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Mother's Pre-pregnancy BMI is an Important Determinant of Adverse Cardiometabolic Risk in Childhood

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Abstract

Objective—Maternal adiposity is associated with poor offspring cardiometabolic health. We aimed to evaluate the relationship of maternal pre-pregnancy body mass index (BMI) on the BMI, body composition and cardiometabolic characteristics of the offspring.

Methods—Forty offspring of overweight/obese mothers (O-OW) and 28 offspring of normal weight mothers (O-NW) underwent evaluation of body composition, abdominal fat distribution, blood pressure measurement, fasting lipids and an oral glucose tolerance test. The anthropometric and cardiometabolic characteristics of O-OW were compared to those of O-NW, and the relationship to maternal BMI was evaluated.

Results—Subjects (mean age 12.6±0.4, Female 52.9%) had similar gestational age, birth weight, age, gender, and Tanner stage. However, O-OW had a significantly higher BMI (24.4±1.2 vs. 19.7±0.8 kg/m² p=0.001), % body fat (31.7±1.6 vs. 24.6±1.1 %, p<0.001), visceral fat (41.9±4.7 vs. 26.1±3.9 cm² p=0.012) with no difference in lean body mass compared with O-NW. O-OW had lower whole body insulin sensitivity index (WBISI) with an adverse cardiovascular disease risk profile (higher BP, triglycerides to HDL ratio, hs-CRP and lower HDL). In addition to offspring's %body fat (β =−0.60, p<0.001), maternal pre-pregnancy BMI (β = −0.19, p=0.046) contributed significantly and independently to the offspring's WBISI (R^2 =0.55, p<0.001).

Conclusions—High pre-pregnancy BMI is an important contributor to excess adiposity, insulin resistance and cardiometabolic disease risk in the offspring during childhood.

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CONFLICT OF INTEREST

The authors did not have any conflict of interest related to this study.

Keywords

In-utero programming; Maternal obesity; Early Childhood Risk Factors of metabolic disease; Insulin Resistance; Cardiometabolic risk

INTRODUCTION

The prevalence of obesity in the United States has continued to increase over the last decades (1, 2). One third of children and adolescents and two thirds of adults in the United States, including pregnant women, are overweight or obese (3, 4). The high prevalence of obesity among women of childbearing age has important implications in the treatment and prevention of childhood obesity and its complications including type 2 diabetes (5). In addition to the well recognized familial clustering of obesity traits, a number of prospective and cross sectional studies have reported a stronger maternal-offspring as compared to paternal-offspring BMI relationship (6, 7, 8). The reasons for such an association have not been fully elucidated but one proposal to explain the link would be the ability of maternal obesity to influence subsequent risk for obesity in the offspring through an intra-uterine programming effect (9). This link has been implied by human observational studies (8, 10) and supported by a number of animal studies that demonstrated an intergenerational transmission of maternal obesity traits (11, 12, 13) and suggested the involvement of an epigenetic mechanism (12). Our study aimed to evaluate the relationship of maternal pre-pregnancy body mass index (BMI) to the BMI, body composition and cardiometabolic characteristics of the offspring in childhood. We hypothesized that children of pre-pregnancy overweight or obese mothers would have a higher BMI, fat mass and more adverse cardiometabolic traits compared to children of mothers were normal weight during the pre-pregnancy period.

MATERIALS AND METHODS

Study Population

Sixty-eight children (mean age 12.6 ± 0.4 years; range 8.0–18.7 years), were recruited from two study centers: 46 from the Children's Nutrition Research Center (CNRC) at Baylor College of Medicine (BCM) and 22 from the University of Pittsburgh. University of Pittsburgh mothers were participants in the Prenatal Exposures and Preeclampsia Prevention (PEPP) project (PO1 HD30367) and children were recruited (1:1) to be either from an uncomplicated gestation or a gestation complicated by pre-eclampsia (PE) or chronic hypertension. At BCM mothers and children were recruited through advertisement. All mothers agreed to provide access to the pregnancy and birth record and perinatal information. The diagnosis of pre-eclampsia or chronic hypertension was verified from medical records. To examine the relationship of maternal pre-pregnancy BMI on the metabolic health of the offspring, the children were divided into two groups based on the mother's pre-pregnancy BMI: offspring of normal weight mothers (O-NW) if maternal pre-pregnancy BMI was $< 25 \text{ kg/m}^2$ ($n=28$), and offspring of overweight or obese mothers (O-OW) if maternal pre-pregnancy BMI was $\geq 25 \text{ kg/m}^2$ ($n=40$). At the time of conception, 25% of mothers were overweight and 33.8% obese. Pre-pregnancy BMIs for 16 mothers (8

