Diabetes Mellitus

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Overview

Diabetes mellitus complicates approximately 7% of all pregnancies. Gestational diabetes mellitus (GDM), or carbohydrate intolerance detected for the first time during gestation, represents about 90% of all cases, whereas pregestational diabetes mellitus, which includes both type 1 and type 2 diabetes mellitus, accounts for the remaining 10%. Type 2 diabetes is now the most common form of pregestational diabetes.

Pathophysiology

The increased perinatal morbidity and mortality associated with the pregnancy complicated by diabetes mellitus can be attributed directly to maternal hyperglycemia. Glucose crosses the placenta by facilitated diffusion. Therefore, maternal hyperglycemia can produce fetal hyperglycemia. During the first trimester, maternal hyperglycemia is associated with an increased risk for abnormal fetal organogenesis. Major fetal malformations, now the leading cause of perinatal mortality in pregnancies complicated by type 1 and type 2 diabetes mellitus, occur in 6–10% of pregnancies complicated by pregestational diabetes. Poorly controlled patients can have up to a 25% risk for fetal malformations. Chronic fetal hyperglycemia in later gestation leads to fetal hyperinsulinemia, which is associated with excessive fetal growth, as well as delayed fetal pulmonary maturation. Intrauterine fetal death, which is observed in pregnancies complicated by poorly controlled diabetes mellitus, can also be attributed to fetal hyperinsulinemia that results in hypoxia and lactic acidosis. The likelihood that any of these complications will occur is directly related to maternal glucose control, as reflected by mean glucose levels or concentrations.
of glycosylated hemoglobin. The presence of diabetic vasculopathy may also affect placental function, thereby increasing the risk for fetal growth restriction, preeclampsia, and preterm delivery.

**Pregestational diabetes mellitus**

**Risk assessment**
Maternal and perinatal risks are increased in the presence of:
1. vasculopathy, such as retinopathy, nephropathy, and hypertension;
2. poor glucose control;
3. prognostically bad signs of pregnancy, including ketoacidosis, pyelonephritis, pregnancy-induced hypertension, and poor clinic attendance or neglect.

**Prepregnancy care**

**Objectives**
1. Assess for maternal vasculopathy by an ophthalmological evaluation, electrocardiogram and 24-hour urine collection for creatinine clearance and protein excretion.
2. Improve maternal glucose control (target glycosylated hemoglobin 7% or lower with normal range 6% or lower) to reduce the risk of fetal malformations and miscarriage; assess for hypoglycemic awareness.
3. Provide contraceptive counseling.
4. Educate the patient and her partner about the management plan for diabetes in pregnancy.
5. Determine rubella immune status and check thyroid function studies.
6. Begin folic acid supplementation to reduce risk of fetal neural tube defects.

**Detection and evaluation of malformations**
1. Identification of women at greatest risk: maternal glycosylated hemoglobin levels in the first trimester.
2. Noninvasive aneuploidy screening and MSAFP.
3. Ultrasonography at 13–14 weeks to detect anencephaly.
4. Comprehensive ultrasonography at 18–20 weeks with careful study of cardiac structure, including great vessels.

**Antepartum care: regulation of maternal glycemia**
Target capillary glucose levels in pregnancy are listed below:
- Mean level: 100 mg/dL
- Before breakfast: less than 95 mg/dL
- Before lunch, supper, bedtime snack: less than 100 mg/dL
• 1 hour after meals: less than 140 mg/dL
• 2 hours after meals: less than 120 mg/dL
• 2 a.m. to 6 a.m.: greater than 60 mg/dL

1 Capillary glucose monitoring with fasting, prelunch, predinner and bedtime levels daily, as well as 1- or 2-hour postprandial values; glycosylated hemoglobin levels in each trimester, target 6% or less.

2 Insulin therapy

   • Multiple insulin injections: prandial insulin (insulin lispro or insulin aspart) with meals, snacks; basal insulin (neutral protamine Hagedorn (NPH)), before breakfast (two-thirds of total NPH dose) and at bedtime (one-third of total NPH dose). If well controlled on insulin glargine or detemir, may continue these basal insulins.
   • Continuous subcutaneous insulin infusion (insulin pump): insulin lispro; continuous basal rate and boluses, in highly compliant patients.

3 Dietary recommendations

   • Plan: three meals, three snacks.
   • Composition: carbohydrate 40–50% complex, high fiber; protein 20%; fat 30–40% (less than 10% saturated).
   • Weight gain: per IOM guidelines.

4 General guidelines for insulin use and carbohydrate intake:

   • 1 unit of rapid-acting insulin lowers blood glucose 30 mg/dL.
   • 10 g of carbohydrate increases blood glucose 30 mg/dL.
   • 1 unit of rapid-acting insulin will cover intake of 10 g of carbohydrate.

