DIABETES IN PREGNANCY: DIAGNOSIS AND MANAGEMENT

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OBJECTIVES

• To review current trends in the diagnosis and management of gestational diabetes.

• To understand current controversies in the diagnosis and management of gestational diabetes.

• To review the use of insulin and oral agents in gestational diabetes.
HOW BIG IS THE PROBLEM?
Statistics About Diabetes Data from the National Diabetes Statistics Report, 2014 (released June 10, 2014)

In 2012, 29.1 million Americans, or 9.3% of the population, had diabetes.

Of the 29.1 million, 8.1 million were undiagnosed –

In 2012, 86 million Americans age 20 and older had prediabetes

Diabetes remains the 7th leading cause of death in the United States in 2010,
The rates of diagnosed diabetes by race/ethnic background are:

- 7.6% of non-Hispanic whites
- 9.0% of Asian Americans
- 12.8% of Hispanics
- 13.2% of non-Hispanic blacks
- 15.9% of American Indians/Alaskan Natives
INCIDENCE OF DIABETES IN PREGNANCY

- Incidence in all pregnancies in the US: 5-14%
- Canada 8-18%
- China 7-10%
- India – possibly as high as 27%
- 80% of patients with diabetes complicating pregnancy have gestational diabetes
- 10-20% of patients with diabetes complicating pregnancy have pre-existing diabetes (Type 1 and Type 2)
GESTATIONAL DIABETES (DEFINITION)

• Carbohydrate intolerance that begins or is first recognized during pregnancy

• Diagnostic Categories: GDM A1 and A2

• 15% of GDM remain diabetic (Type 2)
• 50-60% of GDM will become diabetic in 5-10 yrs
TYPE 2 DIABETES

- Encompasses insulin resistance and relative insulin deficiency.

- Associated with obesity – or increased percentage of body fat.

- May go undiagnosed for many years
BOTH GDM AND TYPE 2 ARE HETEROGENEOUS DISORDERS

Pathophysiology is characterized by
- peripheral insulin resistance
- impaired regulation of hepatic glucose production
- decreased insulin production

* Today both clinical entities are viewed as the same disease with different names
PRE-DIABETES

- In 2010 the ADA committee on diagnosis and classification recognized an intermediate group

- Blood glucose not high enough to have diabetes but also not normal.

- IFG (impaired fasting glucose) fasting 100mg/dl – 125 mg/dl

- IGT (impaired glucose tolerance) 2 hr value on the OGTT of 140mg/dl – 199 mg/dl
PRE-DIABETES

- This is considered an intermediate stage

- IFG and IGT are not diseases in their own right but are risk factors for diabetes and cardiovascular disease.
HGB A1C

- A1C of 5.5-6.0% have a 5 year cumulative incidence of diabetes from 12% to 25%

- NHANES data indicate that A1C of 5.5 -6.0% identifies people with IFG and IGT.
HGB A1C

• Compared to a fasting glucose of 100 mg/dl – using A1C 5.7% or above is 66% sensitive and 88% specific for the development of diabetes in 6 years.

• Individuals with A1C 5.7-6.4 should be informed of the risk and receive counseling regarding changes in lifestyle.
CATEGORIES OF INCREASED RISK

- Fasting 100mg/dl – 125 mg/dl

- 2h values on the 75gOGTT 140mg/dl-199 mg/dl

- A1C of 5.7-6.4
WHY DO WE CARE ABOUT DIABETES IN PREGNANCY?

So wait...why do we have to learn this again?
ADVERSE EFFECTS IN OFFSPRING

- Conception to 8\textsuperscript{th} week
  - Malformations:
    - Caudal regression (3wk)
    - NTD (4 wk)
    - Cardiac (5 wks)
    - Renal (5 wks)
    - GI (6 wks)

- 8\textsuperscript{th} week to delivery
  - Chronic hypoxia
  - Intrauterine death
  - Hyperinsulinism
  - Macrosomia
  - Organomegaly
  - Polyhydraminos

ACOG Tech Bulletin Dec 1994
BIRTH DEFECTS

- Most important FACTOR: glycemic control during embryogenesis

- If Gestational diabetes begins after first trimester; no increase in birth defects

- In women with pre-existing diabetes: 8.5% increase in cardiac defects, 5.3% in CNS defects, and 3.5% in GI and GU defects

- HGA1c levels prior to embryogenesis determine the risks for birth defects. A1c greater than 7 increase the risks
NEONATAL MORBIDITY

- Hypoglycemia
- Polycythemia
- Hyperbilirubinemia
- Hypocalcemia
- Cardiomyopathy
- Respiratory Distress
- Birth Trauma
DIABETES EFFECT ON THE PREGNANCY

- Dystocia
- Preeclampsia
- Pyelonephritis
- Pelvic trauma
The square root of 9 is 3.

