Screening & Management of Diabetes in Pregnancy: What’s New?

Jerrie S. Refuerzo, M.D.
Associate Professor
Division of Maternal Fetal medicine
Department of Obstetrics, Gynecology and Reproductive Sciences
University of Texas Health Science Center at Houston

January 12, 2013
Diagnostic Criteria of Diabetes Non-Pregnant Adults

- Fasting plasma glucose (FPG) ≥ 126 mg/dl
  OR
- Symptoms (polyuria, polydipsia, weight loss) PLUS PG ≥ 200 mg/dl
  OR
- PG ≥ 200 mg/dl 2 hours after 75 gram load
  OR
- HgbA1C ≥ 6.5%
History of GDM Detection

- Risk based screening (1%)
  - Age, ethnicity
  - Family history
  - Previous adverse OB outcome

- Universal screening
  - O’Sullivan criteria (2.5%)
  - Carpenter/Coustan (4-5%)
  - WHO (6-7%)
  - New criteria (18-35%)
When to Screen?

- **Early pregnancy** (<20 wk)
  - Obesity (BMI > 30)
  - Prior GDM
  - PCOS
  - Glycosuria
  - Prior LGA infant (>4kg)
  - First degree relative with DM

- **Everyone** 24-28 wks
Current USA criteria of GDM
2 stage: screening / diagnosis

ACOG Committee Opinion
Number 504, September 2011
Screen and Diagnosis of Gestational Diabetes Mellitus

50 gram OGTT [1 hour]

↓

Fail

↓

100 gram OGTT [3 hour]
## Detection Rate

<table>
<thead>
<tr>
<th>Cut-off value</th>
<th>50 g screen</th>
<th>Requiring 3 hr OGTT (%)</th>
<th>Detection rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-28 wk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 140 mg/dl</td>
<td>15</td>
<td>80-85</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 135 mg/dl</td>
<td>20</td>
<td>90-95</td>
</tr>
<tr>
<td>≥ 130 mg/dl</td>
<td>25</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>
ACOG Committee Opinion
Number 504, September 2011
Screen and Diagnosis of Gestational Diabetes Mellitus

Table 1. Two Diagnostic Criteria for Gestational Diabetes Mellitus

<table>
<thead>
<tr>
<th>Status</th>
<th>Plasma or Serum Glucose Level</th>
<th>Plasma Level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carpenter/Coustan Conversion</td>
<td>National Diabetes Data Group Conversion</td>
</tr>
<tr>
<td></td>
<td>mg/dL mmol/L</td>
<td>mg/dL mmol/L</td>
</tr>
<tr>
<td>Fasting</td>
<td>95  5.3</td>
<td>105  5.8</td>
</tr>
<tr>
<td>One hour</td>
<td>180 10.0</td>
<td>190 10.6</td>
</tr>
<tr>
<td>Two hours</td>
<td>155 8.6</td>
<td>165 9.2</td>
</tr>
<tr>
<td>Three hours</td>
<td>140 7.8</td>
<td>145 8.0</td>
</tr>
</tbody>
</table>

GDM Outcomes

The NEW ENGLAND JOURNAL of MEDICINE

Hyperglycemia and Adverse Pregnancy Outcomes

The HAPO Study Cooperative Research Group®

HAPO
2008
## Diagnosis of GDM with O-GTT

<table>
<thead>
<tr>
<th></th>
<th>New* Criteria 75 g 2 hr</th>
<th>Current** Criteria 100 g 3 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fasting</strong></td>
<td>92</td>
<td>95</td>
</tr>
<tr>
<td><strong>1 h</strong></td>
<td>180</td>
<td>180</td>
</tr>
<tr>
<td><strong>2 h</strong></td>
<td>153</td>
<td>155</td>
</tr>
<tr>
<td><strong>3 h</strong></td>
<td>--</td>
<td>140</td>
</tr>
</tbody>
</table>

