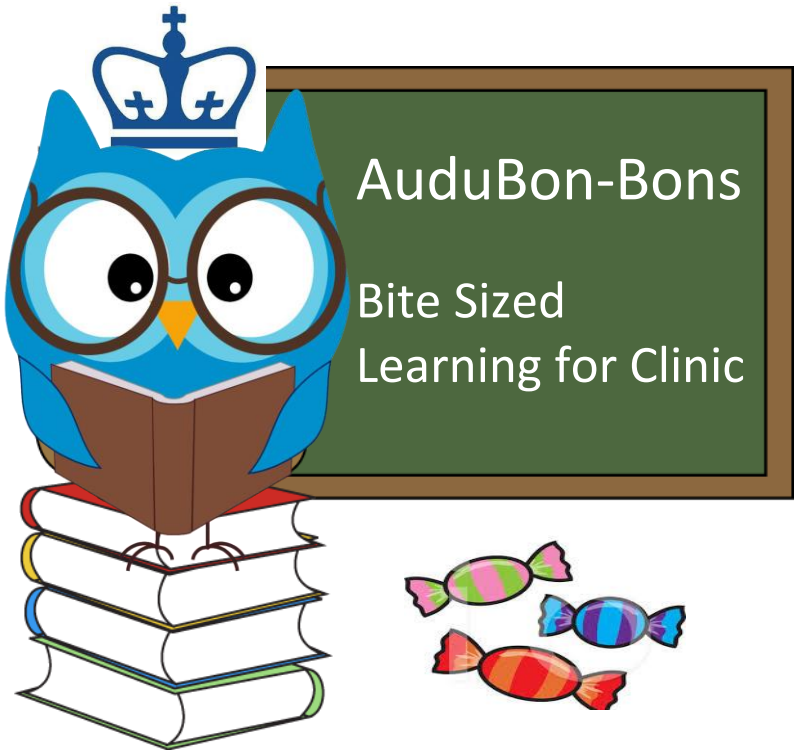
INTRAHEPATIC CHOLESTASIS OF PREGNANCY



Week 60

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With SDH and .phrase slides by Chloé Altchek, MS4

Reading Assignment:
Pearls of Exxcellence: Intrahepatic Cholestasis of Pregnancy

LEARNING OBJECTIVES

- To understand the etiology of intrahepatic cholestasis of pregnancy
- To be able to diagnose intrahepatic cholestasis of pregnancy
- To counsel patients on the management of intrahepatic cholestasis of pregnancy

CASE VIGNETTE

- Ms. Picazon Manos is a 36 yo G1 P0 woman at 36 weeks EGA who presents for a walk-in visit to clinic because her itchy palms are keeping her up at night.
- She denies rash, change in soaps/lotions/detergents, or sick contacts.

FOCUSED HISTORY

What elements of the patient's history are most relevant?

- **PMH:** Eczema
- **PSH:** Adenoidectomy as a child
- **POBH:** **Primigravida. Pregnancy has been uncomplicated thus far.. Denies CTX, LOF, or BPV. +FM.**
- **PGYNH:** Regular menses prior to pregnancy. Denies abnormal paps or STIs. Denies history of fibroids or cysts.
- **MEDS:** PNV
- **All:** NKDA
- **FH:** Mother has T2DM
- **SH:** Married and partner has been supportive. Denies tob, drug, EtOH use. Denies IPV. Works as a HHA. Accepts blood products.

PERTINENT PHYSICAL EXAM FINDINGS

What elements of the patient's physical exam are most relevant?

- **General:** Well appearing woman, VSS
- **FH:** 36cm
- **FHR:** **150s bpm**
- **Skin:** **Normal appearing. No rashes present.** No evidence of jaundice.

INCIDENCE

What is the incidence of intrahepatic cholestasis of pregnancy?

- **0.2-2%**

In which groups is intrahepatic cholestasis of pregnancy most common?

