Early Postpartum Metabolic Assessment in Women With Prior Gestational Diabetes

FELIPE PALLARDO, MD
LUCRECIA HERRANZ, MD
TERESA GARCIA-INGELMO, BM
CRISTINA GRANDE, SCD
PILAR MARTIN-VAQUERO, BM
MERCEDES JAÑEZ, BM
ANTONIO GONZALEZ, MD

OBJECTIVE — To present the results of early postpartum metabolic assessment in women with gestational diabetes mellitus (GDM), to determine predictive factors for subsequent diabetes, and to investigate the association of postpartum glucose tolerance with other components of the metabolic syndrome.

RESEARCH DESIGN AND METHODS — A total of 788 women were evaluated 3–6 months after a GDM pregnancy. A 75-g oral glucose tolerance test (OGTT) was performed. Cholesterol, HDL cholesterol, triglycerides, blood pressure, BMI, and body fat distribution were assessed. Clinical and obstetric history, baseline variables at the diagnosis of GDM, metabolic control during pregnancy, and index pregnancy outcome were compared in women with diabetes and women without diabetes (American Diabetes Association [ADA] criteria) after pregnancy. Multivariate logistic regression analysis was used to ascertain independent predictors of subsequent diabetes. Correlation coefficients were assessed between postpartum glucose tolerance and lipid levels, blood pressure, BMI, and body fat distribution.

RESULTS — According to ADA criteria, 588 (74.6%) women were normal, 46 (5.8%) had impaired fasting glucose, 82 (10.4%) had impaired glucose tolerance, 29 (3.7%) had both impaired fasting glucose and impaired glucose tolerance, and 43 (5.4%) had diabetes. Prepregnancy obesity, recurrence of GDM, gestational age at diagnosis of GDM, glucose values in the 100-g OGTT, number of abnormal values in the 100-g OGTT, fasting C-peptide levels in pregnancy, C-peptide/glucose score in pregnancy, insulin requirement in pregnancy, 3rd trimester HbA_{1c} levels, and macrosomia differed significantly in women with subsequent diabetes. Independent predictors of postpartum diabetes were prepregnancy obesity, C-peptide/glucose score during pregnancy, and the number of abnormal values in the 100-g diagnostic OGTT. The area under the postpartum glucose curve was positively associated with BMI, waist circumference, waist-to-hip ratio, triglycerides, and systolic and diastolic blood pressures.

CONCLUSIONS — Low C-peptide/glucose score during pregnancy together with prepregnancy obesity and severity of GDM (number of abnormal values in the 100-g diagnostic OGTT) are independent predictors of subsequent diabetes. Our data suggest that regardless of obesity and severity of GDM, a β-cell defect increases the risk of postpartum diabetes. The association of postpartum glucose tolerance with triglyceride levels, blood pressure, obesity, and regional distribution of body fat suggests that postpartum glucose intolerance anticipates a high-risk cardiovascular profile that comprises other risk factors besides diabetes.

Diabetes Care 22:1053–1058, 1999

Once pregnancy is over, the implications of gestational diabetes mellitus (GDM) for the future health of the mother comprise potential recurrence of GDM in subsequent pregnancies (1), increased risk for development of type 1 (2) or type 2 (3) diabetes, and possibly, association with other cardiovascular risk factors (dyslipidemia, hypertension, abdominal obesity) that constitute the metabolic syndrome (4).

The incidence of diabetes among women with a history of GDM has been reported to range from 3 to 65% (5). The dispersion in reported incidence rates results from ethnic variation, lack of uniformity in diagnostic criteria for GDM, different means used to define diabetes outside pregnancy, diversity in follow-up practices, characteristics of women lost to follow-up, and differences in statistical management of data.

Several predictors of diabetes after a GDM pregnancy have been identified: severity of glucose intolerance during pregnancy (6) and immediately postpartum (7), insulin requirement during pregnancy (8), earlier diagnosis during pregnancy (9), family history of diabetes (10), recurrence of GDM and increasing parity (8), maternal age (11), prepregnancy obesity (12) and weight gain during (13) and after pregnancy (14), presence of islet cell antibodies (2), and delivery of a macrosomic infant (15).