* Only 1 value is needed

** 2 or more abnormal values are needed
GDM and Type-2 DM

- Decline in β-cell function
- Impaired insulin secretion
- Impaired hepatic glucose production
- Peripheral insulin resistance
# Fetal, Neonatal /Adult Complications

## Uncontrolled GDM / Type 2 DM

### Short Term
- LGA
- Organomegaly
- Birth trauma
- Neonatal hypoglycemia
- TTN / RDS

### Long Term
- Obesity
- Visceral obesity
- Insulin resistance
- Type 2 DM
- Metabolic syndrome
- Cardiovascular disease
Intrapartum Complications
GDM / Type 2 DM

Maternal

- Prolonged labor
- Cervicovaginal tears
- Perineal tears
- C/S delivery
- PPH

Fetal-Neonatal

- Hypoglycemia
- Shoulder dystocia
- Bone fracture
- Nerve palsies
- HIE
Effect of Treatment of Gestational Diabetes Mellitus on Pregnancy Outcomes


A Multicenter, Randomized Trial of Treatment for Mild Gestational Diabetes

Mark B. Landon, M.D., Catherine Y. Spong, M.D., Elizabeth Thom, Ph.D., Marshall W. Carpenter, M.D., Susan M. Ramin, M.D., Brian Casey, M.D., Ronald J. Wapner, M.D., Michael W. Varner, M.D., Dwight J. Rouse, M.D., John M. Thorp, Jr., M.D., Anthony Sciscione, D.O., Patrick Catalano, M.D., Margaret Harper, M.D., George Saade, M.D., Kristine Y. Lain, M.D., Yoram Sorokin, M.D., Alan M. Peaceman, M.D., Jorge E. Tolosa, M.D., M.S.C.E., and Garland B. Anderson, M.D., for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network*
## Pregnancy outcome

### Treatment vs no treatment in GDM

<table>
<thead>
<tr>
<th></th>
<th>ACHOIS</th>
<th></th>
<th>NICHD Network</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Treatment n=506</td>
<td>Control n=524</td>
<td>Treatment n=476</td>
<td>Control n=455</td>
</tr>
<tr>
<td>Induction (%)</td>
<td>39**</td>
<td>29**</td>
<td>27.3</td>
<td>26.8</td>
</tr>
<tr>
<td>Weight Gain (Kg)</td>
<td>8.1 ± 0.3*</td>
<td>9.8 ± 0.4*</td>
<td>2.8 ± 4.5 *</td>
<td>5.0 ± 3.3 *</td>
</tr>
<tr>
<td>C/S delivery (%)</td>
<td>31</td>
<td>32</td>
<td>26.9*</td>
<td>33.8*</td>
</tr>
<tr>
<td>Preeclampsia (%)</td>
<td>12*</td>
<td>18*</td>
<td>2.5*</td>
<td>5.5*</td>
</tr>
</tbody>
</table>

* P < 0.001, ** P = 0.02
# Neonatal outcome

## Treatment vs no treatment in GDM

<table>
<thead>
<tr>
<th></th>
<th>ACHOIS</th>
<th></th>
<th>NICHD Network</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Treatment n=506</td>
<td>Control n=524</td>
<td>Treatment n=476</td>
<td>Control n=455</td>
</tr>
<tr>
<td>Mean BW (g)</td>
<td>3335†</td>
<td>3482†</td>
<td>3302†</td>
<td>3408†</td>
</tr>
<tr>
<td>≥ 4 Kg (%)</td>
<td>10†</td>
<td>21†</td>
<td>5.9†</td>
<td>14.3†</td>
</tr>
<tr>
<td>L GA (%)</td>
<td>13†</td>
<td>22†</td>
<td>7.1†</td>
<td>14.5†</td>
</tr>
<tr>
<td>SGA (%)</td>
<td>7</td>
<td>7</td>
<td>7.5</td>
<td>6.4</td>
</tr>
<tr>
<td>Fat mass (g)</td>
<td>N/A</td>
<td>N/A</td>
<td>427†</td>
<td>464†</td>
</tr>
</tbody>
</table>