in each group) were based on self-reported values due to incomplete records. Epidemiologic studies indicate that mothers can recall pre-pregnant body weight from more than 30 years ago with a 91–95% accuracy (14). Overweight for the children was defined as age- and gender-specific BMI percentile between 85th and 94.9th and obesity 95th and above. Birth-weight for gender and gestational age was determined using reference chart by Oken et al. and small for gestational age (SGA) was defined birth weight < 3rd percentile (15). We excluded children exposed to gestational diabetes, smoking, those with evidence of in-utero infections, chromosomal abnormality and those with history of chronic health problems or on chronic medications that may affect growth. Older children and adolescents were selected because the maternal-offspring BMI correlation is believed to be stronger in older compared to children younger than 7 years of age (7, 16). The study participants recruited from Houston had a greater proportion of Hispanic race-ethnicity and a lower proportion of American White ethnicity compared to those from Pittsburgh. All research procedures received approval from the Institution Review Boards of the University of Pittsburgh and BCM. Parental informed consent and child assent were obtained prior to any research procedure.

Methods

Anthropometrics and body composition—Height was measured on a fixed-wall stadiometer (Holtin Ltd.) to the nearest centimeter three times and then averaged. Weight was measured in light clothing to the nearest 0.1 kg on a balance scale. Waist circumference (WC) was measured from the inferior margin of the last rib and the crest of the ileum to the nearest 0.1 cm three times and averaged. Blood pressure was measured using a Welch Allyn Spot Vital Signs LXi. Body composition including percentage body fat, fat mass and fat free mass, was determined by a dual-energy X-ray absorptiometry (DXA) scan (Delphi-A V12.1, Hologic, Bedford MA). Both computed tomography (CT) and magnetic resonance imaging (MRI) can accurately describe the distribution of visceral and abdominal adiposity with good agreement (17). Abdominal fat distribution was obtained by CT/MRI scan at L4-L5 intervertebral space. Imaging results of 5 participants (1 O-NW, 4 O-OW) were not available due to technical errors.

Fasting measurements and oral glucose tolerance test—Fasting blood sample was obtained for determination of total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides (TG), high sensitivity CRP (hs-CRP) and HbA1c. Each participant underwent a 2-hour OGTT (1.75 g/kg of dextrose [max 75 g]) after an overnight fast (minimum 8 hours). Venous blood samples were obtained at –15 min, 0 min before, and at 15, 30, 60, 90 and 120 min after ingestion of dextrose for measurement of plasma glucose and insulin.

Biochemical Measurements—Plasma glucose was measured using the glucose oxidase method with a glucose analyzer (Yellow Springs Instrument, Yellow Springs, OH), insulin concentration by electrochemiluminescence with a Roche Elecys 1010 analyzer (Roche Diagnostics Corporation, Indianapolis, In). HbA1C was determined by high performance liquid chromatography and hs-CRP was measured at Esoterix, Inc using nephelometry.

