REVIEW ARTICLE

Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD): A Narrative Review

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Abstract

Metabolic dysfunction associated steatotic liver disease (MASLD), formerly known as NAFLD (Non-alcoholic fatty liver disease), is an emerging prevalent disease affecting millions of people worldwide. The article aims to provide a comprehensive review of epidemiology, pathophysiology, diagnostic workups, evolving management options, and outcomes. Primarily factored by insulin resistance, the disease inflammation is affected later by oxidative stress. Patients often have concomitant morbidities such as diabetes, hypertension, obstructive sleep apnea, and obesity, although MASLD itself can be asymptomatic. Liver enzymes, particularly alanine transaminases (ALT), are elevated, along with some blood markers. Diagnostic evaluation includes ultrasound imaging, non-invasive biomarkers, fibroscan, and liver biopsy. To forecast a poor prognosis, fibrosis risk stratification is necessary. The gold standard diagnostic test is liver biopsy, which is limited in use due to invasiveness. The key treatment of MASLD is weight loss by diet and exercise, which are added with limiting alcohol and regular exercise. Therapeutic interventions are yet to be established, although few medications have a narrow spectrum of action. Obese patients may undergo bariatric surgery if the criteria are matched. All the cardiometabolic risk factors should be optimized with proper interventions. Affected individuals should be monitored at regular intervals to assess any changes toward hepatic cirrhosis and carcinoma. To sum up, increasing public awareness and the scopes of scientific research are essential to combat the emerging epidemic.

Keywords: MASLD, MAFLD, NAFLD, MASH, NASH, steatohepatitis, fibrosis, type 2 diabetes

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Introduction:

Metabolic dysfunction-associated steatotic liver disease (MASLD) has emerged as the leading cause of chronic liver disease worldwide and its prevalence has been dramatically increasing affecting more than a third of the adult population. The presence of MASLD is strongly associated with type 2 diabetes, obesity and other cardiometabolic risk factors.[1]

MASLD is the new terminology proposed in 2023 by three multinational liver associations to replace the old term 'non-alcoholic fatty liver disease' (NAFLD).[2] This terminology is non-stigmatizing, accurately describes the pathophysiology highlighting the concept of metabolic dysfunction and acknowledges the overlapping disease mechanisms. Moreover, the revised nomenclature selected an overarching term of steatotic liver disease (SLD) to parse out MASLD from other causes of steatosis. Emerging research reveals that NAFLD and MASLD definitions are highly concordant, with more than 96% of NAFLD patients meeting MASLD criteria; thus, both categories can be used interchangeably.[3]

MASLD includes a spectrum of progressive steatotic liver conditions, ranging from isolated hepatic steatosis to metabolic dysfunction-associated steatohepatitis (MASH) with varying degrees of liver fibrosis, which may progress to cirrhosis.[4] MASLD is also associated with an increased risk of developing cardiovascular disease (CVD), chronic kidney disease (CKD), and certain types of extrahepatic cancers.[5]

Prevalence

MASLD affects nearly 30% of the general population, with a higher prevalence in males compared with females (40% versus 26%).[6] The prevalence of MASLD varies significantly among countries, with 31.2% in North America,

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28.0% in the Asia Pacific regions and 33.8% in South Asia.[1] 1 A study conducted in India found that MASLD is more common in urban areas (16–32%) compared to rural areas (9%).[7] In Bangladesh, MASLD was identified in 18.5% of cases on an ultrasound-based study. Among them it was detected in 36.93% of obese and 7.1% of non-obese persons.[8]

Natural history of disease progression

Fibrosis and the presence of steatohepatitis are the strongest predictors of disease progression. Studies found that those with MASH progressed through one stage of MASLD fibrosis every 7 years, compared to 14 years for those with simple steatosis.[9]

Table I

Revised Nomenclature of MASLD and Related Entities[2]

Revised Nomenclature	Definition
Steatotic liver disease (SLD)	Umbrella term to describe steatosis, diagnosed histopathologically or by imaging, due to different causes
Metabolic dysfunction– associated steatotic liver disease (MASLD)	Steatotic liver disease with the presence of one or more adult or pediatric-specific cardiometabolic risk factors & the exclusion of other causes of hepatic steatosis
MASLD and increased alcohol intake (MetALD) or combination etiology	SLD with one or more cardiometabolic risk factors with the coexistence of other conditions like increased alcohol intake (average daily intake of >20–50 and >30–60 g in females and males, respectively) or other causes of steatosis (drugs, Wilson's disease, inborn errors of metabolism, etc.)