†\( p < 0.001 \)
Comparison of treatment effect in ACHOIS study & NICHD MFMU trial

<table>
<thead>
<tr>
<th>Variable</th>
<th>ACHOIS study</th>
<th>MFMU trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td>Reduced</td>
<td>No difference</td>
</tr>
<tr>
<td>LGA infant</td>
<td>Reduced</td>
<td>Reduced</td>
</tr>
<tr>
<td>Birth weight ≥ 4 kg</td>
<td>Reduced</td>
<td>Reduced</td>
</tr>
<tr>
<td>Neonatal fat mass</td>
<td>--</td>
<td>Reduced</td>
</tr>
<tr>
<td>NICU admission</td>
<td>Increased</td>
<td>No difference</td>
</tr>
<tr>
<td>Shoulder dystocia</td>
<td>No difference</td>
<td>Reduced</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>No difference</td>
<td>Reduced</td>
</tr>
<tr>
<td>Induction</td>
<td>Increased</td>
<td>No difference</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>Reduced</td>
<td>Reduced</td>
</tr>
<tr>
<td>Weight Gain in preg</td>
<td>Reduced</td>
<td>Reduced</td>
</tr>
</tbody>
</table>
GDM Outcomes

The NEW ENGLAND JOURNAL of MEDICINE

Hyperglycemia and Adverse Pregnancy Outcomes

The HAPO Study Cooperative Research Group*

HAPO
2008
# Maternal glucose and pregnancy outcomes

**HAPO Study**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>FPG OR(^b)</th>
<th>95% CI</th>
<th>1-h PG OR</th>
<th>95% CI</th>
<th>2-h PG OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LGA</td>
<td>1.38</td>
<td>(1.32-1.44)</td>
<td>1.46</td>
<td>(1.39-1.53)</td>
<td>1.38</td>
<td>(1.32-1.44)</td>
</tr>
<tr>
<td>C/S</td>
<td>1.11</td>
<td>(1.06-1.15)</td>
<td>1.10</td>
<td>(1.06-1.15)</td>
<td>1.08</td>
<td>(1.03-1.12)</td>
</tr>
<tr>
<td>Neonatal hypoglycemia</td>
<td>1.08</td>
<td>(0.98-1.19)</td>
<td>1.13</td>
<td>(1.03-1.26)</td>
<td>1.10</td>
<td>(1.00-1.12)</td>
</tr>
<tr>
<td>Cord C-peptide &gt;90(^{th}) centile</td>
<td>1.55</td>
<td>(1.47-1.64)</td>
<td>1.46</td>
<td>(1.38-1.54)</td>
<td>1.37</td>
<td>(1.30-1.44)</td>
</tr>
<tr>
<td>PTD, &lt;37 wk</td>
<td>1.05</td>
<td>(0.99-1.11)</td>
<td>1.18</td>
<td>(1.12-1.25)</td>
<td>1.16</td>
<td>(1.10-1.23)</td>
</tr>
<tr>
<td>Shoulder dystocia and/or birth injury</td>
<td>1.18</td>
<td>(1.04-1.33)</td>
<td>1.23</td>
<td>(1.09-1.38)</td>
<td>1.22</td>
<td>(1.09-1.37)</td>
</tr>
</tbody>
</table>
Management of GDM

- Self-blood glucose monitoring
- Dietary counseling (50% of cases)
- Oral hypoglycemic agents → insulin
- Serial US for fetal growth & fluid
- Antenatal testing
- Timely delivery
- Postpartum screening
Target Capillary Glucose Values

- Fasting $\leq 95$ mg/dl
- 1-hour pp < 140 mg/dl
- 2-hour pp < 120 mg/dl
- Before lunch & supper 60-105 mg/dl

