



Obstetric cholestasis: information about the condition, its consequences for women and why this knowledge is important to midwives and others caring for women in pregnancy, labour and afterwards

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Introduction

Itching in pregnancy can be normal, but for some women it is the presenting symptom of an underlying condition that can cause maternal illness and, in severe cases, may result in a stillbirth. This is an uncommon condition of pregnancy and it is called obstetric cholestasis (OC), also known as intrahepatic cholestasis of pregnancy (ICP).

OC has complicated both of my pregnancies but thankfully my babies have been born safe and well. Through reflective practice, I have spent time looking at my own experiences and views about this condition, and how it is managed in order to offer an objective and balanced review (Schott & Priest 2002:24). I am acutely aware of how important it is to continue to raise awareness of this condition as my own experience, together with anecdotal evidence from forums on support websites, confirms that conflicting information is currently given to women about its symptoms, diagnosis, treatment and management. It is also clear from these forums that not all women are aware that itching in pregnancy can be indicative of a possible problem.

In preparation for writing this article, I've spoken to a number of women who have suffered with this condition and asked them to comment on how it felt both physically and emotionally to experience a pregnancy and birth journey complicated by OC.

About the condition

OC is a liver disorder that occurs during pregnancy and resolves spontaneously following birth. It is a condition in which the flow of bile from the liver is reduced leading to raised bile salts (also referred to as bile acids), in the woman's blood. It typically presents in the late second or third trimester (although it is not uncommon for it to occur earlier than this).

OC complicates one in 140 (0.7%) pregnancies in the UK, although it is more common in women of Indian or Pakistani origin, affecting around one in 70–80 (1.2–1.5%) pregnancies (Abedin *et al* 1999). Women expecting twins (or more, eg triplets) seem to be predisposed towards developing the condition and so too are women who have had IVF. Mothers, daughters and sisters of affected women have a higher than average risk of being affected.

Several fetal complications have been reported in OC pregnancies that include an increased risk of preterm delivery (both spontaneous and induced), fetal distress and, in severe cases, stillbirth.

Recurrence in subsequent pregnancies has been estimated as greater than 60% (Mays 2010).

What are the symptoms?

The presenting symptom is pruritus, generally known as 'itching' but which is actually defined as '*an unpleasant sensation that evokes the desire to scratch*' (Geenes & Williamson 2009). This typically presents without a rash and can be mild or so severe that the woman scratches herself until she

bleeds. It can be constant or intermittent and usually begins on the arms, legs, palms of the hand and soles of the feet, although it may occur anywhere on the body including the face. It is usually worse at night, often disturbing the woman's sleep. The cause of itch is poorly understood but recent research has identified lysophosphatidic acid (LPA) as a mediator of potential itch (Kremer *et al* 2010).

Other symptoms that may occur include; steatorrhea (pale stools), dark urine, right upper quadrant pain (this is not common) and jaundice (this too is uncommon), affecting less than 20% of women with OC. It is also not uncommon for the woman to feel generally unwell, tired and to lose her appetite.

What are the concerns?

For the fetus there is an increased risk of premature birth (both spontaneous and iatrogenic), fetal distress, meconium stained liquor and stillbirth. The mechanism for stillbirth is not completely understood but may involve the effect of bile acids on the fetal heart and/or placenta. Incidence of stillbirth is also difficult to quantify but has been quoted as being between 10–15% in some older studies (Laatikainen & Ikonen 1975, Reid *et al* 1976). However, with active management (defined as including weekly blood tests, the possible use of medication such as UDCA and early delivery) several studies have reported a reduction in perinatal mortality to under 3.5% (Lee *et al* 2008, Geenes & Williamson 2009).

For the mother the condition can be very distressing due to the symptoms, especially when the pruritus leads to prolonged periods of sleep deprivation, unless effective treatment can be given to stop the itching. Anxiety also features in OC because of the mother's concerns for the fetus. In most cases, symptoms resolve very soon after the baby is born. There is a small chance that the woman will suffer postpartum haemorrhage (PPH) following delivery but treatment with oral vitamin K has been used as a possible way of preventing this (Kenyon *et al* 2002), although no trials have established its validity as a treatment option. There is no evidence to show that OC has any long term affect on the woman's health, although some studies indicate that gallstones occur more commonly in women who have had OC (Williamson *et al* 2004).