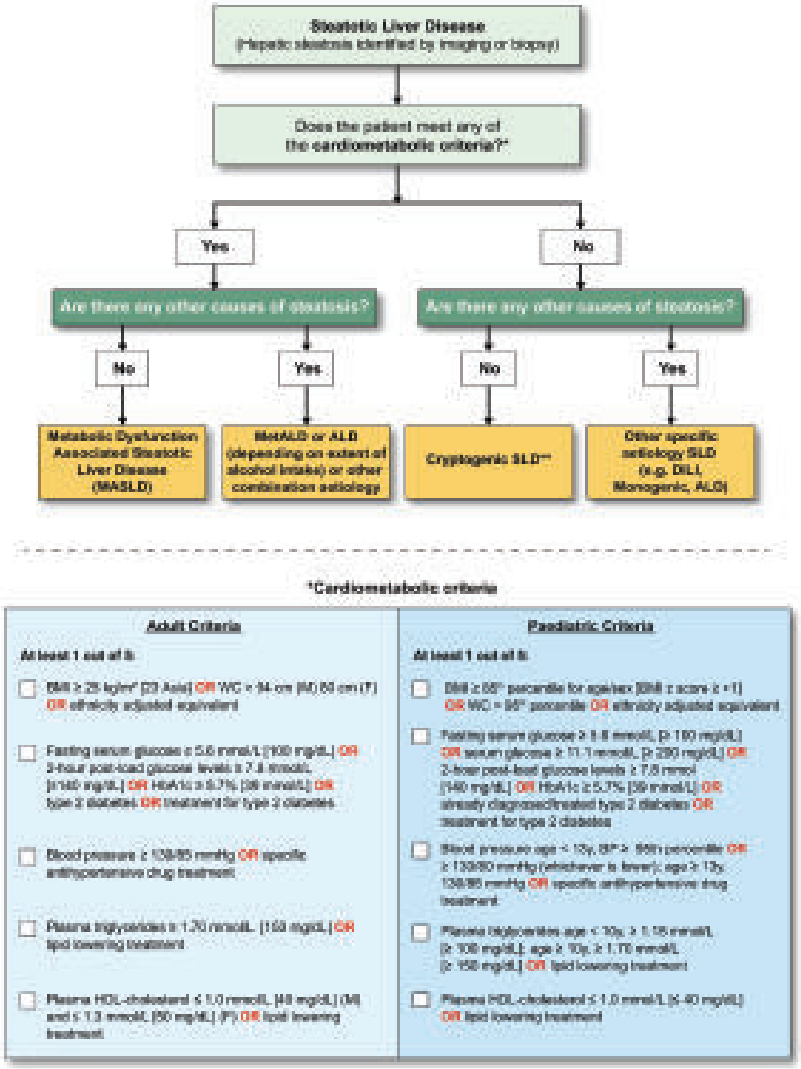

Figure 1: *MASLD diagnostic criteria*[2]

Pathogenesis:

The pathophysiology of MASLD is complex and multifactorial. The most widely supported "two-hit" theory implicates insulin resistance as the ''first hit'' leading to hepatic steatosis. The "second hit" is inflammation brought on by gut-derived endotoxins, oxidative stress, and mitochondrial dysfunction.