- Women from **South America** and **northern Europe**
- Women who conceived with **IVF** (2.7%)
- Women who are **AMA**
- Women who have **multiple gestations** (up to 22%)
- Women who have a history of ICP
  - Up to **90% have recurrence** in subsequent pregnancies

ETIOLOGY

- Overview:
  - **Transport of bile acids from the liver to the gallbladder is disrupted and bile acids become transported from the liver to the blood**
- Genetic:
  - Relates to the cholestatic effect of reproductive hormones in genetically susceptible women
- Hormonal:
  - Estrogen causes reduced expression of hepatic biliary transport proteins through internalization of the bile acid transporter bile salt exporter pump
  - Progesterone metabolites impair hepatic bile acid homeostasis by reducing the function of the main hepatic bile acid receptor
- Environmental:
  - Low selenium and vitamin D levels may contribute

RISKS

What is the relationship between serum bile acid levels and risk of fetal complications?

- **Linear**

What are the risks to the fetus?

- Preterm delivery (spontaneous and indicated)
- Nonreassuring fetal status
- Meconium staining
- Respiratory distress syndrome
- **Intrauterine fetal demise**

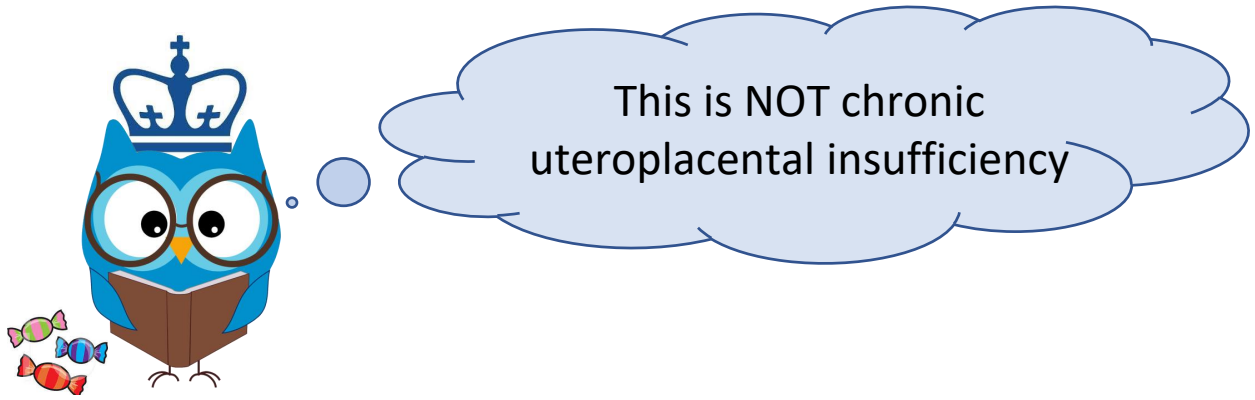
What are the risks to the woman with ICP?

- Preeclampsia
- Gestational diabetes

PATHOPHYSIOLOGY OF STILLBIRTH IN ICP

What is the proposed mechanism of sudden IUFD in ICP?

- *Hypothesis:* bile acids cause sudden cardiac death secondary to **arrythmia**
- Bile acids have also been shown to cause marked **vasoconstriction of placental chorionic vessels**, which may lead to acute anoxia and sudden death



DIAGNOSIS

What is the most common clinical presentation of intrahepatic cholestasis of pregnancy?

- **Third trimester**
- Pruritis, typically of the **palms and soles**
- Potentially abnormal liver function
- **Raised serum bile acid levels**
- May demonstrate dark urine, pale stools, and rarely, jaundice

How do you confirm the diagnosis?

- **Elevated total serum bile acids in the absence of an alternative diagnosis**
  - 11 micromoles/L or higher

MANAGEMENT

What is the preferred management for symptoms of ICP?

- **Ursodeoxycholic acid (UDCA)**
  - Liver indices, bile acids, and pruritis may improve with administration, but unclear if fetal outcomes improve

What is the mechanism of action?

- Reduction of serum bile acids in both maternal and fetal circulations

Do you perform additional antenatal testing?

- **Start at diagnosis**
- Weekly if bile acids <40
- Twice weekly if bile acids >40

Does antenatal testing prevent stillbirths in this setting?

- **No**
- Nor has it been shown to reduce risk or predict those at risk of adverse perinatal outcomes

MANAGEMENT

How often do you monitor bile acids?

- Weekly if bile acids 40 or higher
- **LFTs and bile acids should be rechecked 6-8 weeks after delivery to ensure resolution**

What is the delivery timing for patients with ICP?