This study presents the results of early postpartum metabolic assessment in 788 women with GDM. Factors that may identify women who will develop diabetes after pregnancy are analyzed, and association of postpartum glucose tolerance with other components of the metabolic syndrome is investigated.

RESEARCH DESIGN AND METHODS

This research was conducted in the Diabetes and Pregnancy Unit at the University Hospital La Paz in Madrid, where a total of 1,425 Caucasian women with singleton gestations have been seen for the management of GDM between 1987 and 1997. In the event of there having been a subsequent pregnancy complicated by GDM in the same woman during the years of the study, only the first GDM pregnancy is

From the Division of Diabetes of the Department of Endocrinology (F.P., L.H., T.G.-I., P.M.-V.), the Department of Biochemistry (C.G.), and the Department of Obstetrics and Gynecology (M.J., A.G.), Hospital La Paz, Madrid, Spain.

Address correspondence and reprint requests to Dr. Felipe Pallardo, Jefe de Servicio Endocrinología, Unidad de Diabetes, Hospital Universitario La Paz, Paseo de la Castellana 261, 28046 Madrid, Spain.

Received for publication 25 November 1998 and accepted in revised form 9 March 1999.

Abbreviations: ADA, American Diabetes Association; GCT, glucose challenge test; GDM, gestational diabetes mellitus; LGA, large for gestational age; OGTT, oral glucose tolerance test; WHO, World Health Organization.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Clinical and obstetric characteristics of GDM patients who did or did not attend metabolic testing after pregnancy*

	GDM patients		
	With follow-up	Without follow-up	*P* value
n	788	637	—
Age (years)	33.1 ± 11.7	32.4 ± 5.16	NS
Prepregnancy BMI (kg/m^2)	25.9 ± 16.7	25.8 ± 10.3	NS
GDM class			
A1	81.9	78.3	NS
A2	14.9	18.1	NS
B1	3	3.4	NS
Recurrence of GDM	10.5	11.9	NS
Family history of diabetes	50.7	50.7	NS
Previous macrosomia	10	15.1	<0.01
Previous perinatal mortality	6.4	8.2	NS
Insulin therapy	49.4	36.6	<0.001
Gestational age at diagnosis of GDM (weeks)	26.4 ± 6.4	27.4 ± 6.4	<0.01
Index pregnancy outcome			
Large for gestational age	11.1	10.1	NS
Congenital malformations	2.3	2.3	NS

Data are means ± SD or %, unless otherwise indicated. Continuous variables are compared using independent-samples Student's *t* test, and discrete variables are compared using χ^2 and Fisher exact tests.

considered. Of these women, 788 (55.2%) have attended the initial postpartum metabolic assessment.

In the absence of pregnancy, there are no specific screening programs for diabetes in our environment. The prevalence of known diabetes in the Madrid population is 2.2% (0.17% for type 1 diabetes) and 1.66% for the age-group 30–59 years (16). Other studies in the Spanish population (30–44 years) have shown rates of 0.5% known diabetes and 1.4% unknown diabetes (17).

Selective screening for GDM with a 50-g oral glucose challenge test (GCT) was performed in the first visit to the pregnancy clinic if historical risk factors were present (advanced maternal age, obesity, family history of diabetes, previous GDM, history of poor obstetric outcome). Unless diagnosed at an earlier stage of pregnancy, all women had a GCT at 24–28 weeks' gestation. A positive screen was defined as a 1-h glucose value ≥140 mg/dl (7.8 mmol/l). Each woman with a positive screen was given a fasting 3-h 100-g oral glucose tolerance test (OGTT). The diagnosis of GDM was made using the criteria of the National Diabetes Data Group (18). GDM was subclassified according to fasting glucose value as follows: class A1: <105 mg/dl (5.8 mmol/l); class A2: 105–129 mg/dl (5.8–7.2 mmol/l); and class B1: ≥130 mg/dl (7.2 mmol/l) (11).

