Nonalcoholic Fatty Liver Disease

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KEYWORDS

• Nonalcoholic fatty liver disease (NAFLD) • Nonalcoholic steatohepatitis (NASH)
• Liver disease • Metabolic disease • Dyslipidemia • Insulin resistance • Steatosis

KEY POINTS

- Nonalcoholic fatty liver disease (NAFLD) defines a condition of hepatic steatosis with or without hepatic injury.
- NAFLD is increasing in prevalence worldwide and presents a public health burden. Most patients are asymptomatic, although some present with fatigue and right upper quadrant pain.
- NAFLD is discovered incidentally when patients have elevated liver enzymes or fatty liver is seen on imaging modalities.
- Imaging studies can confirm fatty deposits in the liver, but needle biopsy is needed to determine degree of inflammation.
- The mainstay of treatment is weight loss and controlling diabetes and hyperlipidemia; liver transplantation is considered when disease progresses to cirrhosis.

DESCRIPTION

Nonalcoholic fatty liver disease (NAFLD) describes a condition of fatty infiltration of the liver in the absence of the other common cause of steatosis, heavy alcohol consumption, which is its own entity (ie, alcoholic liver disease). NAFLD is associated with metabolic risk factors such as diabetes mellitus, dyslipidemia, obesity, and in some cases genetic predisposition.[1,2] The clinical and histologic phenotypes of NAFLD extend from a nonalcoholic fatty liver to nonalcoholic steatohepatitis (NASH).

EPIDEMIOLOGY

NAFLD is a common liver disorder that has been gradually increasing worldwide. Prevalence of NAFLD ranges from 6.3% to 33.0%, whereas prevalence of NASH ranges

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from about 3% to 5%. NAFLD affects males more than females. Hispanics have a higher prevalence when compared with non-Hispanic Caucasians, whereas Blacks have a lower prevalence compared with both. Prevalence in Native Americans is also lower, ranging from 0.6% to 2.2%.[1–4] In Asians, however, the disease seems to manifest at a lower body mass index, and many patients do not have insulin resistance as determined by using conventional methods.[2]

DEFINITIONS

NAFLD is divided into 2 categories: nonalcoholic fatty liver and NASH. Nonalcoholic fatty liver describes hepatic steatosis without the significant inflammation that leads to hepatocellular injury or fibrosis. Nonalcoholic fatty liver is usually considered benign and reversible, with minimal risk of progression to cirrhosis or liver failure. In contrast, NASH refers to hepatic steatosis with inflammation and hepatic injury in the form of ballooning of hepatocytes and resulting cellular necrosis. Because NASH is a more severe stage of NAFLD, the risk of progression to cirrhosis, liver failure, and hepatocellular carcinoma, although rare, is higher.[3,4]

PATHOGENESIS

There is significant overlap between the pathologic processes seen in NAFLD and what is seen in alcoholic liver disease. The overlap is to such a degree that a biopsy alone is not able to specify which cause has led to the organic findings. Thus, history is very important to understanding the cause of hepatic steatosis in an undifferentiated patient. Although the 2 conditions have different pathways, they share many similarities. **Fig. 1** demonstrates where these processes overlap. Despite these findings, the treatment is significantly different and therefore attention to the patient's social history is of paramount importance. Pathogenesis can, however, have some overlap in the patient that has both processes cooccurring (eg, a patient with the metabolic syndrome who also abuses ethanol).

The pathogenesis of NAFLD is still being studied. Insulin resistance is the most widely supported key mechanism leading to hepatic steatosis and then steatohepatitis. Many support a 2-hit hypothesis for the progression of NAFLD to NASH, and ultimately, cirrhosis. The initial first hit is that fat gets deposited in hepatocytes. The deposition typically occurs in a macrovesicular pattern. Most authors believe this is brought about by globally active metabolic factors, namely, insulin resistance, central obesity, and fatty acid metabolism dysregulation. The second hit is thought to be the cause of the inflammation and later fibrosis. Oxidative stress plays an important role in this second hit. The process involves induction of cytochrome P450 enzymes that

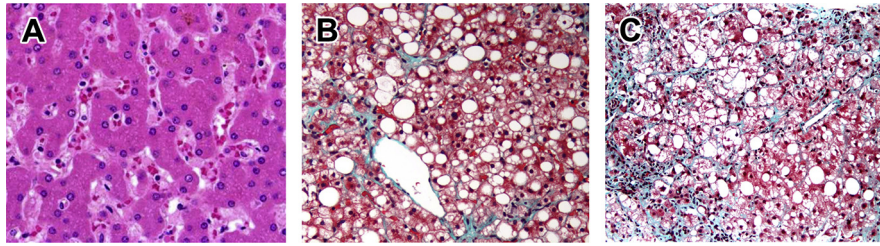

Fig. 1. Histology of (*A*) normal liver, (*B*) nonalcoholic steatosis (NAFLD), and (*C*) nonalcoholic steatohepatitis (NASH).