EXAMINING THE RELATIONSHIP BETWEEN MATERNAL FAT PATTENING
AND INFANT BODY COMPOSITION

By

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ABSTRACT

Background: Maternal obesity is known to effect offspring obesity development. Studies have shown that maternal pre-pregnancy BMI (pre-BMI) and gestational weight gain (GWG) are positively related to infant birth weight and body composition. In addition, maternal fat patterning (central vs. peripheral) before pregnancy is directly related to infant birth weight. However, no study has examined the correlation between quantified maternal fat mass location (central vs. peripheral) and infant body composition.

Purpose: The purpose of this study was to investigate whether maternal central vs. peripheral fat mass (FM) was related to infant body composition (percent body fat (%fat), FM and fat free mass (FFM)).

Methods: Thirty-eight mother–infant pairs were included in this analysis. Maternal central and peripheral FM was measured by dual-energy-x-ray absorptiometry (DXA) at 2 weeks postpartum. Maternal central FM was represented by trunk FM and maternal peripheral FM was represented by the sum of arm and leg FM. Infant body composition was measured by air displacement plethysmography (Pea Pod®) at 1-3 days after birth. Due to the small sample size, first simple linear regression was completed to assess the relationship between infant body composition (dependent variable) and maternal peripheral and central FM (independent variables). Next, the analyses were repeated using multiple linear regression with the following maternal covariates: age, parity, race, socioeconomic status (SES), GWG, weight loss 2 week postpartum, and infant covariates; gender, age at test and gestational age (GA). Only significant covariates were retained in the final model.

Results: In the simple linear regression analysis, maternal peripheral FM was significantly
related to infant FM ($\beta=11.61, p=0.045$) and borderline significant for infant %fat ($\beta=0.28, p=0.055$). The next series of results report the findings when including covariates. When predicting infant %fat, maternal central FM ($\beta=0.43, p=0.011$), maternal age ($\beta=-0.36, p=0.022$), and SES were significantly correlated, (high school vs. some college, $p=0.033$; high school vs. 4-year college, $p=0.041$). When predicting infant FM, maternal peripheral FM ($\beta=13.75, p=0.009$), maternal weight loss 2 weeks postpartum ($\beta=16.604, p=0.041$), and infant age at test ($\beta=-761.74, p=0.019$) were positively related. When predicting infant FFM, only maternal age ($\beta=35.47, p=0.022$), weight loss at 2 weeks postpartum ($\beta=22.33, p=0.023$), and infant GA ($\beta=137.16, p=0.016$) were related.

**Conclusions:** When predicting infant FM, maternal peripheral FM and weight loss 2 weeks postpartum were positively related. However, infant %fat was significantly related to maternal central FM, age and SES. Further studies with a larger sample size are needed to understand these relationships.
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# TABLE OF CONTENTS

Chapter 1. Introduction ................................................................................................. 1  
  Statement of Purpose .............................................................................................. 2  
  Research Questions ............................................................................................... 2  
  Specific aims & Hypothesis .................................................................................. 2  
Chapter 2. Literature Review ..................................................................................... 3  
  Maternal Obesity and Adverse Outcomes .............................................................. 3  
  Fetal Programming Hypotheses .......................................................................... 3  
  Maternal pre-BMI and Infant Birth Weight .......................................................... 4  
  Maternal pre-BMI and Infant Body Composition ............................................... 5  
  Maternal GWG and Infant Birth Weight ............................................................... 6  
  Maternal GWG and Infant Body Composition ................................................... 7  
  Maternal Body Composition and Infant Birth Weight ....................................... 8  
  Maternal Body Composition and Infant Body Composition ......................... 9  
  Maternal Fat Patterning and Infant Birth Weight ............................................ 9  
  Summary ............................................................................................................ 11  
Chapter 3. Methods ................................................................................................. 12  
  Study Overview .................................................................................................... 12  
  Sample .................................................................................................................. 12  
  Inclusion/Exclusion Criteria .............................................................................. 12  
  Research Setting .................................................................................................. 13  
  Ethics .................................................................................................................... 13  
  Data Collection .................................................................................................... 13  
  Instrumentation .................................................................................................... 13  
  Analysis of Maternal Body Composition by iDXA ........................................... 13  
  Infant Body Composition using the Pea Pod® .................................................. 15  
  Statistical Analysis Database Categories ......................................................... 16  
  Database Categories ............................................................................................ 17  
Chapter 4. Results .................................................................................................. 18  
  Subject Characteristics ....................................................................................... 20
Predictors of Infant Body Composition without Covariates .......................20
Predictors of Infant Body Composition including Covariates ....................21
Chapter 5. Discussion .........................................................................................24
Overview ......................................................................................................24
Limitations ...................................................................................................26
Chapter 6. Summary ...........................................................................................27
Chapter 7. References .........................................................................................29
LIST OF TABLES AND FIGURES

TABLES
1. Maternal characteristics and body composition measurements..................21
2. Infant characteristics and body composition measurements ......................22
3. Predicting Infant body composition from maternal central and peripheral FM without covariates .................................................................23
4. Predicting Infant body composition from maternal peripheral FM without covariates .................................................................................23
5. Predicting Infant %fat from maternal central and peripheral FM with covariates ......................................................................................24
6. Predicting Infant FM from maternal central and peripheral FM with covariates ......................................................................................25
7. Predicting Infant FFM from maternal central and peripheral FM with covariates ......................................................................................25

FIGURES
1. DXA measurements of human body composition.....................................16
2. Maternal pre-BMI distribution...................................................................20
Chapter 1
INTRODUCTION

The prevalence of obesity in women of childbearing age has increased in the past few decades (1). The prevalence of obesity in non-pregnant women aged 20-39 years (body mass index, BMI ≥ 30 kg/m²) increased from 28.4% in National Health and Nutrition Examination Survey (NHANES) 1988-1994 (2) to 37.9% in NHANES 1999-2000 (3). According to the latest data from NHANES 2009-2010, the prevalence of obesity for women remains high (35.8% of adult women are obese). Among women aged 20-39 years, over half are overweight (BMI ≥ 25 kg/m²) and 31.9% are obese (1).