**GOAL:** > 50% of within target
Management of GDM

• ADA diet (2000-2200 calories/day)
  • 30 Kcal/kg based on ideal weight
  • 35 Kcal/kg for underweight
  • 25 Kcal/kg for obese

• Exercise (brisk walking)
  • 3-5 times/wk for 30 minutes
Gestational diabetes

Fail 100 gram GTT → GDMA1

Diet and exercise

Self blood glucose monitoring

Prenatal visits every 1-2 wks
Gestational diabetes

Hyperglycemia → GDMA2

- Insulin
- Glyburide
- Metformin

Prenatal visits every 1-2 wks

- Growth US
- Antenatal testing
Medical Therapy

Options

Insulin

Oral hypoglycemic agent
Concern with Insulin

- Difficulty storing medication
- Difficulty administering injections
- Hypoglycemia
Hypoglycemia

- Unaware- asymptomatic
- Moderate hypoglycemia 71%
- Severe hypoglycemia (LOC) 34%
- Peaks as 10-15 wks

Gabbe Obstet Gynecol 2002
Glyburide

- Second generation sulphonylurea
- Micronase, Diabeta
- Does not cross the placenta
- Start at 2.5 mg daily or BID, increase as needed
- Maximum dose is 10 mg BID (total 20 mg/day)
- Onset 4 hrs, duration 10 hrs
Glyburide

Randomized controlled trial

Glyburide (n=201)

Insulin (n=203)

Langer concluded that glyburide was a clinically effective alternative to insulin therapy in women with gestational diabetes

Langer NEJM 2000
Glyburide

- Comparable improvement in glucose control
- The failure rate was 4%
- No difference in maternal complications, neonatal outcomes or cesarean sections
- Glyburide was not detected in the cord serum
- Hypoglycemia was more frequent with insulin (20% vs. 2%)
### Glyburide Failure

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Study Type</th>
<th>n</th>
<th>Failure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Langer</td>
<td>2000</td>
<td>RCT</td>
<td>201</td>
<td>4%</td>
</tr>
<tr>
<td>Kremer</td>
<td>2004</td>
<td>Retrospect</td>
<td>73</td>
<td>20%</td>
</tr>
<tr>
<td>Chmait</td>
<td>2004</td>
<td>Prospect, obs</td>
<td>69</td>
<td>18%</td>
</tr>
<tr>
<td>Conway</td>
<td>2004</td>
<td>Retrospect</td>
<td>75</td>
<td>16%</td>
</tr>
</tbody>
</table>
Glyburide

Risk factors for glyburide failure

- High fasting blood glucose $>110$ mg/dl
- Higher pre-pregnancy weight $>180$ lbs
- Higher weight at delivery $>216$ lbs

Conway Obstet Gynecol Surv 2004
Haileleul SAAOG 2004
Hypoglycemia

- Continuous glucose monitoring for 72 hours
- Glucose < 40 mg/dL

<table>
<thead>
<tr>
<th></th>
<th>Regular Insulin (n=30)</th>
<th>Glyburide (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>63 %</td>
<td>28 %</td>
</tr>
<tr>
<td>Episodes/day</td>
<td>4.2 2.1</td>
<td>2.1 1.1</td>
</tr>
</tbody>
</table>

Hypoglycemia occurred nocturnally on insulin (84%)  

Yogeve Obstet Gynecol 2004
Metformin

- Biguanide
- Glucophage
- Decreases hepatic glucose production
- Crosses the placenta
- PCOS-
  - reduces rate of spont Ab
  - reduces risk of GDM
  - reduces risk of macromia

Glueck Fertil Steril 2002
Simmons MJA 2004
Metformin in pregnancy

- Initially used in prospective studies of type 1 dm
  - Metformin (n=22) vs. insulin (n=42)
  - No differences in perinatal mortality or rate of macrosomia
  - No cases of maternal hypoglycemia, lactic acidosis or congenital anomalies

