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Maternal adiposity is associated with fat mass accretion in female but not male offspring during the first two years of life

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Abstract

Objective—We investigated which antenatal and postnatal factors determine offspring adiposity during the first 2 years of life.

Methods—Participants were mother and child pairs (N= 224). Offspring percent fat mass (%FM) was obtained using quantitative nuclear magnetic resonance at 11 time points between age 0.5 to 24 months. Independent variables included: race, age, gestational weight gain, first-trimester %FM, delivery mode, gestational measures of resting energy expenditure, respiratory exchange ratio, physical activity (PA), serum cytokines and lipids, and dietary intake for the mothers and sex, birth weight and length, breastfeeding duration, and PA at age 2 years for the child. Linear mixed models were used to construct the best-fitted models for the entire cohort and for each sex.

Results—Maternal %FM (p=0.006), HDL (p<0.001) and breastfeeding duration (p=0.023) were positively associated with female offspring adiposity while maternal dietary fiber intake (p=0.016)

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had a negative association. Birth weight (p=0.004), maternal HDL (p=0.013) and breastfeeding duration (p=0.015) were all positively associated with male offspring adiposity.

Conclusions—Antenatal and postnatal factors differentially impact male and female offspring adiposity during the first two years of life.

Keywords

fat mass; pregnancy; high density lipoprotein; sexual dimorphism; dietary fiber; breastfeeding

INTRODUCTION

The prevalence of obesity among women of child-bearing age is >20% (1). In addition, there is a persistent increase in obesity rates among the pediatric population with 18.5% of children in the United States classified as obese (Body Mass Index (BMI)-for-age percentile >95%) (2). Clinical and animal studies have shown that maternal obesity during gestation can program fetal metabolism that results in increased risk of developing obesity (3,4). Infants born to mothers with overweight and obesity experience increased adiposity at birth (5) accelerated postnatal weight gain (6) and carry a 2-fold risk of developing obesity by 2 years of age (7).

BMI is not a true measure of adiposity and may obfuscate the contribution of excess adipose tissue in women with similar BMIs to offspring body composition (8). In addition to excess maternal fat mass, there may be additional maternal factors that predict offspring adiposity such as excessive gestational weight gain (9), poor quality diet through gestation (10), and physical activity (PA) (11) during pregnancies to be independent predictors of offspring adiposity. Furthermore, obesity-induced metabolic disturbances such as increased inflammation (12) and dyslipidemia (13) have been independently associated with infant adiposity.

Identification of maternal and postnatal factors that determine offspring body composition is critical in order to aid in the design of successful prevention strategies as the prevalence of pre-pregnancy overweight and obesity is increasing (1). To overcome this gap in knowledge, we aimed to identify determinants of offspring adiposity during the first two years of life in children born to healthy mothers with non-complicated pregnancies. We further investigated the role of sex in offspring body composition as prior publications have demonstrated a sexual dimorphism in programming of obesity (6). We hypothesized that maternal adiposity, serum lipids, insulin resistance (estimated by HOMA-IR), gestational weight gain, and physical activity during gestation would be associated with offspring adiposity during the first two years of life in a sexual-dimorphic manner.

SUBJECTS AND METHODS

Participants

Participants were women and their offspring enrolled in a longitudinal cohort, the Growing Life, Optimizing Wellness study (GLOWING, NCT01131117) at the Arkansas Children's Nutrition Center. Women were enrolled either before pregnancy (N=37) or within the first

10 weeks of gestation (N=187). Inclusion criteria included: BMI of 18.5–35kg/m^2 at enrollment, second parity, singleton pregnancy, ≥21 years old, and conception without assisted fertility treatments. Exclusion criteria included preexisting or ongoing medical conditions including gestational diabetes, complications during pregnancies, use of medications during pregnancy known to influence fetal growth, smoking during pregnancy, alcohol consumption in any amount, and being a professional athlete. Infants born healthy and at term (≥37 weeks gestation) were eligible for postnatal visits. All study procedures were determined to be in compliance with the ethical research standards set by the Institutional Review Board of the University of Arkansas for Medical Sciences. Written consent was obtained and signed by the participants before any study procedures.

