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

Hod and Yogev **Diabetes Care** 30:S180-S187, 2007
Crowther, et al NEJM 352:2477–2486, 2005
Langer, et al *Am J Obstet Gynecol* 192:989–997, 2005

Gestational Diabetes

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

Hod and Yogev **Diabetes Care** 30:S180-S187, 2007
Crowther, et al NEJM 352:2477–2486, 2005
Langer, et al *Am J Obstet Gynecol* 192:989–997, 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)

Am J Obstet Gynecol 192:1768–1776, 2005
Diabetes Care 31(S1) 2008
Diabetes Care 25:1862-1868, 2002

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

Lancet, 2009, 373(9677): 1773-9

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
Lancet, 2009, 373(9677): 1773-9

TABLE 2. Criteria for Testing for Diabetes or Prediabetes in Asymptomatic Adults

1. Testing should be considered in overweight or obese (BMI ≥25 kg/m^2 or ≥23 kg/m^2 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 ≥92 mg/dl
- 1 h ≥180 mg/dl
- 2 h ≥153 mg/dl

Diabetes Care 35:Supplement 1, 2012
Diabetes Care 2010; 33: 676–682

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 ≥95
- 1 hour ≥180
- 2 hours ≥155
- 3 hours ≥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

Gynecol Obstet Invest 2011;71:207-212
Diabetes Care 34:Supplement 1, 2011
Lancet, 2009, 373(9677): 1773-9

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:S251-S260, 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 21(2):B161–B167, 1998
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
Langer et al *N Engl J Med* 343:1134–1138, 2000
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

Am J Obstet Gynecol 192:1768–1776, 2005
ADA Position Statement
Pettit, et al *Diabetes Care* 3:458–464, 1980
Karlsson, Kjellmer *Am J Obstet Gynecol* 112:213–220, 1972
Langer, et al *Am J Obstet Gynecol* 159:1478–1483, 1988

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 ≤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

Kitzmiller, et al Diabetes Care 30:S225-S235, 2007
Diabetes Care 34:Supplement 1, 2011
Lancet, 2009, 373(9677): 1773-9

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

Lawrence, et al Diabetes Care 31:899-904, 2008
Kitzmiller, et al Diabetes Care 31:1060-1079, 2008

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.

Lawrence, et al Diabetes Care 31:899-904, 2008
Kitzmiller, et al Diabetes Care 31:1060-1079, 2008

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

Lawrence, et al Diabetes Care 31:899-904, 2008
Kitzmiller, et al Diabetes Care 31:1060-1079, 2008

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
Kitzmiller, et al Diabetes Care 31:1060-1079, 2008

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)

Kitzmiller, et al Diabetes Care 31:1060-1079, 2008

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, Creatinine clearance	Initial, f/u as indicated
Serum B12? Celiac?	
Dilated retinal exam	Every 1-6 months as indicated

Kitzmiller, et al Diabetes Care 31:1060-1079, 2008

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

Kitzmiller, 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

Kitzmiller, et al Diabetes Care 31:1060-1079, 2008

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) fetal growth restriction

Kitzmiller, et al Diabetes Care 31:1060-1079, 2008
Management of Preexisting Diabetes and Pregnancy. Alexandria, Virginia, American Diabetes Association, 2008

Pre-existing Type 2 Diabetes Pregnancy

- Metformin and insulin are only recommended drugs
- Many will fail metformin

Diabetes Care January 2016 39(S1)

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

Kitzmiller, et al Diabetes Care 31:1060-1079, 2008

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

Kitzmiller, et al Diabetes Care 31:1060-1079, 2008

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)

Kitzmiller, et al Diabetes Care 31:1060-1079, 2008

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

Klein, et al Arch Intern Med 164:1917–1924, 2004
Kitzmiller, et al Diabetes Care 31:1060-1079, 2008