How is it diagnosed?

The diagnosis of OC is made by excluding other causes of pruritus, which may include viral hepatitis, autoimmune hepatitis and primary biliary cirrhosis (PBC). A liver scan is also prudent to check for gallstones that may be trapped in the common bile duct, although the presence of gallstones in the gallbladder does not necessarily exclude a diagnosis of OC as it is possible to have both OC and gallstones. Women with Hepatitis C are known to have an increased risk of developing cholestasis which may also present earlier in pregnancy (Locatelli *et al* 1999). Dermatological conditions should also be excluded even though in OC the presence of a rash is uncommon, as with gallstones, it is possible to have OC and a dermatological condition (such as eczema). The condition can also present after the woman has taken penicillin based antibiotics and research has identified that some women carry a genetic polymorphism linked to antibiotic sensitivity (Dixon *et al* 2009).

Blood tests

In OC, liver function tests (eg transaminases) and bile acids become elevated although not necessarily concomitantly. In some women bile acids become elevated before liver

transaminases and *vice versa* (Heikkinen 1983). Alanine Transaminase (ALT) and Aspartate Transaminase (AST) are of importance in making the diagnosis, although ALT is specific to liver damage so this enzyme is more helpful. As some liver enzymes drop in the third trimester of pregnancy (Girling *et al* 1997) it is important to use an adjusted reference range for pregnancy as many laboratories report non-pregnant ranges. As a rule of thumb, the upper value of the normal non-pregnant reference range for ALT and AST should be reduced by 20% to establish a corrected reference range that can be used in pregnancy. This will help the clinician to adjust for the pregnancy-related decrease in liver transaminases.

Some studies have demonstrated an increased rate of fetal complications in the presence of raised maternal serum bile acids (Laatikainen & Tulenheimo 1984) So testing for raised levels may prove useful: most laboratories use a normal reference range of $\leq 14 \mu\text{mol/l}$. One Swedish study reported that fetal risks occur after bile acids reach $40 \mu\text{mol/l}$ (fasting sample) and increase 1% for each rise in μMol thereafter (Glantz *et al* 2004).

Some hospitals will also perform coagulation tests to check for clotting as this may be impaired in OC.

What are the treatment and management options?

Treatment typically includes the use of UDCA (ursodeoxycholic acid) which is a hydrophilic 'liver-friendly' bile acid that displaces the hydrophobic 'harmful' bile acids in the bile acid pool (Palma *et al* 1992). UDCA has not been licensed for use in pregnancy, although it has been shown to relieve the mother's symptoms and improve biochemical abnormalities (Glantz 2005). A recent pilot trial, Pregnancy Intervention Trial in Cholestasis (PITCH 2009), investigated UDCA *versus* a placebo but the data are still being evaluated. To date there have been no reports of any problems in using UDCA and standard prescribing involves 500 mg BD increasing to 2g if the woman has no response (defined as reduction in bile acids and/or improvement in pruritus).

The use of rifampicin is a relatively new concept in the treatment of OC. It has been used concomitantly with UDCA in a study that suggests they work in complementary ways to improve cholestasis (Marschall *et al* 2005) and is now being used in some hospitals in the UK where UDCA alone has not improved biochemical markers and/or pruritus.

Oral vitamin K is also sometimes prescribed to women as it is thought to prevent the risk of PPH which has been connected with this condition. As previously discussed this practice is not evidence-based.

Some women are prescribed Chlorpheniramine (Piriton). The helpfulness of Piriton is debatable. It is generally prescribed because of its sedative effect and may help the woman sleep. Any benefit in itch is most likely placebo. Aqueous cream with menthol is often prescribed to help soothe the skin.

