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Cord Blood Leptin and Adiponectin as Predictors of Adiposity in Children at 3 Years of Age: A Prospective Cohort Study

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Abstract

OBJECTIVES—Leptin and adiponectin are adipocyte-secreted hormones that regulate energy homeostasis and metabolism. Because their roles in the neonatal period and in early childhood are poorly understood, we aimed in this prospective cohort study to determine the extent to which umbilical cord blood leptin and adiponectin concentrations predict measures of adiposity and growth at 3 years of age.

PATIENTS AND METHODS—We studied 588 children participating in the prospective prebirth cohort study Project Viva. We examined associations of cord blood leptin and adiponectin levels with weight changes during the first 6 months of life, 3-year circulating leptin and adiponectin concentrations, and the following adiposity-related outcomes at 3 years of age: BMI z score, height-for-age z score, and sums of triceps and subscapular skinfold thicknesses to represent overall adiposity, as well as subscapular/triceps skinfold ratio to represent central adiposity.

RESULTS—Cord blood leptin and adiponectin were each directly associated with the duration of gestation and birth weight for gestational age z scores. Cord blood leptin levels were negatively

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GROUP FINDS FEWER TOYS WITH HIGH LEAD LEVELS

“New York (AP)—After the high-profile recalls of millions of lead-contaminated toys last year, a watchdog group said Wednesday that its tests found fewer toys with high levels of chemicals in them this year. But about a third of the toys tested still contained a worrisome level of chemicals. Healthytoys.org, a project of The Ecology Center, a nonprofit environmental group based in Michigan, in collaboration with other groups, tested about 1500 toys for a variety of chemicals, including lead, arsenic, cadmium and others. About one-third were found to have a significant level of chemicals, while two-thirds had low levels or none of the chemicals the group tested for. Lead was detected in 20% of toys, compared with 35% last year. About half of the toys tested were similar to toys tested last year. The Ecology Center, which also tests for chemical content in other products, began testing toys last year after a spate of recalls. Most significantly, Mattel Inc recalled more than 21 million Chinese-made toys on fears they were tainted with lead paint and tiny magnets that children could accidentally swallow. About 3.5% of toys tested had lead levels above the current 600 parts per million federal standard that would trigger a recall of lead paint. The American Academy of Pediatrics recommends a level of 40 ppm of lead as the maximum that should be allowed in children’s products. Following last year’s recalls, Congress passed legislation that lowers the allowed level of lead paint on toys to 90 ppm and sets a federal limit on lead content within toys for the first time.”

Anderson M. Associated Press. December 2, 2009

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associated with change in weight-for-length, weight-for-age, and length-for-age *z* scores between birth and 6 months of age. Similarly, cord blood adiponectin was negatively associated with change in weight-for-length and weight-for-age *z* scores. After adjusting for several maternal and child factors related to obesity, each 10 ng/mL increment of cord blood leptin was associated with a reduction in BMI *z* score and higher leptin levels at 3 years but not with skinfold thicknesses. Each 10 µg/mL increment of cord blood adiponectin was positively associated with a higher subscapular skinfold thickness/triceps skinfold thickness ratio at 3 years.

CONCLUSIONS—Lower cord blood leptin levels are associated with smaller size at birth but more pronounced weight gain in the first 6 months of life and higher BMI at 3 years of age. Cord blood adiponectin levels are also directly associated with birth weight for gestational age, inversely associated with weight gain in the first 6 months of life, and predict an increase in central adiposity at age 3 years.

