The Interrelationship Between Ethnicity and Gestational Diabetes in Fetal Macrosomia

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OBJECTIVE — To determine the possibility of an ethnic influence on the development of macrosomia (birth weight >90th percentile for gestational age) in gestational diabetes mellitus (GDM).

RESEARCH DESIGN AND METHODS — We prospectively followed all African-American and Latino women enrolled in the Temple diabetes-in-pregnancy program. GDM was diagnosed in 103 African-American and 36 Latino women during the study period (1991–1994) according to the criteria of Carpenter and Coustan. All women were treated according to our previously published protocols. Data were collected on gestational weight gain, previous history of macrosomia, body mass index (BMI), and level of maternal glycemic control.

RESULTS — Insulin therapy was required in 53 women (37.5%) to maintain fasting blood glucose levels at <95 mg/dl and 2-h postprandial levels at <120 mg/dl. Macrosomia developed in 50% of the neonates of Latino women versus 19% of neonates of African-American women (relative risk 2.68; 95% confidence interval 1.57–4.59). Potential confounding factors were not significantly different between the Latino and African-American women: mean blood glucose 96.6 ± 15.7 vs. 96.5 ± 22.4 mg/dl; BMI 29.0 ± 5.5 vs. 31.5 ± 8.2 kg/m^2; pregnancy weight gain 29.2 ± 12.7 vs. 30.9 ± 20.5 lb; and parity 1.8 ± 1.5 vs. 1.6 ± 1.4, respectively.

CONCLUSIONS — We have demonstrated that Latino women with GDM are at higher risk for having macrosomic infants in comparison with African-American women. This ethnic variation in fetal growth may be due to varying influences of in utero growth promoters among these populations as well as underlying genetic factors.

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BMI, body mass index; CI, confidence interval; GDM, gestational diabetes mellitus; IGF, insulin-like growth factors; OR, odds ratio.

Macrosomia continues to be a major factor responsible for the increased morbidity associated with gestational diabetes mellitus (GDM). The mother as well as her macrosomic infant are at risk for a number of potential complications (1,2). Maternal complications include an increased risk for cesarean section, labor abnormalities, and traumatic deliveries. Neonatal complications include shoulder dystocia and its potential neurological sequelae as well as increased risk for metabolic abnormalities such as hypoglycemia, hyperbilirubinemia, and polycythemia. For these reasons, the initiation of intensive treatment regimens to prevent macrosomia have become a major focus of the modern management of the pregnancy complicated by GDM.

The most widely accepted hypothesis (3) regarding the pathogenesis of fetal macrosomia postulates that fetal macrosomia occurs as the result of fetal hyperinsulinemia in response to maternal hyperglycemia. Numerous studies have established a relationship between the level of maternal glucose control and macrosomia. However, despite this knowledge and the increased utilization of intensive therapy protocols, the incidence of macrosomia remains increased in pregnant women with GDM above the background population rate. The current study was undertaken to determine the possibility of an ethnic influence on the occurrence of macrosomia.

RESEARCH DESIGN AND METHODS

Screening and diagnosis

The study population was drawn from the obstetrical clinics of Temple University Hospital, which serves a largely economically deprived inner-city population. All pregnant women were screened for carbohydrate intolerance with a 1-h glucose challenge test between the 24th and 28th week of gestation. If plasma glucose was >135 mg/dl, a 3-h, 100-g oral glucose tolerance test was performed. GDM, de-

Table 1—*Comparison of risk factors for macrosomia*

Variables	Latino women	African-American women	*P* value
Mean blood glucose (mg/dl)	96.6 ± 15.7	96.5 ± 22.4	NS
BMI (kg/m^2)	29.0 ± 5.5	31.5 ± 8.2	NS
Pregnancy weight gain (lb)	29.2 ± 12.7	30.9 ± 20.5	NS
Parity	1.8 ± 1.5	1.6 ± 1.5	NS
Previous history of macrosomia (%)	11	30	NS

Data are means ± SE.

fined as glucose intolerance with onset or first recognition during pregnancy, was diagnosed using the modified criteria of Carpenter and Coustan (4). Only patients with two abnormal values were included in the study population.

