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Maternal obesity influences the relationship between location of neonate fat mass and total fat mass

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Abstract

Background—It is suggested that maternal obesity perpetuates offspring obesity to future generations.

Objective—To determine whether location of neonate fat mass (FM: central vs. peripheral) is related to total neonate FM and whether maternal obesity influences this relationship.

Methods—Neonate body composition and skinfold thicknesses were assessed in healthy neonates (n=371; 1-3 days old). Linear regression models examined the relationship between total FM and location of FM (central vs. peripheral). Location of FM was calculated by skinfolds: peripheral was the sum of (biceps and triceps)/2 and central was represented by the subscapular skinfold.

Results—A significant interaction was found for location of FM and maternal obesity. Holding all predictors constant, in offspring born to non-obese mothers, a 0.5 mm increase in central FM predicted a 15 g greater total FM whereas a 0.5 mm increase in peripheral FM predicted a 66 g greater total FM. However, in offspring born to obese mothers, a 0.5 mm increase in central FM predicted a 56 g total FM whereas a 0.5 mm increase in peripheral FM predicted a 14 g greater total FM.

Conclusions—The relationship between total FM and location of FM is influenced by maternal obesity.

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Author contributions

Paper concept: Hull. **Data collection:** Hull, Paley, Navder, Gallagher. **Analysis and interpretation of data:** Thornton, Hull. Critical review of manuscript for intellectual content: Hull, Paley, Navder, Gallagher. **Statistical expertise:** Thornton. **Study supervision:** Gallagher.

Conflicts of interest

Each author declares that they have no conflict of financial or personal interests in any company or organization sponsoring this study. The authors declare no conflict of interest.

Keywords

maternal obesity; fat pattern; neonate body composition; neonate fat mass

Introduction

The obesity prevalence among women of childbearing age is approximately 30% (1). In the last 3 decades where the rates of maternal obesity have increased, so too have the rates of obesity in children (2, 3). Research has begun to focus on how the maternal *in utero* environment may influence the propensity for obesity development in the offspring and the perpetuation of this trait in later generations (4-6)

Obesity and fat mass (FM) location in adults (7) and children (8) are important predictors of disease risk and development. Visceral fat in adults is greater in individuals with type 2 diabetes when compared to those without diabetes (9) whereas FM located in the femoral-gluteal region is cardioprotective (10).

Prior research has shown a strong relationship between maternal pre-pregnancy body mass index (BMI) and neonate FM (11, 12). Maternal gestational weight gain was directly related to infant FM (13) and this relationship varied by maternal pre-pregnancy BMI (5). Our data (5) showed that neonate FM differs by pre-pregnancy BMI although no difference in fat-free mass was found. One study reported a direct relationship between maternal pre-pregnancy BMI and infant abdominal adipose tissue (14) although location (central vs. peripheral) was not explored.

Given the importance of fat patterning to health outcomes in children and adults, understanding whether a relationship exists between maternal pre-pregnancy BMI (as an indicator of adiposity) and neonatal FM location at birth would be clinically informative. MRI has been used to measure infant adipose tissue in small cohort studies (15, 16), however, due to high costs, it lacks feasibility in larger scale studies. Skinfold thickness has been used to examine fat patterning in children (17). No study to date has investigated the relationship at birth between FM location (central vs. peripheral) and total FM in neonates at birth, and whether maternal obesity influences this relationship.

The primary purpose of this study was to determine in neonates whether FM location is related to total neonate FM and whether maternal obesity influences this relationship. A secondary aim was to explore the maternal factors that relate to the location of neonate FM.

Methods

Subjects

For these analyses, complete data were available for 371 full-term healthy neonates (193 males and 178 females). The subjects were recruited at Roosevelt Hospital in midtown Manhattan and the study was approved by the St. Luke's-Roosevelt Hospital Institutional Review Board (#06-016). A written consent was obtained from a parent before participation.

Race was determined by self-identification of each subject from the following four categories: Asian, non-Hispanic Black (African American), non-Hispanic White, and Hispanic. Subjects were asked to select the category into which each parent and grandparent fell. When all categories were the same, the subject was identified by that category. When multiple categories were selected, the individual was classified as “other”.

