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Newborn adipokines and early childhood growth

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Abstract

Background—While adipokines can regulate satiety and energy metabolism, whether they are associated with childhood growth is unclear.

Objective—To evaluate whether adipokine levels at birth are associated with growth.

Methods—2264 singletons and 1144 twins from Upstate KIDS (born 2008–2010) had adiponectin, leptin, resistin and complement factor D measured in newborn blood spots. Parents reported anthropometry from pediatric visits via questionnaires every 4–6 months. Generalized linear mixed effects models were used to estimate growth trajectories through 3 years of age.

Results—Among singletons, resistin and leptin were associated with greater weight-for-age (0.12 z-score units (95%CI: 0.04, 0.20) [p=0.003] and 0.15 (0.06, 0.24) [p=0.001], respectively) and BMI z-score (0.11; 0.02, 0.20 [p=0.02] and 0.18; 0.07, 0.28 [p=0.002], respectively). After adjusting for birthweight, resistin and a ratio of resistin-to-adiponectin remained associated with weight through 3 years of age and odds of being overweight at 3 years of age in a subgroup of singletons. Among twins, adiponectin was associated with increased weight-for-age and length-for-age z-scores even after adjusting for birthweight (0.18; 0.08, 0.28 [p=0.0006]; 0.20; 0.07, 0.33 [p=0.003], respectively).

Conclusions—Levels of adipokines were associated with early childhood growth in small magnitudes. Resistin may be relevant for further examination in pediatric obesity.

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Keywords

adipokines; adiponectin; resistin; growth; newborn dried blood spots; rapid infant weight gain

Introduction

Adipokines have pleiotropic effects on multiple organ systems to help regulate energy metabolism. Adiponectin and leptin play key roles in energy homeostasis and satiety.¹ Resistin, named for its insulin resisting effects, has been associated with inflammatory responses.² Complement factor D (CFD or adipsin³) has been found to promote adipocyte differentiation.⁴ Cross-sectionally adipokine levels are related to an individual's amount of adiposity, but their ability to indicate longitudinal childhood growth has been unclear. Such associations could be helpful as it would suggest that a newborn's level of adipokines may indicate whether the child will undergo rapid weight gain or continue at larger size. We previously found that adiponectin was associated with gestational age, whereas leptin was positively associated with birth weight.⁵ This investigation expands on those findings to understand how newborn adipokines may be associated with early childhood growth.

Studies evaluating cord blood adipokine concentrations of adiponectin and/or leptin with childhood growth used varying measures of adiposity and included children of different ages.^{6–13} Studies have suggested that cord blood leptin levels are inversely associated with weight at later age, particularly between 2–4 years^{6,8,12,13}, with weaker associations at older age.¹⁴ Lower weight gain in infancy in relation to cord blood leptin has also been observed.^{10,15} There have been mixed results observed for adiponectin, although some reported positive associations with adiposity measures.^{6,7,14,16}

Taken together, longitudinal evidence suggests that leptin and adiponectin levels at birth may be related to early childhood growth. However, twins, whose birth sizes differ from singletons, are generally excluded from previous investigations. In addition, gender differences have been inconsistently reported and there is a lack of studies examining multiple adipokines simultaneously.¹²

Materials and Methods

The Upstate KIDS Study recruited 5034 mothers and their 6171 babies born in New York State (excluding New York City) from 2008 to 2010 and prospectively followed them through 3 years of age.¹⁷ As the study was designed to evaluate the impact of infertility treatment on child health, mothers who used infertility treatment or bore multiple gestations were oversampled.¹⁷ The sampling framework has been detailed elsewhere as are findings that infertility treatment was generally not associated with growth.¹⁸ The New York State Department of Health and the University at Albany (State University of New York) Institutional Review Boards approved the study. Parents provided written informed consent.

