Diabetes and Pregnancy

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Objectives

• Discuss and Review Gestational Diabetes Mellitus (GDM) and Treatment

• Discuss and Review Pre-Existing Diabetes in Pregnancy and Treatment

• Learn management of common problems of Diabetes in Pregnancy
Diabetes and Pregnancy

- Increased rate of GDM and pre-existing DM in pregnancy 1980-2008:
  - 0.95% to 1.81% (pre-existing) whites
  - 4.09% to 6.92% (GDM) whites
  - 1.66% to 3.17% (pre-existing) blacks
  - 3.98% to 6.58% (GDM) blacks

Increasing numbers - obesity, other DM risk

Hunt K, et al  *Obesity Society* 2012
Gestational Diabetes Mellitus
Gestational Diabetes

- Reduced sensitivity to insulin in 2nd and 3rd trimesters
- “Diabetogenic State” when insulin production doesn’t meet with increased insulin resistance

Crowther, et al *NEJM* 352:2477–2486, 2005
Gestational Diabetes

- Human placental lactogen, leptin, prolactin, and cortisol result in insulin resistance
- Lack of diagnosis and treatment - increased risk of perinatal morbidities

Crowther, et al *NEJM* 352:2477–2486, 2005
Gestational Diabetes

- Occurs in 2-9% of pregnancies
- ~135,000 cases in U.S. annually
- Lifestyle management
- Insulin (usually preferred, better efficacy) or sulfonylureas (in very select cases)
Gestational Diabetes and Type 2 Diabetes Risk

• Gestational Diabetes should be considered a pre-diabetes condition
• Women with gestational diabetes have a 7-fold future risk of type 2 diabetes vs. women with normoglycemic pregnancy
• 35-60% go on to have DM

GDM Complications

- Macrosomia
- Fractures
- Shoulder dystocia
- Nerve palsies (Erb’s C5-6)
- Pregnancy outcomes can be very poor with HTN/nephropathy
- Neonatal hypoglycemia

Gabbe, Obstetrics: Normal and Problem Pregnancies 2002
Gestational Diabetes: Outcomes

- Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) Study 28,000 women
- Good GDM management improves outcomes

NEJM (358) 2008
Diabetes Care 2012
Gestational Diabetes (GDM) Screening

- Screen for **type 2 diabetes** first prenatal visit if risk factors
- Not known to have diabetes, screen for GDM at 24 –28 weeks of gestation

Diabetes Care 34:Supplement 1, 2011
### TABLE 2. Criteria for Testing for Diabetes or Prediabetes in Asymptomatic Adults

1. Testing should be considered in overweight or obese (BMI ≥25 kg/m² or ≥23 kg/m² in Asian Americans) adults who have one or more of the following risk factors:
   - A1C ≥5.7% (39 mmol/mol), impaired glucose tolerance, or impaired fasting glucose on previous testing
   - First-degree relative with diabetes
   - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - Women who were diagnosed with GDM
   - History of CVD
   - Hypertension (≥140/90 mmHg or on therapy for hypertension)
   - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
   - Women with polycystic ovary syndrome
   - Physical inactivity
   - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)

2. For all patients, testing should begin at age 45 years.

3. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results (e.g., those with prediabetes should be tested yearly) and risk status.
Gestational Diabetes (GDM) ADA

- Overnight fast, 75g OGTT
- Fasting $\geq 92$ mg/dl
- 1 h $\geq 180$ mg/dl
- 2 h $\geq 153$ mg/dl
Gestational Diabetes (GDM)
ACOG/Others

- 2 Step approach
- 1 hour 50gm OGT (screening) $>135-140$

Then proceed to 3 hour OGTT
Carpenter Coustan
3 hour OGTT

- Fasting $\geq 95$
- 1 hour $\geq 180$
- 2 hours $\geq 155$
- 3 hours $\geq 140$
- 2 or more of the above values

Can follow 1 hour screen, or as initial diagnostic test
GDM Screening

• A1C not ideal for GDM screening, but may be good for type 2 screening
• Fructosamine not good for screening
Gestational Diabetes Management

- Dietician
- Diabetes Educator
- Consider referral to Diabetologist or Endocrinologist
- Moderate Physical Activity ~30 minutes daily if appropriate

Summary and Recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus

Diabetes Care 30:5251-5260, 2007
Diabetes Care 2010; 33: 676–682
Glucose Control in GDM

• Preprandial: <95 mg/dl, and either:
  1-h postmeal: <140 mg/dl
  or
  2-h postmeal: <120 mg/dl
  and Urine ketones negative