Keywords

leptin; adiponectin; children; obesity

The prevalence of adult and childhood obesity has been increasing to epidemic proportions over the past decade.¹ In addition to nutrition and environmental factors early in development, accumulating evidence suggests that the development of obesity and its comorbidities may be influenced by intrauterine factors.^{2–4} Leptin and adiponectin are adipocyte-secreted hormones known to play critical roles in energy homeostasis in adults, but their fetal/neonatal effects are less well understood. Leptin, the product of the *ob* (obesity) gene, was discovered in 1994 and has since been shown to regulate energy homeostasis by relaying information about the body's energy and nutrient stores from the periphery to the brain.⁵ Although secreted primarily from adipocytes, it is also found in other tissues, including placentas.^{6–8} High leptin levels in cord blood have been reported to correlate with fetal adiposity at birth.^{9,10} Adiponectin is another adipokine that is solely derived from adipose tissue, is reduced in obesity in adults, and, in many studies, is inversely related to leptin levels.^{11,12} A large body of evidence supports the role of adiponectin in insulin sensitivity and lipid metabolism. Its role in neonatal and fetal growth remains poorly understood, with studies suggesting that, in contrast to adults, cord blood adiponectin is unrelated to birth weight¹³ or is positively associated with birth weight.^{14,15}

The majority of studies examining the relationship between these adipocytokines and birth weight, as well as other childhood measures of adiposity, have been cross-sectional. Of the few prospective studies, 2 were moderately sized cohort studies (*n* = 185–197) examining only leptin in children ages 5 to 12 years with known risk factors for obesity (childhood obesity, parental obesity, Pima Indian). These studies found that leptin at these ages was positively correlated with weight, thus implying that these children had developed leptin resistance before they reached the 5- to 12-year age range.^{16,17} Two smaller cohort studies (*n* = 52–85) showed that adiponectin was inversely related to weight gain; however, these studies were limited not only by their small size but also by the fact that 1 study examined all of the infants with 1-month follow-up, whereas the other examined only small and average for gestational age infants for 2 years.^{18,19} Limited sample size and duration of follow-up, as well as exclusion of several subgroups and lack of adjustment for numerous potential confounders in previously published prospective studies, have precluded full elucidation of the physiologic role of leptin and adiponectin in early development. Thus, the relationship between cord blood levels of these hormones and ultimate outcomes at birth and beyond remains largely to be determined. We hypothesized that lower leptin levels at birth would activate hypothalamic appetite centers and neuroendocrine mechanisms that would result in increased weight at 6 months and 3 years of age. We also hypothesized that, similar to our recent findings in rodents, increasing adiponectin

levels would be associated with increasing body weight and fat mass measures at 6 months and 3 years of life in children. We sought to clarify this question by analyzing longitudinal data from Project Viva, a larger cohort of pregnant women and their children. The objective of the study was to examine relationships of cord blood levels of adipokines with measures of childhood adiposity 3 years later.

METHODS

Subjects

Subjects were 588 participants from Project Viva, a prospective cohort study of women and their children in eastern Massachusetts enrolled between April 1999 and July 2002. Detailed enrollment criteria were described previously.²⁰ We recruited pregnant women at their initial prenatal visit and obtained informed consent for cord blood collection and longitudinal follow-up of their off-spring.

Of 2128 women who delivered a live infant, 1579 completed prenatal nutritional assessments and consented for their children to be followed up. We collected follow-up information and in-person examinations on 1294 women (82%). For this analysis, we excluded 19 participants who were missing height or weight data at 3 years and 687 from whom we did not collect umbilical cord blood at delivery, leaving a cohort of 588 participants. Comparison of the 588 participants in this analysis with the 1579 who were eligible for 3-year follow-up showed a higher proportion of maternal white race (73% vs 69%) and slightly lower smoking rates during pregnancy (10% vs 12%) but no differences in education status, annual household income, mean maternal prepregnancy BMI, or infant birth weight.

