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Human milk adiponectin impacts infant weight trajectory during the second year of life

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Abstract

Objectives—Serum adiponectin (APN) is associated with lower childhood obesity, and APN concentration in human milk is associated with slower growth during active breastfeeding. Here, we examine infant weight gain in the second year of life after exposure to high or low levels of mother's milk APN.

Methods—Breastfeeding mother-infant pairs were recruited in Mexico City and followed for 2 years; 192 infants with ≥12 months' follow-up were analyzed. Monthly milk samples were assayed for APN; mothers were classified as producing high or low levels of milk APN. Infant and maternal serum APN were assessed during year 1. Infant anthropometry was measured monthly (year 1) or bi-monthly (year 2), and WHO Z-scores calculated. Longitudinal adjusted models assessed weight-for-age (WEI) and weight-for-length (WFL) Z-score trajectories from 1 to 2 years.

Results—Maternal serum APN modestly correlated with milk APN ($r=0.37$, $p<0.0001$) and infant serum APN ($r=0.29$, $p=0.01$). Infants exposed to high milk APN experienced increasing WEI and WFL Z-scores between age 1 and 2 years in contrast to low milk APN exposure (p for group*time=0.02 and 0.054, respectively), adjusting for growth in the first 6 months and other

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Disclosure Statement

LJM and ALM are listed on a U.S. patent application claiming human milk adiponectin as an oral treatment for adiposity and inflammatory disorders, and LJM received a portion of a licensing fee for this technology. The remaining authors report no conflicts of interest.

covariates. In contrast, infant serum APN in year 1 was not associated with rate of weight gain in year 2.

Conclusions—High human milk APN exposure was associated with accelerated weight trajectory during the second year of life suggesting its role in catch up growth after slower weight gain during the first year of life.

Keywords

adiponectin; human milk; breastfeeding; weight gain; infancy

Introduction

Pediatric obesity is a critical public health problem, affecting an increasing number of children and adolescents worldwide [1, 2]. Breastfeeding has been identified as protective against later obesity compared with formula-feeding, with increased duration of breastfeeding often associated with lower obesity in a dose-dependent manner [3–5]. However, the mechanism of action by which breastfeeding confers a protective advantage is unclear. While the macro-nutrient composition of human milk is quite stable, human milk is actually a complex mixture of bioactive factors associated with infant growth and metabolism, including insulin[6], leptin[7, 8], adipocyte fatty acid binding protein (AFABP)[9, 10], several growth factors and their binding proteins[11, 12], and ghrelin[13–15], the composition of which varies from mother to mother and over the course of lactation.

One intriguing component of human milk is adiponectin[9, 10, 16–18], which is secreted by breast adipose tissue [19]. Adiponectin is an insulin-sensitizing and anti-inflammatory molecule, which is typically found in circulation at higher concentrations among individuals with lower adiposity and better metabolic health[20, 21]. Consistent with that concept, we have previously demonstrated that higher maternal milk adiponectin is associated with lower infant weight-for-length Z-scores in the first 6 months of life in two predominantly breastfed cohorts[22]. However, in contrast, another study reported that higher maternal milk adiponectin concentrations were associated with an increased risk of overweight in breastfed infants by age two years [23].

The current study examines the relationship between maternal milk adiponectin, maternal serum adiponectin, infant serum adiponectin and infant growth using a well-characterized longitudinal cohort with frequent follow-up. In this same cohort, we have previously reported that milk adiponectin was associated with lower infant weight during the first 6 months of life[22], but longer-term relationships with growth during the second year of life and with infant and maternal serum adiponectin have not been examined. In particular, we tested the hypothesis that concentrations of human milk adiponectin influences breastfed infants' growth trajectory during the second year of life, beyond the period of active breastfeeding. In addition, we examined the relationships among maternal serum adiponectin, maternal milk adiponectin, and infant serum adiponectin levels to clarify the maternal-infant links with respect to adiponectin in breastfed infants.

Materials and Methods

Methods for this study have been described previously [22], thus are described only briefly here. From March 1998 to April 2003, 306 infants in San Pedro Martir, Mexico City, were enrolled and monitored prospectively from birth to 2 years of age [24]. All enrolled infants were healthy, full-term infants born ≥2.2 kg without congenital defects, whose mothers intended to breastfeed. This study was approved by the IRBs of the National Institute of

Medical Sciences and Nutrition (Mexico City) and Cincinnati Children's Hospital Medical Center, and all mothers provided written informed consent.

Demographic, maternal, household and birth characteristics were ascertained by baseline questionnaire. Infant diet was ascertained by weekly 24-hour recall. Measurements of infant weight (±0.1 kg, Model MP25, CMS Weighing Equipment Ltd., London, England) and length (±0.1 cm using recumbent length board) were collected monthly between 1 and 12 months, and bi-monthly between 12 and 24 months. Milk samples (n=1074) collected at baseline (week 1) and months 1, 3, 5 and 6 were assayed after a single freeze-thaw cycle.

A maternal blood sample was collected at the baseline visit (2 to 20 days postpartum), and infant blood samples were collected at baseline, 3, 6, and 12 months of age. All blood samples were maintained on ice after collection, processed, aliquotted and stored at −70 C until assaying. Serum samples from the mother at baseline (n=274) and a subset of 92 infants at baseline (n=87), 3 months (n=84), 6 months (n=66) and 12 months of age (n=55) were included in the analysis.