Body composition

Whole-body air displacement plethysmography (ADP) (BodPod, Cosmed, Concord, CA, USA) was used to determine maternal fat mass (FM, kg) at enrollment (pre-pregnancy or 4–10 weeks of gestation) under standard conditions. The van Raaij density model was used to determine body composition parameters in pregnant mothers to account for differences from the pre-gravid state (14). Infant body composition was assessed utilizing quantitative nuclear magnetic resonance (QMR, EchoMRI-AH small, Echo Medical System, Houston, TX) at 2 weeks, 1–9, 12, 18 and 24 months of age using mathematical adjustment as previously published (15). Briefly, the following adjustments were applied: if $QMR_{FM} \leq 5.0845$ kg, then adjusted $QMR_{FM} = 0.1160\ (QMR_{FM}\ (kg))^2 + 0.5690\ (QMR_{FM}\ (kg))$; if $QMR_{FM} > 5.0845$ kg, then adjusted $QMR_{FM} = 0.8962\ (QMR_{FM}\ (kg)) + 1.3337$.

Anthropometry

Anthropometric measures were obtained at each study visit using standardized methods. Maternal body weight was measured to the nearest 0.1 kg on a tared scale (Perspective Enterprises, Portage, MI, USA). Standing height was measured using a standard wall-mounted stadiometer to the nearest 0.1 cm (Tanita Corp., Tokyo, Japan) at enrollment.

Objectively assessed physical activity (PA)

Physical activity (PA) was assessed with accelerometry (Actical, Philips Respironics Co. Inc., Bend, Oregon, USA). The Actical was placed on the participant's ankle on the non-dominant side and worn continuously for up to 7 days. To be included in the analyses, each participant needed to record at least three valid days of accelerometer data. Total activity counts (AC) per day were summed over the valid wear period and then divided by the total number of valid days worn to derive average total AC per day. For mothers, data were collected at two time points per trimester and averaged to yield Gestational Activity Counts. In children, data were collected within a week of the 24mo visit. The use of the Actical to objectively assess PA in young children has been validated previously (16). We used the cut-point of 0.083 kcal/min/kg (6.0 metabolic equivalent) to evaluate vigorous activity counts.

Maternal serum cytokines, lipids and Homeostasis Model Assessment of Insulin Resistance (HOMA-IR)

Blood was drawn from the antecubital vein following an overnight fast at 4–10, 12, 24 and 36 weeks of gestation. Serum was processed and stored at −80°C until analysis. Serum glucose (mmol/L), Triglycerides (mg/dL), HDL (mg/dL) and LDL (mg/dL) levels were measured using an RX Daytona® (Randox laboratories–US limited, Kearneysville, West Virginia, USA) clinical analyzer. Serum insulin (mU/L), IL-6 (pg/ml) and leptin (pg/ml) levels were measured using electrochemiluminescence immunoassays (Meso Scale Discovery, Rockville, Maryland, USA). All samples were run in duplicate and averaged for use in subsequent analyses. Results from the 4–10 week and 12 week period were averaged to represent the first trimester. HOMA-IR was calculated from fasting glucose and insulin concentrations for the first trimester.

Resting Energy Expenditure (REE) and Respiratory Exchange Ratio (RER)

REE (kcal/d) and RER (VCO_2/VO_2) were derived from oxygen consumption and carbon dioxide production using indirect calorimetry in mothers during gestation after an overnight fast (Moxus, AEI technologies, IL). REE was calculated using the Abbreviated Weir equation: REE (kcal/d)=[(3.94*V02)+(1.11*VCO2)]. Participants were instructed not to exercise or consume caffeine for twelve hours before the measurement. After 10 minutes of absolute rest (adaptation period), respiratory exchanges were continuously measured for twenty more minutes. Heart rate was constantly monitored using a Polar telemetry system to monitor the participant's safety and evaluate the participant's steady state. A 10-minute steady state period was selected to evaluate REE and RER. Data were collected at 4–10, 12, 24 and 30 weeks of gestation. Values from 4–10 and 12 weeks gestation were average to yield the first trimester estimates in REE and RER. Values from 24 weeks of gestation were used as estimates of REE and RER for the second trimester and finally values from 30 weeks of gestation was used as estimates for REE and RER for the third trimester.