We performed in-person study visits with the mother at the end of the first and second trimesters of pregnancy and with both mother and child immediately after delivery and at 6 months and 3 years postpartum. Participants completed mailed questionnaires at 1 and 2 years postpartum. We collected information about a range of sociodemographic factors, lifestyle habits, and medical and reproductive history.²⁰ At the first-trimester study visit, mothers reported their weights just before they became pregnant. We calculated gestational weight gain as the prepregnancy weight subtracted from the last clinically recorded weight before delivery. Infant birth weight was determined from the hospital clinical record. We calculated gestational age from the last menstrual period, and if the estimate of gestational age from the second trimester ultrasound differed by >10 days, we used that value instead. We calculated birth weight for gestational age (BW/GA) *z* score by using a US national reference.²¹

Cord Blood and Serum Measurements

We collected cord blood samples from the umbilical vein after delivery of the infant, refrigerated whole blood for <24 hours, then spun and aliquoted samples for storage in liquid nitrogen (−80°C). We measured concentrations of leptin and adiponectin in cord blood and in plasma from children at 3 years of age with a radioimmunoassay (Linco Research Inc, St Charles, MO), as described previously.^{22–24}

Outcome Variables

At the 3-year visit, which took place between December 12, 2002, and July 11, 2006, trained research staff measured weight using a calibrated scale (Seca model 881 [Seca Corporation, Hanover, MD]), standing and sitting height using a calibrated stadiometer (Shorr Productions, Olney, MD), and subscapular (SS) and triceps (TR) skinfold thicknesses with a Holtain caliper (Holtain Ltd, Crosswell, Crymych, Dyfed Wales, United Kingdom). Every 6 months, an expert auxologist (Irwin Shorr, MPH) trained or retrained the research staff in all of the anthropometric measurements among volunteer participants of ages similar to Viva participants. In these

training sessions, estimates of interobserver and intraobserver reliability were well within published reference ranges for all of the measurements (example for length: rater 1, 0.22 cm; rater 2, 0.35 cm; rater 3, 0.19 cm; rater 4, 0.25 cm; and between raters, 0.29 cm).²⁵ Experienced field supervisors provided ongoing quality control by observing and correcting the measurement technique every 3 months.

Statistical Analyses

We calculated BMI (kilograms per meter squared) and then each child's age- and gender-specific BMI z score and height-for-age z score using US national reference data (National Center for Health Statistics, Centers for Disease Control and Prevention Growth Charts, www.cdc.gov/growthcharts). We calculated leg length as the difference between standing and sitting heights. We used the sum of skinfolds (SS + TR) to estimate overall adiposity, and the ratio of skinfolds (SS/TR) to estimate central adiposity.²⁶ Spearman correlation coefficients were computed to examine the association between cord blood leptin and adiponectin levels and changes in weight-for-length, weight-for-age, and length-for-age z scores from birth to 6 months.

We examined characteristics of participants and 3-year adiposity outcomes by quintiles of cord blood leptin and adiponectin. To calculate unadjusted trend P values across quintiles, we used Mantel-Haenszel χ^2 for categorical characteristics and linear regression for continuous characteristics with quintiles coded as 1 to 5. In multivariate linear models, we used cord blood leptin and adiponectin as categorical (quintiles) or continuous variables. We adjusted our multivariate model for maternal education, prepregnancy BMI, gestational weight gain and duration of gestation; paternal BMI; and child age, gender, race/ethnicity, and breastfeeding duration. In preliminary modeling, 8 additional potential confounding variables were included, namely, maternal age, glycemic status, hypertension, pregnancy smoking, energy intake and physical activity, and child daily sleep and television viewing. Because inclusion of the confounding variables did not materially change the effect estimates for cord blood leptin or adiponectin, we left them out of the final model. In subsequent models, we additionally adjusted for BW/GA z score. Because we were interested in fat distribution after controlling for overall body size, we further adjusted for child's BMI z score in analysis of the SS/TR ratio. For the continuous cord blood leptin and adiponectin variables, we reported linear regression estimates for a 10 ng/mL increment of cord blood leptin and a 10 μ g/mL increment of cord blood adiponectin. We conducted all of the analyses by using SAS 9.1 (SAS Institute, Inc, Cary, NC).

