Pregestational Diabetes: The On-coming Tsunami

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Outline

• Appreciate the growing magnitude of diabetes in the United States and the impact upon pregnancy

• Understand the common medical and obstetrical concerns of diabetes complicating pregnancy
  – Medical concerns
  – Obstetrical concerns

• Management Pearls
The diabetes epidemic in the United States continues unabated, with a staggering toll in acute and chronic complications, disability, and death.
Diagnosed cases of diabetes in the United States 1980-2004

Undiagnosed cases: 21 million (7%)
Diagnosed cases: 14 million
1 out of 3 cases are undiagnosed
Estimated number of new cases of diagnosed diabetes in people aged 20 years or older, by age group, United States, 2007

Diabetes during pregnancy is increasing every year

• 2006 rate of diabetes during pregnancy was 42.3 per 1000 pregnancies (>4%)
  – 90% gestational diabetes
  – 10% pregestational diabetes

• Rate of diabetes during pregnancy rises approximately 6-7% every year
Risk factors for Diabetes

- Maternal age
- Member of a high risk ethnic group
- Obesity
- A history of gestational diabetes
Diabetes Types

Type 1
• Less common
• Younger age
• Autoimmune process resulting in B cell of Langerhans destruction.
• Characterized by an absolute insulinopenia
• Sensitive to insulin (commonly harder to manage during pregnancy)
• Dependent on exogenous insulin for survival
• At risk for diabetes ketoacidosis

Type 2
• More common (90-95%)
• Common features/risk factors with gestational diabetes such as obesity, non-Caucasian, older.
• Runs in families
• Characterized by relative insulin deficiency and prominent insulin resistance component. Insulin levels typically are normal to high.
Maternal Considerations
Physiology

First trimester:
• Increased insulin sensitivity
• Hypoglycemia is most common at this time

2nd and third trimester:
• Progressively reduced insulin sensitivity (increased resistance)
• Many different hormones involved
• Insulin requirements rise throughout pregnancy
  – Inform your patients
Diabetic retinopathy

Most common cause of blindness in the U.S.

Progresses from background disease to proliferative disease and blindness

Disease exacerbation commonly occurs during pregnancy and is influenced by baseline disease
Unclear if pregnancy or rapid improved control are to blame.

Pregnancy not a contraindication to therapy and immediate photocoagulation should be performed with proliferative disease.
Nephropathy

Fast facts
- Most common cause of chronic renal disease in US
- Commonly defined: 500mg protein over 24 hours
- 5-10% of diabetic women who become pregnant

Severity of disease determined by serum creatinine.
- Mild: <1.4
- Moderate: 1.5-2.5
- Severe: >2.5

Moderate and severe renal disease (1.5)
- Associated with worsening and permanent renal dysfunction.

Associated with additional adverse obstetrical outcomes
- Preeclampsia (as high as 50% of women with class F)
- Fetal growth restriction
- Preterm delivery
Chronic hypertension

5-10% of women with diabetes and pregnancy

Associated with additional adverse obstetrical outcomes
- Preeclampsia
- Fetal growth restriction
- Preterm delivery

Medications
- Commonly used:
  - methyldopa
  - calcium channel blockers
  - beta blockers
- ACE inhibitors contraindicated
  - First trimester: Fetal cardiovascular and CNS defects
  - Second trimester: Renal abnormalities
Hypothyroidism

Strong association with diabetes (as high as 40% in type 1 DM)

Untreated disease associated with:

- Preeclampsia
- Fetal growth restriction
- Preterm delivery
- Developmental delay
- Euthyroid status mitigates these risks.
Diabetes ketoacidosis

Fast facts:
• Incidence: 1-3% of type 1 diabetic pregnancies
• Lack of insulin prohibits use of serum glucose for energy metabolism, alternative sources (fats) required.
  – (insulin is the key that allows glucose into peripheral tissues)
• Pregnancy increases risk in part to increased insulin resistance

Risk factors:
• New infections, non-adherence with therapy
• Treatment with medications (corticosteroids)
  – Betamethasone typically causes hyperglycemia for 5 days.

Concerns:
• Persistent acidemia result in fetal compromise (20% have fetal demise)
• High maternal mortality if not managed properly
Obstetrical considerations
Increased incidence of preeclampsia with diabetes (Sibai AJOG 2000)

**Overall incidence**

- **20%**

**By DM class**

<table>
<thead>
<tr>
<th>Class</th>
<th>Incidence</th>
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<tbody>
<tr>
<td>B</td>
<td>11%</td>
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<tr>
<td>C</td>
<td>22%</td>
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<tr>
<td>D</td>
<td>21%</td>
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<tr>
<td>R+F</td>
<td>36%</td>
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</table>
Increased risk of medically indicated and spontaneous preterm birth with diabetes (Sibai AJOG 2000)

Both medically indicated and spontaneous preterm births are more likely with diabetes when compared to controls.

