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Parental adiposity differentially associates with newborn body composition

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Abstract

Background: Maternal obesity increases offspring's obesity risk. However, studies have not often considered maternal metabolic and exercise patterns as well as paternal adiposity as potential covariates.

Objective: To assess the relationship between parental and newborn adiposity.

Methods: Participants were mother-child pairs (n=209) and mother-father-offspring triads (n=136). Parental (during gestation) and offspring (2 weeks old) percent fat mass (FM) were obtained using air displacement plethysmography. Maternal race, age, resting energy expenditure (indirect calorimetry), physical activity (accelerometry), gestational weight gain (GWG), gestational age (GA), delivery mode, infant's sex, and infant feeding method were incorporated in multiple linear regression analyses. The association between parental FM and offspring insulin-like growth factor 1 (IGF-1) was assessed at age 2 years.

Results: Maternal adiposity was positively-associated with male (β=0.11, p=0.015) and female (β=0.13, p=0.008) infant FM; whereas, paternal adiposity was negatively-associated with male newborn adiposity (β=−0.09, p=0.014). Breastfeeding, female sex, GA, and GWG positively associated with newborn adiposity. Vaginal and C-section delivery methods associated with greater

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adiposity than vaginal induced delivery method. Plasma IGF-1 of 2 year-old boys and girls positively associated with their respective fathers' and mothers' FM.

Conclusions: Maternal and paternal adiposity differentially associate with newborn adiposity. The mechanisms of this finding remains to be determined.

Keywords

body composition; pregnancy; obesity; fetal programming; growth hormone

Introduction

The environment within which fertilization and embryo development occurs has been linked to offspring outcomes. Undeniably, the experiences of the developing embryo/fetus are primarily those of the mother; therefore, it is maternal contributions to programming of offspring health that have captivated research efforts. In the United States where ~50% of babies are being born to women with either overweight or obesity (1,2), a clear link has been established between maternal obesity at conception and offspring's obesity and cardiometabolic risks across the lifespan (3–7). In recent years, however, studies have pointed out that paternal obesity is also contributing to the programming of offspring phenotype, but the results from some of these studies are conflicting (8–10).

In human and animal models, sex-dependent, positive, and even negative associations have been reported between paternal obesity and offspring weight and/or adiposity (8,9,11). For instance, Chen et al.(8), reported that fetal growth is positively associated with paternal BMI in male, but not female babies, while another study found that obesity in fathers increases the risk of intrauterine growth restriction, a known risk factor for cardiovascular disease later in life (11). Murine models of paternal obesity also show different results, with studies reporting that offspring weight and/or adiposity are either unaffected or decreased by paternal obesity (2,10). In the latter case, programming of the growth hormone (GH) insulin-like growth factor (IGF) axis has been proposed as a potential mechanism (2).

Current research evaluating the contribution of parental obesity to offspring phenotype in humans has strong limitations. First, studies in this area have systematically excluded fathers thereby underestimating the role of paternal obesity in the programming of offspring phenotype. Second, these studies are cross-sectional in design and/or rely on BMI as the only indicator of adiposity. Although BMI is a commonly accepted proxy of adiposity, it does not provide information on the relative contribution of individual body compartments to total weight thus wide variations in adiposity can be seen in people with similar BMI (12,13).

The objective of this longitudinal study was to quantify the contribution of parental adiposity, measured in the first trimester of pregnancy using whole-body air displacement plethysmography (ADP), to newborn adiposity at age 2 weeks while accounting for the effect of other variables that may influence offspring phenotype. We hypothesized that newborn adiposity would increase with increasing parental adiposity, but that the influence of maternal adiposity on offspring percent fat mass (%FM) would be stronger than that of

paternal adiposity. To investigate the potential mechanisms underlying the sexual dimorphism observed in the results, we evaluated the associations between parental adiposity and circulating GH, IGF-1 and IGF binding protein (BP)-3 levels in the offspring.

Methods

Subjects

Women were enrolled in the Growing Life, Optimizing Wellness study (GLOWING, NCT01131117) at the Arkansas Children's Nutrition Center between 2011 and 2014 by inviting pregnant or soon to be pregnant women to join the study. The GLOWING study is an ongoing observational study evaluating the impact of maternal health prior and during pregnancy on offspring growth and obesity risk. Participants responded to study advertisements which were distributed in the form of flyers in various locations of Central Arkansas (physician's office, health fairs, daycare centers, etc.) print ads, social media, as well as television and radio advertisement.