Blood spot analyses

At 8 months postpartum, parents provided additional consent for using residual dried blood spots from the Newborn Screening Program. Minor differences in characteristics of parents

providing consent (62%) compared to those who did not and the methods to retrieve the spots have been described elsewhere.^{5,19} Newborn dried blood spot cards were retrieved from cold storage (4°C) and punched.²⁰ Neutral buffer was used to elute the 3.2mm punches. Eluants were frozen until analysis at -80°C. The Human Obesity Panel (R&D Systems, Minneapolis, MN) measuring adiponectin, resistin, complement factor D (CFD), leptin, serpin and c-reactive protein was run using a Luminex¹⁰⁰ analyzer with xPONENT 3.1 software (Luminex System, Austin, TX). Based on replicate measures, the intra-assay coefficients of variation (CV) were 7–9% except for leptin (43%) due to low sensitivity.⁵ Inter-assay CVs ranged 6–9%.⁵ Leptin values were dichotomized at the median level (2.43 pg/ml) due to low detectability (48% undetected).⁵ A resistin to adiponectin ratio was calculated as their relative concentrations may serve as a marker of insulin resistance and provide additional dynamical information on relationships with growth.²¹

Growth measures

At enrollment, mothers received child health journals for recording clinically measured values of weight and length from pediatric visits. Mothers reported these measures and the date or the child's age at each visit in standardized questionnaires. Questionnaires included multiple entries so that we have repeat information about anthropometry, which a mother was queried at 4, 8, 12, 18, 24, 30 and 36 months of age of the child. Thus, in each questionnaire the mother could provide measurements during the intermediate time interval since last questionnaire. Birth weight came from birth certificates. Z-scores for weight, length, weight-for-length and BMI were calculated using the World Health Organization Child Growth Standards for age and sex.

We next examined the association between adipokines and the rapid infant weight gain at 4, 9 and 12 months, respectively. The outcome of rapid infant weight gain was calculated at each time point based on the predicted value of the longitudinal models fitted for each outcome at each of the fixed time points. This allows us to also impute the missing weights based on a fitted model as previously done.¹⁸ Weight gain was calculated by taking the difference between predicted weights and birthweight. Standard deviation scores (SDS) were calculated for each child at each time point by taking the difference between the child's weight gain and average weight gain among singletons in our sample, divided by their standard deviation. Rapid weight gain was defined as having a SDS above 0.5 for 4 or 9 months and above 0.67 for 12 months.

Childhood overweight (85th percentile for BMI) was evaluated among singletons due to a smaller sample of participants with both weight and height reported past 24 months of age (n=1074 singletons and 476 twins). Childhood overweight was evaluated on average at 32 months of age.

Covariates

Mothers reported on race/ethnicity, alcohol, smoking during pregnancy, marital/cohabitation status and paternal anthropometrics at enrollment (approximately 4 months postpartum). Parental ages, insurance status, parity, infant gender, birth weight, and gestational age came from birth certificates. Prepregnancy weight and height information to derive body mass

index (BMI) was from birth certificates and relied on maternal report if missing (n=53). Women were considered to have hypertensive disorder in pregnancy or gestational diabetes if it was indicated on birth records, self-reported or claim filed in the New York State Department of Health Statewide Planning and Research Cooperative System (SPARCS) database of hospital data.

Statistical analysis

Biomarkers were natural log transformed for normality. Of the children with adipokine measurements (n=3637), 133 (3.7%) singletons and 96 (2.6%) twins missing information on weight after birth were excluded from analyses to enable comparisons of growth trajectories. For length analyses, children with only one measure were also excluded (112 singletons and 72 twins). Comparisons were made in baseline characteristics between those excluded due to missing information and those remaining by chi-square or t-test of difference.

Mixed linear models with a random slope and cubic splines for age and age-gender interactions were used to estimate weight-for-age, length-for-age, weight-for-length and BMI z-score trajectories from birth to 36 months. We tested whether the whole curve/trajectory consisting of repeated measures of weight/length/BMI differed by adipokine levels measured at birth. Any significant differences indicate a shift in the whole curve being higher/lower with respect to the adipokine concentration. We did not include time by adipokine interactions in these models but rather tested rapid infant weight gain separately to answer the question of whether rates of growth differed in infancy to an extent that may confer long-term health consequences by concentrations of adipokines. We stratified by plurality and analyses which included twins were clustered on family to account for correlation between sibling pairs. Logistic regression was used to estimate odds ratios (95% CI) for rapid infant weight gain and for risk of childhood overweight. To account for correlation between twins, generalized estimating equations (GEE) were applied. Sampling weights were derived based on vital records data on the births occurring during the recruitment period for infertility treatment, plurality and region of birth.⁵ They were applied to all analyses to account for the oversampling of infertility treatment and twins by design.¹⁷