Obesity is a major health concern for pregnant women. Obese women have higher risks for pregnancy-related complications such as gestational hypertension (4), preeclampsia (5), and gestational diabetes (5). In addition, maternal obesity is related to excessive fetal growth and later offspring disease development (6-8).

Maternal obesity, gestational weight gain (GWG), and maternal body composition, are directly related to fetal over-nutrition as reflected by a high birth weight (9, 10) and an increased infant percent body fat (11, 12). Maternal fat patterning, represented by a central fat distribution (mainly measured by waist to hip ratio (WHR)), has been found to be an independent risk factor for large for gestational age (LGA) and a macrosomic infant (birth weight > 4000g) (13-15). Maternal peripheral fat, although rarely studied, is also related to infant birth weight (16). At this time, no study has quantified maternal central fat or peripheral fat and examined their relationships to infant body composition.
Statement of Purpose

The purpose of this study was to explore the relationship between maternal fat patterning (central versus peripheral) and infant body composition.

Research Question

Does maternal fat patterning (central versus peripheral) relate to infant body composition at birth?

Specific aims & Hypotheses:

Aim 1: To determine whether maternal central fat is related to infant body composition (percentage body fat (%fat), fat mass (FM) and fat free mass (FFM)).
   
   Hypothesis 1.1: Maternal central fat is positively related to infant %fat
   Hypothesis 1.2: Maternal central fat is positively related to infant FM
   Hypothesis 1.3: Maternal central fat is positively related to infant FFM

Aim 2: To determine whether maternal peripheral fat is related to infant body composition (%fat, FM, FFM).

   Hypothesis 2.1: Maternal peripheral fat is positively related to infant %fat
   Hypothesis 2.2: Maternal peripheral fat is positively related to infant FM
   Hypothesis 2.3: Maternal peripheral fat is positively related to infant FFM
Chapter 2

LITERATURE REVIEW

Maternal obesity and adverse outcomes

The obesity epidemic has resulted in an increased number of overweight and obese women of childbearing age in the last three decades (1, 3). Obese women are at risk for a range of complications associated with pregnancy including gestational hypertension, preeclampsia, gestational diabetes and postpartum weight retention (17-20). Maternal obesity is also related to excessive fetal growth and obesity development in the offspring (5, 21-25).

Fetal programming hypothesis

The underlying mechanisms linking maternal obesity to adverse offspring health are proposed by Barker et al. in the “fetal programming hypothesis” (26, 27). Studies of pregnant women from times of war or famine provide insight into the effect of abnormal nutrition on the health outcomes of the infant (28). Data revealed that obesity was higher in offspring conceived during the Dutch famine than those who were conceived before or after (28).

It has been hypothesized that a stimulus or stressor, often seen as maternal under-nutrition, occurs during critical periods in pregnancy and alters the intrauterine environment (29). After being exposed to a restricted nutrient supply in utero, the fetus makes adaptations by prioritizing the development of critical organs such as the brain over the pancreas, liver, or kidney (29, 30). These adaptions can lead to impaired function in the pancreas or liver. Both organs are involved in metabolic homeostasis. Impairment in these organs can lead to inadequate insulin secretion from the pancreas and disturbed fatty acids synthesis in the liver (31). In addition, defects in the development of kidney may influence later blood pressure regulation (30, 32). These permanent changes in the fetus’ physiological systems can lead to coronary heart disease and stroke in adult life (26, 33, 34).

In developed nations, maternal over-nutrition, instead of malnutrition, is more crucial in
influencing fetal growth. Generally, maternal obesity is related to abnormal lipid metabolism, increased insulin resistance, and an altered inflammatory status (35) leading to changes in the intrauterine environment (36). Infants exposed to metabolic abnormalities, such as hypercholesterolemia or high glucose, may have increased growth of adipose tissue and increased insulin resistance, and thus increased risk of developing obesity (36) and future chronic diseases (37). Maternal factors which may influence the intrauterine environment and fetal growth include pre-pregnancy BMI (pre-BMI) (9), body composition (10), and central fat distribution (15).

The relationship between maternal pre-BMI and GWG on infant outcomes

Maternal pre-BMI and infant birth weight

Birth weight is often used to evaluate fetal growth and future disease risk. A high birth weight suggests an intrauterine environment of over-nutrition whereas a low birth weight suggests under-nutrition (38). Researchers have shown that both a low and high birth weight have increased risk of offspring obesity development (39), type 2 diabetes (39) and metabolic syndrome later in life (39-41).

Many studies have focused on maternal factors, such as maternal pre-BMI, in relation to birth weight. Those that have studied these relationships find consistent results (9, 42). May et al (42) used data from the Siouxlan Women, Infants, and Children Program in 233 mother-infant pairs where 58.8% of the study population was white, and 31.8% was Hispanic. Multiple linear regressions were used to predict infant birth weight according to maternal pre-BMI. Covariates included pregnancy weight gain (low and high), smoking, infant gender, and gestational age (wks). Infants born to obese mothers (BMI >29.0 kg/m²) had a 144 g greater birth weight (p=0.026) than infants born to normal moms (BMI: 19.8-26.0 kg/m²) independent of pregnancy weight gain. Frederick et al (9) included 2,670 women (mainly white, mean maternal age: 32.4 ± 5 years) participating in the Omega study using maternal
pre-BMI and infant birth weight obtained from medical records. A positive association was found using self-reported maternal pre-BMI and infant birth weight from medical records ($\beta=44.7$, $p=0.001$).

