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Early-Life Home Environment and Obesity in a Mexican American Birth Cohort: The CHAMACOS Study

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ABSTRACT

Objective: Little is known about the impact of the home environment on biomarkers of obesity, such as adipokines, in children. In this study, we examined the relationship of maternal depressive symptoms and potentially protective social factors, including maternal support and the home learning environment, with body mass index and adipokines.

Methods: Data were obtained from 326 Mexican American participants from the Center for the Health Assessment of Mothers and Children of Salinas cohort. Plasma adipokine levels were assessed in 326 children by enzyme-linked immunoassay at birth or ages 5, 9, or 14 years. Maternal depressive symptoms were evaluated using the Center for Epidemiological Studies Depression Scale when children were 1, 3.5, 7, and 9 years old; social support was assessed by the Duke-University of North Carolina Questionnaire at ages 1 and 5 years; and home learning environment by the Home Observation for the Measurement of the Environment (HOME) at ages of 6 months and 1, 2, 3.5, 7, 9, and 10.5 years.

Results: Age was significantly associated with adiponectin ($B = -5.0$, SE = 0.2) and leptin ($B = 0.01$, SE = 0.003) levels. Individual time point analyses identified significant positive associations of HOME scores in childhood with adiponectin at ages 9 years (HOME score; age 3.5 years: $B = 0.9$, $p = .04$) and 14 years (HOME score; age 7 years: $B = 0.6$, $p = .02$, age 9 years: $B = 0.6$, $p = .05$, age 10.5 years: $B = 0.5$, $p = .04$). We observed significant relationships of maternal depressive symptoms at age 9 years with adiponectin and body mass index z-score at age 14 years ($B = -0.2$, $p = .003$ and $B = 0.02$, $p = .002$, resp.), which were confirmed in longitudinal models.

Conclusions: This study adds new evidence that adverse and protective aspects of the home environment could lead to altered obesity status in children.

Key words: adiponectin, children, home environment, leptin, Mexican American.

INTRODUCTION

Obesity is influenced by life-style, genetic, and environmental risk factors (1) and remains a critical public health issue nationwide (2,3). The burden of the obesity epidemic falls disproportionately on minorities; specifically, Hispanic and non-Hispanic black youth have a higher odds of obesity compared with non-Hispanic white and Asian youth (3). Children diagnosed as obese, based on body mass index (BMI) at or above the 95th percentile, have an increased risk of developing cardiovascular disease and diabetes later in life and becoming obese as adults (4,5).

Increasing evidence suggests that early-life measures of the home environment, including family stability, may influence risk of obesity (6–8). Aspects of the home environment have also been associated with the production of biologically active markers of obesity secreted by adipose tissue, including the adipokines: leptin and adiponectin (9–11). The protein hormone adiponectin, which is primarily derived from adipose tissue, has antidiabetic, antiatherogenic, anti-inflammatory, and insulin-sensitizing properties that mediate the pathogenesis of metabolic and cardiovascular disease (12,13). Studies in adults have shown inverse relationships between self-reported early-life measures of a poor home environment, including abuse, neglect, and household dysfunction, with adiponectin levels assessed in adulthood (9,11,14). Additional research has reported lower adiponectin levels in adult study participants with depressive symptoms in comparison with controls (15–17).

Leptin, another adipokine, is a hormone predominantly secreted by adipose tissue and has also been found in other tissues such as ovaries, placenta, and the brain (18,19). Leptin can moderate energy homeostasis, which can be altered during depression,

BMI = body mass index, **CES-D** = Center for Epidemiological Studies Depression Scale, **CHAMACOS** = Center for the Health Assessment of Mothers and Children of Salinas, **FDR** = false discovery rate, **GEE** = generalized estimating equation, **HPA** = hypothalamic-pituitary-adrenal, **HOME** = Home Observation for the Measurement of the Environment

SDC Supplemental Content

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through interaction with central circuits in the hypothalamus (16,20). Similar to adiponectin, a number of studies in adults have reported associations between leptin levels and early-life family or home dysfunction (9,10,14) and depressive symptoms in adulthood (21). In contrast to adiponectin, the amount of leptin secreted into circulation is higher in adults who have experienced poor home environments or mental illness. However, the only prospective study to date in children (22), using data from 170 12-year-old children from Great Britain, reported suggestive yet insignificant lower levels of leptin in children exposed to early-life maltreatment.

In the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) cohort, we previously reported that 7-year-old children whose mothers consistently demonstrated depressive symptoms had 2.4 times the adjusted odds of overweight/obesity compared with those whose mothers never experienced symptoms of depression (23). Adipokine trajectories from birth to age 9 years have been characterized in a subset of CHAMACOS participants and have shown three distinct risk groups for each adipokine with complex age dynamics through childhood (24). Thus far, studies on aspects of the home and family environment and adipokines have focused primarily on adult populations, are cross-sectional in nature, are predominantly conducted in African American and white populations, and primarily are focused on symptoms of mental health and family dysfunction, rather than protective home environment factors.

In the current study, we examine the relationship of maternal depressive symptoms, as well as the positive influences of social support and a healthy home environment, with BMI and adipokines in children from the CHAMACOS cohort, a Mexican American birth cohort with high levels of childhood obesity (25). We explored these specific psychosocial factors based on previous research that has provided preliminary evidence of how early-life quality of the home environment (26–28), maternal depression (23,29), and offspring social support (30) can impact obesity risk in children, making use of available data measured at multiple time points in early childhood in the CHAMACOS cohort. We hypothesize that children, who were raised in a better home environment with less stress and adversity and whose mothers had better social support and exhibited fewer symptoms of depression, would have increased adiponectin levels and lower BMI and leptin levels through decreased activation of the hypothalamic-pituitary-adrenal (HPA) axis, which can alter levels of hormones that impact obesity risk. We anticipate that recent and previous exposures to home environment factors will influence adipokines and obesity status, given the increasing awareness of how early-life exposures can alter future disease risk. Furthermore, we expand our previous analysis of adipokines to a larger number of participants (n = 326) and extend follow-up from the ages 9 to 14 years.