Analyses were adjusted for covariate models with gestational age and birth weight added separately to evaluate the impact of those covariates previously found associated in this cohort with adipokine levels.⁵ Adipokines were first modeled separately but as the interpretation of results did not differ and correlations between adipokines were low (all $r < 0.25$), only models mutually adjusting for all adipokines are reported. The resistin-adiponectin ratio was correlated with its respective components (i.e., $r = -0.46$ with adiponectin and $r = 0.81$ with resistin) and modeled adjusting only for leptin and CFD and not additionally for adiponectin and resistin levels. Interactions were tested between adipokines and infant sex. All analyses were conducted in SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results

Table 1 shows the baseline characteristics of the participants stratified by plurality. Twins had lower levels of all adipokines due to their smaller birth size and earlier gestation.⁵ The

median numbers of measurements reported by mothers were 9 measures of weight and 8 measures of length/height. Missing longitudinal growth information was associated with sociodemographic factors including younger parental age, non-White race, less than college education, non-private insurance and not married/cohabitating but did not significantly differ by maternal BMI or adipokine levels (data not shown).

Table 2 shows the associations between the adipokines and growth measures from birth through 3 years for singletons. The extensive covariates in model 2 which included pregnancy complications and socioeconomic factors did not materially change estimates. Among singletons, resistin was associated with increased weight-for-age even after adjusting for birthweight and gestational age (0.07 per log unit increase in resistin; 95% CI: 0.01, 0.13). Leptin was also associated with increased weight-for-age, but the association disappeared after accounting for birthweight (model 3). Among twins, adiponectin was associated with increased weight, length and BMI as was the adiponectin to resistin ratio. (Table 2) Associations remained with weight and length even after adjusting for birth measures. In sensitivity analyses, no consistent interactions were detected for infant gender. (data not shown)

In general, adipokine levels were inversely associated with rapid infant weight gain in unadjusted analyses. (Supplemental Table 1) After adjusting for covariates including gestational age (to account for the high risk of rapid weight gain among preterm infants), most results were attenuated. Among singletons, only leptin remained inversely associated with early rapid gain at 4 months, which did not persist at 9 or 12 months. The resistin-to-adiponectin ratio suggests similar findings with resistin for singletons. Among twins, adiponectin was associated with higher odds of rapid weight gain (1.53; 1.10, 2.13). The change in direction of association was solely due to gestational age, as a model without its inclusion was not significant (OR: 0.84; 0.63, 1.13). Resistin-to-adiponectin ratio was inversely associated with rapid weight gain among twins at all infant ages examined in models adjusted for gestational age.

We observed that higher resistin and leptin levels at birth were both associated with increased odds of being overweight (85th percentile) among singletons in the minimal adjustment models. However, like the growth trajectory models, the associations with leptin did not remain after accounting for birth weight although the association with resistin persisted (aOR: 1.33; 95% CI: 1.02, 1.74). Associations were also observed with the resistin-to-adiponectin ratio even after adjusting for birth characteristics (aOR: 1.81; 1.20, 2.75). (Supplemental Table 2)

Discussion

To our knowledge, this is the first examination of long-term growth by adipokine levels measured using newborn dried blood spots in both singletons and twins. Findings demonstrate that associations with growth may be largely due to their correlations with birthweight and/or gestational age and differences detected were relatively small. After accounting for birth characteristics, the associations for twins differed from those observed for singletons. Higher resistin levels were associated with overweight risk at older age as

was the resistin-to-adiponectin ratio among singletons. Among twins, adiponectin was associated with higher weight-for-age and increased weight gain at 12 months but risk of overweight remains to be evaluated in studies with larger numbers of twins. Resistin-to-adiponectin associations coincided with resistin associations among singletons and adiponectin associations among twins.

Previous longitudinal investigations have been based on cord blood or maternal levels of adipokines during pregnancy.^{6–10,12,14} While these concentrations were impacted by placental production, our dried blood spot concentrations are not as both adiponectin and leptin have short half-lives.²² Different sources and study populations may explain the different trends observed across studies. Albeit no studies have shown newborn levels to be strong determinants of childhood growth.