Coetzee S Afr Med J 1984
Coetzee Diabet Research Clin Pract 1986
Metformin in pregnancy

- Cohort study 118 type 2 dm in pregnancy, concern regarding increased risk of preeclampsia
  
  *Hellmuth Diabet Med 2000*

- RCT of women with PCOS
  - Higher live birth rate 75% vs. 34%
  - Reduced rate of spont Ab 17% vs. 62%
  - Reduces rate of GDM 3% vs. 31%

*Glueck Human Reprod 2002
Glueck Fertil Steril 2002
Simmons Med J Aust 2004*
Metformin in pregnancy

Women with GDM randomized to metformin vs. insulin

Australia and New Zealand
363 women with Metformin
370 Women with Insulin

Rowan NEJM 2008
Metformin in pregnancy

Composite Morbidity
- Neonatal hypoglycemia
- RDS
- Phototherapy
- Birth Trauma
- 5 Min Apgar < 7
- Prematurity
Metformin in pregnancy

- Of the women on metformin, 46.3% required supplemental insulin.
- There was no difference in composite morbidity.
- No difference in secondary outcomes.
- No serious adverse events.
Management of GDM who fail oral agents

- Insulin (0.7-1.0 Unit/kg actual wt)
  2/3 total dose in fasting state
  2/3 NPH & 1/3 regular
  1/3 total dose at dinner & bedtime
  1/2 R dinner & 1/2 NPH bedtime
**Starting Dose of Insulin in Mild GDM**

<table>
<thead>
<tr>
<th>Blood Sugars Out of Target</th>
<th>Insulin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting only</td>
<td>.2 units/kg NPH at bedtime</td>
</tr>
<tr>
<td>Post-breakfast</td>
<td>2-4 units regular</td>
</tr>
<tr>
<td>Post-lunch</td>
<td>3-5 units regular at dinner</td>
</tr>
</tbody>
</table>
Fetal Testing
GDM requiring insulin or oral hypoglycemic

- Ultrasound at 32-34 wk for growth/AFI
- EFW prior to induction
- BPP (NST) weekly at 32-34 wk
Timing of delivery
GDM requiring insulin or oral hypoglycemic

• Deliver at 38-39 wk if good control
• Poorly controlled patients
  • Elective delivery ≥ 37 wks
• No amniocentesis
Intrapartum Management of GDM

- Give usual dose of insulin night before
- Omit morning dose prior to induction
- Limit carbohydrate intake
- Maternal blood glucose 70-100 mg/dl
- Use IV insulin if needed
- Offer c/s if EFW > 4500 grams or 4000 grams with other factors
Postpartum Management of GDM

• 75-g oral GTT at 6-8 wk
  • FPG ≥ 108 mg/dl or 2h ≥ 200 (DM)
  • FPG < 108 mg/dl & 2h < 140 (normal)
• Encourage exercise and weight loss
• Low-dose estrogen + progestin OCP/IUD
  • Avoid Progestational agents/Depo-provera
# White Classification for DM

<table>
<thead>
<tr>
<th>Class</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Onset ≥20 yr or duration &lt; 10yr</td>
</tr>
<tr>
<td>C</td>
<td>Onset 10 -19 yr or duration 10-19yr (no vascular dz)</td>
</tr>
<tr>
<td>D</td>
<td>Onset &lt;10 or duration ≥20 yr or retinopathy or HTN only</td>
</tr>
<tr>
<td>F</td>
<td>Nephropathy (≥500mg proteinuria at &lt; 20 wk)</td>
</tr>
<tr>
<td>H</td>
<td>Arteriosclerotic heart disease</td>
</tr>
<tr>
<td>R</td>
<td>Proliferative retinopathy</td>
</tr>
<tr>
<td>T</td>
<td>History of renal transplant</td>
</tr>
</tbody>
</table>
Management of Pre-gestational DM in Pregnancy