Study Procedures

Study procedures have been described elsewhere (5). Briefly, recruitment and testing occurred on the maternity floor before mothers and infants were discharged. The sample consisted of healthy, singleton newborns ranging in age from 1 to 3 days old and greater than 37 weeks in gestation. Maternal medical history was obtained through interview with the mother or by chart review. Exclusion criteria included pre-gestational or gestational diabetes, hypertension, pre-eclampsia, and neonates that had been admitted to the NICU or diagnosed with a congenital anomaly.

After consent and while mothers were inpatient following delivery, maternal pre-pregnancy body weight, height and body weight at admission for delivery were extracted from the medical record. If these data were missing, they were obtained by interview with the mother. These values were used to calculate total GWG and pre-pregnancy BMI. Maternal pre-pregnancy BMI was categorized based on 2009 IOM GWG recommendations (18).

Anthropometrics

Length was measured using an infant length board (Shorr Productions) with neonate lying supine and recorded to the nearest 0.1 centimeter. Two measurements were taken and an average of the measurements was used as input data for the Pea Pod. Skinfolds were measured at the subscapular, biceps and triceps and followed a standard testing protocol uniform to our Body Composition Laboratory for all populations (19). Two measurements were recorded to the nearest 0.1 mm and the average of the two measurements was used in analysis. Location of FM was calculated using the skinfolds measurements: peripheral was the sum of (biceps and triceps)/2 and central was represented by the subscapular skinfold measure. Multiple testers assessed skinfolds. Intraclass correlations (ICC) were calculated between the experienced tester that collected the majority of skinfolds (HRH) and two other testers for each skinfold site. The range of ICC's for the three skinfold sites between the criterion tester and other testers ranged from 0.82 to 0.95 and the technical error of measurement ranged from 0.25 to 0.35.

Air Displacement Plethysmography (PEA POD®)

The Pea Pod® Body Composition System (Software v 3.0.1; COSMED, Rome Italy) was used to measure neonate body composition. Calibration occurred once daily prior to testing. Testing procedures have been described elsewhere (5). Briefly, neonates were undressed and wore a standard tight fitting cap (Allentown Scientific Associates, INC.). The neonate was weighed naked on the Pea Pod® scale and a body weight was obtained to the nearest 0.0001 kg. Items that could not be removed including an umbilical clamp and identification bands were tarred for the body weight and body volume measurements. The neonate was placed

inside the Pea Pod® wearing a cap and body volume was measured. Body density was then converted to percent fat (%fat) using gender specific equations by Fomon (20).

Statistical Analysis

Descriptive statistics, including means and standard deviations were calculated for all variables for the entire group and by pre-pregnancy BMI. Multiple linear regression models were used to examine the relationship between total FM and location of FM (central vs. peripheral). Maternal covariates explored included age, race, parity, gestational weight gain, pre-pregnancy BMI and neonate covariates included gender, age at test and gestational age. Caucasian and normal pre-pregnancy BMI were used as the reference groups for race and pre-pregnancy BMI respectively, to test within group differences and interaction effects. Pearson correlations between maternal characteristics and infant FM location were calculated.

All statistical calculations were performed using SPSS statistical software (SPSS Institute Inc, Cary, NC, version 20.0). The level of significance for statistical tests was 0.05.

Results

Maternal characteristics are presented in **Table 1** and neonate characteristics are presented in **Table 2**. Maternal ethnicity/race breakdown was as follows: Caucasian 52%, African American 12%, Hispanic 21%, Asian 15% and “other” 3%. Maternal pre-pregnancy BMI ranged from a minimum of 16 kg/m² to a maximum of 45 kg/m². Forty-eight percent of the sample gained excess weight based on the Institute of Medicine guidelines. Fifty-two percent of the sample was male neonates born on average at 39 weeks.