Assay of Serum and Milk Adiponectin

Serum total adiponectin was measured in duplicate using radioimmunoassay (Linco Research, St. Charles, MO). Milk adiponectin was measured in skimmed milk by radioimmunoassay (Linco Research, St. Charles, MO) as described previously[17]

Calculated Variables

Breastfeeding durations were calculated using weekly 24-hour recalls, excluding data from the first 7 days of life. Duration of exclusive breastfeeding (EBF) was calculated based on the World Health Organization (WHO) definition as the last age in days at which the infant was reported to receive 100% of all feeds as breast milk. A second breastfeeding variable (BF85%) denoted the last age at which breastfeeding was reported to account for at least 85% of all feeds, regardless of the composition of the rest of the diet; this definition corresponds to "Full or Nearly Full Breastfeeding" [25]. Age of introduction of solid food was determined as the first age (in days) at which the infant was reported to have consumed any solid or semi-solid foods (e.g., cereals, soups, yogurt, fruits or vegetables).

Infant anthropometrics were standardized to the WHO Child Growth Standards [26], and the resulting Z-scores for weight-for-age (WEI), length-for-age (LEN), and weight-for-length (WFL) were analyzed.

Longitudinal assessment of the relationship between milk adiponectin (measured only during the first 6 months) and 2-year growth required two special data manipulations. First, to avoid the use of a single proxy milk adiponectin value to represent longitudinal characterization of milk, individual-level milk adiponectin values were summarized as the median of each mother's milk adiponectin values across her available samples. In this phase, 1 outlier sample was excluded from each of 4 individuals.

Second, to avoid confounding introduced by the decline in milk adiponectin through lactation, which was reported for this cohort previously[22] (e.g., with more or later samples resulting in lower median values), the individual's median was determined to be either above or below the median of the group of mothers with the same number of milk measurements. Group sizes were as follows: 3 (1%) mothers had a single milk measurement, 29 (10%) women had two measurements, 38 (14%) had 3 measurements, 140 (51%) had 4 measurements and 67 (24%) had all five measurements of milk adiponectin. Figure 1 shows the median and interquartile range (IQR) of the milk adiponectin values for the "above median" and "below median" groups of women within each measurement stratum. This

manipulation resulted in a designation of “above median” or “below median” milk APN across the cohort that is not confounded by the duration of breastfeeding or number of samples available. Infant serum adiponectin measurements from months 0, 3, 6, and 12 were treated in the same manner, as 21 infants (23%) had 2 serum adiponectin measurements, 33 (36%) had 3 measurements and 38 (41%) had all 4 measurements.

Statistical Analysis

All analyses were conducted using SAS v.9.1. (SAS Institute, Cary, NC). Descriptive statistics were calculated for the entire cohort (n=277), and were also compared between participants with less than 12 months’ follow-up (n=85) or ≥12 months’ follow-up (n=192), as the latter group was the subset used for the longitudinal anthropometric models. Differences between these follow-up groupings were determined using Student’s t-test or χ^2 tests, as appropriate.

Infant serum adiponectin values were normally distributed at each time point, so were analyzed in original units (μg/ml). Analysis of longitudinal patterns of infant serum adiponectin and comparisons between time points were conducted using repeated measures modeling (PROC MIXED), which allows for missing data and accounts for both the intra- and inter-individual variability present in this data, resulting in larger, and more valid, estimates of standard error (SE) [27]. Differences between infant and maternal serum adiponectin concentrations were evaluated using Student’s t-test. For visual presentation only, serum adiponectin values were plotted using medians and interquartile ranges (IQR), because the standard errors on the estimates were not distinguishable from the plotted symbol. Cross-sectional Spearman correlations among infant serum, maternal serum, maternal milk and infant anthropometry Z-scores during the first year of life were calculated in the entire cohort.

Longitudinal analysis of WFL, WEI and LEN Z-scores were conducted using data from months 12 through 24 to examine growth trajectories during the second year of life. The analysis set for this model thus included only those with at least 12 months of follow-up (n=192). Modeling used repeated measures models, as above, with the intercept and infant’s growth trajectory across time (slopes) allowed to vary by individual. Other covariates considered for model inclusion were: infant sex, birthweight, duration of exclusive breastfeeding, age at introduction of solid food, change in WFL Z-score or WEI Z-score between birth and 6 months, maternal age at delivery, parity, type of delivery, maternal education, and maternal marital status. Changes in WFL and WEI Z-scores during the first 6 months were specifically included to account for the previous finding in this cohort that milk adiponectin was negatively associated with these parameters during this time period[22], and could potentially confound the relationships between 1 and 2 years of age. Covariates were tested in multivariate models if bivariate $p \leq 0.10$, and retained if $p \leq 0.05$. Interaction terms between month and indicators for “above median” or “below median” adiponectin were specifically tested to determine whether high or low milk or serum adiponectin groups demonstrated different weight trajectories in year 2.

Results

Infant Feeding and Anthropometric Characteristics

The patterns of breastfeeding in the present cohort are indicative of a highly breastfed cohort (Figure 2A). Median duration of EBF was 68 days (interquartile range [IQR]: 19 to 130 days), and duration of breastfeeding comprising at least 85% of feeds (BF85%) was 151 days (IQR: 49 to 182 days). Solid food was also introduced at a median of 150 days (IQR:

118 to 177 days). Other characteristics of the infants in this study, previously reported [22], are included in Table 1.

Compared with the WHO growth standard, WFL Z-scores peaked between 1 and 2 months of age, and WEI and LEN Z-scores peaked between 3 and 6 months of age (Figure 2B). During the second year of life, both WEI and WFL Z-scores demonstrate an upward trend relative to WHO growth curves, while LEN Z-scores declined steadily between 5 and 16 months of age.