RESULTS

Higher cord blood leptin was strongly associated with increased cord blood adiponectin (Table 1 and Table 2). Cord blood leptin and adiponectin were also directly associated with gestational age at birth and BW/GA z score. Children who were in lower quintiles of cord blood leptin were more likely to be boys (Table 1). Mothers categorized in the highest quintiles of cord blood leptin had significantly higher prepregnancy BMI.

Although bivariate analysis (Table 1) did not show relationships of cord blood leptin with 3-year BMI, an inverse association was apparent after multivariate analysis (Table 3). This association was strengthened after adjustment for potential confounding effects of maternal and paternal BMI and BW/GA z score.

In contrast, we did not find an association of cord blood adiponectin with 3-year BMI. Figure 1 shows associations of quintiles of cord blood leptin and adiponectin with 3-year BMI z score, after multivariate adjustment for maternal education, prepregnancy BMI, gestational weight gain, duration of gestation, and BW/GA z score; paternal BMI; and child age, gender, race/ethnicity, and breastfeeding duration.

After observing that most associations were nearly linear, we expressed cord blood leptin and adiponectin as continuous variables. The fully adjusted multivariate models (Table 3) show that each 10 ng/mL increment of cord blood leptin was associated with lower BMI *z* score (-0.29 [95% confidence interval (CI): -0.43 to -0.14]; $P = .0001$), lower height-for-age *z* score (-0.16 [95% CI: -0.30 to -0.02]; $P = .03$), shorter leg length (-0.40 [95% CI: -0.77 to -0.04]; $P = .03$), and 3-year leptin levels (0.58 [95% CI: 0.25 to 0.92]; $P = .001$) but was not associated with 3-year skinfold thicknesses or adiponectin levels. Each 10 $\mu\text{g/mL}$ increment of cord blood adiponectin level was associated with higher SS/TR ratio (2.01 [95% CI: 0.09 to 3.93]; $P = .04$) but was not associated with 3-year BMI *z* score, leg length, leptin level, or adiponectin level (0.55 [95% CI: -0.42 to 1.52]; $P = .27$).

Leptin concentration at 3 years of age was directly correlated with BMI *z* score (unadjusted Spearman $r = 0.23$; $P < .0001$), BMI ($r = 0.24$; $P < .0001$), sum of SS + TR ($r = 0.18$; $P < .002$), and SS/TR ratio ($r = 0.12$; $P = .04$) and inversely correlated with leg length ($r = -0.15$; $P = .007$). Three-year adiponectin concentration was marginally associated with the sum of SS + TR ($r = 0.10$; $P = .08$) but was modestly inversely correlated with leg length ($r = -0.14$; $P = .02$) and SS/TR ratio ($r = -0.11$; $P = .05$).

Cord blood leptin was inversely correlated with change in weight-for-length *z* score (unadjusted Spearman $r = -0.28$; $P < .0001$), weight-for-age *z* score ($r = -0.33$; $P < .0001$), and length-for-age *z* score ($r = -0.17$; $P = .01$) from birth to 6 months. Cord blood adiponectin was inversely correlated with change in weight-for-length *z* score ($r = -0.12$; $P = .05$) and weight-for-age *z* score ($r = -0.10$; $P = .04$) from birth to 6 months but was not associated with change in length-for-age *z* score ($r = 0.03$; $P = .61$).

DISCUSSION

In this prospective cohort study, we confirm data from previous observational studies showing that cord blood adiponectin levels are higher than those seen in adults, that cord blood adiponectin correlates with cord blood leptin levels, and that higher leptin and adiponectin levels correlate with higher BW/GA *z* scores. What is first reported herein is that lower cord blood leptin levels predict increased weight and height gain in the first 6 months of life and also predict higher leptin levels at 3 years and higher degrees of both obesity (BMI *z* score) and linear growth (height-for-age/leg length), with or without adjustment for numerous parental and child covariates. Unlike leptin, cord blood adiponectin levels were associated with slower weight gain in the first 6 months of life and were not associated with 3-year BMI or with central adiposity, as measured by the ratio of skinfold thicknesses at 3 years of age. Leptin levels at age 3 years correlated directly with BMI and measures of overall and central adiposity. In contrast, 3-year adiponectin levels were only marginally positively associated with overall adiposity and negatively and significantly associated with central adiposity.

