Screening, Diagnosis and Management of Diabetes in Pregnancy

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Objectives

- Epidemiology of GDM
- Screening of GDM
  - Universal vs. selective screening
  - Screening thresholds
- Diagnosis of GDM
  - GTT: diagnostic thresholds
- Management of GDM
  - Oral hypoglycemic agents vs. insulin injections
- Postpartum follow-up

Epidemiology of Diabetes during Pregnancy in the U.S.

- **154,000 (4%)** of all pregnancies
  - **135,000 (88%)** due to GDM
  - **12,000 (8%)** due to Type 2 DM
  - **7,000 (4%)** due to Type 1 DM

GDM: Obstetric Considerations

- GDM associated with
  - Gestational hypertension
  - Preeclampsia
  - Operative deliveries
  - Postpartum development of Type 2 DM

ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42
GDM: Perinatal Considerations

- GDM associated with
  - Fetal macrosomia
  - Birth trauma
  - Metabolic abnormalities
    - Hypoglycemia
    - Hyperbilirubinemia/polycythemia
    - Hypocalcemia
  - Respiratory distress syndrome
  - Preterm delivery
  - Perinatal mortality

Casey BM et al. Obstet Gynecol 1997;90:867-73

GDM: Postnatal Considerations

- Metabolic syndrome evaluated in a longitudinal cohort of 179 children (at age 6, 7, 9, 11)


GDM: Diabetogenic hormones

- Insulin resistance first recognized during pregnancy
  - Prevalence: 1-14% of all pregnancies

ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S6-42
Risk Factors of GDM

- Maternal age >25 years
- Body mass index >25 kg/m²
- Ethnicity
  - Latina
  - Native American
  - South or East Asian, Pacific Island ancestry
  - African American
- Personal/Family history of DM
- History of macrosomia
- Glycosuria

ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42

Screening of GDM

- ACOG: Universal screening
  - Clinical history
  - Laboratory testing
- ADA: Selective screening
  - Risk assessment at first visit
    - High risk: GCT as soon as feasible
    - Average risk: GCT at 24-28 weeks GA
    - Low risk: No GCT

ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42

Screening of GDM

- U.S. Preventive Service Task Force:
  - Insufficient evidence for universal screening
  - Screening of high-risk women may be beneficial


Low Risk for GDM

- Maternal age < 25 years
- Weight normal before pregnancy
- Members of an ethnic group with a low prevalence of GDM
- No known DM in 1st degree relatives
- No history of abnormal glucose tolerance
- No history of poor obstetric outcome

ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42
Universal vs. Selective Screening

- 94% obstetricians reported universal testing
- Use of risk factors will miss 50% of GDM
- Members of an ethnic group with a low prevalence of GDM


Universal vs. Selective Screening

- Naylor et al: prospective study n=3,131


Universal vs. Selective Screening

- Naylor et al: prospective study n=3,131
- Screening strategy:

<table>
<thead>
<tr>
<th>GCT Postprandial</th>
<th>Screening Thresholds</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 hours</td>
<td>148 mg/dL</td>
</tr>
<tr>
<td>2-3 hours</td>
<td>142 mg/dL</td>
</tr>
<tr>
<td>&gt;3 hours</td>
<td>150 mg/dL</td>
</tr>
</tbody>
</table>

Naylor CD et al. Selective screening for GDM. NEJM 1997;337:1591-6
Universal vs. Selective Screening

Naylor et al: prospective study n=3,131

Screening of GDM

- Screening test
  - 50gm 1-hour glucose challenge test (GCT)
- Screening thresholds
  - 130mg/dL: 90% sensitivity (23% screen +)
  - 140mg/dL: 80% sensitivity (14% screen +)

Screening Thresholds by Ethnicity:
GCT 130 - 150 mg/dL

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>130 mg/dL sensitivity</th>
<th>135 mg/dL sensitivity</th>
<th>140 mg/dL sensitivity</th>
<th>145 mg/dL sensitivity</th>
<th>150 mg/dL sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>99.5 (82.5)</td>
<td>93.9 (87.1)</td>
<td>89.2 (90.7)</td>
<td>75.6 (92.9)</td>
<td>66.2 (95.0)</td>
</tr>
<tr>
<td>African American</td>
<td>98.8 (88.4)</td>
<td>96.5 (91.1)</td>
<td>92.9 (93.8)</td>
<td>81.2 (96.0)</td>
<td>70.6 (97.0)</td>
</tr>
<tr>
<td>Latina</td>
<td>98.3 (80.9)</td>
<td>94.1 (85.5)</td>
<td>89.9 (88.7)</td>
<td>78.2 (91.1)</td>
<td>65.6 (93.5)</td>
</tr>
<tr>
<td>Asian</td>
<td>98.5 (75.9)</td>
<td>93.0 (81.1)</td>
<td>88.8 (86.0)</td>
<td>79.8 (89.0)</td>
<td>69.0 (91.8)</td>
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</tbody>
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Naylor CD et al. Selective screening for GDM. NEJM 1997;337:1591-6