**Maternal pre-BMI and infant body composition**

Although birth weight provides a crude estimate of the intrauterine environment, using solely birth weight may underestimate the true relationship between maternal obesity and fetal development. Measuring infant body composition (FM and FFM) at birth may be better to elucidate the true relationship between maternal obesity and fetal development.

Several studies have suggested a relationship between maternal pre-BMI and offspring body composition (11, 12, 43-45). A higher maternal pre-BMI was related to a higher %fat and FM in infants. Modi. N et al (46) assessed infant adipose tissue (AT) content by whole body MR imaging in 105 full-term infants in UK. Infants were measured within one month and the mean age at test was 11.7 days. Maternal pre-BMI (mean: 23.6 kg/m$^2$) was used as a continuous variable and each unit increase in maternal pre-BMI was associated with an increase in infant total AT (8 mL; 95% CI, 0.09 –14.0; $p = 0.03$), abdominal AT (2 mL; 95% CI, 0.7– 4.0; $p =0.005$), and non-abdominal AT (5 mL; 95% CI, 0.09 –11.0; $p = 0.054$). Infant sex and postnatal weight gain were used as covariates.

Sewell et al (11) measured infant body composition in 220 infants within 72h after birth using total body electrical conductivity (TOBEC) born to overweight/obese women (BMI $\geq$ 25kg/m$^2$) or lean/average women (BMI < 25kg/m$^2$). The population was mainly white and the average maternal age was 28.3 $\pm$ 5.8 years. The researchers found that infants born to overweight/obese mothers had a greater %fat when compared to infants born to lean/average weight women (11.6% $\pm$ 4.7% vs. 9.7% $\pm$ 4.3%, respectively; $p=0.003$). In addition, infant FM was higher in those born to overweight/obese women than those in the lean/average group (420 $\pm$ 220g vs. 380 $\pm$ 170g, respectively; $p=0.01$).
Hull et al (12) measured infant body composition using air displacement plethysmography (ADP) in 72 full-term infants (≤ 35 days old) from normal or overweight/obese mothers (18-45 years of age). They found significant differences between infants born to normal weight and overweight/obese women in %fat (12.5 ± 4.2% vs. 13.6 ± 4.3%, respectively; p<0.0001), FM (414.1 ± 264.2 g vs. 448.3 ± 262.2 g respectively; p<0.05), and FFM (3310.5 ± 344.6 g vs. 3162.2 ± 343.4 g, respectively; p<0.05). The limitation of this study was that infant body composition was measured over a large age range, from 5 days up to 35 days. Other ex utero factors, such as the feeding pattern, might influence infant body composition during that time. This was shown in regression modeling when infant age at test was a significant predictor of infant body composition.

*Maternal GWG and infant birth weight*

Excessive maternal GWG, according to 2009 Institute of Medicine (IOM) recommendations (47), is directly related to larger size at birth (9, 18, 48). Frederick et al (9) included 2,670 women to examine the relationship between maternal GWG and infant birth weight. GWG was calculated as the difference in weight (kg) between last recorded maternal weight within 4 weeks of delivery and self-reported maternal weight at 3 months before conception. Independent of maternal pre-BMI, the prevalence of macrosomia was 76% greater in those women gaining excessive GWG compared to those gaining below the 2009 IOM recommendation (adjusted relative risk: 1.76).

One large-scale study (18) reported data on the relationship between GWG and infant birth weight using the National Longitudinal Survey of Youth from 1979. Information was obtained from 4496 infant and 3733 mothers (difference due to multiple births to the same woman) at aged 15 years of age or older (74% non-Hispanic/non-Black, 18% Hispanic, 8% Black). GWG was calculated as the difference between pre-pregnancy weight and weight at delivery (self-reported) and categorized into inadequate, adequate or excessive, according to
2009 IOM recommendations. Birth weight was recalled by mothers and calculated for gestational age z-values based on 1999-2000 US national reference data (49) to identify LGA (>90th percentile in the reference population) and small for gestational age birth (SGA, <10th percentile in the reference population). Those women with inadequate GWG had an odds ratio (OR) of 1.48 of having a SGA infant. Compared to adequate GWG, women with excessive GWG had an OR of 2.15 of having a LGA infant. Ferraro et al (48) examined 4321 mothers (age 30.39±5.06 years) and infants from the Ottawa and Kingston birth cohort and found consistent results with the previous two studies. Excessive GWG was associated with higher rates of LGA (OR=2.86).

**Maternal GWG and infant body composition**

In addition to its correlation with birth weight, GWG is also related to infant body composition. Crozier et al (50) examined the association between GWG in 948 low-income women from the Southampton Women’s survey and FM in infants at birth using dual energy x-ray absorptiometry (DXA). As a result, they found that almost half of the women (49%) gained excessive weight according to the 2009 IOM recommendations and those women with excessive GWG delivered an infant with a greater FM (7%) at birth compared to women with adequate GWG (SD=0.17, p=0.03). However, the researchers did not consider the interaction between GWG and pre-BMI.

Hull et al (51) conducted a study in 306 full-term infants that considered the effects of GWG on infant body composition by different maternal pre-BMI categories. The categories studied were normal (pre-BMI 18.5-24.9 kg/m²), overweight (pre-BMI 25.0-29.9 kg/m²), and obese (pre-BMI > 30.0 kg/m²). Infant body composition was measured immediately following birth using ADP. The study demonstrated that whether gaining appropriate or excessive GWG, infants born to obese mothers had the greatest %fat (14.6%). Further, there were no within group differences based on whether a normal weight or obese mother gained
appropriately or excessively for infant body fat. The most interesting finding was a within
group difference in offspring body fat born to overweight mothers. Infants born to an
overweight mother that gained appropriately had lower body fat than an infant born to an
overweight mother that gained excessively (9.2 %fat vs. 13.7 %fat, respectively; p<0.05).
This suggests times to intervene to impact infant body composition vary by maternal pre-
BMI. In obese women, interventions may need to occur prior to pregnancy whereas in
overweight women, a significant impact on infant body fat can be made by gaining
appropriate weight during pregnancy.

