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Nonlinear Relationship between Birth Weight and Visceral Fat in Adolescents

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Abstract

Objective—To determine the association of birth weight with abdominal fat distribution and markers known to increase risk for cardiovascular disease and type 2 diabetes in adolescents.

Study design—In 575 adolescents aged 14–18 years (52% female, 46% black), birth weight was obtained by parental recall. Fasting blood samples were measured for glucose, insulin, lipids, adiponectin, leptin, and C-reactive protein. Subcutaneous abdominal adipose tissue and visceral adipose tissue were assessed by magnetic resonance imaging.

Results—When we compared markers of cardiometabolic risk across tertiles of birth weight, adjusting for age, sex, race, Tanner stage, physical activity, socioeconomic status, and body mass index, there were significant U-shaped trends for homeostasis model assessment of insulin resistance, leptin, and visceral adipose tissue (all $P_{quadratic} < .05$). A significant linear downward trend across tertiles of birth weight was observed for triglycerides ($P_{linear} = .03$). There were no differences in fasting glucose, blood pressure, total cholesterol, low-density lipoprotein-cholesterol, high-density lipoprotein-cholesterol, adiponectin, C-reactive protein, or subcutaneous abdominal adipose tissue across tertiles of birth weight.

Conclusions—Our data suggest that both low and high birth weights are associated with greater visceral adiposity and biomarkers implicated in insulin resistance and inflammation in adolescents.

Although many postnatal factors have been associated with the development of obesity, increased attention to prenatal factors has provided important insights into the obesity pandemic. Extrauterine signals received by the developing fetus induce adaptive responses that enable phenotypic advantages for the environment in which the offspring will live.[1,2]

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Birth weight can be an indicator of maladaptive responses to fetal life and has been correlated with obesity and related comorbidities.[3–6] The current paradigm holds that perturbations in prenatal growth may underlie a population at risk for cardiometabolic morbidity and mortality. This notion is supported by studies in animals of nutritional manipulation, which have revealed that both fetal undernutrition and fetal overnutrition may lead to developmental programming of adult cardiovascular disease and diabetes.[7–9] Although postnatal growth may interact with earlier prenatal growth programming to influence adult disease, it is important to determine whether postnatal growth could influence health in its own right or whether it is simply a modifying factor according to prenatal growth programming.[10]

Increased abdominal fat deposition carries a particularly high cardiometabolic risk. Studies relating birth weight to anthropometric measures of central adiposity, such as waist circumference, waist-to-hip ratio, or truncal/peripheral skinfold ratios, have suggested that lower birth weight is associated with greater abdominal adiposity later in life.[11–13] Studies that use more robust techniques to assess abdominal adiposity, including ultrasound imaging, dual-energy X-ray absorptiometry, computed tomography, and magnetic resonance imaging (MRI), however, have found birth weight to be either positively related or unrelated to abdominal adiposity in childhood[14,15] and in adulthood.[16,17] Other studies have shown a U-shape relation between birth weight and later abdominal adiposity.[18–20]

These disparate findings can be attributed in part to differences in populations studied and the study design and instruments used. It is also likely, however, that the specific type of abdominal fat compartment (visceral vs subcutaneous) could be another confounding factor. Given that cardiometabolic abnormalities are associated more strongly with visceral, rather than subcutaneous, adiposity,[21] it is important to consider both types of abdominal fat compartments when determining relationships between birth weight and abdominal adiposity.

The primary objective of this study was to determine linear and nonlinear associations between birth weight and abdominal fat distribution and markers known to increase risk for cardiovascular disease and type 2 diabetes in adolescents living in the southern US. A secondary objective was to determine whether current body size modified relationships between birth weight and the measurements of abdominal fat distribution and cardiometabolic risk.

Methods

The participants in this study were 575 adolescents who were recruited from local high schools in the Augusta, Georgia, area. Inclusion criteria for the study were white or black/African-American race and age 14–18 years. Adolescents were excluded if they were taking medications or had any medical conditions that could affect growth, maturation, physical activity, nutritional status, or metabolism. Informed consent and assent were obtained from all parents and adolescents, respectively. The Institutional Review Board at Georgia Regents University approved the study. All measurements were performed between 2001 and 2005.

