

COMPARISON OF MAGNETIC RESONANCE IMAGING ABDOMINAL
ADIPOSIY AND BODY COMPOSITION IN PRETERM
AND TERM INFANTS

by

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STATEMENT OF THESIS APPROVAL

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ABSTRACT

Recent neonatal research suggests a causal pathway between premature birth, altered fat deposition, and metabolic disease later in life. Specifically, one study reported that preterm infants display altered adiposity with greater visceral adiposity at term-corrected age than term infants. In adults, increased visceral adiposity is associated with glucose intolerance independent of obesity. Therefore, identification of clinical measures of visceral adiposity may improve identification of at-risk infants. We measured anthropometrics, air displacement plethysmography, and visceral and subcutaneous tissue volumes using magnetic resonance imaging in preterm infants (n=12) born at <34 weeks gestational age at hospital discharge, and in term-born infants (n=12).

Our data provide evidence of increased total and visceral adiposity by magnetic resonance imaging in preterm infants. Preterm infants had significantly greater percent body fat by air displacement plethysmography ($p < 0.001$) with higher total ($p < 0.001$) and visceral adiposity ($p = 0.01$) by magnetic resonance imaging at hospital discharge, as compared to term infants. Preterm infant visceral adiposity, when measured by magnetic resonance imaging, was correlated with weight ($r = 0.70$, $p = 0.04$), length ($r = 0.77$, $p = 0.02$), head circumference ($r = 0.75$, $p = 0.02$), mid-arm circumference ($r = 0.72$, $p = 0.03$), subscapular skinfold thickness ($r = 0.86$, $p = 0.003$), and suprailiac skinfold thickness ($r = 0.73$, $p = 0.03$). Overall, the study results indicate that low-cost

anthropometric measures correlate with total, visceral, and subcutaneous adipose tissue by magnetic resonance imaging in preterm infants. Furthermore, these data provide preliminary findings to support the development of regression equations to identify preterm infants at risk of metabolic complications later in life.

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INTRODUCTION

Background/Literature Review

Preterm birth is defined as infants born prior to 37 weeks gestation, as compared to infants born at full-term gestation of 37-42 weeks.¹ In the United States, the preterm birth rate declined from 12.18% in 2009 to 11.99% in 2010.² Recent vital record data indicated a downward trend from 2007 to 2010.² Infants born late preterm (34-36 weeks) account for the current decline; meanwhile, the percent of infants born early preterm (<34 weeks) has remained higher than at any year from 1981 through 2001.² Premature births impact all ethnic groups, with the highest rate among non-Hispanic blacks at 17.47%.² Those infants who survive premature birth have higher rates of morbidity. Acute health consequences include glucose instability, fat malabsorption, apnea, brain injury, and respiratory problems. Long-term consequences include asthma, cerebral palsy, learning disabilities, severe mental retardation, altered adiposity, and impaired vision and hearing.^{1,3,4}

The current nutrition recommendation for preterm infants is to provide adequate intake for catch-up growth.⁵ This accelerated growth is typically achieved through increases in both protein and calories.⁵ Those infants who receive increased protein and calories during the first 3-10 days of life have better long-term neurodevelopmental outcomes.⁶ However, preterm infants with rapid catch-up growth also have higher rates

of cardiovascular disease in later life.⁵ Therefore, those infants who experience increased weight gain in the first weeks of life may still be at risk for later disease.

Recent research has provided evidence of a causal pathway between accelerated postnatal growth and increased total and subcutaneous adiposity in the preterm infant.^{4,7,8} In addition, preterm infants at hospital discharge were found to have altered adiposity with increased visceral adipose tissue (VAT) and decreased subcutaneous adipose tissue (SAT).⁴ In adults, increases in VAT are associated with dyslipidemia and insulin resistance, markers of chronic metabolic disease.⁴ Similarly, visceral fat deposition that develops as a consequence of accelerated postnatal growth may prove to be a marker for preterm infant propensity to later overt disease. The ability to determine body composition and fat distribution in the preterm infant may aid health professionals in identifying those infants at highest risk of later-life disease, thus improving preventative care. Further, accurate assessment of body fatness and distribution may help health professionals modify feeding protocol through macronutrient adjustment, thereby regulating the rate of premature growth.

Currently, nonradiation methods available for assessing body composition in infants include air displacement plethysmography (ADP), magnetic resonance imaging (MRI), and anthropometric measurements, including weight, length, head circumference, and skinfolds. MRI provides the benefit of differentiation between adipose depots. However, it is not routinely used due to high cost and low availability. Anthropometric measurements are commonly used because of ease of administration and low cost. ADP measures the subject's mass and volume to calculate body fat percentage (%BF). The infant ADP system (PEA POD®, LMI, Concord, CA) is specifically made to measure the

body composition of infants and provides the advantage of being portable, radiation free, and requires minimal training to obtain accurate measurements. It is a convenient and readily accessible method for measuring the body composition of infants.

