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Intrahepatic Fat is Increased in Neonatal Offspring of Obese Women with Gestational Diabetes

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Abstract

Objectives—To assess the precision magnetic resonance imaging (MRI) in the neonate and determine if there is an early maternal influence on the pattern of neonatal fat deposition in the offspring of mothers with gestational diabetes (GDM) and obesity compared with the offspring of normal weight women.

Study design—25 neonates, born to normal weight mothers (n=13) and to obese mothers with GDM (n=12), underwent MRI for measurement of subcutaneous and intra-abdominal fat and magnetic resonance spectroscopy for the measurement of intrahepatocellular (IHCL) fat at 1-3 weeks of age.

Results—Infants born to obese/GDM mothers had a mean 68% increase in IHCL compared with infants born to normal weight mothers. For all infants, IHCL correlated with maternal pre-pregnancy BMI but not with subcutaneous adiposity.

Conclusion—Deposition of liver fat in the neonate correlates highly with maternal BMI. This finding may have implications for understanding the developmental origins of childhood NAFLD.

Keywords

Non Alcoholic Fatty Liver Disease; Fetal programming; maternal obesity; gestational diabetes mellitus; abdominal fat; magnetic resonance imaging; magnetic resonance spectroscopy

The increasing recognition of adult metabolic diseases such as obesity and non-alcoholic liver disease (NAFLD) in young children is a leading public health concern. The obesity

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rates in children approach 1 in 5 and it is estimated that 15% of obese children are affected by NAFLD, yet the developmental origins of NAFLD in children remain poorly understood. In rodents, offspring exposure to a maternal high fat diet during pregnancy and lactation accelerates the development of NAFLD and leads to post-natal hepatic dysfunction and histologic features consistent with Non-Alcoholic Steatohepatitis.(1-3). This suggests that the liver is a likely target for excess fat storage due to exposure to maternal over-nutrition. We have previously reported in our Japanese macaque model of maternal obesity that fetal hepatic lipids and oxidative stress were strikingly increased in the early 3rd trimester.(4) However, there is limited human data on the early acquisition of intra-abdominal or hepatic fat in infants exposed to an intrauterine environment characterized by maternal obesity and GDM (5-7). Recent studies in humans have demonstrated that the offspring of women with GDM or obesity demonstrate increased subcutaneous fat at birth (8-11) and that these offspring are at increased risk of metabolic syndrome as early as age 6 years. (12) Given that ~30% of pregnant women are obese and that the prevalence of GDM approaches 20% in some populations, understanding the influence of this gestational environment on the early development of fat depots is of high priority. (13, 14) It is essentially unknown whether this intrauterine exposure to excess fuels alters the pattern of intra-abdominal and hepatic fat accumulation in the infant.

The use of MRI has greatly advanced the capacity for measurement of specific fat depots. (15) However, there is a paucity of data establishing the precision of these techniques in infants. Cross-sectional MRI allows for the isolation and measure of subcutaneous and intra-abdominal fat stores.(16) In the measure of intra-abdominal fat by MRI, one methodological challenge to reproducibility is that this technique requires substantial human interpretation in defining relatively small intra-abdominal fat depots.(17). Magnetic resonance spectroscopy (MRS) is now a well utilized technique in clinical research for the measurement of intrahepatocellular lipid (IHCL) content. Common practice in performance of MRS is to assume a fairly constant hepatic water concentration across a study population and then to use the water concentration as a means of normalizing the fat measure. (18, 19) However, this assumption has not been validated in the neonatal population, where postnatal fluid shifts are known to occur and may impact hepatic water concentration. (20)

To address whether infants of obese/GDM mothers have evidence of ectopic fat deposition in the liver and in the intra-abdominal cavity, we sought to validate MRI techniques in the newborn infant. The aims of the present study were to:(1) determine the reliability of quantifying intra-abdominal and hepatic fat by MRI in neonates, (2) to determine whether a relationship exists between maternal phenotype and intra-abdominal fat and hepatic lipid content in the newborn infant, and (3) to explore the relationships between infant subcutaneous fat, intra-abdominal fat, and hepatic fat depots.

