Management of Pregestational and Gestational Diabetes Mellitus

Background and Prevalence

- **Pregestational Diabetes** - 8 million women in the US are affected, complicating 1% of all pregnancies. Type II is the most common and is characterized by onset later in life, peripheral insulin resistance, relative insulin deficiency, obesity, and development of vascular, renal, and neuropathic complications.
  
  • Accounts for 10% of diabetes in pregnancy.

- **Gestational Diabetes Mellitus** - complicates 6-7% of pregnancies and accounts for 90% of diabetes in pregnancy.

  **Etiology:** Insulin resistance mediated primarily by placental secretion of growth hormone, corticotropin-releasing hormone, prolactin, placental lactogen, and progesterone.

  ➢ Insulin resistance is greatest in the third trimester.

  ➢ Increased prevalence is found among Hispanic, African American, Native American, Asian, and Pacific Islander Women.

Maternal and Fetal Complications

**Pregestational Diabetes** -

- **Maternal:** Miscarriage (uteroplacental insufficiency and fetal anomalies), preterm delivery, preeclampsia, cesarean delivery, diabetic retinopathy, diabetic nephropathy, diabetic neuropathy (gastroparesis), cardiovascular disease, DKA, chronic hypertension, polyhydramnios (often correlated with higher hemoglobin A1C and macrosomia, thought to be related to fetal polyuria), postpartum hemorrhage, 3rd and 4th degree lacerations.

- **Fetal:** Congenital malformations (cardiac, neural tube defects, limb defects, and orofacial clefts associated with hyperglycemia in early pregnancy; Hemoglobin A1C near 10% carries a 20-25% fetal anomaly rate), macrosomia (tight glucose control periconceptionally and in the first trimester seem to have a greater impact on reducing the risk of macrosomia than late glycemic control), stillbirth, increased admission to NICU, neonatal hypoglycemia, higher rates of respiratory distress syndrome, polycythemia, organomegaly, cardiomyopathy, hypocalcemia and hypomagnesemia, hyperbilirubinemia, shoulder dystocia, clavicular fractures, brachial plexus injury, IUGR (usually in setting of hypertension and/or nephropathy).

**Gestational Diabetes Mellitus** -

- **Maternal:** Gestational hypertension, preeclampsia, polyhydramnios, cesarean delivery, increased risk of developing diabetes later in life (50% of women will go on to develop diabetes in their lifetime), postpartum hemorrhage, and 3rd and 4th degree lacerations.

- **Fetal:** Macrosomia, fetal organomegaly, increased admission to NICU, neonatal hypoglycemia, neonatal respiratory distress, hyperbilirubinemia, operative delivery, shoulder dystocia, clavicular fractures, and brachial plexus injury, stillbirth.

- Studies suggest an increased risk of obesity and type II diabetes in infants of mothers with diabetes.
Risk Factors for Development of GDM

- Personal history of impaired glucose tolerance or GDM.
- Member of higher risk ethnic group.
- Family history of first degree relative with diabetes.
- BMI >30 and excessive gestational weight gain.
- Maternal age > 25.
- Previously delivered baby > 9 pounds (4,000 grams).
- Previous unexplained perinatal loss or birth of a malformed infant.
- Maternal birthweight > 9 pounds (4,000 grams).
- Glycosuria at the first prenatal visit.
- Metabolic syndrome.
- PCOS.
- Current use of glucocorticoids (asthmatics, autoimmune disease).
- Hypertension.

Screening and Diagnosis

Indications for early screening prior to 20 weeks:

- BMI > 30.
- Prior history of GDM or known impaired glucose metabolism (GDM carries a 30-50% recurrence rate in subsequent pregnancies).
- PCOS.
- History of macrosomia (> 4,000 grams or 9 pounds).
- First degree relative with diabetes.
  
  ➢ A hemoglobin A1C should also be drawn.
  ➢ A diagnosis of pregestational diabetes can be made with a hemoglobin A1C that is greater than or equal to 6.5% or a fasting glucose that is greater than or equal to 126 mg/dL.

Universal Screening:

- 50 gram, 1 hour oral glucose tolerance test at 24-28 weeks.
- Does not need to be fasting, however women should avoid carbohydrate load prior to the test.
- A value of greater than or equal to 130-140 mg/dL is a positive screen and greater than 200 mg/dL is a diagnosis of GDM.
- ACOG practice bulletin states, “In the absence of clear evidence supporting a cutoff of 135 mg/dL versus 140 mg/dL for the 1 hour glucose screening test, it is suggested that health care providers select one of these as a single consistent cutoff for their practice.”

Diagnosis:

- 100 gram, 3 hour oral glucose tolerance test.
- Women should fast 8 hours prior to the test.
- 2 or more abnormal values indicate GDM.
- In units of mg/dL, the fasting levels should be <95, one hour <180, two hour <155, and three hour <140.
- Consider repeating 3 hour GTT in 4 weeks in high risk individuals.
- Patients with one abnormal value are at risk for fetal macrosomia.
Treatment

**Benefits of Treatment -**
- A 2013 systematic review and meta-analysis of randomized trials for the US Preventive Services Task Force found that appropriate management of GDM (nutritional therapy, glucose monitoring, use of insulin if needed) resulted in a reduction in: **Preeclampsia, birthweight >4,000 gram, and shoulder dystocia** with no significant changes in rates of cesarean delivery, induction of labor, SGA, neonatal hypoglycemia/hyperbilirubinemia, neonatal respiratory complications, birth trauma, or NICU admissions.