METHODS

Study Population

The CHAMACOS is a longitudinal cohort established to assess the health effects of environmental exposures, such as pesticides, on child growth and development (31). A total of 601 pregnant women were enrolled in the study between October 1999 and October 2000. Mothers enrolled in the CHAMACOS study were older than 18 years, less than 20 weeks of gestation at enrollment, eligible for low-income health insurance (Medi-Cal eligible), Spanish or English speaking, and intended to deliver at the county hospital. Of the 536 live births, the number of children with adipokine measurements at different time points was as follows: delivery (adiponectin, leptin; n = 217, n = 211), age 5 years (n = 227, n = 201), age 9 years (n = 250, n = 244), and age 14 years (n = 233, n = 228). The total number of children included in this study was 326, and most had adipokine data for more than three time points (Figure 1).

All study procedures were approved by the Committee for the Protection of Human Subjects at the University of California, Berkeley. Informed consent was obtained from all mothers; oral assent was obtained from children from ages 7 to 11 years, and written assent was obtained starting at 12 years.

Procedures

Women were interviewed at approximately 13 and 26 weeks of gestation, after delivery, and during the developmental assessments of the children at ages 6 months and 1, 2, 3.5, 5, 7, 9, 10.5, and 14 years. To accommodate the study participants, questionnaires and assessments were administered in either English or Spanish by bilingual, bicultural interviewers. Information gathered at each interview included sociodemographic factors, health status, diet, and an assessment of exposure risk factors.

Maternal depressive symptoms and protective factors, including social support and HOME scores, were measured throughout childhood and

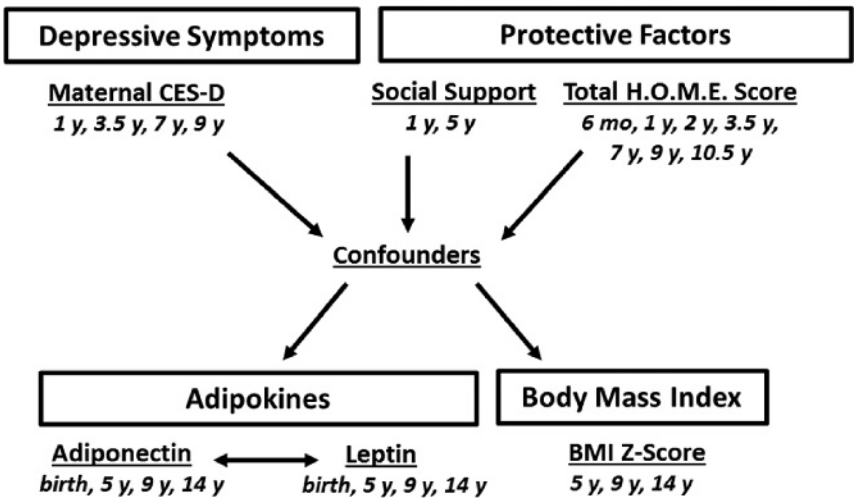

FIGURE 1. Schematic of analysis.

early adolescence in CHAMACOS participants. Maternal depressive symptoms were assessed using the Center for Epidemiological Studies Depression Scale (CES-D) (32) when the children were 1, 3.5, 7, and 9 years old (Figure 1). The recommended cutoff score of 16 (33) was used to identify mothers exhibiting symptoms of depression and the continuous CES-D scores (max range of 0–60, with a score of 60 representing the worst possible score) were used in regression analyses. Social support was characterized in mothers when children were 1 and 5 years using the Duke-University of North Carolina Functional Social Support Questionnaire, with scores representing an average of responses on a 1 to 5 scale to a validated eight-item instrument designed to measure functional social support. Higher scores indicate increased social support (34). Characteristics of the home environment conducive to child development were determined at ages 6 months and 1, 2, 3.5, 7, 9, and 10.5 years using the Home Observation for the Measurement of the Environment (HOME) (35). For earlier visits (ages 6 months–2 years), we used the Infant-Toddler HOME inventory that combines observations of the home environment and mother child interactions by trained bilingual interviewers with questions about toys, books, and the overall home learning environment that were asked of the mothers. The total HOME scores are a combination of the responsivity, avoidance, learning, and involvement subscales with a range of 16 to 45 points. At later time points (3.5–10.5 years), we used a short form of the HOME inventory that was based only on maternal questionnaires that was composed of emotional and cognitive subscales with a range of 5 to 24 points. Higher social support and HOME scores indicate more protective environments, whereas increased depression scale scores refer to more severe maternal depressive symptoms. Cronbach's α, a measure of internal consistency, was 0.77, 0.57, and 0.79 for maternal depressive symptoms, social support, and HOME scores, respectively, measured throughout childhood in the CHAMACOS cohort.

Children were weighed and measured by trained research staff at ages 5, 9, and 14 years. We measured the children's barefoot standing height to the nearest 0.1 cm using a stadiometer. Standing weight was measured to the nearest 0.1 kg using an electronic scale at age 5 years (Tanita 1582) and a foot-to-foot bioimpedence scale at ages 9 and 14 years (Tanita TBF-300A Body Composition Analyzer). BMI was calculated as kilogram per square meter. The Centers for Disease Control and Prevention age- and sex-specific percentiles were used to categorize children as underweight, normal weight, overweight, or obese and BMI z-scores were used in analyses (36).

Adipokine Analysis

Adiponectin and leptin were assessed in blood specimens stored at −80°C collected from CHAMACOS participants at birth (cord blood) and repeatedly at ages 5, 9, and 14 years. We selected samples for analysis based on individuals with plasma available at a given CHAMACOS assessment. The subset of CHAMACOS participants used in this analysis was not significantly different from the main cohort in most demographic characteristics (child sex, baseline poverty, education, gestational age, parity, child overweight status). However, mothers in this sample tended to be slightly older at delivery and had higher average BMI than those not included in the analyses. Plasma adipokines were measured using enzyme-linked immunoassay (ELISA) RayBiotech Human Adiponectin and Human Leptin kits (RayBiotech Inc, Norcross, GA). The protocol developed by the manufacturer was used, with some previously described modifications (37) to increase precision for assessment in children: (*a*) the standard curve for adiponectin was narrowed to obtain better resolution at smaller readings, (*b*) the standard curve for leptin was broadened, and (*c*) plasma samples in the leptin analysis were more diluted. Final dilutions for the RayBio Human Leptin ELISA and the Human Acrp30 ELISA were 1:70 and 1:30,000, respectively. Absorbance values were obtained at a wavelength of 450 nm, with an upper absorbance cutoff of 4.0 optical density units. The minimum detectable concentrations for adiponectin and leptin were 10 and 6 pg/ml, respectively. Internal laboratory controls were included on each plate to ensure reproducibility between the experimental runs, with average intra- and interplate coefficients of variations of less than 5% and 14%, respectively. All plasma samples were measured in duplicate.

