The Impact of Glycemic Control on Neonatal Outcome in Singleton Pregnancies Complicated by Gestational Diabetes

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OBJECTIVE — To identify the impact of suboptimal blood glucose control on neonatal outcomes in women with gestational diabetes mellitus (GDM).

RESEARCH DESIGN AND METHODS — Included were patients with singleton gestation enrolled in an outpatient GDM management program for at least 7 days who delivered at term. Blood glucose control was defined as an average fasting blood glucose of <95 mg/dl, 1-h postprandial of <140 mg/dl, or 2-h postprandial of <120 mg/dl. Data were compared between patients with optimal blood glucose control (n = 2,030) and those with suboptimal blood glucose control (n = 1,188). The primary study outcome was a composite variable consisting of macrosomia, large-for-gestational-age, hypoglycemia, jaundice, or stillbirth.

RESULTS — Over one-third of infants in the poorly controlled group were positive for at least one factor comprising the composite variable compared with 24% from the controlled group ($P < 0.001$).

CONCLUSIONS — Suboptimal glycemic control in women with GDM is associated with adverse neonatal outcome. Careful monitoring of blood glucose levels and initiation of appropriate treatment are essential in the care of women with GDM.

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Gestational diabetes mellitus (GDM) affects 2–5% of pregnancies in the U.S. (1). GDM is defined as a carbohydrate intolerance that begins or is first diagnosed during pregnancy (2). Pregnancies complicated with GDM are at increased risk for cesarean delivery and labor abnormalities as well as adverse neonatal outcomes such as macrosomia, hypoglycemia, stillbirth, and neonatal intensive care unit admission (3). Yet, questions remain regarding the beneficial effects of identification and treatment of GDM, the consequences of failure to diagnose the condition, and the degree of glycemic control necessary during pregnancy (4). Recently, the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) trial revealed that treatment of GDM does improve pregnancy outcome (5).

Current clinical interventions for patients diagnosed with GDM focus on maintaining euglycemia with a combination of diet and exercise. When diet and exercise fail to normalize blood glucose levels, insulin therapy is recommended.

The purpose of this analysis was to compare neonatal outcomes in women diagnosed with GDM whose average blood glucose values were within recommended American College of Obstetricians and Gynecologists guidelines with those with higher-than-recommended blood glucose averages.

RESEARCH DESIGN AND METHODS

— The study population was identified retrospectively from a large centralized perinatal database containing de-identified clinical information on pregnant women receiving outpatient services for surveillance and management of GDM through Matria Healthcare between January 2001 and January 2005. Information stored in the database was collected prospectively from the patient and her health care provider at initiation of outpatient services, as well as during the course of care, and included medical and obstetrical history, current pregnancy risk factors and diagnoses, biometric clinical data relative to care provided, and pregnancy outcome data. All information was collected using standardized forms, plans of treatment, and standard operating procedures. The outpatient service was prescribed by the patient's health care provider and was widely available in the U.S. The outpatient service was voluntary, and signed consent was received from all patients. Additional consent for use of clinical data for reporting and research purposes was obtained from each patient at enrollment. Outpatient services were in addition to and in collaboration with prenatal care provided by the individual health care provider responsible for diagnosis and treatment decisions.

Women enrolled for outpatient GDM management received one-on-one education/counseling and an individualized GDM plan of care designed by a certified diabetes educator (CDE). Education and counseling provided by the CDE included information on blood glucose testing and

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Abbreviations: CDE, certified diabetes educator; FBG, fasting blood glucose; GDM, gestational diabetes mellitus.

