**Diabetes in Pregnancy**

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**GESTATIONAL DIABETES: DIAGNOSIS AND MANAGEMENT**

LEARNING OBJECTIVES:
- To identify risk factors for gestational diabetes.
- To discuss methods of screening and diagnosis of gestational diabetes.
- To discuss the complications of gestational diabetes and pregestational DM.
- To discuss the management of diabetes in pregnancy.

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**GESTATIONAL DIABETES**

"Any degree of glucose intolerance with onset or first recognition during pregnancy..."

*Fourth International Workshop-Conference on GDM 1997*

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**GESTATIONAL DIABETES MELLITUS**

Type II DM (Adult onset DM)

- Long associated with poor obstetrical history, i.e. large babies, stillbirth.
- Gestational DM considered since 1965.

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**Glucose Intolerance in Pregnancy**

- 15% Abnormal 1 hour screen
- 15% Abnormal 3 hour OGTT
- 15% Fail diet therapy

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**GESTATIONAL DIABETES MELLITUS CLASSIFICATION**

- White’s Classification
  - Class A1: diet controlled, blood sugar normal
  - Class A2: insulin required to normalize blood sugar
GDM—WHY DO WE CARE?

- Increased risk for fetal macrosomia (16-45% of GDM fetuses)
- Fetal macrosomia associated with risk of:
  - Maternal trauma at delivery and c-section
  - Neonatal birth injuries
  - Neonatal metabolic changes
  - Childhood obesity
  - DM, questionable decreased IQ
- Insulin requirement in 15% with ↑ PNM risk

Macrosomia

Pathophysiology

Maternal hyperglycemia
→
Fetal hyperglycemia
→
Fetal hyperinsulinemia
→
Denovo lipogenesis
→
Fetal obesity

Gestational Diabetes Mellitus

Significance

↑ Long Term Morbidity
- Childhood obesity
- Type 2 Diabetes

Gestational Diabetes Mellitus

Significance

↑ Subsequent Glucose Intolerance
- Up to 50-70% develop Type 2 diabetes mellitus

Diabetes Mellitus

Fetal Complications

- >4,000 - 4,500 gm
- 50% of GDM
- 40% of pre-gestational DM
  - fetal hyperglycemia results in excessive fetal growth
  - increased risk of birth trauma, fetal loss, childhood/life-long obesity, development of Type 2 diabetes
Shoulder Dystocia
- Brachial plexus injury
  - Erb’s palsy: upper arm paralysis (C5,6)
  - Klumpke: lower arm paralysis (C8,T1)
- Fractured clavicle
- Fractured humerus
- Fetal hypoxemia
- Know maneuvers to treat shoulder dystocia

Respiratory Distress Syndrome
- Exact mechanism unknown
- Decreased with improved control
- Rare after 39 weeks

Congenital Malformations: Pregestational DM
- Insult that causes malformations generally prior to 7 weeks
- A1C < 8.5%—3.4% major anomalies; ≥ 8.5—22.4% major anomalies (Miller et al)
- CNS malformations: 10-fold increase
  - Anencephaly, ONTD, Holoprosencephaly
- Cardiac anomalies: 5-fold increase
  - VSD, Transposition of the Great Vessels

Congenital Malformations: Sacral agenesis or caudal dysplasia
- 200—400 x more common

Congenital Malformations: Pregestational DM
- Teratogenic factors
  - Maternal hyperglycemia
  - Ketone excess
  - Excess free oxygen radicals
- Typical patient profile
  - Poor periconceptional control
  - Long-standing diabetes
  - Vascular disease

Intrauterine Growth Restriction: DM
- Vascular disease causing decreased uterine blood flow
- Pre-eclampsia/CHTN
- Pregestational DM
- Not usually found in GDM
Fetal Death: DM

- More common after 36 weeks with
  - Vascular disease
  - Poor glycemic control
  - Polyhydramnios
  - Fetal macrosomia
  - Pre-eclampsia

Maternal Complications-DM

- Spontaneous abortion
- Pre-eclampsia
- Cesarean section
- Birth trauma
- DKA
- Hypoglycemic coma
- Infections (UTI, pyelo)
- Postpartum hemorrhage

Screening for Diabetes Mellitus

Glucose Metabolism

- Human placental lactogen (HPL)
  - Produced by the placenta
  - Promotes lipolysis
  - Decreased glucose uptake
    - "anti-insulin"
  - Peaks 24 – 28 weeks

Neonatal Complications-DM

- Hypoglycemia
  - Maternal/fetal hyperglycemia
  - 50% of macrosomic babies
- Hypocalcemia
  - Failure of PTH production at birth
- Magnesium deficiency
- Hyperbilirubinemia
  - 25-50% have neonatal jaundice
- Polycythemia
  - Increased erythropoietin

Testing for Gestational DM

Screening Test
- 1 hour glucose challenge

Diagnostic Tests
- 3 hour 100g glucose tolerance test
- 2 hour 75g GTT
Glucose Challenge Test

Performed at 24-28 weeks
Oral glucose load = 50 grams
Normal < 140 mg %

Oral Glucose Challenge

• 140 mg% ~ 90% sensitivity, 15% positive
• 130 mg% ~ 100% sensitivity, 23% positive