Significance of Problem

Preterm births account for 11.99% of all U.S. births (>500,000 annually, 2010).² These preterm infants (<37 weeks gestation) often spend the first weeks of life in newborn intensive care units where they are faced with physiologic and environmental stressors.^{4,9-11} Several studies have shown an association between early life stress and the development of cardiovascular and metabolic disease in later life.¹²⁻¹⁵ For example, Barker et al. (1989)¹² documented an association between intrauterine environment and high blood pressure in adult life. Barker and colleagues (2000)¹³ stated that growth restraint of the female fetus affected the physiology and metabolism of her later offspring. Additionally, Boloker et al. (2002)¹⁴ documented that the offspring of gestational diabetic mothers had an increased risk for obesity, glucose intolerance, and type 2 diabetes in later childhood and as adults. Lastly, an animal study conducted by Langley-Evans et al. (2010)¹⁵ observed that pregnant rodents fed an obesity-inducing hyper-caloric diet produced offspring with disturbed glucose and lipid homeostasis. Consequently, there is concern that the stressors, feeding practices, and metabolic changes experienced by preterm infants may have harmful effects on health in later life.

Recent research indicates that greater abdominal VAT depot in early life may lead to later cardiovascular and metabolic consequences. Hovi et al. (2007)¹¹ reported increased rates of hypertension and glucose intolerance in nonobese preterm children and young adults. A study conducted by Wajchenberg et al. (2002)¹⁶ indicated that regardless

of whether an individual is obese, higher VAT is associated with hypertension and glucose intolerance. Uthaya et al. (2005)⁴ observed that abdominal VAT is 50% higher in preterm infants when measured at 38 weeks gestation, as compared to term-born infants. Together, these studies indicate a propensity of abdominal VAT leading to later disease.

Preterm infant growth and nutritional status have traditionally been measured using anthropometric data, including weight, length, head circumference, skinfold, and arm circumference. These measures are inexpensive and rapid.¹⁷ New technology known as ADP now provides a portable, radiation-free method of measuring total body fat. Although this methodology is safe, precise, and relatively low cost, it is not able to differentiate between the two distinct body fat depots, SAT, located under the skin, and VAT, which surrounds the organs within the abdominal cavity. MRI is able to differentiate between adipose tissue depots. Similar to ADP, MRI is noninvasive and radiation free. However, the disadvantages of MRI include high cost and limited availability.⁴

Research Aims

The aims of this study were two-fold: 1) to compare MRI abdominal VAT depot between preterm infants born 28 to 34 weeks gestation at hospital discharge and full-term infants and 2) to test the strength of relationships between MRI abdominal VAT depot to measured and derived anthropometry, and body fat by ADP in preterm and term infants. The data for this analysis are a subset of data from the study entitled, “Prediction of magnetic resonance imaging-derived visceral adipose tissue by standard anthropometry in preterm infants.”

METHODS

Research Design

This research is a comparative study in which the body composition of preterm infants and term infants were assessed at hospital discharge. The study examined the relationship between MRI abdominal VAT deposition, measured and derived anthropometry, and body fat by ADP. Study measures included body composition by MRI and ADP. Anthropometric measures of body weight, length, head circumference, abdominal circumference, mid-arm circumference, and mid-thigh circumference were collected. Skinfolds measurements were assessed at the bicep, tricep, subscapular, and suprailiac sites. Data including weight, length, head circumference, medical history, dietary intake, and medications were obtained from the infant's electronic medical record in PowerChart® (Cerner, Kansas City, MO). Maternal medical data were obtained via a maternal history questionnaire (Appendix A). Clinical status was obtained from the infant's bedside nurse. The study protocol was approved by the University of Utah Institutional Review Board for Human Subjects.

Subject Selection Criteria

Study participants were recruited from February 2012 to March 2013. Premature (n=12) and full-term (n=12) infants admitted to the University of Utah Hospital NICU or Well Baby Nursery, and born between 28 0/7 and 34 0/7 weeks or 38 0/7 weeks and 42 0/7 weeks gestation, respectively, by maternal dates, midpregnancy fetal ultrasound, and

physical exam at birth and with birth weight, length, and head circumference between the 7th to 90th percentiles (NCHS growth curve) for gestational age were included in the study.

Preterm infant exclusion criteria include gestational age < 28 0/7 weeks and > 34 0/7 weeks at gestation birth, birth weight <10th or >90th percentile, chromosomal abnormalities, major congenital anomalies, major surgery, severe CNS injury, inborn errors of metabolism, infants born to diabetic mothers, or any other condition known to interfere with postnatal growth. However, one preterm infant with weight at the 7th percentile was included. Full-term infant exclusion criteria include gestational age < 38 0/7 weeks and > 42 0/7 weeks gestation at birth, and all other factors described for preterm infants above.