The original data on birth weight were obtained by parental recall. Body weight and height during the study visit were measured and used to calculate sex- and age-specific body mass index (BMI) percentiles for body weight classification: not overweight (<85th percentile), overweight, (85–94.99th percentile), or obese (≥95th percentile).[22]

After the subjects had rested 10 minutes, blood pressure was measured with the Dinamap Pro 100 (Critikon Corporation, Tampa, Florida). Pubertal maturation stage (or Tanner stage) was measured with a 5-stage scale, ranging from I (pre-pubertal) to V (fully mature), as described by Tanner.[23] Participants reported their pubertal stage by comparing their own physical development with the 5 stages in standard sets of diagrams. Socioeconomic status was assessed with the Hollingshead 4-factor index of social class,[24] which combines educational attainment and occupational prestige for the number of working parents in the child's family. Scores ranged from 11 to 51, with greater scores indicating greater theoretical socioeconomic status.

Fasting blood samples were collected for assessment of serum glucose, serum insulin, plasma triglycerides, plasma total cholesterol, plasma high-density lipoprotein (HDL)-cholesterol, plasma low-density lipoprotein (LDL)-cholesterol, serum leptin, plasma adiponectin, and plasma C-reactive protein. Glucose was measured with the Ektachem DT system (Johnson & Johnson Diagnostics, Rochester, New York) and run in duplicate, with intra- and interassay coefficient of variation (CV) of 0.6% and 1.5%, respectively. Specific insulin was measured in serum and assayed in duplicate with a radioimmunoassay kit (RIA HI-14K; Linco Research, St. Charles, Missouri), with intra- and interassay CV of 5% and 5.6%, respectively. Homeostasis model assessment of insulin resistance was calculated by use of the formula: insulin (pmol/L) × glucose (mmol/L)/22.5.[25]

Triglyceride and HDL-cholesterol were measured with the Ektachem DT II system. HDL-cholesterol was analyzed via a 2-reagent system (Equal Diagnostics, Exton, Pennsylvania) involving stabilization of LDL-cholesterol, very LDL-cholesterol, and chylomicrons with cyclodextrin and dextrin sulfate, and subsequent enzymatic-colorimetric detection of HDL-cholesterol.[26] LDL-cholesterol was determined by use of the Friedewald formula.[27]

Leptin was assayed with an enzyme-linked immunosorbent assay (ELISA; R&D Systems, Minneapolis, Minnesota) and run in duplicate, with intra- and interassay CV of 2.2% and 5.3%, respectively. Adiponectin was assayed by ELISA (Linco Research, St. Charles, Missouri) and run in duplicate, with intra- and interassay CV of 7.4% and 8.4%, respectively. C-reactive protein was assayed via a high-sensitivity ELISA (ALPCO Diagnostics, Salem, New Hampshire) and run in duplicate, with intra- and interassay CV of 10% and 10.2%, respectively.

Subcutaneous abdominal adipose tissue (SAAT) and visceral adipose tissue (VAT) were measured with MRI (1.5-T; GE Medical Systems, Waukesha, Wisconsin). Assessments of SAAT and VAT are described in detail elsewhere.[28] To summarize in brief, a series of 5 transverse images was acquired from the lumbar region beginning at the inferior border of the fifth lumbar vertebra and proceeding toward the head; a 2-mm gap between images was used to prevent crosstalk. To calculate volumes for SAAT and VAT, the cross-sectional area

from each slice was multiplied by the slice width (1 cm) and then the individual volumes were summed.

The mean daily minutes spent in moderate and vigorous physical activity was assessed by the use of MTI Actigraph monitors (model 7164; MTI Health, Fort Walton Beach, Florida), uniaxial accelerometers that measure vertical acceleration and deceleration. Participants wore the monitor for 7 days and returned the monitor 1 week later. Daily movement counts were converted to average minutes per day spent in moderate (3–6 metabolic equivalents) and vigorous (>6 metabolic equivalents) physical activity by the software accompanying the device.