All women with a diagnosis of GDM received nutrition counseling and were given a dietary regimen, with individualized caloric intake, including 50% of calories from carbohydrates, 30% from fat, and 20% from protein. Home blood glucose monitoring was performed by the patients on alternate days. Insulin therapy was recommended on the basis of a fasting blood glucose ≥105 mg/dl (5.8 mmol/l) or a 2-h postprandial glucose ≥120 mg/dl (6.7 mmol/l) on two or more occasions.

Patients' age, family history of diabetes, recurrence of GDM, stated prepregnancy weight, parity, and history of obstetric outcome (stillbirth, congenital malformations, preterm delivery, macrosomia, and repeated abortions) were recorded. Prepregnancy obesity was defined as a BMI ≥27 kg/m^2. Characteristics of the index pregnancy included gestational age at the time of diagnosis of GDM, glucose levels of the diagnostic OGTT, mean HbA_{1c} levels during the 3rd trimester of pregnancy, fasting and 2-h postprandial C-peptide levels (standard mixed breakfast, 350 kcal; performed at 28–34 weeks' gestation), insulin requirement, and insulin dose (U/kg). The following data of pregnancy outcome were analyzed: infant weight ascertained as macrosomia (>4 kg), infant considered large for gestational age (LGA) (>90th percentile), and infant birth weight ratio (actual weight at birth/50th-percentile weight for gestational age) (birth weight percentiles were derived from the Battaglia and Lubchenco growth standards [19]); neonatal hypoglycemia (<30 mg/dl for term delivery and <20 mg/dl for preterm delivery, during the first 48 h); birth trauma (fractured clavicles, Erb's palsy, cephalhematoma); and congenital malformations.

All women who deliver a pregnancy complicated by GDM at our unit are advised to return for metabolic testing. A standard 75-g OGTT is performed 3–6 months postpartum, after lactation is concluded. Results of the OGTT were evaluated according to both the 1985 World Health Organization (WHO) criteria (20) and the 1997 American Diabetes Association (ADA) criteria (21). Postpartum metabolic assessment also included current weight, height, waist and hip circumferences (22), blood pressure, and fasting serum lipid concentrations.

Plasma glucose was enzymatically measured on an automated analyzer (Hitachi 704; Boehringer-Mannheim, Indianapolis, IN). Cholesterol and triglyceride levels were determined using enzymatic assays (Kit CHOL-PAP and Kit GPO-PAP; Boehringer-Mannheim). HDL cholesterol levels were measured using an enzymatic assay, after precipitation of LDLs and VLDLs with dextran sulfate (Kit CHOL-HDL; Sclavo Diagnostici, Sienna, Italy). HbA_{1c} values were determined by high-performance liquid chromatography (Biorad, Richmond, CA). C-peptide levels were measured by radioimmunoassay (Medgenix Diagnostics, Brussels, Belgium). The C-peptide/glucose score was calculated as the ratio of C-peptide (ng/ml) to glucose (mg/dl) × 100 (23).

Table 2—*Comparison of clinical and obstetric history between women with diabetes and women without diabetes after pregnancy*

	Diabetic status after pregnancy			
	Diabetes	No diabetes	Odds ratio (95% CI)	*P* value
n	43	745	—	—
Age (years)	32.6 ± 4.8	33. 1 ± 11.9	—	NS
Parity	1.94 ± 0.96	1.89 ± 0.89	—	NS
Prepregnancy obesity (BMI ≥27 kg/m²)	39	22.8	2.16 (1.13–4.14)	<0.05
Recurrence of GDM	20.9	9.9	2.40 (1.11–5.19)	<0.05
Family history of diabetes	65.1	50.7	1.81 (0.95–3.45)	NS
Previous macrosomia	11.6	9.9	1.19 (0.46–3.12)	NS
Previous perinatal mortality	11.6	6.1	1.99 (0.75–5.32)	NS
Previous preterm delivery	2.3	4.8	0.47 (0.06–3.50)	NS
Previous congenital malformations	2.3	5.5	0.41 (0.05–3.04)	NS

Data are means ± SD or %, unless otherwise indicated. Continuous variables are compared using independent-samples Student's *t* test, and discrete variables are compared using χ^2 and Fisher exact tests. The odds ratio and 95% CI were obtained from frequency tables.

Postpartum area under the glucose curve was calculated by the trapezoidal method.

