International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 32, Issue 4, April 2026 ijppr.humanjournals.com ISSN: 2349-7203

# A Review on Non-Alcoholic Fatty Liver and Its Treatments

**Muskan Jain[1], Richa Agarwal[2], Rajesh Asija[3], Shyam Bihari Beniwal[4], Komal Kumari[5]**

[1,4,5]Research Scholar, Maharishi Arvind Institute of Pharmacy, Jaipur, Rajasthan, India.
[2]Associate Professor, Maharishi Arvind Institute of Pharmacy, Jaipur, Rajasthan, India.
[3]Principal, Maharishi Arvind Institute of Pharmacy, Jaipur, Rajasthan, India.

Received: 28 February 2026 Revised: 15 March 2026 Accepted: 31 March 2026

**ABSTRACT**

Non-alcoholic fatty liver disease (NAFLD), now known as metabolic dysfunction-associated liver disease (MASLD), is a spectrum of liver disease. It can be identified by the fact that considerable amount of hepatocytes with minimal or no alcohol use have steatosis. Because of its rising incidence along with increasing rates of obesity, metabolic syndromes, and diabetes mellitus type 2, NAFLD is expected to overtake all other causes of cirrhosis over the next decade, necessitating liver transplantation. Nevertheless, heart disease persists as the most prevalent manifestation of mortality, with only a small percentage experiencing fibrosis and complications associated with the liver. Pathologically, NAFLD is linked to lipid toxicity, oxidative stress, lipid deposits, and endoplasmic reticulum stress. A healthy diet, physical exercise, and a decrease in weight are advised by current international guidelines for the treatment of NAFLD, along with a limited number of medicinal therapies, including vitamin E and pioglitazone. This article assesses MASLD's pathophysiology, diagnosis, treatment, and epidemiology.

**Keywords:** NAFLD, Treatment, Diagnosis, Pathophysiology of NAFLD

## INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is one of the most prevalent chronic liver disorders worldwide. It represents a broad spectrum of conditions marked by excessive fat accumulation in the liver in the absence of other secondary causes, such as heavy alcohol intake. The spectrum spans from non-alcoholic fatty liver (NAFL), a relatively mild form, to non-alcoholic steatohepatitis (NASH), which is more severe. Over time, NAFLD can advance to liver fibrosis and eventually cirrhosis [1,2]. In NAFL, fat deposition occurs in the liver without signs of inflammation, while NASH is distinguished by fat accumulation accompanied by lobular inflammation and cell death, which can further progress to fibrosis and cirrhosis.

Until the mid-2000s, non-alcoholic steatohepatitis (NASH) was largely regarded as a serious condition seen primarily in obese women, frequently linked with type 2 diabetes mellitus (T2DM), and considered to have a relatively benign outcome, despite being a predictor of cardiovascular disease, stroke, and diabetes [1,2,3,4]. In recent years, however, the prevalence of non-alcoholic fatty liver disease (NAFLD) has increased significantly, particularly in Western nations, with an estimated global prevalence of around 25%. NAFLD is now recognized as one of the most common chronic liver disorders in industrialized countries, especially among individuals with central obesity, T2DM, dyslipidemia, and metabolic syndrome.

For the assessment of liver inflammation and injury, liver biopsy remains the gold standard diagnostic tool. In the context of NAFLD and its associated conditions, biopsy findings can vary from the presence of triglyceride droplets within hepatocytes to more advanced manifestations such as non-alcoholic steatohepatitis (NASH). NASH is typically identified by the accumulation of lipid droplets in hepatocytes, accompanied by inflammatory changes and varying degrees of hepatic fibrosis. While most cases of hepatic steatosis are non-progressive, a subset of patients develops NASH, which can advance to liver failure or hepatocellular carcinoma.

According to U.S. guidelines for NAFLD management, the condition is defined by (a) hepatic fat infiltration involving ≥5% of hepatocytes on imaging or histology, and (b) the exclusion of other causes of steatosis, such as alcohol, drugs, or viral infections. Patients with NAFLD may also present with elevated liver enzyme levels.

