

DIABETES IN PREGNANCY



Definition

- For many years, GDM was defined as *any degree of glucose intolerance that was first recognized during pregnancy*, regardless of the degree of hyperglycemia.
- This definition facilitated a uniform strategy for detection and classification of GDM, but this definition has serious limitations.

- The ongoing ***epidemic of obesity*** and diabetes has led to more type 2 diabetes in women of reproductive age, with an ***increase in the number of pregnant women with undiagnosed type 2 diabetes in early pregnancy*** .
- Because of the number of pregnant women with undiagnosed type 2 diabetes, it is reasonable to test **women with risk factors** for type 2 diabetes at their **initial prenatal visit**, using standard diagnostic criteria .

- Women found to have diabetes by the standard diagnostic criteria used outside of pregnancy should be classified as ***having diabetes complicating pregnancy (most often type 2 diabetes, rarely type 1 diabetes or monogenic diabetes)*** and managed accordingly.
- Women who meet the lower glycemic criteria for GDM should be diagnosed with that condition and managed accordingly.
- ***Other women should be rescreened for GDM between 24 and 28 weeks of gestation .***

Table 2.7—Screening for and diagnosis of GDM

One-step strategy

Perform a 75-g OGTT, with plasma glucose measurement when patient is fasting and at 1 and 2 h, at 24–28 weeks of gestation in women not previously diagnosed with diabetes.

The OGTT should be performed in the morning after an overnight fast of at least 8 h.

The diagnosis of GDM is made when any of the following plasma glucose values are met or exceeded:

- Fasting: 92 mg/dL (5.1 mmol/L)
- 1 h: 180 mg/dL (10.0 mmol/L)
- 2 h: 153 mg/dL (8.5 mmol/L)

Two-step strategy

Step 1: Perform a 50-g GLT (nonfasting), with plasma glucose measurement at 1 h, at 24–28 weeks of gestation in women not previously diagnosed with diabetes.

If the plasma glucose level measured 1 h after the load is ≥ 130 , 135, or 140 mg/dL (7.2, 7.5, or 7.8 mmol/L, respectively), proceed to a 100-g OGTT.

Step 2: The 100-g OGTT should be performed when the patient is fasting.

The diagnosis of GDM is made when at least two* of the following four plasma glucose levels (measured fasting and at 1, 2, and 3 h during OGTT) are met or exceeded (Carpenter-Coustan criteria [154]):

- Fasting: 95 mg/dL (5.3 mmol/L)
- 1 h: 180 mg/dL (10.0 mmol/L)
- 2 h: 155 mg/dL (8.6 mmol/L)
- 3 h: 140 mg/dL (7.8 mmol/L)

- The **prevalence** of diabetes in pregnancy has been increasing in the U.S.
- **in parallel** with the worldwide **epidemic of obesity**.
- **Not only** is the prevalence of **type 1 diabetes** and **type 2 diabetes** increasing in women of reproductive age, but there is also a **dramatic increase** in the reported rates of gestational diabetes mellitus.
- Diabetes confers significantly greater **maternal and fetal risk** largely **related to the degree of hyperglycemia** but also **related to chronic complications and comorbidities of diabetes**.

- In general, ***specific risks*** of diabetes in pregnancy include ***spontaneous abortion, fetal anomalies, preeclampsia, fetal demise, macrosomia, neonatal hypoglycemia, hyperbilirubinemia, and neonatal respiratory distress syndrome***, among others.
- In addition, diabetes in pregnancy may ***increase the risk of obesity, hypertension, and type 2 diabetes in offspring later in life .***

- Observational studies show an ***increased risk of diabetic embryopathy***, especially anencephaly, microcephaly, congenital heart disease, renal anomalies, and caudal regression, ***directly proportional to elevations in A1C during the first 10 weeks of pregnancy***

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- Although observational studies are confounded by the ***association between elevated periconceptual A1C and other poor self-care behavior***, the quantity and consistency of data are convincing and support the ***recommendation to optimize glycemia prior to conception***, given that ***organogenesis occurs primarily at 5–8 weeks of gestation***, with an ***A1C ,6.5%*** being associated with the ***lowest risk of congenital anomalies*** .