Associations among infant serum, maternal serum, and maternal milk adiponectin during the first year of life

Serum adiponectin concentrations were 22.5 ± 0.6 μg/ml higher in infants than their mothers at baseline ($p<0.0001$; Figure 3). Infants' serum adiponectin concentrations significantly increased between baseline (mean ± SE: 31.1 ± 0.6 μg/ml) and 3 months (33.2 ± 0.5 μg/ml, $p=0.002$ vs. baseline), then significantly declined by 6 months (28.6 ± 0.6 μg/ml, $p<0.0001$ vs. 3 months) and continued to decline to 12 months of age (23.5 ± 0.8 μg/ml, $p<0.0001$ vs. 6 months; Figure 3 presents medians and interquartile ranges [IQR] of data for clarity). Infant serum adiponectin was not associated with median milk adiponectin concentrations at baseline (Table 2), but by 3, 6, and 12 months of age, higher infant serum adiponectin was associated with higher exposure to milk adiponectin. Infant serum adiponectin at 12 months, but not at earlier ages, was also associated with lower concurrent WEI and LEN Z-scores (both $p<0.01$).

Despite differences in mean levels, maternal and infant serum adiponectin were directly correlated with each other at baseline (Table 2, $r=0.29$, $p=0.007$) and 6 months of age ($r=0.32$, $p<0.01$). Maternal serum adiponectin was also significantly correlated with her own median milk adiponectin concentration ($r=0.37$, $p<0.0001$). Both maternal baseline serum adiponectin and median milk adiponectin were associated with lower infant WEI Z-scores at 0, 3, and 6 months, as previously reported.

2nd year weight trajectories differ by milk adiponectin concentration, but not infant or maternal serum adiponectin

Final longitudinal models for year 2 ZWFL and ZWEI were adjusted for infant sex, birthweight, change in ZWFL or ZWEI between birth and 6 months (as appropriate), and marital status (married vs. not); ZWFL models were further adjusted for delivery type (vaginal vs. C-section). Other covariates were not significantly associated with infant anthropometry in the second year of life.

Infants exposed to high milk adiponectin experienced increasing WEI Z-score during the second year of life, while those exposed to lower milk adiponectin experienced little change in WEI Z-scores between 12 and 24 months of age (Figure 4A). These differences in trajectory over time are significant, even after adjusting for covariates (p for interaction of group by time=0.02). By 24 months of age, WEI Z-scores in infants exposed to high milk adiponectin are 0.21 ± 0.10 units higher than those in the lower milk adiponectin group, after adjusting for covariates ($p=0.04$). Similar patterns are evident for WFL Z-score trajectories (p for interaction=0.054, Figure 4B); however, milk adiponectin concentrations did not affect LEN Z-score trajectories (data not shown).

In the subset of infants with serum adiponectin and at least 12 months' follow-up (n=71), above-median infant serum adiponectin during the first 12 months was modestly associated with lower mean WFL (adjusted β±SE: −0.28 ± 0.14 Z-units, $p=0.05$; Figure 4C) but not significantly lower mean WEI Z-scores (adjusted β±SE: −0.22 ± 0.13 Z-units, $p=0.10$; Figure 4D) during the second year of life. However, infant serum adiponectin did not alter

the infant's growth trajectory between 12 and 24 months (both p for interaction of group by time>0.4). Maternal serum adiponectin at baseline was not significantly associated with either mean ZWFL or ZWEI or growth trajectories during the second year of life (Figures 4E and 4F).

DISCUSSION

This study provides evidence that high exposure to milk adiponectin is part of a complex series of factors associated with increasing weight gain in the second year of life. Using a cohort of breastfed infants and their mothers, we explored the complex relationships among milk adiponectin, maternal serum adiponectin, infant serum adiponectin and changes in infant weight in the second year of life. We found that breastfed infants' weight trajectories during the second year of life are associated with their exposure to human milk adiponectin during breastfeeding, independent of birthweight or growth during the first six months of life.

Previous studies of human milk adiponectin and infant growth have been conflicting. Our previous work in this and a second birth cohort demonstrated that high milk adiponectin concentrations were associated with lower infant weight and weight-for-length Z-scores over the first 6 months of life[22]. However, the present analysis demonstrated that, even adjusting for this early growth pattern, by 24 months of age these same infants exposed to high levels of human milk adiponectin were significantly heavier and had higher WEI Z-scores than those exposed to low levels, indicating a reversal of effect. A recent study also found that higher human milk adiponectin at 6 weeks postpartum was associated with a greater odds of overweight at age 2[23]. By confirming the previous counterintuitive finding, the present study suggests that human milk adiponectin may have different effects during versus after the period of active breastfeeding. This relationship does not appear to be associated with duration of breastfeeding or timing of introduction of solid foods, and appears to be independent of several other covariates in our study.

Potential reasons for why higher milk adiponectin is paradoxically associated with greater second-year weight gain suggest avenues for future analysis. Milk adiponectin has been reported to be positively associated with maternal pre-pregnancy[9] or post-pregnancy BMI[17], although this association is not consistent [23, 28]. It is possible that higher milk adiponectin exposure is a proxy for higher maternal BMI, which may indirectly affect infant weight gain during the first two years of life [29]. Alternately or additionally, milk adiponectin may be physiologically active in infants during the time of active breastfeeding, limiting early weight gain in children otherwise at risk of obesity. A limitation of this study is that maternal anthropometry was not collected, so it is not possible to test these hypotheses in the current study.

Milk adiponectin may also be acting as a proxy measurement for any one of a number of potentially biologically-relevant components of human milk, which may be contributing to increased second-year growth. For example, human milk leptin has been associated with infant weight gain and BMI[23, 30, 31], is postulated to affect food intake and food preferences[32], and has been positively correlated with milk adiponectin[17, 18]. Leptin and other components of human milk were not assessed in the present study, but future research is clearly needed to elucidate the relative roles of the several components of human milk.