The relationship between maternal body composition and infant outcomes

Maternal body composition and infant birth weight

Pre-BMI and GWG are known to influence fetal growth, but studying these variables does
not allow us to explore the individual contributions of measured maternal FM and FFM on
infant outcomes (52). As the techniques for measuring maternal body composition during
pregnancy have become more accessible, several studies have studied the relationship
between maternal body composition and infant birth weight (7, 8, 10, 53-56).

Lederman et al (53) measured maternal body composition in 200 women aged 18-35 years in
New York both early (12-16 weeks) and late in pregnancy (37 weeks). The researchers used
the four-compartment model (underwater weighing, total body water (TBW), and DXA). The
results indicated maternal FM early in pregnancy, but not late in pregnancy, were
significantly related to birth weight (β= -14.3, p=0.049). However, maternal FFM measured
late in pregnancy was significantly (β= 34.9, p=0.0007) related to birth weight whereas early
pregnancy FFM was not (β= -9.8, p=0.4). Based on the results of the study, maternal FM in
early pregnancy and FFM in late pregnancy were significantly related to infant birth weight.
However, maternal FM in late pregnancy or FFM in early pregnancy were not related to birth
weight.
Maternal body composition and infant body composition

Just one study has examined the correlation between maternal body composition and infant body composition. Butte et al (57) measured maternal body composition using the 4-compartment model in 63 women with a low BMI (< 19.6 kg/m²), a normal BMI (19.6-26.0 kg/m²), or a high BMI (> 26.0 kg/m²). Maternal body composition was measured before pregnancy, and at 9, 22 and 36 weeks of pregnancy. Infant body composition was measured by DXA at 2 and 27 weeks of age. No associations were found between maternal body composition (before, during or after pregnancy) and infant body composition at 2 weeks of age. There were some limitations to this study that may have influenced the study results. First, maternal BMI categories were not standard to what is normally studied. In fact, the “high” BMI group was primarily comprised of mothers with an overweight BMI and very few with an obese BMI. Second, infant body composition was measured at 2 weeks and not immediately following birth. As reported by Hull (12), infant age at test is correlated to infant body composition measures. Other factors (e.g. feeding pattern) might influence infant body composition at 2 weeks confounding the associations with the in utero environment.

Maternal fat patterning and infant birth weight

In addition to maternal body composition, studies have also investigated how maternal FM location relates to infant birth weight (14, 15, 58). Studies have shown that central adiposity, measured by waist circumference or WHR, is related to metabolic dysregulation in non-pregnant women, such as altered glucose metabolism and insulin resistance (59-61). Although nothing has been reported in pregnant women, it is possible that in pregnant women, central adiposity can also cause abnormal glucose levels and increased insulin resistance. This in turn can affect placental function and alter the in utero metabolic environment and thereby influence fetal growth.

Three studies assessed the relationship between maternal central fat patterning and infant
birth weight. Brown et al (15) measured maternal WHR before pregnancy in 521 women and suggested it was related to infant birth weight (95% confidence limits, 54-187). A 0.1 unit increase in maternal WHR predicted a 120 g increase in infant birth weight. Data from the Avon Longitudinal Study of Parents and Children (ALSPAC) including a larger sample size (n=3083) found similar results. In the ALSPAC study, the distribution of WHR was categorized into four quartiles, quartile1 used as the reference (median WHR as 0.68), with the remaining quartiles as follows: quartile 2=0.71, quartile 3=0.75, and quartile 4=0.81. Researchers found WHR in the third and fourth quartiles were associated with a greater risk of macrosomia (third quartile, OR 1.59, 95% CI 1.12-2.26, fourth quartile, OR 1.69, 95% CI 1.18-2.42) (14). The Black Women’s Health Study (58) included 6,687 African American women aged 21-44 years and examined the relationship between maternal waist circumference, WHR before pregnancy and macrosomia in full-term infants. Maternal waist and hip circumferences were self-reported and WHR was calculated by waist and hip circumference. All three measurements were validated in a study among 115 participants (r=0.72 for waist circumference, r=0.74 for hip circumference, and r=0.54 for WHR). As a result, they found independent of maternal pre-BMI and GWG, maternal pre-pregnancy waist circumference was positively related to infant macrosomia (p=0.04). The results of this study further indicated maternal central adiposity might explain some of the variation of rates of macrosomia independently and different from what had been explained by maternal pre-BMI and GWG.

So far, no studies have examined how maternal fat patterning (central versus peripheral) using sophisticated techniques relates to infant body composition at birth.
Summary:

The prevalence of obesity in the obstetrics population remains high in recent years (1, 3). Maternal obesity is related to adverse pregnancy complications (17-20), and also to offspring’s overall health (5, 21-25). Maternal factors, such as maternal pre-BMI, GWG and body composition are all positively related to infant birth weight (9, 47, 62, 63) and body composition (11, 12, 15, 51, 57). Furthermore, maternal fat patterning is directly related to infant birth weight (14, 15). However, previous studies did not have a precise measurement of maternal central fat and no studies have related maternal central fat to infant body composition. This study will move the field forward by measuring maternal central fat and peripheral fat using DXA to explore how maternal fat patterning correlates with infant body composition at birth.
Chapter 3

METHODS

Study Overview

This study used the cohort from the Pregnancy Health Study conducted at the University of Kansas Medical Center. The purpose of this study was to explore the relationship between maternal fat patterning (central versus peripheral) and infant body composition.