Inclusion criteria for the study were: normal weight (BMI 18.5–25 kg/m^2), overweight (BMI 25–30 kg/m^2) and class I obesity (BMI 30–35 kg/m^2) at enrollment, second parity (because of birth weights differences between parities (14)), singleton pregnancy, ≥21 years old, and conception without assisted fertility treatments. Exclusion criteria were: maternal preexisting or ongoing medical conditions including gestational diabetes (because of its association with excessive fetal growth which would constitute a strong confounder for the hypothesis (15)), complications during pregnancy, medications during pregnancy known to influence fetal growth, maternal active smoking, alcohol consumption in any amount, and being an athlete. Only children born healthy and at term (≥37 weeks gestation) were eligible for the postnatal portion of the study.

Participants were enrolled either before pregnancy (n=24) or within the first 10 weeks of gestation (8.4±1.5 (SD) weeks, n=185). Thirteen participants were lost to follow-up, 14 withdrew from study participation, and 6 were excluded because they were not pregnant. Ten participants suffered miscarriage, and 15 developed gestational diabetes. Seven infants were born premature and one was stillborn which disqualified them for follow-up. There were 14 families who were unable to attend the two-week visit or were not able to complete the body composition portion of the study visit at the two-week visit. Data for 209 mother-offspring pairs were collected. Fathers were also invited to take part in the study after the mother was enrolled; however, in some cases they refused to participate, mothers were single, or had a different partner at home. A total of 136 fathers completed one research study visit during which body composition, medical history and food intake were assessed and 73 (30%) declined to participate. The study was approved by the Institutional Review Board at the University of Arkansas for Medical Sciences, and all participants gave written informed consent. Participants were compensated based on the number of study visits completed.

Measures

Body composition: Fat mass (FM, kg), fat free mass (FFM, kg), and total body mass (kg) were assessed under standard conditions using whole-body air displacement plethysmography (BodPod© and PeaPod©, Cosmed, Concord, CA, USA). Mothers were evaluated at enrollment (BodPod©), fathers during their study visit (BodPod©), and infants at two weeks of age (PeaPod©, 14.3 ± 1.8 days). Percent fat mass (%FM) was calculated as follows: [FM (kg)/body mass (kg) × 100%].

Anthropometry: Maternal body weight was measured at enrollment, 12 weeks, and every 6 weeks thereafter. Gestational weight gain was computed from the first measured weight to week 36. Weights were measured at the research facility. Adherence to the Institute of Medicine (IOM) gestational weight gain guidelines was evaluated by adjusting the guidelines to reflect the last measure at gestation week 36 (16). Paternal weight was measured at their visit. Weight measures were obtained to the nearest 0.1 kg on a tared scale while wearing a hospital gown only (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. Infant weight was measured to the nearest 0.01 kg using tared scale (SECA 727, SECA, Ontario, CA) and length was measured to the nearest 0.1 cm by using a length board (Easy Glide Bearing Infantometer, Perspective Enterprises, Portage, MI).

Maternal Resting Energy Expenditure (REE): Resting energy expenditure was measured following an overnight fast using a metabolic cart (Moxus, AEI technologies, IL). Participants were instructed not to exercise or consume caffeine for twelve hours prior to the measurement. After 10 minutes of absolute rest (adaptation period), a 10-minute steady state period was selected to evaluate resting energy expenditure (REE) and respiratory exchange ratio (RER). Resting energy expenditure was adjusted for FFM using a log-log regression models as previously described (18).

Demographic characteristics: Participants self-reported their race, age, education, income, date of last menstrual period and estimated delivery date at enrollment. Participants reported their delivery mode (vaginal, vaginal induced, C-section), infant's birth weight and infant's sex at the post-natal two-week visit. Infant feeding details were obtained using food records and were classified into either exclusive breastfeeding, formula or mixed feeding.

Physical activity: Physical activity was assessed with Actical accelerometer (Philips Respironics Co. Inc., Bend, Oregon, USA) at the time of enrollment. The monitor was placed on the participant's ankle on the non-dominant side and programmed to record movement activity beginning at 11:59 PM on a given day. To be included in the analyses, each participant needed to record at least three valid days with at least one weekend day of accelerometer data (device was worn continuously through the day and night). 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.

Offspring GH, IGF-1 and IGFBP-3 levels measurements: Per study design, blood was not drawn at age 2 weeks. However, fasting plasma from 67 offspring (37 boys and 30 girls who had maternal and paternal adiposity data) was available at age 2 years in which GH, IGF-1 and IGFBP-3 levels were measured using ELISA (Invitrogen, California, USA).

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 chi-square test was used to test the frequencies of variables in the ordinal or nominal scales. Maternal associations with offspring %FM were first evaluated using the entire cohort (n=209). Then, a secondary analysis was conducted in the subset of participants (n=136) for whom maternal-father-offspring data were available.