Recent studies have pointed to low birth weight and increased growth rates during infancy as important determinants of obesity during childhood, adolescence and even adulthood [33]. Although the birth weights of this cohort are not low by design, the WEI and LEN Z-scores are consistently below the median, and overweight by age 2 is rare. Thus, it is possible that

the weight gain seen in this cohort during the second year of life represents not pathology (early obesity) but rather positive adaptation (catch-up growth). In this light, higher exposure to milk adiponectin may be delaying catch-up growth that might otherwise occur in the first 6 months. Previous studies have noted that weight gain in the first 6 months is preferentially fat mass, while weight gain thereafter is associated with gain in lean mass [34–36]. Following this reasoning, a delay in catch-up growth in infants exposed to high milk adiponectin may also be associated with less accrual of fat mass during the first 6 months and greater accrual of lean mass later in infancy. While this is speculative, and extends far beyond the scope of the present study, our hypothesis may provide a structure for future investigations on this question.

Interestingly, this study also demonstrates that human milk adiponectin is associated with both the mother's and infant's circulating adiponectin within the first year of life. Weyermann[37] also found positive correlations between maternal milk and maternal serum adiponectin, and additional studies note that adiponectin is secreted from human breast adipose tissue[19]. Furthermore, ingested adiponectin appears in the serum of neonatal mice shortly after administration[38], indicating that milk adiponectin survives digestion in infants. These findings, taken together, suggest that human milk may provide a link between mothers and their infants with regard to this important adipokine.

The present study also extends knowledge about the patterns of infant serum adiponectin during the first year of life in relation to maternal adiponectin and infant growth. Similar to previous studies of cord blood adiponectin [39–42], we report that infants' circulating adiponectin levels during the first month of life are much higher than their mothers'. In addition, we report that maternal and infant serum adiponectin levels are significantly correlated with each other not only at birth, but also at 6 months of age. Previous studies have not typically reported significant correlations between cord blood and maternal adiponectin [39, 41, 43], but this may be due to differences in timing of measurements, cohort composition or breastfeeding exposures. The present study suggests that, despite differences in mean levels, infant serum adiponectin levels are associated with their mothers' levels, whether the reasons for this are genetic, environmental or the in utero or breastfeeding exposures.

Serum adiponectin levels are also dynamic during infancy and early life. We report that total circulating adiponectin significantly increases from birth to 3 months of age, then declines for the remainder of the first year of life. This is consistent with data from other studies showing that total adiponectin increases significantly during late gestation [42, 44–46], increases through the first month after birth[47], then declines during the first year[47] and between the first and second years of life[48]. Circulating high molecular weight (HMW) adiponectin also appears to follow the same pattern [47, 49], which is not surprising given that most cord blood and infant adiponectin occurs in the HMW form [47, 50], and milk adiponectin is also predominantly HMW [38]. The reasons for these fluctuations in infant serum adiponectin are not clear, and future work would be required to determine whether infant serum adiponectin is associated with body composition, as it is in older children.

Infant serum adiponectin does not appear to be related to longitudinal growth patterns in this study. We found no association of infant serum adiponectin with WFL Z-score during the first year, and during the second year of life, higher serum adiponectin was associated with lower mean WFL Z-score, but no difference in growth trajectory. Other studies have also found no association between adiponectin at birth or one month of age with concurrent anthropometric parameters [46, 51], suggesting that the negative association of circulating adiponectin and obesity seen in older children and adults develops after infancy. However, the decline in serum adiponectin between 1 and 2 years of age has been correlated to greater

increases in body fatness, particularly in girls [48]. One study noted that high cord blood adiponectin was associated with greater birth weight, and consistent with our findings, with lower weight gain in the first 6 months of life, yet higher central adiposity by age 3 [52], suggesting a complex relationship between adiponectin and adiposity in early life that is not reported at older ages.

The longitudinal nature of this study, concurrent serum and milk samples, and detailed infant feeding and anthropometric data provided a unique opportunity to study growth trajectories in breastfed infants in relation to milk composition. Despite these several strengths, some limitations of the current study should be noted. Only adiponectin was measured in the human milk samples, so the potential influence of other human milk bioactive components cannot be quantified here. Also, because the original study was designed to focus on infant infectious disease outcomes, maternal BMI was not ascertained, and only a single maternal blood sample was collected. Infant blood samples were limited to a subset of participants. These factors limited inferences about the impact of maternal adiposity, but the strength of the findings suggests that the sample size did not impede our ability to detect significant associations.

In conclusion, this study highlights the potential role of high human milk adiponectin exposure in the accelerated weight trajectory of infants during the second year of life, despite being associated with lower weight gain during the first 6 months in the same cohort. Infant serum adiponectin is also independently associated with lower weight-for-age and weight-for-length Z-scores between 12 and 24 months, and may be influenced by maternal serum and milk adiponectin. These complex relationships in infant growth and feeding in the first two years require additional study, as they may have long-lasting impacts on childhood obesity risk and metabolic adaptation in later life.