Statistical Analysis

We $\log_{10}$-transformed leptin concentrations in CHAMACOS study participants for use in regression and correlation analyses because they were right skewed. Adiponectin concentrations did not require this adjustment. The interrelationships between adiponectin and log-transformed leptin levels measured at birth and ages 5, 9, and 14 years were assessed by Pearson correlation coefficients. Differences in mean adipokine levels by sex were determined by *t* tests, and longitudinal trends of adipokines across childhood were characterized by generalized estimating equations (GEEs) with an exchangeable correlation structure (38). Because leptin demonstrated a difference by sex, we adjusted for sex in the GEE models with leptin as the outcome.

Linear regression models with robust estimates of the SEs were used to determine the association of continuous measures of maternal scores on the CES-D, HOME scores, and total social support scores with concurrent or future child adipokine levels and BMI z-scores, which were assessed at ages 5, 9, or 14 years. CES-D maternal depressive symptom, Duke-University of North Carolina social support, and raw HOME scores were assessed as continuous variables in regression models. We included additional covariates in the models that were identified in previous literature in CHAMACOS (39) and in research assessing the relationship between adversity and obesity trends (6).

Specifically, two regression models were performed to assess the relationship between each independent home environment variable (i.e., continuous measures of maternal depressive symptoms, raw HOME scores, and total social support) and outcome (adiponectin, log-transformed leptin, and BMI z-score): Model 1, the unadjusted model, and Model 2, adjusting for child sex and maternal pregnancy variables. Maternal pregnancy variables in Model 2 included continuous (i.e., maternal pre-pregnancy BMI, years in the United States, pregnancy sugar-sweetened beverage consumption per week), categorical (maternal education level, poverty status), and binary (smoking and alcohol consumption) variables. The maternal education variable was coded as shown in Table 1. Maternal baseline poverty was coded as at or below poverty, greater than poverty to 200% of the poverty level, and greater than 200% of the poverty level. As a sensitivity analysis, we also ran Model 2 with an adjustment for poverty assessed concurrently with the outcome of interest (adipokines or BMI z-score). The results were similar to those of Model 2; thus, they were not presented in the tables.

In addition, regression was used to assess the relationship between longitudinal trends of measures of the home environment and the outcomes (adipokines and BMI). We used GEE-derived SEs based on exchangeable working correlation models to provide robust inference in the presence of repeated measures. For both the maternal depressive symptom and HOME scores, we generated a new variable by using the values for each that were measured at the same time or before the assessment of adipokines or BMI. Specifically, maternal depressive symptom measurements at child age 3 years corresponded to obesity measurements at age 5 years, and depressive symptoms at age 9 years corresponded to adipokine and BMI measurements at ages 9 and 14 years. We used the same time points for the HOME score variable, with the exception of the correspondence of the 10.5-year HOME score with the 14-year outcome assessment. We used social support values from the 5-year child assessment because it was the closest value for all time points of the outcomes. Henceforth, we will designate these variables as time-varying measures of the home environment to distinguish them from the original variables. We used GEE models to assess the relationship between the time-varying variables for maternal depressive symptoms, social support, or home environment and repeated measurements of adipokines and BMI from ages 5, 9, and 14 years. In the models, we adjusted for age and child sex, because they have been previously shown to influence adipokine and BMI trends and would be the most likely confounders in the current analysis. The following model was used:

TABLE 1. Demographic Characteristics of CHAMACOS Mothers and Children With Adipokine Data at Delivery or Age 5, 9, or 14 Years (n = 326)

Characteristic	*N* (%)
Maternal age at pregnancy	
18–24	134 (41)
25–29	107 (33)
30–34	54 (17)
35–45	31 (10)
No. years mother lived in US at pregnancy	
<1	57 (17)
1–10	174 (53)
≥11	95 (29)
Parity	
0	105 (32)
≥ 1	221 (68)
Education	
≤6th grade	144 (44)
7–12th grade	115 (35)
≥High school graduate	67 (21)
Maternal pregnancy BMI[a]	
Underweight (<18.5 kg/m^2)	2 (1)
Normal (18.5–24.9 kg/m^2)	112 (34)
Overweight (25–29.9 kg/m^2)	127 (39)
Obese (≥30 kg/m^2)	84 (26)
Child sex	
Boy	155 (48)
Girl	171 (52)
Gestational age, wk	
34–36	23 (7)
≥ 37	303 (93)
Child birth weight	
Low birth weight (<2500 g)	12 (4)
Normal birth weight (≥2500 g)	314 (96)
Child 5-y BMI (CDC categories)[a]	
Normal (<85 percentile)	139 (47)
Overweight (≥85 percentile, <95 percentile)	61 (20)
Obese (≤ 95 percentile)	98 (33)
Child 9-y BMI (CDC categories)[a]	
Normal (<85 percentile)	134 (45)
Overweight (≥85 percentile, <95 percentile)	50 (17)
Obese (≤95 percentile)	114 (38)
Child 14-y BMI (CDC categories)[a]	
Normal (<85 percentile)	136 (46)
Overweight (≥85 percentile, <95 percentile)	56 (19)
Obese (≤ 95 percentile)	103 (35)

US = United States; BMI = body mass index; CDC = Centers for Disease Control and Prevention.