Statistical analyses were conducted using R-Sigma version 2.0 statistical software (1990, Horus Hardware, Madrid, Spain). Independent-samples Student's *t* test was used to compare continuous variables. χ^2 and Fisher exact tests of significance were used to compare discrete variables. For each categorical variable, the odds ratio and the 95% CI were obtained from frequency tables. Multivariate logistic regression analysis was performed to select the significant factors when the variables were considered jointly. Associations between the postpartum glucose area under the curve and variables related to the metabolic syndrome were determined using linear correlation coefficients. Results have been expressed as percentages or as means ± SD. A *P* value <0.05 was considered significant.

Ethical approval for this research was provided by the Hospital Ethical Committee, and informed consent was obtained from all subjects.

RESULTS — Of the 1,425 women with GDM, 788 (55.2%) participated in the postpartum examination (4.2 ± 1 month after delivery). Table 1 shows clinical and obstetric characteristics of GDM patients who did or did not attend metabolic testing after pregnancy. Women who attended the follow-up examination had been diagnosed as having GDM earlier in pregnancy (26.4 ± 6.4 vs. 27.4 ± 6.4 weeks; $P < 0.01$) and had required insulin therapy during pregnancy more frequently (49.4 vs. 36.6%; $P < 0.001$). History of previous macrosomia was more common among women who did not attend the follow-up examination (15.1 vs. 10%, $P < 0.01$). Age, prepregnancy BMI, family history of diabetes, recurrence of GDM, GDM class, and index pregnancy outcome did not differ significantly between women who did or did not attend the follow-up examination.

Based on a 75-g OGTT, and according to the 1997 ADA criteria, of the 788 women who participated in the postpartum examination 588 (74.6%) were normal, 46 (5.8%) had impaired fasting glucose, 82 (10.4%) had impaired glucose tolerance, 29 (3.7%) had impaired fasting glucose plus impaired glucose tolerance, and 43 (5.4%) had diabetes. Using the 1985 WHO criteria, 634 (80.4%) women were normal, 117 (14.8%) had impaired glucose tolerance, and 37 (4.7%) had diabetes.

To identify predictive factors for subsequent development of diabetes, the 43 women with diabetes according to the ADA criteria were compared with the 745 women without diabetes (normal, im-paired fasting glucose, and impaired glucose tolerance). The proportion of women with GDM classes A1, A2, and B1 differed significantly ($P < 0.001$) between women with postpartum diabetes (39.5, 34.8, and 25.6%, respectively) and women without postpartum dia-

Table 3—*Comparison of baseline variables at diagnosis of GDM between women with and without diabetes after pregnancy*

	Diabetic status after pregnancy		
	Diabetes	No diabetes	*P* value
n	43	745	—
Gestational age at diagnosis of GDM (weeks)	20.6 ± 8.1	26.7 ± 6.1	<0.001
100-g OGTT fasting glucose (mmol/l)	6.46 ± 1.66	5.04 ± 0.34	<0.001
1-h	12.61 ± 1.83	11.63 ± 1.55	<0.001
2-h	11.93 ± 2.88	10.42 ± 1.46	<0.01
3-h	9.59 ± 2.39	7.75 ± 1.88	<0.001
Number of abnormal values in the diagnostic OGTT	3.14 ± 0.78	2.39 ± 0.57	<0.001
Fasting C-peptide level (nmol/l)	0.84 ± 0.34	1.04 ± 0.48	<0.001
Postprandial C-peptide level (nmol/l)	2.40 ± 1.63	2.83 ± 2.93	NS
C-peptide/glucose score*	2.52 ± 1.04	3.67 ± 1.58	<0.001

Data are *n* or means ± SD. Variables are compared using independent-samples Student's *t* test. *C-peptide/glucose score = C-peptide (ng/ml)/glucose (mg/dl) × 100.