Calculations—Fasting indices of insulin sensitivity were calculated using the mean of two fasting glucose and insulin concentration before the start of the OGTT (–15 min and 0 min). Area under the curve (AUC) for insulin-to-glucose ($\text{Ins}_{\text{AUC}}/\text{Gluc}_{\text{AUC}}$) was calculated using the trapezoidal rule. Whole Body Insulin Sensitivity Index (WBISI) was calculated from the OGTT measures. These OGTT-derived indices have been validated against the “gold-standard” hyperinsulinemic-euglycemic clamp measurements in children (18). WBISI was calculated as:

$$\frac{10,000}{\sqrt{(\text{fasting glucose [mg/dL]} \times \text{fasting insulin } [\mu\text{U/mL}]) (\text{OGTT mean glucose [mg/dL]} \times \text{OGTT mean insulin } [\mu\text{U/mL}])}}$$

(19)

Homeostasis Measurement Assessment of Insulin Resistance (HOMA-IR) was calculated as:

$$\frac{\text{fasting glucose (mmol/L/L)} \times \text{fasting insulin } (\mu\text{U/mL})}{22.5}$$

(20)

Statistical analysis—Data were examined for normality of distribution. Log transformation of non-parametric parameters was made as appropriate. Student’s t-test or the Mann-Whitney tests were used to compare the means of normally and non-normally distributed continuous variables. Analysis of co-variance models was used to correct for the differences in race-ethnicity between the comparator groups. Differences in categorical variables were tested using the Chi square test or the Fisher’s exact test. Correlation analyses were performed using Pearson correlation. Linear univariate and multivariate regression analyses were also performed to evaluate the relationship of the measurements of BMI, body fat percentage and insulin sensitivity to maternal pre-pregnancy BMI while accounting for potential confounding factors including offspring’s birth weight, maternal medical condition, Tanner stage, and race-ethnicity. Percent body fat (a known important determinant of insulin sensitivity) was additionally included in the model evaluating the relationship of maternal pre-pregnancy BMI to the offspring’s insulin sensitivity. All analyses were performed using SPSS version 21 (SPSS Inc., Chicago, IL, USA). Data are represented as mean $\pm$ SEM or as percentage as appropriate. A two-tailed p value ≤ 0.05 was considered statistically significant.

RESULTS

Subjects’ Characteristics

Table 1 compares the characteristics of the O-NW and O-OW groups. An equal number of children were exposed to preeclampsia (PE) or chronic hypertension in the two groups (39.3% vs. 43.4%, $p=0.718$). Perinatal characteristics including gender, length of gestation, birth weight and birth weight percentile were not different between the two groups (Table 1). There was a difference in race-ethnicity distribution between the 2 groups. There were 6

SGA births, 5 in O-OW and 1 in O-NW ($p = 0.201$). At the time of study, participants in the 2 groups had similar age. More participants in the O-OW group were pubertal but the difference in pubertal stage distribution between the 2 groups did not reach statistical significance. Despite similar birth weight and gestational age, O-OW had a significantly higher BMI, age- and gender-adjusted BMI percentile, BMI z-score, fat mass and percent body fat with no difference in lean body mass compared with O-NW. They also had significantly greater abdominal fat with O-OW having greater waist circumference, visceral and subcutaneous fat compared with O-NW. The differences observed between the O-OW and O-NW persisted when the participants recruited from our 2 sites were examined separately. There was a higher proportion of overweight/obese children in the O-OW compared with the O-NW group and this translated to an odds ratio of 4.96 (CI=1.65–14.89) for a child born to an overweight/obese mother to be overweight/obese in childhood.

Metabolic Profile

Fasting blood glucose, 2 hour post OGTT glucose, glucose AUC and HbA1c were similar in the 2 groups (Table 2). However, O-OW were more insulin resistant as indicated by the higher values of fasting insulin, HOMA-IR, and $\text{Ins}_{\text{AUC}}/\text{Gluc}_{\text{AUC}}$ reflecting higher insulin for the same degree of glycemia (similar AUC glucose), and had lower WBISI. They also had a more adverse metabolic profile (higher systolic blood pressure, triglycerides, triglycerides to HDL ratio, high sensitivity CRP and lower HDL).

These differences remained significant after adjusting for differences in ethnicity between the 2 groups. The findings of the study did not change when the metabolic parameters of the offspring with and without exposure to maternal chronic hypertension or PE were examined separately. In addition, excluding the children with SGA ($n = 6$) from the data analyses did not change the findings.

