The burden of gestational diabetes mellitus in Jamaican women with a family history of autosomal dominant type 2 diabetes

Rachael R. Irving,[1] *James L. Mills,*[1] *Eric G. Choo-Kang,*[2] *Errol Y. Morrison,*[1] *Santosh Kulkarni,*[3] *Rosemarie Wright-Pascoe,*[4] *and Wayne Mclaughlin*[1]

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ABSTRACT

Objectives. *To determine if Jamaican women of African descent with a family history of early onset autosomal dominant type 2 diabetes have greater odds of developing gestational diabetes mellitus (GDM) than those without a family history of the disease.*

Methods. *A comparative study was conducted of two groups of pregnant Jamaican women: the first with a family history of early onset autosomal dominant type 2 diabetes; the second with no history of the disease. Incidence, odds for developing GDM, and metabolic profiles in first and second trimesters were assessed using SPSS 11.5 (SPSS Inc., Chicago, Illinois, United States).*

Results. *The incidence of GDM was 12.0 % in women with a family history of early onset autosomal dominant type 2 diabetes and 1.5% in women without a family history of the disease ($P < 0.05$). Women with a family history were nine times more likely to develop GDM than those without a family history of diabetes (95% confidence interval: 5.00–16.38, $P < 0.0001$).*

Conclusion. *Family history of early onset autosomal dominant type 2 diabetes appears to increase susceptibility to GDM in Jamaican women. Pregnant women of any age with family history of early onset autosomal type 2 diabetes should be screened for GDM.*

Key words Diabetes mellitus; diabetes gestational; genetics, medical; Jamaica.

[1] Department of Basic Medical Sciences, University of the West Indies, Kingston, Jamaica. Send correspondence to: Rachael Irving, Department of Basic Medical Sciences, University of the West Indies, Mona, Kingston, Jamaica; telephone: 876-9272290; fax: 876-9775233; email: rachael.irving@uwimona.edu.jm.

[2] Department of Pathology, University of the West Indies, Kingston, Jamaica.

[3] Department of Gynaecology, Obstetrics and Child Health, University of the West Indies, Kingston, Jamaica.

[4] Department of Medicine, University of the West Indies, Kingston, Jamaica.

Atypical diabetes seen as an autosomal dominant transmitted disorder is an emerging epidemic among African Americans (1). Families with early onset autosomal dominant type 2 diabetes can be defined as those with two or more first-degree relatives with type 2 diabetes diagnosed before age 35 years, three or more generations affected by diabetes, and diabetes inherited in an autosomal dominant fashion (2). β cell dysfunction is a common feature of autosomal dominant diabetes (2–3). A distinct form of early onset autosomal dominant type 2 diabetes is called Maturity Onset Diabetes of Youth (MODY) and is characterized by a pure insulin secretory defect, rather than impairment of insulin sensitivity as is seen in common early onset autosomal dominant type 2 diabetes (2–3). MODY is mainly a disease of Caucasians (3). Ge-

netic defects in six genes are known to cause MODY: the hepatocyte nuclear factor-4α: HNF-4α/(MODY1); glucokinase: GCK/(MODY2); the hepatocyte nuclear factor-1α: HNF-1α/(MODY3); insulin promoter factor-1: IPFl/(MODY4); hepatocyte nuclear factor-1β: HNF-1β/(MODY5); and transcriptional factor, neurogenic differentiation1: Neuro-D1/(MODY 6) (3–5).

Family history is one of the determining factors of early onset autosomal dominant type 2 diabetes and is also seen in the reports of GDM around the globe (6–8). In population surveys, the prevalence of the disease among relatives of patients with diabetes has been reported as being 4–10 times greater than in controls (9). In addition, emerging data is increasingly showing an association between ethnicity and type 2 diabetes (1). There is an increasing presence of early onset type 2 diabetes not linked to MODY 1–6 in African Americans, this type of diabetes is often termed atypical (1). Like GDM, this type of diabetes is frequently characterized by failure of the β cells to compensate for insulin resistance (2, 10). Ethnicity, family history of diabetes, and β cells failure in compensating for insulin resistance are therefore common factors implicated in the pathophysiology of both GDM and early onset autosomal dominant type 2 diabetes worldwide (2, 7, 10).