Table 4—*Comparison of variables related to index pregnancy outcome and metabolic control during gestation between women with and without diabetes after pregnancy*

	Diabetic status after pregnancy			
	Diabetes	No diabetes	Odds ratio (95% CI)	*P* value
n	43	745	—	—
Birth weight ratio	1.03 ± 0.15	0.98 ± 0.13	—	<0.05
Infant birth weight >4 kg	11.6	3.2	4.02 (1.45–11.13)	<0.05
Large for gestational age	19	10.6	1.97 (0.88–4.40)	NS
Hypoglycemia	9.5	9.7	0.98 (0.34–2.81)	NS
Birth trauma	4.7	2.5	1.89 (0.43–8.42)	NS
Congenital malformations	2.3	2.2	1.04 (0.13–7.99)	NS
Insulin requirement	86	47.2	6.87 (2.87–16.48)	<0.001
Daily insulin dose (U/kg)	0.45 ± 0.2	0.27 ± 0.11	—	<0.001
3rd-trimester HbA_{1c} (%)	5.52 ± 0.66	5.07 ± 0.52	—	<0.001

Data are means ± SD or %, unless otherwise indicated. Continuous variables are compared using independent-samples Student's *t* test, and discrete variables are compared using χ^2 and Fisher exact tests. The odds ratio and 95% CI were obtained from frequency tables.

betes (84.4, 13.8, and 1.7%, respectively). At postpartum assessment, 2.6% of women with class A1, 12.7% with class A2, and 45.8% with class B1 gestational diabetes were found to have diabetes.

Clinical and obstetric history of women with and without diabetes after pregnancy is shown in Table 2. A significantly higher proportion of women with prepregnancy obesity and recurrence of GDM were diagnosed with postpartum diabetes.

Comparison of baseline variables at the diagnosis of GDM between women with and women without diabetes after pregnancy (Table 3) disclosed that diabetic women had been diagnosed as having GDM earlier in the course of pregnancy (20.6 ± 8.1 vs. 26.7 ± 6.1 weeks; $P < 0.001$), had significantly higher glucose levels in the 100-g diagnostic OGTT, significantly greater number of abnormal values in the 100-g diagnostic OGTT, significantly lower fasting C-peptide levels (0.84 ± 0.34 vs. 1.04 ± 0.48 nmol/l; $P < 0.001$), and significantly lower C-peptide/glucose score (2.52 ± 1.04 vs. 3.67 ± 1.58; $P < 0.001$).

Comparison of variables related to metabolic control during pregnancy and index pregnancy outcome between women with and women without diabetes after pregnancy (Table 4) disclosed that a much higher proportion of diabetic women had required insulin (86 vs. 47.2%; $P < 0.001$). Among those who received insulin therapy during pregnancy, women with diabetes after pregnancy had required a higher daily insulin dose (0.45 ± 0.2 vs. 0.27 ± 0.11 U/kg; $P < 0.001$). HbA_{1c} levels in the 3rd trimester were also higher in women with postpartum diabetes (5.52 ± 0.66 vs. 5.07 ± 0.52%; $P < 0.001$). As for pregnancy outcome, the only significant differences were a higher proportion of macrosomia and a higher birth weight ratio in women with diabetes after pregnancy.

Variables that appeared significant in the univariate analysis were entered into a logistic regression analysis. The final model included prepregnancy obesity, C-peptide/glucose score during pregnancy, and the number of abnormal values in the 100-g diagnostic OGTT as independent predictors of subsequent development of diabetes (Table 5).

Postpartum glucose tolerance, evaluated as the area under the glucose curve of the 75-g OGTT, was positively associated with other variables related to the metabolic syndrome assessed after pregnancy: BMI ($r = 0.161$; $P < 0.05$), waist circumference (0.243; $P < 0.05$), waist-to-hip ratio ($r = 0.246$; $P < 0.05$), triglycerides ($r = 0.261$; $P < 0.05$), and systolic ($r = 0.262$; $P < 0.05$) and diastolic ($r = 0.181$; $P < 0.05$) blood pressures. No significant correlation was found for cholesterol ($r = 0.065$) or HDL cholesterol ($r = -0.146$).