Methods

Healthy, full-term infants were studied from two groups of mothers following written, informed parental consent. Mothers were recruited over a 17 month period from prenatal care at either University of Colorado Hospital and Denver Health. The first group consisted of infants born to mothers with a pre-pregnancy BMI <25 kg/m² without GDM (normal weight control). The second group included infants born to mothers with a pre-pregnancy BMI of >30 kg/m² and diagnosed with GDM. GDM was defined using the criteria established by Carpenter and Coustan (21) using a 3 hour oral glucose tolerance test performed between 24-28 weeks of pregnancy. Maternal pre-pregnancy and delivery weights and height were ascertained by self-report and gestational weight gain was defined as difference between delivery weight and pre-pregnancy weight. Neonates were defined as breastfeeding if > 2/3 of their feeds were breastmilk. Both groups were matched for

ethnicity. Infants were excluded for the following maternal conditions: pre-existing diabetes, smoking, hypertension, renal disease, rheumatologic disease, pre-eclampsia, intrauterine growth restriction, or preterm delivery. All research procedures were carried out during a single study visit to Children's Hospital Colorado between 1 and 3 weeks of age. The study was approved by the Colorado Multiple Institution Review Board.

Estimates of Body Composition

Naked weight was obtained on a Detecto electronic scale (Cardinal Scale Mfg. Webb City, MO). Infant length was obtained in the supine position using a standard infantometer (Perspective Enterprises Portage, MI). Triceps and subscapular skin fold thicknesses were obtained using Lange calipers (Beta Technology, Santa Cruz CA). All anthropometric measurements were obtained in triplicate by a single highly experienced investigator and mean values were reported. Total fat-mass and fat-free mass were measured with air displacement plethysmography utilizing the PEA POD system (Life Measurement, Concord CA) as previously reported in infants. (22, 23)

Magnetic Resonance Procedures

MRI measurements were made using an Avanto 1.5T system running Numaris 4.0 software (Siemens, Germany). Studies were performed without sedation after a feeding. The infant was restrained using the MedVac Infant Immobilizer (CFI Medical Solutions, Fenton MI) and placed supine within a moveable plexiglass platform that was modeled on the device used by Harrington.(24) As an external reference for MRS, a sterile container of approximately 100ml of 20% IV fat emulsion (Intralipid, Baxter Healthcare, Deerfield Park, IL) was fastened to the outside of the immobilizer, just above the right costal margin in the mid-clavicular line. For whole body imaging, the area of interest was centered within a Tx/Rx CP Head Coil (Siemens, Germany). Axial images were obtained utilizing a rapid T1-weighted spin echo sequence (TR 409ms, TE 9 ms) every 5mm without gaps beginning at the top of the head in three separate acquisition sequences covering 20cm. Between acquisition sequences, the infant was repositioned within the coil using the mobile platform. Repositioning was precise to allow for a small amount of anatomic overlap between the acquisitions. The upper abdomen was then positioned in the middle of the coil for the performance of 1H- nuclear MRS. A rapid, T1-weighted spin-echo sequence (repetition time (TR) 600ms, echo time (TE) 16ms) was used to position a single 2×2×2cm voxel in the right lobe of the liver, attempting to avoid vascular and biliary structures. Spectra were then obtained from the liver using a PRESS sequence (TR1500ms, TE 35ms) both with and without water suppression, with automatic shimming. All unsuppressed water sequences were performed with 4 signal averages. The water suppression sequences involving the liver were performed with 128 averages. A 2×2×2cm voxel was then placed within the center of the 20% IV fat emulsion reference. A PRESS sequence was obtained with and without water suppression using identical parameters to the liver spectroscopy above. Water suppression within the 20% IV fat emulsion reference was performed with 64 averages. Spectra were analyzed using LCModel software. IHCL was expressed as the ratio of the water suppressed hepatic fat peak to the water suppressed 20% IV fat emulsion fat peak.

