Gestational Diabetes Mellitus

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Gestational diabetes mellitus (GDM) is carbohydrate intolerance with onset or first recognition during pregnancy.1,2 This diagnosis is independent of insulin use or persistence of the condition after the pregnancy and does not apply to pregnant women with previously diagnosed diabetes. Gestational diabetes has been recognized for decades,3 but the potential significance of the condition, as well as criteria for screening and diagnosis, remain controversial. While there is also controversy as to the optimal monitoring and treatment strategy, it is apparent that even mild degrees of maternal hyperglycemia may result in fetal developmental defects.4

Epidemiology

Gestational diabetes affects up to 14% of the pregnant population, approximately 135,000 women per year in the United States.5 Insulin resistance occurs to some degree in all pregnancies,6 but those women who are unable to compensate develop GDM. Women at greatest risk of developing GDM are those who are obese, older than 25 years, have a previous history of abnormal glucose metabolism or poor obstetric outcome, have first-degree relatives with diabetes, or are members of ethnic groups with high prevalences of diabetes. Fetal macrosomia, defined as a birth weight that is either greater than the 90th percentile for gestational age and sex or 2 SDs or more above the normal mean weight,3 may affect up to 40% of the offspring of pregnancies complicated by GDM.7 One study observed macrosomia in 17.9% of pregnancies complicated by GDM despite treatment compared with 5.6% of control subjects.8 Macrosomia is associated with increased risk of birth injuries,9,10 a direct result of the large size of the fetus.9 The risk of shoulder dystocia is increased by as much as 30-fold in diabetic pregnancies when the infants weigh more than 4500 g.10 When the obstetrician delivers the infant early to stop the accelerated in utero growth, complications related to prematurity, such as hyperbilirubinemia, hypocalcemia, and respiratory distress,11 may result. The infant of a woman with GDM is at higher risk of developing obesity, impaired glucose tolerance (IGT), or diabetes at an early age.12-15 Infants whose fathers were diabetic are at a much lower risk for these complications, which appear to be the result of the hyperglycemic intrauterine environment superimposed on a genetic predisposition to diabetes.16

To date there is no evidence-based study indicating that prevention and rigorous treatment of GDM minimize maternal or fetal complications.17 Given the current recommended standards of care,18,19 it is unlikely that such studies could ethically be done today. The risk of GDM recurring in subsequent pregnancies is reported to be 60% to 90%, depending on the woman’s first trimester weight in those pregnancies.20 In addition, after a pregnancy with GDM, the mother has an increased risk of developing type 2 diabetes.20 In 1 study, 7 to 10 years postpartum, 30% of women with GDM had developed diabetes or IGT.3

Optimal Screening and Diagnostic Strategies

The table shows the most commonly recommended screening and diagnostic criteria for GDM.1,2,21 Most of the world uses some modification of the criteria of the World Health Organization (WHO),2 which is based on a glucose load of 75 g. This is the same test load and criteria for diagnosis of diabetes and IGT used in nonpregnant adults, with the recommendation that the diagnosis of gestational IGT should alert the physician to the high-risk nature of the pregnancy, and that gestational IGT should be treated in the same way as GDM.2 These criteria make the diagnosis of GDM at the lowest glucose concentrations. Several studies have shown that the WHO criteria22-24 identify more adverse outcomes than other criteria.

In the United States, the criteria endorsed by the National Diabetes Data Group21 and the American Diabetes Association (ADA)3 are in general use. At the 4th International Workshop Conference on Gestational Diabetes Mellitus, sponsored by the ADA, the glucose concentrations considered diagnostic of GDM were lowered.25 This change was made more than a decade after these criteria were originally proposed. During the intervening years, data were generated suggesting that lower degrees of glucose intolerance were associated with increased risk of adverse perinatal outcome.1 The recommendation to test all pregnant women was changed and women who appear to be at low risk for GDM will no longer be screened with a glucose load test. This recommendation includes women who are members of ethnic groups with a low prevalence of GDM who have no known diabetes in first-degree relatives, are younger than 25 years, were not obese before pregnancy, have no history of abnormal glucose metabolism, and no history of a poor obstetric outcome.1 In an identified low-risk group, the risk of GDM is less than 2%.1
Importance of Blood Glucose Monitoring