Insulin resistance

Primary pathophysiologic abnormality is insulin resistance, leading to an increase in lipolysis, hepatic uptake of free fatty acids (FFA), and accumulation of hepatic triglyceride. Hepatic steatosis, which is characterized by the buildup of fat in the liver, is exacerbated by such excessive triglyceride synthesis.[10]

Oxidative stress

Overproduction of reactive oxygen species (ROS) due to elevated fatty acids in the liver causes oxidative stress, which in turn triggers inflammation and hepatocyte destruction. Liver damage is exacerbated by the vicious cycle created by the interaction of oxidative stress and lipid buildup.[11]

Gut Microbiota Dysbiosis

Emerging research suggests that alterations in gut microbiota can influence MASLD development by affecting metabolic functions and promoting inflammation.[12]

MASLD in lean individuals

Although MASLD is commonly associated with obesity, it can also occur in non-overweight (BMI <25 kg/m^2) patients, with the highest prevalence in Asia (19%).[13] Compared with healthy controls, lean subjects with MASLD have increased insulin resistance, metabolic comorbidities and visceral adiposity. Genetic predisposition, sedentary lifestyle and alterations in the gut microbiome may also contribute to this group.[14]

Diagnostic evaluation

Diagnosis of MASLD is predicated on the presence of hepatic steatosis along with cardiometabolic risk factors and the exclusion of other liver diseases. The majority of patients are usually asymptomatic; however, some may present with fatigue, right upper abdominal discomfort, hepatomegaly and acanthosis nigricans. Stigmata of chronic liver disease are rarely seen until hepatic decompensation occur.[15] Most often, changes in liver enzymes or a pattern of steatosis in the liver seen during imaging for another reason lead to an incidental diagnosis of MASLD.

Targeted screening for MASLD and advanced fibrosis is recommended in the following high-risk groups:[16,17]

- Obesity and/or features of metabolic syndrome
- Type 2 DM (T2DM), prediabetes
- MASLD with moderate alcohol use
- First-degree relative of a patient with cirrhosis due to MASLD/MASH
- Persistently elevated transaminases over six months

The approach to a patient with suspected/confirmed MASLD should be two-pronged:

- Comprehensive evaluation of associated comorbidities and complications
- Assessment of the risk of fibrosis

Table II

Initial Evaluation in Patients with Suspected/Confirmed MASLD.

History	• Comorbidities: diabetes, hypertension, overweight/obesity, obstructive sleep apnea, cardiovascular disease
	• Liver-specific history: evidence of decompensation, portal hypertension
	• Medications• Any alcohol history
Examination	• Blood pressure measurement
	• Features of insulin resistance: acanthosis nigricans
	• Features of chronic liver disease: jaundice, ascites, splenomegaly, gynecomastia, palmar erythema, spider angioma, etc.
Laboratory	• Liver function tests
	• Complete blood count
	• Oral glucose tolerance test, HbA1c
	• Fasting lipid profile
	• Creatinine
	• Urine albumin creatinine ratio• Hepatitis-C
	• Investigations for other causes of steatohepatitis if clinical suspicion
	• Malignancy screening

Laboratory findings:

In MASLD, alanine transaminase (ALT) and aspartate transaminase (AST) level may be either normal or elevated commonly. ALT levels tend to be higher in MASH than in simple steatosis. However, the degree of aminotransferase elevation does not predict the degree of liver inflammation or fibrosis.[18] In addition, alkaline phosphatase (ALP) and glutamyl-transpeptidase (GGT) may be increased by 2 to 3-fold.

In patients with MÁSLD, elevated serum ferritin greater than 1.5 times has been associated with increased risk of ¾tåàtïhåðàtitis, whereas transferrin saturation is elevated in fewer cases.[19]

Imaging in MASLD

Ultrasound

Because of its low cost, safety, and accessibility, ultrasound (USG) is most common imaging technique used in clinical practice. Ultrasonography often reveals a bright liver echotexture with blurring of hepatic vasculature because of diffuse fatty infiltration. The sensitivity and specificity of USG are respectively 85% and 94% in detecting moderate to severe steatosis but, the sensitivity is decreased in patients with obesity.[20] However, it has limitations in accurately quantifying hepatic fat content and differentiating between simple steatosis and steatohepatitis.[21]