Dietary Intake

Dietary intakes were assessed using 3-day food records analyzed with the Nutrition Data System for Research software (Nutrition Coordinating Center; University of Minnesota, MN) following the interview guidelines from the Nutrition Coordinating Center. Participants were instructed to record all food, beverage, medication and supplement intake as they ate throughout the day for 2 week days and 1 week end day. Participants were provided with a booklet to evaluate size or volume of intake. Participants recorded the volume and size of intake for each component of their meal, including drinks, medications or solid foods on the food records. The records were reviewed by a trained nutritionist to clarify any information and query any additional intake that may have been missed. Three-day food records were collected at 4–10, 12 weeks of gestation and every 6 weeks thereafter. Nutrient intakes were averaged for each trimester and reported as kcal, %kcal or g per day. The Healthy Eating Index, which measure diet quality to assess how well intake aligns with key recommendations of the Dietary Guidelines for Americans, was computed according to the current guidelines (10,17). Sensitivity analyses were performed to evaluate results while

excluding women who under-reported energy intake using a validated cut-off of EI greater than 1.35*RMR (18).

Other Covariates

At enrollment, participants self-reported their race, age, date of last menstrual period and estimated delivery date. Delivery mode, infant's birth weight and infant's sex were self-reported by the participant at the 2 week postnatal visit. Gestational age at birth was calculated from the date of their last menstrual period or from the estimated due date obtained by early ultrasound if the date of their last menstrual period was unknown. Gestational weight gain (GWG) was calculated by subtracting the participant's weight at their first visit from their weight at their final prenatal visit (36 weeks of gestation). Breastfeeding duration of infants was determined based on 3-day food records of the child's intake completed by the mother at 2 weeks, 1–9, 12, 18 and 24 months of age. At each study visit, dietary records were reviewed with the mothers during which breastfeeding patterns were identified. Duration was calculated by subtracting the date breastfeeding was initiated (the infant's date of birth) from the date breastfeeding was stopped. Thus the length of breastfeeding may include mixed feeding patterns or inclusion of solid foods.

Statistical Analysis

Variables measured in the interval scale are summarized as means and standard deviations, whereas variables recorded in the ordinal or nominal scale are summarized as counts and percentages. The association between offspring's %FM during the first two years of life and each maternal/infant characteristic was assessed using regressions, whereas mixed models were used to model offspring %FM during the first two years of life and all characteristics simultaneously using a time-varying covariate approach when measures were available at each trimester (e.g. REE, cytokines). The most parsimonious model was constructed using least absolute shrinkage and selection operator (LASSO) linear regression. In light of the sexual dimorphism observed in animal models and clinical studies in response to maternal obesity (6,19) models were further build independently for male (N=128) and female (N=96). Data management and analysis was performed using the Stata version 14.2 statistical software (Stata Corp., College Station Texas) and R version 3.6.1, whereas the recursive partitioning was performed using JMP Pro version 13.0 statistical software (SAS Institute Inc., Cary, NC).

RESULTS

Between 2011 and 2014, 290 eligible women with a BMI between 18–35 kg/m^2 were enrolled in the GLOWING study at the Arkansas Children's Nutrition Center. Of the enrolled participants, 14 voluntarily withdrew from the study, 13 were lost to follow up, 6 did not get pregnant, 15 developed gestational diabetes and 11 suffered miscarriage or stillbirth. Seven babies were born prematurely. In total, 224 mother and child pairs were included in the current study, of which 37 were recruited prior to pregnancy. A total of 102 participants included in the study were classified as normal weight, 81 were overweight and 41 were classified as obese. Thirty participants have partial offspring %FM data between the ages of 2 weeks and 24 months as they were lost to follow up or withdrew from the study

during that time frame. Phenotypic results of mother and infant pairs that were used in subsequent linear regression analyses are listed in Table 1 and Supplemental Table S1. Infant fat mass measures obtained from QMR are presented in Supplemental Table S2.

Maternal gestational serum HDL and LDL (β=0.049, p<0.0001 and β=0.013, P=0.0009, respectively) were significantly, independently and positively associated with offspring %FM (Table 2). Male sex had a significant negative independent association with child %FM (β=−1.206, p=0.0136), whereas infant birth weight (β=1.304, p=0.0083) and length of breastfeeding (β=0.004, p=0.0013) were positively and independently associated with child adiposity during the first two years of life.