We postulated that Jamaican women of African descent with a family history of early onset autosomal dominant type 2 diabetes would have greater odds of developing GDM. We therefore conducted a prospective study evaluating the odds for and incidence of GDM in pre-gravid women with and without a family history of atypical diabetes. The metabolic profiles of these women during the first and second trimesters have also been described.

MATERIAL AND METHODS

A total of 698 pregnant Jamaican women with a family history of early onset autosomal dominant type 2 diabetes were identified from March 2000–September 2003 at the Antenatal Clinic at the University Hospital of the West Indies. Early onset autosomal dominant type 2 diabetes was defined as having a family history of diabetes in multi-generations, at least two first degree relatives diagnosed with type 2 diabetes before 35 years of age, and diabetes only on the maternal or paternal side of the family (2). In addition, 1 000 pregnant women without a family history of diabetes were identified at the same clinic during the same time period. The investigation of both groups of women was carried out simultaneously so that the odds for developing GDM and incidence of GDM could be compared. The study received approval from the Faculty of Medical Sciences of the University of the West Indies and Ethics Committee of the University Hospital of the West Indies. Written, informed consent was also obtained from each participant.

Data collection

Information was collected from the proband and family members that included age, sex, ancestral origin of parents and grandparents, and, if applicable, age at time of diabetes diagnosis and type of diabetes. Body Mass Index (BMI) was calculated at approximately six weeks of gestation by measuring the expectant woman's weight and height. A standard stadiometer was used for measurements. BMI was classified according to the Institute of Medicine (Washington, DC, United States of America) calculations for weight and weight-gain during pregnancy (11). This calculation was correlated with the self-reported BMI before pregnancy. Systolic and diastolic blood pressure measurements were obtained by using a standard sphygmomanometer while the patient was seated.

All participants were screened at nine weeks of gestation for glucose intolerance using the 50 g glucose O'Sullivan Test (12). Those with screening values greater than 7.8 mmol/L were then subjected to a 75-g Oral Glucose Tolerance Test (OGTT) (13). GDM is usually detected in the second trimester; however since the prevalence of diabetes in Jamaica is high and can pre-date the pregnancy (14), it is important to screen for diabetes early in the first trimester (nine weeks). Fasting plasma glucose is used to eliminate women being classified as GDM whose diabetes might likely antedate their pregnancy (15). Baseline samples were also taken at nine weeks for insulin, glucagon, cortisol glucose, triglyceride, and total and HDL cholesterol. The O'Sullivan Test was repeated at 24–27 weeks of gestation on participants with normal O'Sullivan test results or OGTT results.

The diagnosis of GDM was based on the World Health Organization's OGTT criteria (13) because the revised criteria do not affect the prevalence of GDM (16). Fasting samples were repeated at 24–27 weeks of gestation on all participants. The O'Sullivan test was repeated at 32 weeks of gestation on participants with normal O'Sullivan or OGTT results. β cell function and insulin resistance were calculated from fasting insulin and glucose values using the Homeostasis Model Assessment method as this is less invasive, less expensive, and easy to use (17). Women with family history of early onset autosomal dominant type 2 diabetes who were diagnosed with GDM were screened, along with two affected family members, for sequence variants in the MODY genes by polymerase chain reaction single strand conformation polymorphism (PCR-SSCP) analysis (18). Genomic DNA was prepared from peripheral blood by phenol-chloroform extraction. A genome scan was performed by means of PCR and automated fragment analysis. Each individual was genotyped for approximately 425 microsatellite markers with mean distance between markers of < 10 cm. Failure rate averaged across all markers was < 3%. Mutations in glucokinase, HNF-1α, HNF-1β, HNF-4α, IPF-1, and Neuro-D1 genes linked with early onset autosomal type 2 diabetes were searched for by means of a double gradient, denaturing gradient gel electrophoresis. This was followed

by direct sequencing of the products of the PCR that were amplified from the exons, flanking introns and minimal promoters of glucokinase, HNF-1α, HNF-1β, HNF-4α, IPF-1, and Neuro-D1 genes. Finally linkage with markers D7S2846 and D7S1818 flanking the glucokinase locus, D12S395 flanking the HNF-1α locus, D20S478, D20S481 flanking the HNF-4α locus, D17S1293 flanking the HNF-1β locus, and D2S1391 flanking the Neuro-D1 locus were excluded in the families by parametric linkage analysis with logarithmic scores ranging from –0.10 to –10.80 and no significant evidence of linkage heterogeneity.