Medical Spontaneous: 22% vs 3% 16% vs 11%

Preterm delivery in women with pregnancy diabetes mellitus or chronic hypertension relative to women with uncomplicated pregnancies

Both medically indicated and spontaneous preterm births are more likely with diabetes when compared to controls.

Medical Spontaneous: 22% vs 3% 16% vs 11%
Hemoglobin A1c

Mean blood glucose over 8-12 weeks.
A1c of 8% approximates a mean of 180 (1% diff is 30mg/dL)

Predicts risk for first trimester miscarriage and congenital birth defects

First trimester spontaneous abortion (Greene Teratology 1989)
- A1c <9.3% 12.4%
- A1c >14.4% 37.5%

Congenital birth defects (Greene Teratology 1989)
- <9.3% 3%
- >14.4% 40%
- CNS, cardiac are most commonly affected.
- Caudal regression is rare, but pathognomonic

Preconception consultation is critical to prevent
Fetal concerns

Stillbirth
Significant problem before the availability of injectable insulin (50% perinatal loss)

Etiology of stillbirth unclear, combination of fetal hyperinsulinemia and chronic hypoxia?

Fetal growth abnormalities
Macrosomia 20-50%
• Increased fat proportions and larger shoulders than non-diabetics
• Risk of shoulder dystocia and birth injury.

Increased growth restriction risk
• Especially with hypertension and nephropathy.
Fetal concerns

Polyhydramnios

Neonatal metabolic alterations

- Neonatal hypoglycemia
- Hypocalcemia and hypomagnessemia
- Polycythemia, hyperbilirubinemia, jaundice
Management Pearls

Like most veterinary students, Doreen breezes through chapter 9.
Management Goals

Majority of suggestions are not clearly evidence based

1. Identify and minimize impact of maternal medical disease

2. Optimize euglycemia for maternal and fetal health
Baseline maternal assessment

Physical exam
• Blood pressure
• Attention to extremities including soles of feet

Blood work
• Hemoglobin A1c (every trimester)
• Urine culture (every trimester)
• Thyroid stimulating hormone
• Serum creatinine
• 24 hour urine for protein and creatinine clearance
• Liver function testing

Other testing
• Electrocardiogram (do not get excited about left atrial dilation)
• Ophthalmology evaluation
Pregnancy surveillance

First trimester
• Dating ultrasound

Second trimester
• AFP testing
• Level 2 ultrasound
• Fetal echocardiogram (when available)

Third trimester
• Ultrasound for fetal growth every 4-6 weeks after 24 weeks gestation.
• Antenatal surveillance at 32 weeks gestation (at least 1x week)
Treatment: Options Available

- Glucose monitoring
- Diet management
- Hypoglycemic therapy when diet fails
Glucose monitoring recommendations

Self glucose monitoring (ACOG)
- Premeal
- 1 hour after a meal begins
- Prior to sleep
- Middle of the night if concerned about hypoglycemia

ACOG Goals
- Fasting <95 mg/dL
- Premeal <100 mg/dL
- One hour PP <140 mg/dL
- Two hour PP <120 mg/dL
- Glycosylated A1c <6%

ADA Goals
- Preprandial 60-99 mg/dL
- Peak PP 100-129 mg/dL
- Glycosylated A1c <6%
Postprandial glucose monitoring

- Measure glucose levels 4 times/day
  - Fasting
  - 1 or 2 hours after meals

- Postprandial levels associated with improved outcomes
  - Macrosomia (12 vs 42%)
  - Neonatal hypoglycemia (3 vs 21%)
  - Lower caesarean delivery for labor dystocia (24 vs 39%)
Treatment: Diet Control (ACOG)

Calorie estimates:
- Average weight women: 30-35kcal/kg/day
- Underweight: 30-40kcal/kg/day
- Overweight (>120%): 24kcal/kg/day

Caloric composition recommendations:
- Complex carbohydrates: 40-50%
- Protein: 20%
- Unsaturated fats: 30-40%

Each meal (% daily calories):
- Breakfast: 10-20%
- Lunch: 20-30%
- Dinner: 30-40%
- Snacks: 30%
My Plate Planner

Please refer to meal planning guidelines on the back.