Patients with NAFLD frequently present with one or more features of metabolic syndrome (MS), such as systemic hypertension, dyslipidemia, insulin resistance, or overt diabetes [7]. Growing evidence suggests that visceral obesity significantly contributes to

NAFLD, and MS itself is a recognized risk factor for cardiovascular disease [5,7]. Current literature highlights that cardiovascular and vascular complications represent the leading cause of mortality in NAFLD patients, although the exact mechanisms linking NAFLD with cardiovascular disease remain unclear. Insulin resistance is considered a key shared pathway in the development of both conditions.

Interpreting abnormal liver enzyme levels in otherwise asymptomatic individuals can be challenging, even for experienced clinicians. NAFLD is often the underlying cause of unexplained liver test abnormalities in blood donors and accounts for asymptomatic elevations in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in up to 90% of cases, once other liver disorders have been excluded [8,9]. According to data from the World Health Organization Global Health Observatory (2014), global obesity prevalence is approximately 15% in women and 11% in men aged 18 years and older [8,9]. Furthermore, population studies estimate that non-alcoholic steatohepatitis (NASH) affects between 5.7–17% of the U.S. population.

The wide clinical spectrum of NAFLD, along with its close association with metabolic syndrome, presents substantial challenges in diagnosis and management. This review seeks to outline the pathophysiology, risk factors, diagnostic strategies, and both conservative and surgical treatment approaches for NAFLD.

The spectrum of non-alcoholic fatty liver disease (NAFLD) begins with a healthy liver, where fat is present in less than 5% of hepatocytes. Progression starts with simple steatosis or non-alcoholic fatty liver (NAFL), defined as fat accumulation in more than 5% of hepatocytes, which is generally reversible. NAFL can advance to non-alcoholic steatohepatitis (NASH), characterized by steatosis along with inflammation, hepatocyte ballooning, and varying degrees of fibrosis. Approximately 15–25% of NASH cases progress to cirrhosis, representing advanced fibrosis. In about 7% of cases, cirrhosis can further develop into hepatocellular carcinoma. At this terminal stage, the prognosis is poor, and outcomes may require liver transplantation or can result in death.

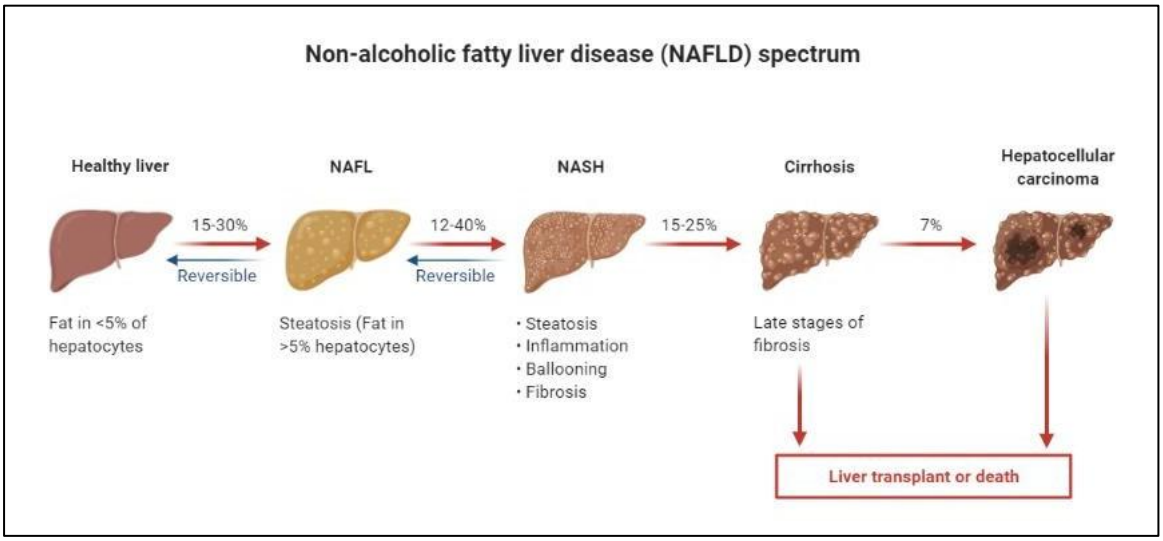


**Fig 1 Progression of NAFLD**

**STAGES OF LIVER DAMAGE:**

**NAFLD:**

In this stage of NAFLD, fat starts to accumulate in **5% or more** of liver cells. This condition, known as **simple steatosis**, is characterized by fat buildup without noticeable inflammation or liver cell damage. Importantly, this phase is **reversible** through lifestyle adjustments such as improved dietary habits and regular physical activity.

