

# NONALCOHOLIC STEATOHEPATITIS IN CHILDREN

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## ABSTRACT

**Background:** Nonalcoholic steatohepatitis occurs commonly in adults with obesity or diabetes mellitus. There are only a few reports of this condition in children.

**Methods:** Prospective consecutive clinical series.

**Results:** Between December 1985 and April 1995, 36 children (21 boys, 15 girls), were diagnosed with nonalcoholic steatohepatitis at the Hospital for Sick Children, Toronto. The median age at diagnosis was 12 years (range, +/- 16 years). Most patients were referred because of elevated serum aminotransferases or abnormal hepatic sonogram. Thirty patients (83%) were obese. Two patients had diabetes mellitus at diagnosis, and it developed later in two. Fifteen patients had palpable hepatomegaly, and one of these had splenomegaly. None had physical signs of chronic liver disease. Thirteen of 36 patients had acanthosis nigricans. Serum aminotransferases were elevated in all but one patient. Tests for Wilson Disease and chronic hepatitis B and C were negative. Serum lipid profiles were abnormal in 18 patients: 7 had hypercholesterolemia, and 11 had hypertriglyceridemia. Twenty-four of 31 examined had abnormal liver sonograms suggestive of fatty infiltration. Twenty-four patients underwent percutaneous liver biopsy: all showed large-droplet fat. Inflammation was present in 88% and fibrosis-cirrhosis in 75%. One 10 year old patient had established cirrhosis at diagnosis.

**Conclusions:** Nonalcoholic steatohepatitis occurs in children, is clinically diverse, and may not be benign. *JPGN* 30: 48-53, 2000, Key Words: Acanthosis nigricans – Fatty liver – Fibrosis – Obesity – Steatohepatitis. © 2000 Lippincott Williams & Wilkins, Inc.

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Nonalcoholic steatohepatitis (NASH) occurs most commonly in adults with obesity, hyperlipidemia, and maturity-onset diabetes. It has also been described in association with pregnancy, starvation, or chronic treatment with drugs, notably corticosteroids. It may also occur, with elevated serum aminotransferases, in adults in the absence of these risk factors. Sufficient evidence has accrued to indicate that NASH, as such, occurs in the absence of obvious causative factors such as starvation and that affected patients are not abusing ethanol secretly. Recent observations suggest, however, that the stereotype of the typical NASH patient as middle-aged, massively obese, and female may not be accurate. Moreover, although initially considered a relatively benign disorder, NASH can progress to cirrhosis in adults.

Nonalcoholic steatohepatitis has been reported in children. Most of these series are small or do not include data from liver biopsies. The purpose of this study was to describe and characterize clinically NASH in children. We report a consecutive prospective series of children with NASH diagnosed at the Hospital for Sick Children during approximately 10 years. This is the one of the largest series of NASH in children reported to date.

## PATIENT AND METHODS

All children diagnosed with NASH at the Hospital for Sick Children, Toronto, from December 1985 through April 1995 were included. Patients were excluded if they were receiving concomitant corticosteroid therapy or if they were found to have a metabolic disorder known to cause fatty liver (e.g., Wilson disease, neutral lipid storage disease, or fatty acid oxidation disorders). The first child was diagnosed as having NASH in December 1985 on the basis of clinical obesity and abnormal serum aminotransferase levels, results of laboratory studies excluding other known liver diseases, and results of a percutaneous liver biopsy showing steatosis and inflammation. Thereafter, NASH was included in the differential diagnosis of children with unexplained elevation of aminotransferases, especially if obese. In

*total, 36 patients were identified. By way of comparison, during this same period, 11 children with symptomatic liver disease were diagnosed as having Wilson disease.*

*Age, sex, weight, height, initial symptoms, other medical conditions, and medications were noted. Laboratory studies included liver function tests, serology for hepatitis B and C, serum copper and ceruloplasmin, immunoglobulins, nonspecific tissue autoantibodies, random serum glucose, and a fasting lipid profile. A random ethanol level was obtained in one patient.*

*Thirty-one patients underwent hepatic sonography. A percutaneous liver biopsy was obtained in 24 patients at the time of diagnosis. Follow-up data were available in 21 patients (mean follow-up, 1.5 years; range, 0.2-5.5 years). Statistical analysis was performed with Student's *t*-test, with  $P < 0.05$  taken as statistically significant.*

*Tomorrow will start with "Results".*

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