

MEDICATION TREATMENT: Ursodeoxycholic acid

- A naturally occurring bile acid that binds toxic bile acids and allows for their elimination
- Prior studies have shown benefits in reducing meconium passage, preventing fetal arrhythmias and transporting bile acids away from the fetus^{9,10}
- A recent meta-analysis showed a reduction in a combination of preterm birth and stillbirth but not stillbirth alone. It may have not been powered to detect a reduction in stillbirth¹¹
- SMFM recommends Ursodiol as a first line treatment for cholestasis even if the fetal benefit on stillbirth is not clear⁴
- Dosing is 10-21 mg/kg/day in divided doses; may increase dose to help control bile acid levels
- May also improve itching

MONITORING:

- Although all stillbirths in cholestasis pregnancies are not able to be prevented by fetal monitoring, it is still recommended
- SMFM also recommends following bile acid levels in pregnancy
 - Exact frequency not determined
 - Should be followed closely in later pregnancy to determine optimal delivery timing
- Betamethasone should also be given for planned delivery prior to 37 weeks gestation

FOLLOW-UP

- Laboratory evaluation postpartum with CMP and total bile acid levels
- Some patients will have an underlying liver condition such as autoimmune hepatitis. This is more common in early or severe cases
- There is also a high recurrence rate of 70-90% in subsequent pregnancies

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<http://icpcare.org/wp-content/uploads/2021/05/Healthcare-Provider-Brochure-References.pdf>

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A GUIDE FOR
HEALTHCARE PROVIDERS

Diagnosis & Management of Intrahepatic Cholestasis of Pregnancy

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WHAT IS INTRAHEPATIC CHOLESTASIS OF PREGNANCY?

A pregnancy disorder in which bile acid transport in the liver is affected by the hormones of pregnancy

- Leads to increased maternal bile acids which can then affect the fetus
- Main symptom is itching
 - Worse at night
 - Classically involves the palms and soles but usually generalized
- Most cases occur in the second and third trimesters but there are cases that have occurred as early as 5 weeks.¹
- Has a genetic predisposition. Some patients have underlying liver conditions such as autoimmune hepatitis or Hepatitis C

WHAT ARE THE RISKS OF CHOLESTASIS?

- Meconium passage
- Preterm labor
- Increased rates of gestational diabetes and preeclampsia
- Respiratory distress in neonate (even when corrected for gestational age at delivery)²
- Stillbirth

WHAT ARE THE RATES OF STILLBIRTH?

- Rates linked to bile acid levels based on recent meta-analysis of 5000 cholestasis pregnancies
- Highest risk of 3.44% with bile acids above 100 $\mu\text{mol/L}$
- Risk for bile acids less than 40 $\mu\text{mol/L}$ was 0.13% and with bile acids 40-99 $\mu\text{mol/L}$ was 0.28%³
- These rates were determined by a meta-analysis where many women were treated with ursodeoxycholic acid and majority delivered by 38 weeks. It is unknown if the active management of these pregnancies might have mitigated some of the stillbirth risk⁴
- Stillbirth is an acute event, possibly a fetal cardiac arrhythmia
- Stillbirth is not prevented with fetal monitoring

DIAGNOSIS OF CHOLESTASIS

- Laboratory evaluation: CMP and total bile acid test
- Serum bile acid diagnostic level of 10 $\mu\text{mol/L}$ agreed upon by research^{4,5,6,7}
- Reference ranges for many bile acid tests are non-pregnancy reference ranges and SMFM notes that the level of 10 $\mu\text{mol/L}$ should be used
- Bile acid test does not need to be fasting. Fasting can artificially lower levels
- Fractionated bile acid tests have a lower reference range for diagnosis⁴



TREATMENT

Delivery timing

- Current guidelines in the US per ACOG and SMFM are based upon bile acid levels^{4,8}

These are:

- For bile acids >100 $\mu\text{mol/L}$: delivery at 36 0/7 weeks. Consideration for delivery 34-36 weeks with unremitting itch, history of stillbirth due to cholestasis or worsening liver functions
- For bile acids 40-99 $\mu\text{mol/L}$: delivery 36 0/7-39 0/7 weeks, with delivery recommended in the early portion of the window
- For bile acids below 40 $\mu\text{mol/L}$: delivery 36 0/7-39 0/7 weeks
- Delivery should be:
 - Based upon highest ever bile acid
 - Individualized per patient
 - In the early portion of the 36 0/7-39 0/7 week window with the exception of mild cases (bile acids below 40 $\mu\text{mol/L}$)
 - Please see our website for an in depth discussion of the evidence behind these recommendations