My Plate Planner
Methods of Use

- Fill 1/2 of your plate with vegetables such as broccoli, carrots, cauliflower, and salad
- Fill 1/4 of your plate with lean meat, chicken or fish; this is about 3 ounces
- Fill 1/4 of your plate with a starchy choice such as 1/2 cup mashed potatoes
- Add 1 serving of fruit
- Choose 1 serving of milk
- Add margarine or oil for preparation or addition at the table

Add other portions as needed to round out your meal plan

For breakfast, use only half the plate
For lunch and dinner, use the whole plate

Free foods

8-ounce glass of milk

9-inch plate
## Treatment: Insulin

<table>
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<th>Type</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
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<tbody>
<tr>
<td><strong>Rapid acting</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lispro (humalog)</td>
<td>5-15 min</td>
<td>1-2h</td>
<td>4-6h</td>
</tr>
<tr>
<td>Aspart (novolog)</td>
<td>5-15 min</td>
<td>1-2h</td>
<td>4-6h</td>
</tr>
<tr>
<td><strong>Short acting</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Regular</td>
<td>30-60 min</td>
<td>2-3h</td>
<td>8-10h</td>
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<tr>
<td><strong>Intermediate acting</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>NPH</td>
<td>2-4 hours</td>
<td>4-10h</td>
<td>12-18h</td>
</tr>
<tr>
<td><strong>Long acting</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Glargine (lantus)</td>
<td>2-4 hours</td>
<td>none</td>
<td>20-24h</td>
</tr>
<tr>
<td>Detemir</td>
<td>3-4 hours</td>
<td>none</td>
<td>20h</td>
</tr>
</tbody>
</table>
Starting insulin

Insulin requirements vary considerably among women.

Typical needs:
- First trimester: 0.7-0.8U/kg/day
- Second trimester: 0.8-1.0U/kg/day
- Third trimester: 0.9-1.2U/kg/day
Greatest experience is with a combination of rapid/fast acting and NPH insulin

Typical insulin requirement

1. Calculate total insulin needs by weight
2. Short acting insulin 50%
   - Divided equally between meals
   - Weight in Kg x 0.1 = insulin per meal
3. Basal insulin insulin 50%
   - In the AM and before bedtime
   - Weight in Kg x 0.2 = insulin in AM and PM
Managing insulin

Elevated fasting  Increase evening NPH
Elevated breakfast  Increase AM short acting
Elevated lunch  Increase AM NPH
Elevated dinner  Increase PM short acting

Inform patient that you expect increases during the pregnancy.

Increase and decrease by increments of 10-20%.
Timing of Delivery

Well controlled diabetic women without medical disease
• May manage expectantly until the due date
• May deliver at 39 weeks

Suboptimally controlled diabetic women or with medical disease
• Case by case
• Induce by 39 weeks gestation
• May consider elective induction at 38 weeks if poorly controlled (especially with elevated A1c or significant LGA status)
Kjos et al AJOG 1993

Randomized trial using 200 women with insulin requiring diabetes at 38 weeks' gestation.

1. Active induction of labor within 5 days
   vs
2. Expectant management

Similar cesarean rate
- Induction: 25%
- Expectant: 31%

Expectant had higher incidence of LGA
- Induction: 10%
- Expectant: 23%

Expectant had higher incidence of shoulder dystocia
- Induction: 0%
- Expectant: 3%

Expectant had high rate of induction for obstetrical issues (49%)
Mode of delivery

Risk of shoulder dystocia for diabetic pregnancies
- 3500g: 5-10%
- 4000g: 10-25%
- 4500g: 25-50%
- 5000g: >25%

Risk of brachial plexus injury (ACOG Pregnancy Bulletin)
- 10-40%
- 4% incidence with CD

Risk of permanent injury
- 10-15%
Mode of Delivery

In light of increasing risk for shoulder dystocia with increasing fetal weight, cesarean may be offered if fetal weight is estimated greater than 4500g to reduce the risk of birth injury.

ACOG Practice Bulletin

In my office, we begin to discuss shoulder dystocia and make cesarean delivery available at 4000g.
After delivery
Significantly reduced insulin requirements post delivery.

Typically may reduce insulin dosing by 50% once eating or discontinue if gestational diabetes.

Contraception
There are no absolute contraindications to any of the available contraceptive methods.

Only caveat: Combined oral contraception may not be appropriate in diabetic women with significant vasculopathy

Postpartum Care
Questions?

Contact email:

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