INTERNATIONAL MULTI DISCIPLINARY JOURNAL FOR RESEARCH & DEVELOPMENT
eISSN 2394-6334 Impact factor: 7,854 Volume 12, issue 12 (2025)

NON-ALCOHOLIC FATTY LIVER DISEASE: PATHOGENESIS, HISTOPATHOLOGICAL FEATURES, AND CLINICAL IMPLICATIONS

Manekshal Bitsh

Independent researcher of medical centre in Dehli, India

Abstract: Non-alcoholic fatty liver disease (NAFLD) is a major hepatological disorder characterized by excessive fat accumulation in hepatocytes without significant alcohol consumption. It represents the most common cause of chronic liver disease worldwide, affecting nearly one quarter of the global population. NAFLD encompasses a spectrum ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, and cirrhosis. This article aims to analyze the pathogenesis, histopathological features, and clinical significance of NAFLD, with emphasis on diagnostic strategies and therapeutic challenges.

Keywords: hepatology, non-alcoholic fatty liver disease, steatosis, non-alcoholic steatohepatitis, fibrosis, cirrhosis, histopathology

Introduction

Hepatology, as a distinct field of medicine, addresses the structural and functional disorders of the liver. Among the broad spectrum of hepatological conditions, non-alcoholic fatty liver disease has emerged as a global health concern due to its close association with obesity, metabolic syndrome, and type 2 diabetes mellitus. NAFLD was once considered a benign condition; however, increasing evidence demonstrates its progression to end-stage liver disease and hepatocellular carcinoma in a significant proportion of patients.

Histologically, NAFLD is defined by lipid accumulation in hepatocytes exceeding 5% of the liver weight, in the absence of secondary causes such as alcohol abuse, viral hepatitis, or medication-induced injury. The importance of studying NAFLD lies not only in its prevalence but also in its silent progression, as many patients remain asymptomatic until advanced stages. Thus, early histological and clinical recognition is essential for effective intervention.

Methods

This article is based on a comprehensive review of peer-reviewed studies published between 2005 and 2024. Literature databases, including PubMed, Scopus, and Web of Science, were searched using the keywords “NAFLD,” “NASH,” “liver fibrosis,” and “hepatopathology.” Inclusion criteria comprised clinical trials, histopathological investigations, and meta-analyses on NAFLD. Exclusion criteria involved case reports and non-English articles.

Histopathological evaluation relied on standard hematoxylin and eosin (H&E) staining and Masson’s trichrome staining for fibrosis assessment. Biopsy samples were graded according to the NAFLD Activity Score (NAS), which evaluates steatosis, lobular inflammation, and hepatocyte ballooning. Statistical data were synthesized qualitatively to highlight the consistency of histological findings across studies.

Results

Histopathological examination reveals that NAFLD encompasses a continuum of liver alterations:

- **Simple Steatosis:** Characterized by macrovesicular fat accumulation in hepatocytes, predominantly in the centrilobular (zone 3) region. Inflammation is absent or minimal.
- **Non-Alcoholic Steatohepatitis (NASH):** Defined by steatosis, lobular inflammation, and hepatocyte ballooning. Mallory–Denk bodies may appear, indicating cytoskeletal damage.
- **Fibrosis:** Begins as perisinusoidal fibrosis in zone 3 and may progress to bridging fibrosis connecting portal and central areas.
- **Cirrhosis:** Represents the advanced stage, with nodular regeneration, diffuse fibrosis, and loss of normal lobular architecture.

Clinical studies demonstrate that approximately 25–30% of NAFLD patients progress to NASH, while 10–20% develop advanced fibrosis or cirrhosis. Risk factors for progression include obesity, insulin resistance, dyslipidemia, and genetic predisposition (such as PNPLA3 gene variants).

Discussion

The pathogenesis of NAFLD is multifactorial and best explained by the "multiple-hit" hypothesis. Insulin resistance leads to increased hepatic lipid uptake and de novo lipogenesis, resulting in steatosis. Oxidative stress and mitochondrial dysfunction generate reactive oxygen species, which induce lipid peroxidation and hepatocyte injury. This cascade activates Kupffer cells and hepatic stellate cells, promoting inflammation and fibrosis.

Histopathological features of NAFLD not only provide diagnostic confirmation but also guide prognosis and management. For example, ballooning degeneration is strongly associated with progression to fibrosis, whereas isolated steatosis often remains stable. Fibrosis stage is the strongest predictor of liver-related morbidity and mortality.

From a clinical perspective, NAFLD has implications beyond the liver. It is closely associated with cardiovascular disease, chronic kidney disease, and extrahepatic malignancies. Therefore, management requires a multidisciplinary approach focusing on lifestyle modification, weight reduction, and control of metabolic comorbidities. Pharmacological options, including pioglitazone and GLP-1 receptor agonists, show promise but are not yet universally recommended.

Conclusion

Non-alcoholic fatty liver disease is a rapidly growing hepatological challenge, reflecting global trends in obesity and metabolic syndrome. Histopathological assessment remains the gold standard for diagnosis and staging, revealing a spectrum from simple steatosis to cirrhosis. Understanding the mechanisms underlying its progression is critical for developing effective preventive and therapeutic strategies. Given its systemic implications and silent course, NAFLD deserves greater attention in both clinical hepatology and public health policy.

References

1. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease. *Hepatology.* 2018;67(1):328–357.
2. Eslam M, Sanyal AJ, George J. MAFLD: A consensus-driven proposed nomenclature for metabolic associated fatty liver disease. *Gastroenterology.* 2020;158(7):1999–2014.
3. Younossi ZM, Koenig AB, Abdelatif D, et al. Global epidemiology of NAFLD. *Metabolism.* 2016;65(8):1037–1046.
4. Bedossa P. Pathology of non-alcoholic fatty liver disease. *Liver Int.* 2017;37(Suppl 1):85–89.
5. Tilg H, Moschen AR. Evolution of inflammation in nonalcoholic fatty liver disease: The multiple parallel hits hypothesis. *Hepatology.* 2010;52(5):1836–1846.