Association between Birth Characteristics and Coronary Disease Risk Factors among Fifth Graders

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Objective To evaluate the associations between selected birth characteristics—prematurity and poor intrauterine growth—and risk factors for coronary artery disease detected among children enrolled in the fifth grade.

Study design Children (n = 3054) with matched birth and fifth grade health screening data on body mass index (BMI), systolic blood pressure, and fasting lipid profiles were analyzed using MANOVA with the following independent variables of weight gain by the fifth grade: BMI percentile, normal or overweight/obese (BMI ≥85th percentile), prematurity, and intrauterine growth (ie, small for gestational age [SGA], appropriate for gestational age [AGA], or large for gestational age [LGA]).

Results LGA status at birth was associated with overweight/obesity later in life. In fifth grade, overweight/obese children had elevated systolic blood pressure and abnormal levels of most fasting serum lipids compared with normal-weight children regardless of birth characteristics. Beyond the effects of BMI percentile, preterm infants had higher levels of triglycerides (TG) than term infants by the fifth grade ($P < .05$). SGA infants who become overweight/obese had higher levels of TGs and very low-density lipoproteins compared with AGA and LGA infants, whether overweight or normal weight ($P < .05$).

Conclusion BMI ≥85th percentile in the fifth grade is associated with abnormalities in most coronary artery risk factors regardless of birth characteristics. Beyond the effects of BMI percentile in the fifth grade, preterm infants had higher TG levels than term infants. SGA infants who were overweight/obese in the fifth grade had higher TG and very low-density lipoprotein levels compared with AGA and LGA infants who were overweight/obese or of normal weight in the fifth grade. *(J Pediatr 2014;164:78-82)*.

Many of the previous analyses examining the associations between birth weight (BW) and subsequent risk factors for coronary artery disease did not include detailed gestational age (GA) assessment.[1] In these studies, lower BW was associated with subsequent findings of coronary artery disease and higher blood pressure (BP) in adults, as well as elevated BP in the pediatric population.[1-4] Relationships between newborn findings and adult disorders have been referred to as the fetal origins of adult disease.[1,5] Several publications have specifically linked these coronary risk outcomes only to those low BW infants who gain excessive weight during childhood or later in life.[4-9]

Lower BW may be related to preterm birth with a normal intrauterine growth pattern, or may be secondary to poor intrauterine growth resulting in a newborn who is small for GA (SGA) at the time of delivery. Many previous analyses relating BW to subsequent outcomes during childhood and adolescence did not include specific GA assessments and thus were unable to clearly delineate whether preterm birth or poor intrauterine growth was responsible for the low BW pattern.[4-9]

In West Virginia, birth data are linked to individual data from coronary artery disease risk factors measured in a fifth grade screening. We undertook an analysis of these matched datasets to determine which early birth factors (ie, prematurity, poor intrauterine growth, or either of these accompanied by excessive weight gain by fifth grade) were associated with coronary disease risk factors.

Methods

The West Virginia Birth Score Project collects data on all newborns delivered in the state within 24 hours of birth, including BW, estimated GA of the newborn, and various maternal risk factors known to be associated with perinatal morbidity and infant mortality[10,11] The project was

AGA	Appropriate for gestational age	LGA	Large for gestational age
BMI	Body mass index	N	Normal
BP	Blood pressure	O	Obese
BW	Birth weight	SBP	Systolic blood pressure
CARDIAC	Coronary Artery Risk Detection in Appalachian Communities	SGA	Small for gestational age
GA	Gestational age	TC	Total cholesterol
HDL	High-density lipoprotein	TG	Triglycerides
LDL	Low-density lipoprotein	VLDL	Very-low-density lipoprotein

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initiated in 1985 to facilitate services for neonates deemed at high risk for infant death.[10] The birth score data are collected by health care professionals, tabulated electronically, and merged with the birth certificate data. In the present study, birth score and birth certificate data for children born between 1993 and 1996 were merged with data collected on fifth grade schoolchildren by the Coronary Artery Risk Detection in Appalachian Communities (CARDIAC) Project between 2004 and 2007. The CARDIAC Project measured body mass index (BMI), systolic BP (SBP), and a fasting lipid profile (ie, total cholesterol [TC], high-density lipoprotein [HDL], low-density lipoprotein [LDL], very-low-density lipoprotein [VLDL], and triglycerides [TG]) on all West Virginia fifth graders with informed consent by the parents and assent by the child.[12] All fifth grade children were given the opportunity to participate with no exclusions. This age group was chosen because they are mostly prepubertal, yet old enough to give assent. The CARDIAC Project and this comparative analysis with birth score cohort was approved by the West Virginia University Institutional Review Board for the Protection of Human Subjects and are described in more detail elsewhere.[12,13]

For the purpose of the present analysis, preterm birth was considered birth at <37 completed weeks of gestation, and term birth was considered birth at 37-42 weeks completed gestation. The growth by GA variables were derived using the GA assessment and the BW on Fenton weight graphs.[14] These variables were defined as follows: SGA, weight <10th percentile for each GA; appropriate for GA (AGA), weight 10th-90th percentile for each GA; large for GA (LGA), weight >90th percentile for each GA.