Study population

All African-American and Latino women enrolled in the diabetes-in-pregnancy program at Temple University Hospital between July 1991 and January 1995 were included in the study and were followed prospectively. Patients with multiple gestations were excluded from the study population. Patients were weighed at the initial visit and at each subsequent visit. Prepregnancy weight was obtained by patient questioning. Body mass index (BMI) was calculated as the patient's self-reported prepregnancy body weight (kg) divided by height squared (m^2). Total pregnancy weight gain was based on the prepregnancy weight and the last weight measured before delivery. The infant's weight, length, sex, gestational age, and perinatal complications were recorded postpartum.

Management approach

Antepartum care was provided by a team of health care providers including perinatologists, postdoctoral fellows, residents, dietitians, and diabetes nurse specialists. Our management approach for pregnant women with GDM has been previously described (5). In brief, after diagnosis of GDM, women were seen for individual counseling and instruction by a registered dietitian. Patients who did not achieve glycemic goals (plasma fasting blood glucose level <95 mg/dl and 2-h postprandial level <120 mg/dl) on diet therapy alone were assigned to diet and insulin therapy. Patients maintained on diet therapy had fasting and postprandial blood glucose levels (2 h after breakfast) performed every 1–2 weeks. Quality control measures including simultaneous laboratory determinations were performed at each clinic session. Women placed on insulin therapy were asked to perform self-blood glucose monitoring (One Touch II, LifeScan) four times a day; fasting and 2-h blood glucose determinations after each meal. However, these self-reported data were only used to adjust therapy and were not included in the analyses.

Neonatal assessment

Gestational age was assigned by menstrual history in conjunction with first trimester ultrasound and postpartum physical examination. Infants were considered macrosomic when their birth weight was ≥90th percentile for gestational age on the basis of growth standards developed by Battaglia and Lubochenco (6). Hypoglycemia was diagnosed if plasma glucose levels were ≤30 mg/dl. Hyperbilirubinemia was characterized by plasma values ≥12 mg/dl (2).

Statistical analysis

Statistical analyses were performed using the Epi Info Statistical software package (Centers for Disease Control and Prevention, Atlanta, GA). Categorical data were analyzed for significance by means of the Mantel-Haenszel χ^2 formula. When a cell value of less than five was encountered, a two-tailed *P* value was obtained with Fisher's exact test. Relative risks and 95% confidence intervals (CIs) were derived using a Taylor series approximation. For continuous variables, a *P* value was calculated through a one-way analysis of variance of the means. Variables that were found to be significantly associated with macrosomia were then entered into multivariate logistic regression analysis using Systat (Evanston, IL). Statistical significance was set at the $P < 0.05$ level.

RESULTS

Maternal characteristics

A total of 139 women with GDM participated in this study. Of the subjects, 36 (25.9%) were of Latino origin and 103 (74.1%) were of African-American descent. The Latino and African-American groups were comparable in demographic characteristics. Mean maternal ages for the two groups were 27.6 ± 5.6 and 27.3 ± 6.5 years, respectively. Of the Latino women, 40% (n = 14) required insulin therapy to maintain blood glucose targets as did 37.9% (n = 39) of the African-American women.

In univariate analysis, history of prior macrosomic birth, mean blood glucose level >100 mg/dl, and Hispanic ethnicity were all associated with macrosomia. No relationship between maternal age, cigarette smoking, chronic hypertension, babies' sex, and macrosomia was found. With multivariate analysis, only Hispanic ethnicity (odds ratio [OR] 4.2, 95% CI 1.6–11.0) and mean blood glucose level >100 mg/dl (OR 3.5, 95% CI 1.2–7.8) were significant factors.

Comparison of risk factors related to an increased incidence of macrosomia can be found in Table 1. No significant differences were found between the Latino and African-American women: mean blood glucose 96.6 ± 15.7 vs.

Table 2—*Delivery and neonatal outcomes*

	Latino women	African-American women	*P* value
Gestational age at delivery (weeks)	38.5 ± 1.9	39.1 ± 1.7	NS
Cesarean section rate	30.5 (11)	24.3 (25)	NS
Birth weight (g)	3,710.9 ± 688.9	3,436.5 ± 635.8	0.05
5-min Apgar <7	2.9 (1)	1 (1)	NS

Data are means ± SE or % (*n*).