Relationship of mother's pre-pregnancy BMI to childhood BMI, body fat percentage and insulin sensitivity

In univariate analyses, pre-pregnancy BMI correlated significantly with BMI Z-score, body fat percent and insulin sensitivity (Table 3). Maternal pre-pregnancy BMI correlated positively with $\text{Ins}_{\text{AUC}}/\text{Gluc}_{\text{AUC}}$ ($r = 0.29$, $p = 0.02$) and inversely with log WBISI ($r = -0.36$, $p = 0.003$).

In multivariate regression analyses with the children's BMI Z-score as the dependent variable and maternal pre-pregnancy BMI, maternal condition, birth weight percentile, race-ethnicity, and Tanner stage as independent variables, maternal pre-pregnancy BMI, race and tanner stage together and independently contributed to the variance in the offspring's BMI Z-score ($R^2 = 0.4$, $p < 0.001$) (Table 3). In the same regression model with % body fat as the dependent variable, pre-pregnancy BMI and race contributed to the variance in % body fat ($R^2 = 0.2$, $p = 0.04$). With log WBISI as the dependent variable, both maternal pre-pregnancy BMI ($\beta = -0.2$, $p = 0.046$) and offspring % body fat ($\beta = -0.6$, $p < 0.001$) contributed to the observed variance ($R^2 = 0.55$, $p < 0.001$). Substituting % body fat with visceral fat in the same model showed both maternal pre-pregnancy BMI ($\beta = -0.26$, $p = 0.01$) and visceral fat ($\beta = -0.65$, $p < 0.001$) contributed independently to the observed variance ($R^2 = 0.52$, $p < 0.001$).

Neither birth weight percentile nor maternal condition had any significant impact on these outcomes.

DISCUSSION

Our study demonstrates that children of mothers who were overweight or obese at the time of conception have a greater tendency to be overweight/obese with increased total body and abdominal adiposity compared to children born to normal weight mothers. They also manifest insulin resistance and an adverse metabolic profile in later childhood. These differences occurred despite similar perinatal characteristics including birth weight and gestational age and independent of ethnic differences. This report adds to the growing body of evidence to support maternal overnutrition not only as an important determinant of offspring obesity and body composition but also predictor of long-term cardiometabolic health (9) by providing objective quantification of adiposity in the offspring using DXA, abdominal fat distribution by CT/MRI, and evaluation of a range of cardiometabolic risk markers and OGTT derived indices of insulin sensitivity.

The observation of higher adiposity in children of overweight/obese mothers are consistent with those of other investigators (21, 22, (23)). Importantly in our study, the impact of maternal obesity on childhood adiposity and indices of insulin resistance occurred in the absence of difference in birth weight between the comparator groups. This is consistent with reports from both human (22, 23) and animal studies (11). Fetuses of obese women with similar birth weight exhibited greater adiposity and insulin resistance based on HOMA-IR measured using cord blood samples (22) but the results from two cross sectional adult studies were mixed. While an earlier study found no differences in insulin sensitivity in lean adult offspring (age 23) of obese (n=23) and lean mothers (n=21) (24), a subsequent study reported that despite the absence of difference in birth weight, adult offspring (age 23) of obese mothers were more insulin resistant than those who had lean mothers (23). These results would suggest that maternal weight likely mediates offspring's insulin resistance through offspring's adiposity. In animal studies, although no difference in birth weight was found in offspring of high-fat diet obese dams compared to offspring of lean dams, this group had a propensity towards greater weight gain, and a higher insulin resistance when exposed to high fat diet in the post-natal period (11).

Although the relationship between maternal-offspring BMI is well recognized, the biologic mechanisms responsible for the ability of maternal obesity to influence subsequent risk for obesity traits in the offspring have not been fully uncovered. In this regard, pre-pregnancy BMI could represent as a surrogate for a wide range of upbringing characteristics and shared socio-economic or lifestyle factors such as dietary and activity patterns and general health behavior.