Segmentation Procedure

120 cross-sectional images were obtained from each infant. Images were analyzed utilizing in-house software. DICOM Images were transferred from the Siemens MRI and formatted as volumes. The image volume was abstracted from surrounding structures, preprocessed with a high pass filter to decrease signal inhomogeneity throughout the volume and segmented into adipose and non-adipose tissue regions using a 3D Markov random field technique. Pixels were allowed partial assignment to a region to compensate for partial volume artifacts. Subcutaneous and intra-abdominal fat compartments were quantified.

Intra-abdominal fat was defined as fat stores internal to abdominal musculature between the dome of the liver and the top of the sacrum. For each subject, a single pediatric radiologist made a blinded determination of the range of cross-sectional images that corresponded to this anatomic region. Bone, blood vessels, organs such as liver and kidneys, and intra-intestinal dietary fat were manually excluded. Two independent observers, blinded to whether the infant was born to an obese or normal weight mother, analyzed each image within the intra-abdominal fat region. For overlapping cross-sectional images, the image with the higher number of subcutaneous fat voxels was retained for quantification. The total number of voxels for each cross-sectional image were then multiplied by the voxel volume (0.00076 cm^3) and then summed for all images to give a total subcutaneous fat volume and total intra-abdominal fat volume. We found that the length of the abdomen (defined as region spanning the dome of the liver to the top of the sacrum) correlated with the infant's total length (Pearson $r=0.40$, $p=0.05$). Our intra-abdominal fat measure was therefore adjusted by infant length, producing the outcome variable intra-abdominal fat/length.

Data Analyses

During study design there was no available data on hepatic and intra-abdominal fat measures upon which to power our study. Assuming a sample size of 12 per group, a power of 80% and statistical significance at 0.05, the detectable effect size was 1.19 (defined as mean difference/standard deviation). Analysis was performed using SAS Version 9.3. Statistical significance was defined as $p<0.05$. Differences in descriptive and measured variables between infants born to obese mothers with GDM and infants born to normal weight mothers were tested for significance using the unpaired t-test for normally distributed variables. Fisher exact test was used for categorical variables. Pearson correlation coefficient was calculated for normally distributed variables. Equality of variance was measured by the F test. Linear regression models were constructed to assess the relationship between IHCL and maternal pre-pregnancy BMI while controlling for measures of infant subcutaneous fat. For assessment of inter-observer variability of intra-abdominal fat quantification, Bland-Altman plots were constructed and the intra-class correlation coefficient was calculated. In all subjects, the volume of intra-abdominal fat increased as one moved inferiorly across the abdomen, graphically resembling a cubic curve (Figure 1). The proportion of the distance from the dome of the liver to the top of the sacrum was introduced as a cubic polynomial into a mixed-effects model for estimation of the intraclass correlation coefficient and construction of the Bland-Altman plot.(25)

Results

Twenty-five infants from 12 mothers with obesity/GDM and 13 normal weight mothers with normal glucose tolerance testing were studied. Pregnancy and infant characteristics are listed in Table I. Of the 13 obese/GDM mothers, two were Class A₁ (diet controlled) GDM and 10 were Class A₂ (requiring insulin or glyburide) GDM. Pre-pregnancy BMI (kg/m^2) was greater in the obese/GDM group (40.1 vs. 21.6, $p<0.05$) by design. Obese/GDM mothers were older than normal weight mothers (29.9 years vs. 24.8 years, $p=0.05$). There were no statistical differences in race/ethnic background or % breastfeeding between the two groups. At birth, infants born to Obese/GDM mothers were heavier than infants born to normal weight mothers (3.5 vs. 3.1 kg, $p=0.01$). By the time of the study at 2 weeks of life, however, there was no statistical difference in infant weight. For other variables that might affect adiposity (gestational age, gestational weight gain, study age of newborn), there were no differences between groups. Although normal weight mothers gained more weight during pregnancy than obese mothers, mean gestational weight gain for normal weight mothers (14.2kg) fell within Institute of Medicine (IOM) recommendations for normal weight women (11.4 to 15.9kg), whereas mean gestational weight gain for obese mothers (9.7kg)

exceeded IOM recommendations for obese women (5 to 9.1kg). (26) Of the 25 infants who participated in the study, 20 infants (10 born to Obese/GDM mothers, 10 born to normal weight mothers) had MRS data available for analysis. In three infants, there was a technical problem in performance of MRS on the 20% IV fat emulsion reference. In two infants (one born to Obese/GDM mother, one born to a normal weight mother), IHCL content was 3 standard deviations above the mean for the cohort of infants, and these outliers were excluded.

