, CLINICAL SPECTRUM, AND CURRENT MANAGEMENT APPROACHES

https://doi.org/10.5281/zenodo.18069592

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Abstract

Metabolic dysfunction–associated fatty liver disease (MAFLD) is a highly prevalent chronic liver disorder worldwide and is closely associated with metabolic abnormalities such as obesity, insulin resistance, and type 2 diabetes mellitus. Despite its growing global burden, no definitive curative therapy has been established. MAFLD exhibits a heterogeneous pathogenesis, resulting in a wide spectrum of clinical outcomes ranging from simple steatosis to advanced fibrosis, cirrhosis, and hepatocellular carcinoma. The recent shift in disease nomenclature emphasizes the central role of metabolic dysfunction and improves patient stratification in both clinical practice and research. Currently, lifestyle modification remains the cornerstone of management, while pharmacological therapies are under active investigation with limited efficacy. A deeper understanding of disease mechanisms is essential for the development of effective and targeted therapeutic strategies.

Keywords

Metabolic dysfunction–associated fatty liver disease (MAFLD), metabolic dysfunction, insulin resistance, obesity, liver fibrosis, lifestyle intervention.

Introduction

Metabolic dysfunction–associated fatty liver disease (MAFLD) has emerged as one of the most common chronic liver conditions worldwide and represents a major global health concern. The increasing prevalence of obesity, type 2 diabetes mellitus, insulin resistance, dyslipidemia, and other components of metabolic syndrome has contributed significantly to the rising incidence of this disease. MAFLD is now recognized as the leading cause of chronic liver disease in many regions, affecting a substantial proportion of the adult population.

MAFLD encompasses a broad clinical spectrum, ranging from simple hepatic steatosis to progressive inflammatory liver injury, fibrosis, cirrhosis, and

hepatocellular carcinoma. Disease progression is highly variable and depends on a complex interaction between metabolic, genetic, inflammatory, and environmental factors. This heterogeneity complicates disease prediction, patient stratification, and therapeutic decision-making.

The transition from the term nonalcoholic fatty liver disease (NAFLD) to MAFLD reflects an improved understanding of disease pathogenesis. The MAFLD concept highlights metabolic dysfunction as the primary driver of liver injury and allows for more accurate identification of patients at increased risk of adverse outcomes. Despite advances in disease recognition, effective pharmacological treatments remain limited, and lifestyle-based interventions continue to be the mainstay of management. This review summarizes current knowledge on the pathogenesis, clinical spectrum, and management strategies of MAFLD.

Pathogenesis of MAFLD

The pathogenesis of MAFLD is complex and multifactorial. Insulin resistance plays a central role by promoting increased lipolysis in adipose tissue, enhanced hepatic uptake of free fatty acids, and de novo lipogenesis within hepatocytes. These metabolic alterations lead to excessive lipid accumulation in the liver, resulting in hepatic steatosis.

In addition to metabolic dysregulation, chronic low-grade inflammation contributes significantly to disease progression. Adipose tissue dysfunction leads to the release of proinflammatory cytokines, such as tumor necrosis factor-α and interleukin-6, which exacerbate hepatic inflammation and insulin resistance. Oxidative stress, mitochondrial dysfunction, and endoplasmic reticulum stress further promote hepatocellular injury and fibrosis.

Genetic and epigenetic factors also influence susceptibility to MAFLD and disease severity. Variants in genes involved in lipid metabolism and inflammation have been associated with increased risk of disease progression. Environmental factors, including dietary patterns and physical inactivity, further modulate disease expression.

Clinical Spectrum and Natural History

MAFLD presents with a wide range of clinical manifestations. Many patients remain asymptomatic and are diagnosed incidentally through imaging or abnormal liver function tests. Simple steatosis is generally considered a relatively benign condition; however, a significant proportion of patients progress to more severe forms of liver disease.

Metabolic dysfunction–associated steatohepatitis is characterized by hepatic inflammation and hepatocyte injury and represents a key step in disease progression. Persistent inflammation may lead to fibrosis, which is the strongest

predictor of long-term outcomes. Advanced fibrosis and cirrhosis are associated with increased risks of liver-related morbidity, mortality, and hepatocellular carcinoma.

