Diabetes: The Effects of Maternal Diabetes on Fetal Development and Outcomes

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Disclosure and Disclaimer

- This webinar is considered a resource, but does not define the standard of care in California. Attendees are advised to adapt the guidelines and resources based on their local facility’s level of care and patient populations served and are also advised to not rely solely on the guidelines presented here.

- I have nothing to disclose.
Objective

The attendee will be able to:

- Discuss the genetic and programmed risk of offsprings of women with diabetes.
- Discuss the effects of a woman having diabetes on her fetus / neonate.
- Discuss ways to prevent or lessen these adverse outcomes.
Pregestational Diabetes

- Type I diabetes
- Type II diabetes
- Pre-diabetes

Gestational Diabetes

- A₁ – Diet/Exercise controlled
- A₂ – Medication required
  - Oral hypoglycemics
  - Insulin
May include undiagnosed Type II DM
Prevalence

- 9.3% Diabetes (29.1 million)
- 37% Pre-diabetes (86 million)
- 5% Type I diabetes (1% pregnancy)
- GDM affects >200,000 women annually – 3 - 18% (dependent on screening type, dx criteria, obesity and ethnicity)

CDC. 2014 National Diabetes Statistics Report
National Diabetes Education Program. 2011
Age-adjusted incidence of Pregestational and Gestational Diabetes in California

Journal of Diabetes and Its Complications 2014 28, 29-34
Prevalence of Pregestational and Gestational Diabetes by Age in California
Age-adjusted prevalence of PGDM and GDM by race/ethnicity.
Effects of Maternal Diabetes on Fetal development and outcomes
Genetic Risk
Infant risk for Diabetes Mellitus

Type 1 Diabetes
- If FOB (father of baby) w/ T1 DM 1 in 17
- If mom w/ T1 DM & < 25 yo 1 in 25
- If mom w/ T1 DM & > 25 yo 1 in 100
- If both parents have T1 DM 1 in 10 - 1 in 4

Type 2 Diabetes
- Stronger link to family history and lineage
- Also dependent on environmental factors
- If parent w/ T2 DM & dx < 50 yo 1 in 7
- If parent w/ T2 DM & dx > 50 yo 1 in 13

ADA, 2013
Programmed Risk
Programming

- The process through which a stimulus or insult establishes a permanent response

- Exposure during a critical period during normal (in utero) fetal development may influence later metabolic or physiologic functions in adult life
The Barker Hypothesis - basic version

Maternal Undernutrition

↓

Fetal Growth Retardation

↓

Structural Change within Organs

↓

Metabolic and Endocrine Dysfunction

Poor Childhood Growth

Disease In Later Life
Fetal Development

• Fetal development is a complex process including many mechanisms that remain elusive

• Appropriate development of the placenta is crucial to normal fetal development
Critical Periods of Placental Development

- Placental function evolves in a carefully orchestrated developmental cascade throughout gestation.

- Disruption of this cascade can lead to abnormal development of the placental vasculature or of the trophoblast (angiogenesis, syncytium formation).

- Timing of a developmental 'insult' will be critical in consequent placental function and hence programming of the fetus.
Proposed Mechanism in the programming of overweight, diabetes and cardiovascular disease

- Perinatal Hyperinsulinism
  - Maternal diabetes and/or overweight during pregnancy
  - Fetal and/or Neonatal overnutrition
  - Acquired malorganization / malprogramming of neuroendocrine regulatory systems of food intake, body weight, and metabolism

- Overweight Obesity
  - Permanent hyperglycemia / hyperinsulinemia
  - Dyslipoproteinemia and atherosclerosis
  - Insulin resistance
  - Impaired glucose tolerance

- Hypertension
  - Cardiovascular disease

- Type 2 Diabetes

Journal of Maternal Fetal and Neonatal Medicine, March 2008; 21(3): 143 - 148
Effects of Maternal Diabetes on Fetal development and outcomes
Effect of diabetes on pregnancy and the baby

“Abortion and miscarriages are said to be frequent ... In our series of 89 pregnancies there were 12 abortions or miscarriages ... The percentage of stillbirths is high. Fourteen stillbirths, or 25 per cent, occurred among our 56 pregnancies coming to term. The possible causes for fetal death in utero are many. The size of the baby is one of the greatest dangers ... One can only speculate as to the cause for this phenomenon. The high glucose content of placental blood in diabetes, in contrast to the normally low content in the placental blood of non-diabetic individuals, is possibly an etiological factor.”

She is recognized for her dedication to the care of pregnant women with diabetes and her contributions to decreasing maternal and perinatal mortality.

