Maternal hormones linking maternal body mass index and dietary intake to birth weight[1–3]

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ABSTRACT

Background: Obese women often give birth to large-for-gestational age infants (typically defined as a birth weight greater than the 90th percentile), who are at risk of birth injuries and of developing metabolic syndrome later in life. The mechanisms underlying increased fetal growth remain to be established.

Objective: We aimed to identify maternal hormones that can explain the link between dietary intake, body mass index (BMI), and birth weight.

Design: Pregnant women with BMIs (in kg/m^2) ranging from 17 to 44 ($n = 49$) were recruited in gestational weeks 8–12. Serum hormone concentrations were measured and dietary history interviews were performed in the first and third trimesters. Multiple regression models were produced to identify hormones that correlate with birth weight and are influenced by BMI or dietary factors.

Results: We found a strong positive correlation between BMI and first- and third-trimester insulin and leptin concentrations and a negative correlation between BMI and first-trimester adiponectin and first- and third-trimester insulin-like growth factor binding protein-1 (IGFBP-1). Maternal total fat intake in the first trimester was positively correlated with maternal leptin and inversely correlated with adiponectin. In addition, third-trimester total fat intake was positively correlated with circulating resistin concentrations. First-trimester maternal serum resistin was positively correlated with birth weight, whereas third-trimester maternal IGFBP-1 was negatively correlated with birth weight.

Conclusions: High first-trimester maternal serum resistin and low third-trimester IGFBP-1 were correlated with increased birth weight. We propose that low serum concentrations of IGFBP-1 represent a link between high BMI and increased fetal growth by increasing the bioavailability of insulin-like growth factor-I, which up-regulates placental nutrient transport. *Am J Clin Nutr* 2008; 87:1743–9.

INTRODUCTION

Overweight and obesity are reaching epidemic proportions (1–3). In 1999–2004 the prevalences of overweight and of obesity were 52% and 29%, respectively, in American women of reproductive age (1). Obese women have an increased incidence of pregnancy complications (2, 4–7), and the fetus of an obese mother has an increased risk of stillbirth and birth defects (5, 8). Fetal overgrowth is common in pregnancies of women with increased body mass index (BMI), and results in the birth of a large-for-gestational age infant (typically defined as a birth weight greater than the 90th percentile). Large-for-gestational age infants have an increased risk of traumatic birth injuries (2, 9) and are prone to developing obesity, diabetes, and hypertension during childhood and later in life (10–12).

The mechanisms underlying fetal overgrowth in pregnancies complicated by maternal obesity are not known. Fetal growth is largely determined by nutrient transfer across the placenta, which is dependent on several factors, including maternal nutrient levels and placental transport capacity. Maternal hormones such as insulin (13, 14), leptin (14), and insulin-like growth factor-I (IGF-I) (15) have been shown to stimulate placental nutrient transporters (16). Leptin and fasting insulin are elevated in late pregnancy in obese women (17), and Clausen et al (18) reported that insulin concentrations in the second trimester were positively correlated with maternal first-trimester body mass index (BMI). Thus, it is possible that increased circulating concentrations of maternal hormones, such as leptin and insulin, constitute a mechanistic link between maternal overweight or obesity and fetal overgrowth mediated by up-regulation of placental nutrient transporters. Furthermore, obesity is associated with elevated maternal plasma concentrations of interleukin-6 (17) and decreased adiponectin concentrations (19) in late pregnancy.

It is well established that severe malnutrition in human pregnancy causes a reduction in birth weight (20). Also, more moderate variations in maternal diet in pregnancy can influence fetal growth (21–23). However, whether these effects are caused by altered maternal nutrient levels per se or by changes in plasma

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concentrations of maternal metabolic hormones is unknown. Indeed, animal experiments suggest that regulation of placental transport capacity by maternal hormones best explains altered fetal growth in response to changes in maternal dietary intake (24). Whether an increased dietary intake contributes to fetal overgrowth in women with overweight or obesity is not well established.

The previously demonstrated positive correlation between BMI and fetal growth (2, 5, 9, 25) provides no mechanistic information. The objective of the current study was to identify hormonal factors that can explain the link between early pregnancy BMI, maternal dietary intake, and birth weight. We focused on dietary factors reported in pregnant women or animal experiments to influence fetal growth and maternal hormones known to regulate placental nutrient transport in vitro.

SUBJECTS AND METHODS

Subjects

Of 56 healthy, nonsmoking, pregnant women recruited during early gestation, 49 completed the study. The study was carried out after written informed consent and was approved by the Committee for Research Ethics at the University of Göteborg, Göteborg, Sweden.