CONCLUSIONS — The group of women with previous GDM who participated in early postpartum metabolic assessment comprised 55.2% of the original group, which is similar to the response rate (52.2–63%) reported by other authors (9,24). Even though they were not different from those who did not participate with regard to age, prepregnancy BMI, family history of diabetes, recurrence of GDM, GDM class, or index pregnancy outcome, use of insulin in pregnancy was more frequent and gestational age at diagnosis of GDM lower in the group attending follow-up examination. Thus, it may be possible that women who returned to postpartum testing were more prone to abnormal postpartum glucose tolerance. However, the

Table 5—*Independent predictive factors of subsequent diabetes in women with GDM according to multiple logistic regression analysis*

	Logistic coefficient	Odds ratio	95% CI	*P* value
Prepregnancy obesity (BMI ≥27 kg/m²)	2.16	8.66	2.27–32.94	<0.01
Number of abnormal values in the diagnostic 100-g OGTT	1.11	3.03	1.43–6.37	<0.01
C-peptide/glucose score*	−0.77	0.46	0.25–0.85	<0.05
Intercept	−4.37			

*C-peptide/glucose score = C-peptide (ng/ml)/glucose (mg/dl) × 100.

likelihood of this bias is not supported by the fact that history of previous macrosomia was more common in the group who did not return to postpartum testing.

The incidence of abnormal glucose tolerance, as defined by the National Diabetes Data Group, up to 1 year after a GDM pregnancy has been reported to be 6.8–57% for combined glucose intolerance and diabetes and 2.6–38% for diabetes alone (6,9,11,24). In our population, use of the WHO criteria yields an incidence rate of 19.5% for combined impaired glucose tolerance and diabetes and 4.7% for diabetes alone. When the ADA criteria are used in our group of women, the incidence rate of diabetes is slightly increased (5.4%) while the incidence rate for combined impaired fasting glucose, impaired glucose tolerance, and diabetes rises to 25.4%. In agreement with previous reports (25), concordance between the diagnosis of impaired fasting glucose and impaired glucose tolerance is low, with only a small overlap (3.7%) between these two classes.

Comparison of clinical and obstetric history between women with and women without diabetes after pregnancy showed that prepregnancy obesity and recurrence of GDM were more common in women with postpartum diabetes, in agreement with other studies (8,12,13). However, family history of diabetes, which tended to be more frequent in diabetic women, was not statistically different between both groups.

As expected and in accordance with previous reports (7,9,26), women with postpartum diabetes had been diagnosed as having GDM earlier in the course of pregnancy and had higher glucose values in the 100-g diagnostic OGTT. Because earlier screening was done only in women with historical risk factors, it is possible that earlier diagnosis of GDM during pregnancy in women with postpartum diabetes merely reflects that these women had more risk factors. In this study, HbA_{1c} levels during the 3rd trimester of gestation, which may be viewed as another measure of the severity of GDM, were higher in women who developed diabetes after pregnancy. Need for insulin therapy during pregnancy, a well-established predictor of subsequent diabetes (8,27), was also more frequent in women with postpartum diabetes.

Fasting C-peptide levels and the C-peptide/glucose score measured during pregnancy were significantly lower in women with subsequent diabetes, even though prepregnancy obesity was more common in these women. Previous reports have shown that lower fasting insulin levels (28), lower insulin response to an OGTT (28,29), and lower first-phase insulin response to an intravenous glucose tolerance test (14) are predictive of abnormal glucose tolerance after a GDM pregnancy. Our data are consistent with the view that pancreatic β-cell dysfunction is an important predictor for later development of diabetes.

Birth of a large infant has previously been related to subsequent development of maternal diabetes (15). In our study, comparison of index pregnancy outcome showed that birth weight ratio was higher and weight >4 kg was more common in infants born to mothers who developed diabetes after pregnancy.

Multivariate logistic regression analysis of our data provides evidence that the risk of subsequent diabetes after a GDM pregnancy is independently increased by three different factors: prepregnancy obesity, severity of GDM (number of abnormal values in the 100-g diagnostic OGTT), and low C-peptide/glucose score during pregnancy. Thus, regardless of obesity and severity of GDM, limited β-cell capacity may be a significant pathogenic factor in subsequent development of diabetes.