Statistical analysis

Statistics were computed using SPSS 11.5 (SPSS Inc., Chicago, Illinois, United States). Frequency tables and accompanying histograms were produced and examined with related descriptive statistics (means, medians, modes, and standard deviations for all 1 968 participants in the first trimester/nine weeks and the 99 diagnosed with diabetes and the 1 599 without diabetes in the second trimester/24–27 weeks). This information along with the Kolmogorov-Smirnov one-sample test were used to assess the variables approximation to normality. Such results were used to determine whether a parametric or non-parametric test should be used for comparison of means and medians. The Mann Whitney U-test was used to compare median differences based on having or not having a family history of diabetes; while the independent group t-test was used to compare mean differences of these two groups. Data are generally presented as mean ± SD; however, because imbalanced sample sizes of women with GDM may affected validity of comparison, mean and median results are reported by group. Using binary logistic regression, odd ratios for getting GDM were derived employing the predicator variables: family history, age, BMI, insulin resistance, hypertension, and cholesterol level.

TABLE 1. Metabolic profile of Jamaican women at nine weeks of gestation, by family history of early onset autosomal dominant type 2 diabetes, 2000–2003[a]

	Family history of early onset autosomal dominant type 2 diabetes	
	Yes (n = 698)	No (n = 1 000)
Total	698	1 000
Age (years)	25.3 ± 4.7	26.6± 5.1
BMI (kg/m^2 at six weeks of gestation)	24.3 ± 4.3	24.5 ± 4.1
Fasting glucose (mmol/L)	5.6 ± 1.4	5.6 ± 1.4
Fasting insulin (mU/L)	10.0 ± 4.6[b]	11.1 ± 7.4[b]
Cortisol (nmol/L × 10^1)	45.8 ± 17.0	44.8 ± 16.0
Glucagon (ng/L)	35.9 ± 9.6	34.9 ± 9.6
HDL-c (mmol/L)	1.3 ± 0.4	1.4 ± 0.3
Total cholesterol (mmol/L)	4.6 ± 0.8	4.9 ± 0.7
Triglyceride (mmol/L)	1.7 ± 0.8[b]	1.3 ± 0.3[b]
β cell function (%)	95.0 ± 24.8[b]	105.6 ± 30.7[b]
Insulin resistance	2.5 ± 1.4[b]	2.7 ± 1.2[b]
Systolic pressure (mmHg)	121.3 ± 6.5	121.5 ± 6.3
Diastolic pressure (mmHg)	80.0 ± 4.9	80.1 ± 4.8

[a] Data are presented as mean ±SD.
[b] Significant difference (P < 0.05) between groups in biochemical parameter.

RESULTS

Metabolic profile in the first trimester

Based on the OGTT WHO criteria (13), no woman was diagnosed with GDM in the first trimester/first nine weeks of gestation. The metabolic profiles of participants at nine weeks of gestation are shown in Table 1. The women with a family history of early onset autosomal dominant type 2 diabetes had lower insulin levels (10.0 ± 4.6 versus 11.1 ± 7.4, P < 0.05), lower β cell function (95.0 ± 24.8 versus 105.6 ± 30.7%, P < 0.05), and were less insulin resistant (2.5 ± 1.4 versus 2.7 ± 1.2, P < 0.05), but had higher triglyceride levels (1.7 ± 0.8 versus 1.3 ± 0.3 mmol/L, P < 0.04) than women without a family history of diabetes. Elevated triglyceride levels (1.7 ± 0.8 mmol/L) (19) were noted in women with a family history of early onset autosomal dominant type 2 diabetes. No significant differences in age, BMI , glucose, cortisol, glucagon, total cholesterol, HDL, or systolic and diastolic blood pressures were noted between women with a family history of early onset autosomal dominant type 2 diabetes and those without.