Estimates of intra-abdominal fat

Inter-observer variability for the measure of intra-abdominal fat was assessed by Bland-Altman and Intra-class Correlation. The Bland-Altman plot (Figure 1) was constructed from independent assessments of a total of 524 abdominal cross-sectional images from 25 subjects. When fat volume was extrapolated from voxels measured, the bias for the Bland-Altman plot was -0.005 cm^3 and the Limits of Agreement were -0.88 cm^3 and 0.87 cm^3 . This result indicated no systematic bias between observers. However, given that the mean intra-abdominal adipose tissue was only 1.04 cm^3 per cross-sectional image for the cohort, the limits of agreement were wide relative to this small volume measure, indicative of poor interobserver agreement. For our study population, the mean intra-abdominal fat volume (21.3 cm^3) was small relative to the mean subcutaneous fat volume (740.7 cm^3). The Intra-Class Correlation for estimation of intra-abdominal fat was 0.50, indicating only modest interobserver agreement.

Variability in intrahepatocellular water content by MRS

We found that the variance in intrahepatocellular water content in our cohort of infants (mean 2580 Arbitrary Units (AU), SD 866) was greater than the variance in water content of our external 20% IV fat emulsion reference (mean 6194 AU, SD 447; Figure 2 available at www.jpeds.com). This difference was statistically significant by the F Test for Equality of Variance ($p=0.006$). This result confirmed our concerns regarding the assumption of a constant hepatic water concentration in young infants.

Impact of Maternal Obesity/GDM on Offspring Adiposity

Adiposity outcomes are summarized in Table II. Percent fat mass and fat-free mass were measured by PEAPOD and were not significantly different between groups. Infants born to Obese/GDM mothers had significantly greater skinfold thickness (mm) compared with infants born to normal weight mothers (11.73 vs. 9.88, $p<0.05$), however there was no difference in total subcutaneous fat as measured by MRI. We did not find significant differences in estimates of intra-abdominal fat/length between groups. The salient finding from this study is that intrahepatocellular lipid (IHCL) was, on average, 68% higher in infants born to obese/GDM mothers compared with those born from normal weight controls (0.030 vs. 0.017, $p=0.04$). Infant subjects were stratified by sex and no significant differences in adiposity outcomes were seen between boys and girls. Univariate analysis was performed for all subjects in the study. There was a significant correlation between IHCL and maternal pre-pregnancy BMI ($r=0.50$, $p=0.02$; Figure 3), but not between IHCL and gestational weight gain ($r=0.03$, $p=0.91$), gestational age ($r=-0.05$, $p=0.85$), or infant study age ($r=-0.09$, $p=0.71$). Intra-abdominal fat/length did not significantly correlate with maternal pre-pregnancy BMI ($r=0.29$, $p=0.16$), gestational weight gain ($r=-0.28$, $p=0.18$), gestational age at birth ($r=-0.11$, $p=0.60$), or infant study age ($r=-0.04$, $p=0.84$). The relationship between offspring IHCL and maternal pre-pregnancy BMI remained significant in regression analysis after controlling for infant subcutaneous fat as measured by either skin folds or MRI.

Relationships between subcutaneous, intra-abdominal, and hepatic fat

There was no relationship between IHCL and subcutaneous fat as measured by MRI ($r=0.18$, $p=0.45$) or skinfold thickness ($r=0.09$, $p=0.71$). Intra-abdominal fat/infant length did not significantly correlate with MRI subcutaneous fat ($r=0.24$, $p=0.25$) or skinfolds ($r=0.19$, $p=0.37$). There was also no correlation between intra-abdominal fat/length and ICHL ($r=0.19$, $p=0.43$).