White Classification

- A₁ – Diet/Exercise controlled
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  - Insulin

<table>
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<th>Age at Dx</th>
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Diabetes Mellitus Associated Maternal Morbidities

**Maternal morbidities**

- Preeclampsia
- Preterm labor
- Microvascular disease (retinopathy, nephropathy, neuropathy)
- Cesarean delivery
- Diabetic ketoacidosis (DKA)
- Hypoglycemia
- Intrapartum trauma due to macrosomia
- Infection
- Polyhydramnios
Diabetes Mellitus Associated Neonatal Morbidities

**Neonatal morbidities / Maternal Effects**
- Miscarriage
- Congenital anomalies
- Macrosomia
- Fetal growth restriction
- Hypertrophic cardiomyopathy
- Respiratory distress
- Metabolic abnormalities
- Perinatal mortality
Pregestational Diabetes

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Risk for 1st Trimester Hyperglycemia

Gestational Diabetes

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Diabetes Mellitus Associated Neonatal Morbidities

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1st Trimester Hyperglycemia
Risk for Spontaneous Abortion

Pregestational DM

- Several studies document an increased rate (15 - 30%) for spontaneous abortion in women with poor control (based on HgbA1c) in the first trimester.

  Annals of Clinical and Laboratory Science. Vol. 21, No. 3

- Rates for women White Class:
  
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<td>D</td>
<td>44%</td>
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- With preconception glycemic control, rates are similar to those in the non-diabetic population.
Neonatal Morbidities / Maternal Effects

**Congenital anomalies**

Hyperglycemia ➔ Teratogenic

- Poor metabolic control during organogenesis
  - Fastings > 120 mg/dL
- Precise mechanism is not completely clear
  - Damage to yolk sac by elevated glucose, production of free O2 radicals, resulting in a disruption of intracellular signaling (genotoxic)
Congenital Anomalies

Period of Organogenesis associated with anomalies

- Spina Bifida 6 weeks
- Anencephaly 6 weeks
- Cardiac
  - Transposition (TOGV) 7 weeks
  - VSD 8 weeks
  - ASD 8 weeks
- Renal 7 weeks
Diabetes Mellitus Associated Neonatal Morbidities

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Risk Beyond the 1st Trimester
Neonatal Morbidities / Maternal Effects

**Macrosomia / LGA**

Birth trauma:
- Shoulder dystocia \(\rightarrow\) brachial plexus Injury
- Severe perineal lacerations

Higher rate of cesarean

Chorioamnionitis

Postpartum hemorrhage
Fetal Growth Rate

- Included 174 women with diabetes and 997 ultrasounds were performed.
- Women with satisfactory control (HbA1c < 6.5%) and with unsatisfactory control (HbA1c ≥ 6.5%) were compared.
- Fetal size difference begins at 18 weeks onward.
- Glucose control has the most significant effect on fetal abdominal growth.
- Suggests that elevated glucose in the first trimester results in early programming of the fetus leading to an accelerated growth pattern.

Wong S, Oats J, Chan F, McIntyre D. Diabetes Care. 2002
BMI / Excessive Weight Gain

- Retrospective analysis looking at % LGA associated with BMI, weight gain and GDM.
- All had increased rates of LGA infants.
- Excessive weight gain contributed the most to LGA.
- Reducing excessive maternal weight gain has the greatest potential to reduce LGA risk.

Kim et al. Obstets Gynecol. 2014
Neonatal Morbidities / Maternal Effects

**Hypertrophic cardiomyopathy**
- Hypertrophy of the septum and ventricular walls that sometimes obstruct blood flow.
- Sometimes cause cardiac failure.
- Cause of intrauterine demise / stillbirth.
- Can regress in the first few months of life.
Neonatal Morbidities / Maternal Effects

**Respiratory distress**

- Hyperinsulinemia delays pulmonary maturation due to a low production of surfactant leading to RDS.
- Six fold increase in women with diabetes.
Neonatal Morbidities / Maternal Effects

**Metabolic abnormalities**

Hypoglycemia

Due to deprivation of maternal glucose supply

Hypocalcemia

Hypomagnesemia

Hyperbilirubinemia

Polycythemia (Hct > 65%)

Chronic hypoxemic state results in activation of erythropoiesis
Neonatal Morbidities / Maternal Effects

Perinatal Mortality
• Etiology often multifactorial
• Hyperinsulinemia → increase oxygen consumption and fetal hypoxia
Summary

- Genetic and environmental factors that influence development of diabetes.
- Fetal programming with initiation as early as placental development and consequences later in life including Type II DM, HTN and CV disease.
- Maternal morbidities that directly or indirectly affect the fetus.
- Neonatal morbidities.
Preconception, Antepartum, and Intrapartum Treatment Goal

Identify and normalize glucose levels in hopes of decreasing morbidity and mortality.
Prevention

- Women with preexisting diabetes should plan their pregnancy
- Preconception / Interconception care
- Normal glycemic control throughout the entire pregnancy
- Encourage breastfeeding as it appears to modify the risk of developing type 2 diabetes and obesity in offspring of diabetic mothers
- Overweight / obesity prevention. Encouraging appropriate weight gain during pregnancy and weight loss after pregnancy could lessen weight retention
QUESTIONS?