

Intrahepatic Cholestasis of Pregnancy

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Intrahepatic cholestasis of pregnancy (ICP) is the most common pregnancy-specific liver disease. The incidence is between 0.2%-2% and is higher in South American and Northern European populations. Risk factors include multifetal gestations, a personal or family history of ICP, in vitro fertilization, cholelithiasis, advanced maternal age, and Hepatitis C.

Genetic, hormonal, and environmental factors each play a role. Transport of bile acids from the liver to the gallbladder is disrupted and bile acids become transported from the liver to the blood, resulting in systemic effects.

ICP classically presents in the third trimester with pruritis, generally of the palms and soles, often worse at night. Patients may have excoriations, but typically do not have a rash. Patients may also demonstrate dark urine, pale stools, and rarely, jaundice. A small proportion of patients may present earlier in gestation, with similar outcomes to patients presenting in the third trimester.

The diagnosis is confirmed by elevated total serum bile acids in the absence of an alternative diagnosis. The primary bile acids are cholic and chenodeoxycholic acid. The reference range for bile acids depends on the technique used and whether a patient has fasted before the collection. Most labs use an upper limit of normal of 10 micromoles/L. Liver enzymes may be elevated, but this is not necessary for the diagnosis. Other etiologies should be investigated if coagulation studies are abnormal.

Bile acids cross the placenta into the fetal circulation, posing significant risk to the fetus. ICP is associated with preterm delivery (spontaneous and indicated), non-reassuring fetal status, meconium staining, respiratory distress syndrome, and stillbirth. These pregnancies are at a increased risk for preeclampsia and gestational diabetes. There is a linear relationship between serum bile acid levels and the risk of fetal complications.

Ursodeoxycholic acid (UDCA) is the preferred treatment for symptomatic ICP. Liver indices, bile acids, and pruritis may improve with treatment. It is unclear if fetal outcomes improve. The

mechanism of action may involve a reduction of serum bile acids in both maternal and fetal circulations. There have been limited studies of other medications.

Given the increased risk of fetal demise after 37 weeks, many experts recommend antenatal testing and serial growth scans. Antenatal testing has not been shown to prevent stillbirth in this setting, but is the standard of care in many practices based on the relatively low risk of surveillance and potential severity of adverse outcomes. Some experts also suggest risk thresholds based upon bile acid levels. Some studies suggest an increased risk of adverse neonatal outcomes when bile acid levels exceed 40 micromoles/L. Weekly monitoring of bile acids may be warranted as those individuals could be managed more aggressively and delivered sooner. Recommendations vary, but most experts suggest delivery by 37 weeks. There is no contraindication to a vaginal delivery.

Patients should have liver function tests and bile acids rechecked 6-8 weeks after delivery to ensure resolution. The biochemical effects of ICP resolve rapidly after delivery and if they persist, an alternative diagnosis should be investigated. There is an up to 90% increased risk of recurrence in future pregnancies and with combined hormonal contraceptive use.

Further Reading:

- Williamson C, Geenes V. **Intrahepatic cholestasis of pregnancy.** [Obstet Gynecol. 2014 Jul;124\(1\):120-33. doi: 10.1097/AOG.0000000000000346.](#)
- Herrera CA, TA Manuck, GJ Stoddard, et al. **Perinatal outcomes associated with intrahepatic cholestasis of pregnancy.** [J Matern Fetal Neonatal Med. 2018 Jul;31\(14\):1913-1920. doi: 10.1080/14767058.2017.1332036. Epub 2017 Jun 5.](#)
- Westbrook RH, Dusheiko G, Williamson C. **Pregnancy and liver disease.** [J Hepatol. 2016 Apr;64\(4\):933-45. doi: 10.1016/j.jhep.2015.11.030. Epub 2015 Nov 30.](#)

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