Factors such as obesity, insulin resistance, and an unhealthy diet are known contributors to NAFL.

**Nonalcoholic steatohepatitis:**

**Non-alcoholic steatohepatitis (NASH)** is a progressive form of non-alcoholic fatty liver disease (NAFLD) that extends beyond simple fat accumulation in hepatocytes. It is characterized by the presence of hepatic steatosis accompanied by inflammation, hepatocyte ballooning, and varying degrees of fibrosis. Unlike simple steatosis, which is often reversible and clinically less

significant, NASH represents a more severe stage that poses a higher risk of progression to cirrhosis, liver failure, and hepatocellular carcinoma. The pathophysiology of NASH is complex and is strongly associated with metabolic abnormalities such as insulin resistance, obesity, dyslipidemia, and type 2 diabetes mellitus. Histologically, NASH is defined by the coexistence of lipid droplets within hepatocytes, lobular inflammation, and cell injury, often progressing silently until advanced damage occurs. Because of its asymptomatic nature and potential for severe outcomes, NASH is considered a critical stage in the NAFLD spectrum, demanding early detection and timely intervention.

**Cirrhosis:**

**Cirrhosis** represents the advanced stage of chronic liver injury that follows persistent inflammation and fibrosis seen in NASH. It is characterized by extensive scarring of the liver tissue, distortion of the normal hepatic architecture, and the formation of regenerative nodules. As scar tissue replaces functional hepatocytes, the liver gradually loses its ability to perform essential metabolic and detoxification processes. Clinically, cirrhosis may remain silent in its compensated stage, but as the disease progresses to decompensated cirrhosis, patients can present with complications such as portal hypertension, ascites, variceal bleeding, hepatic encephalopathy, and impaired synthetic function, including reduced albumin and clotting factor production. This stage marks a significant decline in liver function and is associated with increased morbidity and mortality. Cirrhosis also substantially raises the risk of hepatocellular carcinoma, making it a critical turning point in the NAFLD spectrum where medical management often becomes insufficient and liver transplantation may be the only curative option.

**Hepatocellular carcinoma:**

**Hepatocellular carcinoma (HCC)** is the terminal stage in the progression of chronic liver disease, including NAFLD-related cirrhosis. It is a primary malignancy of the liver that arises due to persistent hepatocyte injury, chronic inflammation, and regenerative nodule formation in the cirrhotic liver. Over time, genetic and molecular alterations caused by oxidative stress, lipid peroxidation, and ongoing fibrosis drive malignant transformation of hepatocytes. Clinically, HCC often develops insidiously and may remain asymptomatic until advanced stages, where patients present with weight loss, abdominal pain, jaundice, or signs of liver decompensation. The prognosis of HCC is generally poor, as it is frequently diagnosed late, and treatment options are limited. Curative interventions such as surgical resection, radiofrequency ablation, or liver transplantation are feasible only in selected patients, while others may require systemic therapies or palliative care. The development of HCC in NAFLD patients underscores the seriousness of the disease spectrum and highlights the need for early diagnosis and long-term monitoring.

**EPIDEMIOLOGY OF THE NAFLD:**

Pooled prevalence of NAFLD globally is 25.24% with wide geographical variation across the world. Highest prevalence rates—mostly ultrasound based—has been reported from Middle East and South American countries (around 30%) whereas the limited number of studies from Africa reports a much lower prevalence (13%) Majority of the studies on NAFLD epidemiology, however, has been from the USA and North America with a NAFLD prevalence rate of 21–24.7%.