A) True.
B) False.
C) Who cares?
SCREENING
2 STEP TESTING

• Universal vs High risk
• 24 – 28 wks

Step 1. 1 hr 50 gram – no fasting necessary
• Venous plasma (<140 mg/dl) identifies 80% of women with GDM. A value >130mg/dl identifies 90% of women with GDM

Step 2. 3 hour 100g after an overnight fast
### Diagnostic Criteria for GDM

<table>
<thead>
<tr>
<th>Status</th>
<th>Carpenter and Coustan</th>
<th>National Diabetes Group</th>
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<tbody>
<tr>
<td>Fasting</td>
<td>95</td>
<td>105</td>
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<tr>
<td>One hour</td>
<td>180</td>
<td>190</td>
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<tr>
<td>Two hour</td>
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<td>165</td>
</tr>
<tr>
<td>Three hour</td>
<td>140</td>
<td>145</td>
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</table>
SCREENING
1 STEP TESTING

- 75 g glucose load after overnight fast
- Fasting 95 mg/dl
- 1 h 180 mg/dl
- 2 h 155 mg/dl
WHEN TO SCREEN

• Assess risk at the first prenatal visit
  Marked obesity
  Family or personal history
  glycosuria
WHEN IS IT OUTRIGHT DIABETES?

- 1. A1C ≥ 6.5%
- 2. Fasting glucose ≥ 126 mg/dl (8 hr fast)
- 3. 2h value ≥ 200mg/dl after 75g load
- 4. Symptomatic pt with random glucose ≥ 200 mg/dl

(1-3 should be confirmed with repeat testing)
A FEW DETAILS

• Hgb A1C ≥ 6.5% identifies one third fewer patients than a fasting ≥ 126 mg/dl

• Certain hemoglobinopathies or anemias may affect the A1C (Sickle cell, iron deficiency)

• There may be discordance between tests.
SCREENING

- Hgb A1C at first prenatal visit. (< 20 weeks)
  \[ \geq 6.5\% \quad \text{dx of diabetes in pregnancy} \]
  counseling on diet
  daily SMBG
  medication as needed

\[ 5.7-6.4\% \quad \text{Impaired glucose tolerance} \]
  counseling on diet
  monitor BG
SCREENING

- <5.7% Test for GDM at 24-28 weeks
WHICH METHOD IS BEST?

—I love controversy"
• World Health Organization (WHO)
• Australasian Diabetes in pregnancy society
• Diabetes in pregnancy study group of India
• International Association of Diabetes and Pregnancy study group (IADPSG)
• American Diabetes Association (ADA)

• ALL SUPPORT 75G ONE STEP TESTING AND THE USE OF THE A1C AT THE FIRST VISIT
• Americal Congress of Obstetricians and Gynecologists (ACOG)

• Supports 2 step testing

• It is estimated that if 75g single step testing is implemented the prevalence of GDM is expected to increase to 20% or higher.
PART 2: MANAGEMENT
ALL DIABETES IS NOT THE SAME

- Diabetes in pregnancy ≠ Diabetes outside of pregnancy

Outside of pregnancy goals are:
To prevent complications of cardiovascular disease
blindness
neuropathy
renal failure
Newborn 13.4 pounds (NSVD !!!)
ALL DIABETES IS NOT THE SAME

During pregnancy – goals are:
Prevent macrosomia
Prevent fetal death
Prevent other fetal complications
THIS MEANS YOU CANT TREAT THEM THE SAME

During pregnancy

- more frequent visits when not controlled
- stricter glycemic goals
CONTROL OF MATERNAL GLYCEMIA (TARGET PLASMA GLUCOSE LEVELS)