[a] Total number of observations for BMI varies because of missing data.

$$Y_{ij} = b_0 + b_1X_{1ij} + b_2X_{2ij} + b_3X_{3i} + e_{ij}$$

where Y_{ij} is either the BMI z-score or adipokine level for the i-th subject at the j-th anthropometric or adipokine assessment in childhood (j = 5, 9, 14). X_{1ij} is the time-varying home environment value (i.e., HOME, social support, or maternal depressive symptom score) for the i-th subject and the j-th assessment, where j is time point of the home environment measurement that is either the same time as the adipokine or BMI assessment or the measurement prior. X_2, X_3 and b_2, b_3 represent the covariates and their respective slopes for the age and child sex variables. e_{ij} is the residual error term.

As a sensitivity analysis, we ran additional models, including one with all the time-varying exposure variables (maternal depressive symptoms, HOME score, and social support) and another model with poverty at outcome assessment. We also examined the potential of social support to moderate the relationship between home environment factors and obesity. We generated interaction terms by multiplying the maternal depressive or HOME time-varying scores by the social support variable and included the new variable in analyses. We also ran mixed-effect regression models to confirm GEE findings. Given the sample size, more complicated longitudinal models did not seem to have sufficient power to detect changes in measures of obesity related to previous or concurrent home environment parameters.

We controlled for the false discovery rate (FDR) in the analysis of individual assessments of measures of the home environment with child adipokines and BMI. All statistical analysis was performed in STATA (version 12.1; STATA Corp, College Station, TX). Statistical significance was set at $p < .05$.

RESULTS

Study Sample Characteristics

Demographic and anthropometric data for CHAMACOS mothers and children (n = 326) with adipokines assessed at least once during childhood (delivery or ages 5, 9, or 14 years) are shown in Table 1. At pregnancy, most mothers were young, had lived in the United States for 10 or fewer years, did not obtain a high school diploma, and had overweight or obesity. In our study, 48% of participants were boys and 52% were girls. More than half of the children at each time point had overweight or obesity: 53% of 5 year olds, 55% of 9 year olds, and 54% of 14 year olds.

Age and Sex Adipokine Trends

Adiponectin levels were highest at birth (M (SD) = 101.2 (32.9) μg/ml), lower as children got older (age 5 years: M (SD) = 36.4 (16.2) μg/ml; age 9 years: M (SD) = 40.7 (18.1) μg/ml), and were lowest in adolescence (age 14 years: M (SD) = 23.7 (11.0) μg/ml) (Table 2, Figure 2). Leptin levels at birth were high (M (SD) = 18.6 (18.7) ng/ml), which could indicate an influence of maternal levels of leptin. Leptin levels were much lower at age 5 years (M (SD) = 3.6 (3.3) ng/ml) and were higher as the children aged (age 9 years: M (SD) = 15.0 (16.7) ng/ml; age 14 years: M (SD) = 22.2 (17.2) ng/ml). Adiponectin levels did not vary by sex, with the exception of a borderline significant (p = .049) difference at age 14 years with higher levels in girls compared with boys (Table 2). Log-leptin levels from delivery through age 14 years were consistently higher in girls. Adiponectin levels were moderately and positively correlated across different time points, becoming stronger as children aged (Table 3). Adiponectin levels at a given time point were most correlated with measurements at adjacent time points (Table 3). Similar trends were observed in the leptin measurements. At each assessment, adiponectin levels were significantly and inversely associated with leptin levels, with the exception of delivery levels, when the negative trend was not

TABLE 2. Plasma Adipokine Levels at Delivery and Ages 5, 9, and 14 Years

	n	M	SD	Min	Max	*p*
Adiponectin, μg/ml						
Delivery						
Boys	103	97.7	30.3	2.5	163.0	.14
Girls	114	104.3	34.9	7.4	186.9	
All	217	101.2	32.9	2.5	186.9	
Age 5 y						
Boys	105	35.5	15.9	0.1	86.1	.46
Girls	122	37.1	16.5	3.9	97.4	
All	227	36.4	16.2	0.1	97.4	
Age 9 y						
Boys	119	40.6	19.2	8.2	93.3	.92
Girls	131	40.8	17.2	2.8	92.4	
All	250	40.7	18.1	2.8	93.3	
Age 14 y						
Boys	107	22.2	11.9	5.5	57.7	.049
Girls	126	25.0	10.2	4.4	47.6	
All	233	23.7	11.0	4.4	57.7	
Leptin, ng/ml						
Delivery						
Boys	98	13.7	15.0	1.9	84.6	<.001
Girls	113	22.8	20.5	1.4	97.1	
All	211	18.6	18.7	1.4	97.1	
Age 5 y						
Boys	82	3.0	2.3	0.2	16.4	.073
Girls	119	4.1	3.7	0.3	22.2	
All	201	3.6	3.3	0.2	22.2	
Age 9 y						
Boys	113	11.4	12.2	0.9	66.1	.017
Girls	131	18.1	19.3	0.7	93.3	
All	244	15.0	16.7	0.7	93.3	
Age 14 y						
Boys	102	14.2	13.7	0.4	55.4	<.001
Girls	126	28.6	17.1	2.8	73.8	
All	228	22.2	17.2	0.4	73.8	

SD = standard deviation; Min = minimum; Max = maximum.

p values obtained from *t* tests comparing adipokine levels in boys and girls at different assessments.

significant ($p = .70$) (Figure 3). Age was a strong predictor ($p < .001$) of leptin and adiponectin levels in the GEE model. For adiponectin, *B* value was close to −5.0 (GEE $B = -4.975$, robust SE = 0.153), and for leptin, *B* value was 0.013 (0.003), respectively.

Maternal Depressive Symptoms and Home Environment Protective Factors

Among the mothers, 50%, 43%, 26%, and 26% were at risk of clinical depression with CES-D scores of 16 or higher when children were assessed at 12 months, 3.5 years, 7 years, and 9 years, respectively (Table 4). Scores reported at 12 months could also reflect symptoms of postpartum depression. Median maternal social support scores were high (1 year: 4.0; 5 years: 4.3). Median HOME scores varied across the collections, reflective of the use of the Infant-Toddler HOME inventory for earlier visits (ages 6 months–2 years) and the short form of the HOME inventory for the later time points (3.5–10.5 years). Specifically, median scores ranged from 26 to 36 and 14 to 18 for the earlier and later visits, respectively.