The literature about stillbirth in OC is limited as all studies are retrospective or small case series. However, some studies have shown that stillbirths have tended to cluster between 37 and 39 weeks of pregnancy. The practice of earlier delivery in the UK evolved following a small study in Australia that reported a reduction in stillbirths in women with the condition if they were delivered by 38 weeks of pregnancy (Fisk & Storey 1988). Trials that are sufficiently powered to produce statistical significance are required to support or refute this practice but given the accepted risk of stillbirth, many clinicians currently choose to expedite delivery in the absence of any robust evidence from appropriate clinical trials (Saleh & Abdo 2007). As previously mentioned it is this combination of delivering early, regular blood tests and the use of medication to treat the condition, often referred to as 'active management' (Kenyon *et al* 2002, Roncaglia *et al* 2002) that is thought by some researchers to reduce the risk of stillbirth.

Some doctors also suggest the woman has regular CTG monitoring as well as additional scans; this can be very comforting for the medical professionals

as well as the woman but there appears to be no evidence that it will identify the 'at risk' baby. Geenes & Williamson (2009) identify several case reports with normal CTG and/or normal fetal movements in the hours preceding fetal loss. It may be more helpful to advise the woman to monitor her own baby's movements and contact her maternity unit if she notices any change in pattern or reduction in movements (Whitworth *et al* 2011).

The aetiology of OC

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

Hormones

- It is thought that the pregnancy hormones oestrogen and progesterone impair the ability of the liver to regulate bile acids and therefore 'unmask' the disease in susceptible women. The exact pathway of this is not fully understood. (Reyes 2008)
- Hormonal factors may explain why it appears that OC is slightly more common in women who have had IVF or women expecting multiple pregnancies.

Genes

- OC is more common in certain populations, including Scandinavians and South Americans, and is known to run in families – these observations raise the possibility of a genetic cause for the disease.
- Researchers have identified a number of mutations and polymorphisms within bile transporter genes that provide an explanation for a component of genetic susceptibility to OC. Work is continuing in this area. (Dixon & Williamson 2008)

Environment

- More women are diagnosed with OC during the winter months – although the reason for this is not clear but may suggest that there is an environmental trigger for the condition, such as a reduced exposure to sunlight or a change in diet (there is a trend to eat food higher in fat in winter).

- Incidence for the condition reduced in South America (specifically Chile) when selenium was added to the diet of the general population supporting the inclusion of an environmental factor.

Following the birth

Liver function abnormalities and bile acid levels generally resolve rapidly following delivery although there have been reports of this taking longer than six months. Generally, clinicians check liver function and bile acid levels around 6–12 weeks postnatally. If levels do not improve after six months, the woman should be referred to a Hepatologist (liver specialist) as she may have another liver condition. It is the resolution of abnormal liver function tests together with the disappearance of the pruritus that will give a final confirmation of diagnosis.

Contraception

There has been little research conducted into this area, but typically women are advised to avoid hormonal contraception if possible to prevent any possible recurrence of pruritus and abnormal liver function. However, some women have reported using the combined oral contraceptive pill with no return of symptoms whilst others have itched almost immediately. Other forms of hormonal contraception that bypass the liver, such as the Mirena intra-uterine device, can be considered although anecdotally some women have also reported itching as a result of this (OC Support UK). It is important to check the liver function before commencing any form of hormonal contraception and it may be prudent to advise women to have an annual liver function check.

Cyclical itching

Many women have reported that they notice their pruritus returns after their pregnancy which can be linked to ovulation and the start of menstruation. Researchers are unsure why this is but it has been postulated that the liver may be left 'sensitive' to hormonal fluctuations. Women have also reported that the itching returns or is worse when they are tired or stressed (OC Support UK).

Where can you get more information about OC?

www.ocsupport.org.uk

www.britishlivertrust.org.uk

<http://www.rcog.org.uk/files/rcog-corp/GTG43obstetriccholestasis.pdf>

Case study

This case study is my personal experience of my second OC pregnancy.

I was 30 years old, with one previous pregnancy that was complicated by OC resulting in a healthy baby boy born at 38 weeks' gestation, weighing 7lb 14oz.

With my history of OC, baseline LFTs were done at the booking in appointment at 12 weeks' gestation. They were: ALT–29, Bilirubin–8, Alkaline Phosphatase–59, Albumin–43. A bile acid test was not performed. All of the values were within normal ranges.