Recruitment

Pregnant women of various adiposity as defined by their early pregnancy BMI [weight (kg)/height (m)^2] were recruited at their first antenatal midwife visit (8–12 wk of gestation) in Göteborg, Sweden, between November 2003 and February 2006. The inclusion criteria were Scandinavian heritage, healthy, and ≥20 y old. The exclusion criteria were smoking, vegetarianism, assisted reproduction, concurrent disease such as eating disorder or diabetes, and development of pregnancy complications such as gestational diabetes, preeclampsia, or intrauterine growth restriction. Of the 56 pregnant women who were recruited, 7 were excluded during the course of the study because of either complications in their pregnancy (one subject each with miscarriage, gestational diabetes, stillbirth, or intrauterine growth restriction), moving away from the area (2 subjects), or lack of compliance with the study protocol after the first trimester (one subject). The remaining 49 women were healthy for the entire pregnancy and delivered between 36 and 43 wk of gestation.

Analyses of maternal serum hormones and adipokines

Maternal fasting blood samples were obtained at 2 time points during pregnancy: at recruitment (gestational weeks 8–12) and in the third trimester (weeks 32–35). Maternal venous samples were obtained in the morning by the midwives at the prenatal care center after the women had fasted overnight (no food after midnight). Blood samples were collected in tubes with and without anticoagulants (lithium heparin) and after 30 min were centrifuged for 10 min at 3000 rpm. Subsequently, tubes were sent to the Laboratory of Clinical Chemistry at Sahlgrenska University Hospital, Göteborg, Sweden, where serum and plasma were collected, aliquoted, and either analyzed directly or frozen at −80 °C. Serum or plasma samples were analyzed for insulin (using immunometric methods), cortisol (immunochemistry), leptin and IGF-I (radioimmunoassay), and IGF binding protein-1 (IGFBP-1), adiponectin, and resistin (enzyme-linked immunosorbent assay). CVs (interassay precision) for these assays ranged from 3% to 12%.

Dietary assessment

Dietary intake data from all subjects were collected by a registered dietitian who interviewed the women at 8–12 wk and at 32–35 wk of gestation, respectively, by using the diet history method (26). The women were interviewed in person at the time of blood sampling after a light breakfast provided at the clinic. The interview was an open, structured, detailed interview designed to capture current habitual dietary intake, meal composition, and eating patterns.

The interview covered all dietary intake over a 24-h period, following the habitual dietary intake meal by meal, seeking day-to-day variation in food choice and meal composition, for weekdays and weekends. All women were asked about food and meal preparation methods, meals at restaurants, and fast food. The number of main-meals, in-between meals, snack-meals, night-meals, and nibbling were recorded. Information on quantities and portion sizes were collected at the end of the interview. Portion sizes of meals were described aided by using a food portion visual (Matmallen, Swedish National Food Administration, 1997). As all pregnant women, our study subjects obtained general dietary information in early pregnancy, at the first or second prenatal visit. However, none of the women in our cohort received special dietary advice from either the midwives or the dietitian. Dietary analyses were performed with the software ALTO DIET 32 (Aivo AB, Solna, Diet32 version 1.2.2.4) and were based on data from the Swedish National Food Administration. An average daily food intake was calculated by determining the mean of the 2 weekdays and multiplying that by 5/7 (5 weekdays out of 7 d) and adding that to the weekend day that was multiplied by 2/7 (2 weekend days out of 7 d).

Data collection

Anthropometric and medical data such as birth size (weight, length), placenta weight, sex, maternal height, weight gain, and pathologic conditions developing during pregnancy were obtained from medical charts after delivery.

Data presentation and statistical analysis

Descriptive univariate statistics including the mean, SE of the mean, and ranges were used to describe dietary intakes and hormone levels in our cohort. Differences between the first and the third trimester were analyzed by using Wilcoxon's signed-rank sum test for the hormones and the paired *t* test for dietary intake. To normalize birth weight and make it independent of sex and gestational age, *z* scores (standard scores) were calculated for all birth weights by using intrauterine growth curves for the Swedish population based on ultrasonically estimated fetal weights (27). The *z* score was derived by subtracting the population mean birth weight for sex and gestational age from an individual birth weight and then dividing the difference by the population SD. Relations between BMI and dietary factors, BMI and maternal hormones, dietary factors and hormones, and hormones and birth weight *z* scores, respectively, were determined by using bivariate analysis and either Pearson's or Spearman's correlation coefficients as appropriate. Subsequently, multiple regression explanatory models were produced for the first and third trimesters,

