Gestational diabetes

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TERMINOLOGY

- Women with type 1 or 2 diabetes diagnosed prior to pregnancy are classified as having preexisting diabetes.
- Historically, the term "gestational diabetes" has been defined as onset or first recognition of abnormal glucose tolerance during pregnancy
- Some organizations have attempted to distinguish women with probable preexisting diabetes that is first recognized during early pregnancy from those whose disease is a transient manifestation of pregnancy-related insulin resistance and diagnosed in the late second or the third trimester.

Prevalence

- The prevalence of gestational diabetes mellitus as traditionally defined is approximately 6 percent of pregnant women in the United States

- The prevalence varies worldwide and among racial and ethnic groups, generally in parallel with the prevalence of type 2 diabetes.

Significance

- Preeclampsia, gestational hypertension
- ●Polyhydramnios
- ●Macrosomia and large for gestational age infant
- ●Maternal and infant birth trauma
- ●Operative delivery (cesarean, instrumental)
- ●Perinatal mortality
- ●Fetal/neonatal hypertrophic cardiomyopathy
- ●Neonatal respiratory problems and metabolic complications (hypoglycemia, hyperbilirubinemia, hypocalcemia, polycythemia)

- Long-term, women with gestational diabetes mellitus are at increased risk of developing type 2 diabetes as well as cardiovascular disease

- Their adolescent and adult offspring appear to be at risk of long-term sequelae, such as obesity, abnormal glucose tolerance, hypertension, or metabolic syndrome.
- In addition, both gestational and pregestational (preexisting) diabetes mellitus have been associated with an increased risk of autism and other adverse neurodevelopmental outcomes in offspring, but it is not clear that these associations are causal

Risk factors

- Personal history of impaired glucose tolerance, A1C ≥5.7 percent, impaired fasting glucose, or gestational diabetes mellitus in a previous pregnancy.
- Member of one of the following ethnic groups, which have a high prevalence of type 2 diabetes: Hispanic American, African American, Native American, South or East Asian, Pacific Islander.
- Family history of diabetes, especially in first-degree relatives
- Prepregnancy weight ≥110 percent of ideal body weight or BMI >30 kg/m^2, significant weight gain in early adulthood and between pregnancies , or excessive gestational weight gain during the first 18 to 24 weeks
- Older maternal age (>25 or 30 years of age).
- Previous unexplained perinatal loss or birth of a malformed infant.
- Glycosuria at the first prenatal visit.
- Previous birth of an infant ≥4000 g (approximately 9 pounds).
- High density lipoprotein <35 mg/dL (0.90 mmol/L), triglyceride >250 mg/dL (2.82 mmol/L).
- Medical condition/setting associated with development of diabetes, such as metabolic syndrome, polycystic ovary syndrome, current use of glucocorticoids, hypertension or cardiovascular disease, acanthosis nigricans.
- Multiple gestation.

- Women at low risk of gestational diabetes mellitus are younger (<25 years of age), non-Hispanic white, with normal BMI (<25 kg/m^2 [<23 kg/m^2 in Asians]), no history of previous glucose intolerance or adverse pregnancy outcomes associated with gestational diabetes mellitus, and no first-degree relative with diabetes .

- Only 10 percent of the general obstetric population in the United States meets all of these criteria for low risk of developing gestational diabetes mellitus, which is the basis for universal rather than selective screening

IDENTIFICATION OF OVERT DIABETES IN EARLY PREGNANCY

- The ADA and ACOG define women at increased risk of overt diabetes based on:Body mass index (BMI) ≥25 kg/m^2 (≥23 kg/m^2 in Asian Americans) **plus** one or more of the following :
- •Gestational diabetes mellitus in a previous pregnancy.
- •Glycated hemoglobin ≥5.7 percent (39 mmol/mol), impaired glucose tolerance, or impaired fasting glucose on previous testing.
- •First-degree relative with diabetes.
- •High-risk race/ethnicity (eg, African American, Latino, Native American, Asian American, Pacific Islander).
- •History of cardiovascular disease.
- •Hypertension (≥140/90 mmHg) or on therapy for hypertension.
- •High-density lipoprotein cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L).
- •Polycystic ovary syndrome.
- •Physical inactivity.
- •Other clinical condition associated with insulin resistance (eg, severe obesity, acanthosis nigricans).
- •Previous birth of an infant weighing ≥4000 g.
- We include older age as a risk factor for early testing and use age 40 years as the threshold.