Individual Assessments of Measures of the Home Environment With Child Adipokines and BMI

We assessed the relationship of measures of the home environment across childhood at individual time points with obesity, as measured by BMI z-score, and adipokines. Maternal depressive symptoms at child ages 3.5 and 9 years were positively associated with BMI z-score at ages 9 and 14 years (Table 5 and Supplemental Table 2, http://links.lww.com/PSYMED/A530). A one-unit increase in CES-D score when children were 3.5 and 9 corresponded to a 0.01-point increase in BMI z-score at age 9 years (3.5 years: 95% CI = 0.003 to 0.02; 9 years: 95% CI = 0.002 to 0.02) and age 14 years (3.5 years: 95% CI = 0.003 to 0.02; 9 years: 95% CI = 0.006 to 0.03). Social support and HOME scores were not significantly associated with 9-year BMI z-scores. However, a unit increase in social support at age 5 years corresponded to a significant 0.2-point decrease in BMI z-score at age 14 years (95% CI = −0.3 to −0.05). In addition, a one-unit increase in HOME score at age 9 years was associated with a 0.05-point decrease in BMI z-score at age 14 years (95% CI = −0.09 to −0.005). The associations of maternal depressive symptoms at age 9 years and social support at age 5 years with BMI z-score at age 14 years remained significant after FDR adjustment (all $p < .01$).

In models with adiponectin as the outcome, we observed a consistent trend across models of higher HOME score, indicating a more enriched home environment, with increased adiponectin at age 9 years. Positive associations with similar magnitudes of effect sizes were with HOME scores at ages 3.5, 7, and 9 years, but only age 3.5 years was significant in crude models, indicating that a one-unit increase in HOME score at age 3.5 years corresponded to a 0.9-point increase in adiponectin at age 9 years (95% CI = 0.03 to 1.8). Similarly, HOME scores were positively associated with adiponectin at age 14 years, with larger-effect sizes observed in crude models with the 7-, 9-, and 10.5-year HOME scores. Specifically, a one-unit increase in the total HOME score at ages 7, 9, and 10.5 years corresponded respectively to a 0.6-point increase (95% CI = 0.1 to 1.2), 0.6-point increase (95% CI = 0.001 to 1.2), and a 0.5-point increase (95% CI = 0.02 to 1.0) in adiponectin at age 14 years.

We identified inverse associations of maternal depressive symptoms and 9-year adiponectin levels; however, results did not reach statistical significance. In the 14-year adiponectin models, a one-unit increase in CES-D score when children were 7 and 9 years corresponded to a 0.2-point decrease (7 years: 95% CI = −0.3 to −0.03; 9 years: 95% CI = −0.3 to −0.07) in adiponectin.

Social support at age 5 years had a positive relationship with adiponectin at age 9 and 14 years. Specifically, a one-unit increase in social support at age 5 years corresponded to a 1.6-point increase in 9-year adiponectin levels (95% CI = −0.9 to 4.0), which

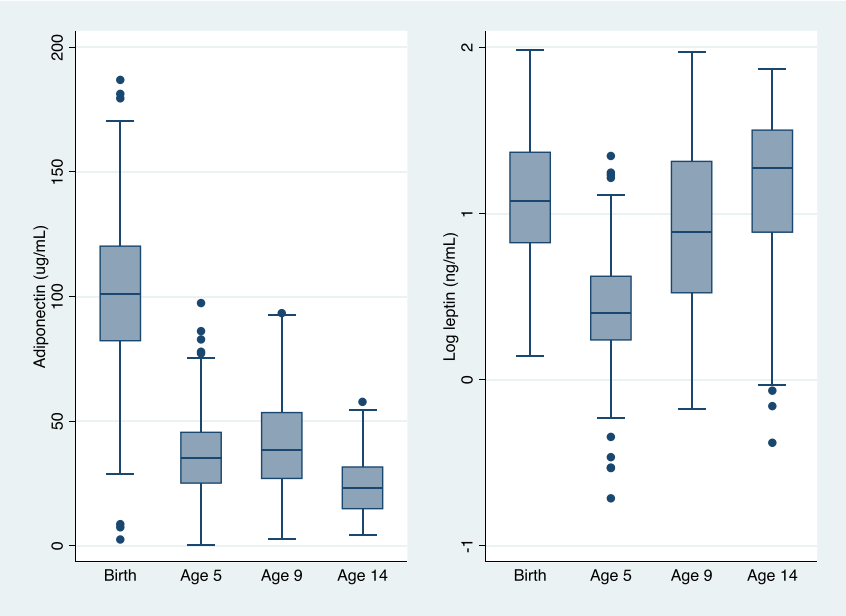

FIGURE 2. Box plots of adipokine trends in CHAMACOS newborns and children at ages 5, 9, and 14 years. The figure presents distributions of adipokines in all study participants with data available at each time point. In addition, GEE models were used to model longitudinal changes in adipokines by age. Age was a significant predictor of adipokine levels ($p < .001$ for all models) for leptin and adiponectin. Color image is available only in online version (www.psychosomaticmedicine.org).

was not significant but was similar in magnitude to a borderline significant 1.3-point increase in 14-year adiponectin (95% CI = 0.003 to 2.7). For the adiponectin models, only the relationship between maternal depressive symptoms and adiponectin at age 14 years remained significant after FDR adjustment ($p = .003$).

We also observed significant associations between symptoms of maternal depression, HOME scores, and social support, predominantly in early childhood, and leptin levels in CHAMACOS children. In crude models, a one-point increase of maternal depressive symptoms at child aged 3.5 years corresponded to a 0.007-point increase in log leptin at age 9 years (95% CI = 0.001 to 0.013), whereas a unit increase in scores at age 7 years significantly related to a 0.007 increase in 14-year log-leptin levels (95% CI = 0.001 to 0.013). A unit increase in HOME score at age 2 years corresponded to a 0.03-point increase (95% CI = 0.003 to 0.055) in log-leptin levels at age 9 years. In the 9- and 14-year leptin models, the direction of association between social support and leptin was consistently negative.