- Most experts recommend delivery by **37 weeks** gestation

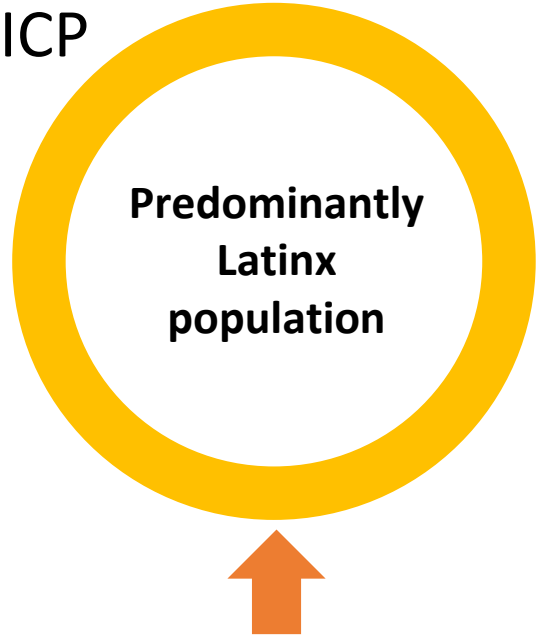
Is this a contraindication to vaginal delivery?

- **No**

SOCIAL DETERMINANTS OF HEALTH

Incidence of ICP differs between populations, and in some, has changed over time, suggesting both genetic and environmental contributions to etiology.

- Latinx obstetric populations have a substantially increased probability of having ICP



3.75%

0.28%

Given the local Latinx population we serve, patient education and screening for ICP must be a focus of ours.

EPIC .PHRASE

.BBonIntrahepCholestofPreg

Description: Intrahepatic cholestasis of pregnancy management counseling

The diagnosis of intrahepatic cholestasis of pregnancy was discussed with the patient. The major complications of ICP were outlined including increased risk for maternal preeclampsia and gestational diabetes and fetal intrauterine demise, meconium-stained amniotic fluid, preterm delivery (spontaneous and iatrogenic), and neonatal respiratory distress syndrome. The goals of treatment were also outlined including relief of pruritus and possible prevention of fetal complications. We discussed treatment options and will begin with ***ursodeoxycholic acid 300mg TID with plan to titrate up to a max of 21 mg/kg/day, deliver by 37 weeks, monitor bile acids weekly if bile acids <40 or twice weekly if bile acids >40, and check liver function and bile acid concentration 6-8 weeks after delivery. The patient was counseled that ICP is not a contraindication for vaginal delivery or breastfeeding. The implications for future pregnancies was also discussed, including the recurrence of cholestasis in 60-70 percent of patients.

CODING AND BILLING

- **ICD-10 Code**
  - O26.619
    - Liver and biliary tract disorders in pregnancy, unspecified trimester
  - **CPT Code**
    - 99214
      - Office or other outpatient visit for the evaluation and management of an established patient, which requires at least two of these three key components:
        - A detailed history; a detailed examination; medical decision making of moderate complexity.
        - Counseling and/or coordination of care with other physicians, other qualified health care professionals, or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs.
        - Usually, the presenting problem(s) are of moderate to high severity.
        - Typically, 25 minutes are spent face-to-face with the patient and/or family.

EVIDENCE

- Coletta, Jaclyn. Columbia University Medical Center Department of Obstetrics and Gynecology OB/GYN Ultrasound Practice Guidelines. Revision October 2016.

- Dikison, Shelby. “Intrahepatic Cholestasis of Pregnancy.” Pearls of Exxcellence. November 2018. Accessed December 2019.

- Williamson, Catherine, and Victoria Geenes. “Intrahepatic Cholestasis of Pregnancy.” *Obstetrics & Gynecology*, vol. 124, no. 1, 2014, pp. 120–133.

- Rook M, Vargas J, Caughey A, Bacchetti P, Rosenthal P, Bull L. Fetal outcomes in pregnancies complicated by intrahepatic cholestasis of pregnancy in a Northern California cohort. *PLoS One*. 2012;7(3):e28343. doi:10.1371/journal.pone.0028343