Influence of Maternal Glucose Level on Ethnic Differences in Birth Weight and Pregnancy Outcome

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Minority ethnicity increases the risk of a poor pregnancy outcome in the United States. The mechanism(s) whereby this occurs is unknown. One possibility is physiologic variation in levels of maternal glucose, the major substrate for fetal growth, which is metabolized from the maternal diet and endogenous gluconeogenic sources. The authors examined whether postload glucose concentration at week 28 was associated with maternal ethnicity or altered the ethnic difference in birth weight after adjustment for duration of gestation (to index fetal growth) and pregnancy outcome (large- and small-for-gestational-age births) among 2,072 diabetes-free gravidas in Camden, New Jersey (1990–2001). After data were controlled for potentially confounding factors, maternal glucose level was significantly lower for African Americans than for Hispanics (mainly Puerto Ricans) or Whites. Maternal glucose was associated with infant birth weight to a similar extent within each ethnic group (1.5–2.0 g of birth weight per mg/dl of maternal glucose). A comparison of regression coefficients from models with and without glucose indicated small but statistically significant effects of glucose on the ethnic difference in birth weight and the risk of large-for-gestational-age birth between African Americans and Whites. Maternal glucose concentration did not differ between Hispanics and Whites; consequently, glucose did not influence this ethnic difference in birth weight and pregnancy outcome. Am J Epidemiol 2002;156:498–506.

birth weight; blacks; ethnic groups; glucose; Hispanic Americans; pregnancy outcome

Abbreviations: LGA, large for gestational age; SGA, small for gestational age.

Maternal glucose concentration has an important relation with fetal growth. Overweight and obese nondiabetic women have larger infants and an increased risk of fetal macrosomia (1). Along with greater plasma volume and the increased placental perfusion associated with obesity, greater maternal insulin resistance with decreased glucose disposal is thought to allow more glucose to be transmitted from mother to fetus (2). The mother’s body mass index also has a consistently positive association with infant birth weight (3), and increasing maternal body mass index is associated with higher maternal glucose levels (4, 5).

Glucose is produced by metabolism from the diet (carbohydrate, glucogenic amino acids) and endogenous gluconeogenic sources (6–8). In pregnancies complicated by diabetes, there is a positive influence of maternal plasma glucose level, especially postprandial glucose level, on infant birth weight (9, 10). Likewise, in women with diabetes it is possible to alter, via dietary modification, the production of glucose and other metabolic fuels (amino acids, triglycerides, free fatty acids, ketones)—fuels that are transported to the fetus and that correlate with fetal growth (6). The literature suggests a similar connection between glucose concentration and fetal growth in pregnancies that are not complicated by maternal diabetes or obesity (5, 11–16).

Membership in an ethnic minority group in the United States increases the risk of a poor pregnancy outcome, for
reasons that are presently unexplained (17–20). For decades, it has been observed that African-American women bear infants of lower birth weight, have a decreased risk of large-for-gestational-age (LGA) birth, and have increased risks of preterm delivery and fetal growth restriction (21). Suboptimal maternal life circumstances undoubtedly contribute a portion of this increased risk. However, there are other unidentified factors which impair fetal growth even among well-educated minority women (16) and which may exert long-term effects by accelerating the prevalence and onset of maternal chronic disease (22).

Results of glucose screening tests vary significantly by ethnic group (4, 15, 23). Although it is unclear whether this difference is due partly to uncontrolled confounding factors, pregnant African-American women appear to have lower circulating levels of glucose than US gravidas who are Hispanic, Asian, or White. Consequently, maternal glucose concentration may be one of the factors underlying the ethnic difference in infant birth weight.

MATERIALS AND METHODS

The Camden Study (5, 24, 25) is an ongoing prospective study of the effects of maternal nutrition and growth during pregnancy in generally healthy young women residing in Camden, New Jersey, one of the poorest cities in the United States. Participants in this analysis included young (<18 years) and more mature (19–29 years) pregnant women enrolling in Camden prenatal care clinics between 1990 and 2001. Gravidas with serious nonobstetric health problems (e.g., lupus, chronic hypertension, type 1 or type 2 diabetes mellitus, seizure disorders, malignancies, or drug or alcohol abuse) are not recruited. Women with gestational diabetes were excluded from this analysis.

