Ref: MM203

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.

Type of change	Why change made	Page number	Date of change	Version 1 to 1.1	Name of responsible person

Contents

1. 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.

These guidelines have been developed for Cwm Taf Morgannwg University Health Board, incorporating previous guidance from Cwm Taf University Health Board and Abertawe Bro Morgannwg University Health Board. These guidelines replace any previous health board versions.

2. Risk Factors

The prevalence of OC is approximately 0.7% in the UK (RCOG 2011). 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.

3. 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

4. Diagnosis

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

Pruritus in pregnancy is common (RCOG 2011), 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 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 ($\geq$14 micromole/litre)
- Exclusion of other causes of abnormal liver function
- Postnatal resolution of symptoms and liver function tests.

5. 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 and GGT elevated, bilirubin 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)
    - FBC and Clotting screen

4) Bile Acids. Bile acids are processed in Biochemistry at PCH on a Tuesday and Thursday pm. RGH send bile acids to PCH for processing. Bile acids are processed in POW on a daily basis. Results should be followed up by Maternity Day Assessment Unit.

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 (eg Altered fetal movements, it is perfectly acceptable to arrange an appointment via MDAU Monday to Friday. Urgent out of hours assessment is not required for itching alone.

6. Associated Risks

Fetal

• Spontaneous or iatrogenic prematurity
• Foetal intracranial bleeding
• Passage of meconium
• Intrapartum fetal distress
• Intrauterine death.

Maternal

- Postpartum haemorrhage secondary to Vitamin K deficiency
- Chronic sleep deprivation

7. 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 and bile acids weekly
- Weekly BP and urine (to exclude other causes)
- Clotting studies should be carried out prior to expected date of birth.

Fetal Monitoring;

- Maternal monitoring of movements.
- Ultrasound and Cardiotocography 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)

8. Treatment

Although there is no current evidence that any specific treatment improves either maternal symptoms or neonatal outcomes, the following may be considered (NICE 2015) (RCOG 2011) (UKTIS 2015);

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

- Bland topical options include Diprobase, calamine lotion and aqueous cream with menthol 1%. There are no trial data to support or refute the use of these products. They are safe in pregnancy and clinical experience suggests that for some women they may provide slight temporary relief of pruritus.

- **Antihistamines -** e.g. chlorphenamine 4 mg TDS or promethazine 25 mg at night may help relieve pruritus and provide some sedation if needed.

- **Ursodeoxycholic Acid**

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, Women should be informed of the lack of robust data concerning protection against stillbirth and safety to the fetus or neonate. The usual dose is 8-12mg/kg per day in 2-3 divided doses. The drug is available as 150mg and 250mg capsules.

- **Vitamin K:**

A discussion should take place with the woman regarding the use of vitamin K. Women should be advised that where the prothrombin time is prolonged, the use of water-soluble vitamin K (menadiol sodium phosphate) in doses of 5–10 mg daily is indicated.

  - Women should be advised that when prothrombin time is normal, water-soluble vitamin K (menadiol sodium phosphate) in low doses should be used only after careful counselling about the likely benefits but small theoretical risk.

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

- **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.

9. 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 (IOL). If the bile acid levels have exceeded 40 micromole/litre at any point, offer IOL at 37+0 weeks of gestation. If the bile acid levels have never risen above 40 micromole/litre, offer IOL at 40 weeks gestation.

- Women should be informed of the increased risk of perinatal morbidity from early intervention.

- Women should be advised that with advancing gestation, the risk of stillbirth versus the risk of delivery may justify offering women induction of labour after 37+0 weeks gestation, but this is not evidence based.

- 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 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.

10. 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 $\geq$ 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 (gastroenterology)

- 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.

11. References

NICE (2015) -Management of Itch in Pregnancy without Rash. NICE Clinical Knowledge Summaries. Last revised July 2015. Accessed 26.06.20 Available from http://cks.nice.org.uk/itch-in-pregnancy#!scenario

RCOG (2011) - Obstetric Cholestasis. Green Top Guideline No 43. Published 19/05/2011. Available from https://www.rcog.org.uk/globalassets/documents/guidelines/gtg_43.pdf

UKTIS (2015) Treatment of obstetric cholestasis. TOXBASE. UK Teratology Information Service. www.toxbase.org

British National Formulary (On-line). London: BMJ Group and pharmaceutical Press. http://www.medicinescomplete.com [Accessed on 08.06.20].

12. Useful Links

- **RCOG Patient Information Leaflet**
  https://www.rcog.org.uk/globalassets/documents/patients/patient-information-leaflets/pregnancy/pi-obstetric-cholestasis.pdf

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

13. Auditable Standards

- Number of women with diagnosed obstetric cholestasis
- Gestational age at birth
- Documentation of appropriate counselling
- Appropriate investigations performed before diagnosis of OC

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Appendix One: Management Flow Chart for Suspected Obstetric Cholestasis

Woman presents with Itching in Pregnancy without a rash

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

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Investigations
- LFTs
- Bile Acids
- FH auscultation (CTG if clinically indicated)

Normal blood results

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Reassure woman

If Midwifery Led Care, no need to transfer to CLC

Repeat assessment in 2 weeks if symptoms

Abnormal Blood Results

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Diagnosis

- ✓ Typical history of pruritus without rash (especially on palms and soles of feet)
- ✓ Abnormal liver function tests
- ✓ Bile acids ≥14 micromoles/litre
- ✓ Exclusion of other causes of abnormal liver function. Viral screen for: Hepatitis A, B, C, Epstein Barr and Cytomegalovius

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Antenatal Care

- ✓ Consultant Led Care
- ✓ Prescribe: topical emollients, Antihistamines, Ursodeoxycholic Acid, Vit K
- ✓ Weekly LFTs, Bile acids, BP and urine via Tuesday am and Thursday am clinic in MDAU in PCH and RGH / any day in POW
- ✓ Perform clotting studies prior to expected date of birth
- ✓ Ultrasound and CTG are not necessary unless other indications for monitoring present

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Birth

- ✓ Should be in an Obstetric Unit
- ✓ **Consider** IOL after 37+0 weeks gestation if bile acids >40 umol/l; 40 weeks if ≤40 umol/l
- ✓ Continuous fetal monitoring in labour

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Postnatal Follow Up

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