Results of studies examining leptin concentrations in cord or maternal blood and childhood BMI (with over 100 participants) are summarized in Supplemental Table 3. Findings are equivocal. However, covariate selection can be important. One study found a positive association between maternal leptin and BMI *z*-prior to adjustment for covariates (0.4; 0.2, 0.6, $p<0.0001$) but reversed direction with adjustment for maternal BMI (−0.2; −0.4, 0.1, $p=0.51$).¹⁵ We did not observe such dramatic changes in the direction of associations, but our study was limited by leptin being difficult to measure in blood spots. The Avon Longitudinal Study of Parents And Children (ALSPAC) first examined cord blood leptin with infant weight gain at 4, 8, 12, and 24 months ($n=197$).¹⁰ They found a similar inverse association between cord leptin concentrations and weight gain in infancy at all time points. At later age, they found that cord blood leptin was associated with higher adiposity by various measures at age 9 but the results were null at age 17.¹¹ The lower risk of rapid weight gain followed by potential higher adiposity is not inconsistent when one accounts for gestational age and birthweight. We previously observed that higher neonatal leptin levels were associated with higher birthweight and odds of being large-for-gestational age (LGA at >90th percentile of birthweight for sex and gestational age).⁵ Here, we see the influence of these associations with birth characteristics carried forward particularly with rapid infant weight gain. That is, higher leptin was protective of rapid weight gain for the first 4 months due to their already larger size as newborns. At 9 and 12 months, the associations with rapid growth did not persist. The risk of overweight may primarily be due to being born larger and remaining larger since the adjustment of birthweight reduced the association which is in keeping with high birthweight as a risk factor of childhood overweight.²³

With regards to adiponectin, if any associations have been found, they tended to be in positive directions with weight and weight gain. Project Viva found no consistent associations although observing higher sum of skinfolds at 3 years with cord blood adiponectin.²⁴ Another study found no associations with rapid infant weight gain at 3 months ($n=340$) with respect to maternal levels of adiponectin measured by fasting serum taken at time of oral glucose tolerance test regardless of whether the pregnancy was complicated by gestational diabetes.²⁵ Among 56 Japanese infants, cord serum adiponectin levels were associated with weight gain from birth to 3 years of age but not with BMI *z*-scores at cross-sectional time points of 6, 12, and 36 months.⁷ One study made similar observations with more direct measures of adiposity.²⁶ They evaluated cord blood high

molecular weight (HMW) adiponectin concentrations with adiposity through 5 years of age, having more direct measures of body fat using MRI.²⁶ Despite some significant positive associations at 3 and 4 years of age with sum of skinfolds and percent body fat, the investigators concluded that cord blood concentrations of HMW adiponectin did not seem to be a useful biomarker of adiposity in early childhood.²⁶ It may even be debated whether birth levels are reflective of neonatal adiposity.²⁷ Our results suggested only positive associations with adiponectin levels among twins. Due to the strong impact of gestational age of delivery on birth levels, as we previously noted⁵, the association of adiponectin among twins may be due to some residual effects of gestational age, as a better biomarker for it than estimated days based on LMP even with ultrasound confirmation. However, we remain the only study to have a large sample of twins to evaluate these differences in associations by plurality.

To our knowledge, no studies have prospectively measured resistin or complement factor D at birth to examine childhood growth beyond 3 months. Thus, our findings are novel with respect to these biomarkers. Resistin, in particular, is associated with insulin resistance but have not exhibited clear associations with obesity. One study found cross-sectional associations with metabolic risk markers including insulin resistance among children but with some indication that the different isoforms of resistin may create discrepant findings.²⁸ Our findings regarding weight gain are similar to those of another study measuring cord blood resistin and other factors (including leptin and adiponectin) among 86 newborns, finding no association for weight gain at 3 months postpartum apart from leptin levels.²⁹ However, we found that higher newborn resistin levels were associated with higher odds of being overweight at 2-3 years of age. Although this association is intriguing and the findings with resistin was most consistent with increased weight over the 3 years among singletons, we acknowledge that after accounting for multiple testing of 4 adipokines the significant association ($p=0.03$) could still be due to chance. CFD expression increases as human adipocytes mature and has proadipogenic effects.⁴ Few studies have measured CFD in humans, although levels of fetal CFD have been found to be positively correlated with maternal BMI.³⁰ Our observation that higher neonatal CFD levels were protective of rapid infant weight gain longer term through 12 months, requires replication.

