Metabolic Dysfunction - Associated Steatotic Liver Disease (MASLD): An Integrative Perspective from Modern Hepatology and Ayurveda

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Abstract

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) has emerged as a major global health concern, closely linked with obesity, insulin resistance, and metabolic syndrome. It represents a spectrum of liver disorders ranging from simple steatosis to steatohepatitis, fibrosis, and cirrhosis. Modern hepatology explains its pathogenesis through a multifactorial "multiple-hit" model involving lipid accumulation, oxidative stress, inflammation, and gut–liver axis dysfunction. Ayurveda offers a holistic perspective that parallels these mechanisms through the concepts of *Agni (*metabolic fire), *Ama* (metabolic toxins), and *Medoroga* (disorder of fat metabolism). The liver (*Yakrit*) is described as a central organ in blood and metabolic regulation, governed by *Ranjaka Pitta*. Impairment of *Agni* leads to *Ama* formation, *Meda* accumulation, and obstruction of bodily channels (*Srotorodha*), which closely resembles the metabolic and inflammatory processes seen in MASLD. This study integrates modern scientific evidence from PubMed, Scopus, and ScienceDirect with classical Ayurvedic principles to explore the pathophysiology, clinical features, diagnosis, complications, and management of MASLD. An integrative 5-step management model is discussed, focusing on lifestyle modification, metabolic correction, inflammation control, gut-liver axis modulation, and long-term maintenance. The findings suggest that an integrative approach combining Ayurveda and modern medicine provides a comprehensive framework for understanding and managing MASLD. Such an approach not only addresses disease progression but also targets its root metabolic causes, offering potential for effective prevention and reversal. Further clinical research is needed to validate these integrative strategies and establish their role in evidence-based practice.

Keywords

MASLD, Fatty Liver Disease, Integrative Medicine, Ayurveda, *Yakrit Roga, Medoroga,* Metabolic Syndrome

1. Introduction

Liver diseases related to metabolic dysfunction are becoming increasingly prevalent worldwide. Metabolic dysfunction-associated steatotic liver disease (MASLD)-formerly known as NAFLD-has become the most common cause of chronic liver disease globally. The change in nomenclature (finalized in 2023) reflects a shift toward a "positive" diagnosis based on the presence of metabolic risk factors rather than just the absence of alcohol use [1]. Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is characterized by excessive accumulation of fat in the liver in individuals with metabolic abnormalities such as obesity, diabetes, and dyslipidemia [2]. It is a broad term used to cover a spectrum of conditions characterized by evidence of hepatic steatosis on imaging or histology.

According to recent epidemiological studies, MASLD affects approximately 25–30% of the global population, making it the most common chronic liver disease [3]. The prevalence is even higher in individuals with metabolic syndrome and type 2 diabetes. The pathogenesis of MASLD involves complex metabolic disturbances including insulin resistance, increased hepatic fat accumulation, inflammation, and oxidative stress.

Ayurveda offers a holistic understanding of metabolic disorders and emphasizes prevention through balanced diet (*Ahara*), lifestyle (*Vihara*), and maintenance of digestive fire (*Agni*). Although MASLD is not described directly in classical Ayurvedic texts, its pathophysiology closely resembles conditions such as, *Medoroga*, *Yakrit Roga*, *Agnimandya*, *Kapha-Medo Dushti.* Exploring MASLD through an integrative approach combining modern hepatology and Ayurvedic principles may provide improved strategies for disease prevention and management.

2. Objectives

1. To study the etiology and pathogenesis of MASLD from a modern hepatology perspective.
2. To review Ayurvedic concepts related to liver diseases and metabolic disorders.
3. To correlate MASLD with Ayurvedic disease conditions such as *Medoroga* and *Yakrit Roga*.

4. To evaluate integrative therapeutic approaches combining modern medicine and Ayurveda.

3. Methodology

This research paper is based on a literature review of both modern medical and classical Ayurvedic sources.

Sources of Data

Modern sources- PubMed, research articles, Hepatology textbooks, WHO reports

Ayurvedic sources- *Charaka Samhita*, *Sushruta Samhita*, *Ashtanga Hridaya*, Ayurvedic pharmacology texts

The collected information was analyzed and correlated to establish an integrative understanding of MASLD.

4. Modern Hepatology Perspective

4.1 Definition

MASLD is defined by ≥5% hepatic steatosis and the presence of at least 1 cardiometabolic risk factor (eg, dyslipidemia or obesity), with no other underlying causes and minimal or no alcohol intake (<20 g/day for females and <30 g/day for males) [4]. Simply MASLD is defined as hepatic steatosis affecting at least 5% of hepatocytes in individuals with metabolic dysfunction and without significant alcohol intake.

4.2 Epidemiology

The global prevalence of MASLD has increased significantly due to modern lifestyle changes, paralleling the "twin epidemics" of obesity and Type 2 Diabetes (T2D) [5]. Most recently done meta-analysis study shows, 38% of adults around the world were shown to have MASLD (years 2016–2019), which was an increase of 50% since 1990–2006 [6]. According to that study, prevalence is highest in Latin America (44.4%) and lowest in Western Europe (25.1%). These trends are expected to grow, and by 2040 the global prevalence of MASLD is forecast to reach 55.4% [7]. The Asia, Northern Africa and Middle East (MENA) regions are experiencing rapid growth in the MASLD risk factors of obesity and T2D withing next few years [8], [9].

MASLD is highly prevalent in India, affecting approximately 38.6% of the general population. It is a major health crisis, with studies indicating rates as high as 68.2% in certain high-risk

groups (e.g., diabetics) and strong regional variations, often with higher burdens in North India and urban, and suburban, areas [10]. MASLD is currently a globally rising major risk factor for metabolic and cardiovascular disease [11][12][13].

4.3 Risk Factors

Recent epidemiological and clinical studies have identified multiple metabolic, lifestyle, demographic, and environmental risk factors associated with the development and progression of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). Research consistently demonstrates that MASLD is strongly linked to cardiometabolic abnormalities and lifestyle behaviors.

4.3.1 Obesity and Adiposity

Obesity is considered the most significant risk factor for MASLD. Excess adipose tissue leads to increased free fatty acid flux to the liver, promoting hepatic fat accumulation and lipotoxicity. Population studies show that individuals with obesity have several-fold higher risk of developing MASLD compared with normal-weight individuals.

A large population cohort analysis demonstrated that obesity significantly increased MASLD risk, with odds ratios exceeding five times compared with individuals without metabolic risk factors [14]. Additionally, longitudinal studies in non-obese populations found that increases in body mass index (BMI) and waist circumference significantly predicted the development of MASLD, indicating that even moderate weight gain can trigger hepatic steatosis [15].