Pre-Conception/First Visit

- Evaluate Prior Ob History

- Evaluate Glucose Control
  - HgbA1C (target< 6%)
  - FBG <100mg/dL

- Evaluate Medications
  - Oral agents/insulin
  - Anti-hypertensives/others

- Evaluate for Co-Morbidities
  - HTN/Proteinuria/Anemia
  - Heart Dz/Eyes/Thyroid
Management of Pre-gestational DM
Antepartum

- Tight Glucose Control
- Frequent adjustment of insulin
- Low threshold for hospitalization
  - Diabetic education, insulin teaching
  - Evaluation of organ damage
- Urine culture Q trimester
- Fetal echo if abnormal HgA1C
- Serial fetal testing @ 32wk
- Delivery ≥ 37 wk
Activity Profiles of Different Types of Insulin

Aspart, lispro, glulisine

Regular

NPH

Detemir

Glargine

Plasma Insulin Levels vs. Hours
## Insulin regimens

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Onset</th>
<th>Peak action(hr)</th>
<th>Duration (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lispro</td>
<td>1-15 min</td>
<td>1-2</td>
<td>4-5</td>
</tr>
<tr>
<td>Regular</td>
<td>30-60 min</td>
<td>2-4</td>
<td>6-8</td>
</tr>
<tr>
<td>NPH</td>
<td>1-3 hr</td>
<td>5-7</td>
<td>13-18</td>
</tr>
<tr>
<td>Lente</td>
<td>1-3 hr</td>
<td>4-8</td>
<td>13-20</td>
</tr>
<tr>
<td>Ultralente</td>
<td>2-4 hr</td>
<td>8-14</td>
<td>18-30</td>
</tr>
<tr>
<td>Lantus</td>
<td>1 hr</td>
<td>No peak</td>
<td>24</td>
</tr>
</tbody>
</table>
Factors Associated with Adverse Pregnancy Outcome

- Pre-eclampsia
- Pyelonephritis
- Polyhydramnios
- Poor compliance
- Poor management
Management of Pre-gestational DM

Intrapartum/Pre-Term

- Magnesium sulfate for PTL
- Avoid terbutaline
- Beware of steroids
- Insulin drip if necessary
  - Target FS: 60-90 mg/dL
- Indications for c/s as for GDM
- Wound infections
Factors Leading to Increased Dose of Insulin

Conditions
Fever / Infection
Terbutaline
Corticosteroids

Adjusting dose of basal insulin
Double dose on day 1
Double dose on day 2
1.5 X dose on day 3
Usual dose on day 4
Diabetic Nephropathy

- **Definition**
  - Protein excretion > 300mg/24 hr at \( \leq 13 \) wk
  - Protein 300-500mg/24 hr at < 20 wk

- **Prevalence of 5-10%**
  - Due to increased Type 2 DM

- **With or without HTN**
  - Various stages of renal involvement

*Sibai, BM. Nephropathy in Diabetic Pregnancy*
Diabetic Nephropathy

Pathophysiology

• #1 cause of renal failure
• Exact mechanism unclear

Disease / progression different in T1 vs T2

Progressive hypertrophy/hyperfiltration

• Glomerular damage
• Renal failure
• Progression of proteinuria
  • Normal
  • Incipient (30–299mg/24)
  • Overt (>300mg/24)
Effect of Pregnancy on Renal Function

Creatinine clearance
- Changes are variable
- 1/3 have an increase

Proteinuria
- 26/46 (58%) \( \uparrow >1g/24 \) from 1\(^{st}\) \( \rightarrow \) 3\(^{rd}\) trimester
- 25/46 (56%) excreted \( >3g/24h \)

Mild renal dysfunction (Cr <1.4; protein <3g/24)*
- Minimal impact on long-term function
- No \( \uparrow \) progression to overt nephropathy

Moderate-severe nephropathy (Cr > 1.4)*
- 45% accelerated, irreversible decline in function
- ESRD /dialysis during or after pregnancy