ADA criteria for diagnosis of diabetes in nonpregnant adults may be used to diagnose overt diabetes in early pregnancy

A1C ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay*. **OR**
2. FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 hours*. **OR**
3. 2-hour plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 gram anhydrous glucose dissolved in water*. **OR** In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

SCREENING FOR UNDIAGNOSED TYPE 2 DIABETES IN EARLY PREGNANCY

- untreated hyperglycemia in early pregnancy is important because it is associated with an increased risk of miscarriage and having a child with a congenital anomaly,

- mothers may have unrecognized complications (eg, nephropathy, retinopathy) from diabetes that place them at increased risk during pregnancy

Candidates for early pregnancy screening

- A1C ≥6.5 percent early in pregnancy, when A1C levels are generally slightly lower than in the nonpregnant state , strongly suggests previously undiagnosed type 2 diabetes.

- A1C <6.5 percent– This is a negative test for diabetes. The author screens these patients for GDM with the two-step test at 24 to 28 weeks of gestation.
- Approximately one-quarter of pregnant people with A1C 5.7 to 6.4 percent suggestive of impaired glucose intolerance) in early pregnancy are diagnosed with GDM when screened with a two-step test later in pregnancy compared with <10 percent of those with A1C <5.7 percent
- the overall value of detecting and treating mildly impaired glucose tolerance in early pregnancy has not been established.

Choice of screening test

- two-step approach ACOG: American College of Obstetricians and Gynecologists

- one-step approach American Diabetes Association criteria

Step one
1. Give 50 gram oral glucose solution without regard to time of day.
2. Measure venous plasma or serum glucose concentration.
3. Glucose ≥135 mg/dL (7.5 mmol/L) or ≥140 mg/dL (7.8 mmol/L) is elevated and requires administration of a 100 gram oral glucose tolerance test.* The lower threshold provides greater sensitivity, but would result in more false positives and would require administering the full glucose tolerance test to more patients than the 140 mg/dL threshold. The lower threshold should be considered in populations with higher prevalence of gestational diabetes.
Step two
1. Measure fasting venous plasma or serum glucose concentration.
2. Give 100 gram oral glucose solution.
3. Measure venous plasma or serum glucose concentration at one, two, and three hours after administration.
4. A positive test is generally defined by elevated glucose concentrations at two or more time points (either Carpenter and Coustan thresholds or National Diabetes Data Group

Diagnostic testing: 100 gram glucose GTT

	Carpenter/Coustan	National Diabetes Data Group
	Plasma or serum: mg/dL (mmol/L)	Plasma: mg/dL (mmol/L)
Fasting	95 (5.3)	105 (5.8)
One hour	180 (10)	190 (10.6)
Two hours	155 (8.6)	165 (9.2)
Three hours	140 (7.8)	145 (8)

75 gram oral glucose tolerance test —

Two-hour 75 gram oral glucose tolerance test	
Fasting	92 mg/dL (5.1 mmol/L)
OR	
One hour	180 mg/dL (10 mmol/L)
OR	
Two hour	153 mg/dL (8.5 mmol/mol)

Management of patients with a positive or negative early pregnancy glucose tolerance test (GTT)

- **Positive GTT** – If a patient in early pregnancy (before significant insulin resistance) meets criteria for diagnosis of diabetes, they are assumed to have had the disorder prior to the pregnancy and their management is similar to those with documented preexisting diabetes mellitus.

- **Negative GTT** – Patients with negative 75 or 100 gram oral GTT in early pregnancy are screened for GDM at 24 to 28 weeks of gestation.

- Those who were screened early in pregnancy using the two-step approach can omit the first step (50 gram oral glucose solution with glucose testing after one hour) later in pregnancy as it is likely to be positive, and go directly to the second step

SCREENING FOR GDM

- the one-step approach resulted in a higher frequency of GDM diagnosis than the two-step approach

- Despite the increased frequency of diagnosis, the proportion of treated patients and perinatal outcomes were similar for both approaches.

