Obstetric Cholestasis (OC)

Jenny Chambers and **Alice Tuson**

share information with midwives on this condition, its symptoms and how to offer women support

SUMMARY Obstetric cholestasis (OC) is the most common liver condition specific to pregnancy and affects around 5,000 women in the UK every year. It's generally benign for the mother although the main presenting symptom of pruritus can sometimes be so severe that the woman scratches herself until she bleeds. However, the main concerns are for the fetus, as the condition is associated with an increased risk of fetal distress, spontaneous premature labour and stillbirth. This article aims to provide information about the condition so that as a practising midwife you can offer women sufficient support should OC be suspected or diagnosed.

Keywords Obstetric cholestasis, intrahepatic cholestasis of pregnancy, stillbirth, itching, pruritus, liver

Author Jenny Chambers, a clinical trials coordinator at Imperial College London and founder of OC Support and Alice Tuson, an NCT student antenatal teacher and trustee for OC Support

For the midwife if a woman presents in the first, second or third trimester with a complaint of 'itching', would obstetric cholestasis come to mind?

For the mother if you were 'itching' during pregnancy, would you think to mention it to your midwife?

'Itching' can be a common discomfort of pregnancy but for some women it's the only symptom of a complex liver condition of pregnancy, obstetric cholestasis (OC), also referred to as intrahepatic cholestasis of pregnancy. OC affects around 5,000 pregnancies per year in the UK (Geenes and Williamson 2009) and is associated with fetal distress, spontaneous premature labour and, in severe cases, stillbirth (Davies and Elias 1993).

Gemma's reflection of OC (page 30) isn't what would be considered a 'typical' case study of the condition but it's a good example of how severe it can be and how early it can present in pregnancy. It also highlights how debilitating it can be for a woman to experience such intense pruritus and how important it is for her to have the appropriate level of care from health professionals.

A 'typical' case

Around 80 per cent of cases of OC present after 30 weeks of gestation (Kenyon et al 2002) but it has been reported as early as eight weeks (Berg et al 1986).

Pruritus (which is defined as an unpleasant sensation that evokes the desire to scratch) (Geenes and Williamson 2009) is the most common symptom of OC, usually presenting in the third trimester and often becoming more severe as the pregnancy progresses. It is typically noticed on the palms of the hands and soles of the feet but can affect anywhere on the body. Women may also report that the ►

itch is worse at night (Geenes and Williamson 2009).

Other symptoms

Some women may also experience dark urine, steatorrhea (pale stools), epigastric pain and jaundice (although jaundice is uncommon, affecting only 20 per cent of women with OC) (Lunzer 1989). It's also not unusual for the woman to feel unwell, tired and to lose her appetite.

Causes of OC

The aetiology of the condition is not yet fully understood but researchers believe that it includes:

- Genetics: it has been identified in several female family members of some cases including grandmother, mother and daughter
- Hormones: it only manifests in pregnancy and women expecting more than one baby are more predisposed towards developing it than those expecting a singleton
- Environment: there are more reported cases in winter months

(Geenes and Williamson 2009).

Diagnosis

OC is a diagnosis of exclusion so other causes of the pruritus need to be investigated. These will include checks for auto immune hepatitis, auto antibody conditions such as primary biliary cirhossis (PBC) and hepatitis C. Liver function tests will focus on the alanine transaminase (ALT) result and a bile acid test is also considered routine in most hospitals. It is possible to diagnose OC with a raised bile acid and normal ALT but not the other way round.

A cause for concern

For the woman there may be an increased risk of postpartum haemorrhage (PPH) (Kenyon et al 2002) although this tends to be low. However, as the condition can cause great anxiety in the woman there may be an increased risk of depression during pregnancy.