The association between infant's %FM at two weeks of age and parental/infant characteristic was assessed using linear regression, whereas multiple linear regression was used to model infant's %FM at two weeks of age and all characteristics simultaneously. The most parsimonious linear regression model was constructed using least absolute shrinkage and selection operator (LASSO) linear regression, although the same model resulted using step-wise linear regression. Data management and analysis was performed using the Stata version 14.2 statistical software (Stata Corp., College Station Texas).

Results

Subject characteristics (Table 1)

Participant characteristics (n=209) are described in Table 1. Women, were in average 30 years old, predominantly Caucasian (85%) with only 32 participants of other races (6 Hispanics, 20 African Americans, 3 Asians, 1 mixed race and 2 unknown), and 35% of them exceeded the IOM recommendations for gestational weight gain (GWG). Their average %FM was 35.7% (range 17.6%–52.1%), and the average BMI was 26 kg/m^2, with 45% of mothers having normal weight, 36% overweight, and 19% obesity. All infants were born full-term (≥37 weeks gestation) per study design with 70% percent of them exclusively breastfeeding for the first two weeks of life. Anthropometric z-scores at birth and at age 2 weeks were comparable between newborn girls and boys. As expected, infant %FM was higher in girls vs. boys (13.6±3.6 % vs. 12.5±3.4 %, p=0.0295). The characteristics of mother-offspring pairs lost due to lack of paternal data (n=73) were comparable to those of the 136 mother-offspring pairs (data not shown). Fathers (n=136, Table 4), were in average 31 years old, and 88% of them were Caucasian. Their average %FM was ~29% (range: 4.1% – 49.7%), and the average BMI was ~29 kg/m^2, with 28% having normal weight, 40% overweight, and 32% obesity. Twelve of them (9%) suffered high blood pressure, and 3 had type 2 diabetes mellitus. Both maternal and paternal blood pressure as well as HOMA-IR results are provided in supplemental table 1. There was no effect of maternal or paternal blood pressure or HOMA-IR on infant adiposity and therefore further analyses were not adjusted for blood pressure or HOMA-IR.

Regression analysis (mother-offspring pairs, n=209)

Boys and girls together—Bivariate linear regression analyses between selected maternal/infant characteristics and infant %FM (n=209) at two weeks of age are summarized in Table 2. When considering all newborns together, maternal %FM, vaginal delivery, delivery by cesarean section, exclusive breastfeeding, and newborn female sex were positively associated with infant %FM at two weeks of age. These associations persisted in multiple regression analysis (Table 3) in which maternal race was also retained as an independent predictive variable of offspring adiposity at age 2 weeks.

Maternal %FM (Table 3), was the strongest predictive variable of newborn %FM (β=0.14, $p<0.001$) and accounted for 8% of observed variance. Maternal race, gestational weight gain and vaginal delivery method each accounted for ~3% of the variance observed in offspring %FM. Children born to non-Caucasian women had in average 1.6% more fat mass than children born to Caucasian women ($p=0.014$). Interestingly, children born via vaginal not-induced delivery method had 1.5% more fat than children born via vaginal induced delivery method ($p=0.010$). Similarly, cesarean-section was positively associated with offspring %FM and explained 2% of the observed variance ($p=0.048$). Percent FM of exclusively breast-fed infants was 1.2% higher than that of formula or mixed-fed infants ($p=0.023$). Offspring sex accounted for 2% of the observed variance with girls having in average 1% more fat than boys ($p=0.041$).

Boys and girls separately—When considering female (n=94) and male (n=115) newborns separately (Table 2), bivariate associations between maternal %FM with girls' %FM (β=0.09, $p=0.044$) and boys' %FM (β=0.10, $p=0.027$) were positive and of similar magnitude. Delivery and feeding methods were associated with girl's %FM only. Percent FM of girls born vaginally was in average ~2% higher than that of girls whose birth had also been vaginal but induced. Exclusive breastfeeding was marginally associated (β=1.51, $p=0.054$) with girl's %FM. Maternal race was associated with boy's %FM only with newborns of non-Caucasian mothers having in average 1.9% more fat than boys born to Caucasian women.

These associations remained in multiple regression analysis (Table 3). Maternal %FM was the strongest predictive variable of girls' and boys' %FM at 2 weeks of age explaining 7% and 5% of the observed variance respectively (Table 3). Delivery mode for girls, and maternal race and gestational age for boys were the next strongest predictive variables.