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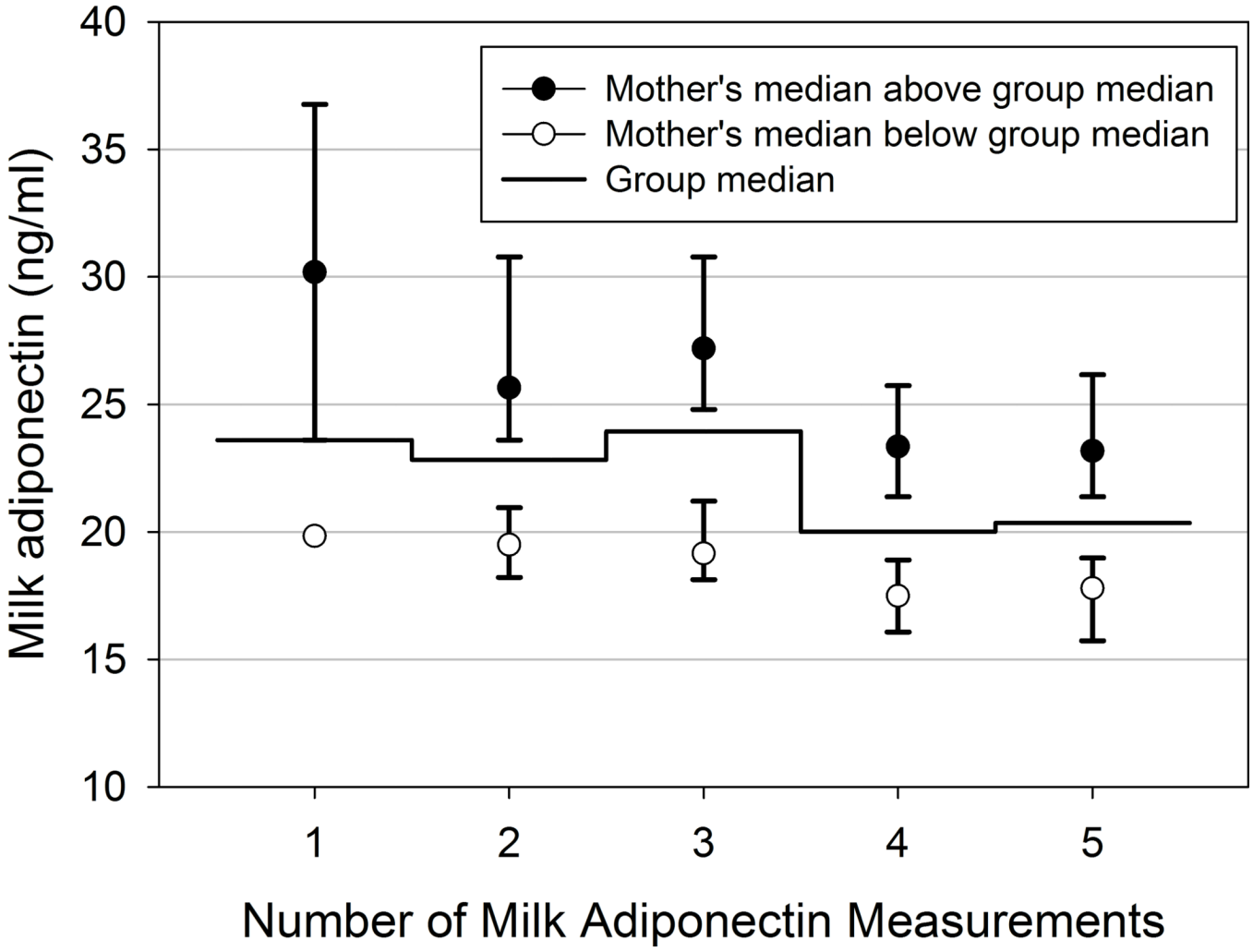
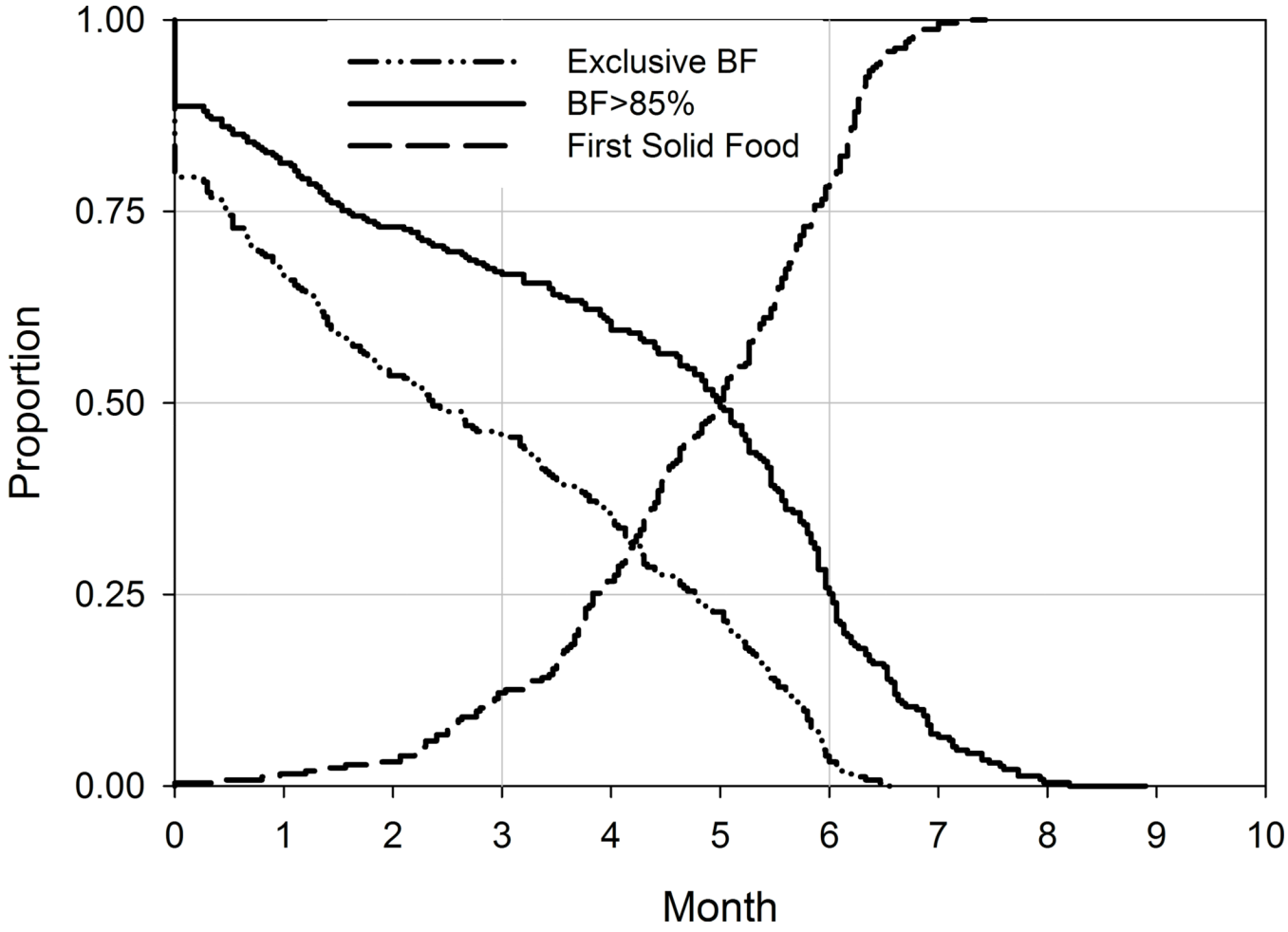