* Outcomes influenced by glycemic control, HTN, preeclampsia
## Diabetic Nephropathy Pregnancy Outcomes (%)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preeclampsia</strong></td>
<td>15</td>
<td>33</td>
<td>35</td>
<td>35</td>
<td>53</td>
<td>40</td>
<td>51</td>
<td>36</td>
</tr>
<tr>
<td><strong>PTB &lt; 35 wk</strong></td>
<td>30.8 *</td>
<td>46</td>
<td>21 **</td>
<td>22.5 *</td>
<td>15.5 *</td>
<td>15 **</td>
<td>25 *</td>
<td>36</td>
</tr>
<tr>
<td><strong>IUGR</strong></td>
<td>20.8</td>
<td>--</td>
<td>19</td>
<td>19.4</td>
<td>11</td>
<td>12</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td><strong>Perinatal Survival</strong></td>
<td>88.9</td>
<td>100</td>
<td>91</td>
<td>93.5</td>
<td>100</td>
<td>95</td>
<td>94</td>
<td>98</td>
</tr>
<tr>
<td><strong>C/S</strong></td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>70</td>
<td>80</td>
<td>--</td>
<td>82</td>
<td>--</td>
</tr>
</tbody>
</table>

* PTB < 34 wk  
** PTB < 32 wk
Pregnancy in Diabetic Nephropathy
Factors associated with Poor Outcomes

- Cr $\geq 1.4$ mg/dl (124 µmol/L)
- Proteinuria $> 3$ g/24 h
- Chronic HTN $> 5$ years
- Left ventricular dysfunction by ECHO
- Ischemic changes on ECG
- Poor compliance with insulin and/or antihypertensive therapy
- Poor outcome in a previous pregnancy
Management of Diabetic Nephropathy

Maternal

• Glycemic control
  • Hg A1C at first visit
  • Frequent self blood glucose monitoring
  • Frequent prenatal visits
Management of Diabetic Nephropathy

Maternal

- Hypertension
  - Goals of therapy 130/80
  - Monthly CBC, CMP starting at 24 wk
  - ACE-I/ARB prior to pregnancy
    - Discontinue at conception
  - Calcium channel blockers
    - 1st line agent
    - Provide renal protection similar to ACE-I
  - Beta blockers – 2nd line agent
Management of Diabetic Nephropathy

Fetal

- Serial growth
- UA Doppler if FGR
- Weekly testing at 28 wk
- Delivery 34-37 wk
  - Dependent on severity
  - Co-morbidities, etc.
Risk Factors for DKA

• Non-compliance with insulin therapy
• Undiagnosed diabetes/GDM
• Acute infections
  • Pyelonephritis
  • Pneumonia
  • Other
• Protracted vomiting
• Use of β-sympathomimetic tocolytics
• Corticosteroids for fetal lung maturity
• Inadequate circulating insulin
• Increased insulin sensitivity

**Reduced glucose utilization/storage**
- Muscles
- Liver
- Adipose cells

**Increased counter regulatory hormones**
- Glucagon
- Cortisol
- Catecholamines
- Growth hormone

**Increased hepatic glucose production**
- Gluconeogenesis, glycogenolysis
- Increased ketogenesis (liver)
- Increased lipolysis

**Release of FFA → Ketone bodies**
- $3\beta$-hydroxybutyrate
- Acetoacetate
- Acetone

**Hyperglycemia**
- Osmotic diuresis
- Hypovolemia
- Loss of potassium
- Fetal hyperglycemia & hyperinsulinemia

**Maternal acidosis**
- Fetal Acidosis

• Maternal acidosis
• Fetal Acidosis
### Signs & Symptoms

<table>
<thead>
<tr>
<th>Signs</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperventilation - tachypnea</td>
<td>Polyuria</td>
</tr>
<tr>
<td>Tachycardia/hypotension</td>
<td>Polydypsia</td>
</tr>
<tr>
<td>Dehydration (dry mucous membranes)</td>
<td>Nausea/vomiting</td>
</tr>
<tr>
<td>Change in sensorium/disorientation</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Fruity breath (increased acetone)</td>
<td>Blurred vision</td>
</tr>
<tr>
<td>Coma</td>
<td>Muscle weakness</td>
</tr>
</tbody>
</table>
Laboratory Findings

