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PROSPECTIVE FIBROSCAN® MEASUREMENTS OF OBESE CHILDREN WITH AND WITHOUT AN INITIALLY ELEVATED ABNORMAL ALANINE AMINOTRANSFERASE (ALT) IDENTIFIES A CRITICAL ROLE FOR ALT IN IDENTIFYING ADVANCED FIBROSIS GROUP

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Background: Nonalcoholic fatty liver disease (NAFLD) has rapidly become the most common form of chronic liver disease in children and adolescents. Abnormal elevations in aminotransferases are commonly used to identify those children who may have more active inflammation, but the possibility of missing advanced disease could be occurring in those who have initially normal levels and subclinical disease activity. Vibration controlled transient elastography using the Fibroscan® device can detect liver steatosis and fibrosis non-invasively. We used Fibroscan® to look for hepatic steatosis and fibrosis in obese children with and without an abnormally elevated ALT to assess the utility of this biomarker as a screening test for more advanced liver disease. **Methods:** All obese subjects (BMI≥30) with abnormal ALT (twice above ULN ≥50 U/L for boys and ≥44 U/L for girls) and normal ALT (twice below ULN, < 50 U/L for boys and < 44 U/L for girls) were prospectively enrolled. Both male and female obese subjects of all races/ethnicities, and age between 8-21 years were included. **Results:** A total of 153 subjects (96 in the normal ALT group, and 57 in abnormal ALT group) were enrolled. White race was predominant (73%) followed by Hispanics (18.9%) and African-Americans (4.5%). Fibroscan® readings in the two groups were compared. In the abnormal ALT group, where more advanced disease was expected, 28% subjects had advanced fibrosis and 26.3% had cirrhosis. In comparison, in the normal ALT group, only 7.2% subjects had advanced fibrosis and none had cirrhosis (p <0.0001). Similarly, in the elevated ALT group 91.2% subjects had grade III steatosis vs 38.5% subjects in the normal ALT group. **Conclusion:** In a prospective study using non-invasive Fibroscan evaluations over a year time period, the ALT was found to be an excellent biomarker for differentiating more advanced liver disease in this cohort of obese children. Based on these findings and as a clinical strategy, regular monitoring of the serum ALT in obese children is suggested, followed by Fibroscan® measurements once their ALT becomes elevated.

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★ 1469

THE PRESENCE OF A TRUNCATING MUTATION IN ABCB11 ABROGATES THE BENEFICIAL EFFECT OF A RESIDUAL FUNCTION MUTATION ON THE COURSE OF SEVERE BILE SALT EXPORT PUMP DEFICIENCY

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Background: Severe bile salt export pump (BSEP) deficiency is caused by mutations in the *ABCB11* gene and frequently leads to end-stage liver disease. Patients with homozygous p.D482G or p.E297G mutations, which are associated with residual BSEP function, have a relatively mild phenotype and respond to surgical biliary diversion (SBD). We now aimed to assess whether genetic categorization of the 2nd mutation in patients harboring one p.D482G or p.E297G mutation allows prediction of their course of disease. **Methods:** From our global NAPPED database, we selected all patients with at least one p.D482G or p.E297G mutation (named "BSEP1" mutations) and divided them into BSEP1/BSEP1 patients (homozygous, n=31), BSEP1/BSEP2 (2nd mutation missense, but not p.D482G/p.E297G, n=22) and BSEP1/BSEP3 (2nd mutation leading to a truncated protein, n=30). We compared native liver survival (NLS), SBD and post-SBD serum bile acids (sBA). Log-rank tests were used. **Results:** In patients without SBD during follow-up, NLS was lowest in BSEP1/BSEP3 patients (NLS at age 15y: 7% vs. 48% BSEP1/BSEP1 and 78% BSEP1/BSEP2, resp., P<0.001, Fig. A). The proportion of patients undergoing SBD was comparable between the three groups (%SBD at age 15y: 21% BSEP1/BSEP1, 40% BSEP1/BSEP2 and 40% BSEP1/BSEP3, P=0.47). Post-SBD sBA levels were negatively associated with NLS (%NLS at 15y post-SBD: 95% in sBA<102 µmol/L, vs. 60% in sBA≥102 µmol/L, P=0.005, cut-off based on ROC). The percentage of patients reaching a post-SBD sBA<102 µmol/L was lowest in BSEP1/BSEP3 (17% vs. 92% in BSEP1/BSEP1 and 60% in BSEP1/BSEP2, P=0.001). NLS at 15 years after SBD was only 22% in BSEP1/BSEP3 patients, vs. 92% in BSEP1/BSEP1 and 82% BSEP1/BSEP2 (P<0.001, Fig B). **Conclusion:** The largest database of severe BSEP deficiency patients allows for the first time prediction of the course of disease and the responsiveness to surgical biliary diversion in patients with at least one *ABCB11* mutation with residual function. A combination of two residual function mutations is associated with long term native liver survival and responsiveness to surgical biliary diversion. However, if one residual function mutation is combined with a second mutation that leads to a truncated protein, the prognosis is poor with regard to native liver survival and responsiveness to surgical biliary diversion, probably due to insufficient combined residual function. These results will allow further personalization of treatment of patients with BSEP deficiency.