Screening Process

Infants were screened for study eligibility within 24 hours of delivery and up to 2 days prior to discharge. The research coordinator identified infants that met inclusion criteria. Attending physician approval was obtained for preterm infants. Parents were then approached, and asked if they had interest in participating in the study. Participating parents were asked to read the consent form and all questions were answered. Written, informed consent was then obtained from one parent, with a study coordinator or a research assistant acting as witness. A copy of the consent form was given to the parent(s) prior to study measurements. Measurements for term and preterm infants were completed 24-48 hours prior to discharge with each infant receiving all measurements within a 24-hour period. Subjects were compensated with a \$25 gift card upon completion of all measurements.

Data Collection

Maternal History Questionnaire

The maternal history questionnaire was completed by the parent at the time of consent. The questionnaire assessed socio-demographic data, including age, ethnicity, marital status, and education level. Anthropometric and health history data included maternal birth weight, prepregnancy weight, predelivery weight, and number of past pregnancies. Additionally, current medical conditions, medications taken during pregnancy, and soy products consumed were addressed as well as paternal age, weight, and height.

Anthropometry and Skinfolds

Body weight (gm) was measured to the nearest 1 gm on a digital electronic scale using the PEA POD (COSMED, formerly Life Measurements Inc., Concord, CA). Infant length (cm) was measured to the nearest 0.1 cm in triplicate using an infant length board (Seca, United Kingdom). Infant head circumference was assessed at the largest occipital frontal circumference. Abdominal circumference was obtained just above the umbilicus with the infant lying in a supine position. Both mid-arm and mid-thigh circumferences were measured on the left limb with the infant lying on the right side. Infant head, abdominal, mid-arm, and mid-thigh circumferences (cm) were each evaluated to the nearest 0.1 cm in triplicate using a vinyl-coated retractable measuring tape with the final value calculated as the average of the three measurements. Triceps, biceps, suprailiac, and subscapular skinfold thicknesses were taken in triplicate using Lange skinfold calipers (Beta Technology, Santa Cruz, CA).

Air Displacement Plethysmography (ADP)

Body composition by ADP utilizes the inverse relationship between volume and pressure in two enclosed chambers to determine whole body density. Data were obtained via the PEA POD (COSMED, formerly Life Measurements Inc., Concord, CA). A two-compartment model used whole body density to calculate fat and fat-free mass percentages. This measurement took approximately 5 minutes. The infant was placed in the PEA POD measurement tray and slid into the measurement compartment. A clear Plexiglas window in the measurement compartment kept the infant in constant visual range of study personnel (technician and nurse) during the measurement period. Once the door was closed, automatic volume calibration began while subject biographical information was entered into the software. Upon conclusion of the first calibration, infant mass (weight) and body volume were measured. Immediately following, fat and fat-free percentage results were tabulated by the software and displayed on the monitor. Test results were printed, entered into the master data files, and stored in the patient's study binder. Measurements were conducted in duplicate with total body fat calculated as an average of these two measurements. A third measurement by ADP was taken if body fat percentage varied by greater than 2% between measurements.

Abdominal MRI

Quantification of total abdominal adipose tissue (TAT), VAT, and SAT was performed with MRI (Siemens scanner, Siemens Corporation, New York, NY). MRI scans were conducted in the University Hospital Department of Radiology Imaging Center just prior to infant hospital discharge. Time within the MRI scanner was < 20 minutes/subject. An experienced, neonatal research nurse accompanied all study infants

to the Imaging Center and was present during the MRI procedure. To minimize difficulties related to infant agitation or restlessness, a standard infant protocol was followed with use of a small amount of sugar water and a pacifier to induce sleep, a positioning device, swaddling, and protective headphones to minimize noise.

Analysis of MRI images was conducted by a practicing board certified radiologist. A sagittal T2-weighted turbo-spin-echo sequence was used to create images of the thoracolumbar spine. Axial gradient recalled echo (GRE) images at three different echo times were then obtained at 1cm intervals encompassing the abdomen and pelvis. Separate fat and water images were created using a three-point Dixon method with phase unwrapping by iterative solution of the Poisson equation.^{18,19} The GRE signal equation and a tissue signal model were then applied to create pixel-by-pixel estimates of fat volume fraction.²⁰ The resulting fat-volume fraction images were then analyzed using Scion Image (NIH). The axial image closest to the L4-5 level of the lumbar spine, as determined by correlation with the sagittal spine images, was analyzed. In most subjects, this level also corresponded to the level of the umbilicus. The validity of a single axial image at L4-5 as a proxy for measurement of abdominal fat over the entire abdomen has been established in adults and in children.^{21,22} Two regions of interest were defined on the L4-5 axial fat volume fraction image, one encompassing the entire abdomen and the other defining the abdominal wall. The fat fraction values of all of the pixels in the ROI's were summed and multiplied by the pixel area to give a total effective fat cross-section area at L4-5 for total fat, intraabdominal fat, and extraabdominal (subcutaneous) fat. Data were also analyzed by a thresholding method in which each pixel with a fat volume fraction greater than 25% was counted as fat. The thresholding method was not used for analysis

due to its ambiguous nature when differentiating between VAT and SAT. It is important to note that when data were analyzed using this method, no significant differences were seen between groups when comparing TAT, VAT, and SAT by MRI.