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

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Table 1—*Maternal characteristics*

	Blood glucose not controlled	Blood glucose controlled	*P*
n	1,188	2,030	
Maternal age (years)	31.3 ± 5.5	31.0 ± 5.7	0.571
≥35 years old	28.2	27.8	0.807
Married	74.9	77.0	0.184
Prepregnancy weight (lbs)	188.3 ± 52.8	162.8 ± 42.8	<0.001
Prepregnancy BMI (kg/m^2)	32.0 ± 8.2	28.0 ± 6.8	<0.001
Obese BMI (>35 kg/m^2)	29.1	13.4	<0.001
Gravidity	2.8 ± 1.8	2.5 ± 1.6	<0.001
A1C at GDM diagnosis	5.5 ± 0.9	5.1 ± 0.7	<0.001
A1C ≥7.0 at diagnosis	5.1	1.8	<0.001
Received insulin	58.4	23.7	<0.001

Data are means ± SD or %.

diabetes diet, exercise, and self-care activities. Blood glucose and ketone values were evaluated daily by a CDE, and immediate adjustments to diet plan or medication were made accordingly. All patients were instructed to perform daily fasting and 1- or 2-h postprandial blood glucose measurements. The decision to have the patient test her blood glucose at 1- or 2-h postprandial was determined by her physician. All testing supplies were delivered to the patient's home. Weekly written reports and as-needed (PRN) telephone report and consultation were provided to the patient's health care provider. The outpatient GDM management program was designed as a 21-day program. Patients discharged before 21 days were generally deemed to be in stable condition and to have adequate blood glucose control by their health care provider. Those enrolled >21 days generally showed signs of suboptimal GDM management that required additional and ongoing education, counseling, and blood glucose surveillance.

For this retrospective analysis, we first identified from the database patients with singleton gestation diagnosed with GDM who had complete pregnancy outcome records. Included were patients who delivered at term (≥37 weeks of gestation) and who received outpatient management for a minimum of 7 days. Each patient's fasting and 1- or 2-h postprandial blood glucose values were averaged, yielding one mean value per patient per blood glucose type (fasting or 1- or 2-h postprandial). Blood glucose control was defined according to American College of Obstetricians and Gynecologists guidelines: a mean fasting value of <95 mg/dl, mean 1-h postprandial of <140 mg/dl, or mean 2-h postprandial of <120 mg/dl. Two groups were identified: women with blood glucose averages within the recommended guidelines (blood glucose controlled; $n = 2,030$) and women with blood glucose averages higher than the recommended guidelines (blood glucose not controlled; $n = 1,188$). Maternal characteristics, A1C levels at GDM diagnosis, and neonatal outcomes were compared using Fisher's exact and Pearson's χ^2 test statistics. $P < 0.05$ was considered statistically significant.

The primary study outcome was a composite variable consisting of the presence of one or more of the following neonatal complications: macrosomia, large-for-gestational-age, hypoglycemia, jaundice, or stillbirth.

RESULTS — Included in this analysis were data from 3,218 women diagnosed with GDM who received outpatient services for management of their condition. In total, 377,372 blood glucose measurements were obtained over 104,405 days (average of 3.6 blood glucose measurements per patient per day). Overall, 63.1% of women achieved recommended levels of mean blood glucose control. Maternal characteristics are compared in Table 1 between patients with and without blood glucose control. Differences were noted in maternal characteristics between the groups. Patients exhibiting suboptimal blood glucose control had a greater BMI and prepregnancy weight as well as a higher A1C at diagnosis of GDM than those patients achieving good blood glucose control. Mean blood glucose values are presented in Table 2. Almost one-third of patients (1,028 [31.9%]) were instructed by their physician to report 1-h postprandial blood glucose values, while 2,190 (68.1%) reported 2-h postprandial results. As expected, fasting and 1- or 2-h postprandial blood glucose values were

Table 2—*Mean blood glucose values*

	Blood glucose not controlled	Blood glucose controlled	*P*
n	1,188	2,030	
Days of blood glucose values	35.6 ± 27.7	30.6 ± 24.1	<0.001
Total blood glucose measurements	151,873	225,499	—
FBG (mg/dl)	97.3 ± 11.4 (40,641)	82.9 ± 7.3 (59,478)	<0.001
1-h postprandial (mg/dl)			
Breakfast	128.7 ± 14.8 (10,080)	114.3 ± 10.7 (19,689)	<0.001
Lunch	130.5 ± 14.8 (9,747)	117.4 ± 10.2 (19,138)	<0.001
Dinner	132.3 ± 15.4 (9,913)	119.3 ± 9.9 (19,180)	<0.001
2-h postprandial (mg/dl)			
Breakfast	110.9 ± 15.5 (27,582)	96.1 ± 9.9 (36,327)	<0.001
Lunch	130.5 ± 14.8 (26,963)	102.4 ± 13.4 (35,921)	<0.001
Dinner	123.7 ± 13.8 (26,947)	106.5 ± 8.0 (35,766)	<0.001

Data are means ± SD (number of blood glucose measurements).