Metabolic profile of women with GDM in the second trimester

Of the 698 women with a family history of early onset autosomal dominant type 2 diabetes, 84 (12.0%) were diagnosed with GDM at 24–27 weeks (second trimester) of pregnancy, while of the 1 000 women without a family history of diabetes, 15 (1.5%) were diagnosed with GDM (Table 2). Women with a family history of early onset autosomal type 2 diabetes were younger (26.4 ± 4.3 versus 32.2 ± 4.1 years, P < 0.02) and had a significantly lower BMI (24.8 ± 4.6 versus 26.6 ± 5.1 kg/m^2 P < 0.04) at six weeks of gestation than did GDM women without family history of diabetes. All of the following were significantly lower in GDM women with a family history of early onset autosomal type 2 diabetes than in GDM women without a family history of diabetes: fasting glucose (6.1 ± 1.3 versus 7.1 ± 2.0 mmol/L, P < 0.05); postprandial glucose (8.5 ± 2.1 versus 10.8 ± 3.4 mmol/L, P < 0.03); fasting insulin (10.9 ± 2.9 versus 19.0 ± 7.9 mU/L); postprandial insulin (14.2 ± 2.2 versus 32.4 ± 6.5 mU/L, P < 0.0001); HDL (1.2 ± 0.3 versus 1.7 ± 0.3 mmol/L, P < 0.05); total cholesterol (4.5 ± 1.2 versus 5.6 ± 0.5 mmol/L,

TABLE 2. Metabolic profile of Jamaican women with gestational diabetes mellitus (GDM) at 24–27 weeks of gestation, by family history of early onset autosomal dominant type 2 diabetes, Jamaica, 2000–2003[a]

	Family history of early onset autosomal dominant type 2 diabetes	
	Yes[a] (n = 84)	No[a] (n = 15)
% GDM	12.0	1.5
Age (years)	26.4 ± 4.3[b] (26)	32.2 ± 4.1[b] (32)
BMI (kg/m^2 at 24–27 weeks of gestation)	24.8 ± 4.6[b] (23)	26.6 ± 5.1[b] (26)
Fasting glucose (mmol/L)	6.1 ± 1.3[b] (6)	7.1 ± 2.0[b] (7)
Fasting insulin (mU/L)	10.9 ± 2.9[b] (11.6)	19.0 ± 7.9[b] (17)
Postprandial glucose (mmol/L)	8.5 ± 2.1[b] (8)	10.8 ± 3.4[b] (8)
Postprandial insulin (mU/L)	14.2 ± 2.2 (14)	32.4 ± 6.5 (26)
Cortisol (nmol/L × 10^1)	46.1 ± 8.6 (45)	45.1 ± 14.0 (45)
Glucagon (ng/L)	36.8 ± 10.1 (34)	36.9 ± 11.8 (34)
HDL (mmol/L)	1.2 ± 0.3[b] (1.1)	1.7 ± 0.3[b] (1.8)
Total cholesterol (mmol/L)	4.5 ± 1.2[b] (4.6)	5.6 ± 0.5[b] (5.6)
Triglyceride (mmol/L)	1.7 ± 0.8[b] (1.6)	1.1 ± 0.1[b] (1.0)
Previous pregnancy	1.2 ± 0.1 (1.2)	1.5 ± 0.1 (1.2)
β cell function	83.4 ± 14.1 (64)	100.4 ± 24.1 (100)
Insulin resistance	2.9 ± 0.7[b] (3.0)	5.7 ± 1.2[b] (6.0)
Systolic pressure (mmHg)	120.1 ± 6.8 (120)	126.9 ± 8.9 (120)
Diastolic pressure (mmHg)	80.0 ± 5.0 (80)	85.3 ± 7.4 (80)

[a] Data are presented as mean ±SD and median in parentheses.
[b] Significant difference (P < 0.05) between groups in biochemical parameter.