Statistical Analyses

We examined the birth weight–cardiometabolic risk factor relationship by comparing the cardiometabolic risk factor variables across tertile groups of birth weight. Birth weight values reported within each group are medians (range) (Tables I and II). Group differences for age, Tanner stage, BMI percentile, socioeconomic status, and physical activity variables were determined by ANOVA. Descriptive statistics for raw variables are presented as mean SD if not stated otherwise. The proportions of male and female and black and white patients were compared between groups by using χ^2 test of goodness of fit. For comparison of the dependent variables, an F test was performed to test the assumption of homogeneity of regression slopes for the interactions between the independent variable (ie, birth weight tertile groups) and the covariates (age, sex, race, Tanner stage, physical activity, and socioeconomic status). Because there were no interactions, linear and nonlinear ANCOVA with polynomial contrast was used to compare the primary dependent variables across birth weight tertile groups after we adjusted for the covariates. Besides linear trends, this method also examines quadratic (U-shaped) trends.[29] The linear contrast compares the lowest with the highest birth weight tertile category, and the quadratic compares both middle with the highest and the lowest birth weight tertile categories together.[30] Additionally, we subsequently tested whether the association between birth weight group and cardiometabolic risk factor variable was dependent on BMI, a variable indicative of postnatal growth.[10] By the use of this approach, if an association with birth weight group was dependent on BMI, there would be no association between birth weight and the dependent variable of interest when controlled for BMI.[31] Adjusted means are reported as mean ± SE. All the analyses were conducted with SPSS software (version 22.0; IBM SPSS Statistics, Chicago, Illinois), and statistical significance was set at P value <.05.

Results

The sample was composed of 575 white and black adolescents aged 14–18 years (52% female, 46% black). The majority of adolescents (92%) reported to be in pubertal stages IV and V; however, 38 participants reported to be in pubertal stage III, and 6 in stage II. The majority of females (97.8%) reported having started menstruation. The percentages of overweight and obese participants were 11.1% and 16.4%, respectively.

Participant characteristics by tertiles of birth weight are described in Table I. Tanner stage, BMI percentile category, physical activity, and socioeconomic status did not differ between

groups; however, a polynomial trend analysis showed a significant positive quadratic effect between BMI percentile and birth weight ($P = .02$). In addition, results of the χ^2 analysis revealed significant differences in sex and racial distributions across tertiles of birth weight (both $P < .01$).

Table II reports measurements of abdominal fat distribution across tertiles of birth weight when we adjusted for age, sex, race, Tanner stage, physical activity, and socioeconomic status. Results of the polynomial trend analysis revealed a significant positive quadratic trend across tertiles of birth weight for VAT ($P_{quadratic} = .002$), and this U-shaped relationship persisted after we included BMI percentile as a covariate ($P_{quadratic} = .028$) (Figure). We found a marginal U-shaped correlation between SAAT and birth weight tertiles ($P_{quadratic} = .054$); however, when BMI percentile was included as a covariate, this relationship no longer remained ($P_{quadratic} = .238$).

When markers of blood pressure, insulin resistance, lipids, and inflammation were compared across tertiles of birth weight with adjustment for age, sex, race, Tanner stage, physical activity, and socioeconomic status (Table II), there were significant U-shaped trends for homeostasis model assessment of insulin resistance and leptin (both $P_{quadratic} < .01$), and these relationships persisted after including BMI percentile as a covariate (both $P_{quadratic} \leq .04$). Further analysis revealed a significant linear downward trend across tertiles of birth weight for triglycerides after adjustment for BMI percentile ($P_{linear} = .03$). There were no differences in blood pressure, fasting glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, adiponectin, or C-reactive protein across tertiles of birth weight (all P_{linear} and $P_{quadratic} > .05$).

Discussion

The present study found U-shaped relationships between birth weight and markers of visceral adiposity, insulin resistance, and inflammation in adolescents living in the southern US. These relationships were independent of potential confounding factors including age, sex, race, Tanner stage, physical activity, socioeconomic status, and current BMI. Collectively, our data are consistent with studies in animals suggesting that both fetal undernutrition and overnutrition are associated with factors known to increase risk for cardiovascular disease and type 2 diabetes.[7–9] The mechanisms by which birth size affects development of visceral obesity and other metabolic abnormalities later in life are unknown. Hypotheses include maternal nutritional factors during pregnancy such as calorie restriction,[32] protein deprivation,[33] and high-fat diet.[34,35] In a rat model of calorie restriction during pregnancy, low birth weight offspring were hyperphagic with increased fasting plasma insulin and leptin levels.[32] With advancing age, these offspring developed marked amplification of hyperphagia, hyperinsulinism, and hyperleptinemia and larger retroperitoneal fat pads (suggestive of visceral fat) relative to body weight compared with offspring of well-nourished mothers.[32] In rodents exposed to high-fat diets during pregnancy, offspring are born larger than normal and later develop a metabolic syndrome phenotype. Insulin resistance, β-cell dysfunction, increased blood pressure, abnormal serum lipid profiles, increased central adiposity, and hyperleptinemia have all been reported.[34–37]

