

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%20cholestasis%20of%20pregnancy%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>)

%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days
%22%5Bdp%5D)

References

- Anzivino C, Odoardi MR, Meschiari E, Baldelli E, Facchinetti F, Neri I, Ruggiero G, Zampino R, Bertolotti M, Loria P, Carulli L. ABCB4 and ABCB11 mutations in intrahepatic cholestasis of pregnancy in an Italian population. *Dig Liver Dis.* 2013 Mar; 45(3):226-32. doi: 10.1016/j.dld.2012.08.011. Epub 2012 Sep 27. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/23022423>)
- Aydin GA, Ozgen G, Gorukmez O. The role of genetic mutations in intrahepatic cholestasis of pregnancy. *Taiwan J Obstet Gynecol.* 2020 Sep; 59(5):706-710. doi:10.1016/j.tjog.2020.07.014. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/32917322>)
- Bacq Y, Gendrot C, Perrotin F, Lefrou L, Chretien 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. Epub 2009 Jul 6. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19584064>)
- 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. Epub 2014 Jul 18. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/25046809>)
- Dixon PH, Sambrotta M, Chambers J, Taylor-Harris P, Syngelaki A, Nicolaides K, Knisely AS, Thompson RJ, Williamson C. An expanded role for heterozygous mutations of ABCB4, ABCB11, ATP8B1, ABCC2 and TJP2 in intrahepatic cholestasis of pregnancy. *Sci Rep.* 2017 Sep 18; 7(1):11823. doi: 10.1038/s41598-017-11626-x. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/28924228>)
- 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. Epub 2008 Nov 5. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18987030>)
- Dixon PH, Williamson C. The pathophysiology of intrahepatic cholestasis of pregnancy. *Clin Res Hepatol Gastroenterol.* 2016 Apr; 40(2):141-53. doi:10.1016/j.clinre.2015.12.008. Epub 2016 Jan 25. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/26823041>)
- 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. Epub 2014 Feb 26. Citation on PubMed (<https://pubmed>)

d.ncbi.nlm.nih.gov/23857305) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4296226/>)

- 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. doi: 10.3748/wjg.14.38. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18176959/>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2673389/>)
- Niemyjska-Dmoch W, Kosinski P, Wegrzyn P, Luterek K, Jezela-Stanek A. Intrahepatic cholestasis of pregnancy and theory of inheritance of the disease. Literature review. *J Matern Fetal Neonatal Med*. 2023 Dec;36(2):2279020. doi:10.1080/14767058.2023.2279020. Epub 2023 Nov 9. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/37945319>)
- Ovadia C, Seed PT, Sklavounos A, Geenes V, Di Ilio C, Chambers J, Kohari K, Bacq Y, Bozkurt N, Brun-Furrer R, Bull L, Estiu MC, Grymowicz M, Gunaydin B, Hague WM, Haslinger C, Hu Y, Kawakita T, Kebapcilar AG, Kebapcilar L, Kondrackiene J, Koster MPH, Kowalska-Kanka A, Kupcinskas L, Lee RH, Locatelli A, Macias RIR, Marschall HU, Oudijk MA, Raz Y, Rimon E, Shan D, Shao Y, Tribe R, Tripodi V, Yayla Abide C, Yenidede I, Thornton JG, Chappell LC, Williamson C. Association of adverse perinatal outcomes of intrahepatic cholestasis of pregnancy with biochemical markers: results of aggregate and individual patient data meta-analyses. *Lancet*. 2019 Mar 2;393(10174):899-909. doi:10.1016/S0140-6736(18)31877-4. Epub 2019 Feb 14. Erratum In: *Lancet*. 2019 Mar 16;393(10176):1100. doi: 10.1016/S0140-6736(19)30504-5. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/30773280>)
- 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. Epub 2010 Apr 26. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20422497>)
- Pillarisetty LS, Sharma A. Pregnancy Intrahepatic Cholestasis. 2023 Jun 4. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from <http://www.ncbi.nlm.nih.gov/books/NBK551503/> Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/31855347>)
- Pusch T, Beuers U. Intrahepatic cholestasis of pregnancy. *Orphanet J Rare Dis*. 2007 May 29;2:26. doi: 10.1186/1750-1172-2-26. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/17535422>)
- Roediger R, Fleckenstein J. Intrahepatic cholestasis of pregnancy. *Clin Liver Dis (Hoboken)*. 2024 Feb 20;23(1):e0119. doi: 10.1097/CLD.000000000000119. eCollection 2024 Jan-Jun. No abstract available. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/38379768>)
- Roediger R, Fleckenstein J. Intrahepatic Cholestasis of Pregnancy: Natural History and Current Management. *Semin Liver Dis*. 2021 Jan;41(1):103-108. doi:10.1055/s-0040-1722264. Epub 2021 Jan 20. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/33764488>)

- Sarker M, Zamudio AR, DeBolt C, Ferrara L. Beyond stillbirth: association of intrahepatic cholestasis of pregnancy severity and adverse outcomes. *Am J Obstet Gynecol*. 2022 Sep;227(3):517.e1-517.e7. doi: 10.1016/j.ajog.2022.06.013. Epub 2022 Aug 18. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/36008054>)
- Williamson C, Geenes V. Intrahepatic cholestasis of pregnancy. *Obstet Gynecol*. 2014 Jul;124(1):120-133. doi: 10.1097/AOG.0000000000000346. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24901263>)
- Zhu B, Yin P, Ma Z, Ma Y, Zhang H, Kong H, Zhu Y. Characteristics of bile acid metabolism profile in the second and third trimesters of normal pregnancy. *Metabolism*. 2019 Jun;95:77-83. doi: 10.1016/j.metabol.2019.04.004. Epub 2019 Apr 5. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/30959040>)

Last updated April 25, 2024