TABLE 3. Metabolic profile of Jamaican women who were "normal" (did not have gestational diabetes mellitus) at 24–27 weeks of gestation, by family history of early onset autosomal dominant type 2 diabetes, Jamaica, 2000–2003[a]

	Family history of early onset autosomal dominanat type 2 diabetes	
	Yes (n = 614)	No (n = 985)
Total	614	985
Age (years)	25.2 ± 4.7	26.5 ± 5.0
BMI (kg/m^2 at 24–27 weeks of gestation)	24.1 ± 3.9	24.4 ± 4.0
Glucose (mmol/L)	5.6 ± 1.4	5.6 ± 1.4
Insulin (mU/L)	10.4 ± 4.8[b]	12.0 ± 7.3[b]
Cortisol (nmol/L × 10^1)	44.9 ± 1.8	44.4 ± 1.7
Glucagon (ng/L)	35.9 ± 9.7	34.8 ± 9.7
HDL-c (mmol/L)	1.3 ± 0.6	1.3 ± 0.3
Total cholesterol (mmol/L)	4.7 ± 0.8	4.9 ± 0.7
Triglyceride (mmol/L)	1.7 ± 0.8[b]	1.3 ± 0.4[b]
β cell function (%)	98.9 ± 24.2[b]	109.7 ± 30.4[b]
Insulin resistance	2.6 ± 1.1[b]	3.0 ± 1.6[b]
Systolic pressure (mmHg)	121.3 ± 6.5	121.4 ± 6.3
Diastolic pressure (mmHg)	80.0 ± 4.9	80.1 ± 4.8

[a] Data are presented as mean ±SD.
[b] Significant difference (P < 0.05) between groups in biochemical parameter.

P < 0.05); insulin resistance (2.9 ± 0.7 versus 5.7 ± 1.2); cell function (83.4 ± 14.1 versus 100.4 ± 24.1%, P < 0.03); systolic blood pressure (120.1 ± 6.8 versus 126.9 ± 8.9 mmHg, P < 0.04); and diastolic blood pressure (80.0 ± 5.0 versus 85.3 ± 7.4 mmHg, P < 0.05). The blood pressures were within normal range (systolic: 120.1 ± 6.8 mmHg; diastolic: 80.0 ± 5.0 mmHg) (19) in women with a family history of early onset autosomal dominant type 2, however triglyceride levels were elevated and significantly higher (1.7 ± 0.8 versus 1.1 ± 0.1 mmol/L, P < 0.05) than that of GDM women with no family history of diabetes.

Metabolic profile without GDM in the second trimester

There were two groups of "normal" (i.e., negative for GDM) women, those with a family history of early onset autosomal dominant type 2 diabetes and those with no history of the disease (Table 3). The 614 normal women with a family history of the disease had elevated triglyceride levels (1.7 ± 0.8 mmol/L) (19). Between the normal group with a family history and the normal group with no history, there were the following significant differences: insulin levels (10.4 ± 4.8 versus 12.0 ± 7.3 mU/L, P < 0.05); , cell function (98.9 ± 24.2 versus 109.7 ± 30.4%, P < 0.04); and insulin resistance (2.6 ± 1.1 versus 3.0 ± 1.6, P < 0.05). There were no significant differences between the two groups in glucose, glucagon, cortisol, HDL, total cholesterol, or systolic and diastolic blood pressure levels at 24–27 weeks of gestation. Women from both groups who had normal glucose tolerance at 24–27 weeks remained normal throughout pregnancy.

Family history and odds of developing GDM

The odds of developing GDM for Jamaican women with a family history of early onset autosomal dominant type 2 diabetes is nine times that of those without a family history of the disease (95% confidence interval: 5.00–16.38, P < 0.0001). Mutation screening via SSCP (18), sequencing (2), and linkage analysis was negative for the six known MODY genes (HNF-4α, GCK, HNF-1α, IPF-1, HNF-1β, and Neuro-D1).

DISCUSSION

The main ethnic groups in Jamaica are Negro/Black (90.5%), mixed/Negro (7.3%), and East Indian (1.3%); other racial groups are less than 1% (20). Marked variations in GDM prevalence among different racial/ethnic groups have been documented, with higher prevalence among Native-Americans, Asians, and African-Americans (8, 21, 22). GDM incidence usually ranges from 3%–5%, and although an incidence rate higher than 11% is rare, up to 14.3% has been reported (6, 21–24).