In clinical reports, birth weight has been correlated positively with obesity and cardiometabolic risk factors in adolescents and adults. Recently, a meta-analysis of 643 902 adults demonstrated that a birth weight of <2500 g was associated with a decreased risk of overweight in later life, and a birth weight >4000 g was associated with an increased risk of overweight.[38] In fact, only one study (of 108) that met the original inclusion criteria demonstrated an inverse relationship between birth weight and obesity in adulthood.[38] Recent studies also have found a positive relationship between high birth weight and adolescent obesity.[39] Although the findings of our study support the positive correlation between birth weight and adolescent BMI, examination of BMI subcategories in each tertile revealed that adolescents in tertiles 1 (<3100 g) and 3 (>3600 g) were more likely to be classified as obese compared with adolescents from tertile 2 (3100–3600 g). Increased obesity prevalence was most dramatic in tertile 3 adolescents, who exhibited a nearly 2-fold increase in classification as obese over study participants in tertile 2.

Although low birth weight does not generally correlate with increased risk for obesity, epidemiologic studies have linked low birth weight with increased visceral adiposity. Rolfe et al[16] demonstrated that birth weight was inversely associated with visceral fat, but not with subcutaneous abdominal fat. Similarly, Ronn et al[40] identified an inverse correlation between birth weight and visceral fat exclusively in males. In these investigations, the correlation between birth weight and visceral fat was dependent on adjustment for current body size (BMI). Although such adjustments have been used to account for the potentially confounding relationship between current body size and health outcomes, they remain controversial and may create a reversal paradox.[41,42] This occurs when a controlled variable is in the causal pathway between the originating event and the outcome of interest and leads to a false or exaggerated inverse relation between the 2.

Some researchers have argued that change in significance after adjustment for current body size does not indicate an “uncovered” association between birth weight and the measured outcome but suggests the influence of postnatal growth up to the time of body size measurement.[10] In our study, visceral fat correlated with both low and high birth weight independent of current BMI. Following Cole logic,[42] the consistency in significance between nonadjusted and adjusted correlations suggests that birth weight (indicative of prenatal growth), rather than current BMI (indicative of postnatal growth) may have a greater influence on visceral adiposity in adolescence. Given the cross-sectional nature of our study, however, it is possible that postnatal growth may also be a contributing factor that interacts with earlier prenatal growth programming to influence greater visceral fat accumulation.

Likewise, low birth weight has been linked to insulin resistance and type 2 diabetes, and this relationship appears more dependent on postnatal vs prenatal growth.[18,43,44] The Health Professionals Follow-up Study and the Nurse’s Health Study demonstrated an inverse relationship between birth weight and risk for type 2 diabetes.[43] Although birth weight and lifestyle were independently associated with risk for type 2 diabetes, the relative risk associated with both variables was more than the additive risk of their independent risk.[43] In a Finnish population, Eriksson et al[44] observed 2 types of BMI-related trajectories during childhood growth that were associated with developing type 2 diabetes in adulthood. The 2

trajectories start with a low birth weight, with a rapid increase in BMI observed in one trajectory and a persistent low BMI in the other. Diabetes development at a lower degree of obesity in the latter trajectory is similar to the insulin resistance pattern observed in Asian populations,[45] where individuals tend to be less obese and develop diabetes. In contrast to these previous studies, Tam et al[20] observed a bimodal relationship between birth weight and insulin resistance in a cohort of Chinese adolescents.

Our results support these findings and are the first to show a U-shaped correlation between birth weight and insulin resistance in a population of adolescents from the US. In both studies, correction for current BMI did not attenuate the relationships. Together, these findings emphasize the role of prenatal vs postnatal growth in the development of type 2 diabetes and suggest that both high and low birth weight may indicate risk for such development.