Sample

The study population was a subset of women participating in an ongoing observational study known as the Pregnancy Health Study. The original study intended to recruit 80 pregnant women, 40 with a normal pre-BMI (BMI 18.5-24.9 kg/m²) and 40 with an obese pre-BMI (BMI 30-40 kg/m²). However, only 37 women were included from the study with pre-BMI ranged from 18.5-39.99 kg/m². The original study was designed to investigate the relationship between maternal body composition and infant body composition.

Inclusion/Exclusion Criteria

Inclusion criteria for the primary study were as follows: women between ages 18 and 45 years, either a healthy BMI (18.5-24.9 kg/m²) or obese BMI (30-40 kg/m²) before pregnancy, singleton pregnancy, English speaking, and delivered at KU Hospital.

Women were excluded if they were underweight (BMI<18 kg/m²) or overweight (BMI, 25-29.9kg/m²) before pregnancy, under the age 18 or over the age of 45, had known infectious diseases (e.g. autoimmune diseases), diabetes mellitus (either gestational diabetes or pre-gestational diabetes), hypertension or preeclampsia, smoke or use any drugs during pregnancy, non-English speaking, expecting multiple infants, and unwilling or unable to do the birth visit or come to the follow up study.
Setting

The study was conducted in the University of Kansas Medical Center from January 2012 to March 2013.

Ethics

The study was approved by Human Subject Committee at KU Medical Center (HSC# 12793). Informed consent was signed by every subject. All the staff was trained before performing any test in the study.

Data Collection

Women seeing an Obstetrician in the KU Obstetrics and Gynecology Clinic were pre-screened by medical chart review. Pregnant women at 28-39 weeks that were eligible for the study were asked if they were interested in participating in a research study. The consent form was explained and signed by eligible and willing participants who met the inclusion criteria. A general questionnaire was distributed to collect demographic data and health information during pregnancy. Recruitment flyers with study information were distributed around KU Medical Center and in KU Hospitals and through a system wide mass email.

The second visit occurred after delivery. Infant body composition was performed using the Pea Pod® within 1-3 days after birth Infant %fat, FM, and FFM were measured. Infant length and weight were also measured at this visit.

The third visit was at two weeks postpartum. Maternal body composition and fat pattern were measured by DXA (GE Healthcare, Madison, WI) in Endocrinology.

Instrumentation:

Analysis of maternal body composition by DXA

DXA is considered to be a valid and reliable measurement to assess central fat compared to computed tomography (CT) and magnetic resonance imaging (MRI) in adults (64, 65). In addition, DXA calculates fat in different regions, such as trunk, arms, and legs (66, 67).
Before a scan, subjects’ weight and height were measured. For each scan, subjects wore a hospital gown and were asked to remove all materials that could attenuate the X-ray beam, including jewelry and wire containing undergarments. Scans were according to the manufacturer’s instructions with subjects in the supine position. All scans were performed by a licensed radiological technician. Manufacturers software (encore version 13.50) was used to analyze the body composition (FM and FFM) and fat pattern.

The central fat was represented by trunk fat that was comprised of neck, chest, abdominal, and pelvic regions. The upper perimeter included the inferior edge of the chin and the lower border intersected the middle of the femoral necks without touching the brim of the pelvis. Peripheral fat was represented by the sum of fat in the arms and legs. The arm region included the arm and shoulder area formed by placing a line from the crease of the axilla and through the glenohumeral joint. The leg region included all the area below the lines that formed the lower borders of the trunk. The upper demarcation was 20% of the distance between the iliac crest and the neck. The lower demarcation was at the top of the pelvis.
Infant body composition using the Pea Pod®

Infant body composition was measured within 72 h after birth using the Pea Pod® (Life Measurement Inc. Concord, CA) (12, 51, 68-72).

First, infant length was measured twice using a length board (Shorr Productions) to the nearest 0.1 cm by trained staff and the average of the two measurements was recorded. Infant length were then entered into the Pea Pod® software. Next, infant body weight was measured with the infant nude using the Pea Pod® integrated scale to the nearest 0.0001kg.

After body weight was measured, a standard head cap was worn by the infant to reduce the air trapped in the hair during the body composition assessment. Then the infant was placed inside the chamber to complete body volume measurements. The total body volume
measurements required approximately 2 minutes. Testing procedure has been described in detail elsewhere (68).

Equations from Fomon (73) was used to convert body volume to body density and infant %fat, FM, FFM. The thoracic gas volume (TGV) was estimated because the direct measurement was not feasible for an infant. Trained staff conducted all tests in Dr. Hull’s research laboratory at KU Medical Center

Densitometry is a safe, quick and easy method to assess infant body composition (68). Several studies have used ADP to measure infant body composition (12, 51, 68-72). Sainz et al (69) compared the accuracy of Pea Pod® with chemical analysis with 24 pig phantoms and found no differences between the results of Pea Pod® and chemical analyses. Yao et al (70, 71) assessed the within and between day reliability of the Pea Pod® in 17 infants and found no significant difference

Statistical Analysis

Simple and multiple linear regression models were used to examine the relationship between maternal fat patterning (central vs. peripheral) and infant body composition. The following confounding variables were explored in the model: maternal age, parity, race, maternal GWG, maternal weight loss 2 weeks postpartum, SES, infant GA, infant age at testing and infant gender. For the SES covariate, dummy variables were created with a high school education only or less as the reference group. To explore the effects of maternal race, dummy variables were created with Caucasian as the reference group. Only significant confounding variables were retained in the final model. Hierarchical step-wise modeling was used to remove non-significant confounding variables. All analyses were conducted using the Statistical Package for the Social Sciences (SPSS for Windows, version 20; SPSS, Chicago,
For tests of significance, $p<0.05$ was used.

