When itching during pregnancy can mean Intrahepatic Cholestasis of Pregnancy

By Caitlin Pieters

What is intrahepatic cholestasis of pregnancy (ICP)?

Intrahepatic cholestasis of pregnancy (ICP) is the most common liver disorder of pregnancy that affects around 5 000 women each year in the UK alone; at present this figure is unknown in South Africa.

What are the symptoms?

Itching (also called pruritus):

- Itching usually presents in the third trimester, however it's important to note that some women may develop ICP as early as the first trimester or second trimester of pregnancy.
- It can be mild or severe, constant or intermittent, localized or general. Many women report that it typically affects their hands and feet.
- It is generally reported as being worse at night, and often interrupts sleep. Researchers are unsure whether this is because women are more active during the day and notice it less or if there is biological reason for the nocturnal increase in severity.
- There is no rash associated with ICP, although scratch marks on the skin are common. Some women scratch until their skin bleeds.
- The severity of the itch does not necessarily correlate with the severity of the condition, and it is possible to itch for some time before blood work becomes elevated.

Other less-common symptoms:

- Dark urine
- Steatorrhoea (pale stools)
- Jaundice (yellowing of the skin and whites of the eyes thought to affect less than 20% of ICP women)
- Anecdotally many women report upper right quadrant pain (pain under or close to the right ribs where the liver is situated) but this has not been researched.
- Nausea
- Fatigue
- Anxiety and depression
- Loss of appetite

What are the risks?

ICP is associated with spontaneous preterm labour, foetal distress, meconium staining and in severe cases stillbirth. There is also an association of PPH (post partum haemorrhage) but this is thought to affect less than 20% of women with the condition. Recent research has suggested that with active management the risk of stillbirth in an ICP pregnancy is believed to be the same as that of a normal pregnancy (1%).

What are the causes?

The causes of ICP are not yet fully understood, but it is likely to be due to a number of different factors, including:

Hormones:

- ICP only occurs in pregnancy suggesting a hormonal link such as oestrogen or progesterone. Recent research has shown that sulfated progesterone metabolites (breakdown products of the hormone progesterone) are always higher in women with ICP and that these also seem to correlate with the bile acid levels. Further research is being undertaken to explore this link.
- Women expecting two or more babies seem to be predisposed towards developing the condition, as are women who have had IVF.

Genes:

- ICP is more common in certain populations, including Scandinavians and South Americans.
- ICP can run in families, including grandmother, mother and daughter (and may also pass down from the male side). Sisters and daughters of women with ICP have around a 14% increased chance of developing ICP in their own pregnancies. The presence of liver conditions and/or gallbladder issues in the mother's family may be indicative of a genetic link.
- Lots of research has been done to try to establish exactly what the link is, and some genetic variation in women with the disease has been found. However, it should be emphasized that researchers are a long way from explaining all cases of ICP by means of genetic analysis.

Environment:

- More women are diagnosed with ICP during the winter months.
- Although the reason for this is not clear, it suggests that there may be an environmental trigger for the condition, such as reduced exposure to sunlight or a change in diet.

How is ICP diagnosed?

To make a diagnosis of ICP, other liver disorders need to be ruled out first with either blood tests and/or liver ultra sound scanning.

These other conditions may include viral hepatitis, autoimmune hepatitis and gallstones. The presence of gallstones does not necessarily exclude a diagnosis of ICP – it is possible to have both ICP and gallstones. Research shows that women with ICP have a higher chance of either already having had gallstones or developing them in later life.

Blood tests:

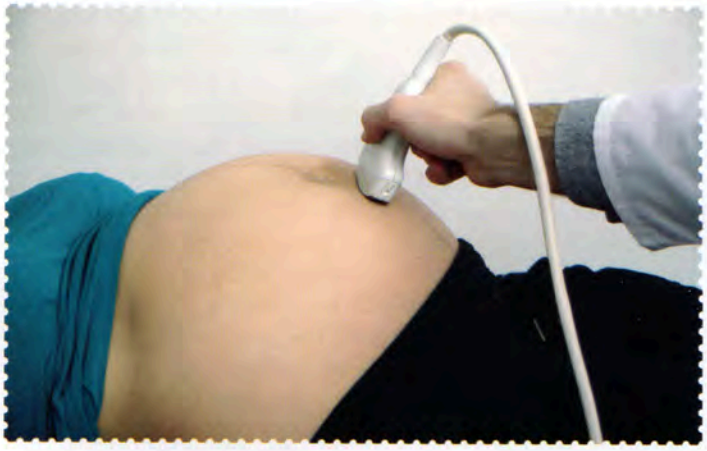
- *Bile acid test:* Bile acids are chemicals produced in the liver to help with digestion. In ICP the flow of bile acid in the liver is reduced and they build up in the blood. A bile acid test is believed to be the most specific test for ICP. Bile acids are thought to be harmful because they may be responsible for some of the complications that could affect the baby. It is largely accepted in the literature that a diagnostic cut-off for the diagnosis of ICP ranges from 10 to 14μmol/L (fasting sample). Anything over 40 mmol/L is considered to be "severe", and is associated with increased risk. In South Africa, bile acid test may be arranged by special request.
- *Liver function test:* This blood test looks at how well the liver is working by measuring the level of different enzymes. ALT (or AST) is the specific one that is used to help make the diagnosis. It is important to note that not all women with ICP will have raised liver functions.