In addition to visceral adiposity and insulin resistance, we also found serum leptin to have a U-shaped relation to birth weight before and after we controlled for current BMI. Leptin is an adipocyte-derived hormone that is augmented in obese individuals, and it plays a central role not only in energy homeostasis but also in the inflammatory response.[46] Evidence is growing that abnormal secretion of leptin causes chronic low-grade systemic inflammation, a well-known risk factor for cardiovascular disease and diabetes.[47] Few studies have investigated how birth weight might be related to this inflammatory-related factor later in life. Phillips et al[48] and Lissner et al[49] found low birth weight children to have high adult leptin concentrations for their BMI, whereas Giapros et al[50] found that children born very large for gestational age (>97th percentile) had high leptin levels during childhood. Our study suggests that both birth weight extremes may be related to greater leptin levels in adolescence, expanding the body of work on this topic.

Strengths of our study include the assessment of abdominal fat distribution via MRI and the consideration of potential confounding variables in our analyses with birth weight.

However, we acknowledge study limitations. First, given that our study used cross-sectional data, we cannot be certain that birth weight has a direct effect on the measures associated with cardiometabolic risk. Other factors linked to birth weight, including parental health and genetics, also may cause predisposition to elevated cardiometabolic risk. Second, birth weight was assigned by maternal recall, which may be inaccurate. However, studies have demonstrated strong agreement between maternal recall and registered birth weight, with one study estimating recall error less than 2%.[51,52] Another limitation is that pubertal maturation stage was measured by self-assessment rather than examination by physician. Previous investigations of the reliability of self-assessment have shown conflicting results. Whereas some researchers report reasonable agreement between self-assessment and examination by a physician,[53,54] others report discrepancies.[55,56] Although self-assessments may have led to a substantial proportion of pubertal stage misclassifications, we elected to use this methodology because physician assessments are time consuming, logistically challenging, and expensive.

Another important limitation is our distribution of participants into tertiles on the basis of birth weight resulted in an unequal sex and race distribution in each cohort. Study participants in tertile 1 were primarily female African Americans, and participants in tertile 3 were primarily white and male, which is representative of the disparity of preterm delivery of low birth weight infants in Georgia as indicated by 2014 data from Centers for Disease Control and Prevention's National Center for Health Statistics.[57] This distribution, as well as other regional differences in socioeconomic status, geographic location, social environment, or lifestyle habits of the study population, may preclude generalizability and limit the study findings to adolescents living in the southern US. Finally, it is important to note how the birth weight and obesity landscapes in the last decade have changed since the data from this study were collected in 2001–2005. Birth weight distributions since the mid-2000s have changed only modestly,[57] and obesity prevalence in children aged 2–19 years, although still high, has been stable during the past decade.[58] These lack of significant changes in birth weight distributions and obesity rates in the last decade lends support to the generalizability of our study findings.

On the other hand, there have been significant changes in lifestyle behaviors in the last decade, which may have implications for the importance of postnatal factors that contribute to obesity. For instance, in a large cross-national study of 30 countries, adolescents spent about 2 hours more per day with "screen time behaviors" in 2010 vs 2002,[59] and although US adolescents reported increased amounts of physical activity over this same time span, most still do not meet recommended guidelines.[60] Factors such as these are clearly integral to the problem of obesity and its related diseases. However, given that the prevalence of diabetes has increased,[61,62] and cardiovascular disease, although decreased, is still the cause of death for 1 in 3 Americans,[63] any insight that might contribute to their prevention is of value. Our study lends support to the importance of considering prenatal factors in reaching this goal.

In conclusion, our data suggest that both low and high birth weights are associated with risk factors related to cardiovascular disease and type 2 diabetes in a population of US adolescents. We also show that both high and low birth weight extremes are associated with greater visceral adiposity and biomarkers implicated in insulin resistance and inflammation. Additional research should target the prenatal environment and the factors associated with fetal undernutrition and overnutrition, because it may offer new insights for public health strategies in reducing cardiometabolic disease risk.