The best fitted model revealed that only maternal %FM (β=0.08, p=0.022), maternal gestational HDL (β=0.05, p=<0.001), birth weight (β=1.27, p=0.016), offspring sex (β=−1.40, p=0.004) and breastfeeding duration (β=0.004, p=0.001) were determinants of offspring adiposity during the first 2 years of life (Table 3).

Given the sexual dimorphism findings in our previous study (6), the analysis was then stratified by child sex. For girls, maternal %FM (β=0.12, p=0.006), maternal HDL (β=0.07, p<0.001), maternal intake of dietary fiber during pregnancy (β=−0.09, p=0.016), and length of breastfeeding (β=0.004, p=0.023) were positively associated with female adiposity during the first two years of life (Table 4). Graphs representing the estimated marginal means of female fat mass (%) for each significant variables in the final models are presented in Supplemental Figures 1 and 2. Of note, maternal fat mass effect on offspring body composition in male is reversed compared to the female. In girls, maternal fat mass effect is significant at age 2 weeks and throughout the first 2 years of life which suggest that differences are set during gestation. Sensitivity analyses conducted on women who reported energy intake at a physiological level (Energy intake/resting energy expenditure >1.35 (18), n=98) found a similar negative association of offspring FM and maternal intake of dietary fiber for the entire cohort (β=−0.07, p=0.046). For boys, birth weight (β=1.95, p=0.004), maternal serum HDL (β=0.04, p=0.013) and breastfeeding duration (β=0.004, p=0.015) were positively associated with male adiposity during the first 2 years of life (Table 5). Sensitivity analyses investigating fat mass index rather than percent fat mass on both maternal and offspring compartments found similar results suggesting a role of maternal HDL and dietary fiber intake as well as birth weight on offspring fat mass index during the first two years of life.

DISCUSSION

In the current study, maternal adiposity, maternal serum HDL, infant birth weight, sex, and breastfeeding duration were identified as independent predictors of offspring adiposity during the first two years of life. When stratified by sex, maternal %FM was the strongest predictor of adiposity in female offspring while birthweight was the strongest predictor in male offspring. In both sexes, maternal HDL and breastfeeding duration were associated with greater adiposity during the first 2 years of life. Interestingly, maternal dietary fiber intake was negatively associated with female offspring adiposity.

Previous publications have pointed out that maternal total cholesterol is critical for neonatal development and birth weight outcomes (26). While others have shown an association between maternal LDL (13,27) or HDL (13,28,29) and infant birthweight, limited studies have investigated the association between maternal HDL and LDL and offspring body composition. Studies have found no association between maternal LDL or HDL levels during pregnancy and offspring adiposity using sum of skinfolds at birth (29), 6 months or 2 years of age (13). However, skinfold measurements are a crude measure of adiposity and are poorly correlated to body fat mass in children (30). In the presented cohort, a positive association was found between maternal serum HDL and offspring adiposity during the first two years. Further studies are needed to elucidate how maternal HDL contributes to metabolic programming and fat accretion in offspring.

A novel finding of this study is that maternal dietary fiber intake during gestation is negatively associated with female offspring adiposity. Very few studies have specifically looked at dietary fiber intake and its contribution to offspring whole body adiposity and none have evaluated its effect in a sexual dimorphic manner. In agreement with our findings, a study by Hallam et al. found that female offspring of rats exposed to a high fiber diet *in utero* had lower birthweight and body fat at 22 weeks of age (adolescence equivalent in humans) and lower levels of hepatic triacylglycerol indicating an effect on hepatic lipid storage (33). Other research has found positive associations with maternal diet quality determined by the Healthy Eating Index (HEI) during pregnancy and neonatal adiposity 72 hours after birth (34) and an inverse association between a higher quality diet during pregnancy and 3 months postpartum and infant body fat (%) at 6 months of age (35). However, we did not find any significant effect of maternal HEI on offspring adiposity during the first 2 years of life. It is possible that maternal diet quality has the largest effect on fetal and early postnatal growth. Further research is sorely needed to delineate the mechanisms that mediate the interaction between maternal obesity and diet intake during different gestational periods and offspring adiposity risk later in life. Our attempt to account for under reporter in sensitivity analyses using a cut off of 1.35*BMR strengthen our findings. However, this cut-off is not intended for pregnant participants and therefore, results should be cautiously interpreted.