4.3.2 Insulin Resistance and Type 2 Diabetes Mellitus

Insulin resistance is a central mechanism in MASLD pathogenesis. When insulin signaling is impaired, adipose tissue releases excessive free fatty acids into the circulation, which are then deposited in hepatocytes.

Clinical studies show that Type 2 diabetes mellitus (T2DM) substantially increases the likelihood of MASLD. Individuals with diabetes have a markedly higher prevalence of fatty liver disease compared with non-diabetic populations. Furthermore, MASLD patients with diabetes also exhibit higher risks of cardiovascular complications and disease progression due to systemic metabolic dysregulation [16].

4.3.3 Dyslipidemia

Abnormal lipid metabolism is another major contributor to MASLD. Elevated triglycerides and reduced high-density lipoprotein cholesterol (HDL-C) promote hepatic lipid accumulation.

Recent research indicates that hypertriglyceridemia, low HDL cholesterol, and elevated blood glucose levels significantly increase both MASLD prevalence and associated cardiovascular mortality risk [17]. In longitudinal studies, increased triglyceride levels and reduced HDL cholesterol were strongly associated with the onset of MASLD in both men and women [18].

4.3.4 Hypertension

Hypertension is frequently observed in individuals with MASLD and is considered a key component of the metabolic syndrome associated with the disease. Above mentioned epidemiological data demonstrate that hypertension independently increases MASLD risk and contributes to disease severity and fibrosis progression. The coexistence of hypertension with other metabolic risk factors significantly amplifies the probability of developing MASLD and its complications.

4.3.5 Gender and Age

Several population studies have reported higher MASLD prevalence in males compared with females. Hormonal differences and higher visceral fat distribution in men are believed to contribute to this disparity. Research findings indicate that MASLD prevalence can reach over 25% in men compared with about 11% in women in certain middle-aged populations. Age is another important determinant, as the prevalence of metabolic risk factors increases with advancing age.

4.3.6 Lifestyle Factors

Lifestyle behaviors play a crucial role in MASLD development. Important lifestyle risk factors include Sedentary lifestyle, High-calorie diet, Excess consumption of refined carbohydrates, Sugar-sweetened beverages, Smoking and stress. Studies have demonstrated that unhealthy dietary patterns and lack of physical activity contribute significantly to hepatic fat accumulation and metabolic dysfunction [19].

4.3.7 Environmental and Genetic Factors

Recent research also suggests that environmental exposures and genetic predisposition may influence MASLD risk. Exposure to environmental chemicals such as per- and polyfluoroalkyl substances (PFAS) has been linked to increased MASLD risk, particularly among adolescents

with certain genetic variants affecting liver fat metabolism [20]. Additionally, genetic polymorphisms such as PNPLA3 gene variants have been associated with increased susceptibility to hepatic fat accumulation.

4.3.8 Combined Cardiometabolic Risk Burden

One of the most important findings in recent MASLD research is the synergistic effect of multiple metabolic risk factors. The presence of obesity, diabetes, and hypertension simultaneously dramatically increases disease risk. Population cohort data indicate that individuals with all three conditions had a more than 17-fold higher likelihood of developing MASLD compared with those without metabolic abnormalities. This highlights the multifactorial nature of MASLD and emphasizes the importance of comprehensive metabolic risk management.

4.4 Pathophysiology

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is a complex metabolic disorder characterized by excessive accumulation of lipids within hepatocytes. It represents the hepatic manifestation of metabolic syndrome and is strongly associated with obesity, insulin resistance, dyslipidemia, and type 2 diabetes mellitus. The disease develops through a multifactorial process involving metabolic disturbances, oxidative stress, inflammatory signaling, mitochondrial dysfunction, and genetic predisposition [21][22].

4.4.1 Hepatic Steatosis: Initial Stage of Disease

The hallmark of MASLD is hepatic steatosis, defined as the accumulation of fat in at least 5% of hepatocytes. This occurs when the balance between lipid acquisition and lipid disposal in the liver becomes disrupted. Fat accumulation results from several mechanisms such as, Increased influx of free fatty acids (FFAs) from adipose tissue, increased de novo lipogenesis (DNL) in hepatocytes, reduced fatty acid oxidation, Decreased export of triglycerides in very-low-density lipoproteins (VLDL). Insulin resistance plays a central role in this process by increasing the delivery of fatty acids to the liver and stimulating hepatic lipid synthesis [23].

4.4.2 Insulin Resistance and Metabolic Dysregulation

Insulin resistance is considered the central pathogenic mechanism in MASLD. Peripheral insulin resistance in adipose tissue increases lipolysis, leading to elevated circulating free fatty acids that are transported to the liver [24].

Within hepatocytes, excess fatty acids are converted into triglycerides and stored as lipid droplets. In addition, insulin resistance stimulates hepatic gluconeogenesis and de novo lipogenesis, further promoting fat accumulation. Molecular studies show that lipid intermediates such as diacylglycerol (DAG) activate protein kinase C (PKC), which interferes with insulin receptor signaling pathways. This impairment worsens insulin resistance and contributes to hyperglycemia and metabolic dysfunction [25].

4.4.3 Multiple-Hit Hypothesis

Earlier models proposed a two-hit theory, where fat accumulation was the first hit and inflammation the second. However, current evidence supports a multiple-hit hypothesis, in which numerous factors act simultaneously to drive disease progression. Key contributing mechanisms include, Insulin resistance, Genetic susceptibility, Nutritional factors, Lipotoxicity, Gut microbiota dysbiosis, Oxidative stress and mitochondrial dysfunction. These mechanisms interact to initiate hepatocellular injury and inflammatory responses [26].

4.4.4 Lipotoxicity and Oxidative Stress

Excess accumulation of free fatty acids and toxic lipid metabolites leads to lipotoxicity, which damages hepatocytes. When the liver's capacity to store triglycerides safely is exceeded, fatty acids enter alternative metabolic pathways that generate reactive oxygen species (ROS) [27].

Lipid peroxidation, Mitochondrial damage and Cellular apoptosis are the causes for Reactive oxygen species. Oxidative stress also activates inflammatory pathways, which further exacerbate liver injury.

4.4.5 Mitochondrial Dysfunction

Mitochondria play a crucial role in energy metabolism and fatty acid oxidation. In MASLD, mitochondrial dysfunction results from oxidative stress and lipid overload. Studies show that mitochondrial calcium overload and oxidative damage impair oxidative phosphorylation and promote hepatocyte injury. These alterations also stimulate the release of pro-apoptotic factors such as cytochrome c, leading to cell death and disease progression [28]. Damaged mitochondria further increase ROS production, creating a self-perpetuating cycle of oxidative injury.

