HEALTH CARE PROFESSIONAL GUIDE
The Signs, Symptoms & Science of Intrahepatic Cholestasis of Pregnancy (ICP)

fight the itch. save a life.
Myths & Misconceptions

A normal liver panel rules out ICP
False. Many cases have been documented where symptoms precede biochemical abnormalities, in some cases by weeks or months. In cases of persistent pruritis in the absence of laboratory abnormalities, retesting is recommended every two weeks.

ICP is not a high risk condition for the fetus
False. Prior to modern active management practices, the reported stillbirth rate was as high as 10-15%. Even with active management there is a significantly higher risk of respiratory distress, meconium staining of the amniotic fluid and/or placenta and membranes, spontaneous preterm labor, and CTG abnormalities.

Ursodeoxycholic acid (UDCA) does not lower fetal risk
False. UDCA has been shown in meta-analysis to lower fetal risk. Additionally it has been shown to have no adverse maternal or fetal side-effects. Laboratory studies have shown that UDCA may help protect the fetus in the following ways:
  a. Preventing changes to the fetal heart induced by bile acids
  b. Preventing premature aging of the placenta induced by bile acids
  c. Facilitating transport of bile acids across the placenta via upregulation of breast cancer resistant protein.

ICP can present only in the third trimester
False. While 80% of ICP cases present in the third trimester, the remaining 20% present earlier, and there have been confirmed reports as early as 8 weeks gestation.

If laboratory values return to normal after treatment with UDCA, early delivery is no longer necessary
False. Early delivery is still recommended. Bile acid levels are subject to sudden and marked increases in the last weeks of pregnancy. Bile acid test results are not readily available and these increases cannot be predicted.

ICP patients are jaundiced
False. Clinical jaundice is rare, typically affecting less than 10% of patients with ICP.
Fetal Risk

1. **Stillbirth**
   Older studies prior to active management practices reported stillbirth rates as high as 10-15%.
   With active management, more recent studies report stillbirth rates similar to an uncomplicated pregnancy.
   Meconium staining of the amniotic fluid (MSAF) is associated with nearly every documented case of ICP-related stillbirth. Recent evidence suggests that this may be a result of premature aging of the placenta due to exposure to elevated bile acids. Discovery of MSAF warrants immediate delivery.

2. **Fetal distress or CTG abnormalities (21-44%)**

3. **Respiratory distress syndrome (17-33%)** can occur even in the presence of a mature lung profile
   Current evidence suggests that this is related to bile acid damage to the lungs

4. **Failure to establish breathing**

5. **Preterm Labor**
   Spontaneous preterm delivery occurs in 20-40% of cases.

6. **Meconium staining of the amniotic fluids and/or membranes and placenta (44-58%)**

7. **Intracranial hemorrhage**

Maternal Risk

1. **Maternal hemorrhage due to vitamin K deficiency**
   This is the only serious maternal risk reported. Older studies prior to current management practices reported rates as high as 20-25%.

2. **More recent literature reports no increased incidence of prolonged prothrombin or partial thromboplastin time**
Symptoms

1. **Pruritis**
   Considered the hallmark symptom of ICP and frequently the only symptom noticed. Moderate to severe pruritis may be intermittent or constant, and in the most severe cases interfere with sleep. Pruritis is sometimes most severe on the hands and feet, but often generalized and sometimes more prominent in other areas. Symptom severity does not correlate with disease severity.

   Pruritis is not typically associated with a rash, but prurigo nodules may develop as a result.

2. **Right upper quadrant pain**

3. **Dark urine**

4. **Pale stool and/or steatorrhea**

5. **Fatigue**

6. **Malaise**

7. **Mild depression**

8. **Clinical jaundice is rare**

Diagnosis

1. **Bile acids (BA)**
   Most authors accept 10-14 µmol/L as the upper limit of normal for total bile acids (TBA) in pregnancy.

   Special attention should be paid to cholic acid, as this is most sensitive for early diagnosis.

2. **Liver function tests (LFT)**
   AST or ALT over 40 IU/L can be used as a partial diagnostic tool.

   Bilirubin is rarely elevated and when it is, only mildly elevated.

   GGT is normal in most patients, elevated in a minority.
1. ICP has a complex etiology that is not fully understood

2. Genetics
   15% of ICP cases are associated with a defect in the ABCB4 (adenosine triphosphate binding cassette, subfamily B, member 4) gene.

3. Hormonal influences – increased estrogen and progesterone
   More common in twin and other multiple pregnancies.
   More common with in vitro fertilization.
   More common with progesterone therapy.
   More likely to present in third trimester when hormone levels are highest.

4. Environmental influences
   Higher prevalence in winter months in some areas.
   Has been linked with selenium deficiency.
   May be initiated or exacerbated by antibiotic use.

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1. Overall incidence in the United States is estimated at 1 in 1000 pregnancies

2. Worldwide, highest incidence rates occur in Scandinavian and South American populations

3. Latina populations in the United States are at higher risk (5.6%)
1. Frontline medication for the treatment of ICP is Ursodeoxycholic Acid (UDCA)
   Typical starting dosage is 600–900 mg/day.
   Dosage is frequently increased as pregnancy progresses. Normal dosages range from 10–20 mg/kg. It is common to exceed this dosage during pregnancy. UDCA has been found to be most effective in doses ranging from 600–2000 mg/day.

2. Early Delivery
   In mild cases (TBA < 40 µmol/L) delivery is recommended at 36–38 weeks.
   In severe cases (TBA > 40 µmol/L) delivery is recommended at 36–37 weeks. Some authors deliver as early as 34 weeks with amniocentesis results indicating a mature lung profile.

3. Monitoring
   Weekly TBA tests can be used to monitor effectiveness of UDCA therapy.
   Non-stress tests and biophysical profiles performed twice weekly. Effectiveness of these tests are under debate. It has been well-documented that it will not prevent all stillbirths, however there have also been documented cases of near-misses that resulted in live birth due to intervention.

4. Vitamin K Supplements
   May be considered for patients who show signs of fat malabsorption such as pale stool or steatorrhea, or patients with abnormal bruising. Prothrombin time and partial thromboplastin time are sometimes tested.

5. Cholestyramine is no longer recommended for treatment of ICP
   It has been shown to be inferior to UDCA in effectiveness and places the patient at increased risk of vitamin K deficiency.

6. Antihistamines and oatmeal baths do not improve pruritis
1. Repeat testing of LFT and FBA at 3-6 months postpartum is recommended to rule out underlying conditions

2. Future Pregnancies
   - Recurrence in subsequent pregnancies can be expected in 60-90% of cases.
   - Baseline FBA and LFT in the first trimester.
   - Repeat testing at symptom onset.
   - UDCA may be given immediately at symptom onset, prior to receipt of laboratory results.

3. Oral Contraceptives
   - Past consensus is that oral contraceptives are contraindicated for patients with a history of ICP.
   - Some authors suggest that low-dose pills may be used safely with LFT monitoring.
   - Newer studies suggest that progesterone may contribute to ICP perhaps even more so than estrogen, bringing into question the practice of using low-dose pills.

Suggested Reading


For more information, self-helps, or support, please visit

www.icpcare.org