In the current study, we found a positive relationship between breastfeeding duration and child adiposity during the first two years of life in both sexes. While exclusively breastfeeding is known to elicit a protective effect against obesity later in life (37), this study agrees with findings by Sauder et al. demonstrating exclusively breastfed babies had increased FM at 5 months of age (9).

Past research has identified a sexual dimorphism between maternal weight status during pregnancy and infant body composition with boys having less FM or body weight than girls as maternal BMI increases (6,9). Interestingly, in the presented results, maternal %FM was only a significant predictor of adiposity during the first two years of life in female offspring suggesting maternal obesity possibly elicits differential developmental effects on fat accretion by sex. Similar results were found by Henriksson et al. that found a positive association between maternal %FM (measured by ADP) at 32 weeks of gestation and %FM of 1 week old infant girls but not boys (39).

Our lack of association between GWG and offspring adiposity are not in agreement with numerous studies linking GWG to offspring body composition outcomes. This can partially be explained by the GLOWING study design which included a behavioral intervention in order to prevent excessive GWG (42). The intervention was successful in mitigating excessive GWG and therefore reducing the range of GWG in normal weight and class 1 obese GLOWING participants which may explain the lack of association between GWG and offspring adiposity during the first two years of life. Offspring PA at 2 years tended to be negatively correlated with their adiposity (P=0.08). This is in agreement with a study by Collings et al. that showed an inverse association between PA and adiposity in children 11 months to 5 years of age (43). These findings emphasizes the importance of PA beginning in early childhood to possibly reverse or mitigate adverse adiposity accrual that occurs in early infancy.

Our study is strengthened by its prospective longitudinal design with detailed phenotypic data of mothers during pregnancy as well as longitudinal measurements of offspring FM using a single methodology. The enrollment of second parity mothers lessen variation in the cohort due to differences in birthweight between parities (44). This study accounted for gestational PA, dietary intake and metabolic rate (REE) that may influence offspring FM accrual. Our study is not without limitations. Only ~87% of participants were able to complete all study visits at 2 years of age resulting in a small reduction in sample size. The BMI range of 18.5–35 kg/m^2 prohibits the generalization of the findings to class II and III obesity. The generalizability of the findings is also limited by two additional factors: 1) the majority of participants were Caucasian (87.1%) from the Central Arkansas region (although the racial distribution reflected the demographics of families living in the four predominant counties [Pulaski, Saline, Faulkner, Lonoke] in Central Arkansas) and 2) recruitment focused on healthy women only.

In conclusion, offspring adiposity during the first two years of life is influenced by maternal adiposity, maternal serum HDL, duration of breastfeeding and infant sex with maternal adiposity being the strongest determinant of adiposity in female offspring and birth weight being the strongest predictor of adiposity in males. Given the complexity of early life influences on infant body composition, continued longitudinal assessment of adiposity into adolescence and adulthood is needed to determine the impact of maternal adiposity on child obesity risk. Development of intervention strategies aiming at reducing maternal adiposity prior to conception may provide protection against obesity later in life by reducing the influences of maternal adiposity on offspring metabolism.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

AC	activity counts
ADP	air displacement plethysmography
BMI	body mass index
FM	fat mass
FMI	fat mass index
GWG	gestational weight gain
HDL	high density lipoprotein cholesterol
HOMA-IR	homeostatic model assessment-insulin resistance
IL-6	interleukin 6
LDL	low density lipoprotein cholesterol
PA	physical activity
QMR	quantitative magnetic resonance
REE	resting energy expenditure
RER	respiratory exchange ratio

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Study Importance Questions

What is already known about this subject?

- Previous research has shown a strong relationship between maternal body mass index (BMI) and risk of obesity development in the offspring.
- Maternal obesity influences offspring body composition in a sexual dimorphic manner.
- Obesity-induced metabolic and inflammatory factors as well as maternal diet and physical activity have been independently associated with offspring body composition.

What does your study add?

