Infants of the Diabetic Mothers: Anticipatory Guidance for Families

Presented by:
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Conflict of Interest Statement
I have no actual or potential conflicts of interest. No recommendations for medications/medical devices are made in this presentation.

Objectives
• Following the presentation and question and answer period, the participant will be able to:
• Describe the incidence of infant of diabetic mothers in California
• Identify the impact of maternal obesity on the fetus.
• Identify 5 complications common to Infants of Diabetic (IDM) and their impact on the intrapartum course of the mother and infant
• Describe management and outcomes for complications seen in IDM.
Anticipatory Guidance

Helping families understand what to expect in a pregnancy complicated by diabetes is vitally important to a healthy outcome of pregnancy. It is every healthcare practitioners responsibility.

Incidence

- 1.0% of all pregnancies are complicated by pre-existing diabetes
- Up to 9.3% of pregnancies are complicated by gestational diabetes
- Approximately 50,000 IDMs born annually in California
- Perinatal mortality: 20/1000 total births


Infant of Diabetic Mother Definitions

- Any offspring of a pre-existing or gestational or diabetic woman
  - Type 1 Diabetes
  - Type 2 Diabetes
  - Gestation Diabetes Mellitus
  - Impaired Glucose Tolerance

- Outcome is largely dependent on consistent blood glucose control from the preconception period through birth.
Maternal Complications of Diabetes That Impact the Fetus and Neonate

- Unstable maternal BG control
- Cardiovascular conditions
- Birth Difficulties
- Post Partum recovery issues
- Psychosocial

Diabetic Embryopathy

- Teratogenic period
- Concentrations of metabolites
  - Blood Glucose fluctuations
  - Ketones
  - Somatomedin inhibitors
  - Oxygen free radicals
  - Aberrant fuels

Increased prevalence of islet cell hyperplasia in fetuses with diabetes-related congenital anomalies, in the absence of diagnosed maternal diabetes (Chambers et al., 2000).
Diabetes in Pregnancy

- Risk for Embryopathy, if poor early control
  - 2 to 4-fold Increased Risk for Malformations
    - Cardiac malformations
    - Central nervous system
    - Renal and urinary tract anomalies
    - Skeletal anomalies
- 7 to 10-fold Increased Risk for Major Anomalies that are fatal or require surgery
  - Cardiac malformations
  - Central nervous system
  - Renal and urinary tract anomalies
  - Skeletal anomalies

Risk for Fetopathy, if poor later control
- Macrosomia
- Hypoglycemia
- Polycythemia/hyperbilirubinemia
- Hypocalcemia/hypomagnesemia
- Cardiomyopathy

Reece et al., Teratology 55:171-184, 1997

Embryopathy - Gestational Diabetic & Obese Women’s Risk

- Bazzar et al., 1990
  - Population-based study
  - Relative risk for major malformations among IDM was 7.9 compared to infants of nondiabetic mothers
  - Gestational diabetics who require insulin in 3rd trimester were 20.6 times more likely to have a child with a cardiovascular defect
  - 4,180 consecutive pregnancies complicated by gestational diabetes (3,764) or type 2 diabetes (416) diagnosed after 20 weeks gestation (County USC).
  - Initial fasting glucose < 120 mg/dL
  - 2.9% malformations
  - Initial fasting glucose 121-200 mg/dL
  - 5.9% malformations
  - Initial fasting glucose > 200 mg/dL
  - 12.9% malformations
- Infants with diabetes-related malformations had significantly elevated fasting glucose and HbA1c
  - Prepregnancy obesity (with no known diabetes) associated with increased risks for spina bifida, omphalocele, heart defects, and multiple anomalies.

Obesity...Diabetes

- Metabolic abnormalities associated with obesity, including dyslipidemia, hyperglycemia, hyperinsulinism, elevated estrogen levels, alterations in growth factors, etc.
- Undiagnosed diabetes
- Nutritional deficits
- Increased nutrient requirement
- Folic Acid, antioxidants
- Excess body fat leads to type 2 diabetes within 20 years
- Excessive abdominal fat independently associated with diseases: cardiovascular, cancer, osteoarthritis, gall bladder, diabetes, etc.