Leptin levels have been widely accepted as a marker for neonatal fat mass, and leptin receptors are expressed in several tissues including fetal cartilage, bone, lung, kidney, and hypothalamus,²⁷ suggesting that leptin may exert biological functions in the fetus and/or early in life. We reported that cord blood leptin predicted weight changes over the first 6 months and anthropometric outcomes at 3 years of life, which is in support of the expected biological function of leptin to regulate food intake, energy expenditure, and, thus, body mass.²⁸ Our data are also consistent with recent experimental evidence indicating that leptin treatment of undernourished rodents with low leptin levels prevents weight gain and metabolic abnormalities later in life.²⁹ Studies in rodents and humans have demonstrated that, in leptin-sensitive states, the role of leptin is first to regulate energy homeostasis by modulating energy intake and expenditure. It also regulates several neuroendocrine axes, including the growth hormone–insulin-like growth factor axis.^{28,30,31} Thus, in contrast to obese adults who develop

resistance to the effects of leptin effects, our data support the notion that infants do not seem to have developed leptin resistance during the first 3 years of life. Thus, it is likely that fundamental differences in the role of leptin to regulate energy homeostasis occur in early development, that is, in the first years of life, before leptin resistance to long-standing circulating higher leptin levels is established.

Both the fetus and the placenta contribute to the total amount of leptin^{32,33} to which the fetus is exposed, but data on any adiponectin production by the placenta remain controversial.^{14, 34–36} Term newborns have ~15% body fat, the majority of which is subcutaneous. In this study, and in contrast to adults whose adiponectin levels are inversely correlated with weight levels, higher cord blood concentrations of adiponectin were associated with higher weight at birth. Similar to previous studies, we found that adiponectin cord blood levels were higher than the usual concentrations seen in adults. These findings are consistent with the results seen in previous studies of animals³⁷ and humans.^{14,15,36}

Several studies have documented a relationship between smaller birth size and increased risk of developing central adiposity and the metabolic syndrome later in life.^{37,38} Therefore, the observation that higher cord blood concentrations of adiponectin were associated in our study with larger birth size, changes in body weight over the first 6 months, and higher 3-year SS/TR ratio, a measure of central adiposity, is intriguing. No previous studies have assessed prospectively the association between baseline adiponectin levels and overall or central obesity in children; thus, it remains unknown to what extent adiponectin alters body composition and/or whether it is only a surrogate marker of other underlying mechanisms or simply changes in adiposity.

With increasing age, the ratio of subcutaneous fat/visceral fat decreases,³⁹ and changes in body fat distribution contribute to the switch from a positive correlation between adiponectin and weight at birth to a negative one later in life. We have shown using longitudinal animal studies that, with progression of age, adiponectin initially increases in relation to increasing body weight and overall fat mass, but over time adiponectin levels plateau and then start decreasing as more intraabdominal fat starts accumulating. The latter leads to decreasing adiponectin levels seen in obese adults, which coincides with the development of insulin resistance.⁴⁰ These longitudinal changes are consistent with the observational data presented herein and may reflect either loss of mitochondria from adipocytes and/or the function of yet-to-be-determined factors that limit adiponectin secretion from adipocytes with increasing age.³⁹ In adult humans, it has been shown that, although short-term changes in weight do not alter adiponectin levels appreciably, significant and long-term weight loss decreases adiponectin levels.⁴¹ Also, decreased central obesity, defined by a low waist/hip ratio and restricted diet, is associated with lower adiponectin levels, whereas the effects of exercise on adult adiponectin levels are not yet clear.⁴² Because adiponectin plays a major role in regulating insulin sensitivity, glucose tolerance, and metabolism,^{40,43,44} it would be expected that higher baseline adiponectin levels seen in larger neonates could be associated with an improved metabolic profile. However, a detailed metabolic assessment of the children studied herein had not been performed at 3 years of age. Thus, longitudinal studies with longer duration of follow-up and assessment of the metabolic syndrome are needed to explore adiponectin changes over time.