Oral Glucose Challenge

Fasting or Fed

- No difference in normals
- GDM, higher if fasting (173.9 ± 28.8) vs. post-meal (154.8 ± 24.1)
- Consider lowering cutoff to 130 mg % if fed
  Coustan et al, 1986

High Risk for GDM (early testing):
>25 BMI + one or more--

• Physical inactivity
• 1st degree relative with DM
• HR race/ethnicity (AA, Asian, Latino, native American)
• Prior baby >4000g
• Prior GDM
• HTN
• PCOS
• A1C > 5.6
• CV disease; low HDL; high TG
• BMI > 40 alone

• ***repeat 24-28 weeks if normal***       ACOG # 180, 2017

Early Screening Tests

1 hr 50 g GTT/3 hr 100g GTT
Positive screen, neg 3 hr—
  repeat 3 hr at 24-28
Hb A1C-poor sensitivity

3 hour GTT

<table>
<thead>
<tr>
<th>Group</th>
<th>Fasting</th>
<th>1hr</th>
<th>2hr</th>
<th>3hr</th>
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<tr>
<td>NDDG</td>
<td>105</td>
<td>190</td>
<td>165</td>
<td>145</td>
</tr>
<tr>
<td>Carpenter</td>
<td>95</td>
<td>180</td>
<td>155</td>
<td>140</td>
</tr>
</tbody>
</table>

**no data to suggest which is superior**
Management

- **Dietary**
- **Glucose monitoring**
- **Medical therapy**
- **Fetal assessment**
- **Labor & Delivery**
- **Postpartum**

**DIETARY MANAGEMENT**

- Enables normalization of glycemia in 80-90% of GDM patients [Class A1]
- Meal plans and caloric requirements individualized based on weight and height -1800-2400 kcal/day [30-35 kcal/kg/day]
- Usually 3 main meals and 2 to 3 snacks
- 35-40% CHO, 20% protein and 40% fat
- Refer diabetic education

**DIET MANAGEMENT**

- Diet achieves euglycemia in most patients.
- “Low CHO” diet [35-40%] is most beneficial.
- Diet should be individualized according to each patient’s response to food ingestion.
- Caloric restriction may be option in motivated patient ie: 1800 cal/day.

**CARBOHYDRATE RESTRICTION**

- RCT N=21 per group
- low CHO < 42%
  - high CHO > 45%
- low CHO group had
  - lower post-prandial BS
  - lower insulin requirement
  - lower LGA and C/s

**EXERCISE EFFECTS**

- Reduces insulin requirements by up to 50%
- Increases insulin sensitivity in Type 2 DM
- Acutely lowers glucose levels, particularly post-breakfast.
- Exact mechanism is unknown
- 30 minutes 5 days weekly aerobic exercise (ACDG, 2017)

**Glucose Monitoring**

- **Home monitoring**
  - Fasting, 1-2 hour post-prandial daily
- **Intermittent weekly monitoring**
  - Fasting, one post prandial weekly
- A1C each trimester (pre-gestational DM)
TARGET PLASMA GLUCOSE
PREGNANCY

FASTING < 95 MG %
1 HOUR POST-MEAL < 140 MG %
2 HOUR POST-MEAL < 120 MG %

Why Check Post-Prandial Values?

• Post-prandial BS become abnormal before fasting and pre-meal BS
• Several authors have correlated post-prandial hyperglycemia in GDMs with macrosomia
• Postprandial-SBGM leads to better glycemic control through more aggressive management \( \rightarrow \) less macrosomia & CS

THRESHOLDS FOR STARTING INSULIN

• Failure to achieve euglycemia
  - FBS > 95 mg/dl
  - 2 hr post-prandial > 120 ; 1 hr >140
    [10-15% values elevated]
• Evidence of developing macrosomia by U/S screening at 29-33 weeks gestation.

Insulin Types

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<tr>
<th></th>
<th>Onset</th>
<th>Duration</th>
<th>Peak</th>
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<tbody>
<tr>
<td>Regular</td>
<td>1 hour</td>
<td>6 hours</td>
<td>2-3 hours</td>
</tr>
<tr>
<td>NPH</td>
<td>2 hours</td>
<td>24 hours</td>
<td>8 hours</td>
</tr>
<tr>
<td>Log</td>
<td>1-10 min</td>
<td>4-5 hours</td>
<td>1-2 hours</td>
</tr>
<tr>
<td>Levemir</td>
<td>1-3 hours</td>
<td>18-26 hrs</td>
<td>Min at 8-10 hr</td>
</tr>
<tr>
<td>Lantus</td>
<td>1-2 hours</td>
<td>24 hours</td>
<td>none</td>
</tr>
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INSULIN LISPRO [Humalog]

• A newer insulin analogue, rDNA
• More rapid onset than Regular, more convenient
• Peaks at 1 hour vs. 2 hours with Regular
• Shorter duration of action
• May benefit GDMs by specifically reducing post-prandial hyperglycemia

INSULIN DOSING

0.5-1.0 UNITS/KG divided doses
(0.5 < 20 weeks; 1.0 > 20 weeks)