**Aim 1:** Maternal central fat is related to infant body composition (%fat, FM, and FFM).

Statistical analyses: Simple and multiple linear regression models assessed the relationship between maternal central FM and infant %fat, FM and FFM. The dependent variable was the respective infant body composition parameter (%fat, FM, FFM) and the independent variable was maternal central FM.

**Aim 2:** Maternal peripheral fat is related to infant body composition (%fat, FM, and FFM).

Statistical analyses: Simple and multiple linear regression models assessed the relationship between maternal peripheral FM and infant %fat, FM and FFM. The dependent variable was the respective infant body composition parameter (%fat, FM, FFM) and the independent variable was maternal peripheral FM.

**Database Categories**

The final list of categories included in the database is as follows:

1. Maternal central FM (trunk)
2. Maternal peripheral FM (arms and legs)
3. Maternal age
4. Maternal race
5. Maternal GWG
6. Maternal weight loss during 2 weeks
7. Maternal parity
8. Maternal socioeconomic status (SES)
9. Infant birth weight
10. Infant gestational age (GA)
11. Infant age at testing
12. Infant gender
13. Infant FM
14. Infant FFM
15. Infant %fat
Chapter 4

RESULTS

This study was designed to determine whether maternal central fat and peripheral fat were related to infant body composition (%fat, FM, FFM).

Subject Characteristics

A total of 38 mother-infant pairs were recruited for the study. Table 1 presents the maternal characteristics. Women in this study had a mean age of 28.9 yrs., a mean pre-BMI of 25.1 kg/m², and a mean GWG of 16 kg. Maternal pre-BMI distribution is presented in Figure 1. Over half of the women in the study were normal. The average maternal central fat was 13.8 kg and peripheral fat was 14.3 kg at 2 weeks postpartum. The majority of women were Caucasian. Infant characteristics are presented in Table 2.

Figure 2. Maternal Pre-BMI Distribution
<table>
<thead>
<tr>
<th>Maternal Characteristics</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>28.9 ± 5.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165.1 ± 6.7</td>
</tr>
<tr>
<td>Pre-BMI (kg/m^2)</td>
<td>25.1 ± 4.9</td>
</tr>
<tr>
<td>GWG (kg)</td>
<td>16.0 ± 6.5</td>
</tr>
<tr>
<td>Weight Loss 2 weeks postpartum (kg)</td>
<td>9.1 ± 3.4</td>
</tr>
<tr>
<td>Highest Weight During Pregnancy (kg)</td>
<td>84.5 ± 14.7</td>
</tr>
<tr>
<td>Pre-pregnancy weight (kg)</td>
<td>68.5 ± 14.6</td>
</tr>
<tr>
<td>Total Fat Mass (kg)</td>
<td>28.9 ± 9.9</td>
</tr>
<tr>
<td>Central Fat Mass (kg)</td>
<td>13.8 ± 4.8</td>
</tr>
<tr>
<td>Peripheral Fat Mass (kg)</td>
<td>14.3 ± 5.4</td>
</tr>
<tr>
<td>Race</td>
<td>N (%)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>29 (76.3)</td>
</tr>
<tr>
<td>African American</td>
<td>6 (15.8)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3 (7.9)</td>
</tr>
<tr>
<td>SES</td>
<td>N (%)</td>
</tr>
<tr>
<td>High School</td>
<td>8 (21.1)</td>
</tr>
<tr>
<td>Some College</td>
<td>9 (23.7)</td>
</tr>
<tr>
<td>4-year College</td>
<td>18 (47.4)</td>
</tr>
<tr>
<td>Graduate School</td>
<td>3 (7.9)</td>
</tr>
<tr>
<td>Parity</td>
<td>N (%)</td>
</tr>
<tr>
<td>Nulliparous, n (%)</td>
<td>14 (36.8)</td>
</tr>
</tbody>
</table>
Table 2: Infant Characteristics and body composition measurements (n=38)

<table>
<thead>
<tr>
<th>Infant Characteristics</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (wks)</td>
<td>0.3 ± 0.1</td>
</tr>
<tr>
<td>GA (wks)</td>
<td>39.6 ± 0.9</td>
</tr>
<tr>
<td>Birth Weight (g)</td>
<td>3438.9 ± 448.2</td>
</tr>
<tr>
<td>Length at Birth (cm)</td>
<td>51.2 ± 3.1</td>
</tr>
<tr>
<td>Head Circumferences (cm)</td>
<td>34.4 ± 1.6</td>
</tr>
<tr>
<td>Percentage Body mass (%)</td>
<td>10.6 ± 4.8</td>
</tr>
<tr>
<td>Fat Mass (g)</td>
<td>351.2 ± 191.7</td>
</tr>
<tr>
<td>Fat Free Mass (g)</td>
<td>2871.0 ± 320.4</td>
</tr>
<tr>
<td>Female</td>
<td>42.1%</td>
</tr>
<tr>
<td>Male</td>
<td>57.9%</td>
</tr>
</tbody>
</table>

Predictors of Infant Body Composition without covariates

Initial regression analyses were conducted using only maternal central and peripheral FM as predictor variables. Maternal central FM was not related to infant body composition. Results from the full model with both maternal central and peripheral FM as independent variables are summarized in Table 3. Next, maternal central FM was removed leaving maternal peripheral FM in the model. In this analysis, maternal peripheral FM was related to infant FM ($\beta=11.607$, $p=0.045$). In addition, maternal peripheral FM had a borderline significance with infant %fat ($\beta=0.276$, $p=0.055$). No relationship was found with infant FFM. These results are summarized in Table 4.
Multiple stepwise regression analysis was conducted including the following covariates: maternal age, parity, SES, race, weight loss 2 weeks postpartum, infant gender, infant age at test, infant GA. Maternal central and peripheral FM were the independent variables and infant body composition variables were the dependent variables. Results for infant body composition are presented in the following tables: infant %fat (Table 5), infant FM (Table 6), infant FFM (Table 7).