Strengths of this study include its study design. Given recent notions that obesity may be influenced by maternal-fetal interactions and infancy may be a period of obesity programming,⁴⁵ a prospective study following children from before birth is of great use. Additional strengths include a larger sample size and longer follow-up than previous studies^{18,19} and a general population study sample rather than children who are at high risk for the development of obesity later in life.^{16,17} This study raises interesting questions regarding the interplay of leptin and adiponectin during the neonatal period, but like all observational studies, it cannot prove

causality. Limitations of this study are that it includes a limited number of time points, and the relatively high socioeconomic position of our participants could limit generalizability.

CONCLUSIONS

This prospective cohort study shows that cord blood levels of leptin and adiponectin predict adiposity-related outcomes over 3 years of follow-up. Unlike in later childhood and adulthood, however, lower leptin levels predicted higher BMI, and higher adiponectin levels predicted increased central adiposity. These findings high-light the fact that the prenatal and early postnatal periods are ones of developmental plasticity.^{46–48} During such critical periods, organisms tend to set long-term metabolic trajectories that later become relatively resistant to change. In the field of obesity, such resistance is evident by the fact that, in adults, the adipoinular axis tenaciously resists sustained weight loss.⁴⁹ These considerations raise the possibility that interventions to prevent obesity and its metabolic consequences may be particularly effective if conducted very early in life. Additional data on long-term effects of these hormones and their determinants are needed to address this possibility.

What's Known on This Subject

Leptin levels have been widely accepted as markers for neonatal fat mass, whereas the role of adiponectin in neonatal and fetal growth is poorly understood. Little is known about these adipokines as predictors of future adiposity in children.

What This Study Adds

Cord blood levels of leptin and adiponectin predict adiposity-related outcomes at 3-year follow-up. Lower leptin levels predicted higher BMI, and higher adiponectin levels predicted increased central adiposity. These results raise the possibility of conducting interventions to prevent obesity in early life.

Abbreviations

BW/GA, birth weight for gestational age; SS, subscapular skinfold thickness; TR, triceps skinfold thickness; CI, confidence interval.

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FIGURE 1.

BMI z score at 3 years of age according to quintile of cord blood leptin (A) and adiponectin (B), adjusted as outlined in "Methods." Values are regression estimates $\pm$ SE. The P value for trend across quintiles is .002 for leptin and .67 for adiponectin.

Table 1
 Characteristics of Participants According to Quintiles of Cord Blood Leptin (N=588)

