



*CDHNF & NASPGHAN – A Partnership for Research and Education for
Children's Digestive and Nutritional Health*

Obesity and NAFLD

Definitions:

Nonalcoholic steatohepatitis (NASH) and nonalcoholic fatty liver disease (NAFLD) have been recognized for more than two decades now^{1,2}. Long term follow up studies of adults with NASH have shown that fibrosis can progress to cirrhosis³. We also understand that NAFLD with hepatic fibrosis and/or inflammation can progress to more severe fibrosis or cirrhosis and have a higher mortality and need for transplantation when compared to individuals with steatosis alone⁴.

Prevalence:

NAFLD is today the most common cause of elevated liver enzymes in children. A recent autopsy series demonstrated that the prevalence of NASH was 2.96% (22/742) in children while closer to 9% had NAFLD. Further 23% of children with NAFLD in this study had NASH while bridging fibrosis or cirrhosis was seen in 9% of children with NASH in this study⁵. Recently Das et al reported significant prevalence of NAFLD even in the non-obese population and potentially significant liver disease related to NAFLD in the developing world as well⁶.

Long term natural history data of pediatric NAFLD/NASH in children are unfortunately very limited. Certain components of routine laboratory tests may be predictive of

NAFLD pattern and advanced fibrosis, but these serologic markers do not at present have adequate sensitivity or specificity to replace liver biopsy data to distinguish NASH from NAFLD⁷. Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) for example are not reliable measures of histological improvement in NASH⁸.

Disease Progression and the importance of liver biopsy:

Liver biopsy therefore provides insight through histology for accurate diagnosis and evaluation of fibrosis progression in patients with NAFLD/NASH. However, the invasive nature and inherent risk of percutaneous liver biopsy, coupled with debated benefit of liver biopsies in guiding therapy or changing clinical outcomes, have hampered the widespread use of liver biopsy by clinicians and prevented a full understanding of the natural history and progression rates of NASH in both children and adults. Smaller studies indicate that NASH may progress rapidly to fibrosis in children within a short span of 3-4 years⁹.

Multiple cross-sectional studies suggest that NAFLD is a significant risk factor for the development of hepatocellular carcinoma (HCC). It is estimated that roughly 1000 cases of HCC in the United States each year can be attributed to NAFLD. One prospective study of adult patients with NASH cirrhosis found HCC to develop in roughly 7% of patients over a 10 year period. Little is known about the risk for HCC in children. However, the long duration of NASH may impact the development HCC for those who have NAFLD as children.

The majority of studies on the pathogenesis of NAFLD have been in the adult population. While pediatric and adult NAFLD share many characteristics, known differences between the two, including histological differences, indicate variation in the development of pediatric versus adult NAFLD^{10, 11}. While our understanding of the pathogenesis is in its infancy, obesity, central adiposity, and insulin resistance are strongly associated with pediatric NAFLD and inflammation with progression to NASH.

Treatment options:

Because poor dietary habits and a sedentary lifestyle lead to obesity and therefore predispose to the development of NASH, the primary therapeutic intervention is gradual and sustained weight loss through a balanced, calorically appropriate along with increased physical activity. Although the direct benefit of lifestyle modification has not been proven for NAFLD, there are enough data to support this recommendation for the typical NAFLD found in obese children

Pharmaceutical Options:

Vitamin E has recently been highlighted by an adult study by Sanyal and his colleagues within the NASH Clinical research network as a potential therapeutic option. The parallel pediatric study from the same group is yet to be published though encouraging results were presented in abstract form in late 2010¹³.

Metformin has also been used specifically in individuals that already have overt insulin resistance though large placebo control trials for NASH in children are not available.

Surgical Options:

The role of bariatric/weight loss surgery in adolescent obesity has become an accepted mainstream therapeutic option. There is now an National Institutes of Health (NIH) funded study evaluating teenagers undergoing bariatric surgery procedures (*Teen-Longitudinal Assessment of Bariatric Surgery*) and their impact on obesity's attendant co-morbidities including NAFLD ¹².

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