CT, MRI

These imaging modalities can detect steatosis but are less sensitive to detect dynamic changes in liver. Magnetic resonance spectroscopy (MRS) & MRI proton density fat fraction (MRI-PDFF) have higher sensitivity and considered gold standard to quantify hepatic fat, but only used in clinical trials rather than in routine practice.[22]

Transient elastography

Vibration-controlled transient elastography (VTCE), known as Fibroscan is a non-invasive method used to assess liver fibrosis by measuring liver stiffness. It is also possible to estimate hepatic steatosis by controlled attenuation parameter measurement at the same time. A liver stiffness cutoff of 6·5–7·9 kPa has approximately 90% sensitivity in excluding stage 3 and 4 fibrosis, whereas patients with cirrhosis typically have liver stiffness more than 12–15 kPa.[23]

Noninvasive biomarkers

Noninvasive tools to predict advanced fibrosis are NAFLD fibrosis score (NFS), Fibrosis-4 (FIB-4) index, AST to platelet ratio index (APRI), serum biomarkers like enhanced liver fibrosis (ELF) panel, hepascore etc. However, FIB-4 index (based on platelet count, age, AST, and ALT) is the most validated. Although the accuracy is modest, these scores have good negative predictive values to exclude advanced fibrosis.[21]

Role of liver biopsy in diagnosis

Liver biopsy is considered as gold standard for the diagnosis. However, it is an invasive procedure and its utility is currently limited to patients with competing etiologies for hepatic steatosis, discordant results on non-invasive tests, and as an endpoint in clinical trials. Characteristic features of steatohepatitis include lobular inflammation and ballooning of hepatocytes with or without fibrosis. The NASH CRN system is widely used for fibrosis staging.[7]

Fibrosis risk stratification

FIB-4 index facilitates primary risk assessment for fibrosis in primary care settings. Significant fibrosis is successfully ruled out by FIB-4 < 1.3, and patients can be monitored on a regular basis in the primary care context. Vibration-controlled transient elastography (VCTE) or an enhanced liver fibrosis (ELF) panel can be used for a secondary risk assessment in patients with an uncertain (1.3–2.67) or elevated (>2.67) FIB-4 index.[16]