20 N/10 LOG AM; 10 LOG SUPPER; 10 N @HS

Target elevated BS
Insulin Therapy

AM 2/3  PM 1/3
↓                     ↓
NPH /Reg or Humalog  R or H /NPH
2/3  1/3             1/2  1/2

Glucose Control and Fetal Size

N=246

• Mean glucose > 105 mg %, 24% LGA
• Mean glucose < 105 mg %, 9% LGA

Langer and Mazze, AJOG, 1988;159

Antepartum Assessment

Serial growth every 4 weeks.
No antenatal testing for A1 well controlled.
BPP or NSTs for A2 well controlled weekly starting at 32 weeks
BPP and/or NSTs twice weekly poorly controlled, vascular disease, etc.

Delivery

• Gestational, pregestational well controlled: 39-40 week delivery
• Poorly controlled gestational or pregestational: individualize-late preterm vs early term (34w-36w6d; 37w0d-38w6d)

Gestational Diabetes

Mode of Delivery

• Vaginal preferred
• Cesarean considered if Efwt > 4500 grams
• Individualize each case

Labor Management

• Blood glucose every 1-2 hours
• BS> 120 mg %, consider insulin drip vs slide scale with log
• Maintain glucose < 120 mg %
• IV Fluid DS 0.45% NS at 125 cc/hour
Glucoregulation during L&D

- Usual dose of PM insulin
- Hold AM insulin, patient is NPO
- If C-section, schedule first case
- If laboring, check every 1 (IDDM)-2 (GDM) hours and maintain glucose 70 – 120 mg/dl
- May need insulin drip to control
- Slide scale SQ is also acceptable

Slide Scale Insulin (log)

**Low dose SQ**

- 121-149        1 unit
- 150-199        2 units
- 200-249        3 units
- 250-299        4 units
- ≥ 300          Call

**High dose SQ**

- 121-149        3 units
- 150-199        6 units
- 200-249        9 units
- 250-299        12 units
- ≥ 300          Call

METFORMIN

- Biguanide
- Inhibits liver gluconeogenesis, absorption of glucose and stimulates glucose uptake in peripheral tissues
- Crosses placenta near maternal levels
- GI upset/diarrhea
- Similar outcomes as insulin
- BUT--- slight increase PTB but lower GHTN (vs insulin)
- 25-45% fail and require insulin

Metformin

- Used in pregestational DM and may be continued in pregnancy
- Frequently used in PCOS patients to improve ovulation and decrease insulin resistance
- Often continued in pregnancy to decrease spontaneous abortion in the first trimester
- Some recommend continued use throughout to reduce the risk of GDM
- Can be used for treatment of GDM

Metformin

- Start 500mg qHS
- Increase up to 3000mg / day divided

INSULIN IS 1ST LINE THERAPY (ACOG, 2017)

Glyburide

- Oral hypoglycemic – 2nd Generation Sulfonylurea
- Outpatient management
- Check LFT’s
- Same diet and therapeutic goals
- Starting dose: 2.5 mg daily
- Maximum dose: 20 mg daily – divided
- Better side effect panel than metformin
- Better patient acceptance
- Associated with larger birthweights; more failures
Glyburide

- Sulfonylurea—avoid with sulfa allergy
- Increases insulin secretion from beta cells
- Increases peripheral tissue insulin sensitivity

Insulin Therapy

- Insulin is initiated when therapeutic goals are exceeded with diet/exercise/oral agent
- Usually started inpatient; outpatient reasonable with reliable, educated patient
- Divided AM and PM dosing
- Mixture of short- and long-acting insulin to achieve therapeutic goals
- May target dosing for specific elevations

Pregestational Diabetes

- Ideally done preconception, but usually done in the first trimester
- Folic acid supplementation
- HgbA1C
- 24 hour urine – protein and creatinine cl
- Renal function
- Eye exam
- EKG if vascular disease or CHTN
- Nutrition consult
- ASA low dose

Pregestational Diabetes

- Early ultrasound for accurate dating
- Offer prenatal diagnosis (1st and 2nd tri)
- Anatomy survey at 18 – 20 weeks
- Fetal echo at 22 weeks

Postpartum Management

- Pregestational diabetics: resume insulin at 50% of the prepregnancy dose and adjust as needed
- GDM resolves following delivery
- GDM check BS while pp in hospital
- Diabetes screening 6 – 12 weeks following delivery
- Increased lifetime risk of Type 2 Diabetes (~50%)

Insulin Drip

50 units regular/500 cc NS

10 cc/hr equals 1 unit/hour
General pregnancy issues

- AMA: NST/BPP from 36 weeks
- BMI>35: serial growth every 6 weeks, testing from 36 weeks
- Hyperthyroid: growth, testing as with CHTN. Serial growth only with hypothyroid (no testing)

- 25 yo G1 at 36w 4d (Thursday)
- A1C 7.3 second trimester, 8.3 at 34 weeks
- US at 32 weeks normal fluid, EFW 50%tile
- Repeat US poly at 38cm, EFW 98%tile (9#12)
- BPP, NST normal
- Plan?