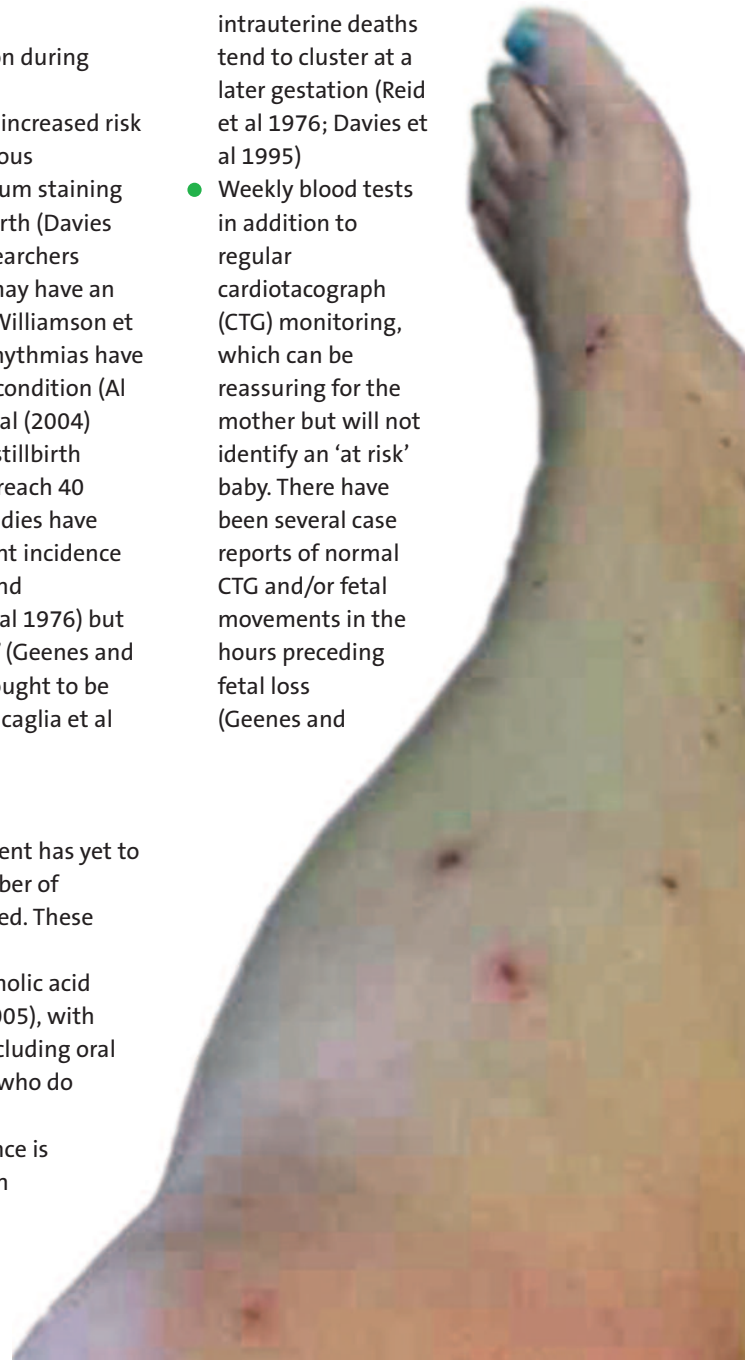
Pruritus is the most common symptom of OC, usually presenting in the third trimester and often becoming more severe as the pregnancy progresses

For the baby there is an increased risk of fetal distress, spontaneous premature labour, meconium staining and, in severe cases, stillbirth (Davies and Elias 1993). Some researchers postulate that bile acids may have an effect on the fetal heart (Williamson et al 2001) as fetal heart arrhythmias have been associated with the condition (Al Inizi et al 2006). Glantz et al (2004) speculate that the risk of stillbirth increases when bile acids reach 40 µmol/l (fasting). Some studies have reported a 10 to 15 per cent incidence of stillbirth (Laatikainen and Tulenheimo 1984; Reid et al 1976) but with 'active management' (Geenes and Williamson 2009), it is thought to be less than 3.5 per cent (Roncaglia et al 2002; Kenyon et al 2002).

Active management

The most effective treatment has yet to be established, but a number of strategies are currently used. These include:

- The use of ursodeoxycholic acid (UDCA) (Glantz et al 2005), with some clinicians also including oral vitamin K. For women who do not respond to UDCA (response in this instance is defined as no reduction in bile acid levels despite increasing the dosage up to 2g per day), a clinician may also prescribe rifampicin (Geenes and Williamson 2009)
- A recent clinical pilot trial of UDCA versus placebo identified that the drug does improve liver function (in that it reduces ALTs) and that the incidence of meconium staining was less in those women who took it (Chappell et al 2012)
- Induction of labour at 37–38 weeks gestation. Inducing birth early has evolved because some researchers have found that the intrauterine deaths tend to cluster at a later gestation (Reid et al 1976; Davies et al 1995)
- Weekly blood tests in addition to regular cardiotacograph (CTG) monitoring, which can be reassuring for the mother but will not identify an 'at risk' baby. There have been several case reports of normal CTG and/or fetal movements in the hours preceding fetal loss (Geenes and



Williamson 2009).

