Zoology, Ecology and Pharma Advances
Content Available at www.uniquepubinternational.com/journals
(An International online peer reviewed Journal) ISSN (O): XXXX-XXXX

Review Article
OPEN ACCESS

PHARMACOLOGICAL MANAGEMENT OF HYPERTENSION IN TYPE 2 DIABETIC PATIENTS: DRUG SELECTION, TREATMENT GUIDELINES, INTERACTIONS, AND SAFETY

YERUVA VENKATA LAKSHMI KEERTHY

Department of Pharmacy Practice, Hindu College of Pharmacy.

Article History: Received: 04 Feb 2026, Revised: 03 Apr 2026, Accepted: 22 Apr 2026

***Corresponding author**
Yeruva Venkata Lakshmi Keerthy

Abstract
Alcohol consumption is a major global determinant of liver disease, spanning a spectrum from reversible steatosis to progressive fibrosis, cirrhosis, and hepatocellular carcinoma. The relationship between the amount, pattern, and duration of alcohol exposure and liver injury is influenced by host genetics, comorbid metabolic disease, nutritional status, gut–liver axis perturbations, and coexisting hepatic insults such as viral hepatitis. This review synthesizes current knowledge on epidemiology, pathophysiology, clinical presentation, diagnostic biomarkers, management strategies, and prevention approaches for alcohol-related liver injury. It highlights mechanisms-including ethanol metabolism, oxidative stress, immune activation, and fibrogenesis-that mediate hepatocellular damage and examines modifiers that shape individual susceptibility. Finally, we outline evidence-based clinical approaches and gaps that require future research.

Keywords: *Alcohol Consumption; Alcoholic Liver Disease; Alcoholic Hepatitis; Steatosis; Fibrosis; Biomarkers; Pathogenesis; Management; Prevention.*

INTRODUCTION

Alcohol-associated liver disease (ALD) remains one of the leading causes of chronic liver disease globally. Alcohol's hepatotoxic effects depend not only on quantity but pattern (binge vs chronic), beverage type, nutritional context, and host susceptibility. While simple steatosis can develop within days of heavy consumption and is often reversible after abstinence, repeated exposure can progress to alcoholic hepatitis (AH), fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). The public-health burden is substantial: alcohol contributes heavily to morbidity and premature mortality, particularly among young adults [1–4].

EPIDEMIOLOGY AND BURDEN

Global studies estimate alcohol use is responsible for a sizeable fraction of liver-related deaths and disability-adjusted life years (DALYs). Analyses from the Global Burden of Disease and WHO show that alcohol-attributable liver disease is concentrated in low- and middle-income regions but remains a major problem worldwide. Trends in several high-income countries indicate increasing ALD-related hospitalizations and liver-transplant listings in recent decades. Population-level risk is not evenly distributed-patterns of heavy episodic drinking and poor access to treatment for alcohol-use disorders (AUDs) amplify the impact [2–5].

SPECTRUM OF ALCOHOL-RELATED LIVER INJURY

ALD comprises a continuum:

Alcoholic fatty liver (steatosis): early accumulation of triglycerides in hepatocytes; often asymptomatic and rapidly reversible with abstinence [6].

Alcoholic steatohepatitis / alcoholic hepatitis (AH): inflammation and hepatocellular injury superimposed on steatosis; can present acutely with jaundice and systemic inflammation; severe AH carries high short-term mortality [7].

Alcohol-associated fibrosis and cirrhosis: progressive deposition of extracellular matrix causing architectural distortion and portal hypertension [8].

Hepatocellular carcinoma (HCC): long-term risk increased in cirrhosis from alcohol, often combined with other carcinogenic exposures [9].

Progression through this spectrum is not inevitable-many drinkers develop only steatosis-but certain exposures and host factors increase risk of progression (see "Modifiers of Susceptibility").