Strengths of our study include the large population-based sampling with measures among both singletons and twins. Newborn dried blood spots remain an important and potentially under-utilized source of biospecimens to conduct population level research. However, some limitations include the measurement of leptin which might have been due to lack of control over ambient conditions, timing of collection and to storage. There was also attrition. However, the linear mixed models are robust to loss to follow-up. As an observational study, residual confounding may be present, including controlling for all determinants previously found to impact adipokines.^{31–35}

Conclusion

While adipokines at birth were associated with early childhood growth, the magnitudes of associations were small and only an association of overweight was evident for resistin levels among singletons. Longitudinal measurements of adipokine levels along with more

comprehensive dietary and physical activity data may prove more informative in understanding their dynamics in development of pediatric obesity. Nevertheless, the availability of blood spots as a valuable source of material for research remains an important avenue to consider.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of participants by plurality with adipokine measures in Upstate KIDS

N	Singletons 2264	Twins 1144
Number of weight measures reported *	9 (6–12)	9 (5–12)
Number of length measures reported *	8 (5–11)	8 (5–11)
Age at last follow-up (months) *	25.8 (13.5–36.7)	24.0 (12.3–36.7)
Maternal age (years)	31.0 (5.9)	32.1 (5.6)
Maternal pre-pregnancy BMI (kg/m ²)	26.9 (6.8)	27.1 (6.9)
Underweight	49 (2.2%)	20 (1.8%)
Normal	1066 (47.1%)	537 (47.0%)
Overweight	579 (25.7%)	293 (25.7%)
Obese	566 (25.1%)	292 (25.6%)
Maternal race		
White	1975 (87.3%)	996 (87.0%)
Black	75 (3.3%)	46 (4.0%)
Asian	68 (2.9%)	36 (3.1%)
Other	87 (3.9%)	46 (4.0%)
Mixed	59 (2.7%)	54 (1.8%)
Maternal education		
Less than high school	77 (3.4%)	41 (3.6%)
HS or GED equivalent	231 (10.2%)	93 (8.1%)
Some college	655 (28.9%)	296 (25.9%)
College	553 (24.4%)	309 (27.0%)
Advanced degree	748 (33.0%)	406 (35.5%)
Private insurance	1815 (80.2%)	946 (82.7%)
Nulliparous	1495 (66.4%)	771 (67.8%)
Smoking during pregnancy		
Never smoked	1408 (64.0%)	718 (65.6%)
Not during pregnancy	604 (27.5%)	313 (28.6%)
Smoked during pregnancy	188 (8.6%)	63 (5.8%)
Male	1196 (52.8%)	549 (48.0%)
Birthweight (g)	3399 (544)	2449 (586)
Gestational age (weeks)	38.8 (1.7)	35.7 (2.7)
Preterm (<37 weeks)	167 (7.4%)	591 (52.0%)
Low birth weight (<2500g)	111 (4.9%)	558 (48.7%)
Adiponectin (µg/ml) **	0.44 (0.43–0.45)	0.38 (0.36–0.39)
Complement Factor D (ng/ml) **	105.8 (103.8–107.7)	87.41 (84.08–89.80)
Resistin (ng/ml) **	24.6 (24.0–25.3)	15.34 (14.78–15.93)
Leptin > median, n(%)	1158 (52.9%)	258 (45.0%)
C-reactive protein (ng/ml) **	25.1 (23.8–26.4)	9.8 (9.1–10.5)

Mean (SD) or N (%) unless otherwise indicated

* Mean (interquartile range) shown

** Geometric mean (95% confidence interval) shown

Number of missing data: 6 for prepregnancy BMI, 1 for private insurance, for 92 smoking status, 19 for parity, 11 for adiponectin, 11 for c-reactive protein, 88 for leptin

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Table 2

Longitudinal association between adipokines and growth over first 36 months of life among singletons in Upstate KIDS

