Guideline for the Management of Obstetric Cholestasis

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Guidelines Definition
Clinical guidelines are systemically developed statements that assist clinicians and patients in making decisions about appropriate treatments for specific conditions.

They allow deviation from a prescribed pathway according to the individual circumstances and where reasons can be clearly demonstrated and documented.

Minor Amendments
If a minor change is required to the document, which does not require a full review please identify the change below and update the version number.

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Equality Impact Assessment Statement
This Procedure has been subject to a full equality assessment and no impact has been identified.

Related Guidelines
- Day Assessment Unit
- Triage
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**Definition**
Obstetric Cholestasis (OC) is a multifactorial condition of pregnancy characterised by intense pruritus in the absence of a skin rash, with abnormal liver function tests (LFTs), which resolves following birth.

The clinical importance of Obstetric Cholestasis lies in the potential fetal risks, which may include spontaneous preterm birth, iatrogenic preterm birth and fetal death. There can also be maternal morbidity in association with the intense pruritus and consequent sleep deprivation.

**Risk Factors**
The prevalence of OC is approximately 0.7% in the UK. The following factors are associated with an increased risk;
- A personal or family history of obstetric cholestasis
- Multiple pregnancy
- Carriage of hepatitis C
- Presence of gallstones.
- Women of Indian and Pakistani descent have a twofold increase in risk

**Presentation**
OC usually presents in the second trimester with history of pruritus. The following symptoms may be indicative of OC;
- Unexplained pruritus, typically worse at night
- Usually no rash (excoriations only)
- Pale stools
- Dark urine
- Jaundice
**Diagnosis**

There is a wide range of definitions of obstetric cholestasis and the absence of agreed diagnostic criteria, which can make diagnosis challenging.

Pruritus in pregnancy is common, and can affect up to 23% of pregnancies, of which only a small proportion will have OC. Itching that involves the palms and soles of the feet is particularly suggestive of OC. Investigations to exclude other causes of pruritus and should be performed, as well as liver function tests (LFTs).

The skin should be inspected and care must be taken to differentiate skin trauma from intense scratching, which may be seen in obstetric cholestasis, from other common skin conditions such as eczema or atopic eruption of pregnancy (previously referred to as eczema of pregnancy, prurigo and pruritic folliculitis). If a rash is present, polymorphic eruption of pregnancy should be considered.

Diagnosis can be made by;

- Typical history of pruritus without rash (pruritus that involves the palms and soles of the feet is particularly suggestive).
- Abnormal liver function tests
- Elevated Bile Acids (>10 micromole/litre)
- Exclusion of other causes of abnormal liver function
- Postnatal resolution of symptoms and liver function tests.
**Investigations**

1) Exclude other causes of pruritus. Remember pruritus can precede elevation of bile acids.

2) LFTs - Pregnancy specific reference range which is 20% lower than non pregnant range should be used. (transaminases elevated, bilirubin and GGT are less commonly elevated)

3) In the presence of deranged LFT’s perform;
   - Viral screen for Hepatitis A, B, C, Epstein Barr and cytomegalovirus
   - Liver ultrasound
   - Liver autoimmune screen for chronic active hepatitis and primary biliary cirrhosis (for example, anti-smooth muscle and antimitochondrial antibodies)
   - Clotting screen **only** if already suspected low platelets/bleeding tendencies or already highly deranged LFTs (ALT>200)

4) Bile Acids. Bile acid levels can raise significantly after a meal therefore blood should be taken after a fast of > 4 hours. Admission should be timed to ensure fasting bloods are taken e.g. planned morning appointment in MDAU. Bile Acids are processed in Biochemistry at PCH on a Monday and Thursday pm. Results should be followed up by MDAU.

If a woman has persistent unexplained itching but liver function tests (LFTs) and bile acids are normal, LFTs and/or bile acids should be monitored every 2 weeks until LFT/bile acids become abnormal or symptoms stop. Seek specialist advice if the itch significantly worsens (NICE 2015).
NB. OC alone is not an obstetric emergency. Therefore, if a woman complains of itching in the absence of other symptoms (ie DFM), it is perfectly acceptable to arrange an appointment via MDAU Monday to Friday. Urgent out of hours assessment is not required for itching alone.

**Associated Risks**

*Fetal*
- Spontaneous or iatrogenic prematurity
- Foetal intracranial bleeding
- Meconium stained amniotic fluid
- Intrapartum fetal distress
- Intrauterine death.

*Maternal*
- Postpartum Haemorrhage secondary to Vitamin K deficiency
- Chronic sleep deprivation

**Monitoring of Obstetric Cholestasis**

Women diagnosed with obstetric cholestasis should be transferred to Consultant led care and advised to give birth in an Obstetric Unit.

*Maternal Monitoring;*
- Measure LFTs weekly
- Weekly BP and urine (to exclude other causes)
- Clotting studies should be carried out prior to expected date of birth.

NB. There is no need to repeat bile acid level once elevated levels are confirmed unless monitoring response to Ursodeoxycholic acid treatment.
**Fetal Monitoring;**

- Maternal monitoring of movements.
- Ultrasound and CTG are **not** reliable methods for preventing fetal death in OC and are **not necessary** unless other indications for monitoring exist.
- Continuous fetal monitoring in labour should be offered.

