

Epidemiology of Nonalcoholic Fatty Liver Disease: A Primer

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Nonalcoholic fatty liver disease (NAFLD) encompasses the spectrum of disease entailing simple steatosis, nonalcoholic steatohepatitis (NASH) with fibrosis, and cirrhosis complicated by portal hypertension and hepatocellular carcinoma. NAFLD is currently one of the most prevalent liver diseases in the industrialized world, and although there has been increasing understanding of the underlying pathophysiological mechanisms, the knowledge of epidemiological estimates and trends continues to grow. This review aims to summarize the geographical characteristics, temporal trends, and natural history of NAFLD.

EPIDEMIOLOGY

Estimates of NAFLD prevalence and incidence vary widely based on the diagnostic modality, age, ethnic group, and geographic location. Although imaging is the most accessible diagnostic modality, ultrasonography and computed tomography have been found to underestimate both the presence of steatosis and NASH in comparison with histological assessments. Population-based studies are thought to more accurately estimate the true prevalence in the general population compared to biopsy or autopsy studies, possibly because of patient selection bias.

Table 1 summarizes the known prevalence estimates of NAFLD across geographic, diagnostic modality, and risk factors for disease. Worldwide, the median prevalence rate of NAFLD was estimated to be 20%, ranging from 6% to 33% worldwide and 10% to 35% in the United States.¹ A recent systematic review estimated an overall worldwide prevalence rate of 25.2%.² The geographic burden of NAFLD disproportionately affects industrialized countries, with higher prevalence attributed to higher burden of associated risk factors linked to NAFLD.³ In addition, race confers additional risk, as found in the Dallas Heart Study, which estimated a high NAFLD prevalence in Hispanic compared with white or black race.⁴ Although Asian ethnicity has been associated with a lower prevalence of NAFLD compared with Hispanic, black, or white ethnicities, the increasing prevalence of obesity and the metabolic syndrome coupled with genetic factors are thought to be the primary risk factors driving the increasing burden of NAFLD in Asian countries.¹ The prevalence rate of NAFLD among children is 3% to 10%, but 40% to 70% among obese children. In addition, the prevalence rate of NAFLD among children has increased in the past decade, from 3% to 5%.⁵

Abbreviations: NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis.

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TABLE 1. PREVALENCE ESTIMATES OF NONALCOHOLIC FATTY LIVER DISEASE

Classification	Group	NAFLD Prevalence in Group	Notes
Geographic	General population	6%-33%	
	North America	11%-46%	
	Europe	4%-49%	Incidence estimate: 29 per 100 000 person-years
	South America	27%-35%	
	Asia	15%-44%	Incidence estimate: 31--86 per 1000 person-years
	Saudi Arabia	15%-55%	
	Africa	9%-20%	
Diagnostic testing	Histology	20%-51%	
	Ultrasonography	17%-46%	Most readily available test but underestimates true prevalence
	Magnetic resonance spectroscopy	31%	
	Abnormal aminotransferase levels	7%-11%	Up to 79% of patients with NAFLD have normal aminotransferase levels
High-Risk Populations	Hispanic race	45%	Whites also higher prevalence rate than blacks (33% and 24%, respectively)
	Obesity	Up to 90%	51% with NAFLD have obesity
	Diabetes mellitus	69%	30%-50% with diabetes have NAFLD
	Dyslipidemia	50%	Up to 90% with dyslipidemia have NAFLD

However, less is known about the epidemiology of NASH, with general population prevalence rates estimated at 3% to 5%, but possibly as high as 12.2%.

TABLE 2. ASSOCIATED RISK FACTORS, COMORBIDITIES, AND COMPLICATIONS OF NONALCOHOLIC FATTY LIVER DISEASE

Host and Demographic Characteristics

Genetic factors
 Race: Hispanic-American, Mexican-American, non-Hispanic white
 Older age
 Male sex
 Asian race (lower incidence and prevalence)
 Children (lower incidence and prevalence)

Associated Lifestyle Factors

Obesity: elevated body mass index, visceral obesity
 Dietary: increased caloric intake, high carbohydrate and fat intake
 Decreased activity frequency

Associated Medical Conditions

Metabolic syndrome
 Type 2 diabetes mellitus
 Other chronic liver disease, especially alcohol use
 Cardiovascular: hypertension, dyslipidemia, acute coronary syndrome, stroke
 Other: hypothyroidism, hypopituitarism, hypogonadism, obstructive sleep apnea, polycystic ovarian syndrome

Hepatic Complications

NASH and associated cirrhosis
 Hepatocellular carcinoma

Extrahepatic Complications

Cardiovascular disease: coronary heart disease, stroke, hypertension
 Type 2 diabetes mellitus
 Chronic kidney disease
 Colorectal cancer: colonic adenoma and adenocarcinoma
 Obstructive sleep apnea
 Endocrinopathy: hypothyroidism, polycystic ovarian syndrome, osteoporosis

However, the prevalence of NASH has been estimated to be as high as 59.1% among individuals with NAFLD.²

NATURAL HISTORY

Individuals with simple steatosis progress to NASH and NASH-associated cirrhosis at estimated rate of only 1.7 per 1000 person-years, highlighting the finding that the majority of patients with NAFLD do not experience development of NASH.¹ A high frequency of remission from NAFLD was observed in the DIONYSOS study, with an observed remission rate of 55 per 1000 person-years (compared with an incidence rate of 18.5 per 1000 person-years) and with high alcohol consumption identified

as the primary risk factor for disease progression.⁶ However, a recent meta-analysis found that 59% of individuals with NAFLD had concomitant NASH, suggesting a higher progression risk than prior estimates.² The general population prevalence of NASH-related cirrhosis is unknown but remains the primary complication of prolonged hepatic inflammation associated with this disease. The incidence of hepatocellular carcinoma (HCC) caused by NAFLD, NASH, and NASH-related cirrhosis has been increasing in the United States and Japan, with advanced fibrosis being the strongest known risk factor for HCC development.⁷

The incidence of liver cirrhosis secondary to NAFLD and NASH is increasing and is currently the second-leading indication for liver transplantation in the United States. The proportion of adults with NASH-associated cirrhosis awaiting transplantation has increased by 170% between 2004 and 2013, and individuals awaiting liver transplantation have been found to have a lower 90-day survival compared with individuals with alcoholic liver disease or hepatitis C infection.⁸ Although liver-related mortality is common among patients with NAFLD, the leading cause remains cardiovascular disease, and therefore patient outcomes in fatty liver disease are closely linked to these metabolic conditions.³ In addition, extrahepatic diseases have also been associated with NAFLD and are summarized in Table 2.^{3,9} The pervasiveness of the risk factors for NAFLD and NASH is thought to play a role in its increasing prevalence and incidence.¹⁰

CONCLUSION

NAFLD represents a growing epidemic, requiring increased understanding of disease process to facilitate development of new treatments to prevent progression to end-stage liver disease. Robust public health interventions are also essential to affect the development of associated metabolic conditions such as obesity, diabetes mellitus, and hyperlipidemia and reduce their increasing incidence in the United States and across the globe. Further knowledge of epidemiological trends and patterns will allow for identification of at-risk populations, thus

facilitating development of public health–related interventions to reduce this burden of disease.

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