Discussion

Our results demonstrate that maternal pre-pregnancy BMI is associated with hepatic fat storage at 1-3 weeks of life across a cohort of infants born to both normal weight and obese mothers with GDM. This relationship is consistent with findings reported by Modi et al.(27) All of our obese mothers also had GDM whereas <10% of mothers had GDM in the cohort described by Modi, (27) suggesting that maternal obesity may be more important than the presence of GDM in predicting infant hepatic fat storage. Our study technically differed from Modi et al in the performance of MRS for measure of hepatic fat, as our study used an external reference. We demonstrated significantly more variability in water content in the liver compared with 20% IV fat emulsion. This finding contradicts the assumption of constancy of intrahepatocellular water concentration in humans. Because hepatic water is conventionally used to normalize the lipid content measured by MRS, our data suggests that this practice may introduce error into the measure of IHCL in neonates. Use of an external reference will add to the reliability of this measure.

We found that the relationship between maternal pre-pregnancy BMI and neonatal hepatic fat may be independent of neonatal subcutaneous fat. This finding suggests that fetal storage of fat in the liver is driven in part by excess fuels present in obese mothers throughout pregnancy and may represent an important process for the early onset of fatty liver, distinct from those factors that determine adipose tissue development in subcutaneous tissue.

After approximately 28 weeks gestation, there are exponentially increasing rates of subcutaneous fat storage that continue through the third trimester.(28) Acceleration of subcutaneous adipose tissue growth in the fetus is synchronous with the development of physiologic maternal insulin resistance in the mother, increasing availability of metabolic substrate such as glucose, triglyceride (TG), free fatty acids(FFA) to the placenta and fetus. (29) In the setting of maternal obesity and pre-existing insulin resistance, however, there are increases in maternal concentrations of nutrients such as lipids early in pregnancy. Recently, we and other investigators have shown that maternal TG and FFA levels in obese women are elevated in pregnancy compared with normal weight women.(8) Further, maternal TG predicted neonatal subcutaneous adiposity as estimated by skinfold thickness more strongly than measures of maternal glycemic control. (30) Increased maternal concentrations of TG and FFA in early pregnancy may drive placental nutrient transport at a time in development when the fetus does not possess the subcutaneous adipose tissue storage compartments necessary to buffer against nutrient excess.(31) This may expose the fetal liver to an excessive lipid load that accumulates when subcutaneous fat stores are underdeveloped. That this depot persisted post-natally in the infants studied here suggests this may have important consequences for the development of early onset NAFLD.

Animal models suggest that in the setting of nutrient overload in early development, the fetus may rely on ectopic sites such as the liver for fat storage. In a well characterized non-human primate model of maternal obesity in which mother Japanese macaque monkeys were fed a high fat diet, we demonstrated excess triglyceride storage in liver tissue in the early 3rd trimester, leading to oxidative stress in hepatocytes that did not completely resolve upon return to a normal diet.(4) In fact, the appearance of the fetal livers was histologically

identical to NAFLD as seen in humans. Murine models of maternal obesity and overfeeding have also demonstrated impairment of expression of genes involved in fatty acid oxidative capacity and lipogenesis in offspring liver at the time of weaning.(3, 32) Of great concern in these animals is that accelerated hepatic fat storage appeared to persist post-weaning and into adulthood, suggesting a lasting impact of the maternal environment on pathways of hepatic lipid metabolism. This enduring phenotype may be influenced by epigenetic changes in hepatocytes and may possibly set the stage for later development of NAFLD in humans. (2)

