Boston Medical Center Maternity Care Guideline
Guideline: Diagnosis and Management of Intrahepatic Cholestasis of Pregnancy
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Background Information

- **Prevalence**
  - The incidence of ICP is between 0.2% to 2%[1, 2]
  - Incidence varies with ethnicity and location; most common in South American, South Asian and northern European patients[2]
- **Risk factors**
  - **Most important risk factor is a history of cholestasis, recurrence rate approaches 90%[2]**
  - Multiple pregnancy, in vitro fertilization, >age 35, positive family history, hepatitis C[2, 3]
  - Women with ICP are also more often later diagnosed with hepatobiliary disease, including fibrosis, gallstone disease, or hepatitis[3]
- Risks: preterm birth (both indicated and spontaneous), meconium stained amniotic fluid, neonatal depression, respiratory distress syndrome, and stillbirth[1, 2, 4, 5, 9-12]
- Fetal demise can be a sudden event without preceding antenatal testing changes [2, 6, 11, 12]
- **The risk of adverse neonatal outcomes increases as bile acid levels increase[5,9]**.
  - Bile acid levels ≥40µmol/L, the risk of stillbirth may be 1.5%[9].
  - Bile acid levels ≥100µmol/L, rates of perinatal death from 9.5%5 to 15.4%[6] have been reported
- The risk of stillbirth is thought to be increased when preeclampsia or gestational DM coexist with ICP[1]
- **Pathophysiology of fetal risk:**
  - Thought to be related to the harmful effects of bile acids, which accumulate in the fetal compartment[2,13]
  - Animal studies have demonstrated effects of high bile acids leading to arrhythmias [14-16]
  - Bile acids can cause isolated vasoconstriction of human placental chorionic veins, which may explain the occurrence of fetal distress, asphyxia, or death[17]

Diagnosis

- **Should be based on symptoms (itching) plus laboratory testing**
- **Symptoms**
  - ICP should be suspected in pregnant women with pruritus without rash
  - Pruritus may occur anywhere, is generally worst on hands and soles

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- Onset of symptoms is usually in the late 2nd or 3rd trimester, although symptoms may present as early as 7 weeks gestation[2, 4]
- If there is clinical suspicion, workup should be pursued regardless of gestational age

- **Laboratory tests**

  To be ordered during workup:

  - **Total bile acids**, **LFTs.** Ideally, bile acids should be obtained fasting, due to the risk of a false positive if not fasting.[7] However, given that this may be logistically prohibitive, it is acceptable to perform them non-fasting, especially when clinical suspicion is high.

  Bile acid testing and levels

  - Onset of pruritus may precede elevation of bile acids by 3 weeks on average, so if labs are negative initially but symptoms persist repeat labs every 1-2 weeks[4]
  - Given that treatment with UDCA may reduce bile acid levels, it is recommended not to start UDCA until a diagnosis is secured.
  - We recommend a cut-off of 10 µmol/L2 [4-6,8]