### Table 3. Predicting Infant body composition from maternal central and peripheral FM without covariates

<table>
<thead>
<tr>
<th>Maternal Central FM (kg)</th>
<th>Infant %fat</th>
<th>Infant FM</th>
<th>Infant FFM</th>
</tr>
</thead>
<tbody>
<tr>
<td>β</td>
<td>p</td>
<td>β</td>
<td>p</td>
</tr>
<tr>
<td>-0.02</td>
<td>0.958</td>
<td>2.13</td>
<td>0.875</td>
</tr>
<tr>
<td>Maternal Peripheral FM (kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β</td>
<td>p</td>
<td>β</td>
<td>p</td>
</tr>
<tr>
<td>0.29</td>
<td>0.334</td>
<td>9.95</td>
<td>0.407</td>
</tr>
</tbody>
</table>

*p<0.05 considered as significant.

### Table 4. Predicting Infant body composition from peripheral FM without covariates

<table>
<thead>
<tr>
<th>Maternal Peripheral FM (kg)</th>
<th>Infant %fat</th>
<th>Infant FM</th>
<th>Infant FFM</th>
</tr>
</thead>
<tbody>
<tr>
<td>β</td>
<td>p</td>
<td>β</td>
<td>p</td>
</tr>
<tr>
<td>0.28</td>
<td>0.055</td>
<td>11.61</td>
<td>0.045*</td>
</tr>
</tbody>
</table>

* *p<0.05. p<0.05 considered as significant.

### Predictors of Infant Body Composition including Covariates

Multiple stepwise regression analysis was conducted including the following covariates: maternal age, parity, SES, race, weight loss 2 weeks postpartum, infant gender, infant age at test, infant GA. Maternal central and peripheral FM were the independent variables and infant body composition variables were the dependent variables. Results for infant body composition are presented in the following tables: infant %fat (Table 5), infant FM (Table 6), infant FFM (Table 7).
When predicting infant %fat, the following relationships were found: maternal central fat mass ($\beta= 0.43$, $p=0.011$), maternal age ($\beta= -0.36$, $p=0.022$), and differences by SES level. The SES level relationships found were for mothers who completed some college ($\beta= 4.19$, $p=0.033$) or a 4-year degree ($\beta= 4.27$, $p=0.041$). These results are summarized in Table 5.

### Table 5. Predicting infant %fat from maternal central and peripheral FM with covariates (adjusted $R^2=0.18$).

<table>
<thead>
<tr>
<th></th>
<th>$\beta$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Central FM</td>
<td>0.43</td>
<td>0.011</td>
</tr>
<tr>
<td>Maternal Age</td>
<td>-0.36</td>
<td>0.022</td>
</tr>
<tr>
<td>High school vs. 4-year college</td>
<td>4.19</td>
<td>0.033</td>
</tr>
<tr>
<td>High school vs. some college</td>
<td>4.27</td>
<td>0.041</td>
</tr>
</tbody>
</table>

$p<0.05$ considered as significant.
Covariates included maternal age, parity, GWG, weight loss 2 weeks postpartum, SES, infant GA, infant age at test, gender.

When predicting infant FM, the following variables were predictors: maternal peripheral FM ($\beta= 13.75$, $p=0.009$) maternal weight loss 2 weeks postpartum ($\beta= 16.60$, $p=0.041$), mother’s with some college education ($\beta= 225.94$, $p=0.028$), and infant age at test ($\beta= -761.74$, $p=0.019$). These results are summarized in Table 6.

### Table 6. Predicting infant FM from maternal central and peripheral FM with covariates (adjusted $R^2=0.30$).

<table>
<thead>
<tr>
<th></th>
<th>$\beta$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Peripheral FM</td>
<td>13.75</td>
<td>0.009</td>
</tr>
<tr>
<td>Maternal Weight Loss 2 weeks postpartum (kg)</td>
<td>16.60</td>
<td>0.041</td>
</tr>
<tr>
<td>Caucasian vs. Hispanic</td>
<td>225.94</td>
<td>0.028</td>
</tr>
<tr>
<td>Infant Age at Test</td>
<td>-761.74</td>
<td>0.019</td>
</tr>
</tbody>
</table>

$p<0.05$ considered as significant.
Covariates included maternal age, parity, GWG, weight loss 2 weeks postpartum, SES, infant GA, infant age at test, gender.
Lastly, in the analysis of infant FFM only maternal age (β = 22.33, p = 0.023), maternal weight loss 2 weeks postpartum (β = 35.47, p = 0.022) and infant GA (β = 137.16, p = 0.016) were significant. These results are summarized in Table 7.

<table>
<thead>
<tr>
<th></th>
<th>β</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Weight Loss 2 weeks postpartum</td>
<td>35.47</td>
<td>0.022</td>
</tr>
<tr>
<td>Maternal Age</td>
<td>22.33</td>
<td>0.023</td>
</tr>
<tr>
<td>Infant GA</td>
<td>137.16</td>
<td>0.016</td>
</tr>
</tbody>
</table>

p<0.05 considered as significant. Covariates included maternal age, parity, GWG, weight loss 2 weeks postpartum, SES, infant GA, infant age at test, gender.
Chapter 5
Discussion
Overview

Previous studies have examined correlations between maternal pre-BMI, GWG, and maternal body composition and infant body composition (11, 12, 43-45, 57). This is the first study to examine data from quantified maternal fat patterning (central vs. peripheral FM) in relation to infant body composition.