Weight gain by the fifth grade was derived using gestational maturity categories (ie, preterm and term) or growth by GA category (ie, SGA, AGA, and LGA), with BMI percentile determination in the fifth grade. The latter was expressed as normal (N; <85th percentile) or overweight/obese (O; ≥85th percentile). For example, an LGA infant who was overweight in the fifth grade was classified as LGA-O, whereas an LGA infant in a more normal weight category by BMI in the fifth grade was classified as LGA-N.

Anthropometric assessment at the fifth grade included measurement of height to the nearest 0.1 cm using a portable stadiometer (Shorr, Olney, Maryland) and weight to the nearest 0.1 kg using an electronic scale (Seca, Hamburg, Germany). BMI was calculated using the following equation: weight (kg)/height $(cm)^2 \times 10\,000$.[15] BMI percentile was calculated using EpiInfo 7 (Centers for Disease Control and Prevention, Atlanta, Georgia). Seated resting BP was measured in duplicate using a standard sphygmomanometer and an appropriate-sized cuff. School health nurses and health science center students collected the measurements.

SBP percentile was calculated using national norms based on the child's age, sex, and height as established by the National Heart Lung and Blood Institute.[16] For each year of age and each height percentile, the SBP followed an approximately normal distribution. The z score from the standard normal distribution was calculated as follows: $z = (\text{SBP} - \text{mean SBP})/\text{SD}$ for year of age by sex. The z score was applied to derive the accumulative probability from the standard normal distribution, which is the same as the SBP percentile. The calculations were performed using SAS version 9.1 (SAS Institute, Cary, North Carolina). In the 2004-2007 CARDIAC Project data, the lipid profile samples were collected as overnight fasting venipunctures by trained phlebotomists at the school.

Mother's first name and surname and child's date of birth were used to merge the children's birth data with their fifth grade CARDIAC data. The birth variables BW and GA assessment were matched with BMI, BP, and lipid profile data as measured by the CARDIAC Project screening. Of the 33 658 children screened in the fifth grade, 6507 (5.17%) were matched with their birth records. We analyzed data from 3054 matched subjects with the most complete data. The loss of subjects was related mainly to the absence of serum lipid data. The slight variation in sample size in groups was due to absent data elements.

To assess potential differences in the children's fifth grade anthropomorphic measurements, BP, and fasting lipids based on GA (with term birth as the reference group) and BW (with AGA as the reference group), we conducted a series of MANOVAs to preserve power and reduce the potential for error. Our models used 2 measures of size at birth (term or preterm and SGA, AGA, or LGA) as the independent variables and BMI percentile, SBP percentile, TC, HDL, LDL, log VLDL, and log TG at the fifth grade as the dependent variables. Childhood obesity (based on BMI percentile) was entered into the models first, to assume much of the variance. The remaining independent variables were then entered, to assess the remaining variance impact. VLDL and TG levels were transformed into log functions because of skewed data. A final MANOVA was performed using the weight gain by fifth grade variables (SGA-N, AGA-N, LGA-N, SGA-O, AGA-O, LGA-O, preterm-N, term-N, preterm-O, and term-O), along with BMI percentile, SBP percentile, and TC, HDL, LDL, log VLDL, and log TG values. Analyses were performed with SPSS 18.0 (SPSS, Chicago, Illinois).

Results

A total of 3054 subjects were available for analysis. The study group had a median age of 11 years and was 53.5% female, 95.7% white, and 2.3% African American. BW and GA data for the birth category groups are presented in **Table I**.

There was no difference between the preterm-born and term-born children in fifth grade in any measure except TG level, with significantly higher TG levels in the preterm children ($P < .05$; **Table II**). SGA infants were smaller and LGA children were larger in fifth grade (**Table I**). Growth by GA group (SGA, AGA, LGA) did not predict SBP percentile in fifth grade (**Table I**). There were no differences in fasting lipid profiles across the GA categories.

There was a relationship between weight gain by fifth grade and cardiac risk factors in both normal-weight and obese