In this study, GDM incidence among Jamaican women with a family history of early onset type 2 diabetes that segregates with autosomal dominant inheritance was 12.0%. This high incidence of GDM is rare and has been reported in only a few populations worldwide, such as among the Cree Indians (12.8%) in Quebec, Canada; the Aboriginal Indians (11.5%) in Saskatoon District, Canada; and the Zuni Indians (14.3%) in New Mexico, United States. The women in these populations were overweight prior to pregnancy, older, and more hypertensive (21–23), thus showing features consistent with the metabolic syndrome (19) that has been linked to GDM (22–24). The Jamaicans with a family history of early onset autosomal dominant type 2 diabetes who developed GDM were normotensive, younger (26.4 ± 4.3 years), and had normal pregnancy BMI at 24–27 weeks of gestation (24.8 ± 4.6 kg/m^2) suggesting that underlying factors, such as genetic and intrauterine, may have taken more prominent roles in the pathophysiology of GDM in this population. At 24–27 weeks of gestation, these women had a mean fasting glucose value of 6.1 mmol/L and a mean insulin value of 10.9 mU/L manifesting 1.79 mU/L of insulin for each mmol/L of glucose in the basal state. When these women were challenged with glucose, their mean postprandial glucose value at 2 hours was 8.5 mmol/L with insulin at 14.2 mU/L thus manifesting 1.67 mU/L of insulin for each mmol/L of glucose; the insulin resistance at this stage was 2.9. This clearly is suggestive of the β cell dysfunction in the face of insulin resistance in pregnancy. Detailed metabolic studies have revealed abnormalities in glucose-mediated insulin secretion in some forms of early onset autosomal dominant diabetes (3, 5).

At 24–27 weeks of gestation, normal pregnant women with a family history of early onset autosomal dominant type 2 diabetes had a mean fasting glucose value of 5.6 mmol/L and insulin of 10.4 mU/L, thus showing 1.85 mU/L of insulin for each mmol/L of glucose in the second trimester. β cell function was at 98.9% and insulin resistance was 2.6. It seems possible therefore, that there is a threshold of insulin sensitivity above which the development of GDM is very unlikely and there is also a stage in the development of GDM too late to protect β cells by reducing insulin resistance. The ability of the pancreatic β-cell to compensate for prevailing insulin sensitivity (i.e., β-cell compensation) is highly heritable (25, 26). Although β cell dysfunction is associated with MODY (3), mutation screening of the women and family members with early onset autosomal dominant type 2 diabetes for the MODY genes 1–6 ruled out β cell defects associated with MODY as the cause of GDM.

Chronic autoimmunity directed at β cells is one mechanism that may contribute to β cell failure in GDM, perhaps even in the absence of chronic insulin resistance. However, evidence for such autoimmunity is present in only a small minority of patients (27–29). The frequency of anti-islet cell and anti-GAD antibodies in GDM parallels ethnic trends in the prevalence of type 1 diabetes outside of pregnancy (10). The prevalence of type 1 diabetes in Jamaicans is low, at about 2.5 per 10 000 (30). We therefore do not believe the 12% incidence of GDM in the women with a family history of early onset autosomal dominant type 2 diabetes is due to autoimmune diabetes.

The hypertriglyceridemia seen in both normal women and those with GDM who had a family history of early onset autosomal dominant type 2 diabetes may be due to defective lipolysis of very low density lipoprotein triglyceride (VLDL-TG) (31, 32). A large number of mutations in lipoprotein lipase (LPL) have been identified (33) and these can cause hypertriglyceridemia. However, it is doubtful that most cases of endogenous hypertriglyceridemia can be explained by mutations in LPL, which appear to be relatively rare. Another attractive suggestion for defective lipolysis of VLDL-TG has recently been proposed. This is an overproduction of apolipoprotein (apo) CIII. This apolipoprotein inhibits the function of LPL (34). The hepatic synthesis of apo CIII apparently is insulin responsive (35); in the presence of insulin resistance, apo CIII may be over-expressed, which can inhibit lipolysis of plasma VLDL-TG and lead to hypertriglyceridemia.