In the current study, using simple regression we found that maternal peripheral FM was related to infant FM and borderline significant to infant %fat. However, after including maternal and infant covariates, maternal central FM predicted infant %fat while maternal peripheral FM predicted infant FM.

Our findings between maternal central FM and infant %fat were in line with previous reports (14, 15, 58). Although no studies have examined maternal central fat and infant body composition directly, three studies showed consistent results with a positive relationship between maternal central fat and infant birth weight (14, 15, 58). This correlation might be explained by glucose intolerance and insulin resistance in pregnant women. Women with higher central fat tend to have greater insulin resistance, higher plasma concentrations of blood glucose and free fatty acids in the plasma regardless of pregnancy (74, 75). Plasma glucose and free fatty acids are the principle energy source supplying nutrients for fetal growth and can be freely transferred to the fetus, and thus increase the energy accumulation and stimulate fetal hyperinsulinemia and macrosomia (76). Infant %fat, in addition to birth weight, was also significantly related to maternal fasting glucose (77).

The mechanism that links maternal central FM to infant %fat might be complex and hyperglycemia is just one of several factors that may explain the association. In addition to its
association with birth weight and %fat, maternal central fat was a significant independent predictor of their children’s metabolic syndrome when adjusted for mothers total triglycerides, cholesterol, and glucose and age (OR, 2.11, 95% CI, 1.36-2.36) (78). This may indicate fetal programming of central fat distribution and high prevalence of metabolic syndrome in the offspring.

The association between maternal peripheral fat and infant body composition has received little study. The only previous study was conducted by Jovanovic-Peterson et al (16) in 20 women with gestational diabetes. They found that peripheral FM (fat in the upper arm) rather than central FM (truncal) using MRI had a stronger relationship with fetal weight (r=0.59, p=0.05) and birth weight ratio (birth weight ratio defined as the actual birth weight divided by the 50th percentile birth weight for the infant’s GA and gender, r=0.68, p=0.001). These findings were inconsistent with previous hypotheses that maternal central body fat was associated with a number of metabolic changes that might influence fetal growth and birth weight. It’s not clear what component of maternal body composition influences fetal FM accumulation. Whether it is subcutaneous fat itself or whether peripheral FM is a surrogate marker of maternal hydration, protein stores or correlated with visceral fat or some other maternal body component is unknown. The links between maternal fat distribution and infant body composition are not completely understood and further research is needed.

Although previous studies confirmed that GWG is an independent determinant of infant body composition, we found no evidence for an effect of GWG on infant %fat, FM, or FFM when taking into account maternal central and peripheral FM. These differentiated effects illustrate that GWG might be closely correlated with maternal peripheral and central FM and could be used interchangeably in predicting infant body composition. Thus, including both GWG and maternal fat distribution in the same model might explain why we did not find any significant results. We also chose not to include maternal pre-BMI in the final analysis as a
potential confounder in the relation between maternal fat patterning and infant body composition. This decision was based on two reasons. First, the majority of women in our study were in the normal BMI category (73.7% were normal). Second, maternal pre-BMI is often used as a surrogate marker for maternal body fat and preliminary analysis showed maternal pre-BMI has stronger and more consistent associations with maternal central and peripheral FM (data not shown).

A reasonable consideration is whether our data reflect maternal race or SES differences that may be driving the relationships with infant body composition rather than absolute maternal fat patterning. Studies have previously shown clear differences in adiposity distributions, but not total FM, between Caucasians and south-Asian Indian babies (46). In this study, we found a significant difference in infant FM between Caucasians and Hispanic babies. However, we acknowledge that distribution across racial groups was unbalanced (76% Caucasians) and this correlation needs to be further assessed.

**Limitations**

This study has a few unavoidable limitations. First, this was an observational study and therefore cannot assess causal relationships. In addition, due to the design of the parent study, only a small number of overweight and obese women were recruited. We are unable to explore these relationships in different pre-BMI groups, thus we cannot conclude that there are no differences among women in different pre-BMI categories.

We are also aware that DXA can differentiate fat location as central and peripheral, but cannot distinguish subcutaneous and visceral fat. Women with central obesity may have different proportions of visceral fat and subcutaneous fat. Those who have more visceral fat may have higher disease risk than those who have more subcutaneous fat even though located in the central region (79)
Chapter 6

SUMMARY

Obesity is a major health concern for pregnant women. The obesity prevalence in women of childbearing age remains high in the past few decades (1). Previous studies have shown that obese women not only have higher risks for gestational diabetes, preeclampsia, and higher rates of C-section during pregnancy (4, 5), but obesity in pregnancy is also related to excessive fetal growth and later offspring disease development (6-8). Maternal central fat distribution, in addition to maternal pre-BMI, GWG and maternal body composition, has been found to be an independent risk factor for LGA and a macrosomic infant (13-15).

This study is a secondary analysis from an ongoing observational cohort study. It was aimed to examine the correlation between maternal fat distribution and infant body composition (%fat, FM, and FFM) at birth. We collected data from 38 pregnant women and their babies. Maternal central FM and peripheral FM were measured by DXA at 2 weeks postpartum. Infant body composition and other anthropometrics were measured by the Pea Pod at 1-3 days after birth.

Our data suggest that maternal central FM was a significant predictor for infant %fat while maternal peripheral FM was significantly correlated with infant FM. Those findings suggest several biological pathways by which increasing maternal central FM might initiate an adverse health outcome in offspring and may help to explain the epidemiological associations with metabolic complications and obesity in later life.

Future directions including precise measurements of visceral and subcutaneous fat and their influence on infant body composition are warranted. More comprehensive research should also assess maternal body distribution, plasma levels of glucose and triglycerides and fetal growth or infant body composition. This might be helpful in evaluating the possible mechanisms between maternal body fat distributions and fetal growth and later disease
development.
References