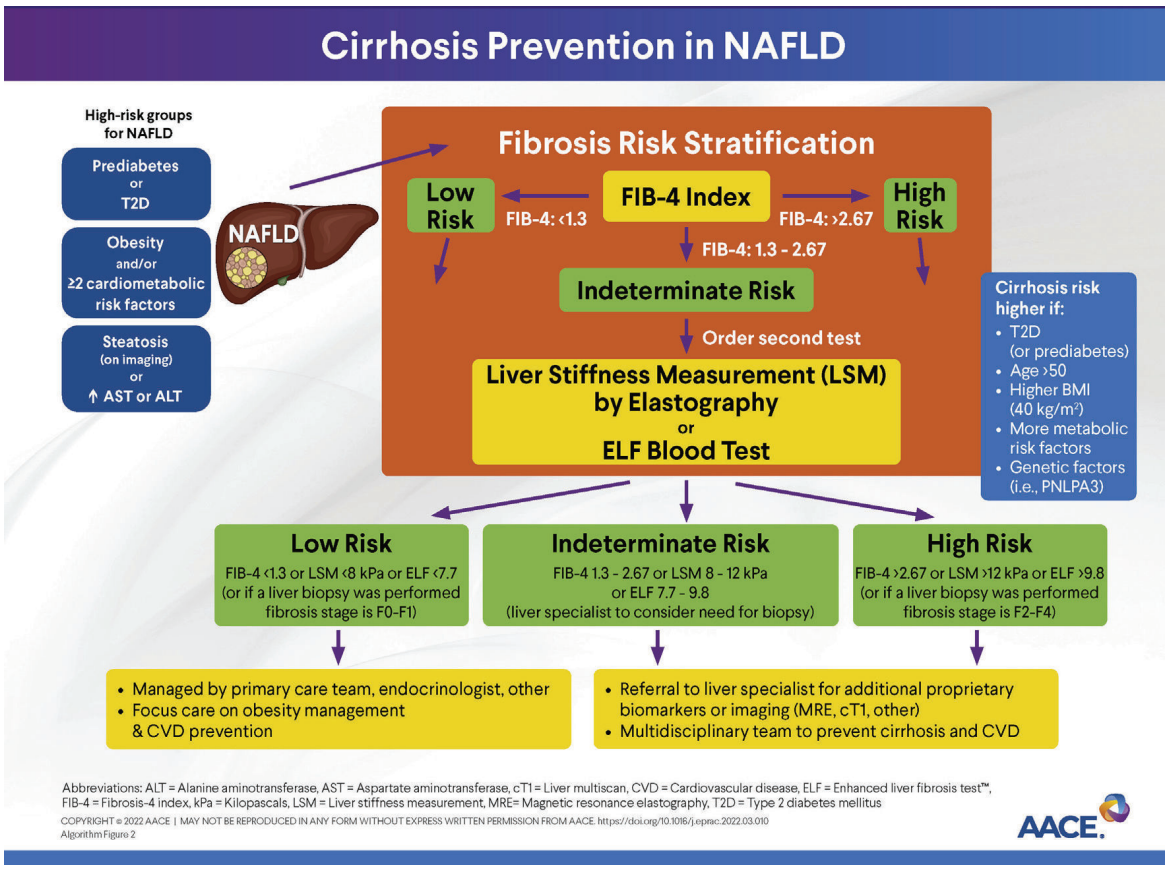

Figure 2: Algorithm for fibrosis risk stratification[16]

Management:

A multidisciplinary holistic approach is needed to reduce the morbidity and mortality associated with the condition, that includes the following:

- Lifestyle education and intervention
- Liver-directed therapies for MASLD
- Assessment and optimization of cardiometabolic risk factors

Lifestyle Interventions for MASLD

Life style modification and weight loss remains the cornerstone of the management of MASLD. There is a dose-response relationship between weight reduction and histological improvement in MASLD. Patients who are overweight or obese and have MASLD should be encouraged to lose at least 7–10% of their body weight. Steatosis can be improved with even mild weight reduction of 3-5%, but MASH and fibrosis can only be improved with weight loss of >10%.[24]

Dietary Interventions

Weight loss achieved through caloric deficit of 500-1,000 kcal/day is effective in reducing hepatic steatosis, irrespective of the specific dietary approach. Caloric restriction is the priority with reduction of saturated fat, starch and added sugars. Several recent studies have shown the value of a Mediterranean diet (low in carbohydrates and saturated fat but higher in monosaturated fat) as it effectively reduces hepatic fat content in addition to cardiovascular benefits.[25]

Exercise

Exercise, independent of weight loss, has hepatic and cardiometabolic benefit and should be routinely recommended and tailored to the patient's preferences and physical abilities.[16] Studies have shown that 30 to 60 minutes of moderate to high-intensity aerobic exercise performed 2–5 days per week, results in a significant reduction in liver fat content.[26]

Alcohol

In patients with obesity and diabetes, synergistic effects of insulin resistance and alcohol increase the risk of fibrosis progression, especially with moderate to heavy alcohol use (>20 g/day in women and >30 g/day in men). Hence, alcohol abstinence should be recommended in these patients, especially with clinically significant fibrosis (≥F2).[17]

Pharmacotherapy in MASLD

The therapeutic landscape in MASLD is rapidly evolving and although several agents have undergone clinical trials, there is currently no FDA-approved drug for management of MASLD.

Anti-diabetic agents in MASLD

Patients with diabetes comprise a particularly high-risk group, with reported prevalence of MASLD and MASH being as high as 55–70% and 30–40%, respectively. On the other hand, nearly half of MASLD patients are diabetic.[27] Due to the close bidirectional relationship, various antidiabetic agents can serve the dual purpose of addressing hyperglycemia as well as MASLD.

