Alpha-1-antitrypsin deficiency in children: liver disease is not reflected by low serum levels of alpha-1-antitrypsin - a study on 48 pediatric patients.

BACKGROUND: Alpha-1-antitrypsin (alpha1-AT) is an important protease inhibitor. The phenotypes are characterized by a low total serum alpha1-AT or by an abnormal protein accumulating in the hepatocytes. The aim of our study was to examine a correlation of total serum alpha1-AT, phenotype, and liver involvement in pediatric patients. METHODS: 48 patients, deficient for alpha1-AT were included. The phenotypes for alpha1-AT were determined by isoelectric focusing. Liver disease was defined either as elevated transaminases or/as elevated conjugated bilirubin and gammaGT. Patients were reexamined after a mean interval of 2 years. RESULTS: Homozygous alpha1-AD was found in 12 patients, heterozygous in 24 patients. In 12 children rare variants of alpha1-AD were diagnosed. Serum alpha1-AT levels less than 60% of normal were found in all patients with homozygous, in 37% of patients with heterozygous alpha1-antitrypsin deficiency (alpha1-AD), and in patients with the homozygous variant PiM(palermo). Liver disease was found in 8/12 patients with the phenotype PiZZ and in 15/24 patients with heterozygous alpha1-AD. Three of 4 patients with the phenotype PiMQ0 had severe liver disease despite normal serum levels for alpha1-AT. In 11 patients with heterozygous alpha1-AD liver disease was apparent despite normal serum levels.
alpha1-AT levels. In two patients with the variant type Mpalermo serum levels were as low as 11% of normal without any signs of liver disease. CONCLUSIONS: Our data clearly show that in the diagnostic workup of neonatal cholestasis measurement of total serum alpha1-AT does not exclude liver disease due to abnormal alpha1-AT variants. We suggest analysis of alpha1-AT-phenotype by isoelectric focussing in patients with unknown liver disease. Heterozygous or rare variant types might remain undiagnosed by measuring total alpha1-AT only.