Subjects identified their ethnicity as African-American, Hispanic, Asian, or White upon entry into prenatal care. Socioeconomic, demographic, and lifestyle data were also obtained by interview and were updated during the pregnancy and postpartum (4–6 weeks after the birth). Maternal weight was measured at each visit, and height was measured at entry into prenatal care; pregravid weight was obtained by recall. Adequacy of gestational weight gain for the entire pregnancy was defined to within 2 completed weeks of delivery using published criteria that adjust weight gain for duration of gestation (26). Body mass index was computed as pregravid weight (kg) divided by the square of height (m²). Institute of Medicine criteria were used to categorize body mass index (3).

Data on current and past pregnancy outcomes, complications, and infant abnormalities were abstracted from the prenatal record, the delivery record, the delivery log books, and the infant's chart. In this analysis, we examined pregnancy outcomes that we found to be directly related to maternal glucose concentration in Camden gravidas (5). Duration of gestation was based on the date of the last normal menstrual period, confirmed or modified by ultrasound. An LGA birth was defined by a birth weight for gestation above the 90th percentile of Brenner's standard (27). Fetal growth restriction was defined by a birth weight for gestation below the 10th percentile of the same standard. Infant birth weight, adjusted for duration of gestation, was used to index fetal growth.

Maternal plasma glucose concentration was examined in 2,072 gravidas without diabetes who underwent a 1-hour 50-g glucose screening test for detection of gestational diabetes (28). This test is routinely conducted in Camden for all gravidas between 24 and 28 weeks’ gestation. As recommended, the test is given without regard to fasting status or time of day. Women testing positive (glucose concentration >140 mg/dl) receive a 3-hour 100-g oral glucose tolerance test. Women diagnosed with gestational diabetes (28, 29) were excluded from this analysis.

Compared with the diagnostic test (the 3-hour oral glucose tolerance test), the sensitivity of the 50-g screening test is 82–89 percent, and its specificity is 82–88 percent, depending on the cutoff of the screening test and the criteria used to diagnose gestational diabetes (30). The test’s positive predictive value ranges between 8 percent and 40 percent, depending on the prevalence of gestational diabetes; its negative predictive value is reported to be 96–99 percent (23, 30).

In the analyses described below, data from the 50-g glucose screening test were used to examine ethnic differences in maternal glucose concentration and the effect of these differences on pregnancy outcome. Confounding was assessed by comparing crude and adjusted odds ratios or regression coefficients. The cumulative distribution function of glucose was estimated for each ethnic group using the PROC LIFEREG procedure in SAS for Windows (version 8.01; SAS Institute, Cary, North Carolina). Multiple logistic regression analyses (for dichotomous dependent variables) or ordinary least-squares regression analyses (for continuous dependent variables) were used to fit separate models for each outcome of interest containing the independent variable(s), maternal age, parity, and potentially confounding factors (31). Adjusted odds ratios and 95 percent confidence intervals were computed from the logistic regression coefficients and their corresponding covariance matrices. The least-squares mean values from the ordinary least-squares models were tested using Bonferroni’s correction for multiple comparisons.

We tested the difference between regression coefficients from models with and without maternal glucose concentration as described by Clogg et al. (32, 33), computing the unconditional variance estimator for linear and generalized linear models (see equation 12 in Clogg et al. (33)). The aim of these comparisons was to determine whether the coefficient(s) characterizing, for example, the relation between maternal ethnicity and infant birth weight (reduced model) differed from the coefficient(s) characterizing the same relation in another model (full model), where the only change was the addition of an extra predictor—maternal glucose concentration.

