Author's response to reviews

Title: Low Birth Weight and Longitudinal Trends of Cardiovascular Risk Factor Variables from Childhood to Adolescence: The Bogalusa Heart Study

Authors:

Maria G Frontini (frontini@tulane.edu)  
Sathanur R Srinivasan (ssriniv1@tulane.edu)  
Jihua Xu (jxu@tulane.edu)  
Berenson S Gerald (berenson@tulane.edu)

Version: 2 Date: 26 August 2004

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We thank the reviewer for the helpful comments and suggestions which we feel helped to clarify and strengthen the manuscript.

1). As suggested by the reviewer, a new analysis was performed using WHO cut point of 2500 gr as measure of low birthweight.

Similar results were obtained. Low birthweight was associated with adverse changes of glucose and triglycerides from childhood to adolescence. However, by using 2500 gr as cut point, the regression model did not show significant interaction between triglycerides or glucose and age_square term. Hence, the final regression model showed faster linear increase of triglycerides and glucose levels from 4 to 18 years of age among those born with weight lower than 2500 gr, and such increases were constant from childhood to adolescence.

The association between changes in diastolic blood pressure and low birth weight showed in this new analysis the same results as those presented in the original report. It is important to note that in the new analysis, 36 subjects (all whites) were reclassified as having “normal birth weight” which increased the total number of controls to 332. None of the subjects who were classified as normal birth weight in the first analysis were reclassified as low birth weight in the second analysis using 2500 gr as cut point. The redistribution of cases caused small increases in the standard error of model beta coefficients that remained significant in the model. The independent association of low birth weight with adverse changes of glucose, triglycerides and systolic blood pressure also remained significant.

2) With respect to lipid analyses, any shift in values can be assumed to be homogeneous among cases and controls, and as source of potential bias, both groups should have been affected at the same level and direction. Further, for example, the average bias in levels of total cholesterol in CDC control samples ranged from -0.1 to -1.6 mg/dL between different cross-sectional surveys with no consistent pattern over time within or between surveys.

3) Table 1. As pointed out by the reviewer, among those subjects with low birth weight vs controls LDL cholesterol and HDL cholesterol mean differences were significant during early childhood but not during adolescence. This is not due to sample size changes, which remained the same in both age groups for all risk variables. The relatively small differences and large variances caused that lack of statistically significant difference in cross-sectional comparisons. To show a statistically significant difference of HDL cholesterol mean values between groups during adolescence (1.1 mg/dL, and sd=24) would have required a sample size of 7,474 subjects in each group (with alpha error =0.05 and beta error=0.20).

The text has been changed to incorporate reviewer’s suggestions.