PATHOPHYSIOLOGY: HOW ALCOHOL HARMS THE LIVER

Ethanol metabolism and toxic intermediates

Hepatocytes metabolize ethanol mainly via alcohol dehydrogenase (ADH) and cytochrome P450 2E1 (CYP2E1), producing acetaldehyde and reactive oxygen species (ROS). Acetaldehyde forms adducts with proteins and DNA, impairing cellular function and promoting inflammation and mutagenesis. CYP2E1 induction during chronic heavy drinking amplifies oxidative stress and lipid peroxidation [10, 11].

Oxidative stress and mitochondrial dysfunction

ROS generation overwhelms antioxidant defenses, damaging mitochondrial DNA and membranes, impairing β-oxidation, and promoting steatosis and cell death. Oxidative stress also triggers stellate-cell activation and fibrogenesis [12].

Gut–liver axis and innate immune activation

Alcohol and its metabolites disrupt gut-barrier integrity, increasing translocation of bacterial products (LPS) to the portal circulation. Kupffer cells sense LPS via TLR4 and release pro-inflammatory cytokines (TNF-α, IL-1β, IL-6), promoting hepatocellular injury and neutrophil recruitment in AH. Chronic immune activation contributes to progression from inflammation to fibrosis [13–15].

Hepatic stellate cells and fibrogenesis

Persistent hepatocyte injury and inflammatory signaling lead to stellate-cell transdifferentiation into myofibroblasts that secrete collagen I and III, driving fibrosis. TGF-β signaling is central to this process and up-regulated in chronic alcohol exposure [12, 16].

Apoptosis, necroinflammation, and regeneration failure

Alcoholic hepatitis features widespread hepatocyte ballooning, Mallory–Denk bodies, and mixed apoptosis/necrosis. Impaired regenerative capacity in severe AH contributes to liver failure [7, 17].

MODIFIERS OF SUSCEPTIBILITY

Not all heavy drinkers develop advanced disease. Major modifiers:

Amount & pattern: cumulative intake and binge frequency increase risk [18].

Sex: women are more susceptible at lower doses [19].

Genetics: PNPLA3, TM6SF2, MBOAT7 variants modulate risk [20].

Coexisting disease: viral hepatitis, obesity, diabetes, iron overload accelerate fibrosis [21].

Nutrition: malnutrition and vitamin deficiency worsen outcomes [13, 22].

Smoking/other toxins: additive hepatotoxic effects [23].

CLINICAL PRESENTATION AND DIAGNOSIS

Presentation ranges from asymptomatic enzyme elevation to decompensated cirrhosis. AH often manifests with jaundice, fever, and tender hepatomegaly after heavy use.

Laboratory findings – AST > ALT (ratio > 2) [24]; elevated GGT & bilirubin, prolonged INR, hypoalbuminemia.

Imaging – ultrasound/CT/MRI show steatosis or nodularity; elastography estimates fibrosis.

Biopsy – steatosis, ballooning, Mallory–Denk bodies, neutrophilic infiltration.

Biomarkers:

Direct: EtG, EtS, PEth for recent/chronic use [25–27].

Indirect: GGT, MCV, AST, ALT, CDT [26].

INTERACTIONS WITH NAFLD AND CO-FACTORS

Metabolic dysfunction and alcohol frequently coexist. Even moderate alcohol may worsen NAFLD and fibrosis. Conversely, metabolic risk factors potentiate alcohol toxicity [28–30]

MANAGEMENT

Abstinence & AUD therapy

Abstinence is the cornerstone; it improves survival across stages. Effective AUD therapy (naltrexone, acamprosate, baclofen) plus psychosocial support are vital [31–33].

Nutrition

Address malnutrition, optimize protein/calories, correct thiamine and micronutrient deficits [13, 22].

Specific therapy for AH

Corticosteroids: prednisolone for severe AH (Maddrey DF ≥ 32) [7, 34].

Other agents: pentoxifylline and anti-TNF not recommended [7, 35].

Supportive: treat infection, manage coagulopathy and renal injury.

Antifibrotic & experimental

Investigational therapies include FXR agonists, anti-IL-1 agents, and microbiome modulation [36].

Liver transplantation

Indicated for end-stage ALD or refractory AH; early transplant may be considered [37].