Studies using serum markers generally report a lower prevalence of NAFLD compared to imaging-based assessments. In Europe, a meta-analysis of studies published up to 2015 found a prevalence of around 24%. In terms of absolute numbers, NAFLD represents a substantial public health challenge, affecting approximately 64 million people in the USA and 52 million in Europe. In Asia, due to its large and rapidly growing population, urbanization, economic development, and lifestyle changes, the burden of NAFLD is rising even faster than in Western countries and is expected to account for a major share of the global NAFLD cases in the coming years.

The prevalence of NAFLD varies widely across Asia due to differences in economic development, diet, lifestyle, and potential genetic factors. Reported rates range from 12.5– 38% in Mainland China, 23–26% in Japan, 27% in Korea, 12–51% in Taiwan, 28% in Hong Kong, 9–32% in India, and 5–30% in other South and Far East Asian countries (Sri Lanka, Malaysia, Indonesia). A noteworthy aspect in Asia is the phenomenon of “lean” or “non-obese” NAFLD, which accounts for about 10% of cases. Initially observed in Asian populations, this highlights the tendency of Asians to develop metabolic syndrome-related conditions even at body measurements below the conventional thresholds for obesity. In these “lean” individuals, NAFLD arises from an expanded adipose tissue distribution not captured by traditional metrics, but the clinical outcomes follow a similar pattern as in typical NAFLD cases.

**RISK FACTORS OF NAFLD:**

Individuals with NAFLD often exhibit features of metabolic syndrome and related cardiovascular risk factors. As mentioned earlier, NAFLD is strongly linked to metabolic syndrome, with obesity, type 2 diabetes, and dyslipidemia being key risk factors. Research has shown that patients with NAFLD have an increased prevalence of cardiovascular disease, regardless of whether they have

diabetes. NAFLD is commonly associated with an unhealthy lifestyle, and evidence suggests that lifestyle modifications can lower liver enzyme levels and improve NAFLD outcomes. In patients with type 2 diabetes, the prevalence of peripheral vascular, coronary, and cerebrovascular diseases is higher in those with NAFLD compared to those without, independent of traditional cardiovascular risk factors, medications, and diabetes-related variables. Numerous studies, both prospective and retrospective, have confirmed a clear and ongoing association between NAFLD and cardiovascular disease.

The link between NAFLD and smoking remains controversial. Smoking is generally recognized as a major risk factor for chronic non-communicable diseases such as cancer, type 2 diabetes, and cardiovascular and respiratory conditions worldwide. Experimental studies in obese rats have shown that cigarette smoke can worsen the histological severity of NAFLD. Some human studies indicate that smokers with NAFLD are more likely to have significant or advanced liver fibrosis compared to non-smokers. A systematic review and meta-analysis suggest a strong association between smoking and NAFLD, highlighting the need for further research into the underlying mechanisms. While smoking has been considered an independent risk factor for NAFLD development, some studies report no significant difference in NAFLD prevalence between smokers and non-smokers, even among heavy smokers.

**SIGNS AND SYMPTOMS:**

Most patients with NAFLD remain asymptomatic, though some may report fatigue, discomfort in the right upper abdominal quadrant, enlarged liver, acanthosis nigricans, or lipomatosis. A notable number of patients who progress to cirrhosis may present with signs of end-stage liver disease. NASH can also be asymptomatic in a large proportion of cases, often being identified incidentally during medical evaluations for unrelated issues. While overt signs of chronic liver failure are uncommon in this group, studies have reported that splenomegaly is present in about a quarter of patients at the time of diagnosis.

NAFLD or NASH is frequently detected due to abnormal liver function tests, particularly elevated aminotransferases (ALT and AST), or as an incidental finding of hepatic steatosis on imaging studies. Physical examination may sometimes reveal hepatomegaly, which is attributable to fat accumulation within the liver.

**CURRENT TREATMENT FOR THE NAFLD:**

**Vitamin E:**

The antioxidant properties of Vitamin E are believed to play a key role in its beneficial outcomes, as shown in randomized trials reporting significant improvements in NASH.

The primary endpoint was defined as histological improvement, characterized by a reduction of at least 1 point in hepatocellular ballooning without any worsening of fibrosis, along with either a decrease in the NAFLD activity score (NAS) to ≤3 or a reduction of at least 2 points, including at least a 1-point decrease in lobular inflammation or steatosis.

