

Intrahepatic cholestasis of pregnancy

Description

Intrahepatic cholestasis of pregnancy (also called ICP) is a liver disorder that typically occurs during the second half of pregnancy. Cholestasis is a condition that impairs the release of a digestive fluid called bile, which is made and released by the liver. In people with cholestasis, bile builds up in the liver, impairing its function. Because the problems with bile release occur within the liver (intrahepatic), the condition is described as intrahepatic cholestasis.

Severe itchiness (pruritus) is typically one of the first symptoms of intrahepatic cholestasis of pregnancy. The itchiness usually begins on the palms of the hands and the soles of the feet before spreading to other parts of the body. People with intrahepatic cholestasis of pregnancy have a buildup of bile acids in the blood. Bile acids are a component of bile and are produced when the liver processes cholesterol. Bile acid levels in the blood are normally low, but they can increase in people with liver disease.

Occasionally, people with intrahepatic cholestasis of pregnancy have yellowing of the skin and whites of the eyes (jaundice). People with intrahepatic cholestasis of pregnancy typically do not continue to have signs and symptoms of the condition after having the baby, though they may have an increased risk of developing disorders of the gallbladder, liver, or heart later in life.

Intrahepatic cholestasis of pregnancy can cause problems for the baby. This condition is associated with an increased risk of premature delivery and breathing problems in the newborn (meconium aspiration). Some infants born to people with intrahepatic cholestasis of pregnancy experience a slow heart rate and a lack of oxygen during delivery (fetal distress). People with higher levels of bile acids in their blood also have an increased risk of stillbirth.

Frequency

Intrahepatic cholestasis of pregnancy is the most common liver disease related to pregnancy. It is estimated to affect up to 2 percent of pregnancies, although the number of people affected varies by country and population. The condition is more common in people in South America and northern Europe. Historically, the highest incidence occurred in the Araucanian Indian population in Chile, although the incidence in this population has declined in recent years.

Causes

Intrahepatic cholestasis of pregnancy is a complex disorder. It is believed to be caused by a combination of genetic, hormonal, and environmental factors. Risk factors for developing intrahepatic cholestasis of pregnancy include underlying liver disease and a form of diabetes called gestational diabetes that occurs during pregnancy. Being pregnant with more than one baby or having a history of intrahepatic cholestasis of pregnancy also increases the risk of developing this condition. Sometimes, multiple people in a family can have intrahepatic cholestasis of pregnancy.

Variants in several different genes are believed to increase the risk of developing intrahepatic cholestasis of pregnancy. Many of these genes provide instructions for making proteins that help with the production (synthesis) or transportation of bile acids. In most cases, the variants that increase the risk of developing intrahepatic cholestasis of pregnancy are present in only one of the two copies of the gene,

The largest genetic contributor is the *ABCB4* gene; variants in this gene have been found in up to 25 percent of people with intrahepatic cholestasis of pregnancy. The *ABCB4* gene provides instructions for making a protein that helps move certain fats called phospholipids across cell membranes before releasing them into bile. Phospholipids attach (bind) to bile acids. Large amounts of bile acids can be toxic when they are not bound to phospholipids. Many of the variants in the *ABCB4* gene that have been found in people with intrahepatic cholestasis of pregnancy cause one protein building block (amino acid) to be substituted for another. A few *ABCB4* gene variants cause the cell to produce an abnormally short protein. Variants in other genes have been found to have a more limited contribution to the risk of developing intrahepatic cholestasis of pregnancy.

Even with these variants, enough protein is still available in most cases to move an adequate amount of phospholipids out of liver cells to bind to bile acids. The added stress on the liver during pregnancy, however, contributes to the buildup of bile acids. Toxic levels of bile acids can impair liver function, including the regulation of bile flow.

[Learn more about the genes associated with Intrahepatic cholestasis of pregnancy](#)

- ABCB11
- ABCB4
- ABCC2
- ATP8B1

Additional Information from NCBI Gene:

- NR1H4

Inheritance

An increased susceptibility to intrahepatic cholestasis of pregnancy typically has an autosomal dominant pattern of inheritance, which means one copy of the altered gene in each cell is sufficient to increase the risk of developing the disorder.

Other Names for This Condition

- Gestational cholestasis
- Obstetric cholestasis
- Pregnancy-related cholestasis
- Recurrent intrahepatic cholestasis of pregnancy

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Cholestasis, intrahepatic, of pregnancy, 1 (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3549845/>)

Genetic and Rare Diseases Information Center

- Intrahepatic cholestasis of pregnancy (<https://rarediseases.info.nih.gov/diseases/9804/index>)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

Clinical Trials

- ClinicalTrials.gov ([https://clinicaltrials.gov/search?cond=%22Intrahepatic cholestasis of pregnancy%22](https://clinicaltrials.gov/search?cond=%22Intrahepatic+cholestasis+of+pregnancy%22))

Catalog of Genes and Diseases from OMIM

- CHOLESTASIS, INTRAHEPATIC, OF PREGNANCY, 1; ICP1 (<https://omim.org/entry/147480>)

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28Cholestasis,+Intrahepatic%5BMAJR%5D%29+AND+%28intrahepatic+cholestasis+of+pregnancy%5BTIAB%5D>)

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