4.4.6 Inflammatory Response and Steatohepatitis

Persistent oxidative stress and lipotoxicity activate inflammatory signaling pathways in the liver. Kupffer cells and infiltrating immune cells release inflammatory cytokines such as, Tumor necrosis factor-α (TNF-α), Interleukin-6 (IL-6), Interleukin-1β (IL-1β). These inflammatory mediators promote hepatocellular injury and trigger the development of metabolic dysfunction-associated steatohepatitis (MASH), a more severe form of MASLD characterized by inflammation and hepatocyte damage [29].

4.4.7 Fibrosis and Disease Progression

Chronic inflammation and hepatocellular injury activate hepatic stellate cells, leading to excessive deposition of extracellular matrix proteins such as collagen. This process results in liver fibrosis, which may progress to cirrhosis and hepatocellular carcinoma if left untreated [30].

4.4.8 Genetic and Epigenetic Factors

Genetic susceptibility also plays a significant role in MASLD pathogenesis. Several gene variants have been identified that influence lipid metabolism and disease progression, including, PNPLA3, TM6SF2, MBOAT7, GCKR. Epigenetic mechanisms such as DNA methylation and histone modification may also contribute to disease susceptibility and progression [31].

4.4.9 Gut–Liver Axis

Emerging research highlights the importance of the gut–liver axis in MASLD pathogenesis. Alterations in gut microbiota can increase intestinal permeability, allowing bacterial endotoxins to enter the portal circulation and trigger hepatic inflammation. This interaction contributes to metabolic disturbances, oxidative stress, and progression of liver disease.

Figure 01 shows pathophysiological process of MASLD.

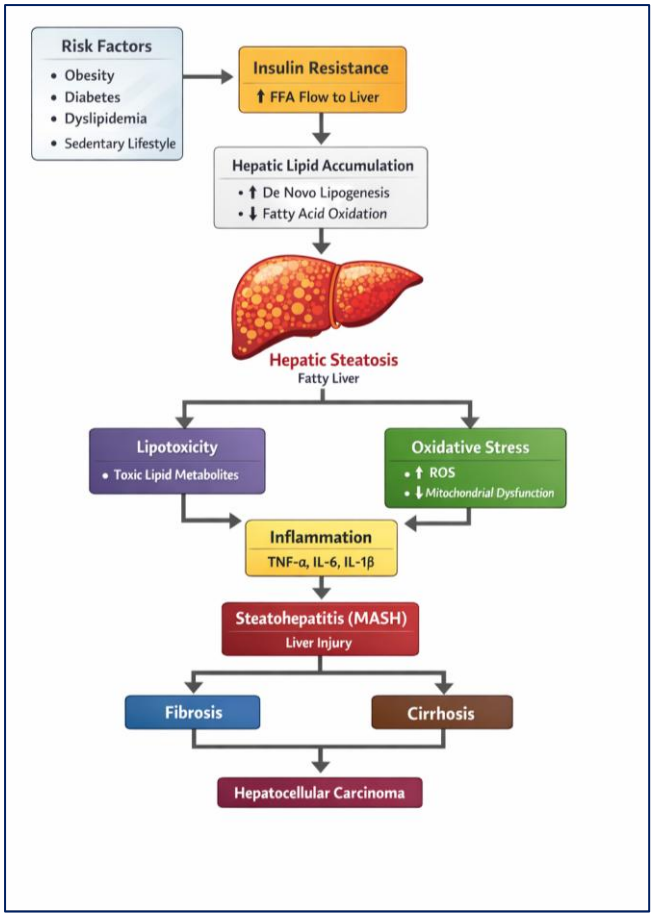

Figure 01: Pathophysiology of MASLD

4.5 Clinical Features

MASLD is often referred to as a “silent disease” because the majority of patients remain asymptomatic in the early stages. Clinical manifestations are usually nonspecific and may only become apparent when the disease progresses to advanced stages such as steatohepatitis, fibrosis, or cirrhosis.

4.5.1 Asymptomatic Nature

One of the most important clinical characteristics of MASLD is that most patients are asymptomatic, especially in the early stages. The disease is frequently detected incidentally during routine laboratory investigations or imaging studies performed for unrelated reasons. Large cohort studies confirm that a significant proportion of MASLD patients have normal liver enzyme levels, further contributing to delayed diagnosis [32].

4.5.2 Nonspecific Symptoms

When symptoms do occur, they are usually mild and nonspecific. Common presenting symptoms are, Fatigue (most common symptom), Malaise, right upper abdominal discomfort or dull pain, Bloating, Thirst and Sleep disturbances. Fatigue is consistently reported as the most frequent presenting symptom in clinical studies and may be related to systemic metabolic dysfunction and low-grade inflammation. These symptoms are often subtle and may not prompt immediate medical evaluation [33].

4.5.3 Physical Examination Findings

In Early-Stage, physical examination may be normal or show minimal findings. The most common clinical sign is mild to moderate hepatomegaly (enlarged liver). Hepatomegaly results from fat accumulation within hepatocytes [34].

Patients often exhibit Central obesity, Hypertension, Insulin resistance, Dyslipidemia as features of metabolic syndrome. These systemic findings are important clinical clues suggesting MASLD.

4.5.4 Laboratory Findings

Although not strictly symptoms, laboratory abnormalities are important clinical indicators such as, Mild elevation of ALT and AST, AST/ALT ratio usually <1, Elevated gamma-glutamyl transferase (GGT). In advanced disease, Hypoalbuminemia, Hyperbilirubinemia and Thrombocytopenia can see [35]. However, many patients may have normal liver enzymes despite significant disease, as supported by multiple studies in PubMed and Scopus databases.

4.5.5 Clinical Features in Advanced Disease (MASH and Cirrhosis)

As MASLD progresses to Metabolic Dysfunction-Associated Steatohepatitis (MASH) and cirrhosis, more severe clinical manifestations appear. Symptoms of Advanced Disease are Nausea and vomiting, Loss of appetite, Jaundice, Pruritus (itching), Ascites (fluid accumulation in abdomen), Easy fatigability, Memory impairment (hepatic encephalopathy) and Easy bruising or bleeding. Signs of Chronic Liver Disease are Jaundice, Spider angiomas, Palmar erythema, Caput medusae, Gynecomastia and Ascites, Petechiae [36].

4.5.6 Extrahepatic Manifestations

MASLD is not only a liver disease but also a systemic metabolic disorder. Common Extrahepatic Features are including cardiovascular disease (most common cause of mortality), type 2 diabetes mellitus, chronic kidney disease, Polycystic ovary syndrome (PCOS), and

obstructive sleep apnea. Research shows that MASLD patients have a significantly increased risk of atherosclerosis and cardiovascular mortality, often exceeding liver-related mortality [37]. These features indicate advanced liver dysfunction and portal hypertension. Figure 02 shows MASLD Spectrum and Clinical Progression.