Fetal evaluation

Assessment of fetal well-being to prevent intrauterine fetal deaths and guide timing of delivery:

1 Biophysical

   • Maternal assessment of fetal activity at 28 weeks.
   • Nonstress test (NST), weekly at 28–30 weeks for women with vasculopathy; twice weekly at 32 weeks and beyond in all pregestational diabetes; may alternate with biophysical profile (BPP).
   • BPP or contraction stress test if NST nonreactive.

2 Sonographic evaluation of fetal growth during the third trimester.

Delivery

Timing

1 Patients at low risk for fetal death (excellent glucose control, no vasculopathy, normal fetal growth, reassuring antepartum fetal testing, no prior stillbirth): may electively deliver after 39 weeks or allow spontaneous labor up to 40 weeks.
2 Patients at high risk for fetal death (poor control, vasculopathy, macrosomia, hydramnios, prior stillbirth): consider delivery prior to 39 weeks. Amniocentesis may be employed to assess for lung maturity.

**Method**

To reduce birth trauma, counsel regarding elective cesarean delivery if estimated fetal weight is 4500 g or more. For estimated weight 4000–4500 g, mode of delivery will depend on prior obstetric history, sonographic growth characteristics, pelvic examination and patient preference.

**Intrapartum glycemic control**

1. Check capillary glucose hourly at the bedside; maintain below 110 mg/dL.
2. Glucose control during labor (first stage) (Table 20.1).

**Contraception for the patient with type 1 or type 2 diabetes mellitus**

**Combination oral contraceptives**

1. Low-dose pills appear safe in patients without vasculopathy.
2. Contraindicated in presence of smoking, hypertension.

**Progestin-only pills**

Acceptable for patients with vasculopathy.

**Mechanical or barrier methods**

Less effective than oral contraceptives but no effect on glucose control or vasculopathy.

**Intrauterine device**

Acceptable for multiparous patients.

**Sterilization**

Consider when family has been completed, especially for patients with significant vasculopathy.

**Table 20.1** Glucose control during first stage of labor

<table>
<thead>
<tr>
<th></th>
<th>Insulin</th>
<th>Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latent phase</td>
<td>1 unit/hr</td>
<td>5 g/h</td>
</tr>
<tr>
<td>Active phase</td>
<td>None</td>
<td>10 g/h</td>
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</tbody>
</table>
Gestational diabetes

Definition
Gestational diabetes is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy. The definition applies irrespective of whether or not insulin is used for treatment or the condition persists after pregnancy. It does not exclude the possibility that unrecognized glucose intolerance may have antedated the pregnancy.

Class A₁ gestational diabetes is diet controlled; Class A₂ gestational diabetes requires diet and pharmacological treatment (insulin or oral agent such as glyburide).

Consequences: Why bother to screen?
2. Fetal and neonatal:
   - excessive fetal growth and birth trauma; neonatal hypoglycemia, hypocalcemia, hyperbilirubinemia;
   - increased perinatal mortality associated with significant maternal hyperglycemia.

Screening and diagnosis
Detection
Most practitioners continue to screen all pregnant women for glucose intolerance since selective screening based on clinical attributes or past obstetric history has been shown to be inadequate. There may be a group of women at low enough risk that screening is not necessary (see below).

According to the Fourth International Workshop Conference on GDM, Screening Strategy, risk assessment for GDM should be ascertained at the first prenatal visit.

Low risk
Blood glucose testing is not routinely required if all of the following characteristics are present:
- Member of an ethnic group with a low prevalence of GDM
- No known diabetes in first-degree relatives
- Age younger than 25 years
- Weight normal before pregnancy
- No history of abnormal glucose metabolism
- No history of poor obstetric outcome.

Average risk
Perform blood glucose screening at 24–28 weeks using one of the following:
- Two-step procedure: 1-hour 50 g GCT (glucose challenge test) followed by a diagnostic OGTT (oral glucose tolerance test) in those meeting the threshold value in GCT (130–140 mg/dl).
- One-step procedure: diagnostic OGTT performed on all subjects.

High risk
- Perform blood glucose testing as soon as feasible, using the procedures described above.
- If GDM is not diagnosed, blood glucose testing should be repeated at 24–28 weeks or at any time a patient has symptoms or signs suggestive of hyperglycemia.


With a GCT cutoff value of 140 mg/dL, sensitivity is 90%, and 15% of patients require a GTT. With a cutoff of 130 mg/dL, sensitivity is nearly 100%, but 25% of patients require a GTT.

A plasma glucose measurement 200 mg/dL or higher outside the context of a formal glucose challenge test, or a truly fasting plasma glucose 126 mg/dL or higher, suggests the diabetic state and warrants further investigation.

Diagnosis
100 g oral glucose load, administered in the morning after overnight fast for at least 8 hours but not more than 14 hours, and following at least 3 days of unrestricted diet (150 g carbohydrate or more) and usual physical activity.

Venous plasma glucose is measured fasting and at 1, 2 and 3 hours. Subject should remain seated and not smoke throughout the test.

Two or more of the following venous plasma concentrations must be met or exceeded for a positive diagnosis (Table 20.2).