Figure 1. Maternal median milk adiponectin in above- versus below-median groups
N per group: n=3, 29, 38, 140, and 67 with 1, 2, 3, 4, or 5 measurements, respectively. Median and interquartile range (IQR) presented.



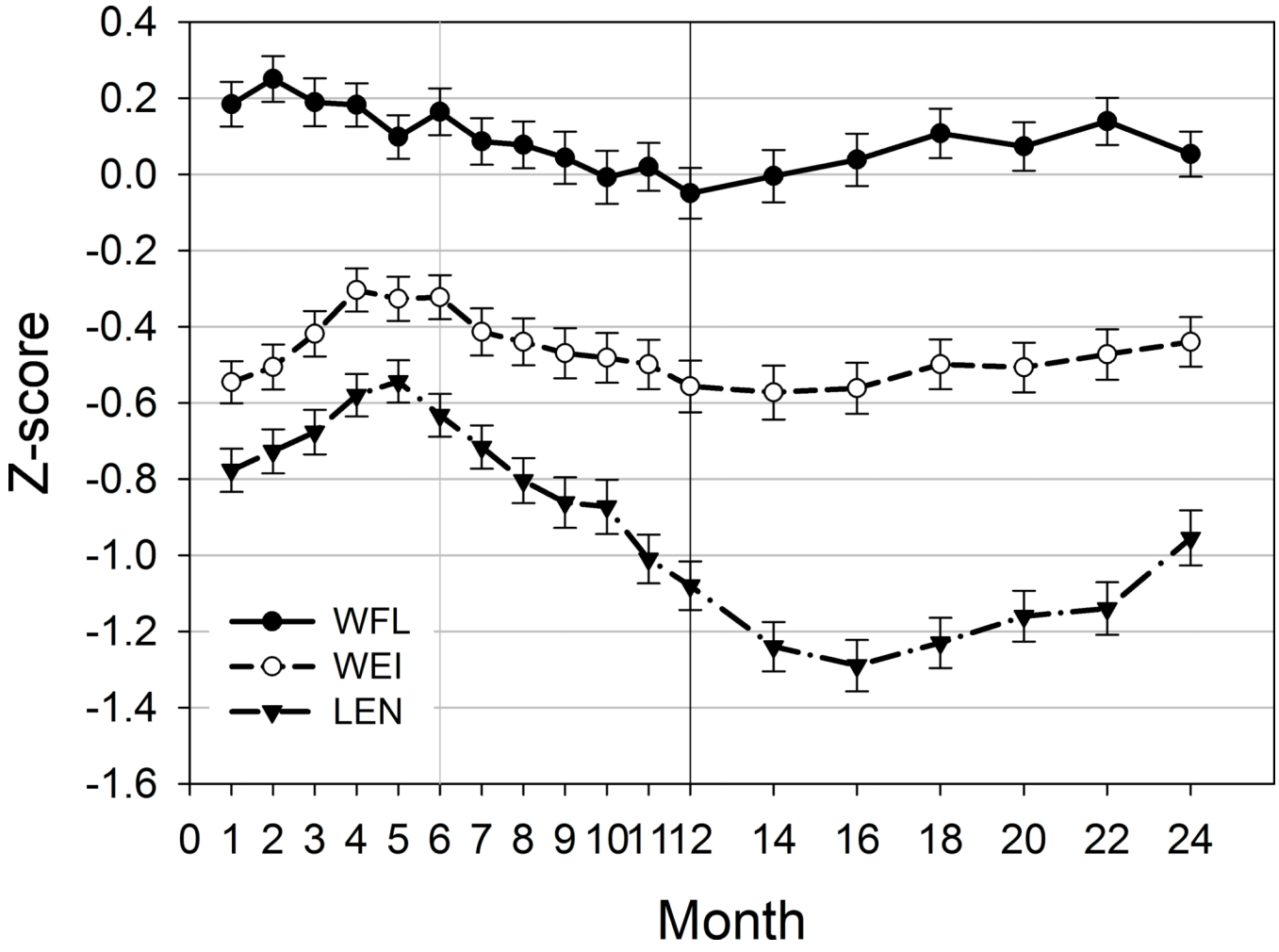


Figure 2. Descriptive presentation of breastfeeding and anthropometry

A. Infant feeding patterns for exclusive breastfeeding (EBF), BF >85% and introduction of solid foods. B. Unadjusted means (± standard error of mean [SE]) of WEI, WFL and LEN Z-scores by month. Vertical solid lines indicate 3, 6 and 12 months of age for visual reference.