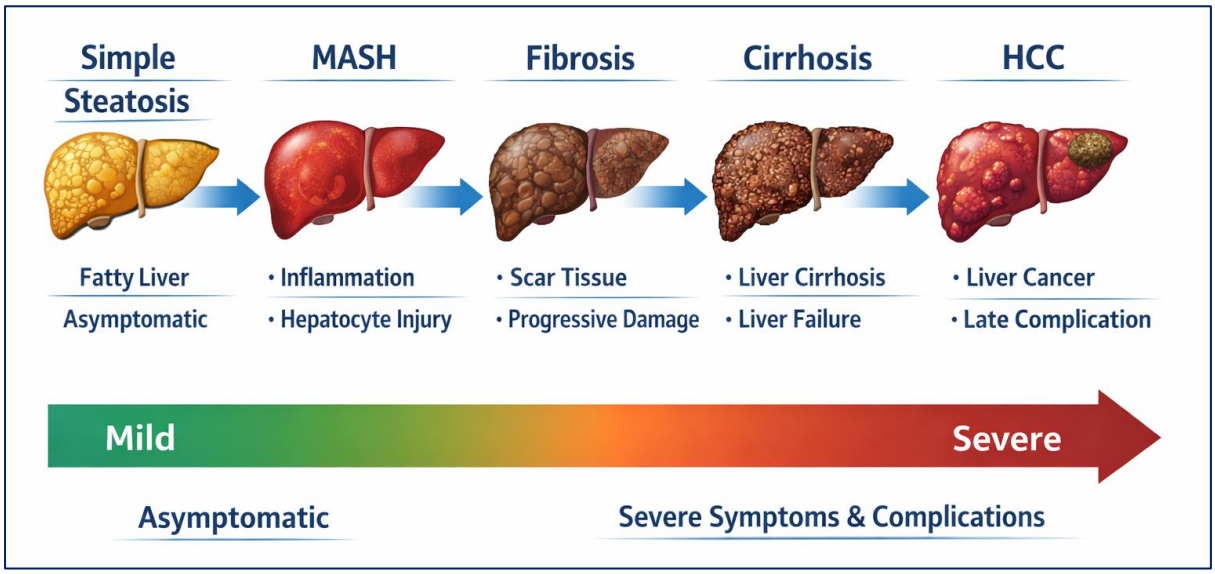

Figure 02: MASLD Spectrum and Clinical Progression

4.6 Diagnosis

The diagnosis of MASLD involves a combination of clinical evaluation, imaging, laboratory investigations, and non-invasive fibrosis assessment tools. Recent guidelines emphasize a multi-step, non-invasive diagnostic approach to identify both hepatic steatosis and the risk of disease progression.

4.6.1 Diagnostic Criteria of MASLD

According to recent consensus guidelines and the referenced PMC study, MASLD is diagnosed when the both Evidence of Hepatic Steatosis and Presence of Metabolic Dysfunction two criteria should be fulfilled. Evidence of Hepatic Steatosis demonstrated by, Imaging (ultrasound, CT, MRI), Controlled attenuation parameter (CAP) via Fibro-Scan and Liver biopsy (gold standard) [38].

At least one cardiometabolic risk factor, such as, Obesity or increased waist circumference, Type 2 diabetes mellitus, Hypertension, Dyslipidemia and Insulin resistance should be present for confirm Presence of Metabolic Dysfunction [39]. This definition reflects a shift from exclusion-based diagnosis (NAFLD) to inclusion-based metabolic criteria (MASLD) [40].

4.6.2 Stepwise Diagnostic Approach

Modern hepatology recommends a structured multi-step diagnostic algorithm [41]. Figure 03 shows that stepwise approach.

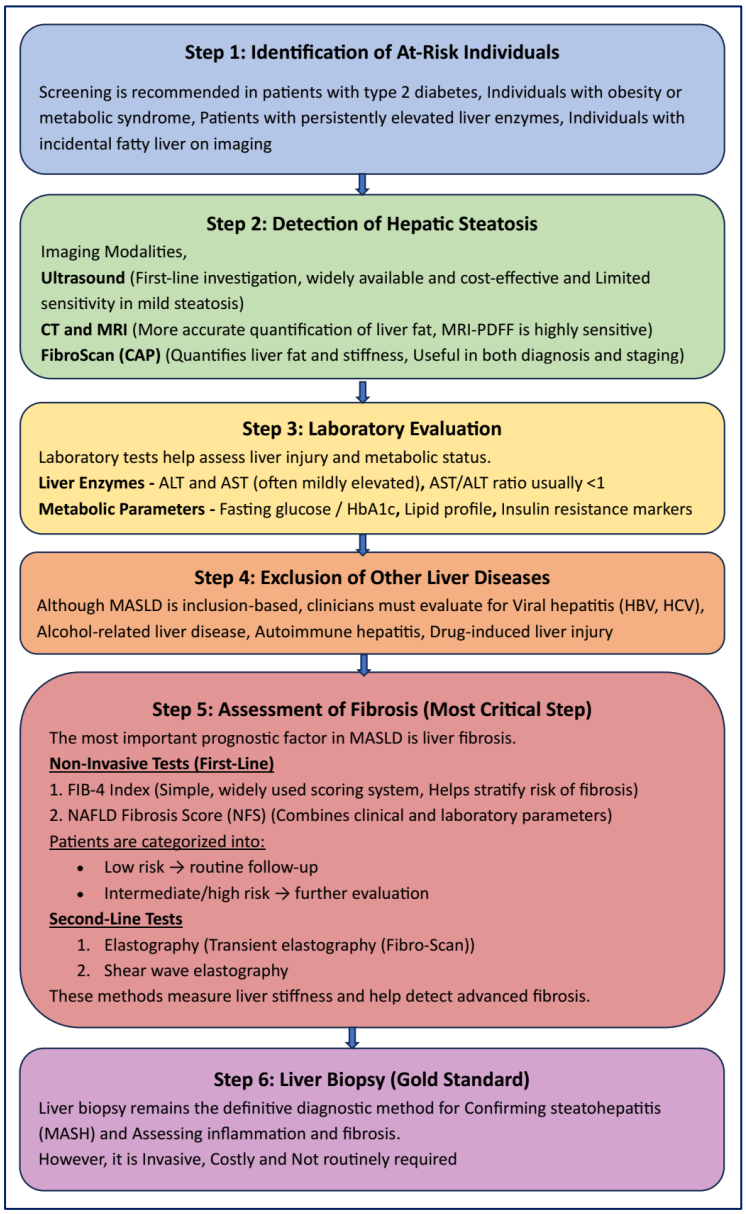

Figure 02: multi-step diagnostic algorithm of MASLD

4.6.3 Diagnosis of MASH (Advanced Form)

Diagnosis of Metabolic Dysfunction–Associated Steatohepatitis (MASH) requires; Hepatic steatosis, Hepatocellular injury (ballooning), Inflammation and ± fibrosis. These features are best confirmed by histological examination (biopsy).