<table>
<thead>
<tr>
<th></th>
<th>NDDG (mg/dL)</th>
<th>Carpenter and Coustan* (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>105</td>
<td>95</td>
</tr>
<tr>
<td>1-hour</td>
<td>190</td>
<td>180</td>
</tr>
<tr>
<td>2-hour</td>
<td>165</td>
<td>155</td>
</tr>
<tr>
<td>3-hour</td>
<td>145</td>
<td>140</td>
</tr>
</tbody>
</table>

Other diagnostic criteria
The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study suggested a continuous relationship between maternal glucose levels (including levels below those currently diagnostic of GDM) and perinatal outcomes. Based on the HAPO data, the IADPSG criteria were derived by consensus. The IADPSG approach utilizes universal 2-hour 75 gram OGTT with the diagnosis of GDM established if one value is abnormal. The IADPSG criteria are as follows: fasting, 92 mg/dl; one-hour, 180 mg/dl; two-hour, 153 mg/dl. This approach results in a 2–3 times increased frequency of GDM. Currently, the ADA endorses either the IADPSG approach or the two-step approach with a diagnostic three-hour OGTT. ACOG endorses only the three-hour 100-gram OGTT criteria.

Antepartum management
Program of care
Visits every 1–2 weeks until 36 weeks, then weekly.

Dietary recommendations in pregnancy
- Plan: 3 meals, bedtime snack.
- Composition: carbohydrate 40–50% complex, high fiber; protein 20%; fat 30–40% (less than 10% saturated).
- Weight gain: 20 lb; 16 lb for very obese.
    Note: Check morning urine for ketones if using caloric restriction in obese patients (1600–1800 kcal/day). Increase caloric intake if fasting ketonuria noted.

Exercise
Encourage regular exercise, 20–30 minutes brisk walking, 3–4 times/week.

Surveillance of maternal diabetes
1 Self-monitoring of capillary blood glucose to check fasting and 1- or 2-hour postprandial glucose levels daily to assess efficacy of diet.
2 If repetitive fasting plasma values are more than 95 mg/dL and/or 1-hour values are more than 140 mg/dL and/or 2-hour values are more than 120 mg/dL, insulin or glyburide therapy is recommended.
3 Starting insulin dose calculated based on patient’s weight: 0.8 U/kg actual body weight per day in first trimester, 1.0 U/kg in second trimester, 1.2 U/kg in third trimester. Give two-thirds of total dose in fasting state: two-thirds as NPH, one-third as regular or insulin lispro; give one-third
of total dose as one-half regular or insulin lispro at dinner, one-half as NPH at bedtime.

4 Glyburide can be used as alternative to insulin, although it is usually not effective if fasting glucose exceeds 115 mg/dL. Glyburide, unlike insulin, does cross the placenta and patients should be informed of this although short-term safety is established. The usual starting dose is 2.5 mg at breakfast and 2.5 mg at dinner with doses as high as 20 mg/day employed.

Delivery

1 Women with well-controlled class A₁ gestational diabetes allow to go to 39 weeks of gestation.
2 If undelivered at 40 weeks, begin fetal assessment with twice-weekly NSTs. Women with prior stillbirth or those with hypertension should be followed with twice-weekly NSTs at 32 weeks.
3 Clinical estimation of fetal size and ultrasonographic indices should be used to detect excessive fetal growth. To reduce birth trauma, counsel regarding cesarean delivery if estimated fetal weight is at least 4500 g. For estimated weight 4000–4500 g, consider prior obstetric history, fetal growth indices, pelvic capacity and patient preference in selecting mode of delivery.
4 Class A₂ women should be followed with twice-weekly NSTs.
5 Suboptimally controlled GDM women may require delivery before 39 weeks.
6 Alert neonatal team as infant may require observation for hypoglycemia, hypocalcemia, and hyperbilirubinemia.

Postpartum care

Evaluation for persistent carbohydrate intolerance

1 Women can continue self-blood-glucose monitoring to evaluate glucose profile although class A₁ patients generally demonstrate normoglycemia.
2 At 6–12 weeks postpartum, oral GTT with 75 g glucose load, administered under conditions described for 100 g oral test. Venous plasma glucose is measured fasting and at 2 hours (Table 20.3).
3 If normal, evaluate at minimum of 3-year intervals with fasting glucose; encourage exercise and, if obese, weight loss.

Effects of oral contraceptives

Deterioration of carbohydrate intolerance not reported with low-dose pills.

Recurrence risk

Approximately 60%.
Table 20.3  Values for venous plasma glucose

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Impaired glucose tolerance (mg/dL)</th>
<th>Diabetes mellitus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting less than 100 mg/dL</td>
<td></td>
<td>100–125</td>
<td>126 mg/dL or higher</td>
</tr>
<tr>
<td>2 h less than 140 mg/dL</td>
<td></td>
<td>140–199</td>
<td>200 mg/dL or higher</td>
</tr>
</tbody>
</table>

**Suggested reading**

**Type 1 and type 2 diabetes mellitus in pregnancy**

**Gestational diabetes mellitus**