Variables	Total, Mean (SD)	Quintile of Cord Blood Leptin ^a					Trend <i>P</i>
		1 (0.5–3.3)	2 (> 3.3–5.5)	3 (> 5.5–8.7)	4 (> 8.7–13.9)	5 (> 13.9–40.0)	
Maternal variables							
Age at enrollment, y	32.3 (5.1)	31.9	32.3	31.9	32.4	32.8	.25
Prepregnancy BMI, kg/m ²	24.8 (5.4)	24.2	24.1	24.7	25.1	26.0	.003
Gestational weight gain, kg	15.7 (5.5)	15.5	15.6	15.8	16.0	15.6	.73
Paternal BMI, kg/m ²	26.4 (3.8)	25.8	25.9	26.5	27.1	26.5	.03
Education ≥ college degree	400 (68) ^b	69%	67%	64%	65%	75%	.45
Married or cohabitating	543 (93) ^b	87%	96%	94%	95%	91%	.43
Household income, more than \$70 000	332 (61) ^b	65%	61%	54%	68%	56%	.45
Newborn/infant variables							
Male	295 (50) ^b	65%	58%	52%	42%	34%	<.0001
Race/ethnicity, white	408 (69) ^b	69%	76%	71%	64%	66%	.16
Cord blood adiponectin, μg/mL	28.5 (6.8)	24.2	27.1	29.8	30	31.7	<.0001
Gestational age at birth, wk	39.7 (1.5)	38.9	39.7	39.7	40.1	40.1	<.0001
BW/GA, z score	0.26 (0.94)	−0.15	−0.08	0.16	0.50	0.84	<.0001
Breastfeeding duration, mo	6.2 (4.5)	6.2	5.6	6.5	5.6	7.3	.08
Child 3-y variables							
Age, y	3.3 (0.4)	3.4	3.3	3.3	3.3	3.2	.002
BMI z score	0.41 (1.03)	0.42	0.32	0.52	0.53	0.24	.61
Weight-for-age z score	0.45 (0.98)	0.47	0.34	0.49	0.62	0.33	.97
Height-for-age z score	0.27 (0.94)	0.26	0.22	0.21	0.39	0.28	.44
Leg length, cm	42.0 (3.1)	42.5	41.7	42.0	42.1	41.8	.30
SS/TR ratio	0.63 (0.15)	0.62	0.62	0.64	0.64	0.64	.19
SS+TR, mm	16.7 (4.2)	16.9	16.2	16.4	17.4	16.7	.63
Leptin, ng/mL	1.7 (1.8)	1.3	1.4	1.8	1.8	2.2	.001
Adiponectin, μg/mL	22.3 (6.0)	23.3	22.9	22.5	21.0	21.4	.02

^aData are means unless otherwise specified.

^bData are *n* (%).

Table 2
 Characteristics of Participants According to Quintiles of Cord Blood Adiponectin (N=588)

Variable	Total Mean (SD)	Quintile of Cord Blood Adiponectin ^a					Trend P
		1 (2.9–23.1)	2 (> 23.1–27.5)	3 (> 27.5–30.9)	4 (> 30.9–33.9)	5 (> 33.9–42.6)	
Maternal variables							
Age at enrollment, y	32.3 (5.1)	32.9	31.9	32.8	31.6	32.1	.20
Prepregnancy BMI, kg/m ²	24.8 (5.4)	25.5	24.8	24.4	25.4	24.0	.14
Gestational weight gain, kg	15.7 (5.5)	15.1	15.6	16.2	16.2	15.4	.42
Paternal BMI, kg/m ²	26.4 (3.8)	26.5	25.9	26.5	26.7	26.2	.76
Education ≥ college degree	400 (68)	71%	62%	67%	69%	72%	.53
Married or cohabitating	543 (93)	91%	96%	94%	92%	90%	.51
Household income, more than \$70 000	332 (61)	61%	61%	61%	58%	62%	.95
Newborn/infant variables							
Male	295 (50) ^b	56%	51%	45%	47%	52%	.38
Race/ethnicity, white	408 (69) ^b	66%	69%	70%	72%	70%	.38
Cord blood leptin, μg/mL	8.8 (6.4)	5.3	7.1	9.7	10.3	11.5	<.0001
Gestational age at birth, wk	39.7 (1.5)	39.2	39.6	39.9	39.8	40.0	<.0001
BW/GA, z score	0.26 (0.94)	0.07	0.17	0.23	0.48	0.33	.002
Breastfeeding duration, mo	6.2 (4.5)	5.7	6.1	6.2	6.6	6.6	.08
Child 3-y variables							
Age, y	3.3 (0.4)	3.4	3.3	3.3	3.3	3.3	.01
BMI z score	0.41 (1.03)	0.35	0.4	0.33	0.64	0.31	.60
Weight-for-age z score	0.45 (0.98)	0.49	0.33	0.37	0.71	0.34	.73
Height-for-age z score	0.27 (0.94)	0.41	0.13	0.24	0.41	0.17	.47
Leg length, cm	42.0 (3.1)	42.5	42.0	41.9	42.1	41.57	.06
SS/TR ratio	0.63 (0.15)	0.61	0.63	0.63	0.64	0.65	0.04
SS+TR, mm	16.7 (4.2)	16.4	16.8	16.3	17.5	16.6	.36
Leptin, ng/mL	1.7 (1.8)	1.5	1.6	1.7	1.7	1.8	.37
Adiponectin, μg/mL	22.3 (6.0)	21.6	21.9	22.9	22.8	22.2	.40

^aData are means unless otherwise specified.