TABLE 1
Maternal demographics and placental and fetal weights

	$\bar{x} \pm$ SEM	*n*	Range
Maternal age (y)	30.0 ± 0.64	49	22–38
Maternal weight first trimester (kg)	71.7 ± 2.90	49	46–133
Maternal height (m)	1.67 ± 0.01	49	1.54–1.86
Maternal BMI first trimester (kg/m^2)	25.5 ± 0.99	49	16.9–44.4
Maternal weight gain (kg)[1]	14.3 ± 0.71	44	7.3–26.8
Birth weight (g)	3490 ± 67	49	2445–4925
Birth length (cm)	50 ± 0.3	48	45–56
Placenta weight (g)	652 ± 20	45	375–970
Gestational age (wk)	40.3 ± 0.2	49	36–43

[1] Maternal weight at week 36 minus maternal weight at first trimester.

respectively. First, BMI and dietary variables were used as explanatory variables for maternal serum hormone concentrations. Second, the relation between maternal hormones and birth weight *z* scores was analyzed. Analyses were carried out by using SPSS 11.0.4.

RESULTS

Maternal demographic data and placental and fetal weights

Maternal demographic characteristics for the 49 patients are presented in **Table 1**. Missing data are due to a lack of information in the medical charts. For birth size, mean values were consistent with expected birth weights at term in the Scandinavian population (27). As expected, maternal first-trimester BMI was positively correlated with birth weight ($n = 49$, $P < 0.01$, $r = 0.420$). To normalize birth weight for sex and gestational age, birth weight *z* scores were calculated and used in subsequent analyses. BMI was also positively correlated with birth weight *z* scores ($n = 49$, $P = 0.017$, $r = 0.343$).

Maternal hormone concentrations and dietary intake in the first and third trimesters

Maternal serum concentrations of insulin, cortisol, IGF-I, resistin, and IGFBP-1 increased significantly from the first to the third trimester, whereas serum adiponectin decreased significantly (**Table 2**). Intake of all dietary components was significantly higher in the third than in the first trimester (Table 2).

Relations between first-trimester BMI, maternal hormones, and dietary intake variables

In bivariate correlation analysis, early pregnancy BMI was positively correlated with first- or third-trimester maternal serum concentrations of insulin, leptin, and resistin and negatively correlated with first- or third-trimester IGFBP-1 and adiponectin (data not shown).

We found that both first- and third-trimester dietary energy intake was highly correlated with BMI (data not shown). In addition, BMI in the first trimester was significantly correlated with macronutrient intake (protein, total fat, saturated fat, monounsaturated fat, polyunsaturated fat, and carbohydrate intake). Similarly, maternal metabolic hormones and dietary variables were highly correlated. For example, insulin was positively and IGFBP-1 and adiponectin were negatively correlated with saturated and monounsaturated fat intake (data not shown).

Multiple regression explanatory models

To identify maternal hormones that could potentially mediate the effect of BMI and dietary factors on birth weight, we carried out multiple regression analyses in 2 steps. First, first-trimester BMI and dietary variables were used as explanatory variables for maternal serum hormone concentrations. Of the dietary variables, we chose to use 2 of the 3 main macronutrient classes in our analysis. Total fat was included because of highly significant correlations with most of the hormones in the bivariate analysis, and total protein intake was included because of reports in the literature of associations between protein intake and fetal growth

TABLE 2
Maternal serum hormone concentrations and dietary intake in the first and third trimesters[1]

	First trimester		Third trimester	
	$\bar{x} \pm$ SEM	Range	$\bar{x} \pm$ SEM	Range
Insulin (mU/L)	7.9 ± 1.3	3–36	11.7 ± 1.4[2]	3–30
Leptin (μg/L)	19.8 ± 2.4	5.2–101	23.8 ± 1.9[3]	8.7–65.4
Cortisol (nmol/L)	602.4 ± 27.0	310–1130	854.5 ± 59.9[4]	310–1580
IGF-1 (μg/L)	150.7 ± 7.4	66–277	270.3 ± 15.9[3]	109–556
Resistin (ng/mL)	14.9 ± 0.8	6.6–31.5	19.6 ± 1.4[3]	7.2–41.5
Adiponectin (μg/mL)	13.0 ± 0.9	3.8–30.8	10.6 ± 0.7[4]	3.8–25.8
IGFBP-1 (ng/mL)	44.3 ± 5.6	3.1–135	106.9 ± 7.6[3]	4–188
Energy (kcal)	2453 ± 59.8	1513–3174	2757 ± 56.0[3]	1855–3612
Protein (g)	97.0 ± 3.5	49–148.5	107.9 ± 3.7[4]	56–169
Total fat (g)	83.7 ± 3.4	35–141	96.6 ± 3.7[3]	31–140
Saturated fat (g)	35.3 ± 1.6	13–51	41.4 ± 1.7[3]	11–65
Monounsaturated fat (g)	30.5 ± 1.4	12–56	34.7 ± 1.5[3]	10–52
Polyunsaturated fat (g)	11.8 ± 0.7	3–25	13.4 ± 0.8[4]	5–26
Carbohydrate (g)	324.4 ± 8.1	176–447	360.7 ± 7.1[2]	268–442