- one-step method increases the number of patients who receive a diagnosis of GDM and thus has the potential for increased patient and medical system burden (eg, more prenatal visits, fetal and maternal surveillance, lifestyle changes, and intervention) with economic, personal, and psychological consequences but without a clear direct benefit over the two-step approach in maternal and newborn outcomes.

- Therefore, we believe it is prudent to use the two-step approach to diagnose GDM followed by treatment of affected patients according to standard guidelines.
- Nevertheless, because of limitations of the available trials, the best approach remains controversial

- patients whose one-hour 50 gram oral GTT plasma glucose concentration was >182 mg/dL had >95 percent probability of an abnormal three-hour 100 gram oral GTT .
- At glucose levels ≥200 mg/dL, others have reported PPVs of 47 to 80 percent for an abnormal three-hour 100 gram oral GTT

- for patients with one-hour 50 gram glucose concentration ≥200 mg/dL, the author makes a presumptive diagnosis of GDM,

Patients unable to tolerate oral hyperosmolar glucose

- The highly concentrated hyperosmolar glucose solution used for the GCT and GTT can cause gastric irritation, delayed emptying, and gastrointestinal osmotic imbalance, leading to nausea and, in a small percentage of patients, vomiting

Options in these cases include:

- Serving the hyperosmolar glucose drink on ice may reduce nausea and vomiting.
- If the patient vomited during the oral GTT and is willing to come back another day for repeat testing, premedication with an antiemetic drug may allow the test to be completed.
- The GTT can be performed intravenously instead of orally, although this is rarely done.
- Periodic fasting and one- or two-hour postprandial blood glucose tests can be obtained in pregnant people at high risk for GDM. For example, they can be asked to keep a weekly log of self-monitored glucose values from 24 to 28 weeks (the gestational age when screening would be performed) and at 32 weeks (the gestational age of peak insulin resistance).

A1C

- no threshold for glycated hemoglobin (A1C) in the second and third trimesters had both good sensitivity and specificity as a screening test for GDM.

Fasting glucose

- fasting plasma glucose level less than 85 mg/dL (4.7 mmol/L) by 24 weeks of gestation performed well for identifying pregnant people who did not have GDM, whereas a value over 85 mg/dL (4.7 mmol/L) performed less well than the one-hour 50 gram oral GTT for identifying those with GDM.

RATIONALE FOR TREATMENT

- Treatment of GDM is important to minimize maternal and neonatal morbidity.

- Preeclampsia
- Birth weight >4000 g
- Shoulder dystocia

- No statistically significant differences in rates of cesarean birth, induction of labor, small for gestational age newborns, neonatal hypoglycemia, neonatal hyperbilirubinemia, neonatal respiratory complications, birth trauma, or neonatal intensive care unit admission were demonstrated compared with no treatment, although the quality of evidence was low.

Intermittent self-monitoring of blood glucose

- Before breakfast (ie, fasting glucose level) **and**
- At one **or** at two hours after the beginning of each meal
- Results should be recorded in a glucose log, along with dietary information

Glucose target (ADA) (ACOG)

- Fasting and preprandial blood glucose concentration: <95 mg/dL (5.3 mmol/L)
- One-hour postprandial blood glucose concentration: <140 mg/dL (7.8 mmol/L)
- Two-hour postprandial glucose concentration: <120 mg/dL (6.7 mmol/L)

Glycated hemoglobin

- A1C values tend to be lower in pregnant compared with nonpregnant people because the average blood glucose concentration is approximately 20 percent lower in pregnant people, and in the first half of pregnancy, there is a rise in red cell mass and a slight increase in red blood cell turnover