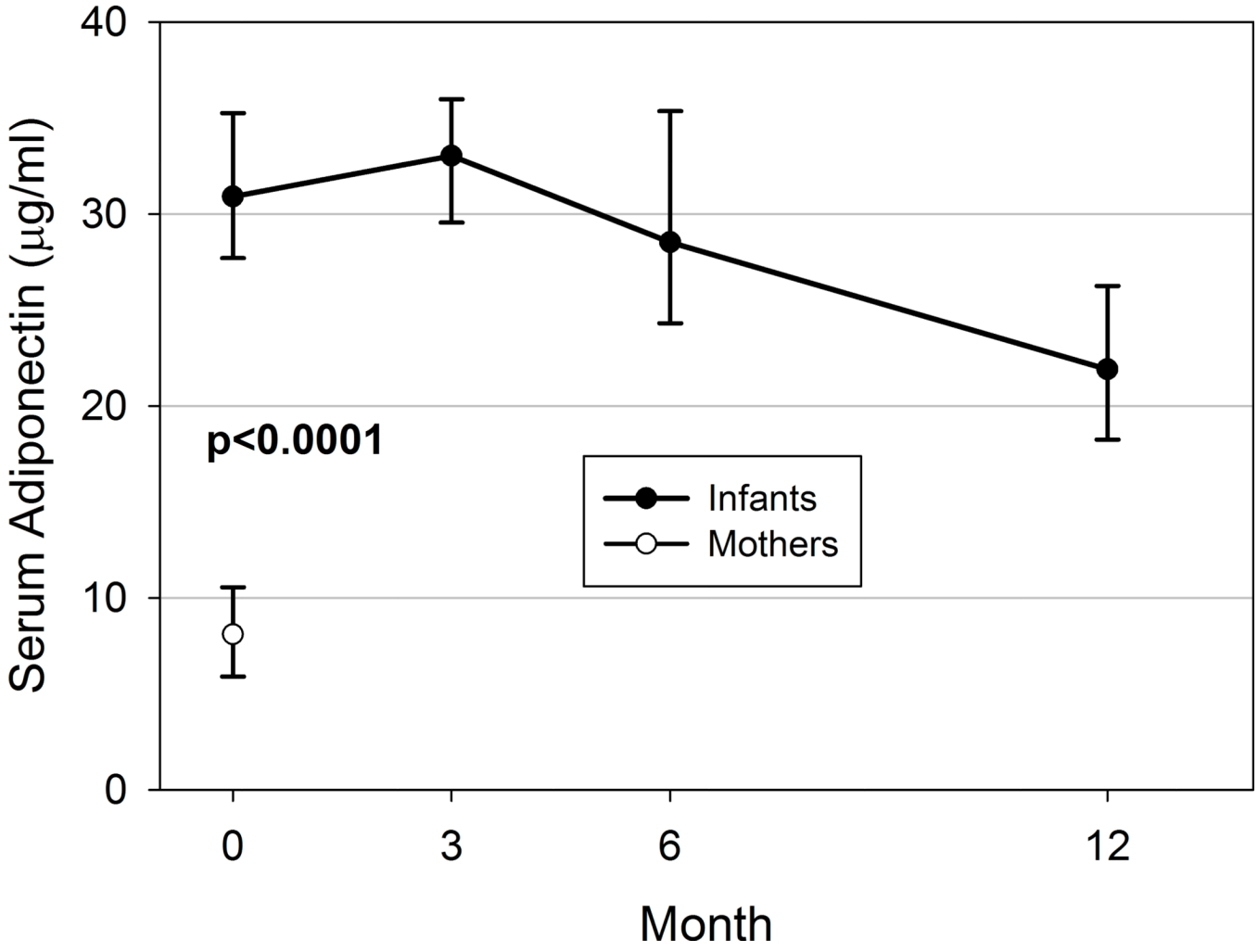


Figure 3. Infant and mothers' serum adiponectin concentrations during first 12 months

Analysis conducted using means and standard errors; however, unadjusted median and IQR are presented for graphical clarity. p≤0.002 for all pairwise comparisons of means among infant serum values; p<0.0001 for cross-sectional comparison of mean maternal and infant serum values at baseline.

