Infant of a Diabetic Mother

Ogata E S. Problems of the infant of the diabetic mother. NeoReviews. (2010); 11, 11: c627-c631
Objectives

Medical Expert
• To review the fetal, neonatal, and long-term effects of gestational diabetes on the infant
• To become familiar with the CPS Position Statement re: newborns at risk for low blood glucose

Scholar
• To discuss recent review articles on clinical manifestations and prognostic outcomes of infants of diabetic mothers (IDMs)
Background

Gestational Diabetes (GDM) = “glucose intolerance that first appears during pregnancy”

• Most common medical complication of pregnancy
  • 3-10% of pregnant women have diabetes → 88% GDM
  • Other 12% had pre-existing diabetes
    • 35% Type I diabetes, 65% Type II diabetes
Background

What is the Gestational Diabetes Screen?
• Performed at GA 24-28 weeks
• If multiple risk factors, recommend early screen at 1\textsuperscript{st} trimester, then repeat in 2\textsuperscript{nd} and 3\textsuperscript{rd} trimesters, even if initially negative
• Baseline bloodwork, then drink 50g glucose, repeat bloodwork 1 hour later

What is a normal/abnormal result?
• Normal glucose = 5.5-7.7 mmol/L
• Positive ≥ 10.3 mmol/L
Background

Risk factors for gestational diabetes

• Family history of Type 2 diabetes mellitus
• Previous GDM or macrosomic infant
• Ethnicity: Asian, SE Asian, First Nations, African, Hispanic
• Obesity, PCOS, acanthosis nigricans
The Case

You are asked to see a GA 39+3 week newborn baby girl, who was born to a 32 year old G2P1 Mom with diet-controlled gestational diabetes. The nursing staff is concerned about persistent hypoglycemia.
Differential Diagnosis

- Sepsis
- LGA, SGA
- Infant of a diabetic mother
- Birth trauma/HIE
- Withdrawal
- Inborn error of metabolism
- Beckwith-Wiedemann Syndrome (BWS)
History

What would you ask?
## History

### Pregnancy History
- Planned pregnancy
- Prenatal screening (MSS, IPS, amniocentesis, CVS...)
- Serologies and GBS
- Ultrasounds (IUGR, LGA)
- HTN, UTIs/illnesses
- Exposures (EtOH, drugs, etc.)
- GDM:
  - When dx
  - Method of control (diet, insulin)
  - HbA1C
  - Frequency of hypo/hyperglycemia

### Birth History
- Gestational age
- SVD vs C/S
- Instrumentation
- Shoulder dystocia
- Resuscitation, APGARS
- Birth weight, Length, HC
- Sepsis RFs:
  - ROM duration
  - Maternal fever
  - Intrapartum antibiotics
### History

#### Maternal PMHx
- Previous GDM or macrosomnic infant
- Previous infant with GBS septicemia
- Obesity, PCOS, acanthosis nigricans
- Medications

#### Family History
- Consanguinity
- Ethnicity
- Type II DM
- Early infant deaths

#### HPI
**Feeds**
- Attempted breastfeeding
- Formula supplementation
- Timing of feeds
- Timing of glucose measurements post-feeds

**Symptoms**
- Lethargy
- Jittery, tremors
- Seizures
- Apneas
- Passage of urine/meconium
Physical Exam

What would you look for?
Physical Exam

- General appearance
  - Well/unwell
  - Dysmorphisms
  - Colour (plethoric, jaundice)

- Vital Signs
  - HR, RR, O2 sats, temp
  - LGA vs AGA vs SGA

- CNS/MSK
  - Tone
  - Lethargy vs Jittery vs Seizures
  - Primitive reflexes (esp. suck)
  - Anencephaly/Spina bifida
  - Caudal regression syndrome

- Head and Neck
  - Fontanelles
  - Birth trauma (clavicles, bleed)
  - Tongue tie, large tongue
  - Ear pits/creases (BWS)

- Cardiorespiratory
  - Respiratory distress
  - Perfusion (fem pulses, cap refill, cyanosis)
  - Murmurs
  - Crackles
  - Anencephaly/Spina bifida
  - Caudal regression syndrome

- Hemihypertrophy (BWS)
Workup

What would you order?
Workup

• Blood work
  • Serum glucose
  • CBC
  • CRP
  • Cord gases
  • +/- blood culture, CSF culture
  • +/- toxicology screen

• Consider Critical Sample if BG <2.6
  • Insulin, Cortisol, Growth hormone
  • VBG, Lactate
  • Ammonia
  • LFTs
  • Plasma amino acids, urine organic acids
  • Serum and urine ketones
  • Acylcarnitines

• Imaging
  • +/- ECHO
  • +/- abdo imaging
  • +/- Head U/S or MRI
Infant of the Diabetic Mother

- **Fetal effects**
  - Embryopathy (1st trimester)
  - Fetopathy (2nd/3rd trimesters)