Regression analysis for mother-father-offspring trios (n=136)

Boys and girls together (Table 4)—When the best fitted model was created, maternal %FM was the strongest predictive variable of offspring %FM accounting for 4% of the observed variance. In agreement with Table 3 (n=209), gestational age, gestational weight gain, female sex and maternal race were all positively and independently associated with offspring %FM. Paternal %FM was not retained as a predictive variable of offspring %FM at age 2 weeks.

Boys and girls separately (Table 4)—When the multiple regression analysis was stratified by sex [boys (n=77) and girls (n=59)], paternal %FM and maternal %FM had independent and opposite effects on male newborn %FM. Male offspring %FM decreased by 0.09% for every 1% increase in paternal %FM (p=0.014). Paternal %FM explained 8% of the observed variance in male offspring %FM. In contrast, maternal %FM was positively associated with boy's %FM and explained 12% of the observed variance. There was a significant loss of power in the female newborn group (sample sized decreased from 94 to 59 girls) which did not allow to accurately evaluate the association between mothers' and father's adiposity with female offspring adiposity.

Association between parental %FM and offspring GH, IGF-1, and IGFBP-3 levels at age 2 years

Growth Hormone—When GH levels of boys and girls were analyzed together, paternal adiposity at conception (β=−0.04, p=0.007), but not maternal adiposity (β=0.01, p=0.459), was associated with GH levels in 2 year old offspring. When analyses were stratified by offspring sex (Table 5), GH levels in male (β=−0.04, p=0.023) and female offspring (β=−0.08, p=0.008) decreased with increasing paternal %FM. On the other hand, increasing maternal adiposity resulted in greater GH levels exclusively in female offspring (β=0.06, p=0.017).

Insulin-like growth factor 1 (IGF-1)—When the overall group was analyzed, paternal adiposity (β=1.25, p=0.009), but not maternal adiposity, was associated with IGF-1 levels. When stratified by sex, IGF-1 levels in girls, were exclusively associated with maternal %FM (β=1.53, p=0.023).This association remained marginally significant (β=1.42, p=0.051) when paternal adiposity was included in the same model (Table 5). On the other hand, IGF-1 levels in boys associated with paternal %FM (β=1.24, p=0.008) but not maternal adiposity. The association between male offspring IGF-1 and paternal %FM remained when maternal adiposity was added to the model (β=1.23, p=0.011; Table 5).

Insulin-like growth factor binding protein 3 (IGFBP-3)—When the overall group was analyzed, plasma IGFBP-3 levels associated with paternal adiposity (β=0.025, p=0.046) but not with maternal adiposity (β=0.012, p=0.251). The former association lost significance when both maternal and paternal %FM were included in the same model (Table 5). When stratified by sex, paternal adiposity associated with neither girls' nor boys' IGFBP-3 plasma levels whereas maternal adiposity associated with girls' but not boys' IGFBP-3 plasma levels. The association between maternal adiposity and girls' IGFBP-3 levels disappeared when paternal adiposity was added to the model (Table 5).

Plasma analyses (growth hormone, IGF-1, IGFBP-3, glucose, insulin, leptin, cholesterol, triglycerides, HDL and LDL) for n=67 children at age 2 years have been summarized in supplementary table 2.

Discussion

The primary aim of this study was to quantify the contribution of parental adiposity to newborn %FM at age 2 weeks. Mother's %FM was measured early in pregnancy therefore

our measurements should closely reflect adiposity at the time of conception. We hypothesized that newborn adiposity would increase in proportion to parental %FM, but that the contribution of maternal adiposity to newborn adiposity would be greater than that of fathers'.

Our results showed that maternal adiposity positively associates with offspring %FM at age 2 weeks, and the magnitude of the association is slightly higher in girls than in boys when other predictive variables were considered. Paternal adiposity associated with that of males, with %FM in newborn boys decreasing with greater paternal %FM at conception. Maternal race, GWG, newborn's sex, gestational age, delivery mode, and infant feeding mode were also independent predictors of newborn adiposity at age 2 weeks.

Novel to our study are the prospective, objectively measured data including physical activity, resting energy expenditure and direct measurements of body composition in both parents and their offspring. All the latter are frequently missing from studies investigating the association between maternal obesity and newborn body composition. We have previously demonstrated a dissociation between BMI-for-age Z-scores and true measurements of adiposity (dual-energy X-ray absorptiometry, DXA) from early infancy to mid-childhood (20). Thus, using direct methods of body composition are of utmost importance when childhood adiposity is the primary outcome of study.