Metabolic assessment after pregnancy showed a positive association between postpartum glucose tolerance and other cardiovascular risk factors: triglyceride levels, blood pressure, obesity, and regional distribution of body fat. O'Sullivan (30) observed that women with previous GDM, after a follow-up period of 22–28 years, had more lipid disturbances (increased cholesterol and triglyceride levels and decreased HDL cholesterol levels), higher blood pressure, and more abnormal electrocardiograms, thus leading to increased cardiovascular events. Meyers-Seifer (4) showed that at 5–6 years postpartum, former GDM mothers had changes in lipid levels and that triglyceride and HDL cholesterol levels correlated with other cardiovascular risk factors. Our present data support the possibility that postpartum glucose intolerance is indicative as well of a constellation of cardiovascular risk factors. Preventive measures directed to lifestyle behavioral patterns, including diet and exercise, which are currently being evaluated (31), may prove beneficial to reduce this high-risk cardiovascular profile.

In conclusion, we have identified many of the reported predictors of diabetes (prepregnancy obesity, recurrence of GDM, gestational age at diagnosis of GDM, severity of GDM, and impaired β-cell function) in the group of GDM women who had diabetes in early postpartum metabolic assessment. Low C-peptide/glucose score during pregnancy together with prepregnancy obesity and severity of GDM (number of abnormal values in the 100-g diagnostic OGTT) are independent predictors of subsequent diabetes. Our data suggest that regardless of obesity and severity of GDM, a β-cell defect increases the risk of postpartum diabetes.

The association of postpartum glucose tolerance with triglyceride levels, blood pressure, obesity, and regional distribution of body fat suggests that postpartum glucose intolerance anticipates a high-risk cardiovascular profile that comprises other risk factors besides diabetes. Accordingly, the need for primary prevention programs targeted at women with prior GDM must be reinforced.

References

1. Moses RG: The recurrence rate of gestational diabetes in subsequent pregnancies. *Diabetes Care* 19:1348–1350, 1996
2. Füchtenbusch M, Ferber K, Standl E, Ziegler AG: Prediction of type 1 diabetes postpartum in patients with gestational diabetes mellitus by combined islet cell autoantibody screening. *Diabetes* 46: 1459–1467, 1997
3. O'Sullivan JB: Diabetes mellitus after GDM. *Diabetes* 40 (Suppl. 2):131–135, 1991
4. Meyers-Seifer C, Vohr BR: Lipid levels in former gestational diabetic mothers. *Diabetes Care* 19:1351–1356, 1996
5. Damm P: Diabetes following gestational diabetes mellitus. In *Diabetes and Pregnancy*. Dornhorst A, Hadden DR, Eds. Chichester, U.K., Wiley, 1996, p. 341–350
6. Catalano PM, Vargo KM, Bernstein IM, Amini SB: Incidence and risk factors associated with abnormal postpartum glucose tolerance in women with gestational diabetes mellitus. *Am J Obstet Gynecol* 165: 914–919, 1991
7. Kjos SL, Peters RK, Xiang A, Henry OA, Montoro M, Buchanan TA: Predicting future diabetes in Latino women with gestational diabetes: utility of early postpartum glucose tolerance test. *Diabetes* 44: 586–591, 1995
8. Henry OA, Beischer NA: Long-term implications of gestational diabetes for the mother. *Baillières Clin Obstet Gynaecol* 5:461–484, 1991
9. Kjos SL, Buchanan TA, Greenspoon JS, Montoro M, Bernstein GS, Mestman JH: Gestational diabetes mellitus: the prevalence of glucose intolerance and diabetes