Table 3—*Neonatal outcomes*

	Blood glucose not controlled	Blood glucose controlled	*P*
n	1,188	2,030	
Mean gestational age at delivery (weeks)	38.7 ± 0.9	38.9 ± 1.0	<0.001
Birth weight (g)	3,491 ± 532	3,364 ± 481	<0.001
Macrosomia (g)	15.7	9.3	<0.001
4,000–4,500	12.3	7.8	<0.001
>4,500	2.5	1.5	0.034
Large-for-gestational-age	19.8	11.1	<0.001
Cesarean delivery	48.5	37.4	<0.001
HLN admission	10.6	7.3	0.002
Neonatal hypoglycemia	9.3	7.1	0.031
Jaundice	10.1	8.4	0.111
Stillbirth	0.3 (4)	0.1 (2)	0.202
Composite outcome*	33.1	24.0	<0.001

Data are means ± SD, %, or % (*n*). HLN refers to higher-level nursery, neonatal intensive care unit, or intermediate care. *Composite outcome refers to one or more of the following outcomes: macrosomia, large-for-gestational-age, hypoglycemia, jaundice, or stillbirth.

higher for women without blood glucose control.

Neonatal outcomes are presented in Table 3. Women with controlled blood glucose delivered fewer large-for-gestational-age ($P < 0.001$), macrosomic ($P < 0.001$), or hypoglycemic ($P < 0.031$) infants than women with uncontrolled blood glucose. Cesarean delivery ($P < 0.001$) and neonatal intensive care unit or intermediate care nursery admission ($P < 0.002$) were also more common for infants from mothers with uncontrolled blood glucose. One-third of infants (33.1%) from mothers with suboptimal blood glucose control had at least one adverse outcome compared with less than one-quarter of infants (24.0%) from the controlled blood glucose group ($P < 0.001$).

The degree of average fasting blood glucose (FBG) >95 mg/dl on the incidence of adverse neonatal outcome is presented in Fig. 1. The rate of adverse neonatal outcome from women with an average FBG ≥123.5 mg/dl (30% > 95 mg/dl) was over twice that of women with an average FBG <95 mg/dl (57.9 vs. 24.8%).

CONCLUSIONS— Our findings suggest that suboptimal glycemic control in women with GDM is associated with adverse neonatal outcomes. For decades, controversy has existed regarding the need for GDM screening and if treatment of GDM is warranted. Many authors have questioned if GDM is even a real clinical entity in need of treatment (6–9).

Previous studies have shown that in general, treatment of GDM does indeed have an impact on pregnancy outcome. A recent randomized trial by Crowther et al. (5) showed that treatment of GDM reduces serious perinatal morbidity when compared with routine care. These authors found the rate of serious perinatal outcomes among infants—defined by one or more of the following: death, shoulder dystocia, bone fracture, and nerve palsy—to be significantly lower in the group that received treatment. Similarly, Langer et al. (3) found that women