Dietary Intake and Medications

Dietary intake was obtained from the electronic medical record, and data including source (IV and/or enteral), type (dextrose solution, human milk, or commercial formula), fluid volume, and energy/nutrient intake calculations. Medication was tracked to identify exposure to medications that may have impacted postnatal growth (caffeine, glucocorticoids).

Infant Clinical Status

The infant's current clinical status and physiologic stability was obtained from the infant's bedside nurse prior to any study-related measurements or procedures. Questions included presence of acute illness or infection, temperature instability, apnea and bradycardia episodes, supplemental oxygen requirement, evidence of enteral feeding intolerance, and anemia. The attending physician or assigned neonatal nurse practitioner was consulted prior to all infant measurements. Infants displaying questionable physiologic stability were not measured until ready for discharge. Measurements were conducted when the infant could maintain body temperature, and all feeds were ad lib by mouth.

Statistical Measures, Data Analysis, and Interpretation

The hypothesis that MRI abdominal VAT depot was greater in infants born preterm at hospital discharge when compared to infants born full term was tested by ANOVA with gender and gestational age treated as cofactors.^{23,24} For the main study,

“Prediction of magnetic resonance imaging-derived visceral adipose tissue by standard anthropometry in preterm infants,” a power analysis was conducted. Given an estimated effect size of 1.8 for VAT depot between preterm vs. term infants, the sample size of 24 preterm and 12 term infants was calculated as sufficient to detect significance with a power = 0.90 and $p < 0.01$. Therefore, the data for this analysis represent preliminary findings. The relationship between MRI SAT and abdominal VAT depot, measured and derived anthropometry, and body fat by ADP in preterm infants and term infants at hospital discharge was measured by Spearman’s correlation with $0.5 < r < 0.7$ considered a moderate correlation, $r > 0.7$ considered a strong correlation, and $p \leq 0.05$ considered significant.²⁵ To achieve this aim, we recruited 12 preterm (28-34 weeks at birth) infants to perform a one-time measure of VAT by MRI and body fat by anthropometry and ADP at discharge (34-40 weeks). Statistical analyses were conducted with SPSS (SPSS, Version 20, SPSS Inc., Chicago, IL).

RESULTS

Maternal characteristics for both preterm and term infants are presented in Table 1. No significant differences were found between the two cohorts for maternal age. Mothers of preterm infants reported a greater number of pregnancies ($p = 0.01$) and living children ($p = 0.005$), as compared to those of term infants. Additionally, a comparison between the two cohorts found no significant difference in maternal pre-pregnancy BMI. Though not significant, more preterm mothers ($n = 6$, 50%) were either overweight ($25.0 \text{ kg/m}^2 < \text{BMI} < 29.9 \text{ kg/m}^2$) or obese ($\text{BMI} > 30.0 \text{ kg/m}^2$) as compared to term mothers (33%, $n = 4$). Mothers ($n = 12$) of preterm infants reported lower

Table 1
Characteristics of Mothers of Preterm and Term Infants.¹

Variable	Preterm infants n = 12	Term infants n = 12
Maternal age (years)	29.2 ± 4.67	26.67 ± 5.76
Gravida (number of pregnancies)	3.17 ± 1.70*	1.58 ± 0.90
Para (number of living children)	2.92 ± 1.50*	1.42 ± 0.67
Prepregnancy body mass index (kg/m ²)	26.80 ± 6.38	24.76 ± 5.99
Prepregnancy weight (kg)	73.49 ± 16.21	64.99 ± 15.14
Total pregnancy weight gain (kg)	10.00 ± 9.67*	17.97 ± 4.57
Number of mothers that took prenatal vitamins	11	10
Physical activity before pregnancy (days per week)	3.50 ± 2.32	2.92 ± 1.73
Physical activity during pregnancy (days per week)	1.58 ± 2.02	2.21 ± 2.76

¹All values are means ± SDs, *significantly different from term infants, $p < 0.02$

maternal weight gain ($p = 0.02$) than mothers of term infants. Regarding prenatal vitamin intake, the frequency of intake by mothers in both groups was comparable. Lastly, physical activity levels, expressed in days per week, were similar for the cohorts both before and during pregnancy. Further maternal history and infant feeding results of this study will be described in an article by Browning et al.

