

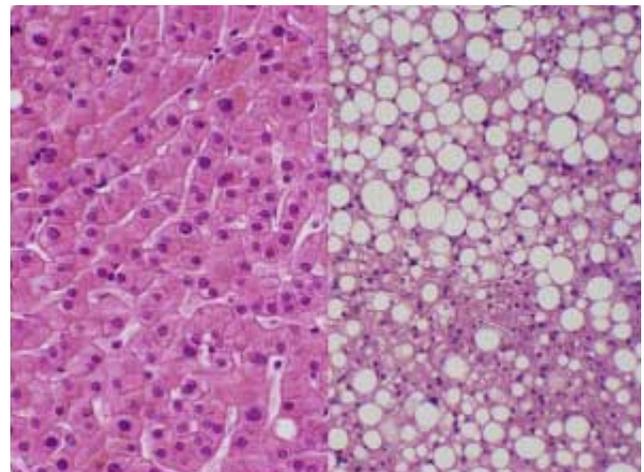
FATTY LIVER: The Epidemic Wolf in Sheep's Clothing, PART 1

Nonalcoholic fatty liver disease (NAFLD) has escalated to the number one liver disease in the United States. No longer just “fatty liver, or fatty liver with focal sparing” noted as almost an afterthought on imaging reports, it has now become an epidemic problem with potential for very real morbidity and mortality. Afflicting children and adults, its pathogenesis is multifactorial, but its increased prevalence strongly coincides with the mounting Western obesity rate. This issue of *The WCC Note* commences a two-part series on hepatic steatosis, beginning with reviews of its prevalence, pathology, and clinical consequences.

NAFLD Defined

How is nonalcoholic fatty liver disease defined?

1. NAFLD is defined as macrovesicular steatosis in more than 5% of hepatocytes (1) in the absence of significant ethanol consumption or other specific cause of liver disease.
2. NAFLD encompasses a spectrum of disease, ranging from:
 - a. Simple steatosis,
 - b. Steatohepatitis (NASH),
 - c. Fibrosis and cirrhosis, to
 - d. Hepatocellular carcinoma. (2)



Normal liver (left); fatty liver (right) (14)

NAFLD Prevalence

How many people have fatty liver?

1. An estimated 31 million Americans, 31% of men and 16% of women have NAFLD. It is thought to be the most plausible cause for the elevated serum aminotransferases and/or gamma glutamyl transpeptidase levels recorded in 24% of U.S. adults. (3)
2. The United States National Institutes of Health estimates that nonalcoholic steatohepatitis (NASH) affects 2% to 5% of Americans, with an additional 10% to 20% having fatty liver, i.e. hepatic fat without current inflammation or liver damage. (4)
3. The true prevalence in children is not known but is reported at 2.6% to 10% and from 8% to 80% in obese children. (5) NAFLD is reported as a common cause of liver disease in children and adolescents. (1, 6)

Who gets fatty liver?

1. The most common associations are:
 - a. Obesity is the number one cause. Eighty percent of patients with NAFLD are obese, and 80% of obese individuals have NAFLD.
 - b. Type 2 diabetes mellitus
 - c. Dyslipidemia (2)
2. NAFLD affects children, adolescents, (1, 6) and adults. It affects boys more than girls (1) and men and women equally. (3)
3. Insulin resistance is reported as almost universal in adult NAFLD and highly prevalent in afflicted children and adolescents. (1)
4. Both genetic and environmental factors are thought to be responsible for the major ethnic variations in prevalence. (1) Recently, for example, variants in the apolipoprotein C3 gene have shown association with NAFLD. (7)
5. The current Western diet, high in saturated fats and fructose, is considered highly responsible. (8)

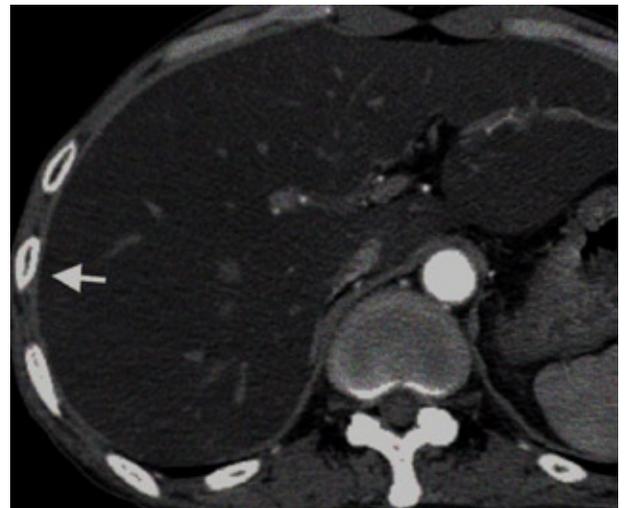
Why does fatty liver disease occur? What is the pathogenesis?