Table 3 describes the results for the regression analysis to predict infant FM (when not considering the interaction with maternal obesity). There were significant main effects for maternal obesity and for central and peripheral FM. Neonates born to obese mothers had 69.5 g greater total FM compared to neonates born to normal weight mothers. The beta values from the regression model found a one unit higher peripheral FM and central FM corresponded to 37.8 g and 121.4 g, respectively, greater prediction of neonate FM. **Table 4** describes the regression model used to explore the interactive effect of maternal obesity on neonate FM location to predict total neonate FM. As presented in **Table 3**, infant peripheral FM contributed 3 times more to total neonate FM compared to the effect of infant central FM. However, when investigating the influence of maternal obesity on neonate FM location, a different effect was observed. In neonates born to obese mothers, the beta values from the regression models found a one unit higher neonate peripheral FM was associated with 105.1 g less neonate FM, whereas a one unit higher neonate central FM deposition was associated with 81.4 g greater neonate FM. Therefore the following effect of maternal obesity was observed. When considering and holding all predictors constant, in offspring born to obese mothers, a 0.5 mm increase in central FM was related to a 56 g greater contribution to total FM whereas a 0.5 mm increase in peripheral FM was related to a 14 g greater contribution to total FM. However this effect was reversed in offspring born to non-obese women. In offspring born to non-obese mothers, a 0.5 mm increase in central FM was related to a 15 g

greater contribution to total FM whereas a 0.5 mm increase in peripheral FM was related to a 66 g greater contribution in total FM. Adjusted R^2 for both models was 0.55.

Regression models were run to explore maternal predictors for infant FM location. Maternal characteristics were minimally predictive of infant FM location (data not presented).

Discussion

This study explored whether neonate FM location (central vs. peripheral) is associated with total neonate FM and whether pre-pregnancy maternal obesity influenced this relationship. First, neonates born to obese mothers had greater total FM compared to neonates born to normal weight mothers. Second, the contribution of neonate peripheral FM to total neonate FM was 3-fold the contribution of neonate central FM to total FM. Third, in offspring born to mothers who were obese, a 0.5 mm increase in central FM predicted a 56 g greater total neonate FM while a 0.5 mm greater peripheral FM predicted a 14 g greater total neonate FM. This relationship was reversed in offspring born to non-obese women.

Our results suggest two things related to offspring fat patterning. First, there are independent relationships between FM location and total FM. Peripheral FM contributed more than 3 times the amount to predicting total FM than did central FM. Second, these relationships are influenced by maternal pre-pregnancy BMI status. In offspring born to obese women, peripheral FM was negatively related with total FM ($\beta=-105$ g) whereas central FM was positively related to total FM ($\beta=81$ g). Therefore, in offspring born to obese women, the more FM located in the “central” region (a cardiometabolic risk factor in adulthood) predicted a greater total FM whereas the often cited cardioprotective peripheral FM predicted a lower total FM. The relationship was different for offspring born to non-obese mothers where greater peripheral FM predicted greater total FM. Could these data be interpreted to infer that offspring born to obese women are programmed to have greater central FM from birth whereas offspring born to non-obese women have greater peripheral FM relative to their total FM?

Few studies have quantified neonate fat distribution at birth and explored factors that influence fat distribution. Brumbaugh and colleagues (15) measured infant body composition using the Pea Pod at age 1-3 weeks, skinfold thicknesses (triceps and subscapular) and MRI derived subcutaneous, intra-abdominal and intrahepatocellular lipids (IHCL). The mothers were normal weight ($n=13$) or obese gestational diabetic ($n=12$). No difference was found between the normal weight or obese gestational diabetic groups for infant body composition (FM or FFM), subcutaneous or intra-abdominal fat but offspring born to obese gestational diabetic women had greater sum of skinfolds and IHCL than offspring born to normal weight women. This suggests a simple measure of total body composition may not be sophisticated enough to detect the programming differences caused by fetal exposure to maternal obesity and diabetes. Group differences by location of skinfold (triceps vs. subscapular) were not explored.

A parallel comparison between the two studies is difficult. Our study and the Brumbaugh et al. (15) study had different research questions, methods and groups. Our study did not

quantify intra-abdominal adipose tissue and Brumbaugh et al. did not explore group differences by location of adipose tissue (peripheral vs. central). Further, Brumbaugh et al. did not include obese non-gestational diabetic mothers thus the influence of obesity outside of diabetes was not explored. Though different outcomes and findings, both studies add to the growing knowledge in this area.