**Pioglitazone:**

Although the PPAR-γ agonist Pioglitazone (30 mg/day) did not achieve the pre-specified primary endpoint in the PIVENS trial—set at a significance threshold of $p = 0.025$ due to two primary comparisons—34% of patients in the Pioglitazone group versus 19% in the placebo group ($p = 0.04$) demonstrated histological improvement as defined by the study criteria. Notably, resolution of definite NASH occurred in 47% of patients receiving Pioglitazone compared to 21% in the placebo group ($p = 0.001$). Similar to Vitamin E, Pioglitazone did not have a significant effect on fibrosis. While overall adverse events were not increased, patients in the Pioglitazone arm experienced a mean weight gain of +4.7 kg at week 96. This weight gain, however, may be linked to its therapeutic mechanism, involving lipid redistribution and expansion of subcutaneous fat stores.

**GLP-1 agonist:**

In a 72-week, double-blind phase 2 trial including 320 patients with biopsy-proven NASH and fibrosis stage 1–3, the glucagon-like peptide-1 receptor agonist semaglutide demonstrated a significantly greater rate of NASH resolution without worsening of fibrosis compared to placebo. While fibrosis improvement was observed in 43% of patients receiving semaglutide versus 33% in the placebo group, this difference did not reach statistical significance. Interestingly, about 38% of participants did not have diabetes mellitus, though all had a BMI greater than 25. It is also noteworthy that the doses of semaglutide used in this trial (0.1, 0.2, or 0.4 mg once daily) were considerably higher than those typically prescribed for its primary indication, type 2 diabetes. DPP-4 inhibitors and SGLT2 inhibitors:

Research on the use of DPP-IV inhibitors in NAFLD has consistently produced unsatisfactory outcomes. As a result, these agents are not recommended for the treatment of NAFLD, except when prescribed for their approved indications. In contrast, research on sodium-glucose cotransporter 2 (SGLT2) inhibitors has consistently demonstrated a decrease in liver transaminase levels along with improvements in imaging-based biomarkers. This suggests that SGLT2 inhibitors could represent a potential therapeutic option for NAFLD, not only in patients with diabetes but also in non-diabetic individuals. However, larger randomized clinical trials are still required to validate these findings.

**PPAR agonist:**

Besides the PPARγ agonist Pioglitazone, which is already included in international guidelines, research has also explored the effects of PPARδ, PPARα/δ, PPARα/γ, and more recently, pan-PPAR agonists. The PPARδ agonist seladelpar has demonstrated improvements in liver enzyme levels, though no changes were observed in hepatic fat content as assessed by MRI-PDFF, and a full manuscript has yet to be released. Elafibranor, a dual PPARα/δ agonist, failed to achieve its primary endpoint of NASH resolution in the large Phase III RESOLVE-IT trial.

## CONCLUSION

NAFLD is a highly common hepatic ailment. Although there is an initial elevated risk of cardiovascular events in individuals with NAFLD, certain patients may develop acute fibrosis or possibly cirrhosis, which increases the risk of hepatic decompensation and liver-related deaths. For the management of NAFLD, there are currently few pharmaceutical treatments available; the mainstays of any therapeutic plan are exercise, decreasing weight, and a balanced diet. Pharmaceutical therapies now in use include pioglitazone and vitamin E.