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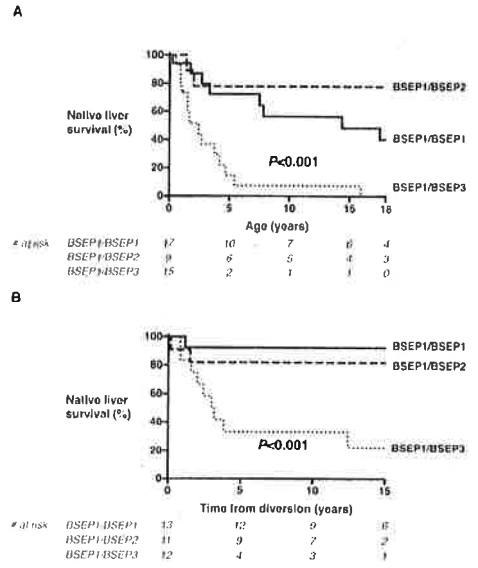

Figure:
A: Native liver survival in severe BSEP deficiency patients without surgical biliary diversion, with a homozygous (BSEP1/BSEP1, solid line), compound heterozygous missense (BSEP1/BSEP2, dashed line) or compound heterozygous truncated (BSEP1/BSEP3, dotted line) genotype. Log-rank test.
B: Native liver survival in severe BSEP deficiency patients after surgical biliary diversion in patients with a homozygous (BSEP1/BSEP1, solid line), compound heterozygous missense (BSEP1/BSEP2, dashed line) or compound heterozygous truncated (BSEP1/BSEP3, dotted line) genotype. Log-rank test

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TRENDS IN THE PREVALENCE OF NONALCOHOLIC FAT LIVER DISEASE (NAFLD) AMONG ADOLESCENTS AND ADULTS IN THE UNITED STATES, 2007-2016

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Background: NAFLD is associated with obesity ac age groups. Understanding the prevalence of NAFLD adolescents and young adults is relevant to the public efforts. Aim: To provide estimates of NAFLD prevale adolescents and young adults and evaluate trends from 2007-2008 through 2015-2016 in the United **Methods:** Data were obtained from National Heal Nutrition Examination Survey (NHANES) from 200 Adolescents and young adults aged 12 to 29 year included. NAFLD was determined by US-Fatty Live (US-FLI) in the absence of secondary causes of liver d and the difference prevalence trends were analyzed on age, gender, and race. **Results:** Complete clinic and US-FLI were available for 4,654 adolescents and adults (mean age 21 years; 50.5% male; 57.1% white Hispanic, and 13.9 % Black). The overall prevale NAFLD among adolescents and young adults was ranging from 13.2% among early and middle adolesce 17 years) to 18.7% among late adolescents and young (18-24 years) to 24.0% among older young adults years) (trend P<.001). The prevalence of NAFLD was among boys than among girls (aged 12-17: 15.1% vs aged 18-24: 21.1% vs. 16.2%; aged 25-30: 28.7% vs all p<.030). Among adolescents, Hispanics (26.9% higher prevalence of NAFLD than Whites (9.8%) and (7.9%) (pairwise P<.001). This was also true for young aged 18-24 (32.2% vs. 17.7% and 7.5%, P<.001); and adults aged 25-30 (38.3% vs. 22.4% and 14.0%, P Over the study time period, the prevalence of NAFLD adolescents and young adults (24-30 years) did not (trend P>0.80). In contrast, NAFLD prevalence a adults aged 18-24 increased from 10.7% (2007-200 (2015-2016) (trend P=0.014). Interestingly, the of other liver diseases including excessive alcoho hepatitis decreased from 9.1% to 4.6% (trend P fact, White and Hispanic young adults aged 18-24 drivers behind this increase in the prevalence of this period, accounting for 62.3% and 21.0% of the respectively (trend P=0.047 and 0.003). **Conclusion** data indicate an increasing trend in the prevalence among young adults aged 18-24 years, especial non-Hispanic White and Hispanic Americans. These have important public health and policy implications