There is evidence supporting that offspring weight and BMI at birth increase in proportion to maternal obesity (21,22). However, studies evaluating the effect of maternal BMI on offspring adiposity *per se* have not always agreed. For instance, Eriksson et al. (23) did not find pre-pregnancy maternal BMI to affect newborn adiposity measured with ADP. In contrast, several other studies also using combined (direct and indirect) measurements of adiposity in mothers and their offspring have shown opposite results (24–27). Here, using laboratory-based body composition analysis techniques in newborn offspring and parents we provide conclusive evidence of maternal adiposity as a main contributor to newborn offspring %FM.

A novel finding from our study was that paternal adiposity had a negative and sex-dependent association with male newborn %FM. There is scarcity of longitudinal studies in humans evaluating the effects of paternal adiposity on intrauterine growth and newborn body composition. Case-control studies have shown that lower birthweight and intrauterine growth restriction are more likely to occur in offspring of men with higher abdominal obesity and insulin resistance, but no sex-specific correlations were reported (11,28–30). More recently, contrasting results were reported by Chen el al. (8) who found intrauterine growth and birthweight positively correlate with paternal BMI in boys but not in girls.

The observation of sex-dependent associations between paternal health and offspring outcomes were first seen in epidemiological studies. Kaati et al. (31) found that boys exposed to high food availability (an indicator of overfeeding) at 9 to 12 years of age had increased cardiovascular disease and type-2 diabetes mortality risks in male descendants. Since then, murine models have shown that paternal nutritional experiences and obesity status can exert transgenerational and sex-specific effects on offspring health (10,32,33).

However, when it comes to the primary outcome of the present study (newborn adiposity) insufficient and contrasting data exist in the literature which do not allow to clearly elucidate the effect of paternal obesity on newborn phenotype.

In a rat model of diet induced paternal obesity and insulin resistance, for example, birthweight did not differ between exposed and control male and female offspring (10). The study, led by Ng et al.(10), focused on females and found paternal obesity to induce sustained pancreatic β-cell dysfunction in the offspring without altering growth or adiposity. More recently, and using a similar murine model, Lecomte et al. (2) reported birthweight and growth trajectories of male offspring are dramatically affected by paternal obesity, with lower birthweight, stunted growth, and decreased adiposity occurring in association with low levels of GH and IGF1 factor (2).

Similarly to the aforementioned study, we found that independent of maternal adiposity, fat accretion in male newborns decreased with increasing paternal %FM. A limitation of our study, though, is that we did not collect blood from offspring at 2 weeks of age thus evaluation of the GH axis was not done at this timepoint. However, using plasma from 67 children of this same cohort at age 2 years, we found that IGF-1 levels of boys and girls positively associated with their respective fathers' and mothers' adiposity. Our findings at age 2 years, however, should not be extrapolated to the neonatal period. Larnkjær et al.(34) recently reported 28% lower plasma levels of IGF-1 in 9-month old infants born to women with obesity when compared to infants born to women with normal weight. The study, did not report on the effect of paternal obesity on offspring IGF-1 levels even though 54% of participating fathers had either overweight or obesity. Assessing the influence of parental adiposity on the adrenal axis is also of interest. Chen et al. (8) reported birth weight and cortisol levels from umbilical cord blood in male offspring increase in proportion to paternal BMI but not maternal BMI. It is unknown if the association between paternal obesity and male newborn cortisol levels relates to lower adiposity in offspring. Further studies assessing the effect of parental adiposity on the programming of endocrine axes involved in in the regulation of *in utero* growth and newborn body composition phenotypes are needed.

As expected, in the current study, higher GWG and exclusive breast feeding predicted greater offspring adiposity. This is in line with previous studies showing GWG as a main contributor to fetal growth and overall adiposity (7,26,27,35–37). We and others have previously shown breastfed babies carry greater adipose content and less fat free mass than formula fed babies (38,39). In contrast to infant formulas, human milk is characterized by dynamic changes in macronutrient composition and bioactive components (40,41). Thus, compositional differences between human milk and infant formulas may explain the differences in body composition reported here.

The evidence on neonatal sex differences in body composition is conflicting. Carberry et al. (42) and Eriksson et al. (23) did not find differences in body composition in males vs. females after 4 and 7 days of birth, respectively. In contrast, Carlsen et al. (7) found that independent of maternal obesity status and GWG, males have lower %FM than females do at birth (<48h). Our data agree with the latter study as multiple linear regression analyses show female-sex as an independent predictor of higher %FM at two weeks of age.