4.6 Complications

MASLD is not merely a benign accumulation of fat in the liver but a progressive multisystem disorder associated with significant hepatic and extrahepatic complications. According to recent hepatology literature, including the Journal of Hepatology, MASLD contributes substantially to morbidity and mortality worldwide, primarily due to cardiovascular disease, liver-related complications, and systemic metabolic effects [42]. Table 01 shows common complications of MASLD.

Table 01: Complications of MASLD

Hepatic Complications	**Progression to Steatohepatitis (MASH)** The initial stage of MASLD (simple steatosis) can progress to MASH, characterized by, Hepatocellular injury, Inflammation, Ballooning degeneration. This stage significantly increases the risk of fibrosis and long-term complications.
	Liver Fibrosis Fibrosis is the most important predictor of prognosis in MASLD. Chronic inflammation activates hepatic stellate cells and it leads to excessive deposition of collagen and extracellular matrix. Studies show that advanced fibrosis is strongly associated with increased liver-related events and mortality [43].
	Cirrhosis and Hepatic Decompensation Progressive fibrosis may lead to cirrhosis, which represents irreversible liver damage. Complications of Cirrhosis (Ascites, Portal hypertension, Variceal bleeding, Hepatic encephalopathy) Patients with cirrhosis are at high risk of liver failure and death.
	Hepatocellular Carcinoma (HCC) MASLD is increasingly recognized as a major cause of hepatocellular carcinoma, even in the absence of cirrhosis. Rising incidence globally Can occur in non-obese individuals. Recent studies confirm that MASLD significantly increases the risk of HCC due to chronic inflammation and metabolic dysregulation [44].

Cardiovascular Complications (Most Common Cause of Death)	Cardiovascular disease (CVD) is the leading cause of mortality in MASLD patients. Responsible mechanisms are insulin resistance, atherogenic dyslipidemia, systemic inflammation. Clinical Outcomes are coronary artery disease, stroke, heart failure Large-scale studies confirm that MASLD is strongly associated with increased cardiovascular morbidity and mortality [45]. **Cardiac Arrhythmias** Recent meta-analyses show that MASLD is associated with an increased risk of atrial fibrillation, independent of traditional risk factors [46].
Metabolic Complications	MASLD is closely linked with metabolic syndrome and contributes to Type 2 diabetes mellitus, Worsening insulin resistance, Dyslipidemia. The relationship is bidirectional-MASLD both results from and exacerbates metabolic dysfunction.
Extrahepatic Complications [47]	**Chronic Kidney Disease (CKD)** MASLD is associated with an increased risk of chronic kidney disease, likely due to shared mechanisms such as, Inflammation, Endothelial dysfunction, Insulin resistance.
	Endocrine and Reproductive Disorders Polycystic ovary syndrome (PCOS) Hormonal imbalance
	Obstructive Sleep Apnea MASLD patients frequently exhibit sleep disorders due to obesity and metabolic dysregulation.
Malignancies (Extrahepatic Cancers)	Recent studies highlight increased risk of extrahepatic cancers, including Gastrointestinal cancers, Breast cancer, Gynecological cancers.

	MASLD is therefore considered a systemic disease with oncogenic potential [48].
Infectious Complications	Emerging evidence suggests that MASLD is associated with increased susceptibility to infections. Higher risk of serious bacterial infections. Risk increases with severity of fibrosis. Meta-analysis shows MASLD patients have significantly higher odds of hospitalization due to infections [49]
Mortality and Disease Burden	MASLD contributes to increased overall mortality due to cardiovascular disease (most common), Liver-related complications, Malignancies. The burden of disease is increasing globally due to rising obesity and diabetes prevalence.

4.7 Treatment of MASLD

The management of MASLD focuses on targeting underlying metabolic dysfunction, preventing disease progression, and reducing cardiovascular and liver-related complications. Recent guidelines from hepatology societies emphasize a multidisciplinary, stepwise, and primarily non-pharmacological approach, with pharmacotherapy reserved for selected patients.

4.7.1 Lifestyle Modification (Cornerstone of Management)

Lifestyle intervention is the first-line and most effective treatment for MASLD.

- **Weight Reduction** - Target is 5–10% body weight loss, ≥10% weight loss can improve Steatosis, Inflammation, Fibrosis. Sustained weight loss significantly reduces liver fat and improves histological outcomes [50].
- **Dietary Management** - Recommended Diet is Mediterranean diet which is high in Fruits and vegetables, Whole grains, Lean proteins and Healthy fats (olive oil, nuts). Avoid Refined carbohydrates, Sugary beverages (fructose). Saturated and trans fats. Dietary quality plays a crucial role in metabolic regulation and liver health [51].
- **Physical Activity** - 150–200 minutes/week moderate exercise. It can be combination of aerobic exercise, resistance training. Exercise improves liver fat and insulin sensitivity even without weight loss [52].

- **Alcohol Restriction** - Avoid or minimize alcohol intake. Even moderate intake may worsen fibrosis

4.7.2 Management of Metabolic Risk Factors

MASLD is strongly linked with metabolic syndrome; therefore, management must include Diabetes, hypertension and dyslipidemia management mainly. Managing comorbidities reduces both liver-related and cardiovascular complications.

4.7.3 Pharmacological Therapy

Currently, no universal drug is approved specifically for MASLD, but several agents are used in selected patients, especially those with MASH and fibrosis. High-risk patients, Failure of lifestyle intervention and MASH with fibrosis stage ≥F2 are indications for Drug Therapy. Common Pharmacological Agents are Insulin Sensitizers (Improves steatosis and inflammation), GLP-1 Receptor Agonists (It will promote weight loss and improve liver histology), Lipid-Lowering Drugs (Reduces cardiovascular risk). And emerging Drugs (thyroid hormone receptor agonist, Targets lipid metabolism and fibrosis). These therapies act on key mechanisms such as insulin resistance, inflammation, and lipotoxicity [53].

4.7.4 Bariatric and Surgical Interventions

These interventions use when the patient is severe obesity and failure of lifestyle and medical therapy. Benefits are significant weight loss, improvement or resolution of MASLD and reduction in fibrosis progression. Bariatric surgery is an effective option in selected patients [54].

