**TITLE: INTRAHEPATIC CHOLESTASIS OF PREGNANCY (ICP)**

**Subtitle: Diagnosis and management.**

**SUMMARY:** Intrahepatic cholestasis of pregnancy (ICP) causes intense pruritus and is associated with an increased risk of adverse pregnancy outcome including fetal loss when total bile acids are significantly elevated. Increased fetal surveillance and late preterm/early term delivery are warranted.

**Rationale:** ICP typically presents in the third trimester of pregnancy with itching on the palms and soles, usually worse at night, in the absence of a rash. Liver function tests may be abnormal. Elevation of total bile acids (TBA) above 10umol/L is confirmatory. While levels above 99 umol/L clearly confer a significantly increased risk of adverse perinatal outcomes, including spontaneous preterm birth meconium stained amniotic fluid, and stillbirth, TBA levels between 40 and 99 umol/L may also have some degree of increased risk. Although treatment with ursodeoxycholic acid (UDCA) improves pruritus for many patients and may lower bile acids, it may not lower the risk of adverse pregnancy outcome, particularly stillbirth. An evidence based approach for antenatal care and timing of delivery is not available: however, expert opinion supports antenatal surveillance and late preterm/early term delivery.

**Eligible patients:** Any patient presenting with severe pruritus in the third trimester of pregnancy, (although earlier disease onset has been reported), in the absence of a rash, should be evaluated for ICP if other dermatologic conditions, both pre-existing and pregnancy associated, are not evident (eg: allergic reactions, dry skin, atopic dermatitis, biliary cirrhosis, drug reaction, atopic eruption of pregnancy, polymorphic eruption of pregnancy (formerly known as PUPPS), acute fatty liver of pregnancy). Particular populations at high risk for ICP include those with multiple gestation, hepatitis C, cholelithiasis, IVF conception, age >35 y/o, and, most importantly, prior pregnancy affected by ICP.

**Contraindications:** None

**Technique:**

Obtain liver function tests (LFT) and TBA immediately on pregnant patients presenting with either generalized pruritus or that limited to the palms and soles in the absence of a rash. If symptoms persist with no other explanation, and initial labs are normal, repeat labs are indicated since pruritus can precede lab abnormalities by several weeks. If treatment with UCDA has been initiated empirically, these repeat labs can be normal.

In all cases, repeat LFT and TBA at 34 weeks. Weekly TBA are not recommended. Although fasting TBA were previously recommended, random values have been used in more recent studies and are more convenient for the patient.

First line treatment of pruritus consists of UDCA 300-500 mg BID with adjustment based on symptoms up to a total daily dose of 2000 mg. Women with high BMI, may need higher doses, up to 21 mg/kg/day. Hydroxyzine, emollient creams, and menthol creams may lessen itching but have not been studied in randomized controlled trials.

Recent clinical trials and meta-analyses support the use of fetal surveillance, which results in substantially lower rates of adverse perinatal outcomes compared with earlier reports. Institute fetal surveillance at a gestational age when delivery would be performed in response to abnormal fetal testing results or at the time of diagnosis if the diagnosis is made later in gestation. The optimal frequency and type of testing is unknown and may be determined by criteria such as comorbidities or TBA levels (eg, more frequent for TBA of 100 mmol/L or more). Twice weekly NST or weekly BPP with NST is reasonable.

Delivery timing is stratified based on maximum TBA level:

Symptoms c/w ICP but no TBA results: Deliver at 37+0 wks (or diagnosis if later)

TBA <40 umol/L: Proceed with delivery at 36+0 wks to 39+0 wks (or diagnosis if later). 37+0 wks is the local standard.

TBA 40-99 umol/L: Proceed with delivery at 36+0 wks to 39+0 wks (or diagnosis if later). No later than 37+0 wks is the local standard.

TBA 100 umol/L or greater: Proceed with delivery at 36+0 wks (or diagnosis if later)

TBA 100 umol/L or greater **AND** any of the following: (1) excruciating and unremitting maternal pruritus not relieved with pharmacotherapy (2) a history of stillbirth before 36 weeks of gestation due to ICP with recurring ICP in the current pregnancy (3) pre-existing or acute hepatic disease with clinical or laboratory evidence of worsening hepatic function: Proceed with delivery 34-36+0 wks.

**Special Considerations:**

Administer antenatal corticosteroids (ACS) for fetal lung maturity when delivery is pursued prior to 37+0 wks **AND** ACS haven not been administered previously.

 The risk of stillbirth is clearly increased in pregnant people with ICP and TBA of 100 umol/L or more: however, most affected pregnant people will have TBA under this threshold and possibly a risk of stillbirth that is similar to that of pregnant people in the general population, provided that repeat TBA testing is done. Data are confounded by treatment plans designed to prevent stillbirth which may have mitigated stillbirth risk. Co-existing pregnancy complications, such as pre-eclampsia or gestational diabetes, might increase the risk of stillbirth.

Due to the higher risk of stillbirth, patients with ICP should be placed on continuous fetal monitoring during labor.

Pre-eclampsia is a common complication which develops in patients with ICP. Onset is typically 2-4 weeks after the diagnosis of ICP.

Consider hepatitis C testing if not done previously in patients with risk factors who are diagnosed with ICP.

If symptoms persist 4-6 weeks postpartum, repeat TBA and LFT and refer to a liver specialist as appropriate, since complete resolution and correction of labs is expected shortly after delivery.

**References:**

Catherine Williamson and Victoria Geenes, Intrahepatic Cholestasis of Pregnancy. Obstet Gynecol. Vol 124, No.1, July 2014.

Ovadia, C et al. Association of adverse perinatal outcomes of intrahepatic cholestasis of pregnancy with biochemical markers: results of aggregate and individual patient data meta-analysis. Lancet. Vol 393. March 2, 2019.

Chappell LC et al. Ursodeoxycholic acid versus placebo in women with intrahepatic cholestasis of pregnancy (PITCHES): a randomized controlled trial. Lancet. Vol 394. September 7, 2019.

Lee RH et al for the Society for Maternal-Fetal Medicine Publications Committee. Society for Maternal-Fetal Medicine Consult Series #53: Intrahepatic cholestasis of pregnancy. pubs@SMFM.org. 2021.

ACOG Committee Opinion Number 818. Interim update: Medically Indicated Late Preterm and Early-Term Deliveries. Obstet Gynecol. Vol 137 No 2, February 2021.

Reviewed: February 2021

Updated 3/31/2022