Interestingly, we found that vaginal delivery and delivery by cesarean section were associated with greater infant %FM compared to induced vaginal delivery. Peripartum exposure to synthetic oxytocin (SynOT) is common in the U.S. where induction or augmentation of labor occurs in up to 50% of childbirths (43). There is paucity of data on the effects of SynOT in newborn offspring. Some studies have found an association between SynOT peripartum exposure and increased incidence of unwanted breastfeeding cessation as well as changes in newborn offspring feeding behavior including lower prefeeding cues, suction, and swallowing (44,45). However, results in this area of research are mixed. An integrative review of the literature (46) found that 17 out of 34 studies have linked SynOT to suboptimal breastfeeding outcomes. The authors suggest there is a potential for SynOT to cross the placenta and newborn brain barrier which would in turn affect newborn eating behaviors. The latter hypothesis strives from animal experiments showing SynOT exposure during the neonatal period results in long-term behavioral changes in exposed animals (47). Here we show lower adiposity in infants exposed to SynOT, but the mechanisms involved remain to be determined. It is unclear whether fetal growth influenced the delivery mode or whether the delivery mode influenced fat accretion during the first two weeks of life. In addition, our study has not accounted for the use of other procedures commonly used in vaginal induced childbirths such as epidural analgesia, and this should be taken into consideration when interpreting our results.

Our study had some limitations including a sample that was mostly Caucasian (85% of mothers) and living in Arkansas, which may limit the generalizability of the current findings to other racial or ethnic groups. Additionally, we had a limited sample size for body composition measures in fathers (136 fathers vs. 209 mothers), and due to the limited number of female newborns with paternal body composition measurements (n=59), this study cannot draw conclusions on the effects of paternal %FM on female adiposity. However, the study also had numerous strengths including longitudinal collection of data, measurement of maternal anthropometrics directly in clinic, consideration of maternal activity and energy expenditure, and most importantly direct objective measures of maternal, paternal, and infant body composition using whole-body air displacement plethysmography.

In this cohort, maternal adiposity at conception was the strongest predictive variable of newborn boys' and girls' adiposity. Paternal fat mass was the second strongest predicted variable of adiposity in boys with fat accretion in male newborns decreasing with increasing paternal adiposity. Also, an interesting finding from this study was induced vaginal delivery associated with lower adiposity at 2 weeks of age. The underlying mechanisms as well as the long-term clinical implications of these findings warrant further investigation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

GH	growth hormone
IGF	Insulin-like growth factor
IGFBP-3	Insulin-like growth factor binding protein 3
ADP	air displacement plethysmography
%FM	offspring percent fat mass
FM	fat mass
FFM	fat free mass
IOM	Institute of Medicine
RER	Resting energy expenditure
AC	activity counts
GWG	gestational weight gain
DXA	dual-energy X-ray absorptiometry
SynOT	synthetic oxytocin

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Table 1.

Mother-offspring pairs characteristics (n=209)

Variables	All (n=209)		Boys (n=115)		Girls (n=94)		*p*-value
Maternal age, years	29.5	± 3.6	29.4	± 3.6	29.7	± 3.6	0.5269
Maternal race, n (%)							0.1636
Caucasian	177	(84.7)	101	(87.8)	76	(80.9)	
AA/Asian/Hispanic/Mixed race/Unknown	32	(15.3)	14	(12.2)	18	(19.1)	
Maternal education, n (%)							0.7432
High school or GED	13	(6.2)	9	(7.8)	4	(4.3)	
Partial college or graduate	127	(60.8)	68	(59.1)	59	(62.8)	
Graduate training or degree	63	(30.1)	35	(30.4)	28	(29.8)	
Specialized training	6	(2.9)	3	(2.6)	3	(3.2)	
Maternal % FM	35.7	± 7.4	35.7	± 6.9	35.7	± 7.9	0.9900
Annual family income n (%)							0.2225
≤ $60,000	85	(40.7)	52	(45.2)	33	(35.1)	
> $60,000-$90,000	62	(29.7)	29	(25.2)	33	(35.1)	
≥ $90,000	62	(29.7)	34	(29.6)	28	(29.8)	
Maternal total AC/day × 1000	320	± 121	318	± 138	323	± 96	0.7904
Maternal REE, kcal/day$^{0.70}$	87.7	± 8.9	87.9	± 8.7	87.4	± 9.2	0.6745
Maternal RER	0.85	± 0.04	0.85	± 0.04	0.85	± 0.04	0.8478
GWG, kg	11.8	± 4.1	12.2	± 3.8	11.3	± 4.5	0.1213
IOM recommendations for GWG, n (%)							0.0589
Below	28	(13.4)	10	(8.7)	18	(19.1)	
Ideal	107	(51.2)	65	(56.5)	42	(44.7)	
Above	74	(35.4)	40	(34.8)	34	(36.2)	
Gestational age, wks.	39.3	± 0.9	39.3	± 0.9	39.2	± 0.8	0.8891
Delivery method, n (%)							0.1427
Vaginal induced	58	(27.8)	38	(33.0)	20	(21.3)	
Vaginal not induced	77	(36.8)	41	(35.7)	36	(38.3)	
C-section	74	(35.4)	36	(31.3)	38	(40.4)	
Birth weight, (kg)	3.5	±± 0.5	3.6	± 0.5	3.5	± 0.5	0.0228
Birth Length, (cm)	51.0	± 2.6	51.4	± 2.5	50.6	± 2.6	0.0123
Weight-for-age z-score at birth	0.45	± 0.98	0.47	± 0.96	0.42	± 1.00	0.7357
Length-for-age z-score at birth	0.79	± 1.35	0.82	± 1.32	0.76	± 1.39	0.7136
BMI-for-age z-score at birth	0.06	± 1.14	0.07	± 1.12	0.05	± 1.17	0.9272
Feeding mode, n (%)							0.3430
Formula or mixed fed	62	(29.7)	31	(27.0)	31	(33.0)	
Breast fed only	147	(70.3)	84	(73.0)	63	(67.0)	
Length at age 2 wks, (cm)	51.3	± 2.0	51.7	±1.9	50.8	± 2.0	0.0015
Weight at age 2 wks, (kg)	3.7	± 0.5	3.8	±0.5	3.6	± 0.4	0.0022