4.7.5 Management of MASLD Based on Disease Stage

4.7.5.1 Early MASLD (Simple Steatosis)

Management at this stage primarily involves lifestyle modification, including weight loss, a healthy diet, and regular physical activity. These measures can effectively reduce liver fat and prevent disease progression. Patients are advised regular monitoring with liver enzymes and non-invasive fibrosis assessment tools to detect any worsening of disease. Pharmacological treatment is generally not required unless risk factors persist.

4.7.5.2 MASH (Steatohepatitis)

In this stage, management includes lifestyle interventions combined with pharmacotherapy in selected patients, particularly those with fibrosis. Drugs such as insulin sensitizers and GLP-1 receptor agonists may be used. In addition, strict control of metabolic risk factors like diabetes, dyslipidemia, and hypertension is essential to reduce both liver-related and cardiovascular complications.

4.7.5.3 Advanced Fibrosis / Cirrhosis

Patients with advanced disease require specialist care and close surveillance for complications such as portal hypertension and hepatocellular carcinoma. Management focuses on preventing disease progression and managing complications. In cases of end-stage liver disease, liver transplantation is considered the definitive treatment.

5. Ayurvedic Perspective

5.1 Concept of *Yakrit* in Ayurveda

In Ayurveda, the liver is referred to as *Yakrit*, a vital organ with profound physiological, pathological, and metabolic significance. Classical Ayurvedic texts such as Charaka Samhita, Sushruta Samhita, and Ashtanga Hridaya describe *Yakrit* not only as an anatomical structure but as a functional hub of metabolism, blood formation, and *doshic* balance.

The term *Yakrit* is derived from two components.“Ya” - to maintain and “Krit” – to perform or act [55]. Thus, Yakrit is defined as “the organ that performs and maintains multiple vital functions in the body.” This reflects the Ayurvedic understanding of the liver as a dynamic metabolic organ, similar to its role in modern hepatology.

n Ayurveda, *Yakrit* (liver) is described as a “*Mamsa Pinda*” (mass of flesh) located in the right upper abdomen, closely corresponding to modern anatomical descriptions. It is considered a *Matruja Avayava* (organ derived predominantly from maternal factors) and a *Shonitaja Avayava* (originating from blood tissue), highlighting the importance of maternal nutrition and fetal development in liver formation. *Yakrit* is regarded as the primary seat of Rakta Dhatu (blood tissue) and plays a crucial role as a *Raktashaya* (blood reservoir). It is also associated with *Raktadhara Kala*, responsible for blood formation and maintenance, and serves as the root (Moola) of *Raktavaha Srotas* (blood channels), along with the spleen (*Pleeha*). These concepts correlate with modern understandings of hepatic hematopoiesis, blood storage, and metabolic regulation [56][57].

Yakrit is the principal site of *Ranjaka Pitta*, a subtype of *Pitta Dosha,* which facilitates the transformation of Rasa Dhatu into Rakta Dhatu, imparts color to blood, and supports metabolic processes. This function is comparable to modern liver roles such as bilirubin metabolism, hemoglobin synthesis, and enzymatic activity. Functionally, *Yakrit* is central to metabolic regulation, blood formation, and systemic homeostasis, paralleling contemporary liver functions including carbohydrate, lipid, and protein metabolism, detoxification, and plasma protein synthesis [58].

Pathologically, disorders of *Yakrit* (*Yakrit Vikara*) arise due to disturbances in *Pitta Dosha, Raktadhara Kala*, and *Raktavaha Srotas*, leading to conditions such as *Pandu* (anemia), *Kamala* (jaundice), and *Yakritodara* (hepatomegaly). These conditions can be correlated with modern liver diseases including hepatitis, MASLD, and cirrhosis. Overall, the Ayurvedic concept of *Yakrit* presents a holistic and functional understanding of liver physiology and pathology, which shows significant parallels with modern hepatology and supports integrative approaches to liver diseases [59][60].

5.2 *Agni* and Metabolism

In Ayurveda, *Agni* (digestive and metabolic fire) is considered the central principle governing digestion, metabolism, and overall homeostasis. It is responsible for the transformation (*Paka*) of ingested food into absorbable nutrients, which are then utilized for tissue formation and energy production. According to Ayurvedic physiology, Agni operates at multiple levels through a hierarchical system of 13 types, including *Jatharagni* (primary digestive fire), *Bhutagni* (elemental metabolism), and *Dhatvagni* (tissue-level metabolism). *Jatharagni* initiates digestion in the gastrointestinal tract, while *Bhutagni* and *Dhatvagni* regulate cellular and tissue metabolism, closely resembling modern concepts of enzymatic digestion and biochemical pathways [61][62].

A properly functioning *Agni* ensures efficient digestion, absorption, and assimilation of nutrients, thereby maintaining energy balance, immunity, and tissue nourishment. Conversely, impaired Agni (*Mandagni*) leads to incomplete digestion and the formation of *Ama* (metabolic toxins), which accumulate in the body, obstruct physiological channels (*Srotas*), and contribute to systemic inflammation and metabolic disorders [63]. This concept is comparable to modern mechanisms such as metabolic dysregulation, oxidative stress, and chronic low-grade inflammation seen in conditions like obesity and MASLD [64].

From a modern scientific perspective, Agni can be correlated with digestive enzymes, metabolic pathways, mitochondrial function, and hormonal regulation, which collectively control nutrient metabolism and energy production. Ayurveda further emphasizes that Agni is influenced by diet, lifestyle, circadian rhythm, and mental state, aligning with emerging research in chronobiology and metabolic regulation. Thus, *Agni* represents a comprehensive and integrative concept of metabolism, bridging traditional Ayurvedic knowledge with modern biomedical understanding [65].

5.3 Correlation of MASLD with *Medoroga*

MASLD shows a strong conceptual and pathophysiological correlation with *Medoroga* described in Ayurveda. *Medoroga* is characterized by excess accumulation and vitiation of *Meda Dhatu* (adipose tissue) due to improper diet, sedentary lifestyle, and impaired metabolism (*Agni Dushti*) [66]. Classical Ayurvedic texts describe *Medoroga* as a disorder of *Medovaha Srotas*, where abnormal fat deposition occurs in various parts of the body, leading to systemic metabolic disturbances. Contemporary Ayurvedic studies have correlated *Medoroga* with dyslipidemia, obesity, and metabolic syndrome, which are the primary drivers of MASLD [67].