Thiazolidinediones

Pioglitazone, a PPARã agonist, improves histology and insulin resistance in MASLD. Studies demonstrated that pioglitazone was better than placebo in achieving MASH resolution as well as fibrosis improvement.[28] Potential side effects include weight gain, osteoporosis and risk for worsening heart failure in those with preexisting cardiac dysfunction.

GLP-1 receptor agonists (GLP-1RAs)

GLP-1RAs comprise another class of agents that have changed the landscape of diabetes and obesity. In a small study of patients with NASH, liraglutide improved steatosis and reduced fibrosis progression compared with placebo.[29] Semaglutide was reported to improve MASH resolution to a similar degree in people with or without type 2 diabetes.[30] Tirzepatide, a novel dual agonist at GLP-1 and GIP receptors demonstrates weight loss and reduction in liver fat content of 8.1%, suggesting a possible benefit in MASH.[17]

SGLT-2 inhibitors (SGLT-2i)

In addition to the management of hyperglycemia, SGLT-2 inhibitors induce 2%–3% weight loss and have cardiorenal protective benefits. SGLT-2 inhibitors may be considered as adjunctive pharmacotherapy for MASLD as they reduce hepatic steatosis by 10-39%.[31] However, their therapeutic impact on hepatic fibrosis requires further studies.

Non-diabetic agents in MASLD

Vitamin E

Vitamin E is a strong antioxidant that has been demonstrated to reduce transaminases, steatosis, and inflammation in non-diabetic patients with MASH at doses of 800 IU/day, while having no effect on fibrosis.[32] Vitamin E treatment leads to a drop in serum ALT to ≤40 U/L and ≥30% of baseline values, resulting in improved histological parameters.[33]

Saroglitazar (Dual PPAR á/ã agonist)

Recently, Saroglitazar, a dual potent PPAR-á/ã agonist has been recommended to use in MASH with F1–F3 fibrosis and in MASLD with comorbidities (obesity, T2DM, dyslipidemia).[34]

Upcoming disease-modifying drugs

Newer drugs that modify the disease pathogenesis are in the pipeline for phase 3 trials in patients with MASH. Examples include obetacholic acid, lanifibranor, aramchol, resmetirom, aldafermin, pegbelfermin.[7]

Bariatric Surgery

In addition to sustained weight loss, bariatric surgery significantly reduces the risk of fibrosis progression in obese patients. Hence, bariatric surgery should be considered as an option to treat MASLD patients with a BMI ≥35 kg/m^2 (≥32.5 kg/m^2 in the Asian population), especially with coexisting T2DM.[16]

However, new or worsening features of MASLD, like fibrosis was reported in 12% of cases after surgery. Caution has to be exercised in patients with advanced fibrosis and cirrhosis due to risk of hepatic decompensation and mortality.[35]

Optimization of Management of Comorbidities:

Metabolic risk factors modification is an essential part of comprehensive management to improve long term outcome**.** Statins are safe for CVD risk reduction across the spectrum of MASLD, except in decompensated cirrhosis. For the management of hypertriglyceridemia, omega-3 fatty acids, icosapent ethyl, or fibrates can be helpful. ACE inhibitors/ARBs are preferred first-line agents to optimize hypertension; but has to be avoided in decompensated cirrhosis.[16]

Monitoring progress and response to treatment

- Patients without fibrosis can be monitored every 2 or 3 years, in the absence of worsening of metabolic risk
- Patients with fibrosis should be monitored annually
- Patients with cirrhosis should undergo monitoring at 6-month intervals including screening for hepatocellular carcinoma.[7]

Mortality

In individuals with MASLD who do not have severe fibrosis, cardiovascular disease and nonhepatic malignancies are the leading causes of death; whereas liver-related mortality predominates in patients with advanced fibrosis. Therefore, screening for hepatocellular carcinoma (HCC) is recommended for patients with MASH -related cirrhosis.[17]

Conclusion:

MASLD is a growing epidemic creating an increasing health burden, but still the awareness remains low among patients and clinicians regarding multidisciplinary approach. There is an increasing need to develop simplified clinical algorithms for early diagnosis and management. Identification and early treatment of comorbid conditions like diabetes, dyslipidemia and cardiovascular diseases can significantly improve the prognosis. Currently lifestyle modifications with weight loss are the only effective treatment for MASLD. However, it can be anticipated that novel pharmacological agents will become available soon and transform the current MASH management into a more comprehensive strategy.