Active management:

The most effective treatment is still to be established, but it is believed that with active management the risk of foetal complication drops to that of a normal pregnancy. Current practice includes prescribing the medication UDCA (ursodeoxycholic acid), monitoring bile acid levels and delivering the baby at around 36–38 weeks.

Medication:

- *UDCA (ursodeoxycholic acid)*: This is believed to be a "friendly" bile acid that displaces the more harmful bile acids from the blood. Many doctors believe that UDCA helps to protect the baby from the damaging effects of bile acid as well as helping to relieve symptoms. A recent pilot trial that looked at UDCA versus placebo showed that the incidence of meconium staining was reduced in those women who received UDCA and that the ALT/AST levels improved. However, it did not show that bile acid levels were improved for a significant number of women. A further larger-powered trial is planned.



UDCA is typically administered starting at 500mg per day, and rising in 500mg increments to a maximum dose of 2 000mg per day. Some clinicians still adhere to the recommended prescribing policy of basing the dosage on weight i.e. 12-15mg per kg of bodyweight but in the UK where the condition is the subject of extensive research most clinicians begin with 500mg twice a day. UDCA is still unlicensed for use during pregnancy but is prescribed to women with "informed consent".

- *Rifampicin:* This is a powerful antibiotic that is traditionally used to treat tuberculosis (TB). Recently it has been found to be helpful in treating ICP if UDCA is not effective. It must be given in addition to UDCA but there has been little research to evaluate its efficacy in treating ICP.
- *Piriton (Chlorpheniramine):* This is an antihistamine. This type of drug is used to treat itching in other conditions (e.g. allergies). There is no evidence to prove that it helps in ICP, and indeed many women would agree with this. However, another effect of Piriton is that it causes people to feel drowsy, and this may help if the itch is interrupting sleep.
- *Body cream with menthol:* Some women report a temporary relief from itching due to the cooling effect of menthol. It is relatively simple for a pharmacist to make up some aqueous cream with menthol added (1-2% of menthol).
- *Oral vitamin K: This practice evolved in the UK because clinicians hoped that it would help to reduce any risk of PPH. However there is no research to support its use although researchers in the UK will prescribe it if the woman reports steatorrhoea (pale stools).* There is no evidence to suggest that taking oral vitamin K is harmful to mother or baby.

Monitoring the blood:

- Both bile acid and liver function tests should be performed regularly. While liver function tests are indicative of how well the maternal liver is working, researchers believe that bile acid levels are most important in gauging the risk to the baby.
- Bile acid levels can be unpredictable and may go up and down during an ICP pregnancy. Given their association with foetal risk it is reasonable to implement a practice of weekly bile acid levels, perhaps twice weekly from 34 weeks.

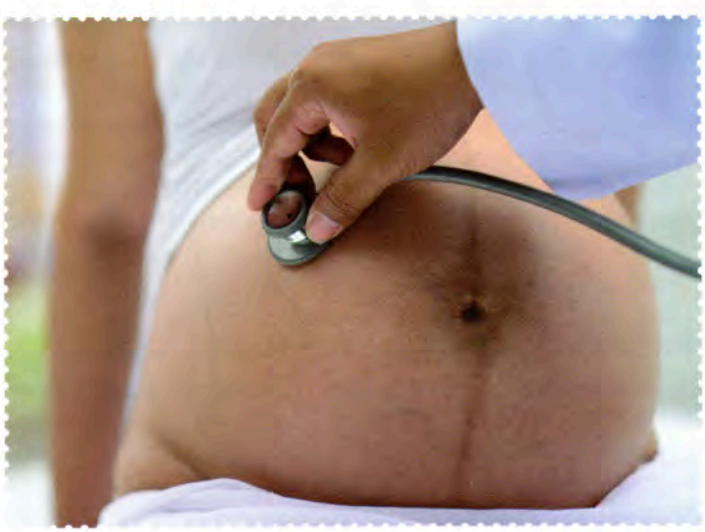
Monitoring the baby and early delivery:

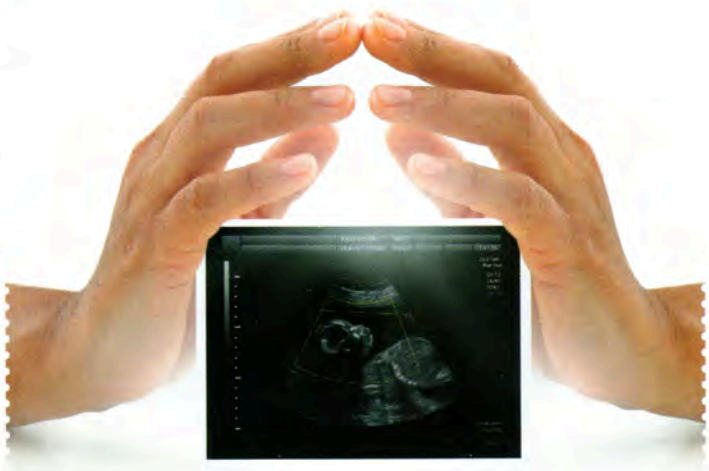
- Weekly monitoring from diagnosis is followed by many doctors in the UK but can vary in what it involves. However, it generally includes weekly blood tests (bile acids and liver function), with some hospitals adding biophysical profiles and Doppler flow studies.

- Non-stress tests that evaluate the foetal heart rate may be offered twice weekly, but they are only offered as a way of reassurance. The reason for this is because there have been reported cases of stillbirths 12-hours after a non-stress test was passed so there is no evidence to suggest that conducting this procedure will identify an "at risk" baby.
- Because research has shown that stillbirths tend to occur from 36 weeks the practice of early delivery has evolved. As the risk of sudden IUD (intra-uterine death) is also associated with bile acid levels (and recent research has shown a 200% increase in risk if the bile acids double for a mother who is in the "severe" category) it may be necessary to consider an earlier delivery than 36 weeks. This is a challenging decision for clinicians who have to weigh up the risk of early delivery and increased risk of the baby being admitted to the neonatal unit versus exposure to high bile acid levels and possible stillbirth. Research is currently investigating the exact mechanism for foetal death and has suggested that it is linked to the affect of bile acids on the foetal heart but further research is required before there are any definitive answers.
- Some women choose to keep a kick-chart to help monitor the baby's movements, although there is much debate on the value of these.

Other things that may help:

- There is no research to suggest that reducing saturated fats in the diet will help but as all women are advised to follow a healthy diet in pregnancy and saturated fats are not of any nutritional benefit it makes sense to let women know this.
- There is no research that suggests that rest and relaxation can help with the condition but it may help women to be able to cope with the psychological impact of having ICP.
- Some women report that cool clothing helps with the itch, as does applying an icepack to the affected area (but these need to be applied carefully to prevent any ice-burns).
- ICP can be a distressing condition, and many women feel depressed and anxious, which is exacerbated by lack of sleep due to itching. Just being able to talk to someone about this may help her feel supported. Referring women to specialist organizations such as ICP Support that has the benefit of having some trained counselors in the team may help. ICP Support is a science-based charity that also offers support via the phone, Facebook groups and an online forum. They can also be contacted via email.





What happens after the baby is born?

- Usually the condition resolves within 48 hours of delivery, but it can take several weeks for the itching to disappear completely.
- Around 6-12 weeks postpartum (although it can take longer for everything to settle), the mother's liver function and bile acid level should be checked to confirm that it has returned to normal. This is important, as there may be an underlying liver condition that has caused the itching and abnormal liver readings during pregnancy. If this is the case and the mother's bloods have not improved after several months she should be referred to a hepatologist (liver specialist) or gastroenterologist who has a special interest in the liver for further investigation.
- It is worth noting that some women report a return of ICP symptoms post-partum when using hormonal contraceptives, in which case alternative contraceptive methods may be discussed. It may be a case of trial and error, as what works for some women may not work for others.
- Some women experience "cyclic itching" during ovulation or at the start of menstruation. It generally only lasts for a few days and is not as intense as the itching experienced during an ICP pregnancy. There has been no research to explain why this happens, but current thinking suggests that it happens because the liver has been left 'sensitive' to hormone fluctuations.
- Some women have reported that they experience itching again in times of extreme tiredness and stress, but the reasons for this are not yet known.

Will ICP reoccur?

Reported recurrence rates vary, with some researchers stating 60% and others up to 90%. What is known is that women who have ICP in one pregnancy are very likely to develop it again in a subsequent one.

More information and support

All information in this article was sourced from ICP Support, a UK-based charity who are involved with research into the condition, and who are linked to ICP specialists. Other information and current research papers can be downloaded directly from their website. For more information, please visit:
Website: www.icpsupport.org
Facebook group: www.facebook.com/groups/icpsupportsa