- Fasting
- Preprandial
- 1 hr after meals
- 2 hr after meals
- 60-90 mg/dl
- 60-105 mg/dl
- <140 mg/dl
- <120 mg/dl
GLUCOSE MONITORING

• Daily SMBG superior to intermittent monitoring

• Fasting blood sugar

• Post prandial sugars most predictive of macrosomia. The most difficult glucose to control - post breakfast (dawn phenomenon) most predictive of fetal demise

• Verify glucometer with your facility’s lab
MEDICAL NUTRITION THERAPY (MNT)

- Goal: to provide calories and nutrients to sustain pregnancy, but does not cause post-prandial hyperglycemia
DIETARY RECOMMENDATIONS

• 3 meals and 3 snacks

• Composition: CHO-30%-prot-20%;fat-30-40%

• Wt gain: 25-35 lb; if overwt (15-25); underwt (30-40)

• Caloric distribution; 10%-breakfast, 20-30 % for lunch, 30-40 % for dinner, 30% for snacks

• Exercise is also very important in the management of all women with diabetes
CARBOHYDRATE BUDGET

- Breakfast: 1-2 carbohydrate choices
- Lunch: 3-4 carbohydrate choices
- Supper: 3-4 carbohydrate choices
- Snacks (1-3): 1-2 carbohydrate choices

- Amount of CHO typically found in a 2200 calorie diet
NUTRITION GUIDELINES

- Carbohydrate counting/label reading
- CHO restriction at breakfast
- Avoid sugar, concentrated sweets, refined/processed starches
- Eliminate liquid CHO (juices), test milk
- Ok to use aspartame (Equal), sucralose (Splenda), saccharine (Sweet n Low)

Increase high fiber foods (25-30 grams)
### Nutrition Facts

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<th>Nutrient</th>
<th>Amount Per Serving</th>
<th>% Daily Value</th>
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<td><strong>Total Fat</strong></td>
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<tr>
<td>Saturated Fat</td>
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<tr>
<td>Trans Fat</td>
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<td><strong>Sodium</strong></td>
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<tr>
<td><strong>Protein</strong></td>
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**INGREDIENTS:** UNBLEACHED ENRICHED WHEAT FLOUR (WHEAT FLOUR, MALTED BARLEY, BORONIC DINITRATE, REDuces FRUCTOSE CONTENT, MONONITRATE, RIBOFLAVIN, FOLIC ACID), WATER, YEAST, HIGH FRUCTOSE CORN SYRUP, SALT, CALCIUM PHOSPHATE, SOY FLOUR, CALCIUM SULFATE, NITRATE.
<table>
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<td>Servings Per Container</td>
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<table>
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<td>Calories from Fat</td>
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<td>% Daily Value**</td>
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<tr>
<td>Total Fat</td>
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<td>Saturated Fat</td>
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<tr>
<td>Protein</td>
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</table>
• After a meal
• Peak glucose levels approximately 1 hour
• Preprandial levels 2-3 hours
• Should you check 1 hour or 2 hour postprandial?
WHEN TO INITIATE PHARMACOTHERAPY

- GDM A1 to A2
- >2 values exceed goal in 1 to 2 weeks
- FBS >95
- 2 hour PP>120
- Fetal abdominal circumference >70% at 29-33 wks

(Buchanan diabetes care 1998)
INSULIN THERAPY LISPRO (HUMALOG)

- Rapid Acting—good for pre-meals!
- Onset—15 min
- Peak—30-90 min
- Duration—3-5 hours
- Little antibody formation; more effective than regular insulin
- Disadvantages: expensive, once thought to increase risk for proliferative retinopathy
INSULIN THERAPY
NPH

- Intermediate Acting Insulin
- Onset 1-2 hours
- Peak 4-8 hours
- Duration 12 hours
- Good for HS to Fasting window
- May add in Am to cover midday
INSULIN THERAPY
ULTRALENTE

- Long Acting
- Onset 4-6hr
- Duration 24-36 hours
- Peaks 16-18 hours
- Large day to day variability
- Not recommended
LANTUS(GLARGINE-DNA ORIGIN)

- Long acting
- Once a day insulin injection
- No peak
- Steady release of insulin
- Acidic pH 4. After SQ injection it is neutralized forming micro precipitates.
- Cannot be mixed with any other insulin
- Category C
INSULIN TOTAL DAILY DOSE REGIMEN