1. NAFLD is considered to be the liver's manifestation of a metabolic syndrome called "syndrome X" or "insulin resistance syndrome." The syndrome links NAFLD with obesity, diabetes mellitus type 2, hypertension, and hyperlipidemia. (1)
2. Evidence points to a two-hit theory.
 - a. The first hit:
 - i. The "first hit" involves accumulation of fat in the liver.
 - ii. Free fatty acids (FFA) are elevated in the serum, become oversupplied to the liver, and lead to steatosis. (2)
 - b. The second hit:
 - i. Steatosis makes the liver vulnerable to additional biochemical insults, the "second hit." These include oxidative stress, mitochondrial dysfunction, pro-inflammatory cytokines, adipocytokine imbalance, dysregulated apoptosis, and stellate cell activation. The result can lead to inflammation causing NASH and fibrosis. (5, 9)

What is the pathology of nonalcoholic fatty liver?

1. Liver steatosis consists of large and small vesicles of fat, predominantly triglycerides, inside hepatocytes. (3)
2. The histology may differ between children and adults. (10)

Figure at right: Fatty liver in a 44-year-old man. Axial contrast-enhanced CT scan shows linear high attenuation along the hepatic surface (arrow), a finding that represents pseudoenhancement. The diaphragm has high attenuation relative to the decreased attenuation of the fatty liver and thus mimics an enhanced hepatic capsule. (14)



NASH Pathology

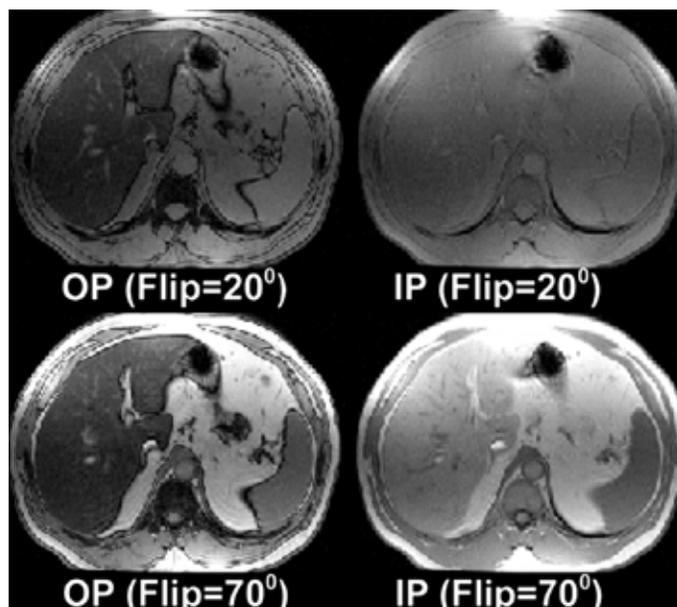
What is the pathology of nonalcoholic steatohepatitis (NASH)?

1. Steatosis, multifocal parenchymal inflammation, Mallory hyaline, hepatocyte death from ballooning degeneration and also apoptosis, and sinusoidal fibrosis occur. (3)

NAFLD Effects

What effect does fat have on the liver?

1. NAFLD is suspected to be responsible for up to 70% of chronic hepatitis cases of “unknown” cause. Studies suggest that cirrhosis may eventually develop in up to 10% to 30% of those with NAFLD. (3)
2. NAFLD may contribute to progression of other liver diseases. (3)



Transverse IP and OP images (155/2.3 [OP], 4.6 [IP]) of the liver in a patient suspected of having nonalcoholic steatohepatitis, obtained at low T1 weighting (flip angle, 20°) and high T1 weighting (flip angle, 70°). (15)

NAFLD and Nutrition

What are some recent nutritionally related studies?

1. Daily fructose ingestion by patients with NAFLD shows association with increased hepatic fibrosis. (11)
2. In contradistinction, berry consumption has been shown to enhance liver function. (12)

NAFLD Associated Diseases

What other diseases are associated with NAFLD?

1. Chronic kidney disease and retinopathy show higher prevalence in type 1 diabetic patients who have NAFLD. (13)
2. Hepatic steatosis is an independent marker for increased cardiovascular risk. (10)

CONCLUSION

Conclusion: Nonalcoholic fatty liver disease has become the most common chronic liver disease in Western children, adolescents, and adults. It can have association with hepatitis, cirrhosis, and hepatocellular carcinoma. ■

The next issue of *The WCC Note* will review imaging literature of nonalcoholic fatty liver disease.

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