	Crude	Model 1	Model 2	Model 3
Weight-for-age z-score	2264	2176	2167	2176
Adiponectin	0.13 (0.01, 0.25)	0.09 (−0.04, 0.21)	0.08 (−0.04, 0.2)	0.002 (−0.09, 0.09)
Complement Factor D	0.08 (−0.03, 0.19)	0.02 (−0.09, 0.13)	0.01 (−0.1, 0.13)	−0.01 (−0.1, 0.07)
Resistin	0.14 (0.06, 0.21)	0.14 (0.06, 0.21)	0.12 (0.04, 0.2)	0.07 (0.01, 0.13)
Leptin	0.17 (0.08, 0.26)	0.15 (0.06, 0.24)	0.15 (0.06, 0.24)	−0.003 (−0.07, 0.07)
Resistin-to-adiponectin ratio	0.15 (0.004, 0.30)	0.17 (0.02, 0.32)	0.14 (−0.02, 0.29)	0.11 (0.01, 0.22)
Weight for length z-score	2138	2051	2042	2051
Adiponectin	0.11 (−0.02, 0.24)	0.09 (−0.04, 0.22)	0.08 (−0.05, 0.22)	0.07 (−0.06, 0.2)
Complement Factor D	0.03 (−0.09, 0.15)	0.01 (−0.12, 0.13)	0.04 (−0.08, 0.17)	−0.001 (−0.12, 0.12)
Resistin	0.04 (−0.04, 0.12)	0.04 (−0.05, 0.12)	0.10 (0.01, 0.19)	0.03 (−0.05, 0.12)
Leptin	0.19 (0.08, 0.30)	0.16 (0.05, 0.27)	0.15 (0.05, 0.26)	0.08 (−0.02, 0.19)
Resistin-to-adiponectin ratio	−0.005 (−0.17, 0.16)	0.01 (−0.16, 0.17)	0.10 (−0.08, 0.28)	0.01 (−0.15, 0.17)
BMI z-score	2143	2056	2047	2056
Adiponectin	0.16 (0.02, 0.3)	0.13 (−0.01, 0.27)	0.12 (−0.01, 0.26)	0.09 (−0.03, 0.22)
Complement Factor D	0.06 (−0.06, 0.18)	0.02 (−0.1, 0.14)	0.05 (−0.07, 0.17)	0.004 (−0.11, 0.12)
Resistin	0.07 (−0.02, 0.15)	0.06 (−0.02, 0.15)	0.11 (0.02, 0.2)	0.04 (−0.05, 0.12)
Leptin	0.21 (0.1, 0.32)	0.17 (0.07, 0.28)	0.17 (0.06, 0.28)	0.08 (−0.02, 0.18)
Resistin-to-adiponectin ratio	0.01 (−0.16, 0.18)	0.02 (−0.16, 0.20)	0.09 (−0.09, 0.27)	0.00 (−0.17, 0.17)
Length z-score	2152	2065	2056	2065
Adiponectin	0.02 (−0.12, 0.17)	−0.03 (−0.18, 0.13)	−0.03 (−0.18, 0.13)	−0.10 (−0.23, 0.02)
Complement Factor D	0.08 (−0.05, 0.21)	0.04 (−0.11, 0.18)	−0.02 (−0.16, 0.13)	−0.005 (−0.12, 0.11)
Resistin	0.13 (0.03, 0.22)	0.13 (0.03, 0.23)	0.04 (−0.06, 0.15)	0.05 (−0.03, 0.13)
Leptin	0.09 (−0.02, 0.21)	0.09 (−0.02, 0.21)	0.11 (−0.01, 0.22)	−0.05 (−0.16, 0.05)
Resistin-to-adiponectin ratio	0.20 (0.005, 0.40)	0.23 (0.03, 0.42)	0.09 (−0.11, 0.29)	0.15 (−0.002, 0.30)

Crude: infant age, age*gender; Model 1: infant age, age*gender, prepregnancy BMI, maternal age, maternal race, and all adipokines; Model 2: Model 1 and insurance status, maternal education, hypertensive disorder in pregnancy, GDM, C-reactive protein; Model 3: Model 1 with birth weight and gestational age. Bolding indicates $p < 0.05$; Associations are per log unit increase in adiponectin, resistin and CFD. Associations for leptin are high (above median) versus low. Associations for resistin-to-adiponectin ratio are per unit increase.

