

Review of Treatment Options for Nonalcoholic Fatty Liver Disease

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KEYWORDS

• NAFLD • NASH • Epidemiology • Diagnosis • Treatment

KEY POINTS

- Nonalcoholic fatty liver disease (NAFLD) has become the most common cause of chronic liver disease in the United States and other western countries, and its prevalence has mirrored the rising obesity and diabetes mellitus epidemics.
- Among those with NAFLD, patients with nonalcoholic steatohepatitis (NASH) represent a large potential public health concern with risk for development of cirrhosis and hepatocellular carcinoma.
- NAFLD is characterized by hepatic steatosis as determined by imaging (ultrasound, MRI, or CT) or histology from liver biopsy.
- Patients are commonly first diagnosed by mild (1.5-fold to 4-fold) elevations in their serum aminotransferase, alanine aminotransferase, and aspartate aminotransferase, and/or by incidental radiographic evidence of steatosis.
- Although the future of NAFLD and NASH treatment has many promising agents, clinicians are currently faced with limited options and an emphasis on lifestyle modification.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD), a major cause of chronic liver disease globally, encompasses a vast spectrum of disease that spans from isolated fatty liver (IFL) to nonalcoholic steatohepatitis (NASH), which is defined by necroinflammation with

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hepatocyte injury and ballooning, along with a variable amount of fibrosis and potential for progression to cirrhosis. Over the past few decades, a rising NAFLD prevalence has reflected increasing obesity prevalence, suggesting a strong correlation between NAFLD and the escalating global obesity epidemic. Many experts now consider NAFLD to be a hepatic manifestation of metabolic syndrome, which is defined by the presence of three of the following: visceral obesity, elevated fasting plasma glucose, hypertension, hypertriglyceridemia, or low high-density lipoprotein levels.¹ This article details the pathogenesis of NAFLD, with an emphasis on the steps that result in the NASH phenotype, along with the current state of diagnosis and treatment of this common chronic liver disease.

EPIDEMIOLOGY

Global NAFLD prevalence rates range from 2.8% to 46%.^{2,3} With time, NAFLD has become the most common cause of chronic liver disease in the United States and other western countries, and its prevalence has mirrored the rising obesity and diabetes mellitus (DM) epidemics. Recent global analysis estimates 1.5 million adults are overweight with a body mass index (BMI) of 25 kg/m² or greater, and 500 million adults are obese with a BMI of 30 kg/m² or greater.⁴ In the United States, approximately 33.8% of the population is obese and 10.6% have DM type 2.⁵

The National Health and Nutrition Examination Surveys (NHANES) performed in the United States from 1988 to 2008 showed stable prevalence rates for chronic liver diseases, such as hepatitis B, hepatitis C, and alcoholic liver disease. However, the prevalence of NAFLD dramatically increased from 5.5% to 11%. Overall, NAFLD represented approximately 47% of all chronic liver disease in 1988, rising to 75% by 2008.⁶ During this same time, the prevalence of several metabolic syndrome features, such as obesity, DM, insulin resistance (IR), and hypertension increased and, in one study, multivariate analysis found obesity to be an independent predictor of NAFLD.⁷

Estimating the true incidence and prevalence of NAFLD, specifically NASH, remains a challenge due both to the asymptomatic presentation of the disease as well as the lack of accurate and noninvasive diagnostic measurements. The prevalence of NAFLD was first estimated to be 36% in lean patients and 72% in obese patients in 1990 via autopsy. The prevalence of NASH in this same cohort was found to be 2.7% in lean patients and 18.5% in obese patients.⁸ The evaluation of patients undergoing bariatric surgery confirmed the high prevalence rates among obese populations in which the prevalence of NAFLD and NASH was found to be 91% and 37%, respectively.⁹ Of note, although NAFLD is strongly associated with obesity and other metabolic syndrome components, it can occur in patients without obesity and obesity does not guarantee the presence of NAFLD.

There have been several population based studies designed to ascertain NAFLD prevalence. In 2005, magnetic resonance spectroscopy (MRS) was used to identify asymptomatic steatosis in 31% of the 2100 adults in the Dallas Heart Study.¹⁰ In 2011, a prospective study using ultrasound (US) evaluated 328 asymptomatic middle-aged subjects from Texas and found a 46% prevalence of NAFLD. Subsequent liver biopsies in patients with NAFLD demonstrated a 12.2% prevalence of NASH.¹¹ Studies have suggested that ethnicity plays a role in the development of NAFLD, with Hispanics at greatest risk, followed by whites, and then African Americans.¹⁰⁻¹² In adults, NAFLD is most commonly diagnosed during the fourth decade of life for men and sixth decade of life for women.¹³ NAFLD is not only a disease of adults; it affects children and adolescents. Within these populations, NAFLD prevalence has proven to rise with increasing BMI.¹⁴

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