We found no significant difference in infant subcutaneous fat by MRI but skinfold thickness was higher in the offspring of obese GDM women. Our sample size may have limited our ability to demonstrate a consistent difference in subcutaneous fat across multiple measurement techniques. We were not able to demonstrate a difference in intra-abdominal fat stores, which is likely due to the very small intra-abdominal fat depot size as well as inter-observer variability in its measure. Although Modi et al reported a relationship between newborn abdominal adipose tissue and maternal pre-pregnancy BMI, (27) their abdominal adipose tissue measurement did not discriminate between intra-abdominal fat and abdominal subcutaneous fat, and therefore this relationship may have been driven principally by abdominal subcutaneous adipose tissue. In our study, the low amount of intra-abdominal fat relative to subcutaneous fat made it challenging to precisely measure intra-abdominal fat and suggests that these internal adipose stores are not readily available for storage in the newborn. The increased deposition of fat in the liver of the developing fetus from obese-GDM mothers may reflect a process whereby the liver stores fat due to the unavailability of intra-abdominal or subcutaneous fat stores early in pregnancy.

With greater attention towards the importance of depot-specific fat in children, and with the acceptance of technologies such as MRI for their measure, it is important to establish potential limitations of these techniques in children. Our study demonstrated only modest inter-observer reliability in the measurement of intra-abdominal fat in neonates. There is a paucity of data concerning the reliability of the measurement of intra-abdominal fat in children.(15) Harrington et al. reported a coefficient of variation of 17.6% for the measurement of internal adipose tissue in a cohort of neonates.(24) We analyzed inter-observer variability for measurement of the intra-abdominal fat depot across all cross-sectional images obtained for our entire cohort, thus producing what we feel is a robust assessment of reliability.

Several factors specific to measurement of intra-abdominal fat in infants may explain our modest inter-observer agreement. As is typical with the performance of MRI in young infants, our study was performed in a post-prandial state. Intra-intestinal dietary lipid appears very similar to adipose tissue on T1 weighting. Discrimination of the intra-abdominal adipose depot from surrounding tissue requires considerable manual manipulation, which can lead to inter-observer differences. Additionally, the size of the intra-abdominal depot is small in neonates, both in absolute terms (mean volume of 21cm³ in our cohort) and relative to total adipose tissue (<3% of total fat). For our cohort, the mean ratio of intra-abdominal fat to subcutaneous fat was 0.029, identical to that reported by Harrington et al in a cohort of 25 term infants. (33) In 19 adults who underwent whole body imaging, the mean ratio of intra-abdominal fat to subcutaneous fat was 0.067.(34) Relative to total fat, it appears that the intra-abdominal depot increases in size with age. Inter-observer variation in the measurement of the intra-abdominal depot is therefore likely to be more pronounced when its total volume is smaller, as in the infant.

Our study was limited by a small sample size, which we feel was the reason we did not find significant differences in our two groups for total fat by Pea Pod and subcutaneous fat by

MRI. The absence of finding consistent differences between these fat measures between offspring groups does not undermine the observation that intrahepatic fat was significantly different between these offspring, despite a small sample size. We did not capture maternal dietary information nor did we obtain measures of maternal glycemic control or triglyceride levels during the third trimester of pregnancy, variables which may influence neonatal adiposity outcome.(8, 30) Therefore we do not know whether obesity alone, the degree of maternal insulin resistance, or differences in glucose, lipids or other maternal metabolic factors are the driving force behind offspring hepatic fat accretion.

In summary, our data contribute to a growing body of literature regarding development of precise methods for the measure of specific fat locations in young children. We also demonstrate that a higher maternal pre-pregnancy BMI leads to an increase in fetal hepatic fat deposition. Considerable data have shown the increased risk of obesity and metabolic disease for offspring of obese and GDM women. This inter-generational transmission of risk derives heavily from genetic risk and obesogenic lifestyle choices shared in families, but the demonstration of physiologic differences at birth relating to maternal metabolic factors strongly suggests a role for the gestational environment.(35) Further characterization of the maternal metabolic environment that contributes to excess fetal fat accretion, in particular early in pregnancy before subcutaneous depots are present in the fetus, is a future challenge. Unclear still are whether or not increased hepatic fat persists in these infants and the role for increased infant hepatic fat in the pathogenesis of NAFLD. There may also be critical developmental windows after birth when nutritional interventions such as breastfeeding may ameliorate metabolic risks that are acquired during fetal life.(36, 37) Longitudinal studies will be required to address these questions. The achievement of a more normal weight in women of childbearing age prior to pregnancy may be a critical target in the public health battle against human obesity and metabolic disease.