Adjusted* Odds Ratios for Pregnancy Complications by Maternal BMI

*Adjusted for maternal age, smoking, education, marital status, trimester prenatal care began, payer, and weight gain during pregnancy; BMI<20.0 (lean) reference group.

Fetal & Neonatal Complications

- Hypoglycemia
- Macrosomia
- Congenital Anomalies
- Respiratory Distress Syndrome (RDS)
- Hypocalcemia
- Hypermagnesemia
- Hyperammonemia
- Polycythemia
- Renal vein thrombosis
- Complications associated with delivery
  - Brachial plexus palsy
  - Fractured clavicle
  - Shoulder dystocia
- Cephalopelvic Disproportion
- Risks associated with operative vaginal deliveries (vacuum extraction, forceps, etc.)

Neonatal Guidelines of Care: Infant of a Diabetic Mother; PAC/LAC, 2012

Neonatal Outcomes by Degree of Maternal Obesity

- SGA
- LGA
- Neonate aspiration
- Total delivery
- LGA
dis
- Early Neonatal death

Cedergren, Obstet Gyn 103:219, 2004

Collaborative Management

- Careful review of maternal history
- Risk Appropriate Care and Timely Intervention: Preconception, Prenatal, Intrapartum, Postpartum and Intraconception
- Sensitive neonatal assessment for gestational age, birth trauma and complications of maternal diabetes
- Monitor for sign and symptoms of complications
- Educate
  - Risks associated with IDM
  - Opportunities to minimize risk
  - Ways to prevent or delay diabetes in offspring
    - onset of diabetes
    - metabolic syndrome
    - perinatal complications in future generations
Macrosomia

- Large for Gestational Age
  - Birth weight $>4$ kg or above the 90th percentile for gestational age
- Physical findings
  - Increased adipose tissue
  - Full face covered with vernix
  - Disproportionate head/shoulder ratio
  - Plathoric
  - Large placenta & cord
- Complications
  - Birth trauma
  - Increased cesarean rate

Respiratory Distress Syndrome (RDS)

**Signs and Symptoms**
- Diagnosis
- Tachypnea
- Grunting
- Cyanosis
- Apnea
- Hypoxemia

**Treatment**
- Supplemental oxygen
- Intubation/Nasal Continuous Positive Airway Pressure
- Monitor Arterial Blood Gases
- Surfactant replacement

Hypoglycemia

**Signs and Symptoms**
- Jitteriness
- Seizures
- Apnea/cyanosis
- Irritability
- Hypotonia
- Respiratory Distress Syndrome
- Poor feeding
- Hypothermia

**Treatment**
- If stable give early feeding, preferably breastfeeding
- If unable to achieve adequate oral intake, IV required
- Wean IV fluids as oral intake increases
Oral Feedings

- Breastmilk: Colostrum, Mature milk: fore and hindmilk
- Formulas: only when medically indicated or when mother has given informed consent
- Keep mother and infant together continuously
- Offer breast as soon as possible but at least within 1 hour of delivery
- Encourage feedings whenever oral cues noted or at least every 3 hours
- Support mothers to nurse 10-12 times/day
- If mother and infant are separated because of medical complications protect mother's breastmilk supply
  - Pump within first 12 hours postpartum
  - Pump every three hours with hospital grade, double pump
  - Pump at least once or twice a night

Hypocalcemia/Hypomagnesemia

- Related to severity of maternal diabetes
- Hypocalcemia develops in first 3 days
- May be secondary to hypoparathyroid function
- Symptoms:
  - Irritability
  - Jitteriness
  - Agnea
  - Lip smacking
  - Tongue thrusting
- Treatment:
  - Transfer to Neonatal Intensive Care Unit
  - Calcium gluconate
  - Magnesium sulfate

Hyperbilirubinemia

Elevate indirect (unconjugated) bilirubin >2 mg/dl in term infant, no safe levels determined for late preterm or preterm infants.