The demographic information for the preterm ($n = 12$) and term ($n = 12$) infants participating in the study are detailed in Table 2. Male subjects represented half the preterm population ($n = 6$ M, 50%) and slightly greater than half of the term sample population ($n = 7$ M, 58%). Mean gestational age at birth was 32.18 weeks ($SD = 1.72$) in preterm infants, as compared to 39.96 weeks ($SD = 1.11$) in term infants. Regarding birth weight, 92% of preterm ($n = 11$) were appropriate for gestational age (AGA), and 100% of the term infants ($n = 12$) were AGA. Non-Hispanic white infants ($n = 20$) represented 83% of the sample population, with infants of Hispanic ethnicity ($n = 4$) as the remaining 17%. At the time of measurement, postmenstrual age was significantly lower ($n = 12$, $p < 0.001$) in preterm infants ($M = 37.21$ weeks, $SD = 1.48$ weeks) than term infants ($M = 40.28$, $SD = 1.10$ weeks). No significant differences were found between the cohorts for weight, length, and head circumference. Preterm infants as compared to term infants had a significantly lower mid-arm circumference and mid-thigh circumference ($p = 0.004$) when adjusting for corrected gestational age at the time of measurement. No significant differences were found in abdominal circumference when adjusting for corrected gestational age. However, the total body fat percentage by ADP was significantly higher in preterm infants ($n = 9$, $M = 17.72\%$, $SD = 5.64\%$), as compared to term infants ($n = 12$, $M = 8.42\%$, $SD = 3.43\%$, $p < 0.001$). Additionally,

Table 2
 Characteristics of Preterm and Term Infants at Hospital Discharge¹

Variable	Preterm Infants n = 12	Term Infants n = 12
Number of infants	12	12
Number of male subjects	6	7
Gestational Age, birth (PMA weeks)	32.18 ± 1.72	39.96 ± 1.11
Number of non-Hispanic white	11	9
Number of Hispanic	1	3
At time of measurement		
Postmenstrual Age	37.21 ± 1.48*	40.28 ± 1.10
Weight (kg)	2.80 ± 0.49	3.16 ± 0.29
Length (cm)	47.20 ± 1.99	49.63 ± 1.49
Head circumference (cm)	33.29 ± 1.36	34.56 ± 0.29
Mid-arm circumference (cm)	9.51 ± 1.08*	10.16 ± 0.18
Mid-thigh circumference (cm)	14.15 ± 2.16*	14.70 ± 1.46
Abdominal circumference (cm)	29.65 ± 1.92	29.36 ± 0.49
ADP Body Fat %	17.72 ± 5.64*	8.55 ± 3.25
BMI (kg/m ²)	12.41 ± 1.53*	12.75 ± 1.06
Ponderal index (kg/m ³)	26.19 ± 2.84	25.65 ± 2.37

¹All values are means ± SDs unless otherwise noted.

*Significantly different from term infants, $p < 0.05$

when adjusting for corrected gestational age at the time of measurement, preterm infants had significantly higher BMI when compared to term infants ($n = 12$, $M = 12.41$ kg/m², $SD = 1.53$ kg/m², $p = 0.02$). No significant differences were found between preterm and term infants for ponderal index. Regarding gender differences, no significant differences were found between males and females in the preterm group. Within the term group, the gestational age at birth was significantly lower for male infants ($M = 39.38$ weeks, $SD = 1.06$ weeks) than female infants ($M = 40.77$ weeks, $SD = 0.54$ weeks, $p = 0.03$ weeks).

During the first week of life, 100% ($n = 12$) of preterm infants received a combination of enteral and parenteral feeds. At discharge, 67% ($n = 8$) of preterm infants

were given fortified breast milk with the remainder receiving formula (n = 4, 33%). Term infants were all exclusively breastfed. Throughout the hospital stay, 33% (n = 4) of preterm infants received at least one dose of caffeine and 92% (n = 11) of preterm infants were provided with a supplemental multivitamin with iron.

Skinfold thickness measurement data for preterm and term infants at hospital discharge are presented in Table 3. Preterm infants had significantly higher tricep skinfold thickness (p = 0.05), subscapular skinfold thickness (p = 0.01), and bicep skinfold thickness (p = 0.03) than term infants when adjusting for corrected gestational age. Suprailiac skinfold thickness (p < 0.001) was found to be significant in the pretest for ANCOVA; therefore, significance could not be determined when correcting for postmenstrual age.

A comparison of total abdominal adipose tissue, visceral adipose tissue, and subcutaneous adipose measurements by MRI in preterm and term infants are depicted in Table 4. Three of the preterm infants (n = 12) were on nasal cannula and could not be measured with MRI and ADP. Preterm infants were found to have significantly higher

Table 3
Skinfold Thickness Measurements
in Preterm and Term Infants at Hospital Discharge¹

Variable	Preterm infants n = 12	Term infants n = 12
Tricep skinfold thickness (mm)	3.37 ± 0.78*	3.02 ± 0.48
Subscapular skinfold thickness (mm)	4.23 ± 0.80*	3.48 ± 0.71
Bicep skinfold thickness (mm)	2.91 ± 0.59*	2.64 ± 0.12
Suprailiac skinfold thickness (mm)	3.12 ± 0.72*	2.61 ± 0.10

¹All values are means ± SDs unless otherwise noted.