Risk factors for GDM include age and obesity (21–23). In our study, 1.5% of women with no family history of diabetes developed GDM. These women were overweight at 24–27 weeks of gestation, over 30 years of age, and hypertensive with elevated total cholesterol and high insulin resistance. This subset of women without family history of diabetes who developed GDM had many of the features of the metabolic syndrome, associated with increased incidence of GDM (19, 21–23). In the face of increasing insulin resistance in the second trimester, appropriate hyperinsulinemia occurred. The fasting glucose value was 7.1 mmol/L and insulin 19.0 mU/L. They manifested 2.71 mU/L of insulin for each mmol/L of glucose in the basal state. With a glucose challenge, the mean postprandial glucose value was 10.8 mmol/L and the insulin 32.4 mU/L thus showing 2.99 mU/L of insulin for each mmol/L of glucose. β cell function was 100.4%. Robust plasticity of β cell function in time of insulin resistance is the hallmark of normal glucose regulation during pregnancy (10). The myriad of obesity, age, high blood pressure, and elevated total cholesterol in these women are markers of increased insulin resistance (19) to which the insulin resistance of pregnancy was additive. This exaggerated resistance to insulin and ability to sup-

press glucose production and stimulate glucose uptake resulted in hyperglycemia in pregnancy. During the fasting state in GDM, severe insulin resistance is characterized by an overproduction of glucose by the liver; while in the fed state, severe insulin resistance is characterized by a decrease in insulin-mediated glucose uptake by the muscle (36).

Although family history is a risk factor for GDM (3, 6, 7, 37), not much is known about its genetics. Allele frequencies of candidate genes in women with GDM and controls have not documented any specificity for phenotypic sub-classification (10, 38). Variants that differed in frequency between GDM and controls have been identified in genes coding for the (a) islet specific promoter of glucokinase, said to be important for glucose sensing by the β cells; (b) Calpain 10, a gene associated with type 2 diabetes in some ethnic groups; and (c) the sulfonylurea receptor-1 that is involved in glucose-stimulated secretion (39–41). Several studies have also evaluated a series of *a priori* candidate genes for a role in early-onset type 2 diabetes (42). Sequence variants have been identified in genes such as HNF-3β, NeuroD4, Neurogenin-3, HNF-6, and GLUT-2; however, none of these have been conclusively shown to predispose to type 2 diabetes or GDM (40). Therefore, GDM appears to be multifaceted and may be caused by both genetic and environmental factors that characterize other types of diabetes.

The environmental factors that cause GDM in Jamaican women with a family history of early onset autosomal dominant type 2 diabetes may be absent after delivery, thus with a usual incidence rate of 12%, GDM presents a unique opportunity to investigate the early pathogenesis of the disease. Because of the increased suceptibility to GDM that Jamaican women with a family history of early onset type 2 diabetes have at any age, it is important that they be screened for GDM early in pregnancy.

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RESUMEN

La carga de la diabetes mellitus gestacional en mujeres de Jamaica con antecedentes familiares de diabetes autosómica dominante tipo 2

Objetivos. Determinar si las mujeres jamaicanas de ascendencia africana con antecedentes familiares de inicio temprano de diabetes autosómica dominante tipo 2 tienen mayor probabilidad de desarrollar diabetes mellitus gestacional (DMG) que las que no tienen esos antecedentes familiares.

Métodos. Se realizó un estudio comparativo con dos grupos de mujeres jamaicanas embarazadas: el primero con mujeres que tenían antecedentes familiares de inicio temprano de diabetes autosómica dominante tipo 2 y el segundo con mujeres sin antecedentes familiares de esa enfermedad. Se empleó el programa SPSS v. 11.5 (SPSS Inc., Chicago, Illinois, Estados Unidos de América) para analizar los resultados y calcular la incidencia, la probabilidad de desarrollar DMG y los perfiles metabólicos en el primer y el segundo trimestres de gestación.

Resultados. La incidencia de DMG fue de 12,0% en las mujeres con antecedentes familiares de inicio temprano de diabetes autosómica dominante tipo 2 y de 1,5% en las mujeres sin antecedentes familiares de esa enfermedad ($P < 0,05$). Las mujeres del primer grupo tuvieron nueve veces más probabilidades de desarrollar DMG que las del segundo grupo (intervalo de confianza de 95%: 5,00 a 16,38; $P < 0,0001$).

Conclusión. Los antecedentes familiares de inicio temprano de diabetes autosómica dominante tipo 2 aumentaron la predisposición a sufrir DMG en mujeres jamaicanas. Las mujeres embarazadas con antecedentes familiares de inicio temprano de diabetes autosómica tipo 2 deben someterse a pruebas de tamizaje para DMG, independientemente de su edad.

Palabras clave Diabetes mellitus, diabetes gestacional, genética médica, Jamaica.