- The study identifies maternal first-trimester fat mass and serum high density lipoprotein cholesterol, infant sex, and breastfeeding duration as significant determinants of offspring adiposity from birth to age 2 years.
- Maternal first-trimester adiposity and dietary fiber intake during pregnancy is associated with adiposity only in girls during the first two years of life.
- Early-life adiposity in boys is associated with their birth weight but not determined by maternal fat mass.

How might your results change the direction of research or the focus of clinical practice?

- Results from this study suggests further research is needed to understand how maternal HDL impacts offspring body composition and metabolism later in life.
- New research that investigates the relationship between maternal dietary fiber intake and offspring body composition outcomes is warranted.
- These results provide possible windows of opportunity to mitigate obesity in offspring through the development of intervention strategies aimed at reducing maternal cholesterol and adiposity and improving maternal diet prior to or during pregnancy.

Table 1.

Maternal and child characteristics

		N=224
Maternal Variables		
Race		
Caucasian		195 (87.1%)
Non-Caucasian		29 (12.9%)
Delivery method		
Vaginal induced		65 (29.0%)
C-section		78 (34.8%)
Vaginal		81 (36.2%)
Age at Delivery (years)		30.2 (3.6)
Weight before gestation week 10 (kg), (n=37)		66.8 (9.2)
Fat Mass (% Fat) *		35.7 (7.4)
Fat Mass Index (fat mass (kg)/height $(m)^2$)		9.6 (3.4)
RER (gestation)		0.85 (0.04)
REE (kcal/d, gestation)		1528.7 (184.5)
Gestational Weight Gain (kg)		11.9 (4.2)
Gestational Weight Gain (g/week)		0.43 (0.17)
Gestational Age (weeks)		39.2 (0.9)
Physical Activity Counts (avg/day, x1000) (gestation)		309.1 (89.8)
Serum (gestation)		
HOMA-IR *		1.7 (0.9)
Leptin (pg/L)		26.5 (22.4)
IL-6 (pg/ml)		0.42 (0.35)
Triglycerides (mg/dL)		136.9 (66.3)
HDL (mg/dL)		63 (15.6)
LDL (mg/dL)		95 (44)
Dietary Intake (gestation)		
Energy (kcal/day)		1947 (447.8)
Fat (% kcal/day)		35.6 (4.9)
Carbohydrate (% kcal/day)		50.5 (5.9)
Protein (% kcal/day)		15.5 (2.8)
Dietary Fiber (g/day)		17.5 (5.9)
Added Sugar (g/day)		62.9 (31.5)
Healthy Eating Index		48.6 (8.2)
Offspring Variables		
	Males	**Females**
N	128 (57.1%)	96 (42.9%)
Birth Weight (kg)	3.6 (0.5)	3.4 (0.5)
Birth Length (cm)	51.5 (2.6)	50.5 (2.6)
Breastfeeding Duration (days)	244.7 (222.6)	241.5 (212.7)

		N=224
Physical Activity at 2 years of age		
Total Activity Counts (avg/day, x1000)	497.9 (117.8)	436.7 (110.9)
Sedentary Activity Counts (avg/day, x1000)	4.9 (7.6)	4.7 (7.5)
Vigorous Activity Counts (avg/day, x1000)	14.0 (23.5)	14.6 (62.8)

Data is presented as mean (SD), counts or %. RER, respiratory exchange ratio; REE, resting energy expenditure; HOMA-IR, homeostatic model assessment-insulin resistance; IL-6, interleukin 6; HDL, high density lipoprotein cholesterol; LDL, low density lipoprotein cholesterol.

* Designates variables accounted for in the first trimester only.

Table 2.

Association between each characteristic and offspring fat mass (%) between 0.5 and 24 months of age (N=224)