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

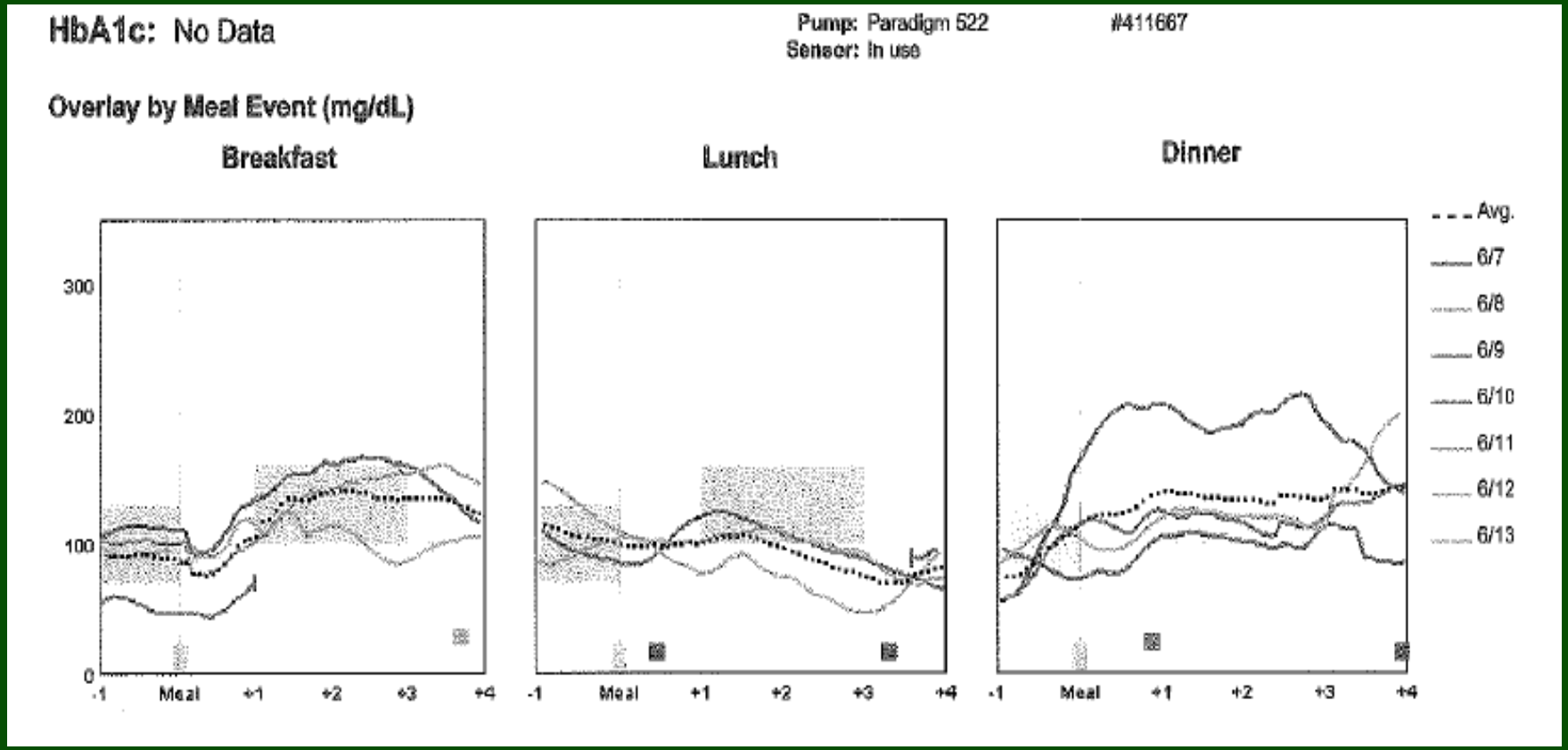
Case #1

- 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
Pump: Paradigm 522
Sensor: In use
#411667
Overlay by Meal Event (mg/dL)
Breakfast
Lunch
Dinner
300
200
100
0
-1
Meal
+1
+2
+3
+4
Avg.
6/7
6/8
6/9
6/10
6/11
6/12
6/13

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

- OGTT
- 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

Contact Info/Slide Decks/Media

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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)
http://www.webmd.com/eric-l-johnson

Diabetes e-columns (archived):
http://www.diabetesnd.org/

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Slide and Content Review