Our data were collected immediately following birth whereas Brumbaugh et al. assessed measures at 1-3 weeks. The time difference post-birth when measures were acquired may confound results. Factors including illness (ie., hyperbilirubin) (21) or feeding mode (formula fed vs. exclusive breast feeding) (22) can influence neonate postnatal body weight and body composition change. Neonates typically experience weight loss starting within the first 24 hours up to 11 days of life (23-25). Within the first 24 hours and 36 hours of life, exclusively breast fed neonates lost an average of 2.0% and 3.3% of birth weight, respectively (23). The total percentage of birth weight lost and days to return to birth weight vary by feeding mode. On average, formula fed infants lost 3.5% of birth weight and returned to birth weight by 6.5 days old (upper end 20 days) whereas exclusively breast fed infants lost an average 6.6% of birth weight and returned to birth weight by an average 8.3 days old (upper end 24 days). Our laboratory has shown periods of body weight change can influence neonate body composition measures (5) as measured using the Pea Pod where measures were acquired at birth, 24 hours and 48 hours old. A significant decrease in body mass and fat free mass was found in the first 24 hours, but no further differences were found at later times. Therefore we avoid measurements in the first 24 hours and test when body mass and body composition stabilized between 24 and 48 hours.

The current study provides information obtained using a cross-sectional design immediately following birth. This study did not measure infants longitudinally to characterize fat distribution changes. Positive but moderate correlations have been found between infant body composition and body composition measured in childhood (13). Other studies have reported on the role of postnatal infant rate of weight gain in relation to FM distribution at 6 months or at 1 year (26, 27). In the Generation R study (26), skinfolds were measured at 6 weeks and 6 months to estimate body fat and FM distribution. Infants who experienced rapid weight gain (>0.67 SD) between 6 weeks and 6 months had a greater central/peripheral FM ratio suggesting different fat distribution patterns based on the rate of infant weight gain. A second study (27) investigated weight change throughout infancy in relation to DXA assessed FM at 12 months. Weight gain in the first 6 months was related to DXA measured total FM and trunk FM at 12 months (27).

Strengths and Weaknesses

A strength of this study is the objective measure of infant body composition using the Pea Pod in a large and diverse sample. This provides a superior measure of infant body composition to assess effects of the maternal environment on fetal programming. All measurements were acquired between 24 and 36 hours following birth, therefore *ex utero* influences that change body weight and influence body composition in the first weeks of life are largely avoided.

This study is not without weaknesses. First, skinfold measurements were used to represent central and peripheral FM. Ideally, a more direct method such as MRI that separates subcutaneous from visceral fat would be preferential. Second, we did not characterize the maternal environment by measuring diet and physical activity. Physical activity, sedentary time and dietary quality may play a role in programming infant fat distribution. Last, we do not have measures beyond birth therefore it is not clear if this relationship continues into infancy or childhood.

Lifecourse relevance

The question exists as to whether fat patterning in neonates has relevance to disease risk later in life. There is increasing evidence that many adult onset diseases may have their origins in early life, including from critical developmental phases in the prenatal period. Though the relationships we found are somewhat intuitive, they cannot be interpreted to conclude that offspring exposed to maternal obesity are at a greater disease risk due to a different fat pattern (ie greater central FM and less peripheral FM). Data are lacking that translates how the *in utero* environment (ie, maternal environment) that the fetus is exposed to (maternal diet, physical activity, inflammation) and the environment during early infancy might influence the phenotype of the offspring in childhood (ie, fat pattern) and what this means (ie, consequences) for long term health. Data from the Dutch famine studies (28) that used birth weight and length as a proxy for infant adiposity measures cannot inform what different fat patterns found at birth mean for the long term health of the offspring. Studies that target how maternal factors (including physical activity and diet) and the period of infancy impact fat patterning and thereby disease risk are needed.

Conclusion

In healthy neonates born at term, the relationship between total FM and where that FM is located (central versus peripheral) is influenced by pre-pregnancy maternal obesity. Future studies are needed to determine predictors of infant FM location at birth and to understand how infant FM distribution is related to later health.

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What is known:

- Data have shown infants born to overweight and obese mothers have greater body fat than infants born to normal weight mothers.
- Infant body fat is influenced by whether the mother gains excessive weight during pregnancy and this relationship differs by pre-pregnancy BMI category.

What this adds:

- Neonate total FM is influenced by the location of FM (central vs. peripheral) and this relationship is related to maternal obesity.

Table 1

Maternal characteristics for the total sample and each pre-pregnancy BMI group.