Maternal Variables	*β*	95% CI	*p*-value
Race			
Caucasian	Reference		
Non-Caucasian	0.003	−1.452, 1.457	0.9971
Delivery method			
Vaginal induced	Reference		
C-section	−0.216	−1.421, 0.989	0.7253
Vaginal	0.321	−0.876, 1.518	0.599
Age at Delivery (years)	−0.03	−0.165, 0.105	0.6657
Fat Mass (% Fat) *	0.063	−0.002, 0.127	0.0591
RER (gestation)	−2.006	−6.392, 2.380	0.3700
REE (kcal/d, gestation)	0.0010	−0.0004, 0.0024	0.1622
Gestational Weight Gain (kg)	0.05	−0.066, 0.166	0.3958
Gestational Age (weeks)	0.347	−0.179, 0.872	0.1961
Physical Activity Counts (avg/day, x1000) (gestation)	0.003	−0.003, 0.008	0.3161
Serum (gestation)			
HOMA-IR *	0.314	−0.274, 0.902	0.2957
IL-6 (pg/ml)	−0.078	−0.841, 0.686	0.8417
Leptin (pg/ml)	0.002	−0.013, 0.017	0.8189
Triglycerides (mg/dL)	0.003	−0.003, 0.008	0.2871
HDL (mg/dL)	0.049	0.027, 0.071	<0.0001
LDL (mg/dL)	0.013	0.005, 0.021	0.0009
Dietary Intake (gestation)			
Energy (kcal/day)	−0.0003	−0.0009, 0.0004	0.4185
Total Fat (%kcal/day)	0.071	−0.052, 0.194	0.2602
Total Carbohydrate (%kcal/day)	−0.076	−0.176, 0.024	0.1341
Total Protein (%kcal/day)	0.115	−0.092, 0.322	0.2775
Total Dietary Fiber (g/day)	−0.031	−0.082, 0.019	0.2234
Added Sugars (by Total Sugars) (g/day)	0.002	−0.009, 0.014	0.6799
Healthy Eating Index	0.011	−0.024, 0.045	0.5426
Offspring Variables			
Sex			
Female	Reference		
Male	−1.206	−2.164, −0.248	0.0136
Birth Weight (kg)	1.304	0.336, 2.271	0.0083
Birth Length (cm)	0.129	−0.055, 0.314	0.1696
Breastfeeding Duration (days)	0.004	0.001, 0.006	0.0013
Physical Activity at 2 years of age			
Total Activity Counts at 24mo (x1000)	−0.004	−0.009, 0.000	0.0806

Maternal Variables	β	95% CI	p-value
Sedentary Activity Counts at 24mo (x1000)	0.214	−0.504, 0.931	0.5598
Vigorous Activity Counts at 24mo (x1000)	−0.0002	−0.0125, 0.0121	0.9758

RER, respiratory exchange ratio; REE, resting energy expenditure; HOMA-IR, homeostatic model assessment-insulin resistance; IL-6, interleukin 6; HDL, high density lipoprotein cholesterol; LDL, low density lipoprotein cholesterol.

* Designates variables accounted for in the first trimester only.

Table 3.

Best subset selection model for predicting childhood fat mass during the first two years of life for the entire cohort (N=224)

Variable	*β*	95% CI	*p*-value
Maternal Fat Mass (%Fat) (first trimester)	0.08	0.01, 0.14	0.022
Maternal HDL(mg/dl) (gestation)	0.05	0.03, 0.07	<0.001
Sex			
Female	Reference		
Male	−1.40	−2.35, −0.45	0.004
Birth Weight (kg)	1.27	0.24, 2.30	0.016
Breastfeeding Duration (days)	0.004	0.001, 0.006	0.001

CI, confidence interval; HDL, high density lipoprotein cholesterol

Table 4.

Best subset selection method for predicting female fat mass during the first two years of life (N=96)

Variable	*β*	95% CI	*p-value*
Maternal Fat Mass (%Fat) (first trimester)	0.12	0.03, 0.21	0.006
Maternal HDL (mg/dl) (gestation)	0.07	0.04, 0.10	<0.001
Average Total Dietary Fiber (g/day)	−0.09	−0.16, −0.01	0.016
Breastfeeding Duration (days)	0.004	−0.001, 0.007	0.023

CI, confidence interval; HDL, high density lipoprotein cholesterol

Table 5.

Best subset selection method for predicting male fat mass during the first two years of life (n=126)

Variable	*β*	95% CI	*p*-value
Maternal HDL (mg/dl) (gestation)	0.04	0.01, 0.06	0.013
Birth weight (kg)	1.95	0.63, 3.26	0.004
Breastfeeding Duration (days)	0.004	0.001, 0.007	0.015

CI, confidence interval; HDL, high density lipoprotein cholesterol