Variables	All (n=209)		Boys (n=115)		Girls (n=94)		*p*-value
Length z-score at age 2 wks	-0.34	± 1.01	−0.33	± 0.98	−0.35	± 1.06	0.8898
Weight z-core at age 2 wks	0.01	± 0.86	0.01	± 0.89	0.01	± 0.83	0.9347
Weight for length z-score at age 2 weeks	0.11	± 0.90	0.13	± 0.87	0.08	± 0.94	0.6792
Offspring % FM at age 2 wks	13.0	± 3.5	12.5	± 3.4	13.6	± 3.6	0.0295

Data presented as mean±SD, counts and %. AA=African American; GED=general education development; AC=activity counts; REE=resting energy expenditure; RER=respiratory exchange ratio; GWG=gestational weight gain; IOM=Institute of Medicine

Table 2.

Association between selected characteristics and infant's percent fat mass at two weeks of age

Variables	All (n=209)		Boys (n=115)		Girls (n=94)	
	β	***p*-value**	***β***	***p*-value**	***β***	***p*-value**
Maternal %FM	0.10	0.0029	0.10	0.0265	0.09	0.0441
Maternal age (years)	−0.06	0.3662	0.01	0.9299	−0.16	0.1244
Maternal race						
Caucasian	Reference					
Non-Caucasian	1.19	0.0773	1.91	0.0489	0.35	0.7134
Family Income						
≤ $60,000	Reference					
> $60,000 – $90,000	−0.10	0.8600	−0.26	0.7464	−0.35	0.6956
≥ $90,000	−0.23	0.6970	0.11	0.8853	−0.84	0.3680
GWG (kg)	0.02	0.6757	0.01	0.8989	0.06	0.4625
Gestational weight gain above IOM	0.37	0.4710	0.16	0.8064	0.58	0.4560
Total AC/day	0.00	0.5773	0.00	0.4222	−0.00	0.7985
REE (kcal/kg of $FFM^{0.74}$)	0.03	0.2345	0.03	0.4644	0.04	0.2939
Gestational age (weeks)	0.36	0.2037	0.59	0.0946	0.04	0.9297
Delivery mode						
Vaginal Induced	Reference					
Vaginal	1.35	0.0265	0.68	0.3781	2.02	0.0438
C-section	1.41	0.0221	1.31	0.0991	1.37	0.1650
Newborn sex						
Male	Reference					
Female	1.06	0.0295				
Feeding mode at age 2 weeks						
Formula or mixed-fed	Reference					
Exclusively breastfed	1.08	0.0430	0.83	0.2469	1.51	0.0540

%FM=percent fat mass, GWG=gestational weight gain, IOM=Institute of Medicine, AC=activity counts, REE=resting energy expenditure, FFM=fat free mass.

(mother-offspring pairs, n=209)

Table 3.