Screening Thresholds by Ethnicity: Sensitivity of GCT 130 - 150 mg/dL

<table>
<thead>
<tr>
<th></th>
<th>GLT 130 mg/dL sensitivity (specificity)</th>
<th>GLT 135 mg/dL sensitivity (specificity)</th>
<th>GLT 140 mg/dL sensitivity (specificity)</th>
<th>GLT 145 mg/dL sensitivity (specificity)</th>
<th>GLT 150 mg/dL sensitivity (specificity)</th>
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Is GCT Ever Diagnostic for GDM

- **GCT, GDM diagnosis & Perinatal outcomes**

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|                |                                          |

Diagnosis of GDM

- **Diagnostic test**
  - FS >126 mg/dL or random BG >200 mg/dL
  - 100gm 3-hour glucose tolerance test (GTT)
  - 2 or more abnormal values

<table>
<thead>
<tr>
<th></th>
<th>Carpenter and Coustan</th>
<th>National Diabetes and Data Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Fasting 95 mg/dL</td>
</tr>
<tr>
<td>1hr</td>
<td></td>
<td>180 mg/dL</td>
</tr>
<tr>
<td>2hr</td>
<td>155 mg/dL</td>
<td>165 mg/dL</td>
</tr>
<tr>
<td>3hr</td>
<td>140 mg/dL</td>
<td>145 mg/dL</td>
</tr>
</tbody>
</table>

ADA position statement: Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42

Cheung et al. Markedly elevated GLT & perinatal outcomes. JMFNM 2006;19:728-34
Diagnosis of GDM

**Diagnostic test**
- 75gm 2-hour glucose tolerance test (GTT)
  - 2 or more values exceeding threshold (ADA)
  - Fasting or 2hr value exceeds threshold (WHO)

<table>
<thead>
<tr>
<th></th>
<th>WHO</th>
<th>ADA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>126mg/dL</td>
<td>95mg/dL</td>
</tr>
<tr>
<td>1hr</td>
<td>--</td>
<td>180mg/dL</td>
</tr>
<tr>
<td>2hr</td>
<td>140mg/dL</td>
<td>155mg/dL</td>
</tr>
</tbody>
</table>

ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42

Diagnosis of GDM: 75gm GTT

- ADA vs. WHO diagnostic criteria
- Cohort study: 4,977 women with 2-hr 75gGTT
- GDM by either diagnostic criteria associated with:
  - Perinatal death (RR 1.59; 3.10)
  - Preeclampsia (RR 2.28; 1.94)
  - Macrosomia (RR 1.29; 1.45)

Schmidt MI et al. GDM diagnosed with a 75gm-2-hr OGGT and adverse perinatal outcomes. Diabetes care 2001;24:1151-5.

Diagnosis of GDM

**75gm 2-hr GTT vs. 100gm 3-hr GTT**
- Poor concordance: kappa index 0.18-0.21
  - 16-20 weeks: 15/277 (2hrGTT) vs. 41/277 (3hrGTT), 11 concordant
  - 26-31 weeks: 25/484 (2hrGTT) vs 60/484 (3hrGTT), 13 concordant
- Omission of the 3rd hr value (100mg GTT):
  - 87% sensitivity (Attila et al 1999)
  - 26.4 vs. 28.4% GDM, no difference in perinatal outcomes of 18 omitted cases (Jakobi 2004)

Mente G et al. Lack of concordance between 75g and 100g GTT for diagnosis of GDM. Clin Chem 2006; 52:1679-82
Jakobi E et al. A 2-hr vs. 3-hr 100gm GTT for diagnosis of GDM. J Perinatal Med 2004;32:120-2

Diagnosis of GDM

- ADA and the 4th International Workshop-Conference on GDM:
  - Carpenter & Coustan diagnostic criteria
- Carpenter & Coustan vs. NDDG:
  - Women with GDM by Carpenter and Coustan only have higher odds of
    - Macrosomia
    - Hypoglycemia
    - Hyperbilirubinemia

ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42
Ferrara A et al. Diabetologia 2006
**Diagnosis of GDM**

- Women with false-positive GCT
  - Retrospective cohort study (Stamilio 2004)
    - Cesarean delivery
    - Macrosomia
    - Shoulder dystocia
    - Composite morbidity
  - Retrospective cohort study (McLaughlin 2006)
    - Cesarean delivery
    - Preeclampsia
    - Macrosomia
    - ICN admission

Stamilio et al. False positive 5-hour GCT and adverse perinatal outcomes. Obstet Gynecol 2004;105:146-56