There are 3 studies that suggest that the risk of fetal macrosomia increases as the maternal postprandial glucose increases. Keeping 1-hour postprandial blood glucose levels between 120 mg/dL (6.7 mmol/L) and 140 mg/dL (7.8 mmol/L) minimizes the risk of macrosomia. Although therapy begins with diet, insulin therapy should be initiated when peak postprandial response exceeds this target.7,26-28

Women with GDM have been known to deliver large newborns despite only modest elevations of glucose. Continuous glucose monitoring system use has enabled the detection of previously missed postprandial blood glucose peaks in GDM. We used the continuous glucose monitoring system in 10 women with GDM and discovered that, on average, the women spent 1.8 hours per day with glucose concentrations 120 mg/dL (6.7 mmol/L) or greater. In these women, the continuous glucose monitoring system has revealed high postprandial blood glucose levels, which were previously unrecognized by intermittent fingerstick evaluation.30

Diets Designed to Minimize Postprandial Glycemia

Diabetic fetopathy, which is a result of maternal postprandial hyperglycemia, can be minimized when the peak postprandial response is blunted. This is best accomplished by carbohydrate restriction. The optimal dietary prescription provides the caloric and nutrient needs to sustain pregnancy but does not cause postprandial hyperglycemia. To date, there are no randomized controlled trials specifically focused on the development of an optimal diet for women with GDM; therefore, the standard ADA recommendations were adopted. The ADA’s diet for nonpregnant persons suggests that meal plans could have up to 60% carbohydrate composition. Instituting this high-carbohydrate diet for GDM results in the need for insulin therapy in greater than 50% of women. The National Academy of Sciences concluded that healthy

## Table. Criteria for the Diagnosis of Gestational Diabetes Mellitus*

<table>
<thead>
<tr>
<th>Time, h</th>
<th>National Diabetes Data Group†</th>
<th>American Diabetes Association‡</th>
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</tbody>
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*All data are mg/dL, unless indicated otherwise. To convert mg/dL to mmol/L, multiply by 0.0555. Two or more concentrations as high as or higher than those shown (National Diabetes Data Group and American Diabetes Association) and 1 or more concentrations as high or higher than those shown (World Health Organization) make the diagnosis of gestational diabetes. NA indicates time points not performed.
†May be done as primary test or only if screening glucose 1 hour after a 50 g oral glucose load of 140 mg/dL or higher.
‡May be done as primary test or only if screening glucose 1 hour after a 100 g oral glucose load of 140 mg/dL or higher.

Ketonuria develops in pregnancies complicated by GDM. Some obstetricians believe that women who require insulin therapy are at a higher risk for difficulties during delivery and liberalize criteria for cesarean delivery. Others have shown that decreased incidence of macrosomia decreases the cesarean delivery rate if the indications for operative delivery are not changed for the woman with GDM who requires insulin.42

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The type of insulin and its dosage schedule should be prescribed to lower the baseline and postprandial glucose levels. The basal need may be given by using an insulin pump or multiple doses of isophane insulin (neutral protamine Hagedorn) (NPH).44 The meal-related hyperglycemia peaks should be treated with rapid-acting insulin. Insulin lispro, an analog of human insulin, possesses unique properties that facilitate lowering the postprandial glucose concentration and is a valuable therapeutic option in the treatment of GDM.44 The rapid absorption of insulin lispro allows for a faster peak insulin concentration vs regular human insulin, possesses unique properties that facilitate lowering the postprandial glucose concentration and is a valuable therapeutic option in the treatment of GDM. The rapid absorption of insulin lispro allows for a faster peak insulin concentration vs regular human insulin.

**REFERENCES**