- Serum glucose > 300 mg/dl (> 200mg/dl)*
- Arterial pH < 7.30 (< 7.25)*
- Serum bicarbonate < 15 m Eq/L*
- Anion gap > 12 m Eq/L
- Serum Ketones (+)**

* These values are variable
** Acetest or ketosticks only detect acetoacetate
Monitoring of DKA

- Medical/Obstetric ICU
- Vital signs every 15 mins
- Large bore IV catheter or central line
- ABG, glucose, electrolytes, ketones (q 1-2 hr)
- Urine for analysis, culture, ketones
- Oxygen by face mask at 6 L/min
- Continuous pulse oximetry
- Continuous FHR monitoring (≥ 24 wks)
- Evaluate for infection
- Bedside flow-sheet
  - Intake - output
  - Results of serial blood tests
  - Medications
Treatment of DKA

- **Insulin**
  - Bolus 10-15 U, maintenance 0.1 U/kg/h
  - Fluid replacement (deficit ~ 100 ml/kg body weight)
  - 1 L (0.9% NS) first & second hr
  - 0.5 L/hr, third hr
  - 0.25 L/hr, 4-24 hrs

- Add 5% dextrose to IV if glucose < 250 mg/dl

- Monitor serum glucose & ketones every hr

- Potassium replacement if serum $K^+ < 5$ mEq/L
  - Potassium chloride (20-40 mEq/hr)
  - Potassium phosphate

- Continuous FHR monitoring
Maternal DKA
Reversible Fetal Hypoxia-acidosis*

- Metabolic acidosis
  - Increased Hgb affinity to $O_2$
  - Less oxygen to fetus
  - Fetus unable to exchange acids

- Reduced tissue perfusion

- Hyperglycemia
  - Fetal hyperglycemia, ↑ insulin
  - Increased oxygen requirements

*Usually last 6 hrs before correction*
Transient Changes in Fetal Testing in DKA

- Fetal heart rate
  - Tachycardia
  - Absent accelerations
  - Poor variability
  - Late decelerations
- Abnormal biophysical profile
- Doppler (redistribution of blood flow)
  - Increased umbilical artery PI
  - Reduced middle cerebral artery PI
Absent variability
Absent variability with decelerations
Biophysical profile = 2/10
Minimal variability and repetitive late decelerations
Incipient Nephropathy

Normal serum CR and/or microalbuminuria (30-300 mg/24 h) or proteinuria (190-499 mg/24 h) < 20 wk

<table>
<thead>
<tr>
<th>Study - Author</th>
<th>No. of women</th>
<th>Preeclampsia</th>
<th>PTB &lt;34 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coombs et al (1993)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;190 mg/24hr</td>
<td>204</td>
<td>20 (10)</td>
<td>47 (23)</td>
</tr>
<tr>
<td>190-499 mg/24hr</td>
<td>45</td>
<td>18 (40)</td>
<td>23 (51)</td>
</tr>
<tr>
<td>&lt;190 mg/24hr</td>
<td>94</td>
<td>16 (17)</td>
<td>12 (13)</td>
</tr>
<tr>
<td>190-499 mg/24 hr</td>
<td>35</td>
<td>7 (20)</td>
<td>5 (14) *</td>
</tr>
<tr>
<td>Ekbom et al (2000-01)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-278 mg/24hr (2000)</td>
<td>26</td>
<td>11 (42)</td>
<td>16 (62)</td>
</tr>
<tr>
<td>30-300 mg/24hr (2001)</td>
<td>30</td>
<td>13 (43)</td>
<td>NR</td>
</tr>
</tbody>
</table>