mellitus in the first two months post partum. *Am J Obstet Gynecol* 163:93–98, 1990
10. Pendergrass M, Fazioni E, DeFronzo RA: Non-insulin-dependent diabetes mellitus and gestational diabetes mellitus: same disease, another name? *Diabetes Rev* 3: 566–583, 1995
11. Metzger BE, Bybee DE, Freinkel N, Phelps RL, Radvany R, Vaisrub N: Gestational diabetes mellitus: correlations between the phenotypic and genotypic characteristics of the mother and abnormal glucose tolerance during first year postpartum. *Diabetes* 34 (Suppl. 2):111–115, 1985
12. Coustan DR, Carpenter MW, O'Sullivan PS, Carr SR: Predictors of subsequent disordered glucose metabolism. *Am J Obstet Gynecol* 168:1139–1145, 1993
13. Dornhorst A, Bailey PC, Anyaoku V, Elkeles RS, Johnston DG, Beard RW: Abnormalities of glucose tolerance following gestational diabetes. *Quart J Med* 77: 1219–1228, 1990
14. Buchanan TA, Xiang A, Kjos SL, Lee WP, Trigo E, Nader I, Bergner A, Palmer JP, Peters RK: Gestational diabetes: antepartum characteristics that predict postpartum glucose intolerance and type 2 diabetes in Latino women. *Diabetes* 47:1302–1310, 1998
15. Larsson G, Spjuth J, Ranstam J, Vikbladh I, Saxtrup O, Astedt B: Prognostic significance of birth of a large infant for subsequent development of maternal non-insulin-dependent diabetes mellitus: a prospective study over 20–27 years. *Diabetes Care* 9:359–364, 1986
16. Monereo Megías S, Fernandez San Martín MI, Pedrosa Jamar S, Elviro Peña R, Belmonte Tomás E, Aliaga Maraver A: Prevalencia de diabetes mellitus registrada en un área sanitaria de la comunidad de Madrid. *Endocrinología* 44:208–212, 1997
17. Tamayo-Marco B, Faure-Nogueras E, Roche-Asensio MJ, Rubio-Calvo E, Sanchez-Oriz E, Sabrada-Olivan JA: Prevalence of diabetes and impaired glucose tolerance in Aragon, Spain. *Diabetes Care* 20:534–536, 1997
18. National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes* 28:1039–1057, 1979
19. Battaglia FC, Lubchenco LO: A practical classification of newborn infants by weight and gestational age. *J Pediatr* 71:159–163, 1967
20. World Health Organization: *Diabetes Mellitus: Report of a WHO Study Group*. Geneva, World Health Org., 1985, p. 10–11 (Tech. Rep. Ser., no. 727)
21. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 20:1183–1197, 1997
22. Van der Kooy K, Seidell JC: Techniques for the measurement of visceral fat: a practical guide. *Int J Obesity* 17:187–196, 1993
23. Tanenberg RJ, Alster DK, Tuttleman M, Zawadzki JK: Diagnosis and monitoring of diabetes mellitus and diabetic complications. In *Diagnostic Endocrinology.* 2nd ed. Tabb Moore W, Eastman RC, Eds. St. Louis, MO, Mosby, 1996, p. 243–282
24. Dacus JV, Meyer NL, Muram D, Stilson R, Phipps P, Sibai BH: Gestational diabetes: postpartum glucose tolerance testing. *Am J Obstet Gynecol* 171:927–931, 1994
25. Larsson H, Berglung G, Lindgárde F, Ahren B: Comparison of ADA and WHO criteria for diagnosis of diabetes and glucose tolerance. *Diabetologia* 41:1124–1125, 1998
26. Damm P, Küll C, Bertelsen A, Molsted-Pedersen L: Predictive factors for the development of diabetes in women with previous gestational diabetes mellitus. *Am J Obstet Gynecol* 167:607–616, 1992
27. Lam KSL, Li DF, Lauder IJ: Prediction of persistent carbohydrate intolerance in patients with gestational diabetes. *Diabetes Res Clin Pract* 12:181–186, 1991
28. Metzger BE, Cho NH, Roston SM, Radvany R: Prepregnancy weight and antepartum insulin secretion predict glucose five years after gestational diabetes mellitus. *Diabetes Care* 16:1598–1605, 1993
29. Damm P, Kühl C, Hornes P, Molsted-Pedersen L: A longitudinal study of plasma insulin and glucagon in women with previous gestational diabetes. *Diabetes Care* 18:654–665, 1995
30. O'Sullivan JB: The interaction between pregnancy, diabetes and long-term maternal outcome. In *Diabetes Mellitus in Pregnancy*. 2nd ed. Reece EA, Coustan DR, Eds. New York, Churchill Livingstone, 1995, p. 389–398
31. Dornhorst A, Rossi M: Risk and prevention of type 2 diabetes in women with gestational diabetes. *Diabetes Care* 21 (Suppl. 2): 43–49, 1998