COMMENTS AND RESPONSES

Intrauterine Growth Retardation, Insulin Resistance, and Nonalcoholic Fatty Liver Disease in Children

Response to Nobili et al.

We read with interest the article by Nobili et al. (1), who reported results of a case-control study that demonstrated an association between intrauterine growth retardation (defined as small for gestational age [SGA]) and pediatric nonalcoholic streatohepatitis (nonalcoholic fatty liver disease [NAFLD]).

Nobili et al. (1) compared children with NAFLD with hospital control subjects. The choice of control subjects may result in an underestimate of the association between SGA and NAFLD if hospitalized children suffer from conditions associated with SGA. Furthermore, hospital control subjects may differ from the general population. Another interesting question is whether associations persist into adulthood.

In the British Women's Heart and Health Study (2,101 women aged 60–79 years), an increase of 1 SD (691 g) of retrospectively reported birth weight was associated with a 2% (95% CI 0–4%, $P = 0.021$) decrease in the geometric mean of alanine aminotransferase (ALT) and a 4% decrease in γ-glutamyltransferase (GGT) (1–6%, $P = 0.008$), after adjustment for potential lifestyle confounders. Associations were not attenuated after further adjustment for components of the insulin-resistance syndrome (2). ALT and GGT are commonly used biomarkers of NAFLD in the absence of other established causes of liver damage. These results are in line with the results found by Nobili et al. (1) and suggest that this association persists into adulthood and that birth weight and NAFLD may be associated via pathways other than insulin resistance.

However, among 798 men aged 53–70 years from the Caerphilly Study, the fully adjusted ratio of geometric means of ALT per change of 1 SD of self-reported birth weight (1 SD = 869 g) was 1.02 (95% CI 1.00–1.05, $P = 0.09$) and that of GGT, 0.97 (0.93–1.00, $P = 0.09$).

Any of these results could be chance findings; alternatively, they could represent a real difference in the nature of the association of birth weight with NAFLD in men and women. Unfortunately, Nobili et al. (1) did not present results by sex, and it is unlikely with 90 case subjects that there would be adequate power for exploring sex differences.

In conclusion, further studies are required to determine whether there is a developmental origin to NAFLD and whether the nature of any developmental effect differs in males and females.

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