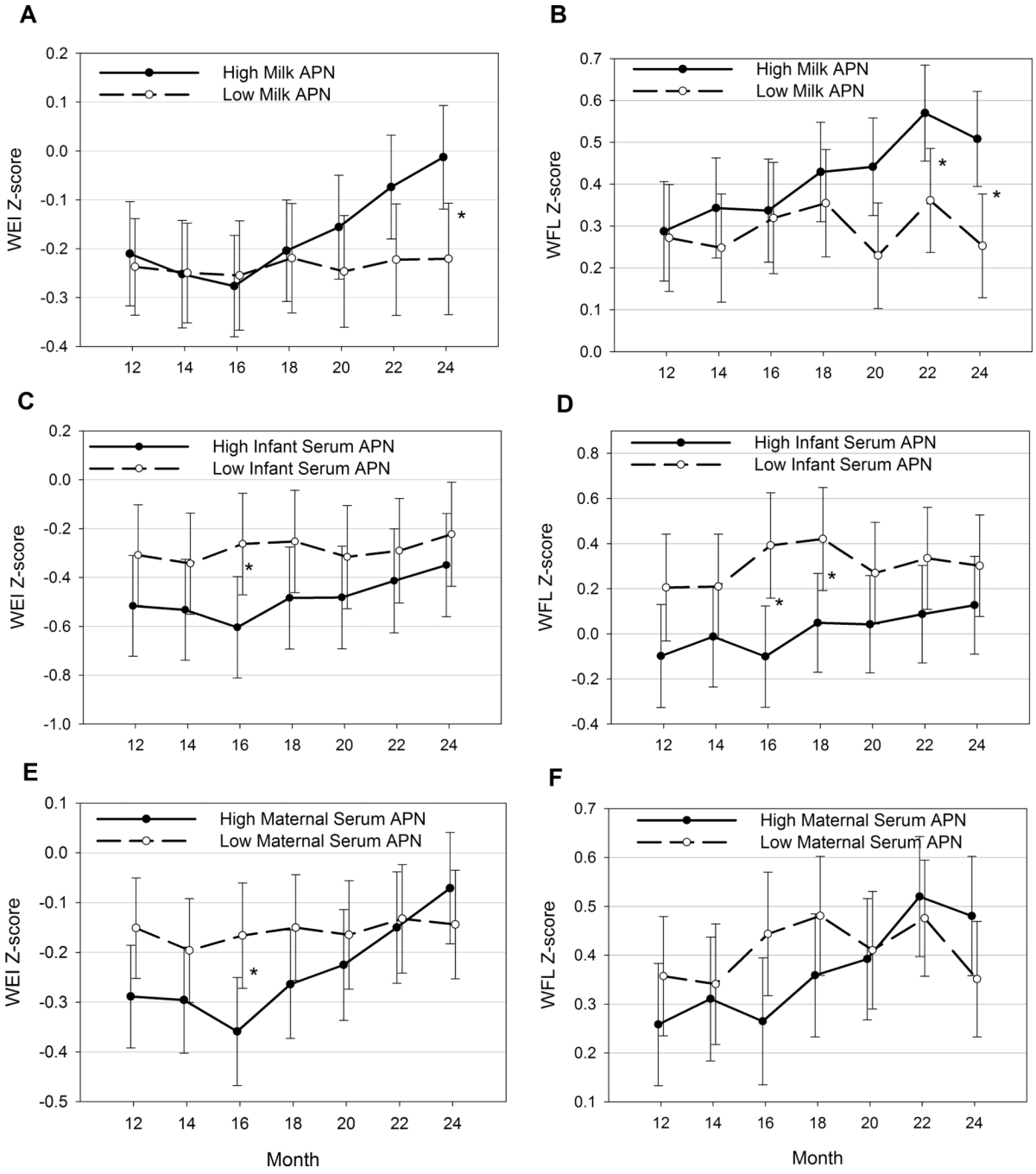


Figure 4. Year 2 infant growth trajectories by adiponectin concentrations

Least square means ± SE presented from fully adjusted models. A. WEI Z-score, Milk adiponectin; B. WFL Z-score, Milk adiponectin; C. WEI Z-score, Infant serum adiponectin; D. WFL Z-score, Infant serum adiponectin; E. WEI Z-score, Maternal serum adiponectin; F. WFL Z-score, Maternal serum adiponectin. APN: Adiponectin. *p≤0.05 for adjusted pairwise comparison between high and low groups.

Table 1

Baseline characteristics of cohort

	Entire cohort	≥12 months' followup	<12 months' followup
N	277	192	85
Maternal Characteristics			
Age at delivery	25.0 ± 5.7	25.4 ± 5.7	24.0 ± 5.5*
Employed (n [%] yes)	39 (14%)	31 (16%)	8 (9%)
Education			
≤Elementary	104 (38%)	68 (35%)	34 (40%)
≤High school	133 (48%)	95 (49%)	38 (45%)
≤College	42 (15%)	29 (15%)	13 (15%)
Marital status (% married)	261 (94%)	183 (95%)	78 (92%)
Delivery type (% vaginal)	183 (66%)	121 (63%)	62 (73%)
Parity	1.2 ± 1.2	1.3 ± 1.2	1.1 ± 1.2
Infant Characteristics			
Sex (% male)	125 (45%)	90 (47%)	35 (41%)
Birth weight (kg)	3.2 ± 0.4	3.2 ± 0.4	3.2 ± 0.4
Follow-up duration (months)	17.2 ± 8.5	22.4 ± 3.5	5.4 ± 3.2*
Infant Feeding			
Exclusive BF duration (days)	78.1 ± 62.8	83.8 ± 63.6	65.0 ± 59.2*
Age at food introduction (days)	143.7 ± 41.0	146.3 ± 38.5	134.1 ± 48.2
Adiponectin			
Maternal serum (μg/ml)	8.37 ± 3.36	8.49 ± 3.43	8.09 ± 3.19
Infant Serum (μg/ml)	31.08 ± 5.49	30.69 ± 5.79	32.37 ± 4.25
Milk adiponectin (ng/ml)	21.57 ± 5.12	21.11 ± 5.13	22.63 ± 4.95*

Unadjusted mean ± standard deviation (SD) or frequency (percent) presented.

*$p \leq 0.05$ for difference by duration of follow-up, by Student's t-test or χ^2 test, as appropriate.

Table 2

Correlations among infant serum adiponectin, maternal serum adiponectin, milk adiponectin and infant anthropometry in the first year of life

		Adiponectin		Anthropometry		
	N	Maternal baseline serum APN	Median milk APN	Infant WFL Z-score	Infant WEI Z-score	Infant LEN Z-score
Infant serum APN at:						
Baseline	87	**0.29****	0.04	0.02	0.11	0.002
3 months	84	0.20	**0.22***	−0.02	−0.20	**−0.23***
6 months	66	**0.32****	**0.38****	0.07	−0.06	−0.09*
12 months	55	0.18	**0.28***	−0.26	**−0.34****	**−0.40****
Median infant serum APN	92	**0.28****	**0.25****	−0.08 0.03 0.01 −0.16	−0.16 −0.06 −0.12 −0.19	−0.003 −0.11 −0.17 **−0.24***
Maternal baseline serum APN	274	--	**0.37*****	−0.11 −0.07 **−0.17**** −0.09	**−0.15**** **−0.15**** **−0.14*** −0.12	−0.11 −0.10 0.01 −0.08
Median milk APN	276	--	--	−0.11 **−0.15*** **−0.14*** −0.07	**−0.17**** **−0.20**** **−0.14*** −0.04	**−0.13*** −0.10 −0.09 −0.02

Unadjusted Spearman rank correlations presented. The 4 values in each box in the lower right panel correspond to correlations of adiponectin values with indicated z-scores at 0, 3, 6 and 12 months, respectively.

* p≤0.05

** p≤0.01

*** p≤0.0001