In MASLD, excessive lipid accumulation occurs in hepatocytes due to insulin resistance, altered lipid metabolism, and chronic inflammation, which closely parallels the Ayurvedic concept of *Meda Dushti* and *Srotorodha* (channel obstruction). Research integrating Ayurveda and modern science highlights that *Medovaha Srotodushti* plays a central role in fatty liver disease, linking impaired fat metabolism with hepatic steatosis [68]. Additionally, case-based and clinical studies indicate that conditions like non-alcoholic fatty liver disease (now MASLD) are frequently interpreted in Ayurveda under the spectrum of *Medoroga* and *Yakrit Vikara*, due to shared etiological factors such as overnutrition, sedentary habits, and metabolic imbalance [69].

From a pathophysiological perspective, both MASLD and *Medoroga* originate from Agni impairment leading to Ama formation, followed by accumulation of lipids and obstruction of metabolic pathways. This results in progressive disease involving fat deposition, inflammation, and tissue damage. Modern research supports this correlation by demonstrating that metabolic

dysfunction, particularly lipid dysregulation and insulin resistance, is central to MASLD progression, mirroring Ayurvedic descriptions of Meda accumulation and systemic imbalance. Thus, MASLD can be understood as a hepatic manifestation of *Medoroga*, where deranged fat metabolism and systemic metabolic dysfunction converge at the level of the liver.

5.4 Pathophysiology of MASLD with Ayurvedic Correlation

The pathophysiology of MASLD is complex and multifactorial, involving insulin resistance, lipid accumulation, oxidative stress, inflammation, and fibrosis, commonly explained by the "multiple-hit hypothesis." The primary initiating factor is insulin resistance, which leads to increased lipolysis in adipose tissue and excessive influx of free fatty acids into the liver. This results in hepatic steatosis, characterized by triglyceride accumulation in hepatocytes. Subsequent "hits," including mitochondrial dysfunction, oxidative stress, and inflammatory cytokine release, promote hepatocellular injury, leading to steatohepatitis (MASH) and progressive fibrosis [70].

From an Ayurvedic perspective, this entire cascade can be understood through the concepts of *Agni Dushti, Ama* formation, and *Medoroga.* The pathogenesis begins with *Mandagni* (impaired metabolic fire) due to improper diet and sedentary lifestyle, resulting in incomplete digestion and formation of *Ama* (metabolic toxins). *Ama* circulates in the body and causes *Srotorodha* (obstruction of channels), particularly affecting *Medovaha* and *Raktavaha Srotas*, which regulate lipid and blood metabolism. This leads to *Meda Dhatu Vriddhi* (excess fat accumulation), analogous to dyslipidemia and obesity, which are key drivers of MASLD [71].

The accumulation of vitiated *Meda* in *Yakrit* (liver) results in *Yakrit Meda Dushti*, corresponding to hepatic steatosis. Additionally, disturbance of *Ranjaka Pitta* impairs normal metabolic transformation and blood-related functions, contributing to inflammation and hepatocellular damage. As the disease progresses, persistent *Ama* and *Meda* accumulation lead to chronic inflammation and tissue injury, which parallels modern mechanisms of oxidative stress, cytokine-mediated damage, and activation of hepatic stellate cells, ultimately resulting in fibrosis and cirrhosis [72].

Furthermore, Ayurvedic literature describes that prolonged *Srotorodha* and *Dhatu Dushti* disrupt systemic homeostasis, which correlates with the systemic nature of MASLD, including its association with metabolic syndrome, cardiovascular disease, and chronic inflammation. Thus, MASLD can be conceptualized as a hepatic manifestation of *Medoroga*, where deranged

Agni initiates a cascade of *Ama* formation, Meda accumulation, and progressive liver damage. Figure 03 shows integrated flowchart of MASLD pathophysiology.

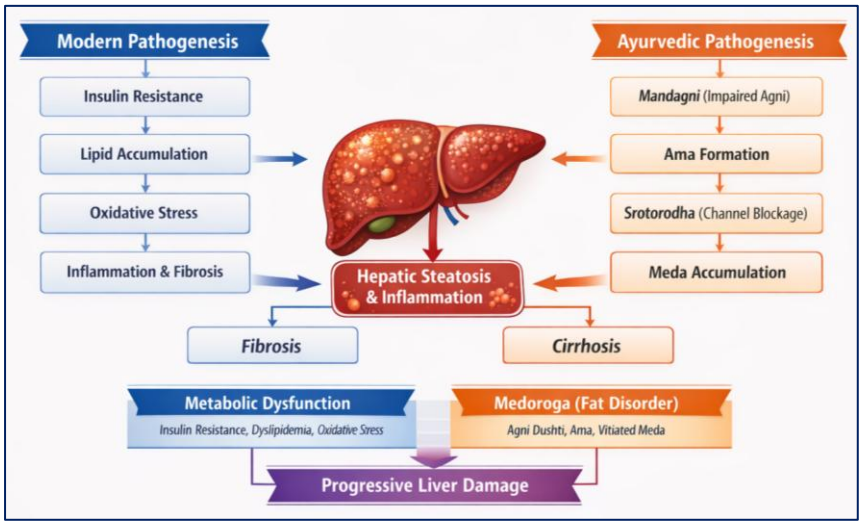

Figure 02: Integrated Pathophysiology of MASLD with Ayurveda

6. Ayurvedic Management of MASLD

Ayurvedic management of MASLD (correlated with *Medoroga* and *Yakrit Vikara*) is based on correcting the root cause-*Agni Dushti, Ama* accumulation, and *Meda* imbalance-rather than only treating symptoms. The therapeutic approach is broadly divided into *Nidana Parivarjana, Shodhana, Shamana*, and lifestyle regulation.

6.1 *Nidana Parivarjana* (Removal of Causes)

The first and most essential step is elimination of causative factors such as high-fat diet, sedentary lifestyle, excessive calorie intake, and stress. Modern hepatology also emphasizes lifestyle correction as the cornerstone of MASLD management, particularly weight reduction and metabolic control [73].

6.2 *Shodhana Chikitsa* (Bio-purification Therapy)

Ayurveda recommends Panchakarma therapies, especially *Vamana Karma* (therapeutic emesis) and *Virechana Karma* (purgation). These help in eliminating *Ama* and *vitiated Doshas*, improving metabolic function and reducing lipid accumulation. Studies suggest that such detoxification therapies may help restore metabolic balance and improve liver parameters [74].

6.3 Shamana Chikitsa (Herbal and Drug Therapy)

Various *Medohara* (fat-reducing) and *Yakrit*-protective drugs are used, such as *Guduchi (Tinospora cordifolia*), *Kutki (Picrorhiza kurroa)*, *Bhumyamalaki (Phyllanthus niruri*). Evidence from systematic reviews and RCTs shows that Ayurvedic formulations can reduce liver enzymes (ALT, AST), improve lipid profile, and reduce hepatic fat accumulation [75].