References:

1. Miao L, Targher G, Byrne CD, Cao YY, Zheng MH. Current status and future trends of the global burden of MASLD. Trends Endocrinol Metab. 2024;35(8):697-707.
2. Rinella ME, Lazarus JV, Ratziu V, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Hepatology. 2023;78(6):1966-1986.
3. Hagström H, Vessby J, Ekstedt M, Shang Y. 99% of patients with NAFLD meet MASLD criteria and natural history is therefore identical. J Hepatol. 2024;80(2):e76-e77.
4. Kaya, E. and Yilmaz, Y. (2022) Metabolic-associated fatty liver disease (MAFLD): a multi-systemic disease beyond the liver. J. Clin. Transl. Hepatol. 10, 329–338.
5. Rosato V, Masarone M, Dallio M, Federico A, Aglitti A, Persico M. NAFLD and Extra-Hepatic Comorbidities: Current Evidence on a Multi-Organ Metabolic Syndrome. Int J Environ Res Public Health. 2019;16(18):3415.
6. Riazi K, Azhari H, Charette JH, et al. The prevalence and incidence of NAFLD worldwide: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol 2022; 7:851.
7. Eslam M, Sarin SK, Wong VW et al. The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic-associated fatty liver disease Hepatol Int. 2020;14:889-919.
8. Rahman MM, Kibria MG, Begum H, et al. Prevalence, risk factors and metabolic profile of the non-obese and obese non-alcoholic fatty liver disease in a rural community of South Asia. BMJ Open Gastro 2020;7(1):e000535.
9. Dulai PS, Singh S, Patel J, Soni M, Prokop LJ, Younossi Z, et al. Increased risk of mortality by fibrosis stage in nonalcoholic fatty liver disease: systematic review and meta-analysis. Hepatology. 2017;65:1557–65.
10. Sanyal AJ, Campbell-Sargent C, Mirshahi F, et al. Nonalcoholic steatohepatitis: association of insulin resistance and mitochondrial abnormalities. Gastroenterology 2001; 120:1183.
11. Narasimhan S, Gokulakrishnan K, Sampathkumar R, Farooq S, Ravikumar R, Mohan V, Balasubramanyam M: Oxidative stress is independently associated with non-alcoholic fatty liver disease (NAFLD) in subjects with and without type 2 diabetes. Clin Biochem. 2010, 43:815-21.
12. Boursier J, Mueller O, Barret M, et al. The severity of nonalcoholic fatty liver disease is associated with gut dysbiosis and shift in the metabolic function of the gut microbiota. Hepatology 2016; 63:764.
13. Fan JG, Kim SU, Wong VW. New trends on obesity and NAFLD in Asia. J Hepatol. 2017;67:862–73.
14. Long MT, Noureddin M, Lim JK. AGA Clinical Practice Update: diagnosis and management of nonalcoholic fatty liver disease in lean individuals: expert review. Gastroenterology. 2022;163: 764–4.
15. Bacon BR, Farahvash MJ, Janney CG, Neuschwander-Tetri BA. Nonalcoholic steatohepatitis: an expanded clinical entity. Gastroenterology. 1994;107(4):1103–9.
16. Cusi K, Isaacs S, Barb D, et al. American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings: co-sponsored by the American Association for the Study of Liver Diseases (AASLD). Endocr Pract. 2022;28(5):528–562.
17. Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology. 2023;77(5):1797-1835.
18. Wong VW, Wong GL, Tsang SW, et al. Metabolic and histological features of non-alcoholic fatty liver disease patients with different serum alanine aminotransferase levels. Aliment Pharmacol Ther 2009; 29:387.
19. Kowdley KV, Belt P, Wilson LA, et al. Serum ferritin is an independent predictor of histologic severity and advanced fibrosis in patients with nonalcoholic fatty liver disease. Hepatology 2012; 55:77.
20. Hernaez R, Lazo M, Bonekamp S, et al. Diagnostic accuracy and reliability of ultrasonography for the detection of fatty liver: a meta-analysis. Hepatology 2011; 54:1082.
21. Chaudhry A, Noor J, Batool S, Fatima G, Noor R. Advancements in Diagnostic and Therapeutic Interventions of Non-alcoholic Fatty Liver Disease: A Literature Review. Cureus. 2023;15(9):e44924.
22. Caussy C, Reeder SB, Sirlin CB, Loomba R. Noninvasive,quantitative assessment of liver fat by MRI-PDFF as an endpoint in NASH trials. Hepatology 2018; 68: 763–72.
23. Siddiqui MS, Vuppalanchi R, Van Natta ML, et al. Vibrationcontrolled transient elastography to assess fibrosis and steatosis in patients with nonalcoholic fatty liver disease. Clin Gastroenterol Hepatol 2019; 17: 156–63.e2.
24. Vilar-Gomez E, Martinez-Perez Y, Calzadilla-Bertot L, et al. Weight loss through lifestyle modification significantly reduces features of nonalcoholic steatohepatitis. Gastroenterology. 2015;149(2): 367–378, e5, e14-e15.