RESULTS

Despite the fact that women in Camden live in a poor urban environment, there was ethnic variation in their background characteristics (table 1). While there was little difference in pregravid body mass index or the proportion of

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women who were overweight, White women were slightly older than the other gravidas, were more likely to be smokers, and were less likely to have their prenatal care financed by Medicaid or to have inadequate weight gain during pregnancy. Parous White women were somewhat less likely to have had a low birth weight infant previously. Of the factors shown in table 1, maternal pregravid body mass index \((r = 0.13, p < 0.001)\), age \((r = 0.15, p < 0.001)\), nulliparity \((r_{pb} = -0.048, p < 0.05)\), and number of cigarettes smoked per day \((r = 0.038, p < 0.1)\) correlated with the mother’s glucose concentration on the 50-g screening test along with maternal ethnicity.

African Americans evinced a somewhat different distribution of plasma glucose than Whites and Hispanics, most of whom (75 percent) were of Puerto Rican descent. More African Americans had plasma glucose levels in the lower ranges of the distribution than gravidas from other ethnic groups (figure 1). On average, glucose concentration was approximately 5 percent lower (5 mg/dl) for African-American gravidas than for Whites or Hispanics \((p < 0.001)\), and control for potentially confounding factors did little to alter it (table 2). On the other hand, after data were controlled for body mass index and other factors, Hispanic and White women had nearly identical concentrations of plasma glucose.

We found no interaction between maternal ethnicity and glucose concentration for birth weight \((p > 0.5)\) or any other pregnancy outcome examined. Thus, maternal glucose concentration was associated with infant birth weight to approximately the same extent in each ethnic group. After data were controlled for duration of gestation and potentially confounding factors, birth weight increased among White women by slightly less than 2 g per mg/dl increase in plasma glucose; for Hispanics, the increase in birth weight amounted to slightly more than 2 g per mg/dl increase in plasma glucose; and for African Americans, the increase was

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<tr>
<td>Maternal ethnicity</td>
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<tr>
<td>African-American ( (n = 1,040) )</td>
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<tr>
<td>Age group (years)</td>
</tr>
<tr>
<td>&lt;16</td>
</tr>
<tr>
<td>16–18</td>
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<tr>
<td>≥19</td>
</tr>
<tr>
<td>Nulliparity</td>
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<td>Smoking (cigarettes/day)</td>
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<td>1–9</td>
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<tr>
<td>10–20</td>
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<td>&gt;20</td>
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<td>Medicaid payment status</td>
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<td>Body mass index†</td>
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<td>&lt;19.8</td>
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<td>19.8–26.0</td>
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<tr>
<td>&gt;26.0</td>
</tr>
<tr>
<td>Inadequate weight gain during pregnancy</td>
</tr>
<tr>
<td>23.7</td>
</tr>
<tr>
<td>Prior preterm birth (&gt;20 weeks' gestation)‡</td>
</tr>
<tr>
<td>9.0</td>
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<tr>
<td>Prior low birth weight infant‡</td>
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*p < 0.1; ** p < 0.01; *** p < 0.001 (chi-squared test).
† Weight (kg)/height (m)².
‡ Among parous women \( (n = 876) \).
slightly less—approximately 1.5 g per mg/dl (table 3). The 95 percent confidence intervals for these regression coefficients overlapped, suggesting a similar influence of maternal plasma glucose on birth weight for each ethnic group.

While glucose concentration had a similar influence within groups, a difference in glucose concentration between ethnic groups (table 2) was associated with a portion of the ethnic differences in infant birth weight (table 4). After data were controlled for potentially confounding factors (age, parity, cigarettes per day, clinic payment status, a prior low birth weight infant, duration of gestation, gestational weight gain, fetal sex, and pregravid body mass index), the model that did not include maternal glucose concentration (the reduced model) showed significant differences in infant birth weight (−178 g between African Americans and Whites and −142 g between Hispanics and Whites), whereas the model that included plasma glucose (the full model) explained 11 g of the 178-g difference ($p < 0.001$) in birth weight between African Americans and Whites. Hispanics and Whites had equivalent concentrations of glucose. Thus, the addition of plasma glucose to the model showed little change (−1.5 g) in the birth weight difference between Hispanic women and White women (table 4).