**Pregestational Diabetics -**
- Goal Hemoglobin A1C levels should be no higher than 6% and ACOG recommends checking levels each trimester.
- CMP, TSH, dilated retinal exam, EKG and 24 hour urine is recommended at initial visit.
- Treatment will include diet and exercise along with pharmacotherapy if indicated.
- Growth scans should be performed q4 weeks after the anatomy scan.
- Fetal Echocardiogram may be indicated in cases of suspected cardiac defects or when the fetal heart and great vessels cannot be visualized by ultrasonography.
- Twice weekly antenatal testing starting at 32 weeks.
- Daily fetal movement counting.
- Women should be seen in the office every 1-2 weeks during the first two trimesters and weekly after 28 weeks.
- Delivery is not indicated prior to 39 weeks unless comorbid conditions are present.
- Although an ultrasound estimate of fetal weight may help rule out macrosomia, ultrasound has not proved to be more accurate than clinical assessment in determining the size of the large fetus (Leopolds, fundal height).
- Cesarean delivery may be considered if the EFW is greater than 4,500 grams.
- Cesarean delivery can be discussed if the EFW is between 4,000-4,500 grams.
- Patients are referred to MFM for co-management.

**Diet Controlled Diabetics -**
- Nutritional therapy:
  - Carbohydrate intake should be limited to 33-40% of calories (complex carbohydrates high in fiber are less likely to produce postprandial hyperglycemia, which is correlated with macrosomia risk).
  - Fat intake should be 40% of total calories.
  - Protein intake should be 20% of total calories.
  - The intake should be divided over 3 meals and 2-4 snacks.
- Glucose monitoring:
  - Fasting levels in the morning should be less than or equal to 95 mg/dL.
  - 1 hour postprandial should be less than or equal to 140 mg/dL.
  - 2 hour postprandial should be less than or equal to 120 mg/dL.
- A moderate exercise program is recommended (20-30 minutes of cardio fitness three times per week or use of a recumbent bicycle).
- Daily fetal movement counting.
- There is no consensus regarding antepartum testing in women with well-controlled GDM.
- Sibley MFM does not currently recommend antenatal testing or growth scans.
- The onset of spontaneous labor can be anticipated.
Although an ultrasound estimate of fetal weight may help rule out macrosomia, ultrasound has not proved to be more accurate than clinical assessment in determining the size of the large fetus; however, it is reasonable to assess fetal growth by ultrasound late in the third trimester.

Cesarean delivery may be considered if the EFW is greater than 4,500 grams.

Cesarean delivery can be discussed if the EFW is between 4,000-4,500 grams.

**Diabetics who require insulin and oral hypoglycemics** -

- Pharmacotherapy is usually initiated when fasting glucose levels are persistently greater than 95 mg/dL, 1 hour postprandials are greater than 140 mg/dL, or 2 hour postprandial levels are greater than 120 mg/dL.
- Insulin, glyburide, and metformin have been shown to be equivalent in efficacy and any can be an appropriate first-line therapy (although, oral hypoglycemics have not been approved by the FDA for this indication).
- Glyburide should not be used in a patient with a sulfa allergy.
- Metformin users are more likely to require supplemental insulin to maintain euglycemia than glyburide users (35% of metformin users vs. 16% of glyburide users).
- MFM will consult on patients requiring glyburide and co-manage with patients requiring insulin.
- Daily fetal movement counting.
- Growth scans should be performed every 4 weeks after initiation of medication.
- Antenatal testing should begin weekly at 32 weeks.
- Delivery is indicated at 39 weeks.
- Cesarean delivery may be considered if the EFW is greater than 4,500 grams.
- Cesarean delivery can be discussed if the EFW is between 4,000-4,500 grams.

**Poorly controlled diabetics managed with nutritional therapy or medication** -

- Daily fetal movement counting.
- Growth scans should be performed every 4 weeks.
- Antenatal testing should be increased to twice weekly.
- Timing of delivery will depend on testing, however, if reassuring, delivery is not indicated prior to 39 weeks.
- MFM will consult and/or co-manage with these patients.

**Postpartum Screening**

- Breastfeeding should be encouraged as it can improve glucose metabolism in the short-term.
- Up to one third of women will have diabetes or impaired glucose metabolism at postpartum screening.
- Up to 50% will develop type 2 diabetes later in life.
- Having GDM increases patients risk for development of type 1 diabetes, type 2 diabetes, metabolic syndrome, and cardiovascular disease.
- Screening is recommended at 6-12 weeks with a 75 gram, 2 hour oral glucose tolerance test.
- Cutoffs include a fasting value greater than or equal to 92 mg/dL, 1-hour value greater than or equal to 180 mg/dL, and 2-hour value greater than or equal to 153 mg/dL.
- Women with DM should be referred for diabetes management.
- Women with an impaired fasting glucose or impaired glucose tolerance should be referred for nutritional management, counseled on importance of weight loss and exercise, starting metformin can be considered for combined impaired fasting glucose and impaired glucose tolerance, and women should have yearly assessment of glycemic status.
- Women with a normal test should have glycemic status assessed every 3 years and counseled on the importance of nutritional status and physical activity.
References


Caughey, Aaron, MD, PhD. Gestational Diabetes Mellitus: Obstetrical Issues and Management. UpToDate, July 2015.