## REFERENCES

1. Pouwels S, Sakran N, Graham Y, Leal A, Pintar T, Yang W, et al. Non-alcoholic fatty liver disease (NAFLD): a review of pathophysiology, clinical management and effects of weight loss. BMC Endocrine Disorders [Internet]. 2022 Mar 14;22(1).
2. Ahmed A, Wong RJ, Harrison SA. Nonalcoholic fatty liver disease review: diagnosis, treatment, and outcomes. Clin Gastroenterol Hepatol. 2015;13(12):2062–70.
3. Machado MV, Diehl AM. Pathogenesis of nonalcoholic Steatohepatitis. Gastroenterology. 2016;150(8):1769–77.
4. Nasr P, Ignatova S, Kechagias S, Ekstedt M. Natural history of nonalcoholic fatty liver disease: a prospective follow-up study with serial biopsies. Hepatol Commun. 2018;2(2):199–210.
5. Nasr P, Ignatova S, Kechagias S, Ekstedt M. Natural history of nonalcoholic fatty liver disease: a prospective follow-up study with serial biopsies. Hepatol Commun. 2018;2(2):199–210.
6. Browning JD, Szczepaniak LS, Dobbins R, Nuremberg P, Horton JD, Cohen JC, et al. Prevalence of hepatic steatosis in an urban population in the United States: impact of ethnicity. Hepatology (Baltimore, Md). 2004;40(6):1387–95.
7. Chalasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice guideline by the American Gastroenterological Association, American Association for the Study of Liver Diseases, and American College of Gastroenterology. Gastroenterology. 2012;142(7):1592–609.
8. Dixon JB, Bhathal PS, O'Brien PE. Nonalcoholic fatty liver disease: predictors of nonalcoholic steatohepatitis and liver fibrosis in the severely obese. Gastroenterology. 2001;121(1):91–100.
9. Erbas O, Erdogan MA, Khalilnezhad A, Gürkan FT, Yiğittürk G, Meral A, et al. Neurobehavioral effects of long-term maternal fructose intake in rat offspring. Int J Dev Neurosci. 2018;69:68–79.
10. Lau JK, Zhang X, Yu J. Animal models of non-alcoholic fatty liver disease: current perspectives and recent advances. J Pathol. 2017;241(1):36–44.
11. Day CP, Saksena S. Non-alcoholic steatohepatitis: definitions and pathogenesis. J Gastroenterol Hepatol. 2002;17(Suppl 3):S377–84.
12. Pandey S. Preliminary phytochemical screening and in vitro antibacterial activity of Bauhinia variegata Linn. against human pathogens. Asian Pacific Journal of Tropical Disease. 2015 Feb;5(2):123–9.
13. RajKapoor B, Jayakar B, Murugesh N, Sakthisekaran D. Chemoprevention and cytotoxic effect of Bauhinia variegate against N-nitrosodiethylamine induced liver tumors and human cancer cell lines. J Ethnopharmacol 2006; 104: 407- 409.
14. Balamurugan G and Muralidharan P. Antiobesity effect of Bauhinia variegata bark extract on female rats fed on hypercaloric diet. Bangladesh J Pharmacol 2010; 5: 8- 12.
15. Sharma RK, Rajani GP, Sharma V, Komala N. Effect of ethanolic and aqueous extracts of Bauhinia variegata Linn. on gentamicin-induced nephrotoxicity in rats. Ind J Pharm Edu Res 2011 ; 45(2):192-198.
16. Surendra BH and Alpana R. Hepatoprotective properties of Bauhinia variegata bark extract. The Pharmaceutical Society of Japan 2007; 127(9): 1503-1507.
17. Rajkapoor B, Jayakar B, Anandar R and Kavimani S. Antiulcer effect of Bauhinia variegata Linn. in rats. Journal of Natural

Remedies 2003; 3(2): 215-217.
18. Ou H, Fu Y, Liao W, Zheng C, Wu X. Association between smoking and liver fibrosis among patients with nonalcoholic fatty liver disease. Can J Gastroenterol Hepatol. 2019;2019:6028952
19. Dr K.R. Khandelwal , Practical Pharmacognosy Techniques andExperiments , Nirali prakashan page no. 25.1 – 25.8
20. Ci chandharan Kavitha and G Indira Quantitative estimation of total phenolic, flavonoids, tannin and chlorophyll content of leaves of Strobilanthes Kunthiana (Neelakurinji) Journal of Medicinal Plants Studies 2016; page no.282-286.
21. Kumar P, Shailesh Baraiya, Gaidhani SN, Gupta MD, Wanjari MM. Antidiabetic activity of stem bark of Bauhinia variegata in alloxan-induced hyperglycemic rats. Journal of Pharmacology and Pharmacotherapeutics 2012.

How to cite this article:
Muskan Jain et al. Ijppr.Human, 2026; Vol. 32 (4): 720-725.
Conflict of Interest Statement: All authors have nothing else to disclose.