[1] Paired first and third trimester values for the 49 subjects in the study. IGF-1, insulin-like growth factor-1; IGFBP-1, IGF binding protein-1.
[2–4] Significantly different from the first trimester [Wilcoxon signed rank test (hormones) and paired *t* test (dietary variables)]: [2] $P < 0.05$, [3] $P < 0.001$, [4] $P < 0.01$.

(2, 28, 29). In this multiple regression model, we found a strong positive correlation between BMI and first- and third-trimester insulin and leptin and a negative correlation between BMI and first-trimester adiponectin and first- and third-trimester IGFBP-1 (**Table 3**). With the exception of a positive correlation between first-trimester protein intake and leptin concentrations, protein intake had no effect on maternal hormone concentrations independent of BMI and total fat intake (Table 3). Maternal intake of total fat in the first trimester was positively correlated with maternal serum leptin and inversely correlated with adiponectin concentrations. Interestingly, we found that third-trimester total fat intake was positively correlated with circulating resistin concentrations (Table 3).

As a second step in our multiple regression modeling, we explored the relations between maternal hormones and birth weight. Because wide inclusion criteria in selecting variables for the multiple regression model are recommended in the literature (30), we included hormones that were correlated with birth weight *z* score below the 20% level ($P < 0.20$) in bivariate correlations. The hormones meeting these criteria were resistin and IGFBP-1 in the first trimester and adiponectin and IGFBP-1 in the third trimester. BMI was not used as a primary input variable in the multiple regression analysis because the modeling aimed at being explanatory to identify hormonal factors linking BMI mechanistically to fetal growth. Our primary approach was a full regression model, and these results are summarized in **Table 4**. In first-trimester maternal serum, resistin was a significant factor determining birth weight *z* score. When BMI or total fat and protein were introduced into the model, the B for resistin decreased from 0.75 to 0.59 (with BMI) and to 0.63 (with total protein and fat) and resulted in borderline significances ($P = 0.081$ and $P = 0.094$, respectively) with birth weight *z* score, which suggests that the influence of first-trimester maternal resistin on fetal growth is partly independent of BMI and dietary intake. To assess the effect size, we performed forward stepwise multiple regression, and the results suggested that resistin is the factor with the strongest relation to birth weight, explaining 12% (*R*-square) of the total variance in fetal growth (data not shown).

TABLE 4
Results of the multiple regression analysis with birth weight *z* score as the dependent variable

	B	*P*	*R*
First trimester			
IGFBP-1	0.051	0.283	
Resistin	0.754	0.023	0.380
Third trimester			
IGFBP-1	−0.084	0.038	
Adiponectin	−0.617	0.168	0.452

[1] IGFBP-1, insulin-like growth factor binding protein-1. Multiple regression analysis was performed with hormones that were associated ($P < 0.20$) with birth weigth.

Adding BMI explained an additional 4.5% of the variance in birth weight.

In the third trimester, the full regression model identified IGFBP-1 as significantly related ($P = 0.038$) to birth weight *z* score (Table 4). Adding BMI to the model changed B from to −0.084 to −0.066 (data not shown), and the relation between third-trimester IGFBP-1 and birth weight *z* score became insignificant ($P = 0.133$). In contrast, dietary factors, such as total energy, had little effect on the relation between IGFBP-1 and birth weight, which remained significant (data not shown). Forward stepwise multiple regression was performed, and the results indicated that maternal third-trimester IGFBP-1 could explain 16% of the variation in birth weight. Adding BMI explained an additional 2% of the variance in birth weight.