More recently, a body of emerging evidence is suggesting that an intra-uterine programming effect that is independent of other post-natal factors could also be involved. In animal studies, the intrauterine exposure to maternal obesity could be limited to the gestation period by the cross fostering of offspring after birth. Using this technique in rats, Shankar et al. reported greater adiposity and subsequent weight gain in offspring of high-fat diet obese

dams who were only exposed to maternal obesity during the in utero period (11). Human observational studies that examined the differences in BMI of sibling-pairs born following temporal changes in maternal weight as a result of bariatric surgery have also supported this proposal. Children born after mothers had experienced dramatic weight-loss (36%) following bariatric surgery had significantly lower BMI z-scores and better indices of insulin sensitivity than siblings born before surgery (10). Such differences among sibling-pairs were less likely to be explained by socio-economic differences or maternal genotype, although a positive modification in lifestyle following maternal weight loss cannot be excluded. An environmental effect would be consistent with observation of similar childhood growth patterns in offspring of mothers with gestational diabetes and their non-exposed siblings (25). On the other hand, influence of in-utero factors are supported by the observation of worse atherogenic index in non-obese children born idiopathic large for gestational age to non-obese mothers, compared with AGA children (26). More recently, pre-clinical models have suggested the transmission of obesity could be mediated via an epigenetic mechanism during the intra-uterine period. Waterland et al. demonstrated the amplification of obesity when the agouti viable yellow (A^{vy}) allele was passed through successive generation of A^{vy} female mice. Dietary manipulation through supplementation of dams with a methyl-rich diet that induces DNA hypermethylation during development prevented the transgenerational effect thereby highlighting the importance of maternal nutrition during the periconceptional period (12).

Some limitations of our study need to be acknowledged. A causality effect is limited by the inherent nature of a cross-sectional study. Our results support the independent effect of maternal pre-pregnancy BMI on various offspring cardiometabolic risk factors but additional information such as dietary and activity pattern, general health behavior of the study population would enable a more comprehensive evaluation of the biological underpinnings including those from an intra-uterine programming effect. Nonetheless, regardless of the potential mechanism, our results clearly show that maternal pre-pregnancy BMI is an important marker for future risk to children and a potential target for intervention. Maternal pre-pregnancy BMI was self-reported in some of our women. However, multiple studies have shown self-reported BMI correlates well with measured BMI ($r > 0.9$) (27, 28) and has been shown to be reliable when evaluating the pre-pregnancy/pregnancy period (29). The exclusion of self-reported maternal pre-pregnancy BMI in our study did not alter the findings. We did not assess gestational weight gain. While excessive maternal weight gain during pregnancy might be critical for the body size of offspring in later life (30), (31, 32) maternal pre-pregnancy obesity may have a greater effect (32). Animal studies that controlled for and reported similar gestational weight gain in lean and obese dams also reported greater weight gain and adiposity in offspring of obese dams (11). An equal proportion of study participants in the NW and OW groups were exposed to maternal chronic hypertension or pre-eclampsia and while such adverse intra-uterine exposure may have an effect, the relationship of maternal weight to childhood BMI and insulin resistance indices was independent of maternal condition and was still evident when the 2 groups were analyzed separately. Such findings are consistent with the results of the Avon Longitudinal Study where the positive effect of gestational hypertension on offspring overweight or obesity was attenuated to null when maternal pre-pregnancy BMI was taken into account

(33). SGA is a well-known risk factor for insulin resistance and adverse cardiometabolic phenotypes. There were a small number of SGA children in our cohort equally distributed between the two comparator groups. Their exclusion did not alter our results. Paternal BMI was not available in our cohort but maternal rather than paternal factors are believed to have a more important contribution to offspring BMI. In the Cardiovascular Risk in Young Finns Study, maternal and not paternal BMI was reported be a significant predictor of later development of T2DM and outperformed genetic risk score in a large cohort of children (n=1835) followed over 20 years (34).