Importantly, MAFLD is also associated with increased cardiovascular risk, which represents the leading cause of death in affected patients. Therefore, comprehensive management should address both hepatic and extrahepatic complications.

Diagnosis and Patient Stratification

The diagnosis of MAFLD is based on evidence of hepatic steatosis in the presence of metabolic dysfunction. Noninvasive imaging techniques, such as ultrasound, transient elastography, and magnetic resonance imaging, are commonly used for disease detection and staging. Serum biomarkers and scoring systems aid in the assessment of fibrosis risk and disease severity.

The MAFLD diagnostic framework allows for improved patient stratification by recognizing the coexistence of liver disease with metabolic comorbidities. This approach facilitates earlier identification of high-risk individuals and supports more personalized management strategies.

Lifestyle Modification

Lifestyle intervention remains the cornerstone of MAFLD management. Weight loss through caloric restriction and increased physical activity has been shown to reduce hepatic steatosis and improve metabolic parameters. Even modest weight reduction can lead to meaningful improvements in liver histology.

Pharmacological Therapies

Currently, no pharmacological agent has been approved specifically for the treatment of MAFLD. Several drugs targeting insulin resistance, lipid metabolism, inflammation, and fibrosis are under investigation. While some agents demonstrate beneficial effects on liver enzymes and histological features, therapeutic responses remain variable and often modest.

Management of Comorbidities

Effective control of metabolic comorbidities, including diabetes, hypertension, and dyslipidemia, is essential in patients with MAFLD. A multidisciplinary approach involving hepatologists, endocrinologists, and primary care physicians is recommended to optimize patient outcomes.

Future Perspectives

Advances in understanding the molecular mechanisms underlying MAFLD may enable the development of more effective and targeted therapies. Improved disease phenotyping and biomarker discovery are expected to enhance patient

stratification and treatment selection. Ongoing clinical trials will provide further insights into novel therapeutic approaches.

Conclusion

Metabolic dysfunction–associated fatty liver disease is a prevalent and heterogeneous condition driven primarily by metabolic abnormalities. Despite its increasing global impact, effective curative therapies remain unavailable, and lifestyle modification continues to be the foundation of management. The adoption of the MAFLD nomenclature represents a significant step toward improved disease recognition and patient stratification. Continued research into disease mechanisms and therapeutic targets is essential to address the growing burden of MAFLD and improve long-term patient outcomes.

REFERENCES:

1. Eslam M, Newsome PN, Sarin SK, et al. A new definition for metabolic dysfunction–associated fatty liver disease: An international expert consensus statement. J Hepatol. 2020;73(1):202–209.
2. Eslam M, Sanyal AJ, George J; International Consensus Panel. MAFLD: A consensus-driven proposed nomenclature for metabolic associated fatty liver disease. Gastroenterology. 2020;158(7):1999–2014.e1.
3. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease—Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016;64(1):73–84.
4. Younossi ZM, Golabi P, de Avila L, et al. The global epidemiology of NAFLD and NASH in patients with type 2 diabetes: A systematic review and meta-analysis. J Hepatol. 2019;71(4):793–801.
5. Rinella ME. Nonalcoholic fatty liver disease: A systematic review. JAMA. 2015;313(22):2263–2273.
6. Friedman SL, Neuschwander-Tetri BA, Rinella M, Sanyal AJ. Mechanisms of NAFLD development and therapeutic strategies. Nat Med. 2018;24(7):908–922.
7. Tilg H, Moschen AR, Roden M. NAFLD and diabetes mellitus. Nat Rev Gastroenterol Hepatol. 2017;14(1):32–42.
8. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the AASLD. Hepatology. 2018;67(1):328–357.
9. Byrne CD, Targher G. NAFLD: A multisystem disease. J Hepatol. 2015;62(1 Suppl):S47–S64.

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10. Loomba R, Friedman SL, Shulman GI. Mechanisms and disease consequences of nonalcoholic fatty liver disease. Cell. 2021;184(10):2537–2564.