

Clinical and Economic Burden of Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis



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KEYWORDS

• Prevalence • Risk factors • Mortality • Health-related quality of life

KEY POINTS

- The prevalence of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) continues to increase around the world as a result of the increase in obesity and other metabolic disorders.
- The true incidences of NAFLD and NASH are unknown because of the lack of accurate noninvasive diagnostic methods and lack of awareness of this disease outside of gastroenterology and hepatology practices.
- The economic burden of NAFLD/NASH, which is projected to be immense, must be more precisely defined for an effective national and global strategy to deal with the epidemic of NAFLD-related liver disease.

THE EPIDEMIOLOGIC BURDEN OF NONALCOHOLIC FATTY LIVER DISEASE

Nonalcoholic fatty liver disease (NAFLD) is a complex liver disease, which affects up to one-quarter of the adult population in the world.^{1,2} In a recent meta-analysis, the worldwide prevalence of NAFLD was estimated to be 25.24% (95% confidence interval [CI]: 22.10–28.65).² This prevalence varied across the globe, with the highest prevalence reported in the Middle East and the lowest in Africa.² Interestingly, the prevalence of NAFLD in Asian countries seems to follow a rural-to-urban gradient,

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with lower prevalence rates reported from the rural areas of India and China and higher prevalence rates from the urban areas.³⁻⁵

In the United States, the prevalence of NAFLD varies according to ethnicity.⁶⁻¹⁵ NAFLD is more common among Mexican Americans when compared with non-Hispanic whites and non-Hispanic blacks.¹⁰ Even within an ethnic group, there are differences according to the country of origin.^{8,11-17} In one study, Hispanics of Mexican origin had a significantly higher prevalence of NAFLD compared with the Hispanics of Dominican and Puerto Rican origin.⁹ In contrast to Hispanic Americans, African Americans have a lower prevalence of NAFLD despite having a higher rate of metabolic conditions associated with NAFLD (obesity, type 2 diabetes mellitus, and hypertension).^{14,15,17} These variations in prevalence rates suggest a dual impact of genetic predisposition coupled with environmental factors playing a role in determining the risk for NAFLD.¹⁸⁻²⁶

As previously noted, NAFLD is considered the liver manifestation of metabolic syndrome and is highly associated with obesity, type 2 diabetes mellitus, hypertension, and hyperlipidemia.¹⁸ The data from the meta-analysis revealed that the prevalence of these comorbidities within people with NAFLD were high, which included obesity at 51.34% (95% CI: 41.38-61.20), type 2 diabetes at 22.51% (95% CI: 17.92-27.89), hyperlipidemia at 69.16% (95% CI: 49.91%-83.46%), hypertension at 39.34% (95% CI: 33.15-45.88), and metabolic syndrome at 42.54% (95% CI: 30.06-56.05).² As the prevalence of obesity and diabetes increases, the incidence and disease burden from NAFLD will continue to increase.²⁷⁻³³

Although most patients with NAFLD are obese, it is important to recognize that some patients with NAFLD are considered lean. A study using the National Health and Nutrition Examination Survey's data suggested that the prevalence of lean NAFLD in the United States general population was about 7.8%, comprising 17% of all NAFLD cases.³⁴ In contrast, lean NAFLD may be the predominant type of NAFLD in certain geographic areas.³⁻⁵ In one study, from rural India, lean NAFLD subjects comprised more than 50% of all NAFLD cases.³⁻⁵ These data suggest that factors other than obesity, such as environmental factors or gut microbiome, may contribute to the development of lean NAFLD in the Asian countries.

It is important to note that the minority of patients with NAFLD will progress to cirrhosis, hepatocellular carcinoma, and liver-related death. In this context, NAFLD has been divided into different histologic subtypes.³⁵⁻³⁸ Most long-term studies of NAFLD suggest that only patients with documented histologic evidence of non-alcoholic steatohepatitis (NASH), which comprises about 20% of NAFLD cases, are at the greatest risk for progression and adverse outcomes.^{28-34,39-44} In other words, most patients with NAFLD have non-NASH NAFLD and are primarily at risk for cardiovascular mortality.^{16,17,31,45-51} In contrast, about 15% to 20% of patients with NASH can have a progressive liver disease and may succumb to liver-related mortality.^{39-44,51} Although mostly nonprogressive, it is important to note that a few patients with non-NASH NAFLD may progress and develop NASH and advanced fibrosis.⁴⁰ In contrast, a few patients with NASH and even NASH-related fibrosis can regress.⁵⁰ The exact circumstances under which patients with NASH can progress or regress has not been well defined. Nevertheless, in general, the progressive course of NASH has been closely linked to the increasing number of metabolic comorbidities, especially type 2 diabetes mellitus^{34,45,47,52} (Figs. 1 and 2).

Finally, it is important to note that the risk of progressive liver disease for an individual patient with NAFLD is relatively small.² However, given the considerable prevalence of NAFLD in the United States, the total number of patients with

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