Multiple regression analyses to identify predictors of newborn %FM in the overall group, and in boys and girls separately (mother-offspring pairs, n=209)

Variables	β	SE	95% CI	Pr^2	*p*-value
Overall Group (n=209)					
Maternal %FM	0.14	0.03	0.07, 0.20	0.0803	<0.001
Maternal race					
Caucasian	Reference				
Non-Caucasian	1.61	0.64	0.34, 2.87	0.0304	0.014
Newborn sex					
Male	Reference				
Female	0.95	0.46	0.04, 1.87	0.0209	0.041
GWG (kg)	0.16	0.06	0.04, 0.27	0.0342	0.009
Gestational age (weeks)	0.63	0.27	0.10, 1.17	0.0265	0.021
Delivery mode					
Vaginal Induced	Reference				
C-section	1.21	0.61	0.01, 2.40	0.0197	0.048
Vaginal	1.54	0.59	0.37, 2.70	0.0330	0.010
Feeding mode at age 2 weeks					
Formula or mixed-fed	Reference				
Exclusively breastfed	1.15	0.50	0.16, 2.15	0.0257	0.023
Stratified by Sex					
Girls (n=94)					
Maternal %FM	0.13	0.05	0.03, 0.22	0.0711	0.008
Delivery mode					
Vaginal Induced	Reference				
C-section	0.95	0.96	−0.96, 2.87	0.0095	0.325
Vaginal	2.22	0.99	0.25, 4.18	0.0277	0.028
Feeding mode					
Formula or mixed-fed	Reference				
Exclusively breastfed	1.32	0.77	−0.21, 2.84	0.0284	0.090
Boys (n=115)					
Maternal %FM	0.11	0.04	0.02,0.20	0.0515	0.0157
Maternal race					
Caucasian	Reference				
Non-Caucasian	2.02	0.93	0.18, 3.86	0.0409	0.0317
Gestational age (weeks)	0.64	0.34	−0.03,1.32	0.0312	0.0615

%FM=percent fat mass, GWG=gestational weight gain, SE=standard error, Pr^2=square partial correlation

Table 4.

Multiple regression analyses to identify predictors of newborn %FM in the overall group, and in boys and girls separately (mother-father-offspring triads, n=136).

Variables	β	SE	95% CI	Pr^2	*p*-value
Overall group (n=136)					
Maternal %FM	0.09	0.04	0.01, 0.17	0.0399	0.022
Maternal race					
Caucasian					
Non-Caucasian	1.65	0.83	0.00, 3.30	0.0295	0.050
Newborn sex					
Male					
Female	1.16	0.55	0.08, 2.25	0.0303	0.035
GWG	0.17	0.07	0.03, 0.32	0.0407	0.015
Gestational age (weeks)	0.82	0.29	0.24, 1.40	0.0528	0.006
Stratified by Sex					
Girls (n=59)					
Maternal age	−0.36	0.15	−0.66, −0.07	0.0992	0.017
Family Income					
≤ $60,000	Reference				
> $60,000 – $90,000	2.63	1.15	0.32, 4.93	0.0846	0.026
≥ $90,000	0.9948	1.34	−1.70, 3.69	0.0089	0.462
Boys (n=77)					
Maternal %FM	0.12	0.04	0.04, 0.21	0.0977	0.006
Paternal %FM	−0.09	0.04	−0.16, −0.02	0.0807	0.014
Gestational age (weeks)	1.06	0.34	0.38, 1.75	0.1159	0.003

%FM= percent fat mass, SE=standard error; Pr^2=square partial correlation.

Table 5.

Multiple regression analysis showing the association between parental %FM measured early in pregnancy with offspring plasma growth hormone levels at age 2 years.

Growth Hormone	β	SE	95% CI	Pr^2	*p*-value
Girls (n=30)					
Paternal %FM	−0.08	0.03	−0.13, −0.02	0.23	**0.008**
Maternal %FM	0.06	0.02	0.01, 0.11	0.19	**0.017**
Boys (n=37)					
Paternal %FM	−0.04	0.02	−0.07, −0.01	0.14	**0.023**
Maternal %FM	−0.01	0.01	−0.03, 0.02	0.01	0.564
IGF-1					
Girls					
Paternal %FM	0.35	0.77	−1.23–1.93	0.01	0.651
Maternal %FM	1.42	0.69	−0.01–2.84	0.14	**0.051**
Boys					
Paternal %FM	1.23	0.45	0.03–2.16	0.19	**0.011**
Maternal %FM	0.02	0.37	−0.67–0.71	0.00	0.946
IGFBP-3					
Girls					
Paternal %FM	0.00	0.03	−0.05–0.06	0.00	0.889
Maternal %FM	0.03	0.02	−0.02–0.08	0.07	0.181
Boys					
Paternal %FM	0.01	0.02	0.02–0.05	0.02	0.388
Maternal %FM	0.00	0.01	−0.02–0.03	0.00	0.855

%FM= percent fat mass, IGF-1= Insulin-like growth factor 1, IGFBP-3= Insulin-like growth factor binding protein 3, SE=standard error; Pr^2=square partial correlation.