Diabetes Care 2010; 33: 676–682
Gestational Diabetes-Medications

- Patients who do not meet metabolic goals within one week or show signs of excessive fetal growth
- **Insulin** has been the usual first choice
- Sulfonylureas (glyburide) or metformin- select cases? Long term safety lacking (metformin-prematurity?)
- Other diabetes medications not recommended in GDM
- Metformin for PCOS need not continue in pregnancy

Summary and Recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus

*Diabetes Care* 30:S251-S260, 2007


Diabetes Care 40 (S1) 2017
Insulin Safety in Pregnancy

• All insulins are pregnancy category B except for glargine, glulisine, and degludec, which are labeled category C
• Human Insulins-Least Immunogenic
• Breastfeed-All insulins considered safe

Data from Package Inserts
Gestational Diabetes-Management

- Fasting, pre-meal, 2-hour post-prandial blood glucose probably all important
- Mean blood glucose >105-115, greater perinatal mortality
- A1C in GDM probably not important except for type 2 screening

ADA Position Statement
Insulin Dosing-GDM

- Insulin dosing:
  - Can use usual weight based dosing (i.e., 0.5 u/kg)
  - Practical dosing can be to start 10 units NPH or detemir with evening meal
  - Most NPH will titrate to BID, with eventual addition of Regular or Rapid Acting BID
Alternate Insulin Dosing in GDM

- Regular or rapid acting (lispro or aspart) with meals,
  NPH or detemir at bedtime
- NPH + Regular or rapid acting in AM,
  regular or rapid acting at supper,
  NPH at bedtime
Insulin Titration in GDM

Titrate insulin based on SMBG values:

- Fasting 60-90
- Pre-meal $\leq 95$
- 2 hour post-meal $< 120$
- Bedtime $< 120$
- Occasional 3 AM
Gestational Diabetes: Post-natal

- Blood glucose testing first few days after delivery
- Fasting glucose rechecked 4-12 weeks following delivery
- Screen at least every 3 years thereafter to be screened for Type 2 Diabetes-high risk of developing Type 2 Diabetes (7x higher) and/or CVD

Diabetes Care 34:Supplement 1, 2011
Pre-existing Type 1 or Type 2 Diabetes in Pregnancy
Preconception Counseling

Also need to evaluate/treat

- Nephropathy
- Neuropathy
- Retinopathy
- Cardiovascular disease (CVD)
- Hypertension
- Dyslipidemia
- Psych
- Thyroid disease/Celiac disease
- Tobacco

Preconception Counseling

Meds to be evaluated

- Statins, many BP meds, many DM meds not used in pregnancy

- Continue multidiscipline patient-centered team care throughout pregnancy and postpartum.

Preconception Counseling

- Educate pregnant diabetic women about the strong benefits of
- Long-term CVD risk factor reduction
- Effective family planning with good glycemic control before the next pregnancy

Diabetes: Pregnancy Complications

- Cardiac: VSD, transposition of great vessels
- Anencephaly, Spina Bifida
- Sacral agenesis or caudal dysplasia
- Complications associated with polyhydramnios, oligohydramnios (i.e. growth retardation)
- Others as per GDM

Gabbe, Obstetrics: Normal and Problem Pregnancies 2002
Pre-Existing Diabetes and Pregnancy

• Pre-conception counseling (includes diabetes educator and dietician)

• Recommended pre-conception A1C as close to normal (6.0%)

• More Type 2 patients in child bearing years (diagnosed at younger age)

Lab Testing Pre-existing DM

**Initial Evaluation** (in addition to routine prenatal testing)

A1C  
Every 1-3 months

Fasting Lipid Profile  
Initial, f/u as indicated

TSH and thyroid anti-bodies  
Initial, f/u as indicated

CBC, serum ferritin  
Initial, f/u as indicated

LFT’s, consider liver U/S  
Initial, f/u as indicated

Urine microalbumin/protein  
If positive, 24 hour urine for total protein, creatinine clearance

Serum creatinine,  
Initial, f/u as indicated

Creatinine clearance  

Serum B12? Celiac?  
Every 1-6 months as indicated

Dilated retinal exam  

Lab Testing Pre-existing DM

**Initial Evaluation**
Assess risk factors for CHD

- Resting ECG* in asymptomatic patients age 35 years or older
- Other studies, i.e., stress testing, echocardiography if suspect for heart disease

*Kitzmillar, et al Diabetes Care 31:1060-1079, 2008*
Lab Testing in Pre-existing DM

Special Considerations in type 1 DM

• Celiac Screening: anti-tissue transglutamase or anti-endomysial antibody plus IgA level or TTG IgA and TTG IgG

• Thyroid testing

Glucose Targets in Pregnancy with Pre-existing Diabetes

- Premeal, hs, overnight glucose 60–99 mg/dl
- Peak postprandial glucose 100–129 mg/dl
- Mean daily glucose <110 mg/dl
- A1C ~6.5 or less with little or no hypoglycemia
- Higher glucose targets may be used in patients with hypoglycemia unawareness or the inability to cope with intensified management
- Control ‘too tight’ (avg <80-90 mg/dl)