PROGNOSIS

Severity and prognosis are assessed by Maddrey DF, MELD, Lille, and Child–Pugh scores [7, 38].

PUBLIC HEALTH, PREVENTION, AND POLICY

Population-level control measures: taxation, minimum pricing, advertising limits, and health warnings [40]. Screening and brief interventions in primary care reduce risky drinking [2, 31, 38].

FUTURE DIRECTIONS

Research priorities:

- Identify genetic / microbiome predictors of progression
- Develop robust early biomarkers [25, 18]

- Test novel immunomodulatory and regenerative therapies
- Scale integrated hepatology–addiction models
- Evaluate policy impacts on ALD incidence

CONCLUSION

Alcohol consumption remains a leading, preventable cause of liver disease. Ethanol metabolism, oxidative stress, immune activation, and fibrogenesis drive injury, modulated by genetics and comorbidities. Abstinence, nutrition, and AUD care are central to management. Strong policy and ongoing research are essential to reduce global burden.

REFERENCES

1. Griswold MG, Fullman N, Hawley C, Arian N, Zimsen SRM, Tymeson HD, et al. Alcohol use and burden for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2018;392(10152):1015–35.
2. World Health Organization. Global status report on alcohol and health 2018. Geneva: WHO; 2018.
3. Rehm J, Mathers C, Popova S, Thavorncharoensap M, Teerawattananon Y, Patra J. Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders. Lancet. 2009;373(9682):2223–33.
4. Rehm J, Shield KD. Global burden of disease and the impact of alcohol. Biomedicines. 2019;7(4):99.
5. National Institute on Alcohol Abuse and Alcoholism (NIAAA). Surveillance Report #118: Apparent Per Capita Alcohol Consumption: National, State, and Regional Trends, 1977–2019. Bethesda (MD): NIAAA; 2020.
6. Stickel F, Hampe J. Genetic determinants of alcoholic liver disease. Gut Liver. 2017;11(2):173–87.
7. Crabb DW, Im GY, Szabo G, Mellinger JL, Lucey MR. Diagnosis and treatment of alcohol-associated liver diseases: 2019 practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2020;72(1):31–64.
8. Thursz MR, Kamath PS, Mathurin P, Szabo G, Shah VH. Alcohol-related liver disease: areas of consensus, unmet needs and opportunities for further study. J Hepatol. 2018;69(1):154–88.
9. Rehm J, Samokhvalov AV, Shield KD. Global burden of alcoholic liver diseases. Addiction. 2010;105(5):817–43.
10. Kale SR. Diabetes associated complicated disorders and its treatment a review article. World Journal of Current Medical and Pharmaceutical Research. 2023 Jul 22:99-106.
11. Zakhari S. Overview: how is alcohol metabolized by the body? Alcohol Res Health. 2006;29(4):245–54.
12. Zeng T, Zhang CL, Song FY, Zhao XL, Xie KQ. Molecular mechanisms of hepatotoxicity induced by alcohol: oxidative stress and mitochondrial dysfunction (Review). J Immunol Res. 2016;2016:1–9.
13. KOTHA P, Vasabhakthula NV, Undurthi C. A study on the effect of exacerbations on the quality of life of patients with chronic obstructive pulmonary disease. World Journal of Current Medical and Pharmaceutical Research. 2020 Dec 15:319-21.
14. Malnick SDH, Alin P, Katan MB, Levi Z. Alcohol, gut microbiome and liver: The role of the gut–liver axis in the pathogenesis of alcohol-related liver disease. Front Med (Lausanne). 2022;9:9783455.
15. Idalsoaga F, Kulkarni AV, Mousa OY, Arrese M, Arab JP. Alcoholic liver disease: pathogenesis, management, and novel targets for therapy. Front Med (Lausanne). 2020;7:448.
16. Tom AA, Antony N, Ashok P, PS MA, Jojo J. Assessment of patient knowledge, practice and adverse events of insulin administration and storage techniques in patients with diabetes. Journal of Innovations in Applied Pharmaceutical Science (JIAPS). 2023 Nov 30:42-6.
17. Shield KD, Parry C, Rehm J. Chronic diseases and conditions related to alcohol use. Addiction. 2013;108(6):989–1000.
18. Northcote J, Livingston M. Accuracy of self-reported drinking: observational study of differences between self-reported and actual alcohol consumption. Alcohol Alcohol. 2011;46(5):593–6.
19. Stickel F, Buch S, Lau K, Meyer C, Berg T, Ridinger M, et al. Genetic variation in the PNPLA3 gene is associated with alcoholic liver disease. Semin Liver Dis. 2015;35(2):170–92.
20. Chayanupatkul M, Liangpunsakul S. Alcoholic liver disease: Clinical aspects and treatment. World J Gastroenterol. 2014;20(44):15563–75.
21. European Association for the Study of the Liver (EASL). EASL Clinical Practice Guidelines on nutrition in chronic liver disease. J Hepatol. 2019;70(1):172–93.
22. Kaur M, Barwal A, Kumari S, Atteri S. Diabetes Mellitus: An Incisive Review. International Journal of Pharmaceutics and Drug Analysis.;4(11):494-504.
23. Peterson KP. Alcohol biomarkers: clinical utility and limitations. Ann Clin Biochem. 2004;41(Pt 6):116–27.
24. ARUP Laboratories. Alcohol Use Biomarkers: Choose the Right Test. Salt Lake City (UT): ARUP Consult; 2024.
25. Poojitha D, Narendra JB. Prevalence of comorbidities associated with COVID19 in andhra pradesh, India. International Journal of Pharmaceutics and Drug Analysis. 2020;8(10):1-4.
26. Basu VR, Shanthi G, Shirisha A. A review on recent trends of diabetes mellitus. Journal of Innovations in Applied Pharmaceutical Science (JIAPS). 2022 Jan 6:01-9.