^bData are *n* (%).

Table 3

Regression Estimates of Child 3-Year Adiposity-Related Measures on Continuous Cord Blood Leptin (per 10 ng/mL) and Adiponectin (per 10µg/mL) Exposure

Variable	Cord Blood Leptin		Cord Blood Adiponectin	
	Estimate (95% CI)	P	Estimate (95% CI)	P
BMI z score at 3 y of age				
M1	−0.09 (−0.22 to 0.04)	.20	0.06 (−0.07 to 0.18)	.38
M2	−0.16 (−0.30 to −0.02)	.02	0.08 (−0.04 to 0.21)	.18
M3	−0.29 (−0.43 to −0.14)	.0001	0.07 (−0.06 to 0.19)	.29
Weight-for-age z score at 3 y of age				
M1	−0.03 (−0.15 to 0.10)	.67	0.001 (−0.12 to 0.12)	.98
M2	−0.10 (−0.23 to 0.03)	.15	0.03 (−0.09 to 0.15)	.63
M3	−0.28 (−0.42 to −0.14)	<.0001	0.002 (−0.11 to 0.12)	.98
Height-for-age z score at 3 y of age				
M1	0.05 (−0.07 to 0.17)	.42	−0.08 (−0.19 to 0.03)	.16
M2	−0.00 (−0.14 to 0.14)	.99	−0.07 (−0.19 to 0.05)	.26
M3	−0.16 (−0.30 to −0.02)	.03	−0.10 (−0.21 to 0.02)	.10
Leg length at 3 y of age				
M1	−0.20 (−0.59 to 0.19)	.30	−0.42 (−0.79 to −0.05)	.02
M2	−0.06 (−0.41 to 0.30)	.75	−0.09 (−0.40 to 0.22)	.57
M3	−0.40 (−0.77 to −0.04)	.03	−0.16 (−0.46 to 0.15)	.31
SS+TR				
M1	0.19 (−0.36 to 0.74)	.50	0.40 (−0.11 to 0.91)	.13
M2	−0.02 (−0.63 to 0.58)	.94	0.45 (−0.08 to 0.98)	.09
M3	−0.24 (−0.88 to 0.41)	.48	0.42 (−0.11 to 0.95)	.12
SS/TR				
M1	0.92 (−1.03 to 2.87)	.35	1.83 (0.01 to 3.66)	.05
M2	−0.43 (−2.64 to 1.79)	.71	1.96 (0.04 to 3.88)	.05
M3	−0.22 (−2.61 to 2.17)	.86	2.01 (0.09 to 3.93)	.04
3-y leptin				
M1	0.59 (0.27 to 0.91)	.0003	0.20 (−0.06 to 0.47)	.14
M2	0.59 (0.28 to 0.90)	.0002	0.23 (0.00 to 0.45)	.05
M3	0.58 (0.25 to 0.92)	.001	0.20 (−0.03 to 0.43)	.08
3-y adiponectin				
M1	−1.15 (−2.26 to −0.03)	.04	0.65 (−0.26 to 1.56)	.16
M2	−0.91 (−2.22 to 0.41)	.18	0.61 (−0.36 to 1.57)	.22
M3	−1.38 (−2.81 to 0.05)	.06	0.55 (−0.42 to 1.52)	.27

M1 was unadjusted. M2 was adjusted for maternal education, prepregnancy BMI, gestational weight gain and duration of gestation; paternal BMI; and child age, gender, race/ethnicity, and breastfeeding duration. SS/TR outcome was additionally adjusted for BMI z score at 3 years of age. M3 was M2 plus BW/GA z score.