*Significantly different from term infants, p < 0.05

Table 4
Comparisons of Adipose Tissue by MRI Between Preterm
and Term Infants at Hospital Discharge

Variable	Preterm infants n = 9 Mean ± SD	Term infants n = 12 Mean ± SD
Total Abdominal Adipose Tissue (cm ²)	169.19 ± 48.56**	129.09 ± 36.15
Visceral Adipose Tissue (cm ²)	79.87 ± 20.28*	55.70 ± 19.18
Subcutaneous Adipose Tissue (cm ²)	89.32 ± 40.75	73.39 ± 27.57

*p < 0.05, **p < 0.01

TAT ($p < 0.001$) and VAT ($p = 0.01$) than term infants, when adjusting for corrected gestation. No significant differences in SAT deposition were found between the preterm and term cohorts. Analysis of variation in adiposity by gender found term females ($M = 154.301 \text{ cm}^2$, $SD = 16.48 \text{ cm}^2$) to have significantly greater TAT ($p < 0.03$) when compared to males ($M = 111.08 \text{ cm}^2$, $SD = 36.15 \text{ cm}^2$). No significant differences were found between preterm male and female infant adiposity by MRI.

The relationship between MRI SAT and abdominal VAT depot, measured and derived anthropometry, and body fat by ADP in preterm infants measured at hospital discharge were tested with Spearman correlations. These correlation results are depicted in Table 5. In this subset, preterm infant weight was strongly associated with MRI TAT ($r = 0.85$, $p = 0.004$) and moderately correlated with VAT ($r = 0.70$, $p = .04$). Relationships between length ($r = 0.77$, $p = .02$), head circumference ($r = 0.75$, $p = .02$) and MRI VAT revealed significant moderate correlations. Of note is the strong correlation found between mid-arm circumference and TAT ($r = 0.93$, $p = 0.001$), VAT ($r = 0.72$, $p = 0.03$), and SAT ($r = 0.75$, $p = 0.02$). A strong correlation was found between

Table 5
Correlations of Adipose Tissue By MRI, Anthropometry, and ADP
in Preterm Infants (n = 9) at Hospital Discharge

	MRI TAT	MRI VAT	MRI SAT
Weight (kg)	0.85*	0.70**	0.65
Length (cm)	0.55	0.77**	0.40
Head Circumference (cm)	0.37	0.75**	0.17
Mid-arm circumference (cm)	0.93*	0.72**	0.75**
Mid-thigh circumference (cm)	0.87*	0.58	0.77**
Abdominal circumference (cm)	0.13	0.60	-0.12
Tricep skinfold thickness (mm)	0.38	0.63	0.08
Subscapular skinfold thickness (mm)	0.61	0.86*	0.30
Bicep skinfold thickness (mm)	0.72**	0.58	0.47
Suprailiac skinfold thickness (mm)	0.83*	0.73**	0.63
ADP Percent Body Fat	0.90*	0.54	0.80*
BMI (kg/m ²)	0.91*	0.63	0.77**
Ponderal index (kg/m ³)	0.80*	0.38	0.77**

*p < 0.05, **p < 0.01

mid-thigh circumference and MRI TAT ($r = 0.87$, $p = 0.008$), and SAT ($r = 0.77$, $p = 0.02$). Analyses revealed no significant correlations for abdominal circumference and tricep skinfold thickness. Subscapular skinfold thickness had a strong positive association with MRI VAT ($r = 0.86$, $p = 0.003$). Additionally, a moderate correlation was found between bicep skinfold ($r = 0.72$, $p = .03$) and MRI TAT. Suprailiac skinfold strongly correlated with MRI TAT ($r = 0.83$, $p = 0.005$) and moderately correlated with MRI VAT ($r = 0.73$, $p = 0.03$). Furthermore, body fat by ADP was strongly associated with TAT by MRI ($r = 0.90$, $p = 0.002$), and SAT ($r = 0.80$, $p = 0.009$). Analysis of derived anthropometry in the preterm infant revealed that BMI was strongly correlated with MRI TAT ($p < 0.001$) and SAT ($p = 0.02$) while ponderal index had a strong positive association with MRI TAT ($p = 0.01$) and MRI SAT ($p = 0.02$).

