Current Trends in Diagnosis and Management of Gestational Diabetes

Shreela Mishra, MD
Assistant Clinical Professor
UCSF Fresno Medical Education Program

2/2/2019
Disclosures

- No disclosures
Objectives

- Learn the diagnostic criteria for gestational diabetes mellitus
- Understand treatment goals and glycemic targets used in management of gestational diabetes mellitus
- Review management of gestational diabetes mellitus with medical nutrition therapy and pharmacologic therapy
What exactly is gestational diabetes mellitus (GDM)?

- In the past, GDM was defined as any degree of glucose intolerance first recognized during pregnancy.
- This did not account for women with undiagnosed diabetes existing prior to conception.
- GDM: Diabetes that is first diagnosed in the 2nd or 3rd trimester of pregnancy, that is not clearly either pre-existing Type 1 or Type 2 diabetes.
Hyperglycemia and Adverse Pregnancy Outcomes

The HAPO Study Cooperative Research Group*
HAPO Study

Multinational cohort study of >23,000 pregnant women

- 75-g OGTT done at 24-32 weeks gestation
- Data remained blinded if FPG < 105 mg/dl & 2 hour glucose < 200 mg/dl
- Primary outcomes:
  - Birth weight > 90th percentile for gestational age
  - Primary cesarean delivery
  - Clinically diagnosed neonatal hypoglycemia
  - Cord-blood serum C-peptide level > 90th percentile
Frequency of Primary Outcomes across Glucose Categories

A Birth Weight >90th Percentile

- FPG <75
- 1-hr glucose < 105
- 2-hr glucose < 90

B Primary Cesarean Section

- FPG ≥ 100
- 1-hr glucose ≥ 212
- 2-hr glucose ≥ 178
Frequency of Primary Outcomes across Glucose Categories

- **C Clinical Neonatal Hypoglycemia**
- **D Cord-Blood Serum C Peptide >90th Percentile**

Frequency (%)

![Graphs showing frequency of primary outcomes across glucose categories.](image)
Overall Results of HAPO Study

- Maternal hyperglycemia less severe than that used to define overt diabetes is related to clinically important perinatal disorders

- For most complications, there was no threshold for increased risk

- The risk of adverse outcomes continuously increased as a function of maternal glycemia at 24-28 weeks gestation
How do we diagnose gestational diabetes mellitus?
Will be referencing guidelines from:

- American Diabetes Association (ADA) Standards of Medical Care in Diabetes 2019
  - [http://care.diabetesjournals.org/content/diacare/suppl/2018/12/17/42.Supplement_1.DC1/DC_42_S1_Combined_FINAL.pdf](http://care.diabetesjournals.org/content/diacare/suppl/2018/12/17/42.Supplement_1.DC1/DC_42_S1_Combined_FINAL.pdf)

- California Diabetes and Pregnancy Program (CDAPP) Sweet Success Guidelines for Care
  - [https://www.cdappsweetsuccess.org/Guidelines-for-Care](https://www.cdappsweetsuccess.org/Guidelines-for-Care)

- American College of Obstetrics and Gynecology (ACOG) Practice Bulletin on Gestational Diabetes Mellitus
  - [https://journals.lww.com/greenjournal/fulltext/2017/07000/Practice_Bulletin_No__180___Gestational_Diabetes.51.aspx](https://journals.lww.com/greenjournal/fulltext/2017/07000/Practice_Bulletin_No__180___Gestational_Diabetes.51.aspx)
ADA Guidelines for GDM diagnosis

- Test for undiagnosed pre-existing DM at first prenatal visit in women with risk factors, with the usual screening used for non-pregnant adults (fasting glucose and Hgb A1c)

- If no risk factors for pre-existing DM, test for GDM at 24-28 weeks gestation in pregnant women not previously known to have diabetes

- GDM is diabetes first diagnosed in 2nd or 3rd trimester of pregnancy, and is not clearly pre-existing type 1 or type 2 diabetes
Who should be screened for undiagnosed DM?