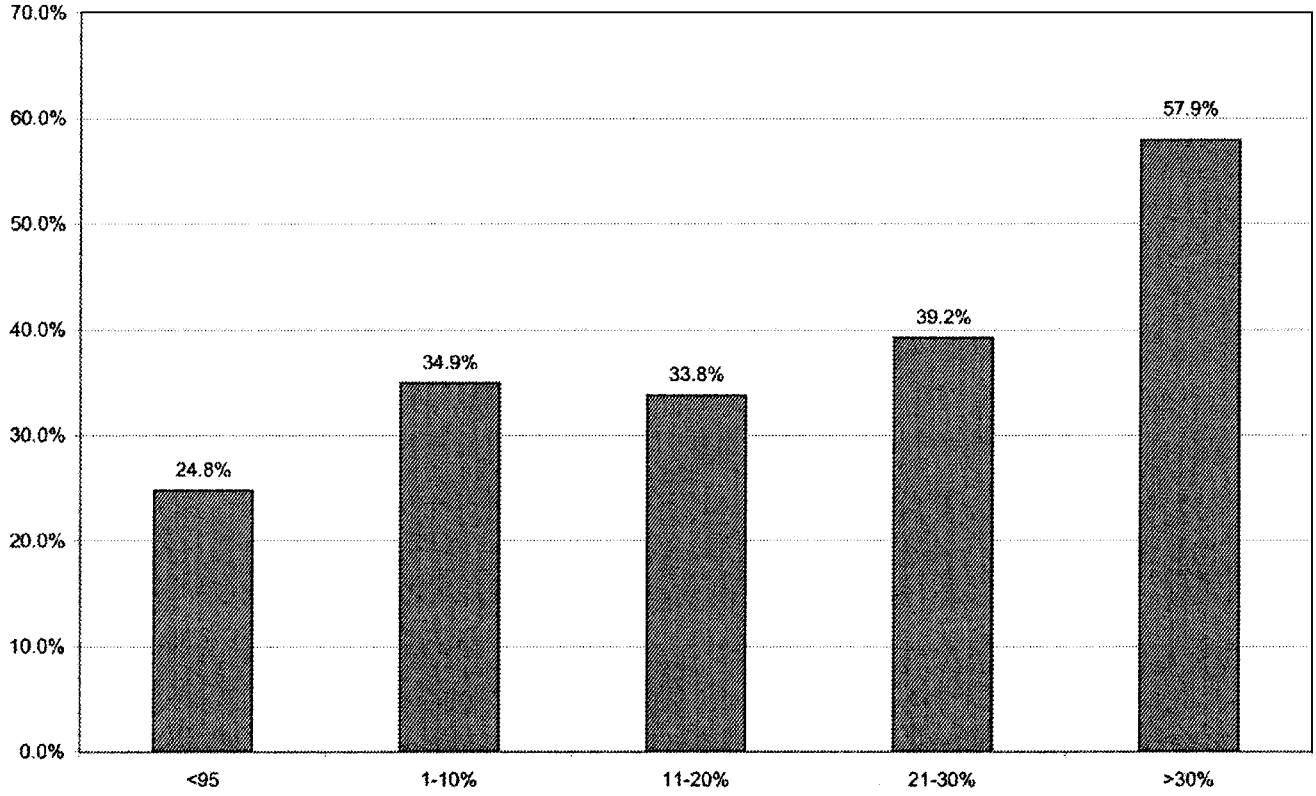

Figure 1—*Percent of patients with composite outcome by FBG % >95 mg/dl. All P < 0.05 compared with control subjects <95 mg/dl.*

with untreated GDM had significantly higher rates of adverse neonatal outcome. Our study results are consistent with these findings and take them one step further by showing the impact of blood glucose control.

In the present study, all patients received similar outpatient management for their GDM. Data were stratified into two groups depending on optimal versus suboptimal blood glucose control. Women with suboptimal control had a higher incidence of adverse events measured by the composite outcome, which included the presence of macrosomia, large-for-gestational-age, hyperglycemia, jaundice, or stillbirth. We found higher rates of cesarean delivery, higher-level nursery admission, macrosomia, and neonatal hypoglycemia in the group of women with suboptimal blood glucose control. Furthermore, we found that a cumulative effect with respect to suboptimal glucose control may be present. As the average FBG increased > 95 mg/dl so did the incidence of the composite outcome.

Limitations of our study include those inherent in a retrospective study. Information on race and ethnicity was not available for the analysis. In the present study, all patients received similar daily outpatient surveillance and management of their GDM. We cannot report on pregnancy outcomes of patients who did not receive daily blood glucose management.

In summary, suboptimal glycemic control in women with GDM is associated with adverse neonatal outcome. Careful monitoring of blood glucose levels and initiation of appropriate treatment are essential in the care of women with GDM.

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