Table 6
Correlations of Adipose Tissue by MRI, Anthropometry, and ADP
in Term Infants (n = 12) at Hospital Discharge

	MRI TAT	MRI VAT	MRI SAT
Weight (kg)	0.69*	0.60*	0.45
Length (cm)	0.06	0.61*	-0.05
Head Circumference	0.15	0.37	0.03
Mid-arm circumference (cm)	0.59*	0.29	0.57*
Mid-thigh circumference (cm)	0.65*	0.66*	0.40
Abdominal circumference (cm)	0.20	0.03	0.20
Tricep skinfold thickness (mm)	0.48	0.59*	0.05
Subscapular skinfold thickness (mm)	0.48	0.17	0.51
Bicep skinfold thickness (mm)	0.33	0.46	-0.03
Suprailiac skinfold thickness (mm)	-0.04	0.06	-0.28
ADP Percent Body Fat	0.49	0.10	0.59
BMI (kg/m ²)	0.69*	0.22	0.70*
Ponderal index (kg/m ³)	0.51	0.20	0.65*

*p < 0.05, **p < 0.01

Term infant relationships between measured and derived anthropometry, ADP, and TAT, VAT, and SAT are summarized in Table 6 using Spearman correlations. Analyses revealed that weight moderately correlated with total (r = 0.69, p = 0.01) and visceral (r = 0.60, p = 0.04) adipose tissue. Length (r = 0.61, p = 0.04) moderately correlated with VAT. A moderate positive association was found between mid-arm circumference and TAT (r = 0.59, p = 0.05), SAT (r = 0.57, p = 0.05). Mid-thigh moderately correlated with TAT (r = 0.65, p = 0.02) and VAT (r = 0.66, p = 0.02)). Finally, tricep skinfold was moderately associated with VAT (r = 0.59, p = 0.05). No significant relationship was observed with subscapular skinfold, bicep skinfold, suprailiac skinfold, ADP percent body fat, and adipose tissue by MRI. Finally, derived anthropometry in the term infant revealed that BMI was moderately correlated with MRI

TAT ($p = 0.02$) and MRI SAT ($p = 0.01$), while ponderal index had a moderate positive association with MRI SAT ($p = 0.02$).

DISCUSSION

In premature infants, the early postnatal period is a crucial time that influences the development of appropriate growth and metabolism in childhood and adult life.²⁶ We have made the observation that preterm infants at hospital discharge have significantly greater TAT and VAT than term infants, when adjusting for corrected gestational age. These findings support previous studies showing altered adiposity in preterm infants at hospital discharge/term corrected age.^{7,8,27,28}

Preterm infants were not found to have significantly lower weight or length than term infants when correcting for postmenstrual age. These findings diverge from research by Cooke et al. and Uthaya et al.^{4,29} Cooke reported that preterm infants had reduced linear growth and fat-free mass while Uthaya et al. and Harrington et al. observed that preterm infants were both lighter and shorter when compared to term infants at hospital discharge.^{4,29} Additionally, our analyses showed weight, length and head circumference to be associated with VAT in preterm infants. However, we did find that preterm infants had lower mid-arm and mid-thigh circumferences suggesting less regional subcutaneous fat deposition than that found in term infants.

Our research found significantly higher bicep, tricep, and subscapular skinfold measurements in preterm infants at hospital discharge than in term infants. These results suggest higher total body fatness in preterm infants as compared to term infants. Higher total body adiposity in the preterm infant as compared to the term infant contradicts

findings by Uthaya et al. showing lower total adipose tissue in the preterm infant.⁴ This variance may be explained by the differences in study populations and methods. Our results revealed higher percent body fat by ADP, higher TAT by abdominal MRI, and higher VAT by abdominal MRI in preterm infants than in term infants. In contrast, Uthaya et al. observed lower total adipose tissue and subcutaneous adipose tissue and greater intraabdominal adipose tissue in extremely premature infants at term-corrected age than term infants.⁴ In addition, Harrington et al. reported reductions in total percentage adipose tissue and subcutaneous adipose tissue mass, yet not intra-abdominal adipose tissue mass in growth-restricted infants, as compared to (AGA) infants.²⁴ This author speculated that in growth-restricted infants, the deposition of subcutaneous and visceral adipose tissue may be under different regulatory control during intrauterine life.²⁴ In contrast to these studies, our research was conducted in preterm infants without growth restriction. Furthermore, we employed abdominal MRI as compared to the use of whole-body MRI by Uthaya et al. and Harrington et al. Therefore, differences in infant characteristics and study methodology may explain the divergent results, with increased TAT in addition to VAT observed in our preterm cohort data.

Visceral adiposity is a known predictor of metabolic disease in adulthood.³⁰ Greater central adiposity in adulthood has been associated with adults born premature.^{31,32} Furthermore, the risk of high blood pressure in adulthood increases with prematurity.^{33,34} Increases in TAT and VAT in the premature infant at body weights similar to the term infant suggests possible overfeeding in an effort to achieve catch-up growth. A reduction in overall fat deposition in the preterm infant and therefore decreased visceral adiposity may be key to reducing metabolic syndrome risk factors in

adulthood.³⁵ Additionally, our findings of increased TAT and VAT in the appropriately grown preterm infant also suggest a possible difference in the nutrition needs of preterm AGA infants versus those born small for gestational age. Thus, the development of specific measures of VAT may be beneficial in determining appropriate preterm nutrition.