At my booking appointment the midwife assured me that I was under consultant led care should this be needed and no set plan was made as to when LFT and bile acid tests would be taken throughout the pregnancy. It was suggested that I should ask for them to be done regularly or if any symptoms arose, for tests to be performed immediately.

At my request bloods were taken a couple of times between 12 and 30 weeks but all results remained within normal values. I often felt itchy on the soles of my feet and legs, and on reflection I know I was anxious waiting to see if the condition would recur.

At 30 weeks' gestation I had very bad cramps at the top right corner of my abdomen. I would describe the cramps as a very bad stitch that made me fold over in pain which then took up to two hours to slowly subside. It also caused a very strong Braxton Hicks contraction to occur. On contacting the delivery suite I was asked to come in where they monitored me for signs of labour. They didn't think it could be connected to OC and didn't do LFT and bile acid tests, but on reflection I think that these pains were right upper quadrant pains which can be associated with this condition. They advised me to rest.

At 31 weeks' gestation LFT and bile acid tests were done at my request.

ALT-32, Bilirubin-6, ALP-141, Albumin-35, GGT-37, Bile Acid-6. In retrospect the ALT was a little elevated but not thought to be of concern, especially when the bile acid result was within normal values.

For the next few weeks, the cramps continued at different points and I felt progressively more unwell, experiencing nausea and exhaustion. Reflecting on this I know that OC may have been causing this but, without the clinical sign of itching, LFT and bile acid tests were not repeated until 36 weeks' gestation.

At 36 weeks' gestation I attended my routine midwife appointment. The fundal height was measuring 39 weeks instead of 36, which caused concern so a glucose tolerance test was carried out along with LFT and bile acids. After a couple of hours I was called and told that the ALT result was raised but that they would have to wait another two days for the bile acid result.

The following day I went to the day assessment unit for measuring, monitoring and a scan. From here on, LFT and bile acid tests were performed every couple of days together with monitoring of the fetus. This showed that the ALTs were increasing quite substantially as were the bile acids. ALT's: Friday-67, Monday-122, Wednesday-152. Bile acids: Friday-8, Monday-11, Wednesday-16.

By now I was experiencing itching which got worse throughout the week and was far worse than I remembered in my first pregnancy. So, this, along with the cramping, meant that I was not feeling at all well. I also noticed that I had pale stools and dark urine, which are associated with this condition.

At 36+6 weeks' gestation, following the highest results in the blood tests, I saw a registrar who explained that he didn't think OC was a serious condition and he would not be discussing induction until 40 weeks. I felt very anxious at this advice and was concerned that the registrar did not have any research to support his management. The itchiness became so bad at night that I had to resort to having cold showers, hot showers and rubbing my feet on the carpet but nothing relieved the intense itching.

So, two days later, now 37+1 weeks' gestation I woke up in the early hours of the morning with a severe cramp down one side of the abdomen and on contacting the delivery suite, was admitted to the maternity unit. On the CTG monitors, it appeared that I was having contractions and so I was admitted in the hope that the natural labour would progress and if not that I would be induced. The Glucose Tolerance Test (GTT) result also came in, 5.6mmol/l, which was abnormal but no investigation was made in to this as I was in hospital when they saw the result.

Unfortunately, the natural labour did not progress, but after two attempts with a pessary for induction and an artificial rupture of the membranes (ARM) I thankfully gave birth to a healthy baby girl, Erin Mary who was born 3 hours 40 minutes later weighing 7lb 11.5oz.

Psychological impact

Throughout the last weeks of pregnancy, along with feeling unwell, I felt acute anxiety over my condition and the lack of support from the health care professionals. Once Erin was born and the symptoms of OC disappeared, I felt a sense of elation – a rejoicing for both my baby and I were safe. However, following this initial elation, I felt I needed to reflect on my experience of OC and understand the feelings I had experienced in the final weeks of my pregnancy. Writing this article has helped the process.

Lasting effects

I am one of the few women who cannot tolerate any hormonal contraception and experiences cyclical itching around ovulation and menstruation.