6.4 *Ahara* and *Vihara* (Dietary Management & Lifestyle and Behavioral Therapy)

Diet plays a central role in restoring *Agni* and reducing *Meda.* Light, easily digestible food (*Laghu Ahara),* Low-fat, high-fiber diet, Avoidance of processed, fried, and sugary foods. This aligns with modern dietary strategies focusing on caloric restriction, Mediterranean diet, and reduced saturated fat intake. Lifestyle modification is considered the foundation therapy in both Ayurveda and modern medicine for MASLD. Especially regular physical activity, yoga and pranayama, adequate sleep and circadian rhythm regulation [76].

7. 5-Step Integrative Model for MASLD Reversal

The management of MASLD requires a multidimensional, stepwise approach targeting metabolic dysfunction, inflammation, and liver injury. Recent integrative research emphasizes lifestyle, metabolic correction, gut-liver axis, pharmacotherapy, and long-term maintenance as key pillars [77].

7.1 Step 1: Lifestyle & Metabolic Correction (Foundation Phase)

The first and most critical step is lifestyle modification, including weight loss, dietary changes, and physical activity. Evidence shows that 5-10% weight reduction significantly improves hepatic steatosis and inflammation [78].

- Modern: Calorie restriction, Mediterranean diet, exercise
- Ayurveda: *Nidana Parivarjana, Agni Deepana*

Mechanism of this step to target improving insulin sensitivity and lipid metabolism, reducing fat accumulation in the liver.

7.2 Step 2: Metabolic & Hormonal Regulation

MASLD is strongly linked with insulin resistance, obesity, and endocrine imbalance. Modern therapies such as GLP-1 receptor agonists, THR-β agonists, and metabolic modulators are emerging as effective strategies [79]. This step targets to restoring systemic metabolic homeostasis and reduces hepatic fat influx.

- Ayurveda: Correction of *Agni* and *Dhatvagni*
- Modern: Glycemic control, lipid regulation

7.3 Step 3: Targeting Inflammation & Oxidative Stress

Progression from steatosis to MASH is driven by oxidative stress, mitochondrial dysfunction, and inflammatory cytokines. This step prevents hepatocyte injury and disease progression [80].

- Modern: Antioxidants, anti-inflammatory therapies
- Ayurveda: *Ama Pachana, Pitta Shamana*

7.4 Step 4: Gut–Liver Axis Modulation

Emerging evidence highlights the role of gut microbiota dysbiosis in MASLD progression. Modulating the microbiome improves liver outcomes by restoring metabolic signaling. Improves intestinal barrier function and reduces endotoxemia, lowering liver inflammation [81].

- Modern: Probiotics, microbiome therapies
- Ayurveda: Ahara regulation, Ama reduction, gut cleansing

7.5 Step 5: Hepatoprotection, Fibrosis Prevention & Long-Term Maintenance

Advanced MASLD requires prevention of fibrosis and long-term disease control. A multidisciplinary and personalized approach is recommended. Mechanism of this step aims to promote hepatic regeneration, prevents fibrosis, and reduces recurrence risk [82].

- Modern: Antifibrotic drugs, surveillance, comorbidity control
- Ayurveda: *Rasayana therapy, Dinacharya, Ritucharya*

8. Discussion

The present study highlights that Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is not merely a hepatic disorder but a systemic metabolic condition driven by complex interactions between insulin resistance, lipid metabolism, inflammation, and lifestyle factors. Modern hepatology explains MASLD through the “multiple-hit hypothesis,” where metabolic overload, oxidative stress, and inflammatory pathways collectively contribute to disease progression from simple steatosis to steatohepatitis, fibrosis, and cirrhosis.

Interestingly, Ayurvedic principles provide a parallel and holistic framework to understand this condition. The concept of *Agni* (metabolic fire) plays a central role, where its impairment

(Mandagni) leads to the formation of *Ama* (metabolic toxins) and subsequent disturbance in *Meda Dhatu* (fat metabolism). This aligns closely with modern mechanisms such as insulin resistance and lipid dysregulation. The Ayurvedic description of *Medoroga* as a disorder of fat accumulation and metabolic imbalance strongly correlates with MASLD, especially in the context of obesity, dyslipidemia, and sedentary lifestyle.

Furthermore, the involvement of *Yakrit* (liver) as a key organ in Rakta (blood) metabolism and transformation through *Ranjaka Pitta* reflects modern understanding of hepatic metabolic, enzymatic, and detoxification functions. The concept of *Srotorodha* (microchannel obstruction) can be interpreted as impaired metabolic pathways, lipid deposition, and inflammatory cascades seen in MASLD. These similarities suggest that Ayurveda, although described in classical terminology, captures the systemic and metabolic nature of liver diseases with remarkable depth.

From a therapeutic perspective, both systems converge on the importance of lifestyle modification as the cornerstone of management. Weight reduction, dietary regulation, and physical activity are universally emphasized. Ayurvedic interventions such as *Nidana Parivarjana* (removal of causative factors), *Agni* correction, *Ama Pachana,* and *Medohara* therapies complement modern strategies targeting metabolic correction and inflammation control.

The 5-step integrative model further strengthens this alignment by combining evidence-based modern interventions with Ayurvedic principles. This model addresses MASLD at multiple levels-metabolic, inflammatory, microbial, and regenerative-thereby offering a more comprehensive and patient-centered approach. In particular, the inclusion of gut-liver axis modulation and long-term lifestyle sustainability reflects emerging scientific understanding as well as classical Ayurvedic wisdom.

However, despite promising correlations, there remains a need for high-quality clinical trials and standardization of Ayurvedic interventions to validate their efficacy in MASLD management. Integrative approaches should be scientifically evaluated to ensure safety, reproducibility, and global acceptance.

9. Conclusion

MASLD represents a growing global health challenge rooted in metabolic dysfunction and lifestyle imbalance. This study demonstrates that Ayurvedic concepts such as *Agni, Ama,*

Medoroga, and Yakrit Vikara provide a comprehensive and holistic framework that closely parallels modern hepatological understanding of the disease.

The integration of Ayurveda with contemporary medical science offers a multidimensional approach to MASLD management-focusing not only on symptom control but also on correction of underlying metabolic disturbances. The 5-step integrative model highlights the importance of lifestyle modification, metabolic regulation, inflammation control, gut health, and long-term maintenance in achieving disease reversal.

In conclusion, MASLD can be effectively approached through an integrative paradigm, where the strengths of both systems are utilized to enhance patient outcomes. Future research should focus on generating robust clinical evidence to further validate and refine these integrative strategies, paving the way for more personalized and sustainable management of metabolic liver diseases.

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