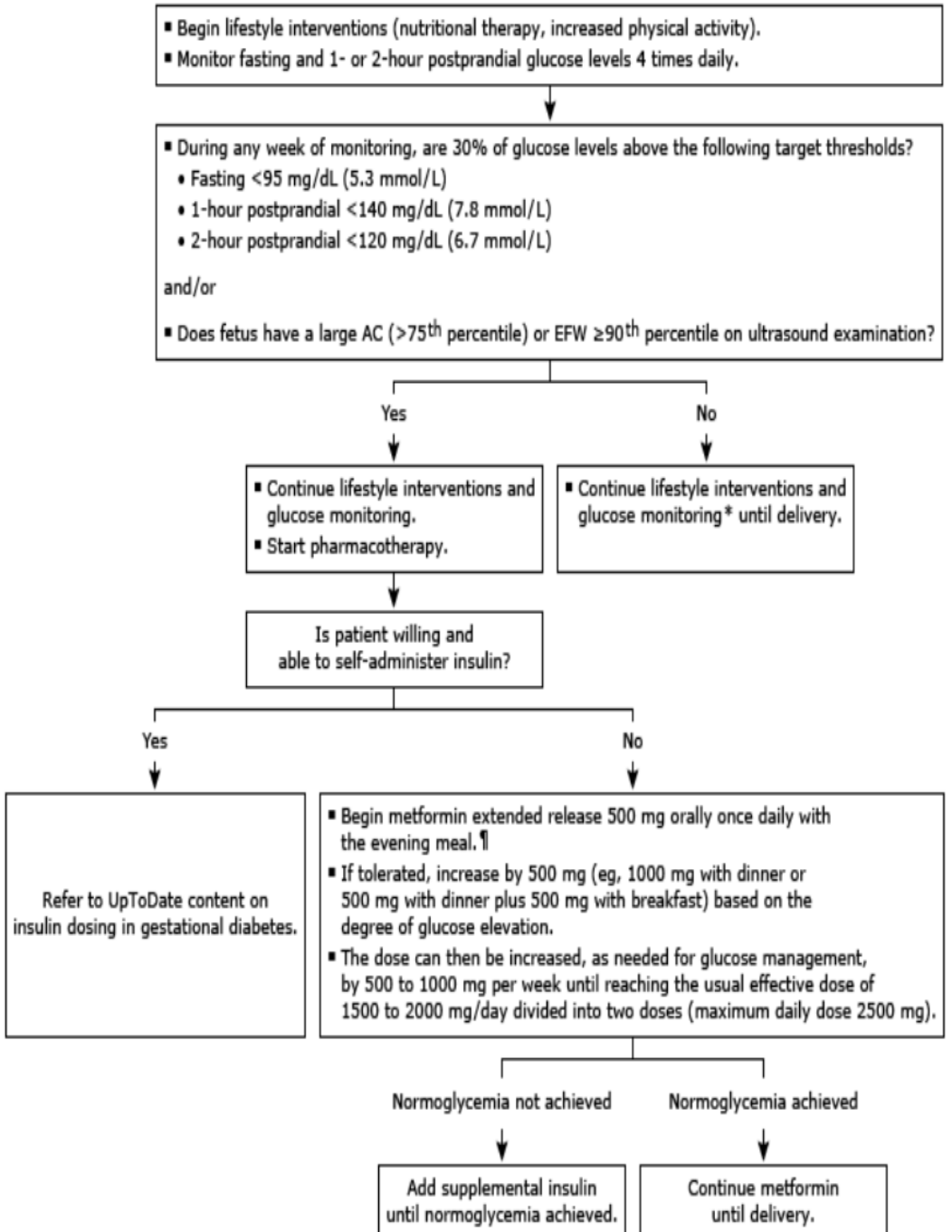
- Other factors that have been reported to affect A1C levels include race and iron status (chronic iron deficiency anemia increases A1C, treatment of iron deficiency anemia with iron lowers A1C).

Choice of pharmacotherapy

- There are two pharmacologic options in pregnant patients who require pharmacotherapy: insulin (and some insulin analogs) and selected oral antihyperglycemic agents (eg, metformin, glyburide).

- We favor insulin because it is effective and easily adjusted based on glucose levels, and data are lacking regarding long-term outcomes in offspring exposed to oral antihyperglycemic drugs in utero.
- We believe that oral antihyperglycemic agents are a reasonable alternative to insulin for patients in whom pharmacotherapy is indicated but who decline to take, or are unable to comply with, insulin therapy

Initial approach to glucose management in patients with newly diagnosed gestational diabetes mellitus at 24 to 28 weeks of gestation



- A long-acting insulin analog (insulin glargine or detemir) may be used instead if NPH insulin is not available.
- Insulin regular
- rapid-acting insulin analogs (aspart or lispro)


Thank you