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List of abbreviations

NAFLD	Non-Alcoholic Fatty Liver Disease
GDM	Gestational Diabetes Mellitus
MRI	Magnetic Resonance Imaging
MRS	Magnetic Resonance Spectroscopy
IHCL	Intrahepatocellular lipid

Figure 1.

A, Each point represents the mean of two observers for the MRI-measured voxels of intra-abdominal fat according to location within the abdominal cavity. There is a non-linear trend in intra-abdominal fat across the abdominal cavity. As one moves inferiorly through the abdomen (left to right on x-axis), intra-abdominal fat first increases and then decreases. B, For measure of inter-observer variability, a Bland-Altman Plot of the difference in abdominal visceral fat measured by two independent observers against the mean abdominal visceral fat measured in 524 abdominal cross-sectional images. When voxels are converted to cm^3 (1 voxel = 0.00076 cm^3), the bias for the Bland-Altman plot is -0.005 cm^3 and the Limits of Agreement are -0.88 cm^3 and 0.87 cm^3 .

Figure 2. Box-and-Whisker plot of distribution of water content in liver and 20% IV Fat Emulsion external reference as measured by Magnetic Resonance Spectroscopy in 20 neonates. Box shows 25%-75% range of values, whiskers show entire range of values.

Figure 3. Relationship between Intrahepatocellular lipid and maternal pre-pregnancy BMI. Intrahepatocellular lipid = ratio hepatic fat to 20% IV Fat Emulsion fat. White circles = infants born to normal weight mothers. Black circles = infants born to obese, GDM mothers.

Table 1

Subject Characteristics; values are mean (SD)

Variable	Normal Weight Mothers (n=13)	Obese/GDM Mothers (n=12)	p value
Pre-pregnancy BMI (kg/m ²)	21.6 (2.3)	40.1 (5.8)	<0.001
Gestational weight gain (kg) *	14.2 (3.2)	9.7 (8.6)	0.11
Gestational age (weeks)	39.6 (0.9)	39.3 (0.4)	0.21
Maternal age (years)	24.8 (6.5)	29.9 (5.9)	0.05
Infant birth weight (kg)	3.1 (0.3)	3.5 (0.4)	0.01
Infant weight at study visit (kg)	3.5 (0.3)	3.7 (0.5)	0.15
Infant length (cm)	51.6 (1.6)	51.5 (2.0)	0.82
Infant age (days)	16.9 (2.3)	15.6(2.2)	0.15
Male (%)	53.8	66.7	0.69 [†]
Race/ethnicity (%)			
White	46.2	33.3	0.69 [†]
Black	0	8.3	
Hispanic	53.8	58.3	
Breastfeeding (%)	69.2	50.0	0.43 [†]

* Based on maternal prepregnancy weight, Institute of Medicine recommends gestational weight gains of 11.4kg to 15.9kg for normal weight women and 5.0kg to 9.1kg for obese women. (26)

[†] p value from Fisher's exact test

Table 2

Infant Adiposity Outcomes; values are mean (SD)

Outcomes	Infants of Normal Weight Mothers	Infants of Obese/GDM Mothers	<i>p</i> value
Pea Pod % Fat Mass	13.1(5.0)	14.7 (3.0)	0.36
Pea Pod % Fat Free Mass	86.9 (5.0)	85.3 (3.0)	0.37
Sum Skin Folds (mm)	9.88 (1.96)	11.73 (1.30)	0.01
MRI Subcutaneous fat (cm ³)	707 (138)	777 (159)	0.26
MRI Intra-Abdominal fat/length (cm ²)	0.39 (0.09)	0.43 (0.16)	0.42
IHCL (AU) ^{*†}	0.017 (0.0045)	0.030 (0.016)	0.04

^{*} IHCL is expressed as the ratio of hepatic fat peak to Intralipid fat peak.

[†] There were 20 subjects (10 Obese/GDM infants and 10 Normal Weight infants) for whom ICHL was calculated.