- Continuous relationship between carbohydrate intolerance and adverse outcome
  - No single cutoff can separate
    - those with high risk
    - those with no risk at all
  - GDM diagnostic criteria validated by
    - Predictive value for subsequent diabetes in the mother
    - Rather than ability to identify risk to the fetus/newborn
  - Diagnostic criteria appropriate but arbitrary


**Management of GDM**

- Nutrition therapy
- Home self glucose monitoring
- Medical therapy if glycemic control not achieved with diet/exercise
  - Subcutaneous insulin
  - Oral hypoglycemic agents
    - Glyburide
    - Metformin
- Antenatal monitoring

Gable MG. Management of diabetes mellitus by ObGyn. Obstet Gynecol 2004;103:1228-34

**Goals of Glycemic Control**

- Blood glucose goals during pregnancy
  - Fasting < 95mg/dL
  - 1-hr postprandial < 130-140mg/dL
  - 2-hr postprandial am < 120mg/dL
  - 2am < 120mg/dL
Treatment of GDM

Table 1. Primary Clinical Outcomes among the Infants

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Insulin Group (%)</th>
<th>Carbohydrate Add (%)</th>
<th>Carbohydrate Add (%)</th>
<th>Fetal</th>
<th>Insulin (%)</th>
<th>Carbohydrate Add (%)</th>
<th>Fetal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g)</td>
<td>3150±550</td>
<td>3150±550</td>
<td>3150±550</td>
<td>0.01</td>
<td>0.004</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>Large for gestational age (%)</td>
<td>15 (21)</td>
<td>21 (12)</td>
<td>21 (12)</td>
<td>0.07</td>
<td>0.32</td>
<td>0.07</td>
<td>0.32</td>
</tr>
<tr>
<td>Macrosomia (%)</td>
<td>10 (15)</td>
<td>15 (12)</td>
<td>15 (12)</td>
<td>0.04</td>
<td>0.002</td>
<td>0.04</td>
<td>0.002</td>
</tr>
<tr>
<td>Small for gestational age (%)</td>
<td>12 (18)</td>
<td>18 (12)</td>
<td>11 (12)</td>
<td>0.00</td>
<td>0.001</td>
<td>0.00</td>
<td>0.001</td>
</tr>
<tr>
<td>Stillbirth (%)</td>
<td>3 (5)</td>
<td>5 (3)</td>
<td>5 (3)</td>
<td>0.07</td>
<td>0.40</td>
<td>0.07</td>
<td>0.40</td>
</tr>
<tr>
<td>Hypoglycemia requiring therapy (%)</td>
<td>1 (2)</td>
<td>2 (1)</td>
<td>2 (1)</td>
<td>0.00</td>
<td>0.001</td>
<td>0.00</td>
<td>0.001</td>
</tr>
<tr>
<td>Neonatal conditions (%)</td>
<td>3 (5)</td>
<td>5 (3)</td>
<td>5 (3)</td>
<td>0.00</td>
<td>0.001</td>
<td>0.00</td>
<td>0.001</td>
</tr>
<tr>
<td>Respiratory distress syndrome (%)</td>
<td>2 (3)</td>
<td>3 (2)</td>
<td>3 (2)</td>
<td>0.00</td>
<td>0.001</td>
<td>0.00</td>
<td>0.001</td>
</tr>
</tbody>
</table>


Langer et al 2000
- Randomized controlled trial (n=404)
- Similar glycemic control

Table 2. Blood Glucose Concentration, Measured at Home and Glycated Hemoglobin Values, During Treatment in Women with GDM

<table>
<thead>
<tr>
<th>Variable</th>
<th>Glucose (mg/dl)</th>
<th>Hemoglobin (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning glucose</td>
<td>87±16</td>
<td>5.1±1.4</td>
<td>0.03</td>
</tr>
<tr>
<td>No. of measurements</td>
<td>150</td>
<td>112</td>
<td></td>
</tr>
<tr>
<td>Mean glucose (log)</td>
<td>9.0±1.3</td>
<td>0.1±0.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Hemoglobin (log)</td>
<td>9.0±1.3</td>
<td>0.1±0.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Total glucose</td>
<td>9.0±1.3</td>
<td>0.1±0.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Hemoglobin (log)</td>
<td>9.0±1.3</td>
<td>0.1±0.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Glycated hemoglobin (log)</td>
<td>9.0±1.3</td>
<td>0.1±0.1</td>
<td>0.01</td>
</tr>
</tbody>
</table>