Preconception Care

- In addition to focused attention on achieving glycemic targets.
- A, standard preconception care should be augmented with extra ***focus on nutrition, diabetes education, and screening for diabetes comorbidity and complications.***

- Women with *preexisting type 1 or type 2 diabetes* who are planning pregnancy or who have become pregnant should be counseled on the *risk of development and/or progression of diabetic retinopathy*.
- *Dilated eye examinations* should occur ideally *before pregnancy or in the first trimester*, and then patients should be *monitored every trimester and for 1 year postpartum as indicated* by the degree of retinopathy and as recommended by the eye care provider.

- *Diabetes-specific testing* should include **A1C, creatinine, and urinary albumin-to-creatinine ratio.**
 - Special attention should be paid to the review of the medication list for potentially *harmful drugs* (i.e., **ACE inhibitors , angiotensin receptor blockers , and statins.**
 - The *use of aspirin* (81–150 mg) can be considered ***preconception*** as it is recommended for ***all pregnant women with diabetes*** (if no contraindication) **by 16 weeks of gestation to reduce the risk of preeclampsia**
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***GLYCEMIC TARGETS IN
PREGNANCY***

- **Glucose targets** are **fasting plasma glucose ,95 mg/dL** and either **1-h postprandial glucose ,140 mg/dL** or **2-h postprandial glucose ,120 mg/dL** .
- Due to **increased red blood cell turnover**, **A1C is slightly lower in normal pregnancy** than in normal nonpregnant women.
- Ideally, the **A1C target in pregnancy is ,6%** if this can be achieved **without significant hypoglycemia**, but the target may be **relaxed to ,7% if necessary to prevent hypoglycemia**.

Insulin Physiology

- Given *that early pregnancy* is a time of *enhanced insulin sensitivity* and *lower glucose levels*, many women with type 1 diabetes will have lower insulin requirements and increased risk for hypoglycemia .
- The situation rapidly *reverses by approximately 16 weeks as insulin resistance increases* exponentially during the *second and early third trimesters to 2–3 times the preprandial requirement*.
- The *insulin requirement levels off toward* the *end of the third trimester* with placental aging.
- *A rapid reduction in insulin requirements can indicate the development of placental insufficiency* .

Glucose Monitoring

- Reflecting this physiology, *fasting and postprandial monitoring* of blood glucose is recommended to achieve metabolic control in pregnant women with diabetes.
- *Preprandial testing* is also recommended when *using insulin pumps or basal-bolus therapy* so that premeal rapid-acting insulin dosage can be adjusted. Postprandial monitoring is associated with better glycemic control and lower risk of preeclampsia .

MANAGEMENT OF GESTATIONAL

DIABETES MELLITUS

Lifestyle Management

- ***After diagnosis***, treatment ***starts*** with ***medical nutrition*** therapy, ***physical activity***, and ***weight management*** depending on pregestational weight, as outlined in the section below on preexisting type 2 diabetes, and ***glucose monitoring*** aiming for the targets recommended .
- ***70–85% of women*** diagnosed with GDM under CarpenterCoustan can control GDM with ***lifestyle modification alone***;

Medical Nutrition Therapy

- ***The food plan*** should provide ***adequate calorie intake*** to promote fetal/neonatal and maternal health, achieve glycemic goals, and ***promote weight gain*** .
- There is ***no definitive*** research that identifies a specific optimal calorie intake for women with GDM or suggests that their calorie needs are different from those of pregnant women without GDM.
- The DRI for all pregnant women recommends a minimum of ***175 g of carbohydrate***, a ***minimum of 71 g of protein***, and ***28 g of fiber***.
- The diet should ***not be high in saturated fat***. As is true for all nutrition therapy in patients with diabetes, the amount and type of carbohydrate will impact glucose levels. ***Simple carbohydrates*** will result in ***higher postmeal excursions***.