- Increased bilirubin production
  - Late preterm delivery
  - Intraventricular exposure to excess growth factors
  - Decrease in bilirubin binding and excretion
  - Slight immaturity of liver
  - Potential metabolic derangement
- Prevention
  - Early, adequate breastfeeding

- Diagnosis:
  - Serum bilirubin at 24 hours of age, or at signs of increasing jaundice
- Treatment:
  - Adequate hydration and nutrition
  - Phototherapy
  - Exchange transfusion
  - Family teaching
  - Appropriate follow-up after discharge
Polycythemia

- Elevated venous hematocrit of >65%
- Signs and symptoms
  - Plethora
  - Jitteriness
  - Tachypnea, or Cyanosis (general or circumoral)
  - Poor feeding
- Screening: obtain central hematocrit at 24 hours of life or if symptoms noted
- Treatment
  - Treat underlying symptoms
  - Hydration
  - Hyperbilirubinemia treatment
  - Partial-exchange transfusion
- Common complications
  - Renal vein thrombosis
  - Hypertension

Birth Defects, Congenital and Chromosomal Anomalies

Associated with Diabetes
- CNS
- Cardiopulmonary
- Skeletal
- Mid-line facial defects
- Ear and hearing
- Third trimester cardiac hypertrophy
- Numeric sex chromosomal anomalies
- Multiple congenital anomalies

Associated with Maternal Obesity
- Neural tube defects
- Heart defects
- Cleft lip +/− palate
- Multiple congenital anomalies

Risk of Congenital Anomalies by Maternal HbA1C

<table>
<thead>
<tr>
<th>HbA1c*</th>
<th>% Malformations</th>
<th>RR (95% CI)</th>
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<tbody>
<tr>
<td>&lt;6</td>
<td>3.0%</td>
<td>1.0</td>
</tr>
<tr>
<td>6.1-9.0</td>
<td>5.2%</td>
<td>1.7 (0.4-9.7)</td>
</tr>
<tr>
<td>9.1-12.0</td>
<td>4.3%</td>
<td>1.4 (0.3-8.3)</td>
</tr>
<tr>
<td>12.1-15.0</td>
<td>38.9%</td>
<td>12.8 (4.7-35.0)</td>
</tr>
<tr>
<td>&gt;15.0</td>
<td>40.0%</td>
<td>13.2 (4.3-40.4)</td>
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Diabetic Embryopathy – Central Nervous System, Cardio/Pulmonary/Vascular, Gastrointestinal

Central nervous system
- Neural tube defects
  - Anencephaly
  - Meningomyelocele
- Hydrocephaly
- Holoprosencephaly

Cardio/Pulmonary/Vascular
- Transposition of great vessels
- Coarctation of the aorta
- Atrial & ventricular septal defects
- Dextrocardia
- Single ventricle, hypoplastic right heart
- Patent ductus arteriosus
- Pulmonary hypoplasia and arterial atresia
- DiGeorge sequence

Gastrointestinal: Small Left Colon Syndrome

Diabetic Embryopathy – Midfacial Defects

Case control study of hemifacial microsomia and microtia/anotia:
- Diabetes in 1st half pregnancy reported in:
  - 10.3% of 155 case mothers versus
  - 1.4% of 854 control mothers

Multivariate-adjusted odds ratios (and confidence intervals):
- Diabetes: 6.3 (2.7 - 14.9)
- Diabetes + Multivitamin with Folic Acid: 5.5 (2.0 - 15.0)
- Diabetes - Multivitamin with Folic Acid: 9.8 (1.1 - 89)

Werler et al., Birth Defects Research 70:258, 2004

Diabetic Embryopathy – Skeletal Anomalies

Cervical vertebral anomalies and Caudal Regression Syndrome
Long Term Prognosis

- Metabolic Complications
  - Obesity
  - Glucose Intolerance
  - Dyslipidemia
  - Hypertension
- Predisposing factors
  - Infant of a diabetic mother
  - Infant of an obese mother
  - Large for gestational age infant
- Growth Development
- Childhood obesity
- Neurological development indefinite

Questions?