By way of comparison, a full model that controlled for number of cigarettes smoked per day (in lieu of glucose), when compared with a reduced model that did not, significantly increased the ethnic difference in birth weight rather than reduce it as glucose did. The ethnic difference in birth weight increased by 13.5 g (standard error 5.1; $p < 0.01$) for African Americans and by 13.0 g (standard error 5.0, $p < 0.01$) for Hispanics in comparison with Whites.

We also examined other indices of fetal growth (fetal growth restriction, LGA birth) that are directly related to maternal glucose concentration. None of the models suggested any effect of an interaction between maternal glucose concentration and ethnicity on the outcomes of interest. Both Hispanic and African-American gravidas had a greater than twofold decrease in risk of an LGA birth and a nearly fourfold increase in risk of fetal growth restriction (table 5). A comparison of the logistic regression coefficients in the reduced (without plasma glucose) and full (with plasma glucose) models suggested that, like birth weight, inclusion of maternal glucose concentration modestly but significantly diminished the difference in LGA births between African Americans and Whites but had little effect on the Hispanic-White difference. However, the inclusion of maternal glucose concentration in models of fetal growth

![FIGURE 1. Cumulative distribution function (CDF) for maternal plasma glucose concentration 1 hour after a 50-g glucose challenge, by ethnic group, Camden, New Jersey, 1990–2001. White (W) women are represented by a solid line, African-American (AA) women by a dashed line, and Hispanic (H) women by a broken dashed line.](image-url)
restriction had no effect on the ethnic disparity in fetal growth restriction for either African-American women or Hispanic women (table 5). Likewise, the inclusion of maternal plasma glucose level did not have a statistically significant effect on ethnic differences in duration of gestation and preterm delivery (data not shown).

**DISCUSSION**

Glucose, the main substrate for fetal growth, is transported across the placenta in proportion to its concentration in the maternal bloodstream. The change in levels of glucose and other substrates after a meal promotes the passage of nutrients across the placenta and provides energy for fetal growth (34, 35). In healthy women, reduced glucose transfer from mother to fetus, as indexed by the screening test for gestational diabetes, is linked to slower fetal growth, smaller birth size, a reduced risk of LGA birth, and an increased risk of fetal growth restriction (4, 5, 11–14, 16). A higher maternal glucose concentration may also be a marker for inflammation and infection, and it is associated with shorter gestation and increased risks of chorioamnionitis, cesarean section, and preeclampsia in women who are not diabetic (5, 36).

Several studies have suggested that pregnant African Americans have lower glucose concentrations than US women of other ethnic groups. Nahum and Hufnaker (23) and Green et al. (4, 15) examined data from a substantial number of California gravidas 60 minutes after a 50-g glucose screening test and found that African-American women consistently had the lowest glucose concentrations of any ethnic group examined. As in the current study, their glucose concentration was approximately 5–6 percent below

### TABLE 3. Results of regression of infant birth weight on maternal plasma glucose level, by ethnic group, in the Camden Study, Camden, New Jersey, 1990–2001.*,†

<table>
<thead>
<tr>
<th>Predictor variable</th>
<th>Maternal ethnicity</th>
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<tr>
<td></td>
<td>African-American</td>
<td>Hispanic</td>
<td>White</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n = 1,040)</td>
<td>(n = 750)</td>
<td>(n = 282)</td>
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<td></td>
</tr>
<tr>
<td>Maternal glucose level (mg/dl)</td>
<td>1.56 0.63 0.34, 2.79</td>
<td>2.19 0.66 0.89, 3.48</td>
<td>1.98 0.95 0.11, 3.84</td>
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<td></td>
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</tbody>
</table>

* Data were adjusted for age, parity, smoking (cigarettes/day), pregravid body mass index, gestational weight gain, clinic payment status, a prior low birth weight infant, and duration of gestation. A separate model was fitted for each ethnic group.
† Results of regression of birth weight on maternal plasma glucose adjusted for gestational duration alone were as follows: African Americans, 1.96 g per mg/dl of glucose (SE 0.63), 95% CI: 0.73, 3.19; Hispanics, 2.57 g per mg/dl of glucose (SE 0.66), 95% CI: 1.28, 3.86; Whites, 2.45 g per mg/dl of glucose (SE 0.99), 95% CI: 0.51, 4.39.
‡ Change in birth weight (g) per unit of plasma glucose (mg/dl).
§ SE, standard error; CI, confidence interval.