96.5 ± 22.4 mg/dl; BMI 29.0 ± 5.5 vs. 31.5 ± 8.2 kg/m^2; pregnancy weight gain 29.2 ± 12.7 vs. 30.9 ± 20.5 lb; and parity 1.8 ± 1.5 vs. 1.6 ± 1.4, respectively.

Neonatal outcomes

Neonatal and delivery information is summarized in Table 2. No significant difference was found between the two groups with regard to gestational age at delivery, cesarean section, and 5-min Apgar scores <7. However, the mean birth weight of infants born to Latino women was significantly higher (3,711 ± 689 vs. 3,436 ± 636 g; $P = 0.05$). Macrosomia developed in 50% of the neonates of Latino women versus 19% of neonates of African-American women. This difference was statistically significant with a relative risk of 2.68 (95 CI% 1.57–4.59). This association remained significant even after controlling for levels of glycemic control, BMI, insulin therapy, and maternal weight gain.

CONCLUSIONS — This is the first study reporting an ethnic variation in the incidence of macrosomia among offspring of women with GDM. Macrosomia is known to be associated with a number of risk factors including maternal obesity, pregnancy weight gain, previous history of macrosomia, parity, and blood glucose control (7–9). In our study population, we did not find a difference in the occurrence of these risk factors between the two ethnic groups. Therefore, our finding of an increased incidence of macrosomia in the infants of Latino women when compared to African-American women could not be attributed to any of the known factors associated with excessive fetal growth.

It is important to note that our blood glucose criteria for the initiation of insulin therapy were lower than the current national recommendations (10). Despite the use of more stringent criteria for the initiation of insulin therapy, the rate of macrosomia remained elevated in our population of women. Our patients, however, were not intensively and meticulously monitored for their glycemic control throughout pregnancy; hence, it is possible that the high incidence of macrosomia could be attributed to a slightly less satisfactory level of metabolic control despite early initiation of insulin therapy. The infrequency of blood glucose sampling may have given a false impression of the actual level of metabolic control achieved. Although we believe this is improbable, we recognize it may be a possible explanation. Furthermore, both groups of individuals received the same level of care, thus making the above an unlikely explanation for the differences found between the two groups. Despite the fact that our rates of macrosomia were high, the incidence of other perinatal morbidities related to glucose control were relatively low. Hypoglycemia occurred in 5.0% of the neonates, hyperbilirubinemia in 5.8%, respiratory distress syndrome in 1.4%, and shoulder dystocia in 3.6%. These rates are comparable to the incidence recently reported by Langer et al. (11) in a group of intensively treated women with GDM. This supports our belief that glycemic control was not responsible for the differences in rates of macrosomia found between the two groups.

These authors found that mean blood glucose levels were a good predictor of perinatal outcome. Latino women appear to be a higher risk population for macrosomia for unclear reasons at present. Fetal ultrasound criteria as suggested by Buchanan et al. (12) may offer additional criteria for the initiation of insulin therapy in patients with GDM. These investigators examined the utility of fetal abdominal circumference measurements by ultrasound in the early third trimester to identify women at high risk for macrosomia. Their patient population consisted of Latino women with GDM and fasting blood glucose levels <5.8 mmol/l. Women with fetuses whose abdominal circumference was >75th percentile for gestational age were randomized to an unblinded trial of diet compared with diet-plus-insulin therapy for the remainder of the pregnancy. The authors found that insulin treatment significantly reduced the rate of macrosomia, suggesting that fetal ultrasound can be used to guide metabolic therapy in pregnancies complicated by mild GDM.

We postulate that this ethnic variation in fetal growth may be related to varying expression, levels, and/or actions of in utero growth promoters, including insulin and insulin-like growth factors (IGFs). Current evidence suggests that IGFs play an important role in fetal growth. The IGFs have been shown to be potent growth-promoting stimuli for many different cultured cell populations (13,14). Moreover, many clinical and animal studies have demonstrated an association between fetal and infant growth and IGF-I levels (13,15,16). The precise role that IGFs play in deviant fetal growth needs further investigation. However, the ethnic variation found in our study may be related to influences of these in utero growth promoters or other underlying genetic factors.

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