The most difficult issues for me to adjust to were related to the professional support and management of my condition. I had an expectation that I would be 'looked after' and that the midwives and doctors would know how to manage this condition and yet I experienced such difference in opinion from two registrars. I was very lucky in that I had consistent care from the midwife at the day assessment unit, who took the time to listen to my concerns.

From my experiences, and further exploration into this condition, I feel there are some aspects of professional care that need addressing which may offer improvement in the care of other women with this condition. I also offer some insight into how women themselves feel who have experienced and, managed to cope with, the more difficult aspects of OC.

How a midwife can support a woman with OC (See Box 1)

In a recent article about caring for pregnant women with diabetes, Rogers & Hughes (2010:179) said 'It is imperative that midwives are knowledgeable about matters outside the sphere of normality', but it is also important that the midwife can empathise with the woman's

Box 1.

Helpful questions the midwife can ask for a woman who has a skin irritation and raised blood levels suggestive of OC

- How are you feeling? Sounds simple but quite often this very important question can get forgotten and then denies access to further information from the woman.
- How is your itching?
- What do you find helps to relieve it? It's important to make sure that women haven't been driven to finding extreme solutions to their itch. There was one reported case of a woman who continually put her feet in buckets of water with ice and had to be admitted to hospital with severe ice burns.
- What is your biggest worry at this moment? Asking this question may help a woman to voice her fear about stillbirth. Whilst no pregnant woman can be totally reassured that her baby will be fine she can be given the facts about the condition and reassured that everything that can be done is being done for her.
- What support do you have? If the woman is on her own dealing with this, she may need even more support or more guidance on where to seek support, for example, directing her to www.ocsupport.org.uk

experience, so that they can be more intuitive about understanding how it may really feel for a woman suffering with this condition. In addition, they also need to be prepared to answer any questions and give support that may help relieve the woman's anxiety about what is happening to her and her pregnancy. Anxiety is linked to raised levels of the stress hormone, cortisol, during pregnancy which have been reported to have deleterious effects for both mother and fetus (Evans *et al* 2001, Teixeira *et al* cited in Fraser & Cooper 2009).

How a woman may feel

Physically

OC can make a woman feel very ill and we have heard of some women who itch so badly that they scratch until they bleed. The woman may also find it impossible to sleep. When I asked women with OC how they felt physically, they mentioned: itchy, uncomfortable, heavy, sore, exhausted, tired, ill, and nauseous.

Some of the statements I have heard from women include:

'I would give myself carpet burns because that was more preferable'

'A couple of times I rubbed my feet outside on the concrete in our garden – it felt nice at the time but maybe a bit sore afterwards'

'Putting my hands and feet in buckets of freezing ice cold water did seem to help'

Psychologically

Along with feeling so unwell, suffering with a pregnancy condition that has a risk of stillbirth can be very frightening. Words that were mentioned when I asked women with OC how they emotionally felt include: scared, anxious, tired, nervous, frightened, lonely, confused, worried, afraid, frustrated, depressed, isolated, and desperate. This suggests that while there is a risk of this happening, it might have helped the women to have shared their fears with someone prepared to listen and put their fears into perspective.

Conclusion

OC is a complex condition involving many variables that require further research and trials before comprehensive guidelines on treatment and management can be implemented. However, midwives have a valuable role to play in helping to ensure that a woman who presents with itchiness is investigated for the possibility of OC and is fully supported following diagnosis. OC Support UK offers information and support to women with this condition. Their website (www.ocsupport.org.uk) has valuable information for both women and health care professionals: there is also a help line for women to ring. Listening to women who have OC should never be underestimated as a valuable tool for guiding them through what can be a challenging and anxious time.

Alice Tuson is an NCT student antenatal teacher and a volunteer for OC Support UK. Alice has had both of her pregnancies complicated by OC.

Jenny Chambers founded OC Support UK in 1991 after being told she had OC. She has two sons but suffered two stillbirths before being diagnosed with the condition. She works as part of a research group investigating OC at Imperial College London and practises as a counsellor at a fertility clinic local to where she lives in the Midlands.

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