Pre-existing Type 2 Diabetes Pregnancy

- Metformin and insulin are only recommended drugs
- Many will fail metformin
Pre-existing Type 2 Diabetes Pregnancy

• If already on insulin, continue
• Insulin needs increase as pregnancy progresses
• Controversy: Switch glargine to detemir or NPH?
• Continue lispro, aspart, or R if already using

Pre-existing Type 1 Diabetes and Pregnancy

• All continue on insulin
• Controversy: continue glargine or converted to detemir or NPH?
• Continue Regular/Rapid Acting
• If on pump, continue

Pre-Existing DM: Insulin

- In type 1 patients, may have a period of increased insulin sensitivity at 10-14 weeks.
- Type 1 and type 2 patients usually have marked increase in insulin requirements as pregnancy progresses.
- Converting type 2 patients to insulin as per discussion in GDM, may need larger doses initially (0.7-1.0 unit/kg).

Hypertension and Lipid Management

• Medications for Cholesterol discontinued
• BP: Same recommendations as GDM (i.e., methyldopa)
• Dietician consult (already in place, but to account for dyslipidemia if pre-existing or newly diagnosed)
• CHD present in 1 in 10,000 pregnancies, but 1 in 350 women with DM
• Stroke 4-8 times more common in women with type 1 or type 2 DM

Case #1

- 30 y/o white female
- Known Type 2 DM on Metformin 500mg BID
- Previous successful pregnancy 2 years ago on insulin, male infant 7lbs 11 oz. (3.5 kg)
- No known infertility history
- Now at 11 weeks, referred by primary provider
- A1C 3 weeks prior to consult 5.8, but some AM glucose elevations prior into 130’s
Case #1

- Metformin continued (but could consider stopping)
- Patient started on NPH 10 units at HS, and was told to titrate upwards 2-3 units every 3 or 4 nights until fastings <90 with no significant hypoglycemia
- Patient required BID NPH by 16 weeks
- R was started in evening with largest meal (along with NPH), eventually on BID NPH/R, although evening NPH moved to HS at approx week 25 to improve fasting glucose
- A1C not over 6.2 during pregnancy (checked q 8 weeks)
Case #2

- 25 y/o with Type 1 Diabetes of 12 years duration
- Had been on pump 5 years ago, now on MDI with detemir and aspart
- No previous pregnancies
- A1C at first visit (21 weeks gest) 7.8
- Went on sensor augmented pump (records blood sugar every 5 minutes 24 hours a day)
Sensor Data

HbA1c: No Data

Overlay by Meal Event (mg/dL)

- Breakfast
- Lunch
- Dinner

Pump: Paradigm 522
Sensor: In use

#411667
Case #2

- A1C’s after pump restart 5.4-5.6 for remaining pregnancy
- C-section for failure to progress at 39 weeks, stayed on pump entire hospitalization
- Mom, baby no complications
Case #3

- 24 y/o, first pregnancy, 28 weeks
- Difficulty gaining weight
- Fatigue for last month
- “urinating a lot, don’t you do that in pregnancy?”
Case #3

- OGGT
- Fasting 342
- 1 hour 460
- 2 hour 420
- What now?
Case #3

- Urine showed 3+ ketones
- This patient has type 1 diabetes
- Pregnancy is coincidental
- Started on MDI insulin immediately
Inpatient Diabetes Management

- Diabetes Educator and Dietician consult - Diabetes needs/program changes within hours of delivery of infant.
- Need to account for breast feeding (giving away calories)
- Continued pump or insulin drip most appropriate for patients on insulin, particularly more than one injection daily.
- Supplemental subcutaneous may be appropriate for well controlled GDM for a short period of time (24 hours or less)
- Often return to previous pre-pregnancy program within hours or days of delivery
Summary

• GDM: Start insulin if not meeting goals after one week
• Pre-existing type 2: Convert to insulin
• Pre-existing type : Continue insulin
• Meet targets, avoid hypoglycemia
• Continued comprehensive approach
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Slide Decks (Diabetes, Tobacco, other)
http://www.med.und.edu/familymedicine/slidedecks.html

iTunes Podcasts (Diabetes) (Free downloads)
http://www.med.und.edu/podcasts/ or search North Dakota Diabetes Podcasts

WebMD Page: (under construction)
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Diabetes e-columns (archived):
http://www.diabetesnd.org/
Acknowledgements

- William Zaks, M.D., Ph.D., Assistant Medical Director, Altru Diabetes Center, Grand Forks, ND

Slide and Content Review