We also examined the relationship between positive and negative aspects of the home environment and adipokines at age 5 years (Supplemental Table 1, http://links.lww.com/PSYMED/A530). Results were similar in magnitude to the 9- and 14-year adipokine and BMI models but did not reach statistical significance, suggesting that obesity status and biomarkers of obesity in later childhood may be more sensitive to the effects of maternal depressive symptoms or protective home environment factors.

TABLE 3. Pearson Correlation Matrix of Adipokines Assessed at Delivery and Ages 5, 9, and 14 Years

	A_0	A_5	A_9
A_5	**0.26**	—	—
A_9	**0.26**	**0.49**	—
A_{14}	**0.21**	**0.35**	**0.52**
	L_0	L_5	L_9
L_5	**0.19**	—	—
L_9	**0.37**	**0.51**	—
L_{14}	**0.28**	**0.35**	**0.56**

A_0 = adiponectin at delivery; A_5 = adiponectin at age 5 years; A_9 = adiponectin at age 9 years; A_{14} = adiponectin at age 14 years; L_0 = log-transformed leptin at delivery; L_5 = log-transformed leptin at age 5 years; L_9 = log-transformed leptin at age 9 years; L_{14} = log-transformed leptin at age 14 years.

Bolded values are significant at $p < .05$.

Longitudinal Assessment of Measures of the Home Environment With Child Adipokines and BMI

Longitudinal models of adipokines and BMI z-score showed significant relationships with the most recent measures of maternal depressive symptoms and social support (Table 6). Maternal depressive symptoms were significantly associated with increased BMI z-score ($B = 0.007$; 95% CI = 0.0004 to 0.014) and decreased adiponectin ($B = -0.248$; 95% CI = −0.376 to −0.119). Social support at age 5 years, which was the closest assessment to all childhood adipokine measurements (age 5, 9, and 14 years) was negatively associated with BMI z-score ($B = -0.162$; 95% CI = −0.273 to −0.050) and leptin ($B = -0.056$; 95% CI = −0.096 to −0.016). Cumulative HOME score was not significantly associated with longitudinal levels of adiponectin across childhood ($B = -0.285$; 95% CI = −0.694 to 0.124; $p = .17$), contrary to the results observed in the individual models. In the sensitivity analysis, we found no significant differences in the model including all the

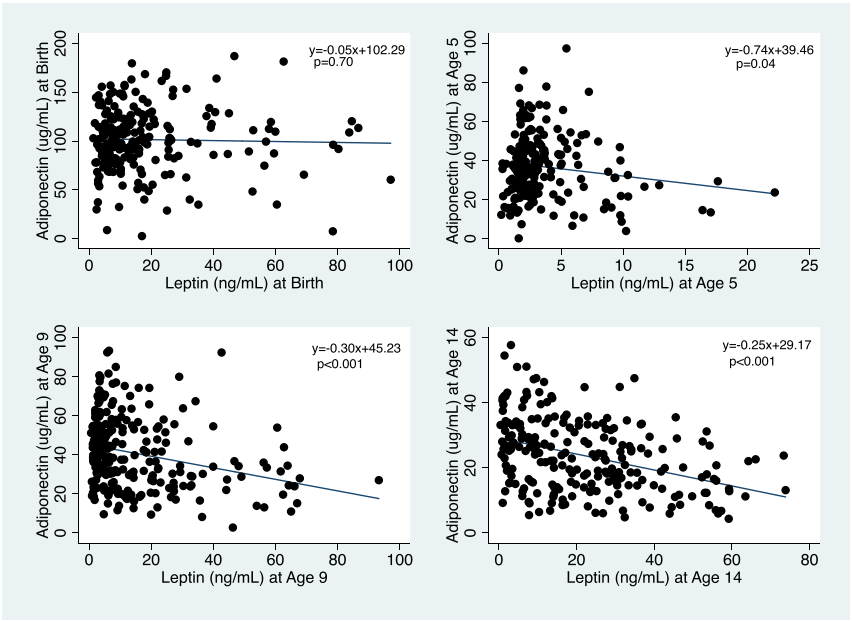

FIGURE 3. The relationships between leptin and adiponectin in CHAMACOS children at birth and age 5, 9, and 14 years. The figure shows the relationship between adiponectin and leptin measurements at a given assessment. At all time points, with the exception of birth, leptin and adiponectin are significantly and inversely associated. Color image is available only in online version (www.psychosomaticmedicine.org).

exposure variables (maternal depressive symptoms, HOME score, and social support) and another model with poverty at outcome assessment. The results of the analyses of a potential social support moderation of the relationships of HOME score and maternal depressive symptoms with obesity indicated a lack of interaction. Mixed-effect models produced similar results to the GEE models.

DISCUSSION

In this longitudinal study, we examined adipokine levels and BMI throughout childhood and assessed their relationship with early-life measures of the home environment in a Mexican American birth cohort. Adiponectin levels in CHAMACOS children were high at birth and, on average, lower as the children aged. Leptin levels were high at birth and during adolescence, but lower during early childhood (age 5 years). Previous mixture modeling analyses that reported trajectory clusters for adiponectin and leptin in a subset of CHAMACOS children up to age 9 years observed similar patterns in adipokine levels, including the large difference in adiponectin levels at birth and early childhood (24). We found consistent positive associations between HOME score in late childhood and adiponectin at ages 9 and 14 years indicating that a protective home environment is associated with beneficial profiles of adiponectin in children. Significant associations were observed between maternal depressive symptoms and HOME score in

TABLE 4. Distribution of Home Environment Parameters in CHAMACOS Participants

Adversity Parameter	Child Age	*n*	M	SD	Min	Max
Maternal Depressive Symptoms (CES-D)	1 y	301	16.7	11.0	0.0	50.0
	3.5 y	291	15.0	10.9	0.0	49.0
	7 y	308	10.8	9.5	0.0	43.0
	9 y	278	10.5	10.4	0.0	46.0
Duke Social Support	1 y	303	3.8	1.0	1.0	5.0
	5 y	299	4.0	1.0	1.1	5.0
Total HOME Score	6 mo	325	31.8	4.3	16.0	43.5
	1 y	325	35.6	3.3	19.3	43.5
	2 y	325	25.8	2.7	13.3	31.0
	3.5 y	325	17.2	2.4	11.1	23.9
	7 y	319	17.7	2.8	9.0	24.0
	9 y	307	14.3	2.8	5.0	20.0
	10.5 y	298	14.5	2.8	6.0	20.0

SD = standard deviation; Min = minimum; Max = maximum; Center for Epidemiological Studies Depression Scale; HOME = Home Observation for the Measurement of the Environment.