27. Bryazka D, Reitsma MB, Griswold MG, et al. Population-level patterns of liver disease mortality attributable to alcohol use. Lancet Public Health. 2022;7(8):e633–43.
28. Mackowiak B, Mellinger JL, Hines IN. Alcohol and metabolic-associated fatty liver disease: interactions and implications. Clin Liver Dis (Hoboken). 2024;23(1):1–10.
29. World Health Organization. Recommendations for screening and brief interventions for hazardous and harmful alcohol use. Geneva: WHO; 2017.
30. Raju AK. Newer Insights of Relationship between Obesity and Pregnancy Complications-a single Centered Prospective Study. World Journal of Current Medical and Pharmaceutical Research. 2023 Jul 21:94-8.
31. Mathurin P, Louvet A, Duhamel A, Nahon P, Carbonell N, Boursier J, et al. Early liver transplantation for severe alcoholic hepatitis. N Engl J Med. 2011;365(4):403–11.
32. 32.Thursz M, Gual A, Lackner C. Treatment and prognosis of alcoholic hepatitis. Gastroenterology. 2016;150(1):183–94.
33. Shanmugam H, Liu Y, Sheth D, et al. Emerging therapies in alcohol-associated liver disease. Hepatology. 2022;76(3):1034–49.
34. Vyshnavi P, Venkatesh P. Review on diabetes mellitus. Journal of Innovations in Applied Pharmaceutical Science (JIAPS). 2022 Jan 26:24-7.
35. Saberi B, Dadabhai AS, Jang YY, Mezey E. Advances in clinical management of alcoholic liver disease. J Clin Transl Hepatol. 2016;4(3):206–15.
36. Khan A, Sheron N, Anand AC. Emerging and experimental therapies in alcoholic hepatitis. Clin Liver Dis. 2021;25(4):829–48.
37. World Health Organization. Cancer warning labels and stronger alcohol policy action: policy brief. Geneva: WHO; 2025.
38. AL-Habsi KA, AL-Mahdouri HN, Amaresh N, Mullaicharam AR. Retrospective Study on Diabetes Patients in Two Different Regions in Oman. International Journal of Pharmaceutics and Drug Analysis.;3(4):91-7.