

# Intrahepatic Cholestasis of Pregnancy

Subjects: Genetics & Heredity

Contributor: Camila Xu

Intrahepatic cholestasis of pregnancy is a liver disorder that occurs in pregnant women.

Keywords: genetic conditions

---

## 1. Introduction

Cholestasis is a condition that impairs the release of a digestive fluid called bile from liver cells. As a result, bile builds up in the liver, impairing liver function. Because the problems with bile release occur within the liver (intrahepatic), the condition is described as intrahepatic cholestasis. Intrahepatic cholestasis of pregnancy usually becomes apparent in the third trimester of pregnancy. Bile flow returns to normal after delivery of the baby, and the signs and symptoms of the condition disappear. However, they can return during later pregnancies.

This condition causes severe itchiness (pruritus) in the expectant mother. The itchiness usually begins on the palms of the hands and the soles of the feet and then spreads to other parts of the body. Occasionally, affected women have yellowing of the skin and whites of the eyes (jaundice). Some studies have shown that women with intrahepatic cholestasis of pregnancy are more likely to develop gallstones sometime in their life than women who do not have the condition.

Intrahepatic cholestasis of pregnancy can cause problems for the unborn baby. This condition is associated with an increased risk of premature delivery and stillbirth. Additionally, some infants born to mothers with intrahepatic cholestasis of pregnancy have a slow heart rate and a lack of oxygen during delivery (fetal distress).

## 2. Frequency

Intrahepatic cholestasis of pregnancy is estimated to affect 1 percent of women of Northern European ancestry. The condition is more common in certain populations, such as women of Araucanian Indian ancestry in Chile or women of Scandinavian ancestry. This condition is found less frequently in other populations.

## 3. Causes

Genetic changes in the *ABCB11* or the *ABCB4* gene can increase a woman's likelihood of developing intrahepatic cholestasis of pregnancy.

The *ABCB11* gene provides instructions for making a protein called the bile salt export pump (BSEP). This protein is found in the liver, and its main role is to move bile salts (a component of bile) out of liver cells, which is important for the normal release of bile. Changes in the *ABCB11* gene associated with intrahepatic cholestasis of pregnancy reduce the amount or function of the BSEP protein, although enough function remains for sufficient bile secretion under most circumstances. Studies show that the hormones estrogen and progesterone (and products formed during their breakdown), which are elevated during pregnancy, further reduce the function of BSEP, resulting in impaired bile secretion and the features of intrahepatic cholestasis of pregnancy.

The *ABCB4* gene provides instructions for making a protein that helps move certain fats called phospholipids across cell membranes and release them into bile. Phospholipids attach (bind) to bile acids (another component of bile). Large amounts of bile acids can be toxic when they are not bound to phospholipids. A mutation in one copy of the *ABCB4* gene mildly reduces the production of *ABCB4* protein. Under most circumstances, though, enough protein is available to move an adequate amount of phospholipids out of liver cells to bind to bile acids. Although the mechanism is unclear, the function of the remaining *ABCB4* protein appears to be impaired during pregnancy, which may further reduce the movement of phospholipids into bile. The lack of phospholipids available to bind to bile acids leads to a buildup of toxic bile acids that can impair liver function, including the regulation of bile flow.

Most women with intrahepatic cholestasis of pregnancy do not have a genetic change in the *ABCB11* or *ABCB4* gene. Other genetic and environmental factors likely play a role in increasing susceptibility to this condition.

### 3.1. The genes associated with Intrahepatic cholestasis of pregnancy

- *ABCB11*
- *ABCB4*

## 4. Inheritance

Susceptibility to intrahepatic cholestasis of pregnancy is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to increase the risk of developing the disorder. Some women with an altered gene do not develop intrahepatic cholestasis of pregnancy. Many other factors likely contribute to the risk of developing this complex disorder.

## 5. Other Names for This Condition

- obstetric cholestasis
- pregnancy-related cholestasis
- recurrent intrahepatic cholestasis of pregnancy

---

## References

1. Bacq Y, Gendrot C, Perrotin F, Lefrou L, Chrétien S, Vie-Buret V, Brechot MC, Andres CR. *ABCB4* gene mutations and single-nucleotide polymorphisms in women with intrahepatic cholestasis of pregnancy. *J Med Genet*. 2009 Oct;46(10):711-5. doi:10.1136/jmg.2009.067397.
2. Brouwers L, Koster MP, Page-Christiaens GC, Kemperman H, Boon J, Evers IM, Bogte A, Oudijk MA. Intrahepatic cholestasis of pregnancy: maternal and fetal outcomes associated with elevated bile acid levels. *Am J Obstet Gynecol*. 2015 Jan;212(1):100.e1-7. doi: 10.1016/j.ajog.2014.07.026.
3. Dixon PH, van Mil SW, Chambers J, Strautnieks S, Thompson RJ, Lammert F, Kubitz R, Keitel V, Glantz A, Mattsson LA, Marschall HU, Molokhia M, Moore GE, Linton KJ, Williamson C. Contribution of variant alleles of *ABCB11* to susceptibility to intrahepatic cholestasis of pregnancy. *Gut*. 2009 Apr;58(4):537-44. doi: 10.1136/gut.2008.159541.
4. Geenes V, Chappell LC, Seed PT, Steer PJ, Knight M, Williamson C. Association of severe intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes: a prospective population-based case-control study. *Hepatology*. 2014 Apr;59(4):1482-91. doi: 10.1002/hep.26617.
5. Meier Y, Zodan T, Lang C, Zimmermann R, Kullak-Ublick GA, Meier PJ, Stieger B, Pauli-Magnus C. Increased susceptibility for intrahepatic cholestasis of pregnancy and contraceptive-induced cholestasis in carriers of the 1331T>C polymorphism in the bile salt export pump. *World J Gastroenterol*. 2008 Jan 7;14(1):38-45.
6. Pauli-Magnus C, Meier PJ, Stieger B. Genetic determinants of drug-induced cholestasis and intrahepatic cholestasis of pregnancy. *Semin Liver Dis*. 2010 May;30(2):147-59. doi: 10.1055/s-0030-1253224.
7. Williamson C, Geenes V. Intrahepatic cholestasis of pregnancy. *Obstet Gynecol*. 2014 Jul;124(1):120-33. doi: 10.1097/AOG.0000000000000346. Review.

---

Retrieved from <https://encyclopedia.pub/entry/history/show/11605>