It is also important to acknowledge that there is no treatment for the itch at present, although some women find that UDCA does reduce the sensation and others find relief with anti allergy tablets (the side effects can help them to sleep) and by applying aqueous cream with menthol to the skin. The recent findings from the Pregnancy Intervention Trial in Cholestasis (PITCH) showed that UDCA significantly reduced pruritus, but that following a survey conducted amongst clinicians and affected women the size of the benefit was considered too small for most doctors to recommend the drug, or for women to want to take it. However, for those women who experience severe itching any relief might be considered beneficial and so some women may still want to try to see if it helps them (Chappell et al 2012).

One very recent promising finding by researchers is that it is not the bile acids that directly cause the 'itch' but instead a naturally occurring lipid called lyposophatidic acid (LPA) (Kremer et al 2010). It is hoped that this information may lead to a treatment for the pruritus.

Recurrence in subsequent pregnancies

Recurrence has been quoted as being more than 60 per cent (Mays 2010). Interestingly, some women develop the condition after one or more non-OC pregnancies and those who do develop it in more than one pregnancy seem to demonstrate variations in itch and blood results that show no obvious pattern (Reyes 1997).

Conclusion

We hope this article together with Gemma's reflection (page xx) has furthered your knowledge and understanding of this complex condition. There is still much to be discovered by researchers but clinicians can help with the management of OC by simply listening to women. As Gemma's piece illustrates, she knew something was wrong but found it challenging to convince other health professionals. One is left to ponder on what might have happened had she not been a midwife. **TPM**

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Further resources

www.ocsupport.org

References

Al Inizi S, Gupta R and Gale A (2006). 'Fetal tachyarrhythmia with atrial flutter in obstetric cholestasis'. *Int jour gynecol obstet*, 93(1): 53-54.

Berg B, Helm G, Petersohn L et al (1986). 'Cholestasis of pregnancy. Clinical and laboratory studies'. *Acta obstet gynecol Scand*, 65(2): 107-113.

Chappell LC, Gurung V, Seed PT et al (2012). 'Ursodeoxycholic acid versus placebo, and early term delivery versus expectant management, in women with intrahepatic cholestasis of pregnancy: semifactorial randomised clinical trial'. *Brit med jour*, 344: doi: 10.1136.

Davies MH and Elias E (1993). 'Intrahepatic cholestasis of pregnancy pathogenesis and management'. *Trop gastroenterol*, 14: 79–86.

Davies MH, da Silva RC, Jones SR et al (1995). 'Fetal mortality associated with cholestasis of pregnancy and the potential benefit of therapy with ursodeoxycholic acid'. *Gut*, 37: 580-584.

Geenes V and Williamson C (2009). Intrahepatic cholestasis of pregnancy. *World J Gastroenterol*, 15(17): 2049-2066.

Glantz A, Marschall HU, Lammert F et al (2005). 'Intrahepatic cholestasis of pregnancy: a randomized controlled trial comparing dexamethasone and ursodeoxycholic acid'. *Hepatology*, 42(6): 1399–1405.

Glantz A, Marschall HU and Mattsson LA (2004). 'Intrahepatic cholestasis of pregnancy: relationships between bile acid levels and fetal complication rates'. *Hepatology*, 40(2): 467-474.

Kenyon AP, Piercy CN, Girling J et al (2002). 'Obstetric cholestasis, outcome with active management: a series of 70 cases'. *Brit jour obs gyn*, 109(3): 282-288.

Kremer AE, Martens JJW and Kulik W (2010). 'Lysophosphatidic acid is a potential mediator of cholestatic pruritus'. *Gastroenterology*, 139(3): 1008-1018.

Laatikainen T and Tulenheimo A (1984). 'Maternal serum bile acid levels and fetal distress in cholestasis of pregnancy'. *Int j gynaecol obstet*, 22(2): 91-94.

Lunzer MR(1989). 'Jaundice in pregnancy'. *Baillieres clin gastroenterol,* 3(2): 467–483.

Mays JK (2010). 'The active management of intrahepatic cholestasis of pregnancy'. *Curr Opin Obstet Gynecol*, 22(2): 100-103.

Reid R, Ivey KJ, Rencoret RH et al (1976). Fetal complications of obstetric cholestasis. *Br med j,* 1(6014): 870-872.

Reyes H (1997). Review: intrahepatic cholestasis. A puzzling disorder of pregnancy. *Jour gastroenterol hepatol*, 12(3): 211-216.

Roncaglia N, Arreghini A, Locatelli A et al (2002). 'Obstetric cholestasis: outcome with active management'. *Eur j obstet gynecol reprod boil,* 100(2): 167-170.

Williamson C, Gorelik J, Eaton BM et al (2001). 'The bile acid taurocholate impairs rat cardiomyocyte function: a proposed mechanism for intrauterine fetal death in obstetric cholestasis'. *Clin sci*, 100(4): 363–369.