

Intrahepatic Cholestasis of Pregnancy (ICP) – Fact or Fiction?

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Intrahepatic cholestasis of pregnancy (ICP), also known as obstetric cholestasis (OC), is the most common liver condition specific to pregnancy. Research has identified that hormones, genetics and the environment all play a part in why a woman develops ICP, but it is still unclear what role each plays. Studies have shown an increased risk of stillbirth in affected pregnancies, but there is limited evidence to prove the mechanisms by which complications occur. These complexities have resulted in an absence of standardised management for ICP, resulting in conflicting information about diagnosis, treatment and management. The following article clarifies questions commonly asked and separates fact from fiction about this enigmatic condition of pregnancy.

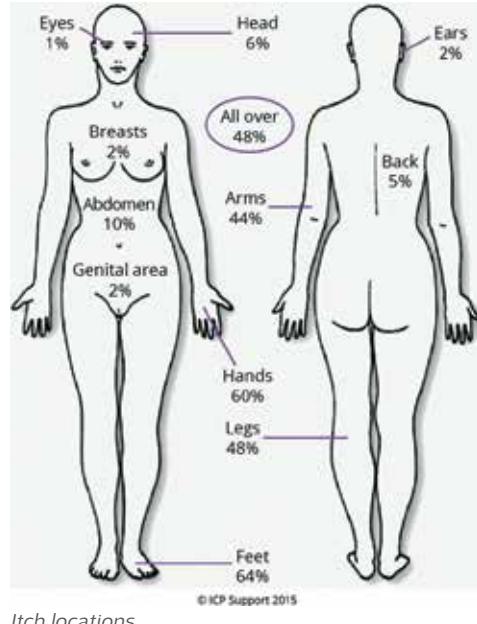
FICTION – ICP only presents in the third trimester

FACT – Approximately 80% of women will be diagnosed after 30 weeks of gestation (Kenyon et al 2002), although there are reports in the literature of diagnosis as early as eight weeks and anecdotal evidence that it can develop as early as 6 weeks.

Diagnosis of ICP is made by excluding and investigating other causes of pruritus (itching). Blood tests should include liver function, non-fasting bile acids, anti-mitochondrial and anti-smooth muscle antibodies, and hepatitis B and C serology. Most typically in ICP it is the liver function test (namely, alanine transaminase or aspartate transaminase) and bile acid test that shows abnormalities. It is not uncommon for bile acid levels to be elevated with a normal liver function test result (Geenes and Williamson 2009), but it is also documented that alanine transaminase may rise before bile acids do. Itch often precedes blood abnormalities by some weeks, so repeat testing is essential if itching persists and no other cause has been identified.

FICTION – Pruritus only presents on the palms of the hands and soles of the feet; otherwise it's not ICP

FACT – Pruritus can present anywhere on the body and can vary from mild to so severe that skin breakage occurs from repeated and frantic scratching. It is known to be typically worse at night (Ovadia and Williamson 2016).



Itch locations

Initially, bile acids were first thought to be the direct cause of pruritus, but it is now known that the itch does not typically correlate with bile acids levels and other pruritic agents have been identified, including lysophosphatidic acid (Kremer et al 2010) and sulphated progesterone metabolites, both of which have been shown to correlate more directly with levels of itch.

Given that women can be diagnosed with ICP as early as the first trimester, and that 20% of women will itch in pregnancy, some health professionals are concerned about over testing. There is no easy way to distinguish women who simply have pregnancy pruritus from those who have ICP, although the nocturnal nature of the itch in ICP may be a marker. It is possible that the combination of measuring the pruritic agents in conjunction with bile acids would be a better way of identifying women with ICP, but this needs further research and to be cost-effective. For now,



Impact of scratching

recognising that itch is not always purely on hands and feet is important for detecting those women who may be missed simply because their itch is not 'typical'.

FICTION – ICP doesn't cause stillbirth

FACT – Elevated maternal serum bile acid concentrations $\geq 40 \mu\text{mol/L}$ are associated with an increased risk of fetal distress, premature labour (spontaneous and iatrogenic), meconium staining and, in severe cases, stillbirth (Geenes et al., 2014). Geenes' work also identified concomitant conditions such as pre-eclampsia and gestational diabetes mellitus, supporting emerging data (Dixon and Williamson 2016) that suggest that all three conditions have an overlap, given their abnormal metabolic backgrounds.

The specifics of why and how complications occur are not clear, but observations suggest that bile acids may be elevated in the fetal/placental circulations (Ovadia and Williamson, 2016). Researchers suggest that when this occurs the fetal heart develops subtle arrhythmias that cannot be detected using standard obstetric surveillance, such as cardiotocography, leading to unpredictable and sudden fetal death.

Studies suggest the current drug of choice for treating women with ICP, UDCA, may reduce this risk and protect the fetal heart, although this requires more research (currently being undertaken) (Schultz et al 2016).

FICTION – All births should take place around 38 weeks

FACT – Women with ICP are commonly induced at around 37-38 weeks of pregnancy. . However the research suggests women, whose bile acids do not rise above the suggested threshold for fetal risk, could await spontaneous labour. (Geenes et al., 2014). Given that to date there have been no large trials and the mechanism for fetal death has still to be proven, it would seem appropriate to adopt a cautious approach about when women with ICP should meet their babies. The caveat should always be that bile acid levels are monitored frequently, with results available within 24 hours.

FICTION – It's only a condition of pregnancy

FACT – ICP has longer term health implications. Recurrence has been quoted as being greater than 60% in future pregnancies (Mays 2010). Outside of pregnancy women have a greater risk of developing gallstones and recent research suggests that women also have an increased chance of developing type 2 diabetes, cardiovascular disease and a lesser risk of biliary tree cancer in later life (Wikström Shemer et al 2015). Nonetheless, these studies highlight that ICP is not the transient condition it was first thought to be, and that it has future health implications for some women. It is therefore important that all women who have had ICP have liver function and bile acid tests after the birth of their baby to ensure that all biochemical abnormalities have resolved, and it may be prudent to repeat these tests on an annual basis. More research is clearly needed to better understand the impact of ICP on women so that clearer guidance on health monitoring can be given to health professionals.

FICTION – Women should only be seen by doctors

FACT – ICP is a complex condition requiring specialist knowledge. In midwifery-led care models the midwife may be the first health professional women tell about their pruritus. Although women will need to be seen by doctors, the midwife plays an important role in providing emotional support to the woman, who may be exhausted due to lack of sleep and anxious because of the risk of stillbirth. We know from the support lines and groups run by ICP Support that the risk of stillbirth is something that women can (understandably) become fixated on, and an empathetic response from midwives to this fear can make all the difference to how women cope.

We also know from these support groups that women tend to focus purely on the survival of their baby, with little thought given to birth. Whilst we would never minimise the very real risks that ICP brings, we would encourage health professionals to engage in discussion with women about labour and birth.

Conclusion

We have only really been able to scratch (pun intended!) the surface of this complex condition, but hope we have given you further insight into ICP and resolved common misconceptions about the condition. Clear, honest and up-to-date information given to women from those caring for them can make all the difference in supporting them, and improving your own knowledge of the condition may give you the confidence to be able to provide that support.

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