Table 2.3—Criteria for testing for diabetes or prediabetes in asymptomatic adults
1. Testing should be considered in overweight or obese (BMI ≥25 kg/m² or ≥23 kg/m² in Asian Americans) adults who have one or more of the following risk factors:
   - First-degree relative with diabetes
   - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - History of CVD
   - Hypertension (≥140/90 mmHg or on therapy for hypertension)
   - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
   - Women with polycystic ovary syndrome
   - Physical inactivity
   - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)

2. Patients with prediabetes (A1C ≥5.7% [39 mmol/mol], IGT, or IFG) should be tested yearly.
3. Women who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other patients, testing should begin at age 45 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.
How do we diagnose pre-existing diabetes in pregnancy?

- DM diagnosed in 1st trimester with standard diagnostic criteria of:
  - Hemoglobin A1c $\geq 6.5\%$ or
  - Fasting plasma glucose of $\geq 126$ mg/dL or
  - 2-hr glucose of $\geq 200$ mg/dL on 75-g OGTT or
  - Classic symptoms of hyperglycemia/hyperglycemic crisis and random plasma glucose $\geq 200$ mg/dL
Diagnosis of GDM

- Can use either of 2 strategies, at 24-28 weeks gestation

- One-Step Approach: 75-g OGTT
  - Done in AM after 8 hr overnight fast
  - Diagnosis of GDM made if any one of the following criteria is met or exceeded:
    • Fasting glucose ≥ 92 mg/dL
    • 1 hr: ≥ 180 mg/dL
    • 2 hr: ≥ 153 mg/dL

- Two-Step Approach
  - Step 1: Perform 50-g oral glucose load. If glucose ≥ 130, 135, or 140 mg/dL at 1 hr, proceed to step 2.
  - Step 2: Do fasting 100-g OGTT *
    • Fasting glucose ≥ 95 mg/dL
    • 1 hr: ≥ 180 mg/dL
    • 2 hr: ≥ 155 mg/dL
    • 3 hr: ≥ 140 mg/dL

* Per ADA criteria: need at least 2 elevated values for GDM diagnosis
Per ACOG criteria, need only elevated value for GDM diagnosis
ACOG Guidelines for GDM Screening

- The two-step approach is most commonly used in the US
- Institutional screening thresholds vary for the 1-hour glucose challenge, from 130 mg/dL – 140 mg/dL
- No randomized trials examining if one cutoff is more effective than others
- There are also different cutoffs for the 3-hour OGTT, by the National Diabetes Data Group and by Carpenter and Coustan, which uses lower thresholds
- Practitioners and institutions should select a single set of diagnostic criteria for consistent use within patient populations
What is the recommended management of GDM?
Management of GDM

Self-monitoring of blood glucose

- Monitor 4x/day initially
- Fasting and postprandial values, either 1-hr or 2-hr postprandial
- Postprandial BG monitoring is more effective in preventing obstetrical and neonatal complications

Glycemic Targets

- Fasting glucose < 95 mg/dL and either
- 1-hour postprandial < 140 mg/dL
  Or
- 2-hour postprandial < 120 mg/dL
Hemoglobin A1c in GDM

- A1c levels fall during normal pregnancy due to physiological increase in red blood cell turnover

- A1c can be used to monitor control, but should be used as a secondary measure of glycemic control in pregnancy, after self-monitoring of blood glucose

- A1c of < 6% in 2nd and 3rd trimesters → lowest risk for large-for-gestational age infants, pre-term delivery and pre-eclampsia.
Lifestyle Modification

- 70-85% of women can control GDM with lifestyle modification alone
- Medical nutrition therapy
  - Individualized nutrition plan, developed with RD
  - Maintain adequate caloric intake
  - Total 175 g daily carbohydrate intake is recommended in pregnancy
  - Generally recommend 30-45 g carb with 3 main meals and 15 gram carb snacks in between meals
- Physical activity should be encouraged, can help improve insulin sensitivity
When to initiate pharmacologic therapy?

- When target glucose levels cannot be consistently achieved through nutrition therapy and exercise
- No specific threshold value identified for when medical therapy should be started
- Suggestions per CDAPP Sweet Success guidelines are to initiate therapy when > 20% of BG values are out of range in one week, or BG values are repeatedly high at same time of day
Pharmacologic Therapy

- Insulin is first-line agent recommended for treatment of GDM in U.S.