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Glossary

BMI	Body mass index
CV	Coefficient of variation

ELISA	Enzyme-linked immunosorbent assay
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
MRI	Magnetic resonance imaging
SAAT	Subcutaneous abdominal adipose tissue
VAT	Visceral adipose tissue

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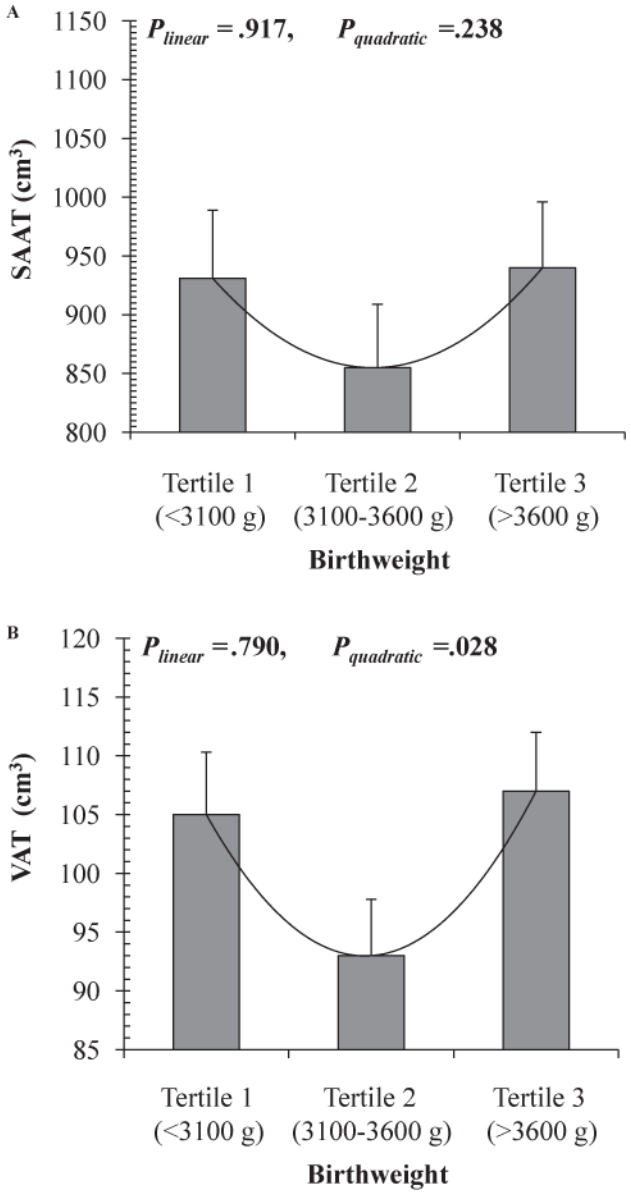

Figure.

Associations of **A**, SAAT and **B**, VAT across tertiles of birth weight in 575 adolescents aged 14–18 years. P_{linear} and $P_{quadratic}$ refer to *P* values obtained from the ANCOVA analysis for linear and quadratic terms, respectively, adjusted for age, sex, Tanner stage, moderate/vigorous physical activity, socioeconomic status, and BMI percentile.

Table I

Participant characteristics *

	Birth weight†			*P* value‡
	Tertile 1 2900 g (1040–3080 g)	**Tertile 2 3400 g (3100–3600 g)**	**Tertile 3 3900 g (3620–5260 g)**	
n	189	199	187	
Age, y	16.1 ± 1.1	15.9 ± 1.2	16.0 ± 1.2	.21
Female, %§	60.8	52.3	41.7	<.01
Blacks, %§	59.3	44.2	33.2	<.01
Tanner stage (1–5)	4.5 ± 0.7	4.6 ± 0.6	4.6 ± 0.6	.50
BMI percentile	62.0 ± 27.5	58.7 ± 28.8	66.9 ± 27.5	.02
BMI percentile category (%)§				.16
Not overweight	74.0	75.8	67.4	
Overweight	10.1	12.1	11.2	
Obese	15.9	12.1	21.4	
Moderate/vigorous physical activity, min/d	41 ± 30	45 ± 27	46 ± 30	.25
Socioeconomic status	34 ± 9	34 ± 9	36 ± 8	.11

* Values are means ± SD or %.

† Values are median (range) of birth weight in a given tertile.

‡ *P* values comparing differences between tertile groups of birth weight were calculated with ANOVA.

§ Test of significance between groups were based on χ^2 test.