Table 3

Longitudinal association between adipokines and growth over first 36 months of life among twins in Upstate KIDS

	Crude	Model 1	Model 2	Model 3
Weight-for-age z-score	1144	1116	1109	1116
Adiponectin	0.53 (0.39, 0.69)	0.53 (0.38, 0.68)	0.54 (0.40, 0.69)	0.18 (0.08, 0.28)
Complement Factor D	0.16 (0.03, 0.28)	-0.0004 (-0.12, 0.12)	-0.01 (-0.13, 0.11)	-0.03 (-0.13, 0.06)
Resistin	0.01 (-0.07, 0.10)	0.003 (-0.08, 0.09)	-0.03 (-0.13, 0.06)	-0.07 (-0.13, -0.01)
Leptin	0.07 (-0.05, 0.19)	-0.01 (-0.13, 0.11)	-0.01 (-0.13, 0.10)	-0.05 (-0.14, 0.04)
Resistin-to-adiponectin ratio	-0.44 (-0.63, -0.26)	-0.41 (-0.59, -0.23)	-0.50 (-0.70, -0.30)	-0.24 (-0.36, -0.11)
Weight for length z-score	1050	1022	1017	1022
Adiponectin	0.15 (-0.01, 0.30)	0.15 (0.004, 0.30)	0.15 (0.0002, 0.30)	0.10 (-0.048, 0.25)
Complement Factor D	0.03 (-0.11, 0.18)	0.01 (-0.14, 0.15)	0.01 (-0.13, 0.16)	-0.004 (-0.14, 0.13)
Resistin	-0.03 (-0.12, 0.07)	-0.02 (-0.11, 0.07)	0.001 (-0.11, 0.10)	-0.02 (-0.11, 0.07)
Leptin	-0.04 (-0.18, 0.09)	-0.09 (-0.23, 0.04)	-0.09 (-0.22, 0.05)	-0.13 (-0.26, -0.003)
Resistin-to-adiponectin ratio	-0.16 (-0.36, 0.03)	-0.15 (-0.33, 0.04)	-0.12 (-0.32, 0.08)	-0.11 (-0.28, 0.07)
BMI z-score	1068	1040	1035	1040
Adiponectin	0.31 (0.14, 0.48)	0.32 (0.18, 0.47)	0.33 (0.18, 0.49)	0.13 (-0.004, 0.27)
Complement Factor D	0.11 (-0.05, 0.28)	0.04 (-0.09, 0.18)	0.04 (-0.12, 0.17)	0.02 (-0.11, 0.14)
Resistin	-0.01 (-0.12, 0.09)	-0.02 (-0.11, 0.07)	-0.01 (-0.13, 0.09)	-0.05 (-0.13, 0.03)
Leptin	-0.01 (-0.17, 0.15)	-0.09 (-0.22, 0.04)	-0.08 (-0.21, 0.08)	-0.12 (-0.24, -0.01)
Resistin-to-adiponectin ratio	-0.29 (-0.47, -0.10)	-0.27 (-0.45, -0.09)	-0.29 (-0.48, -0.10)	-0.18 (-0.34, -0.03)
Length z-score	1072	1044	1039	1044
Adiponectin	0.61 (0.43, 0.78)	0.61 (0.42, 0.80)	0.63 (0.45, 0.82)	0.20 (0.07, 0.33)
Complement Factor D	0.11 (-0.05, 0.28)	-0.06 (-0.22, 0.10)	-0.06 (-0.22, 0.10)	-0.09 (-0.22, 0.04)
Resistin	0.03 (-0.08, 0.15)	0.02 (-0.09, 0.14)	-0.03 (-0.15, 0.08)	-0.08 (-0.18, 0.01)
Leptin	0.13 (-0.02, 0.28)	0.06 (-0.09, 0.21)	0.05 (-0.10, 0.19)	0.05 (-0.07, 0.17)
Resistin-to-adiponectin ratio	-0.46 (-0.70, -0.22)	-0.43 (-0.67, -0.19)	-0.57 (-0.82, -0.32)	-0.27 (-0.45, -0.10)

Crude: infant age, age*gender; Model 1: infant age, age*gender, prepregnancy BMI, maternal age, maternal race, and all adipokines; Model 2: Model 1 and insurance status, maternal education, hypertensive disorder in pregnancy, GDM, C-reactive protein; Model 3: Model 1 with birth weight and gestational age Bolding indicates p<0.05