- Oral options in pregnancy:
  - Metformin and glyburide - Not recommended as first-line treatment for GDM because they are known to cross placenta
Sulfonylureas in GDM

- Known to cross placenta
- Associated with increased neonatal hypoglycemia
- Glyburide associated with higher rate of neonatal hypoglycemia and macrosomia than insulin or metformin
- Long-term safety data for offspring not available
Metformin in GDM

- Crosses the placenta
- Advantages over glyburide:
  - Lower mean birth weight in offspring
  - Lower risk of macrosomia
  - Less maternal weight gain
- Compared to insulin: Lower risk of neonatal hypoglycemia and less maternal weight gain
- Metformin may slightly increase risk of prematurity
- Long-term metabolic influence on offspring is unknown
Insulin in GDM

- Does not cross the placenta

- Frequent titration of insulin needed to match changing requirements during pregnancy due to progressive increase in insulin resistance

- Frequent self-monitoring of BG is crucial
Which insulin to use in pregnancy?

- Regular insulin (U-100 and U-500), insulin aspart, insulin lispro, NPH and insulin detemir → All pregnancy Category B
  - FDA has enough human data to allow these to be considered low risk in pregnancy
- Insulin glulisine, insulin degludec, inhaled human insulin → all pregnancy Category C. No human data in pregnancy.
- Insulin glargine – No longer has pregnancy category. No well-controlled clinical studies in pregnant women.
- Since 2015, FDA no longer using lettering system for pregnancy categories
Insulin in GDM Management

- For fasting hyperglycemia, NPH or insulin detemir can be started at bedtime.

- For postprandial hyperglycemia, prandial coverage should be started before the meal.

- Rapid-acting insulin analogs lispro and aspart are preferred over regular insulin.
CDAPP Sweet Success guidelines for insulin dosing

**Table 6. INSULIN CALCULATION BY GESTATIONAL AGE AND BODY WEIGHT FOR GDM**

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>Insulin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12 weeks</td>
<td>0.6-0.7 units per kg actual body weight</td>
</tr>
<tr>
<td>13-28 week</td>
<td>0.7-0.8 units per kg actual body weight</td>
</tr>
<tr>
<td>29-34 weeks</td>
<td>0.8-0.9 units per kg actual body weight</td>
</tr>
<tr>
<td>35-40 weeks</td>
<td>0.9-1 units per kg actual body weight</td>
</tr>
</tbody>
</table>
GDM: Immediate Postpartum Period

- Insulin and oral medications started for GDM can all be discontinued after delivery
GDM: Postpartum Long-Term Follow-up

- Test women with GDM for prediabetes or diabetes at 4-12 weeks postpartum using 75-g OGTT rather than A1c, and clinically appropriate nonpregnancy diagnostic criteria

- Continue lifelong screening for development of diabetes of prediabetes at least every 3 years

- GDM associated with increased lifetime maternal risk for DM at 50-70% after 15-25 years

- Women with history of GDM found to have prediabetes require intensive lifestyle interventions or metformin to prevent diabetes
Summary

- Screen for pre-existing, undiagnosed DM in women with risk factors at first prenatal visit
- Test for GDM at 24-28 weeks gestation in pregnant women not previously known to have diabetes
- Use either one-step or two-step approach for diagnosis
- Monitor BG 4x/day, fasting and 1 or 2 hr. postprandial
- Treatment of GDM reduces risk of pre-eclampsia, shoulder dystocia, macrosomia
Summary

- Majority of women can control GDM with lifestyle changes only
- Insulin is the first line agent recommended for pharmacologic therapy
- Perform 75-g OGTT at 4-12 weeks postpartum to screen for pre-diabetes and DM
- Must continue lifelong screening for diabetes in women with GDM due to increased risk
References


- Shields L, and Tsay GS. Editors, California Diabetes and Pregnancy Program Sweet Success Guidelines for Care. Developed with California Department of Public Health; Maternal Child and Adolescent Health Division; revised edition, updated September 2015.