	Total (n=371)	Underweight (n=20)	Normal (n=252)	Overweight (n=59)	Obese (n=40)
Age (years)	31.8 ± 5.5	32.1 ± 4.9	32.0 ± 5.7	32.1 ± 5.6	30.2 ± 4.4
Height (cm)	163.6 ± 7.0	167.8 ± 6.9	163.7 ± 6.7	163.8 ± 7.8	161.4 ± 7.1
Pre-pregnancy body weight (kg)	63.3 ± 12.8	49.9 ± 4.8	58.2 ± 6.0	73.1 ± 8.3	88.0 ± 13.1
Pre-pregnancy BMI (kg/m²)	23.6 ± 4.6	17.7 ± 0.7	21.7 ± 1.7	27.2 ± 1.4	33.7 ± 3.6
Gestational weight gain (kg)	14.4 ± 4.9	15.0 ± 3.7	14.8 ± 4.4	14.2 ± 5.2	12.0 ± 7.2
Maternal race/ethnicity n(%)					
<i>Caucasian</i>	182 (49%)				
<i>African American</i>	45 (12%)				
<i>Hispanic</i>	78 (21%)				
<i>Asian</i>	56 (15%)				
<i>Other</i>	10 (3%)				

Means ± standard deviation

Table 2

Neonate characteristics for the total sample and each pre-pregnancy BMI group.

	Total (n=371)	Underweight (n=20)	Normal (n=252)	Overweight (n=59)	Obese (n=40)
Age (weeks)	0.3 ± 0.1	0.3 ± 0.2	0.3 ± 0.1	0.3 ± 0.1	0.3 ± 0.1
Gestational age (weeks)	39.5 ± 1.3	39.8 ± 1.1	39.6 ± 1.3	39.2 ± 1.4	39.4 ± 1.4
Body mass (g)	3205.7 ± 460.5	3168.5 ± 316.9	3167.9 ± 437.5	3304.7 ± 585.7	3316.0 ± 429.3
Length (cm)	49.4 ± 2.4	49.9 ± 1.6	49.4 ± 2.4	49.6 ± 2.5	49.7 ± 2.2
Body fat (%)	11.9 ± 4.5	11.9 ± 5.6	11.5 ± 4.2	12.6 ± 4.6	14.1 ± 4.8
Fat mass (g)	392.2 ± 179.5	384.1 ± 195.7	370.6 ± 165.2	431.3 ± 211.5	475.6 ± 179.9
Fat-free mass (g)	2809.1 ± 353.6	2784.4 ± 265.5	2793.2 ± 341.9	2864.9 ± 425.8	2840.3 ± 349.5
Central fat mass (mm)	3.6 ± 0.9	3.6 ± 0.9	3.6 ± 0.8	3.8 ± 1.1	3.8 ± 0.9
Peripheral fat mass (mm)	3.7 ± 0.8	3.7 ± 0.7	3.6 ± 0.7	4.0 ± 0.9	4.0 ± 0.8

Means ± standard deviation

Table 3

Multiple regression to predict infant fat mass (g) (n=371).

Predictor	Regression coefficient (β)	<i>p</i> value
Infant gender (0=male)	33.0	0.01
Gestational age at birth (weeks)	17.5	<0.001
Maternal race "other" (0=Caucasian)	-94.9	0.009
Gestational weight gain (kg)	3.7	0.006
Maternal pre-pregnancy obese (0=normal)	69.5	0.001
Central fat mass (mm)	37.8	0.001
Peripheral fat mass (mm)	121.4	<0.001

Adjusted $R^2=0.55$

Table 4

Multiple regression to predict infant fat mass (g) and explore the interaction of maternal obesity and neonate fat mass location (n=371).

Predictor	Regression coefficient (β)	<i>p</i> value
Infant gender (0=male)	35.2	0.006
Gestational age at birth (weeks)	17.8	<0.001
Maternal race "other" (0=Caucasian)	-83.2	0.026
Gestational weight gain (kg)	3.5	0.009
Maternal pre-pregnancy obese (0=normal)	179.3	0.095
Central fat mass (mm)	30.0	0.013
Peripheral fat mass (mm)	132.2	<0.001
Central fat mass $\times$ Maternal obesity	81.4	0.018
Peripheral fat mass $\times$ Maternal obesity	-105.1	0.04

Adjusted $R^2=0.55$