### TABLE 4. Results of regression analyses predicting infant birth weight from models with and without maternal glucose level in the Camden Study (n = 2,072), Camden, New Jersey, 1990–2001†,‡

<table>
<thead>
<tr>
<th>Predictor variable</th>
<th>Change in birth weight</th>
<th>Difference§</th>
<th>Z score¶</th>
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<tbody>
<tr>
<td></td>
<td>Reduced model</td>
<td>Full model</td>
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<tr>
<td></td>
<td>β# Standard error</td>
<td>β# Standard error</td>
<td>Δ Standard error</td>
</tr>
<tr>
<td>Maternal ethnicity</td>
<td></td>
<td></td>
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<tr>
<td>African-American††</td>
<td>−178.02** 29.08</td>
<td>−167.18** 29.05</td>
<td>−10.85 3.68</td>
</tr>
<tr>
<td>Hispanic††</td>
<td>−142.42** 30.05</td>
<td>−140.88** 29.92</td>
<td>−1.54 2.86</td>
</tr>
<tr>
<td>White</td>
<td>—‡‡</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Maternal glucose level (mg/dl)</td>
<td>1.90* 0.43</td>
<td></td>
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</tr>
</tbody>
</table>

* p < 0.005; ** p < 0.001.
† Data were adjusted for age, parity, smoking (cigarettes/day), pregravid body mass index, gestational weight gain, clinic payment status, a prior low birth weight infant, fetal sex, and duration of gestation.
‡ Results for the ethnic difference in birth weight adjusted for duration of gestation alone were as follows: 187.6 g (SE 28.78) for African Americans versus Whites (p < 0.001) and −149.04 g (SE 29.93) for Hispanics versus Whites (p < 0.001).
§ Difference between the reduced model (without glucose) and the full model (with glucose).
¶ Reduced model versus full model.
# Change in birth weight (g) per unit of plasma glucose (mg/dl).
†† Dummy coded variable comparing this ethnic group with Whites.
‡‡ Reference category.
that of either Hispanic or non-Hispanic Whites; Hispanic Whites and non-Hispanic Whites had nearly identical concentrations. A lower postload glucose concentration suggests that a lower cutpoint may be needed when screening African Americans for gestational diabetes (23). Thus, a disproportionate number of cases of gestational diabetes among African Americans may be missed. Untreated or undiagnosed gestational diabetes places the mother at higher risk of morbidity and the fetus at greater risk of morbidity and perinatal mortality (37–39). Type 2 diabetes that is not recognized before pregnancy also increases risk of fetal and neonatal death (40). Women with a history of gestational diabetes have an increased long-term risk of developing type 2 diabetes (39). A subsequent pregnancy may accelerate onset and increase risk of diabetic complications (41). Fetuses exposed to maternal diabetes in utero also have increased long-term risks of obesity and impaired glucose tolerance (42, 43). Epidemiologists should investigate whether gestational diabetes is being underdiagnosed among African Americans and whether this has led us to think of some of the associated morbidity and mortality as “ethnic differences.”

Interestingly, recent data suggest that in pregnant women, the ethnic difference in glucose concentration is noted only after “eating” (i.e., after a glucose load), not in the fasting state (44). The reason(s) why African Americans have lower plasma glucose levels is not known. Nonpregnant African-American girls and women also have lower postprandial glucose concentrations than Whites (45–48). The difference is not unique to pregnancy, but it may be related to underlying insulin secretion, resistance, or clearance (44, 49, 50). The habitual antecedent composition of the diet increases insulin secretion and resistance, including diets with a low fiber content (a high glycemic index) or a high fat content (51–54). Some studies (55, 56) but not all (57) suggest that dietary differences such as these exist between African Americans and Whites.

