Published in final edited form as:
Dig Liver Dis. 2014 August ; 46(8): 760–761. doi:10.1016/j.dld.2014.03.014.

High Prevalence of Hepatitis B Non-Immunity in Pediatric Non Alcoholic Fatty Liver Disease Patients

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Dear Editor:

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in both adults and children in the United States today [1]. While achieving a healthy weight is optimal management of NAFLD and nonalcoholic steatohepatitis (NASH), equally important is preventing secondary damage to the liver that might accelerate liver fibrosis. Hepatitis B is one such preventable cause of secondary liver damage and therefore prevention of hepatitis B has been a public health priority. As this is most effectively done with vaccination against hepatitis B. Primary hepatitis B vaccination is part of the universal vaccination schedule for infants and children. Unfortunately, however obesity has been identified as a predictor of poor serologic antibody development after Hepatitis B vaccination [2, 3]. The objective of this study was to determine the sero-prevalence of immunity against hepatitis B in a cohort of consecutively evaluated pediatric NAFLD patients. We hypothesized that positive hepatitis B surface antibody (HBs Ab) sero-prevalence would be low in children with NAFLD, despite universal immunization practices in place against hepatitis B.

We conducted a retrospective review of prospectively collected clinical and histological data obtained from children and adolescents, age 6-18, enrolled in an IRB-approved single center NAFLD registry at the Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio. The registry collected anthropometric data, laboratory assessments for other causes of chronic liver disease, and liver biopsies. Enrollment criteria included chronically elevated liver enzymes after exclusion of other liver diseases including: hepatitis B, hepatitis C, alpha 1 antitrypsin deficiency, Wilson disease, autoimmune hepatitis, and iron indices for hemochromatosis. The presence of HBs Ab was used as a surrogate for immunity after vaccination. The absence of HBs Ab after vaccination indicated a decreased immunogenic response. Patients were grouped into non-immune and immune groups and analyzed for demographic, and biochemical differences.

All 200 subjects had negative HBs Ag levels and negative hepatitis B core antibody levels, indicating no past or active hepatitis B infection. Therefore, HBs Ab positivity was a result

Conflict of Interest Statement:
There are no potential conflicts of interest, real or perceived. Minesh Mehta wrote the first draft of the manuscript and no honorarium, grant, or other form of payment was given to anyone to produce the manuscript.

of vaccination rather than exposure to the virus. Of 200 subjects, 96 (48%) had no documented HBs Ab serology and had not been evaluated for hepatitis B immunity. No significant clinical differences in age, body mass index (BMI), aspartate aminotransferase (AST), alanine aminotransferase (ALT) or gender were found between those with documented HBs Ab and undocumented HBs Ab status. Of the 104 subjects with documented HBs Ab status, only 29 were found to have positive HBs Ab serology, indicating immunity. The remaining 75 subjects (72%) were considered Hepatitis B non-immune. No significant clinical differences in age, BMI, AST, ALT or gender were found between the two groups.

We identified a very high prevalence of hepatitis B non-immunity (72%) in a prospective, single center cohort of children with NAFLD [4]. No prior reports exist evaluating the status of hepatitis B immunity in children affected by NAFLD. Our study's findings raise legitimate concern, but should be considered preliminary as they are derived from a single center Midwestern cohort of children with NAFLD. Incomplete immunization records limit our study. However, data from the Centers for Disease Control and Prevention (CDC) indicate high immunization rates in the Midwestern region. We further speculate that the lack of hepatitis B immunity observed in our pediatric NAFLD patients is more likely to be from a diminished immunogenic response to hepatitis B vaccination in the setting of obesity. In conclusion, our data suggest that there is potentially an extremely high rate of non-immunity against hepatitis B in children with NAFLD. We propose that children with NAFLD should undergo comprehensive screening for hepatitis B immunogenicity, in addition to screening for infection, and catch up or booster vaccinations should be administered to non-immunized patients with confirmatory immunity testing thereafter.

Acknowledgements

NASH CRN (SD): U01 DK61732; K23 (SAX): K23 DK080888; K08 (RK): K08 DK84310. Digestive Health Center: P30 DK078392; Institutional CTSA NIH/NCRR: 1UL1RR026314-01

Abbreviations

ALT	Alanine amino transferase
AST	Aspartate aminotransferase
BMI	body mass index
CCHMC	Cincinnati Children's Hospital Medical Center
CCSC	Cincinnati Children's Steatohepatitis Center
GGT	gamma glutamyltransferase
NAFLD	nonalcoholic fatty liver disease
NASH	nonalcoholic steatohepatitis
TIBC	total iron binding capacity

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