No specific method of antenatal fetal monitoring for the prediction of fetal death can be recommended. Ultrasound and cardiotocography are **not** reliable methods for preventing fetal death in obstetric cholestasis.

The current additional risk of stillbirth in obstetric cholestasis above that of the general population has not been determined but is likely to be small.

(See Appendix One for Management Flow Chart)

**Treatment**  
Although there is no current evidence that any specific treatment improves either maternal symptoms or neonatal outcomes, the following may be considered;

- **Topical emollients** - These are safe in pregnancy and clinical experience suggests that for some women they may provide slight temporary relief of pruritus.

- **Antihistamines** (e.g. chlorpheniramine 4 mg TDS or promethazine 25 mg at night) may help relieve pruritus and provide some sedation if needed.
• **Ursodeoxycholic Acid** commencing at 250 mg TDS increasing to a maximum dose of 500 mg TDS. This is a hydrophilic bile acid that decreases the hydrophobic hepatotoxic bile acids, and may reduce pruritus and abnormal liver function. Ursodeoxycholic acid is not licensed for use in pregnancy, but there are no reports of adverse fetal or maternal effects.

• **Dexamethasone** should not be used for the treatment of obstetric cholestasis, nor should it be used outside of a randomised controlled trial without a thorough consultation with the woman.

• **Vitamin K** A discussion should take place with the woman regarding the use of vitamin K. The usual dose is 10 mg daily by mouth, aiming to improve both maternal and neonatal levels, which are assumed to be deficient, and therefore reduce postpartum haemorrhage and fetal or neonatal bleeding. Where the prothrombin time is prolonged, the use of water-soluble vitamin K (menadiol sodium phosphate) 5–10 mg daily is indicated.

  NB. Postnatal vitamin K must be offered to the babies in the usual way.

**Timing of Birth**

Poor outcome cannot currently be predicted by biochemical results and decisions regarding timing of birth should not be based on results alone

• A discussion should take place with women regarding induction of labour after 37+0 weeks of gestation.
• Women should be informed of the increased risk of perinatal morbidity from early intervention.
• Women should be informed that the case for intervention (after 37+0 weeks of gestation) may be stronger in those with more severe biochemical abnormality (transaminases and bile acids).
• Women should be advised that there is currently no good evidence that induced early delivery affects the risk of stillbirth.
• Women should be informed of the increased risk of maternal morbidity from intervention at 37+0 weeks of gestation.
• Women should be informed of the inability to predict stillbirth if the pregnancy continues.

Post Natal Follow Up
Postnatal resolution of symptoms and normalisation of LFTs can be crucial in confirming the diagnosis of OC.

• LFTs should be checked ≥ 10 days postpartum to ensure they have returned to normal (LFTs increase in the first 10 days of the puerperium)
• If, after 8 weeks, the results are still abnormal, seek specialist advice from appropriate specialist team.
• An appointment should be made in GOPD for 8 weeks postpartum to provide appropriate counselling to ensure that the mother has fully understood the implications of obstetric cholestasis (Risk of recurrence in future pregnancies is approximately 45% - 90%).
• Advise women that there is a 10% risk of developing pruritus or hepatic impairment or both with oestrogen containing contraception and have their LFTS monitored if they are used.
References


Useful Links

RCOG Patient Information Leaflet

Obstetric Cholestasis Patient Support Group
http://www.ocsupport.org.uk/

Auditable Standards

• Number of women with diagnosed obstetric cholestasis
• Gestational age at birth
• Postnatal follow-up completed
• Appropriate investigations performed before diagnosis of OC
Appendix One: Management Flow Chart for Suspected Obstetric Cholestasis

Woman presents with Itching in Pregnancy without a rash

Refer to MDAU for assessment (Suspected OC alone is not an emergency situation)

Investigations
- LFTs
- Bile Acids (at least 4 hours since food)
- FH auscultation (CTG if clinically indicated)

Normal blood results
- Reassure woman
- If MLC, no need to transfer to CLC
- Repeat assessment in 2 weeks if symptoms persist

Abnormal Blood Results
- Diagnosis
  - Typical history of pruritus without rash (especially on palms and soles of feet)
  - Abnormal liver function tests
  - Fasting bile acid ≥10 micromoles/litre
  - Exclusion of other causes of abnormal liver function. Viral screen for; Hepatitis A, B, C, Epstein Barr and Cytomegalovirus

Antenatal Care
- Consultant Led Care
- Prescribe; topical emollients, Antihistamines, Ursodeoxycholic Acid, Vitamin K
- Weekly LFTs, BP and urine via Tuesday clinic in MDAU
- No need to repeat bile acid level once its elevation is confirmed.
- Perform clotting studies prior to expected date of birth
- Ultrasound and CTG are not necessary unless other indications for

Birth
- Should be in an Obstetric Unit
- Consider IOL after 37+0 weeks gestation.
- Continuous fetal monitoring in labour

Postnatal Follow Up
- LFTs ≥ 10 days postpartum to confirm diagnosis of OC
- If results remain abnormal after 8 weeks refer to specialist team.
- GOPC at 8 weeks - counselling to ensure that the mother has understood the implications of OC and future pregnancies