Pharmacologic Therapy

- ***Treatment of GDM*** with ***lifestyle and insulin*** has been demonstrated to improve perinatal outcomes.
- ***Insulin is the first-line*** agent recommended for treatment of GDM in the U.S.
- While individual RCTs support ***limited efficacy of metformin and glyburide in reducing glucose levels*** for the treatment of GDM, these agents are not recommended as first-line treatment for GDM because they are known ***to cross the placenta*** and data on long-term ***safety for offspring is of some concern*** .

Sulfonylureas

- Sulfonylureas are known to *cross the placenta* and have been associated with *increased neonatal hypoglycemia*.
- Concentrations of glyburide in umbilical cord plasma are approximately *50–70% of maternal levels* .
- Glyburide was associated with a higher rate of neonatal hypoglycemia and *macrosomia than insulin or metformin* in a 2015 metaanalysis and systematic review .

Metformin

- Metformin was associated with a *lower risk of neonatal hypoglycemia* and *less maternal weight gain* than insulin in systematic reviews ..
- However, metformin readily *crosses the placenta*, resulting in umbilical cord blood levels of metformin *as high or higher than simultaneous maternal levels* .

- However, due to the ***potential for growth restriction or acidosis*** in the setting of ***placental insufficiency***, ***metformin should not be used in women with hypertension, preeclampsia, or at risk for intrauterine growth restriction*** .

Insulin

- *Both multiple daily insulin* injections and *continuous subcutaneous insulin* infusion are reasonable deliver strategies, and neither has been shown *to be superior to the other during pregnancy* .

Type 1 Diabetes

- Women with type 1 diabetes have an ***increased risk of hypoglycemia in the first trimester*** and, like all women, have altered counterregulatory response in pregnancy that may decrease hypoglycemia awareness.
- ***Pregnancy is a ketogenic state***, and women with type 1 diabetes, and to a lesser extent those with type 2 diabetes, are ***at risk for diabetic ketoacidosis*** (DKA) at ***lower blood glucose levels*** than in the nonpregnant state.

Type 2 Diabetes

- Type 2 diabetes is often associated *with obesity*.
- Recommended *weight gain during pregnancy* for overweight women is 15–25 lb and for obese women is 10–20 lb .
- *There is no adequate data* on *optimal weight gain* versus weight maintenance in women with a BMI ≥ 35 kg/m².
- *Glycemic control is often easier* to achieve in women with type 2 diabetes *than in those with type 1* diabetes but can *require much higher doses of insulin*,.

- Women with ***type 1 or type 2*** diabetes should be prescribed ***low-dose aspirin*** 60–150 mg/ day (***usual dose 81 mg/day***) by the ***end of the first trimester*** in order to ***lower the risk of preeclampsia.***

- ***Insulin resistance decreases dramatically immediately postpartum***, and insulin requirements need to be evaluated and adjusted as they are often ***roughly half the prepregnancy requirements for the initial few days postpartum.***
- ***Screen women*** with a recent ***history of gestational diabetes mellitus at 4–12 weeks postpartum***, using the ***75-g oral glucose tolerance*** test and clinically appropriate nonpregnancy diagnostic criteria.
- Women with a ***history of gestational diabetes mellitus*** found to ***have prediabetes*** should receive ***intensive lifestyle interventions and/or metformin to prevent diabetes.***

- Women with a ***history of gestational diabetes mellitus*** should have ***lifelong screening*** for the development of type 2 diabetes or prediabetes at ***least every 3 years.***
- Women with a ***history of gestational diabetes mellitus*** should seek ***preconception screening for diabetes*** and preconception care to identify and treat hyperglycemia and prevent congenital malformations.