DISCUSSION

This is, to the best of our knowledge, the first prospective study of pregnant women with a wide range of early pregnancy BMI that assessed maternal dietary intake and metabolic changes in both the first and the third trimester and their impact on birth weight. In the analysis of our data, we used a model in which dietary intake and BMI were assumed to not have direct effects

TABLE 3
Multiple regression analysis with maternal hormone as the dependent variable[1]

	BMI		Protein		Total fat	
Trimester and hormone	B	*P* value	B	*P* value	B	*P* value
First						
Insulin	0.633	<0.001	0.017	0.752	−0.008	0.863
Leptin	1.724	<0.001	0.187	0.047	−0.209	0.022
IGF-1	−1.371	0.287	−0.071	0.878	−0.345	0.425
IGFBP-1	−2.367	0.010	0.516	0.081	0.124	0.672
Cortisol	−10.452	0.049	1.660	0.374	0.371	0.830
Adiponectin	−0.320	0.021	0.068	0.126	−0.095	0.036
Resistin	0.167	0.208	0.002	0.970	0.063	0.154
Third						
Insulin	0.616	<0.001	0.110	0.895	0.007	0.065
Leptin	1.379	<0.001	0.022	0.625	0.036	0.782
IGF-1	−0.050	0.800	0.223	0.173	−0.305	0.342
IGFBP-1	−2.507	0.023	−0.732	0.334	0.360	0.071
Cortisol	−9.777	0.284	−2.897	0.275	3.455	0.388
Adiponectin	−0.137	0.200	−0.062	0.618	0.018	0.119
Resistin	0.252	0.163	0.155	0.792	0.0168	0.030

[1] IGF-1, insulin-like growth factor-1; IGFBP-1, IGF binding protein-1. $P < 0.05$ was considered significant.

on fetal growth, but were primarily mediated via changes in maternal metabolic hormones, which affect placental nutrient transport, thus resulting in altered fetal nutrient supply and growth (**Figure 1**). In general support of this model, maternal metabolic hormones such as insulin, leptin, and IGF-I have been shown to stimulate the activity of placental amino acid transporters in vitro (13, 14). Furthermore, we recently published evidence that intrauterine growth restriction developing in response to maternal protein malnutrition in rats may be due to decreased concentrations of maternal IGF-I, insulin, and leptin, which down-regulate the placental amino acid transporters (24).

The current study has several strengths. First, it was a prospective cohort study, which allows the collection of detailed and extensive data on dietary intake and metabolic hormones and adipokines from both the first and the third trimester in the same subject. Second, our study population consisted of a homogeneous group with respect to ethnicity and socioeconomic background; the subjects were nonsmokers, delivered at term, and had no pathologic conditions. Third, relatively few (12.5%) were lost from the study. The primary limitation with the study is the relatively small number of subjects studied ($n = 49$), which decreases our ability to detect biologically relevant differences. Despite this potential limitation, using a multiple regression explanatory approach, we identified maternal factors that may be of particular importance in determining fetal growth. Our study provides new information on first-trimester metabolism in overweight and obese women. We report extensive changes in hormone concentrations, qualitatively similar to those in the third trimester, already early in pregnancy in women with high BMI. This is significant because perturbations in maternal metabolism (31–33) or dietary intake (28) in early pregnancy may have marked effects on the fetal growth trajectory for the remainder of pregnancy.

As evidenced by the positive correlations between early pregnancy BMI and the intake of protein, carbohydrate, and fat, obese women have a higher intake of all macronutrients, in particular in early pregnancy. These findings support the concept of obesity in pregnancy as a condition of overnutrition. There is a growing body of evidence from both animal and epidemiologic studies that maternal nutritional status affects fetal growth and development. However, most previous studies focused on the effects of maternal undernutrition (20, 34, 35, 36). Studies in women primarily focused on subjects within the normal BMI range and the relation between dietary intake and fetal growth. In some of these studies, no significant correlation between maternal energy or macronutrient intake and birth weight was shown (37, 38), whereas other studies reported that birth weight is associated with the percentage of energy obtained from dairy products in gestational week 16 (29), high carbohydrate intake in early pregnancy, and low intake of meat protein in relation to carbohydrate intake in late pregnancy (28). A significant effect of maternal protein intake on birth weight was also observed in a study by Cucó et al (23), who reported that proteins were the macronutrient with the largest effect on birth weight independent of energy intake or preconceptional BMI. The mechanisms linking dietary intake in pregnant women to fetal growth in these studies, however, are unclear.