- **Neonatal effects**
  - Congenital Anomalies
  - Growth (macrosomia vs. IUGR)
  - Respiratory Distress Syndrome
  - Metabolic and Hematologic Complications

- **Long-term outcomes**
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Diabetic Embryopathy (1st trimester)

- Rosenn *et al.* (1994)
  - Women with 1st trimester HbA1C >12% had ↑ risk of major congenital abnormalities and spontaneous abortions
- Better glycemic control = ↓ risk

Greene MF *et al.* *Teratology.* (1989); 39;225.
Infant of the Diabetic Mother

• Diabetic Fetopathy (2\textsuperscript{nd}/3\textsuperscript{rd} trimester)
  – Pedersen’s Hypothesis for macrosomia and fetal hyperinsulinemia
    • Maternal hyperglycemia $\rightarrow$ fetal hyperglycemia
    • Causes premature maturation of fetal pancreatic islets: hypertrophy of $\beta$-cells
    • Results in fetal hyperinsulinemia

– Hyperinsulinemia
  • Stimulates storage of glycogen in liver
  • $\uparrow$ activity of hepatic enzymes used in lipid synthesis
  • Accumulation of fat in adipose tissue
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- **Macrosomia**
  - More common in diabetic mothers (n=76,000)
    - 21% vs 8%
  - Excessive growth related to poor glucose control, especially in 3rd trimester
  - Increased fetal growth, esp. insulin-sensitive tissues → macrosomia
    - Liver, cardiac muscle, subcutaneous fat
    - Disproportionate abdominal girth (fat deposition + visceromegaly), sparing head
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Features of IDM macrosomia:
- BW >90th %ile or >4000g
- Plethoric, puffy, fat pads over upper back + lower jaw
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Labour and Delivery

• Prematurity
• Perinatal asphyxia
• Macrosomia/IUGR
• Birth Trauma
  – Shoulder dystocia
  – Cesarean section?
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- Prematurity
  - PROM more common in diabetic vs. non-diabetic pregnancies (31% vs 20%)
    - related to higher rate of UTIs
  - Maternal preeclampsia more common
    - iatrogenic premature delivery

- Perinatal asphyxia
  - Correlated with hyperglycemia while in labour, prematurity, and diabetic nephropathy
  - Maternal vascular disease (causing nephropathy) → fetal hypoxia → perinatal asphyxia
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- Macrosomia/IUGR
  - Macrosomia ~4X more often in IDM
  - IUGR more common in GDM with vasculopathy
    - Preeclampsia → placental insufficiency
    - Excessively aggressive glucose control

- Birth Trauma
  - Shoulder dystocia
    - 1/3 of IDMs >4000g; 1.7X greater risk
    - Distribution of fat in shoulders and upper back
    - Brachial plexus injury, clavicular/humaral #, cephalohematoma, subdural hemorrhage, facial palsy
  - Cesarean section?
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Post-natal Complications

• Congenital anomalies
  – CNS
  – Cardiovascular
  – GI
  – GU

• Respiratory Distress Syndrome

• Metabolic complications

• Hematologic complications
  – Polycythemia
  – Hyperbilirubinemia
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CNS Anomalies

- Anencephaly and spina bifida are 13–20X more common in IDMs
- 200X increased risk of Caudal Regression Syndrome
  - Caudal agenesis, sacral dysgenesis, caudal dysplasia
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Cardiovascular Anomalies

- 30–50% of IDMs
- ↑ risk for hypertrophic cardiomyopathy
  - Most common is thickened interventricular septum
  - Can reduce size of ventricles → LV outflow obstruction
- 5–10% may have respiratory distress, poor cardiac output, or heart failure
  - Cardiomegaly on CXR
  - Best diagnosed by ECHO
- Cardiomyopathy is transient
  - Resolves within 2–3 weeks as fetal insulin normalizes
  - ECHO findings resolve within 6–12 months
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Gastrointestinal Anomalies
- Small left colon syndrome
  - Transient inability to pass meconium that spontaneously resolves (vs. Hirschsprung's)
- Duodenal atresia, imperforate anus

Genito-urinary Anomalies
- Ureteral duplication, renal agenesis, hydronephrosis
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Respiratory Distress Syndrome

- Especially ↑ risk if GA <38 weeks
- Why? Unclear
  - Delayed maturation of surfactant synthesis due to hyperinsulinemia
  - Interference with lung maturation by glucocorticoids
- Also consider transient tachypnea of the newborn
  - C/S delivery due to macrosomia
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Hypoglycemia

- Occurs frequently (25–40%) in IDMs
- Most commonly in macrosomia
  - Persistent hyperinsulinemia without supply of glucose from mother
  - Transient hyperinsulinemia resolves in 2–4 days
  - Need to maintain normal serum glucose, while weaning supplemental glucose
  - Avoid repeated boluses → rebound hypoglycemia

- Also in IUGR infants
  - Poor glycogen stores
  - Often started on D10W IV
CPS Position Statement: Neonatal Hypoglycemia