In conclusion, our study highlights the importance of maternal overweight/obesity during conception as a contributing factor for excess adiposity and cardiometabolic disease risk in the offspring during later childhood. Uncovering the biologic mechanism(s) responsible for the inter-generational transmission of adiposity and insulin resistance traits (genetic/epigenetic vs. the role of shared social-environmental factors) needs to be addressed in future studies and has profound implications in formulating effective strategies to better manage childhood obesity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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HC Tan analyzed the data and wrote the first draft of the manuscript; JR contributed to data collection and interpretation, reviewed and edited the manuscript; JC, RS, and RK contributed to data collection and interpretation, reviewed and edited the manuscript; FB obtained funding, conceived and carried out the study, analyzed and interpreted the data, critically reviewed and edited the manuscript, and is the guarantor of this work. All authors were involved in writing the paper and had final approval of the submitted and published versions. The authors would like to thank the nurses and staff of the Metabolic Research Unit at the Children's Nutrition Research Center, Baylor College of Medicine and of the Pediatric Clinical and Translational Research Center at the Children's Hospital of Pittsburgh; Lori Bednarz, RN, Sarah Mauch, MS, Janette Gonzalez and Elizabeth Garnes, RN for their research coordinating efforts; Susan Sharma for the laboratory expertise and the support of the Arslanian's Lab at the University of Pittsburgh. We are very thankful to the study volunteers and their parents.

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Table 1

Characteristics of study participants at birth and at study evaluation according to maternal pre-pregnancy BMI.

	O-NW (n= 28)	O-OW (n= 40)	P-value
Maternal Characteristics			
Maternal pre-pregnancy BMI (kg/m ²)	22.0 ± 0.4	31.5 ± 0.8	< 0.001
Gestational Age (Weeks)	38.4 ± 0.5	38.0 ± 0.4	0.4
Birth Characteristics			
Birth Weight (kg)	3.2 ± 0.1	3.1 ± 0.1	0.5
Birth weight percentile (%)	50.0 ± 5.5	43.4 ± 5.2	0.4
SGA/AGA/LGA	1/26/1	5/35/0	0.23
Characteristics at Study Evaluation			
Age (years)	12.5 ± 0.6	12.7 ± 0.5	0.8
Race-ethnicity (n) AW/AA/H/BR	17/5/5/1	12/11/17/0	0.03
Gender (Male/Female)	15/13	17/23	0.4
Tanner stage (%)			
I	39.3	30	0.7
II–III	25	25	
IV–V	35.7	45	
BMI (kg/m ²)	19.7 ± 0.8	24.4 ± 1.2	0.001
BMI z-score	0.29 ± 0.17	1.07 ± 0.19	0.004
BMI percentile (%)	57.2 ± 5.1	75.5 ± 4.9	0.013
BMI 85 th percentile (%)	21.4	56.5	0.003
Fat mass (kg)	17.5 ± 3.9	22.2 ± 2.2	0.009
Fat free mass (kg)	34.3 ± 2.6	38.0 ± 2.2	0.3
Body fat (%)	24.6 ± 1.1	31.7 ± 1.6	0.001
Waist circumference (cm)	67.2 ± 2.3	78.8 ± 3.0	0.015
VAT (cm ²) *	26.1 ± 3.9	41.9 ± 4.7	0.012
SAT (cm ²) *	103.2 ± 16.5	197.0 ± 25.9	0.003

O-OW = Offspring of overweight or obese mothers, O-NW = Offspring of normal weight mothers. AW= American white, AA = African American, H= Hispanic, BR= Bi-racial. VAT = Visceral Abdominal Adipose Tissue, SAT = Subcutaneous Abdominal Adipose Tissue. Data are

Means $\pm$ S.E.M. P-values for t-test or equivalent non-parametric test for continuous variables and Chi-square or Fisher's exact test for categorical variables. * CT/MRI data were available for 27 offspring of NW and 36 offspring of OW mothers.

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Table 2

Metabolic characteristics of study participants examined according to maternal pre-pregnancy BMI group.