In our model (Figure 1), we proposed that one important mechanism by which diet influences fetal growth is by altering the circulating concentrations of key maternal metabolic hormones, which regulates placental nutrient transport and therefore fetal growth. This hypothesis was indirectly supported by significant correlations between dietary variables, in particular fat intake, and maternal serum concentrations of metabolic hormones. We therefore proceeded by carrying out a multiple regression analysis, which showed that first-trimester protein and fat intake were positively correlated with leptin concentrations and first-trimester fat intake was inversely associated with circulating adiponectin, associations that could not be explained by BMI. In the third trimester, total fat intake was correlated with serum resistin independently of BMI. These data show that maternal dietary intake variables influence concentrations of maternal hormones, which may alter fetal growth by affecting maternal metabolite levels and placental function.

We proceeded by assessing the relation between maternal hormones and birth weight. Using multiple regression modeling, we found that first-trimester maternal plasma resistin was positively and third-trimester maternal plasma IGFBP-1was negatively correlated with birth weight z score. IGFBP-1 generally inhibits IGF-I action and also has direct effects independent of IGF-I and the IGF-I receptor (39). We propose that the mechanistic link between low IGFBP-1 and increased fetal growth is increased IGF-I bioavailability. Ample experimental evidence exists showing that maternal IGF-I increases fetal growth and up-regulates placental nutrient transporters. Maternal IGF-I administered to pregnant guinea pigs midgestation increased placental and fetal growth (40). IGF-I has been shown to stimulate system A uptake in cultured term primary trophoblast cells (15) and to increase glucose and amino acid uptake in a first-trimester trophoblast cell line (41). Furthermore, in pregnant guinea pigs, in vivo evidence suggested that chronic infusion of IGF-I midgestation was associated with an increased placental capacity to

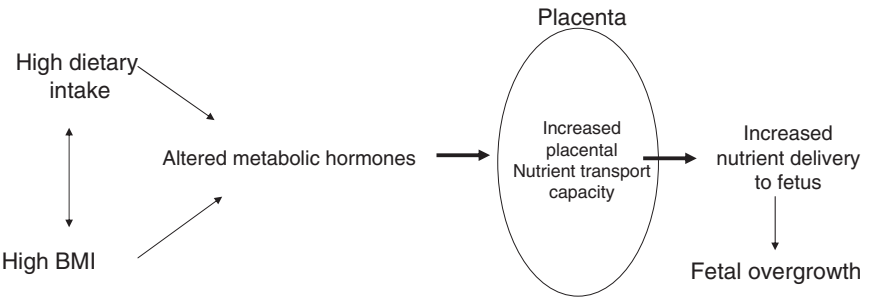

FIGURE 1. Model for mechanistic links between overweight or obesity in pregnancy and fetal overgrowth. We propose that a high BMI and high dietary intake alter the maternal circulating concentrations of metabolic hormones, which up-regulates placental nutrient transport and results in increased nutrient delivery to the fetus and fetal overgrowth.

transport glucose (42). Because BMI was inversely correlated with serum IGFBP-1 in our multiple regression analysis (Table 3), serum IGFBP-1 concentrations may constitute one mechanistic link between BMI and birth weight.

Resistin, a cytokine secreted by adipocytes, was identified in 2001 and has been shown to cause insulin resistance in mice (43); however, the effects of resistin on insulin sensitivity in humans remain less well defined (44, 45). Maternal circulating concentrations of resistin are higher in pregnant than in nonpregnant women and have been reported to decrease with advancing gestation in women with normal BMI (46). In contrast, we observed an increase in maternal serum resistin between the first and third trimesters (Table 2). This apparent discrepancy may be due to the inclusion of overweight and obese women in our cohort, because pregnant women with a high BMI have a high fat intake, and total fat intake in the third trimester was positively correlated with resistin concentrations (Table 3). First-trimester resistin was positively correlated with birth weight, and this association was independent of BMI and dietary variables. The mechanism linking first-trimester resistin to fetal growth remains to be established. To the best of our knowledge, the effects of resistin on placental function and fetal growth have not been studied. However, it was recently reported that resistin stimulates lipoprotein lipase in 3T3-L1 adipocytes (47). If resistin has similar effects in placenta, it will result in increased transplacental transfer of free fatty acids, which may stimulate fetal growth and fat deposition.

In summary, high first-trimester maternal serum resistin and low third-trimester IGFBP-1 were correlated with increased birth weight. We propose that low serum concentrations of IGFBP-1 represent a link between high BMI and increased fetal growth by increasing the bioavailability of IGF-I, which upregulates placental nutrient transport.

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