**ALGORITHM FOR THE SCREENING AND IMMEDIATE MANAGEMENT OF BABIES AT RISK FOR NEONATAL HYPOGLYCEMIA**

1. **NEWBORN BABY**
   - Is the baby unwell?
     - **YES**
       - CHECK GLUCOSE NOW: INVESTIGATE FOR CAUSE AND TREAT ANY UNDERLYING CONDITION
     - **NO**
       - ROUTINE CARE: INITIAL FEED
         - Is the baby at risk? SGA, LGA, IDM or premies?
           - **YES**
             - ROUTINE CARE: FEED ON DEMAND AS LONG AS INFANT REMAINS WELL
           - **NO**
             - CHECK GLUCOSE AT 2 HRS. AND EVERY 3-6 HOURS BEFORE FEEDS AS LONG AS INFANT REMAINS WELL. UNTIL FEEDS ARE ESTABLISHED AND GLUCOSE ≥2.6 mmol/l

2. **<2.6 mmol/l in an unwell baby**
   - CONSIDER IV TREATMENT
   - Refeed and recheck glucose in 1 hour
     - Remains <2.6 mmol/l despite feeding
       - CONSIDER IV TREATMENT
     - Rises to ≥2.6 mmol/l after feeding
       - ONCE ONLY

3. **≥2.6 mmol/l**
   - INITIATE INTRAVENOUS INFUSION OF 10% DEXTROSE AT A RATE OF 80−120 mg/kg/day (5−5.5 mg/kg/min).
   - CHECK GLUCOSE 30 min AFTER ANY CHANGE AND ADJUST THERAPY (UP TO 100 ml/kg/day and/or 12.5% DEXTROSE) IN ORDER TO MAINTAIN GLUCOSE LEVEL ≥2.5 mmol/l. IF RATES IN EXCESS OF 100 ml/kg/day OF 12.5% DEXTROSE ARE REQUIRED INVESTIGATION, CONSULTATION AND/OR PHARMACOLOGICAL INTERVENTION ARE INDICATED. MAY START WEANING IV 12 HOURS AFTER A STABLE BLOOD GLUCOSE LEVEL IS ESTABLISHED. CONTINUED BREASTFEEDING IS ENCOURAGED.

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Figure 1) Screening for neonatal hypoglycemia. IDM Infant of diabetic mother; IV Intravenous; LGA Large for gestational age; SGA Small for gestational age. CPS Statement: www.cps.ca/english/statements/FN-sm0101.htm
Infant of the Diabetic Mother
Hematologic Complications

- Polycythemia
  - 13–33% of IDMs
  - Increased erythropoietin 2° chronic fetal hypoxemia
  - Hyperviscosity syndrome: vascular sludging, ischemia, infarction of organs
  - Consider hematocrit within 12 hours

- Hyperbilirubinemia
  - 11–29% of IDMs
  - ↑ bruising with birth trauma + polycythemia
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Long-term Metabolic Risks

- Type 2 DM more common in IDMs (45%) than in prediabetic (8.6%) or non-diabetic (1.4%)
- Type 1 DM more common in children of diabetic fathers (6.1%) than mothers (1.3%)
- Macrosomia usually resolves by age 1, but obesity often recurs
  - BMI higher in IDMs than controls (24.6 vs. 20.9kg/m²)
Test Your Knowledge

All of the following are possible complications for an infant of a diabetic mother EXCEPT:

A. Jaundice
B. IUGR
C. Omphalocele
D. Cardiomyopathy
The Answer

Omphalocele

- Omphaloceles are associated with Beckwith-Wiedemann Syndrome, which commonly presents as macrosomnia and hypoglycemia.
Test Your Knowledge

A newborn GA 35 weeker has a blood glucose of 1.9mmol/L at 2 hours of age after a feed. The baby is fed again and the next blood glucose 1-hour post feed is 2.2mmol/L. According to the CPS Position Statement on Neonatal Hypoglycemia, what is the next most appropriate step?

A. Supplement the next breast feed with formula
B. Start IVF D5NS at a TFI of 80ml/kg/day
C. Start IVF D10W at a TFI of 120ml/kg/day
D. Start IVF D10W at a TFI of 80ml/kg/day
Start IVF D10W at TFI of 80ml/kg/day (GIR of 5.5mg/kg/min)
Summary

- Labour and Delivery
  - Prematurity
  - Perinatal asphyxia
  - Macrosomia/IUGR
  - Birth trauma (shoulder dystocia, C/S)
- Congenital Anomalies
  - Hypertrophic cardiomyopathy
  - Spina bifida/anencephaly, caudal regression syndrome
  - Small left colon syndrome, GI atresia
  - Ureteral duplication, renal agenesis, hydronephrosis
- Hypoglycemia
- Polycythemia, Hyperbilirubinemia
- Later: Increased risk of Type II DM, Obesity