	O-NW (n = 28)	O-OW (n= 40)	P-value	Adjusted *P-value
Fasting Glucose (mg/dL)	88.0 ± 1.6	88.3 ± 1.6	1.0	-
Fasting Insulin (μU/mL)	10.8 ± 0.9	16.7 ± 2.6	0.009	0.021
HOMA-IR	2.3 ± 0.2	4.1 ± 0.6	0.004	0.025
2-hour Glucose (mg/dL)	116.1 ± 3.8	127.2 ± 5.4	0.1	-
2-hour Insulin (μU/mL)	64.2 ± 8.2	118.7 ± 13.8	0.001	0.035
AUC Glucose	14989.9 ± 446.2	16044.7 ± 605.5	0.2	-
AUC Insulin	8749.5 ± 728.7	15253.4 ± 1470.0	< 0.001	0.007
Ins _{AUC} /Gluc _{AUC}	0.6 ± 0.006	1.0 ± 0.10	0.001	0.033
WBISI	4.8 ± 0.4	3.4 ± 0.4	0.001	0.019
HbA1C (%)	5.5 ± 0.1	5.5 ± 0.1	0.6	-
Cholesterol (mg/dL)	150.2 ± 6.1	149.2 ± 1.9	0.9	-
TG (mg/dL)	59.9 ± 1.6	85.6 ± 6.0	0.001	0.011
HDL (mg/dL)	54.2 ± 1.6	47.0 ± 1.9	0.002	0.038
TG / HDL	1.1 ± 0.1	2.0 ± 0.2	< 0.001	0.004
CRP (mg/L)	0.6 ± 0.1	1.7 ± 0.6	0.001	0.018
SBP (mmHg)	106.9 ± 1.7	113.4 ± 1.6	0.010	0.014
DBP (mmHg)	65.2 ± 1.4	67.6 ± 1.1	0.2	-

O-OW = Offspring of overweight or obese mothers, O-NW = Offspring of normal weight mothers, HOMA-IR = Homeostasis Measurement Assessment of Insulin Resistance, Ins_{AUC}/Gluc_{AUC} = Area under the curve for insulin/ AUC for glucose during the OGTT, WBISI = Whole Body Insulin Sensitivity Index. Data are Means ± S.E.M,

* P-value adjusted for ethnicity differences between the 2 groups. To convert to SI units: for cholesterol in millimoles per liter, multiply by 0.02586, for triglycerides in millimoles per liter, multiply by 0.01129 and for glucose in millimoles per liter, multiply by 0.05551.

Table 3

Univariate and Multivariate Regression Analyses of Maternal Pre-pregnancy BMI to Childhood BMI Z-score Percent Body Fat and Insulin Sensitivity.

	BMI Z-score						Body Fat Percentage						Log WBISI					
	Univariate			Model 1			Model 2			Univariate			Model 1			Model 2		
	$R^2 = 0.4$, $p < 0.001$	β	p	$R^2 = 0.64$, $p < 0.001$	β	p	$R^2 = 0.2$, $p = 0.04$	β	p	$R^2 = 0.2$, $p = 0.006$	β	p	$R^2 = 0.55$, $p < 0.001$	β	p	$R^2 = 0.55$, $p < 0.001$	β	p
Maternal Pre-pregnancy BMI	0.40	0.001	0.33	0.003	0.19	0.02	0.03	0.23	0.056	-0.36	0.003	-0.34	0.005	-0.2	0.046			
Birth Weight Percentile	0.02	0.9	0.06	0.55	0.004	0.956	0.7	0.09	0.47	-0.07	0.59	-0.14	0.224	-0.09	0.353			
Race-Ethnicity	0.39	0.001	0.25	0.026	0.09	0.303	0.33	0.27	0.029	-0.31	0.009	-0.22	0.07	-0.05	0.580			
Maternal Condition	-0.1	0.3	-0.02	0.827	-0.06	0.47	0.002	0.07	0.55	-0.02	0.88	-0.13	0.287	-0.08	0.379			
Tanner Stage	0.40	0.001	0.29	0.009	0.25	0.003	0.17	0.08	0.50	-0.20	0.1	-0.14	0.232	-0.11	0.269			
Body Fat %	0.72	< 0.001	-	-	0.59	< 0.001	-	-	-	-0.69	< 0.001	-	-	-0.60	< 0.001			

Dependent variables: Offspring BMI Z-score, Body Fat Percent, or Log Whole body Insulin Sensitivity Index (log WBISI).

Model 1: Adjusted for Maternal Pre-pregnancy BMI, Birth Weight Percentile, Race-Ethnicity, Maternal Condition, Tanner Stage.

Model 2: Adjusted for Model 1 + body fat %.