Table II

Measurements of abdominal fat distribution, BP, insulin resistance, lipids, and inflammation across tertiles of birth weight in adolescents aged 14–18 years *,†,‡

	Birth weight				
	Tertile 1 2900 g (1040–3080 g)	**Tertile 2 3400 g (3100–3600 g)**	**Tertile 3 3900 g (3620–5260 g)**	P_{linear}	$P_{quadratic}$
n	189	199	187		
SAAT, cm^3					
Model 1	895 ± 71	803 ± 66	1026 ± 68	.191	.054
Model 2	931 ± 58	855 ± 54	940 ± 56	.917	.238
VAT, cm^3					
Model 1	104 ± 6.2	87 ± 5.6	114 ± 5.8	.277	.002
Model 2	105 ± 5.3	93 ± 4.8	107 ± 5.0	.790	.028
Systolic BP, mm Hg					
Model 1	111 ± 1	110 ± 1	111 ± 1	.995	.310
Model 2	112 ± 1	111 ± 1	111 ± 1	.492	.696
Diastolic BP, mm Hg					
Model 1	60 ± 1	60 ± 1	60 ± 1	.179	.759
Model 2	60 ± 1	60 ± 1	59 ± 1	.134	.875
Fasting serum glucose, mg/dL					
Model 1	89.8 ± 0.5	89.7 ± 0.5	88.9 ± 0.6	.285	.590
Model 2	89.8 ± 0.5	89.8 ± 0.5	88.7 ± 0.6	.175	.368
HOMA-IR					
Model 1	3.73 ± 0.14	3.14 ± 0.14	3.71 ± 0.14	.931	.001
Model 2	3.73 ± 0.13	3.27 ± 0.13	3.58 ± 0.13	.403	.014
Plasma triglycerides, mg/dL					
Model 1	72.4 ± 3.1	65.9 ± 2.9	65.1 ± 3.1	.097	.439
Model 2	72.8 ± 3.1	67.2 ± 2.8	63.3 ± 3.0	.026	.798
Plasma total cholesterol, mg/dL					
Model 1	148.5 ± 2.3	145.9 ± 2.2	148.3 ± 2.3	.936	.364
Model 2	148.6 ± 2.3	146.1 ± 2.2	148.0 ± 2.3	.861	.419
Plasma HDL-cholesterol, mg/dL					

	Birth weight				
	Tertile 1 2900 g (1040–3080 g)	**Tertile 2 3400 g (3100–3600 g)**	**Tertile 3 3900 g (3620–5260 g)**	P_{linear}	$P_{quadratic}$
Model 1	46.8 ± 0.8	47.1 ± 0.8	46.1 ± 0.8	.517	.503
Model 2	46.7 ± 0.8	46.7 ± 0.7	46.6 ± 0.8	.942	.930
Plasma LDL-cholesterol, mg/dL					
Model 1	93.3 ± 2.2	89.4 ± 2.1	93.7 ± 2.2	.894	.112
Model 2	93.5 ± 2.2	89.9 ± 2.1	93.0 ± 2.2	.865	.195
Serum leptin, μg/L					
Model 1	12.7 ± 0.9	9.9 ± 0.8	14.4 ± 0.9	.205	.001
Model 2	12.7 ± 0.7	11.1 ± 0.7	13.0 ± 0.7	.880	.040
Plasma adiponectin, mg/L					
Model 1	8.4 ± 0.4	8.4 ± 0.4	8.4 ± 0.4	.998	.973
Model 2	8.4 ± 0.4	8.2 ± 0.4	8.5 ± 0.4	.721	.545
Plasma C-reactive protein, mg/L					
Model 1	1.19 ± 0.18	1.08 ± 0.17	0.97 ± 0.18	.381	.998
Model 2	1.20 ± 0.16	1.17 ± 0.16	0.86 ± 0.18	.165	.479

BP, blood pressure; *HOMA-IR*, homeostasis model assessment of insulin resistance.

*Values are means ± SEM.

†Model 1 was adjusted for age, sex, race, Tanner stage, moderate/vigorous physical activity, and socioeconomic status; model 2 was adjusted for the same covariates in model 1 and further adjusted for BMI.

‡P_{linear} and $P_{quadratic}$ refer to *P* values obtained from the ANCOVA for linear and quadratic terms, respectively.