TABLE 5. Relationship of Aspects of the Home Environment During Childhood With Adipokines or BMI Z-score at Age 14 Years

	β[a] (95% CI)						
	Depression Scale				Duke Social Support		
	1 y	3 y	7 y	9 y	1 y	5 y	
BMI z-score							
Model 1	0.010 (−0.001 to 0.021)	**0.014 (0.003 to 0.024)**	0.009 (−0.002 to 0.020)	**0.016 (0.006 to 0.026)[b]**	−0.022 (−0.140 to 0.097)	**−0.164 (−0.278 to −0.050)[b]**	
Model 2	0.006 (−0.005 to 0.017)	0.009 (−0.002 to 0.019)	0.009 (−0.002 to 0.020)	**0.012 (0.001 to 0.023)**	−0.009 (−0.127 to 0.110)	**−0.157 (−0.268 to −0.046)[b]**	
Adiponectin							
Model 1	−0.078 (−0.204 to 0.048)	−0.102 (−0.235 to 0.031)	**−0.169 (−0.311 to −0.027)**	**−0.203 (−0.336 to −0.070)[b]**	−0.391 (−1.854 to 1.073)	**1.342 (0.003 to 2.682)**	
Model 2	−0.028 (−0.160 to 0.103)	−0.059 (−0.202 to 0.084)	**−0.177 (−0.326 to −0.028)**	**−0.172 (−0.318 to −0.026)**	−0.496 (−2.026 to 1.033)	1.236 (−0.187 to 2.660)	
Leptin							
Model 1	0.004 (−0.001 to 0.009)	**0.006 (0.001 to 0.011)**	**0.007 (0.001 to 0.013)**	0.004 (−0.002 to 0.010)	−0.047 (−0.102 to 0.009)	−0.053 (−0.106 to 0.001)	
Model 2	0.002 (−0.004 to 0.007)	0.002 (−0.003 to 0.007)	**0.006 (0.0004 to 0.012)**	0.003 (−0.002 to 0.009)	−0.032 (−0.087 to 0.023)	−0.054 (−0.110 to 0.002)	
	HOME Score						
	6 mo	1 y	2 y	3 y	7 y	9 y	10.5 y
BMI z-score							
Model 1	−0.007 (−0.034 to 0.020)	−0.002 (−0.040 to 0.036)	0.033 (−0.016 to 0.082)	0.005 (−0.042 to 0.052)	−0.033 (−0.073 to 0.007)	**−0.046 (−0.086 to −0.005)**	−0.016 (−0.057 to 0.026)
Model 2	−0.013 (−0.041 to 0.016)	−0.00001 (−0.037 to 0.037)	0.030 (−0.019 to 0.079)	0.004 (−0.041 to 0.048)	−0.016 (−0.054 to 0.023)	−0.029 (−0.069 to 0.011)	0.0002 (−0.04 to 0.04)
Adiponectin							
Model 1	0.172 (−0.152 to 0.495)	0.323 (−0.141 to 0.786)	0.241 (−0.351 to 0.834)	0.100 (−0.423 to 0.623)	**0.641 (0.104 to 1.178)**	**0.588 (0.001 to 1.176)**	**0.523 (0.018 to 1.028)**
Model 2	0.120 (−0.243 to 0.483)	0.211 (−0.293 to 0.716)	0.089 (−0.583 to 0.760)	0.064 (−0.484 to 0.612)	0.493 (−0.09 to 1.075)	0.354 (−0.28 to 0.988)	0.325 (−0.229 to 0.878)
Leptin							
Model 1	0.003 (−0.011 to 0.016)	0.002 (−0.017 to 0.021)	0.019 (−0.004 to 0.041)	−0.002 (−0.030 to 0.025)	−0.018 (−0.040 to 0.004)	−0.009 (−0.030 to 0.012)	0.004 (−0.018 to 0.025)
Model 2	−0.004 (−0.019 to 0.010)	0.009 (−0.006 to 0.025)	0.014 (−0.007 to 0.036)	−0.0002 (−0.024 to 0.024)	−0.008 (−0.029 to 0.013)	−0.005 (−0.027 to 0.016)	0.003 (−0.018 to 0.024)

CI = confidence interval; BMI = body mass index.

Bolded values are significant at $p < .05$.

Model 1: crude.

Model 2: crude + sex + smoking + alcohol + education + pre-preg BMI + preg SSB + baseline poverty + years United States.

[a] Linear regression coefficient.

[b] Significant after FDR adjustment.

TABLE 6. Results of GEE Analyses of the Relationship of Longitudinal Trends in Aspects of the Home Environment With Adipokines or BMI Z-score

Exposure	Outcome	β[a] (95% CI)
Depressive Symptoms	BMI z-score	**0.007 (0.0004 to 0.014)**
	Adiponectin	**−0.248 (−0.376 to −0.119)**
	Log leptin	−0.0004 (−0.004 to 0.003)
Social Support	BMI z-score	**−0.162 (−0.273 to −0.050)**
	Adiponectin	1.191 (−0.236 to 2.618)
	Log leptin	**−0.056 (−0.096 to −0.016)**
HOME Score	BMI z-score	−0.002 (−0.022 to 0.018)
	Adiponectin	−0.285 (−0.694 to 0.124)
	Log leptin	−0.009 (−0.021 to 0.003)

BMI = body mass index; HOME = Home Observation for the Measurement of the Environment.

Bolded values are significant at $p < .05$.

[a] Coefficient from GEE models adjusting for age and sex.

early childhood and leptin at ages 9 and 14 years, but effect sizes were relatively small. We also report positive associations between maternal depressive symptoms when children were 3 and 9 years with BMI z-scores at ages 9 and 14 years, suggesting that increased maternal depressive symptoms are related to higher BMI z-scores in offspring. These data indicate that aspects of the home environment of CHAMACOS children could lead to altered obesity status and the expression of biomarkers of obesity. Clinical implications of these findings could include the direct impact of psychosocial factors on child health status and indirect effects, such as increased medical costs due to obesity comorbidities.