25. Gepner Y, Shelef I, Komy O, et al. The beneficial effects of Mediterranean diet over low-fat diet may be mediated by decreasing hepatic fat content. J Hepatol. 2019; 71(2):379e388.

26. Hashida R, Kawaguchi T, Bekki M, et al. Aerobic vs. resistance exercise in non-alcoholic fatty liver disease: a systematic review. J Hepatol. 2017;66(1):142–152.

27. Stefan N, Cusi K. A global view of the interplay between non-alcoholic fatty liver disease and diabetes. Lancet Diabetes Endocrinol. 2022;10(4):284-296.

28. Belfort R, Harrison SA, Brown K, Darland C, Finch J, Hardies J, et al. A placebo-controlled trial of pioglitazone in subjects with nonalcoholic steatohepatitis. N Engl J Med. 2006;355:2297–307.

29. Armstrong MJ, Gaunt P, Aithal GP, Barton D, Hull D, Parker R, et al. Liraglutide safety and efficacy in patients with nonalcoholic steatohepatitis (LEAN): a multicentre, double-blind, randomised, placebo-controlled phase 2 study. Lancet. 2016; 387:679–90.

30. Newsome PN, Buchholtz K, Cusi K, et al. A placebocontrolled trial of subcutaneous semaglutide in nonalcoholic steatohepatitis. N Engl J Med. 2021;384(12):1113–1124.

31. Kuchay MS, Krishan S, Mishra SK, Farooqui KJ, Singh MK, Wasir JS, et al. Effect of empagliflozin on liver fat in patients with type 2 diabetes and nonalcoholic fatty liver disease: a randomized controlled trial (E-LIFT trial). Diabetes Care. 2018; 41:1801–8.

32. Sanyal AJ, Chalasani N, Kowdley KV, et al. Pioglitazone, vitamin E, or placebo for nonalcoholic steatohepatitis. N Engl J Med. 2010;362(18):1675–1685.

33. Hoofnagle JH, Van Natta ML, Kleiner DE, Clark JM, Kowdley KV, Loomba R, et al. Vitamin E and changes in serum alanine aminotransferase levels in patients with non-alcoholic steatohepatitis. Aliment Pharmacol Ther. 2013;38: 134–43

34. Chaudhuri S, Dutta A, Chakraborty SBD. Efficacy and safety of saroglitazar in real-world patients of non-alcoholic fatty liver disease with or without diabetes including compensated cirrhosis: a tertiary care center experience. JGH Open. 2023;7(3):215–220.

35. Wirth KM, Sheka AC, Kizy S, et al. Bariatric surgery is associated with decreased progression of nonalcoholic fatty liver disease to cirrhosis: a retrospective cohort analysis. Ann Surg. 2020;272(1):32–39.