Green et al. (4) examined the effect of glucose concentration on birth weight among full-term births (>37 weeks) within several ethnic groups. They reported a significant effect of maternal glucose concentration for all groups combined, as well as a separate effect within each group.
except for the African Americans, in whom the regression coefficient was not statistically significant. Our study confirms these results among births of all gestations, extends them to African Americans, and demonstrates regression coefficients in the same general range as those reported by Green et al. (4). Our study suggests that the effect of glucose on fetal growth (birth weight adjusted for length of gestation) is similar for each of the ethnic groups examined.

After testing the difference between models that did and did not include maternal plasma glucose, we demonstrated that adding glucose concentration to the list of predictors reduced the ethnic differences in infant birth weight and risk of LGA birth. US Hispanic gravidas, who are mainly of Puerto Rican descent, have infants of lower birth weight than Whites (58), but they do not have lower concentrations of maternal glucose. Consistent with this, we found no effect of maternal glucose concentration on the ethnic difference in fetal growth or birth weight between Hispanics and Whites. We demonstrated a statistically significant effect in the ethnic group with a lower postprandial glucose concentration (African Americans), a finding that has biologic plausibility for pregnancy. Consistent with Pedersen’s hypothesis (35), less stimulation of beta cells in the fetal pancreas by lower concentrations of maternal glucose should result in slower fetal growth.

We used Brenner’s standard (27) to examine ethnic differences in LGA and small-for-gestational-age (SGA) birth. This standard is based on gestational age measured to the nearest week rather than in completed weeks. This means, for example, that an infant born at 36 weeks and 5 days of gestation would be considered more mature according to Brenner’s standard. The effect would be to decrease the proportion of SGA infants and increase the proportion of LGA infants. Since more LGA infants are born at term, this might also exaggerate ethnic differences, particularly if one ethnic group (Whites) has a longer duration of gestation than others.

While we explained a small portion of the overall difference in gestational-age-adjusted birth weight (approximately 5–7 percent) and risk of LGA birth between African Americans and Whites, maternal glucose level did not explain ethnic differences at the low end of the spectrum, that is, differences in the risk of SGA birth. Recently, unexplained SGA birth was linked to increased maternal insulin sensitivity on the euglycemic hyperinsulinemic clamp test (59). Thus, it may be necessary to measure the sensitivity of insulin to a glucose load rather than plasma glucose concentration itself to “explain” ethnic differences in SGA birth.

There is little ethnic difference in birth weights at weeks 24–28, the point in gestation at which ethnic differences in glucose concentration were examined. Rather, the difference in birth weight between African Americans and Whites arises with advancing gestation (21). In gravidas who do not have diabetes, results of the 50-g glucose screening test at 24–28 weeks correlate only moderately ($r = 0.35$) with measures of longer-term plasma glucose control, including glycosylated hemoglobin (past 3–4 months) and glycosylated plasma protein (past 3–4 weeks) (60). Thus, one limitation is that results from the 50-g screening test may not be a good indicator of maternal glucose concentration later in pregnancy, and this may have attenuated the results examined in this study.

African Americans with controlled diabetes have a reduced risk of infant macrosomia and bear infants of lower birth weight than Hispanics at the same controlled glucose concentration (61). Thus, during pregnancy, there may also be ethnic differences in other insulin-sensitive diet-driven metabolic fuels—fuels that correlate with fetal growth and infant birth weight (62, 63). For example, African-American girls and women have lower concentrations of free fatty acids and triglycerides (46, 64), and one study reported a lower concentration of certain amino acids, including the branch chain amino acids, in the umbilical cord blood of low birth weight African-American infants compared with those of higher birth weight (65). Thus, measurement of glucose concentration along with other maternal fuels at a later point in gestation would also improve our insight into these ethnic differences.

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