In addition to previous adipokine trajectories research in the CHAMACOS cohort (24), there have been only a few studies that have assessed trends of repeated measurements of adipokines throughout childhood. Mantzoros et al. (40) examined the relationship between cord blood and 3-year adipokine levels in 588 children in the Project Viva cohort. The authors found that although there was not a significant relationship between adiponectin levels at birth and age 3 years, leptin levels at the assessments were positively associated (crude model $p = .0003$). Gruszfeld et al. (41) studied trends in adipokines in 459 children from infancy to age 8 years, observing a decrease in adiponectin and leptin levels from infancy, with an increase around school age for adiponectin only. This finding is similar to our observations in the CHAMACOS cohort for a longer period from birth to 14 years. Another study in 519 Japanese children aged 9 to 10 years observed positive associations ($p < .001$) between adipokine levels at baseline and values measured at the 3-year follow-up (42). In the current study, we also observed positive associations between adipokine assessments throughout childhood, with the strongest correlation observed for consecutive measurements. At each time point, we found that leptin values were higher in girls compared with boys, which is consistent with previous reports (42,43). The sex difference observed for leptin, but not for adiponectin, could be a result of differences in body composition, as well as the potential of serum androgen levels to reduce the amount of leptin in boys (44).

In addition to assessment of trends in adipokine levels across childhood and by child sex, we examined the relationship of BMI, adiponectin, and leptin with maternal depressive symptoms and protective factors of the home environment, including social support and HOME scores. Previous research has identified relationships of early-life aspects of the home environment (26–28), maternal depression (23,29), and offspring social support (30) with obesity risk in children. In the CHAMACOS cohort, we identified consistent and positive associations between maternal depressive symptoms at child aged 3 and 9 years with BMI in adolescence. The positive relationship identified in the current study is similar to a previous study conducted by Audelo et al. (23) in 332 7-year-old CHAMACOS children, where youth whose mothers demonstrated depressive symptoms at the 1-, 3.5-, and 7-year child assessments had 2.4 times the adjusted odds of overweight/obesity relative to those whose mothers never experienced symptoms of depression. A similar study (29), including 1090 children with anthropometric assessments at three time points during early childhood, reported that children with mothers exhibiting depressive symptoms, assessed by CES-D when the child was 1 month, as well as 2 and 3 years old, were 1.7 times more prone to be overweight than their counterparts whose mothers did not report depressive symptoms. Taken together, these studies suggest a possible role of maternal depression in offspring obesity status and a potential avenue for obesity intervention.

Most of the research regarding the relationship between adversity and adipokine measurements has been conducted in cross-sectional assessments of adult populations. Positive associations were found between abuse, family instability, and depressive symptoms, in early childhood or adulthood, and adult leptin levels (9,10,21,45), whereas negative relationships were observed between home and family measures and adiponectin in adulthood (9,11,15–17,46). In our prospective analysis in Mexican American children, we also saw positive associations between maternal depressive symptoms and leptin levels throughout the child's youth and negative associations with adiponectin, particularly in older children. In addition, the positive associations we observed between HOME score and adiponectin at 9 and 14 years concur with trends seen in the literature; in this case, as HOME scores decrease, indicating poor home learning environment, adiponectin levels decline. Because adiponectin has many beneficial immunological and metabolic properties, a profile of lower levels is less desirable. The association between HOME scores and adiponectin in the longitudinal models did not reach statistical significance ($p = .17$) and thus was unable to completely corroborate the individual time point findings.

Although the current study relies on maternal assessment of adversity as children age into adolescence, it is plausible that maternal depressive symptoms, social support, and home environment could impact mental well-being, and biomarkers of obesity, of their children through several pathways. Numerous studies have demonstrated associations between stress and depressive symptoms in mothers and altered risk of obesity in their children, potentially mediated by parenting behaviors (i.e., through unhealthy dietary practices or sedentary lifestyles) or parent-child interactions (47–50). Maternal stress can induce a subsequent stress response in their children, as a result of augmented levels of cortisol (51). In addition, pervasive stress during childhood has been shown to activate the HPA axis, resulting in the release of hormones such as glucocorticoids that have downstream effects on obesity risk (52).

The biological pathways whereby family instability, stress, and depression in an individual can affect their adipokine profiles are well documented in humans. As an anti-inflammatory adipokine, adiponectin can inhibit the function of macrophages and tumor necrosis factor-α and increase the secretion of anti-inflammatory cytokines, including interleukin-10 and interleukin-1 receptor antagonist (53–55). However, during symptoms of depression, proinflammatory cytokines, such as interleukin 6, can alter HPA activity, releasing glucocorticoids that can prevent adiponectin from exerting its anti-inflammatory effects (56). Conversely, glucocorticoid secretion as a response to stressors enhances the production of leptin in humans (57,58).

The main strengths of the current study include the use of data collected longitudinally to assess the relationship between maternal depressive symptoms, social support, and the home environment and adipokine trends in a well-characterized Mexican American birth cohort. Understanding the relationship between the home environment and biomarkers of obesity in this population is particularly relevant because of the high prevalence of both parental prepregnancy and childhood obesity. However, we recognize certain limitations, because we did not examine more data on child behavior, adverse experiences, and emotional well-being, which could mediate the relationship between maternal psychosocial factors and child obesity risk. In addition, other home environment factors that were not examined in the current study, such as single parent household and crowding, could influence adipokine levels in children. Given the projected growth in the Hispanic population in the United States (59) and the high prevalence of obesity in Mexican American children (3), which we have observed in the CHAMACOS cohort, this research can have health implications in the general population and in minority populations at high risk of obesity. This study provides novel support for the relationship between early-life exposure to maternal depressive symptoms and protective factors, such as social support and an enriching home environment, and their association with adipokines. This research can inform potential public health strategies to address early childhood factors that contribute to the obesity epidemic and comorbidities of obesity.

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