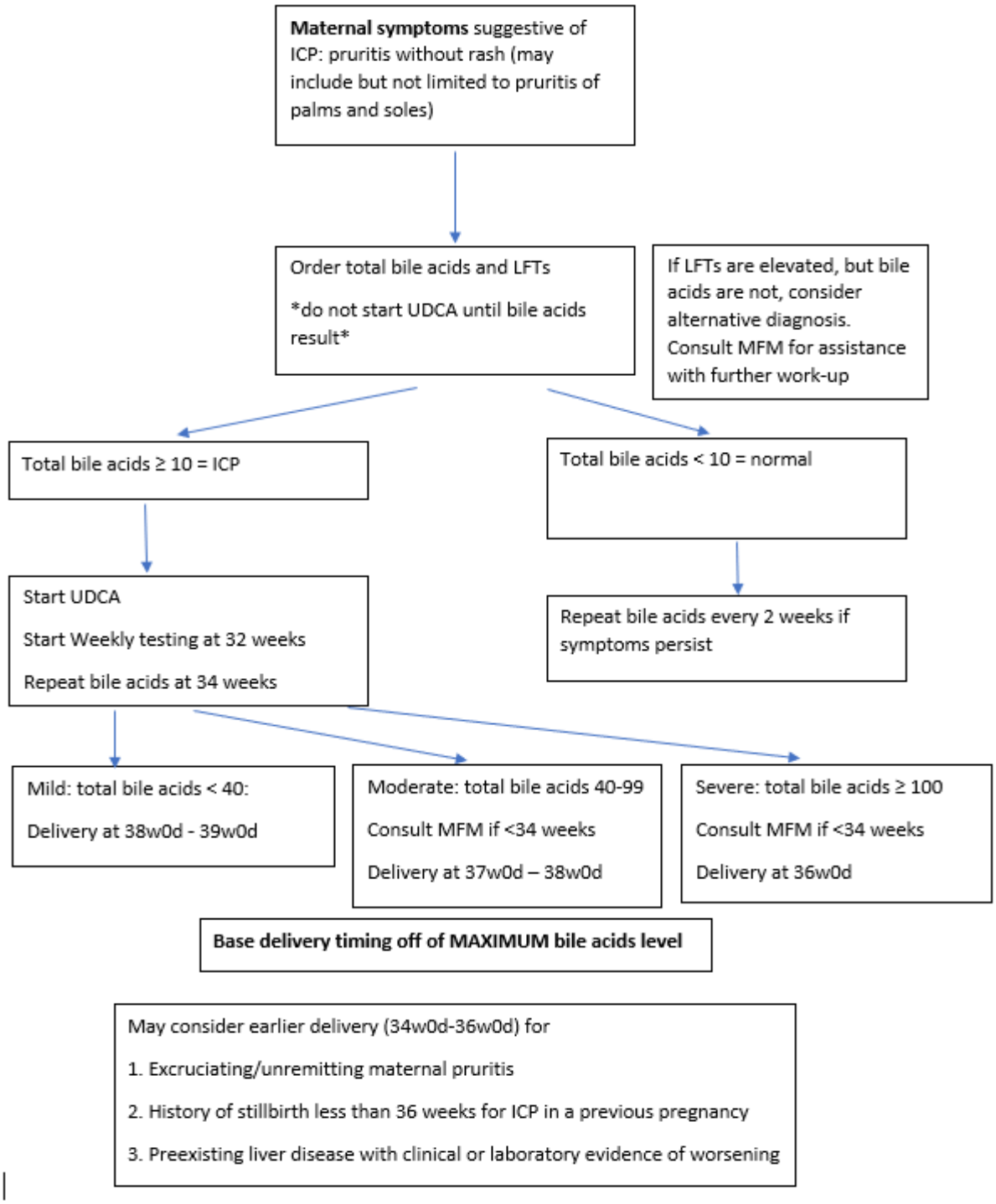
  AST and ALT levels

  - Elevation of AST/ALT is seen in the majority of cases[2]
  - Elevation of AST/ALT may precede increase in bile acids by 1-2 weeks[4]
  - Liver enzyme elevation may vary widely in ICP
  - ALT is more sensitive than AST[2]

Treatment/Management

- **Uresodeoxycholic acid** (UDCA aka Ursodiol, Actigall) is the **only** drug shown consistently decrease maternal symptoms and improve serum bile acids and liver function tests[18-20]
  - There may be some fetal benefit to treatment as well[18]
  - Starting dose of UDCA is 10mg/kg/day, divided into BID or TID dosing.
  - May increase further to maximum of 15mg/kg/day as needed for symptom control
  - Actigall (the most commonly prescribed form of UDCA) is available in 300mg tabs, and doses can be rounded as appropriate
  - For example, a 100kg patient could be started on a 1,000mg/day dose (600mg BID or 300mg TID), and increased to a maximum of 2000mg/day
- **Symptomatic treatment:** cool compresses, Benadryl, or aqueous cream with 2% menthol[2] may be considered

Delivery Timing and Logistical Practice for BMC and CHC providers



Algorithm adapted from University of North Carolina Dept. of Ob/Gyn with permission.

Note – if there are clinician concerns regarding inconsistent clinical picture, please consult MFM for management and delivery plan.

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