Similar neonatal outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Glyburide (N=203)</th>
<th>Insulin (N=203)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational age</td>
<td>24.1 (12)</td>
<td>26.1 (13)</td>
<td>0.70</td>
</tr>
<tr>
<td>Birth weight</td>
<td>3.25 (1.3)</td>
<td>3.14 (1.1)</td>
<td>0.28</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>3.0 (1.0)</td>
<td>3.1 (1.0)</td>
<td>0.36</td>
</tr>
<tr>
<td>Macrosomia (%)</td>
<td>3 (1.0)</td>
<td>3 (1.0)</td>
<td>0.36</td>
</tr>
<tr>
<td>Birth complications (%)</td>
<td>1.0 (1.0)</td>
<td>1.0 (1.0)</td>
<td>0.99</td>
</tr>
<tr>
<td>Phototherapy (%)</td>
<td>3 (1.0)</td>
<td>4 (1.2)</td>
<td>0.74</td>
</tr>
<tr>
<td>Birth injury (%)</td>
<td>3 (1.0)</td>
<td>3 (1.0)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

Similar neonatal outcomes

<table>
<thead>
<tr>
<th>Neonatal Outcome</th>
<th>Glyburide % (n)</th>
<th>Insulin % (n)</th>
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<tbody>
<tr>
<td>Preeclampsia</td>
<td>12 % (28)</td>
<td>6 % (16)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Birth weight &gt; 4000 gms</td>
<td>24 % (63)</td>
<td>25 % (60)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean birth weight</td>
<td>3661 gms</td>
<td>3599 gms</td>
<td>NS</td>
</tr>
<tr>
<td>Birth injury</td>
<td>3 % (8)</td>
<td>1 % (3)</td>
<td>0.08</td>
</tr>
<tr>
<td>Phototherapy</td>
<td>9 % (21)</td>
<td>5 % (12)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Jacobson et al 2005

Retrospective cohort study (n=504)

<table>
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<th>Insulin % (n)</th>
<th>p-value</th>
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Langer 2000: Insulin vs. Glyburide

GDM: Medical Therapy vs. Insulin

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<tr>
<td>Birth weight &gt; 4000 gms</td>
<td>7 (14)</td>
<td>4 % (9)</td>
<td>0.26</td>
</tr>
<tr>
<td>Lung complications (%)</td>
<td>8 (16)</td>
<td>6 % (12)</td>
<td>0.43</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>9 % (18)</td>
<td>6 % (12)</td>
<td>0.25</td>
</tr>
<tr>
<td>Hyperbilirubinemia (%)</td>
<td>6 (12)</td>
<td>4 % (8)</td>
<td>0.36</td>
</tr>
<tr>
<td>Composite morbidity (%)</td>
<td>30 %</td>
<td>20 %</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Multivariable logistic regression adjusting for maternal age, parity, education level, GA at delivery, GA at GDM diagnosis, BMI, and gestational weight gain
GDM: Postnatal Considerations

- Metabolic syndrome evaluated in a longitudinal cohort of 179 children (at age 6,7,9,11)

![Graph showing prevalence of MS]

- ObesOB: Pediatrics 2005;115:e290-6

Medical Management of GDM

- ACOG Practice Bulletin:
  - No oral agents other than glyburide has been shown to be safe and effective in GDM
  - Further study recommended before use of newer oral hypoglycemic agents can be supported for use in pregnancy


Postpartum Follow-up

- Diagnosis of DM in non-pregnant state:

<table>
<thead>
<tr>
<th>Normal Values</th>
<th>Impaired fasting glucose or impaired glucose tolerance</th>
<th>Diabetes Mellitus</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG &lt;110mg/dL</td>
<td>FPG 110-125mg/dL</td>
<td>FPG ≥126mg/dL</td>
</tr>
<tr>
<td>75g 2hr GTT 2hr PG &lt;140mg/dL</td>
<td>75g 2hr GTT 2hr PG 140-199mg/dL</td>
<td>75g 2hr GTT 2hr PG ≥200mg/dL</td>
</tr>
<tr>
<td>Symptoms of DM &amp; random PG ≥200mg/dL</td>
<td></td>
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Postpartum Follow-up

- Cost-effective screening:
  - Fasting PG, 2hr GTT, Hgb A1c
  - Annually, every 2 years, every 3 years
    - Assume negative 6-week screen progress to DM 8% per year
    - Each positive FPG, Hgb A1c followed by confirmatory GTT
  - GTT every 3 years: lowest cost per case DM detected

Diabetes and Pregnancy: Summary

- **Gestational Diabetes**
  - Screening and Diagnosis
    - Universal screening
    - GCT Thresholds: 130 mg/dl vs. 140 mg/dl
    - GTT diagnostic criteria: Carpenter and Coustan
  - Management
    - Diet/exercise, nutritional consult
    - Self-monitoring of blood glucose
    - Insulin vs oral hypoglycemic agents if indicated
  - Postpartum screening