Our study found significant correlations between anthropometrics and VAT by MRI in both preterm and term infants. Specifically, weight, length, head circumference, mid-arm circumference, subscapular skinfold thickness, and suprailiac skinfold thickness were positively correlated with VAT by MRI in the preterm infant. In the neonatal intensive care unit, infant weight, length, and head circumference are used as indicators of appropriate growth. Therefore, the use of mid-arm circumference, subscapular skinfold thickness, and suprailiac skinfold thickness, in addition to weight and head circumference, may be beneficial in determining body composition in the clinical setting as the use of MRI for testing is cost prohibitive.

Our results add to the existing literature confirming altered adiposity in the preterm infant. However, the preliminary nature of this study indicates the need for further research to confirm the relationship between preterm infant anthropometric measures and VAT by MRI. Overall, this study supports the need to test relationships between MRI measures of SAT and VAT, anthropometry, and body fat by ADP in a larger sample size of preterm infants.

Strengths and Limitations

A major strength of the study is the inclusion of varied methods of body composition measurement, which provide a more in depth view of the relationship

between body composition and anthropometric measures in the preterm and term infant. In addition, the research design included an examination of confounding factors, such as maternal health history and infant gender.

A limitation of the study is the sample population size and demographic. The sample population was restricted to infants born prematurely and admitted to the University of Utah Hospital Well-Baby Nursery or Newborn Intensive Care Unit. Additionally, of the preterm infants ($n = 12$), three infants were on nasal cannula and could not be measured with MRI and ADP. Another limitation of the study population was that participants were recruited from a single location. Only infants admitted to the University of Utah Hospital in Salt Lake City, UT participated, making this study regionally specific to the demographics of the study location. Therefore, the sample population may not reflect the demographics of neonates in the United States. Additionally, these preliminary analyses with a small sample size did not allow for full consideration of potential confounding variables. Specifically, data on infant postnatal weight gain, mean kcal and protein intake, and serum adipocytokine levels as potential biomarkers of abdominal VAT depot in preterm infants will be addressed in a future manuscript.

Furthermore, the study was limited by the technical approach in evaluating MRI data. Images of both the preterm and term infants were observed to have greater edema in the subcutaneous fat when compared to adult images. To our knowledge, no current research is using MRI to explain this anomaly. However, comparison between the two infant groups is unlikely to be affected. Lastly, the study is limited by ambiguity in identifying the L4-5 vertebrae as well as variability in the quality of the images.

Conclusion

Results of this study demonstrate that preterm infants display greater visceral adiposity than term infants at hospital discharge. Our findings may explain the connection between preterm birth and factors of metabolic disease, such as high blood pressure in adulthood. Moreover, our data show a correlation between anthropometric measures and visceral adiposity in the preterm infant. More research is needed to further elucidate the factors contributing to increased preterm adiposity and to confirm effective, low-cost methods for monitoring preterm infant body composition.

APPENDIX

MATERNAL HISTORY QUESTIONNAIRE

Contact Information:

Name: _____ Date: _____
Address: _____ Date of Birth: _____
_____ Home Phone: _____
Best Time to Reach You: _____ Second Phone: _____
E-mail address (if available): _____

Personal Information:

Maternal

Ethnicity: White Hispanic Asian Black
 Native American Pacific Islander Other: _____

Baby's

Ethnicity: White Hispanic Asian Black
 Native American Pacific Islander Other: _____

What was your birth weight? _____

What is your education level?

High school/GED Some college/technical school
 Associate's degree Bachelor's degree
 Post-Graduate degree Other: _____

What was your pre-pregnancy weight? _____ Height? _____

What was your pre-delivery weight? _____

Please provide the following information in relation to the baby's *father*:

Age: _____ Weight: _____ Height: _____

Pregnancy Information:

How many children do you have (not counting this pregnancy)? _____

How many pregnancies have you had (not counting this pregnancy)? _____

Have you done any of the following during your current pregnancy?

- Smoke Consume Alcohol
 Used Recreational Drugs Used Over-the-Counter or Prescription Medications
 Taken Prenatal Vitamins

Consumed Soy Products (i.e. soy milk, soy flour, soy protein, tofu, tempeh, miso soy burgers/sausage, soy yogurt/cheese, etc.)

If you have consumed soy products during your pregnancy, please complete the table below:

Soy Product Consumed	Circle which trimester	Servings per week?	Servings per day?
	1 2 3		
	1 2 3		
	1 2 3		

Do you have any medical conditions, either diagnosed prior or subsequent to this pregnancy? **No**
Yes If yes, please specify: _____

If you have used over-the-counter or prescription medications during your pregnancy, please complete the table below.

Medication	Reason for Use	Dose	Start Date	Duration of Use

Physical Activity Information:

How many days towards the end of your pregnancy (on average per week) did you perform physical activity where your heart beats faster and your breathing is harder than normal for 30 minutes or more? (can be 30 minutes in a row or 3, 10 minute blocks)

0 days 1 day 2 days 3 days 4 days 5 days 6 days 7 days

How many days in a typical week did you perform activity such as this?

0 days 1 day 2 days 3 days 4 days 5 days 6 days 7 days

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