• 1\textsuperscript{st} trimester \hspace{1cm} .7 u/kg
• 2\textsuperscript{nd} trimester \hspace{1cm} .8u/kg
• 3\textsuperscript{rd} trimester \hspace{1cm} 1.0u/kg

• Dose range \hspace{1cm} .25u/kg to 1.0u/kg
INSULIN THERAPY – DAILY BREAKDOWN
LISPRO COVERAGE

- TDD x 40% Pre Breakfast
- TDD x 30% Pre Lunch
- TDD x 20% Pre Dinner
- TDD x 10% Bedtime
- NPH is added for coverage at bedtime
BEWARE OF VICIOUS CYCLE

↑ Appetite
↑ Wt Gain
↑ Insulin resistance

↑ BG

Insulin
MANAGEMENT OF GDM/TYPe 2 ORAL AGENTS

• First line glyburide (not used in Type 1)
• Max dose 20mg/day
• Usual dose 5-10mg targeted for time when glucose abnormal (there is a 2.5mg dose)

• It’s a sulfonylurea - don’t use in patients with sulfa allergy
• Long tail – most common side effect is hypoglycemia
ORAL HYPOGLYCEMIC AGENTS
GLYBURIDE

• An effective alternative to insulin in the treatment of gestational diabetes (Langer NJMED, 2000)

• 30–40% failure rate in some series of studies

• Patients prefer oral agents rather than injections!

• Other agents Metformin (biguanide)

• Precose?
MANAGEMENT OF GDM/TYP 视 2

ORAL AGENTS

• Metformin – insulin sensitizer
• Maximum dose studied 2000mg/day but have seen patients on up to 2500.
• Crosses the placenta in appreciable amounts
• Doesn’t cause hypoglycemia
• Can be combined with glyburide
• Most common side effect is GI upset
MANAGEMENT OF GDM/TYPE 2 MEDICATION

• When to add medication
• Goals: fasting ≤ 95mg/dl
• 2 hr postprandial ≤ 120mg/dl
• Check 4 x day = 28 values/week
• 15-20% abnormal values consistently indicates a need for medication.
MEDICATION MANAGEMENT
RULES OF THE ROAD

1. There must always be a combination of medicine and diet.

2. Starting medication is just that. A start. Patient will not be controlled immediately after you start medication. It will have to be adjusted. This is particularly true of insulin.

3. Exercise makes everything better.

4. Oral agents won't work if blood glucose consistently ≥ 170mg/dl.
FETAL SURVEILLANCE

- Ultrasound
  Early dating and viability scan
  Every 4 weeks for growth

Quad screen marker at 15-20 weeks or Free fetal DNA > 10 weeks

Kick count at 28 weeks (+/-)

Pre-existing diabetes, GDM A-2, NST twice/week starting at 30-32 weeks, or BPP once/week starting at 32-34 weeks
DELIVERY

- Induce at 38-39 6/7wks (pre-existing DM and GDM A-2)
- ADA (2004)
- NICE (2008)

- Amniocentesis for fetal lung maturity if there is uncertainty in gestational age (especially in the borderlands)
- Keep BG at 70-90 mg/dl during labor
- Most important determinant of risk for early neonatal hypoglycemia is intrapartum control
POST PARTUM CARE

• Breastfeeding is encouraged

• 2 hour 75 –gm glucola at 6 weeks post-partum)

• Euglycemia, IFG, IGT, Overt Type 2

• 50-60% of GDM will develop Type 2 diabetes in 5-10 years
MAJOR GOALS

• Manage all diabetes patients with a team approach

• Major Goals: To prevent Macrosomia, hyperbilirubinemia, birth trauma, neonatal hypoglycemia in the baby

• To prevent: operative deliveries (including – vacuum extraction, forceps delivery, and cesarean deliveries), genital trauma, and prevent preeclampsia in the mother
QUESTIONS

Interesting facts about SUMO
- Eat 20,000 calories a day
- Ideal weight is 400-600 lbs
- They never eat breakfast
- Each meal 5-10 bowls of rice and up to 6 pints of beer
- Surprisingly low incidence of diabetes (5%)