Manchester University
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DOCUMENT CONTROL PAGE	
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Minor Amendment	Date Notified To Date Summary of amendments –
Author	Originated by: Dr B Singhania, Dr N Zahid Modified By: Dr K MacLeod, Dr R Agass Designation: Consultant Obstetrician
Ratification	Ratified by: Obstetric Clinical Effectiveness Group Date of Ratification: 23rd August 2017 Ratified by: Medicines Management Committee Date of Ratification: 14th September 2017
Application	All Staff formerly under CMFT
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1. Introduction

Obstetric Cholestasis (OC), also referred to as intrahepatic cholestasis of pregnancy, is a multifactorial condition of pregnancy. It is characterised by intense pruritus in the absence of a skin rash and raised serum bile acids in association with deranged liver function tests which do not have an alternative cause, and which resolve postnatally.

In England, obstetric cholestasis affects 0.7% of pregnancies (RCOG 2011).

2. Detail of guideline

2.1. Risk factors for developing Obstetric Cholestasis:

- Personal or family history
- Multiple pregnancy
- Hepatitis C carrier
- Gall stones

  (RCOG 2011)
- IVF pregnancy
- Age > 35 years

  (Williamson and Geenes, 2014)

2.2. Fetal risks:

- Premature delivery – Mostly iatrogenic, however the risk of spontaneous preterm delivery is marginally increased compared with the general population. (Overall risk of prematurity is 7-25% vs background risk of 4-12%) (RCOG 2011, Geenes et al 2014)
- Higher risk of meconium-stained liquor, typically occurring at earlier gestation (Geenes et al, 2014, Kenyon et al, 2002).
- Higher occurrence of intrapartum fetal distress (RCOG, 2011).
- Risk of stillbirth is unclear but reported to be up to 1-2% when bile acids are > 40mmol/L (Glantz et al, 2004).

2.3. Maternal risks:

- Maternal morbidity associated with severe pruritus leading to insomnia and exhaustion.
- Iatrogenic risks from increased rate of induction of labour (Geenes et al, 2014; RCOG, 2011).
- Increased risk of delivery by caesarean section, although the role of obstetric cholestasis itself is not easy to establish (RCOG, 2011).
- Women may have fat malabsorption leading to vitamin K deficiency and subsequent prolongation of prothrombin time (PT), which may

increase postpartum haemorrhage risk (Geenes et al, 2014; RCOG, 2011). A history of steatorrhoea may be present.

2.4. Diagnosis

Obstetric Cholestasis is a diagnosis of exclusion. Other pregnancy related liver diseases include HELLP and acute fatty liver of pregnancy; both of which are very uncommon.

2.4.1. **Take a detailed clinical history**

- Pruritus typically starting on palms of hands and soles of feet, often worse at night
- Excoriation marks from scratching may be seen, but other rash is not present
- May be associated with signs of fat malabsorption: dark urine, pale stools, steatorrhoea
- Jaundice is rare
- Ask about other clinical signs of liver disease (nausea and vomiting, abdominal pain, fatigue, telangiectasia, bruising).

2.4.2. **Perform a clinical examination**

- Blood pressure, urinalysis, heart rate and temperature
- Examine for signs of other causes of itching, e.g. Eczema

2.4.3. **Investigations**

- See also *appendix 2* for investigation and management algorithm
- Liver function tests (LFTs) and bile acids at initial presentation
- If results are normal but symptoms persist, repeat blood tests every two weeks if less than 34 weeks gestation or once a week if over 34 weeks gestation whilst symptomatic:

Mild Obstetric Cholestasis:	bile acids > 14mmol/L
Moderate Obstetric Cholestasis:	bile acids > 40mmol/L
Severe Obstetric Cholestasis:	bile acids > 100mmol/L

  Increasing fetal risks are directly associated with increasing maternal serum bile acids (Glantz et al, 2004).
- Coagulation Screen – if there are clinical signs of fat malabsorption, bile acids >40mmol/L, rapidly rising bile acid levels, or in labour/prior to an elective LSCS if abnormal LFTs
- Viral Serology: Hepatitis A, Hepatitis B, Hepatitis C, Epstein-Barr Virus (EBV), Cytomegalovirus (CMV)

- Liver Auto-antibodies: anti-smooth muscle, anti-mitochondrial
- Ultrasound scan of the liver

2.5. Antenatal Management

- See also *appendix 2* for investigation and management algorithm
- Following diagnosis, women should have a consultant review on AAU and induction date given/discussed. An antenatal clinic appointment should be made with the next available consultant for counselling and to create a management plan for her pregnancy if any of the following:
    - < 32 weeks gestation,
    - bile acids (BA) > 100mmol/L,
    - AAU staff concerns,
    - Unacceptable delay in waiting time.
- Send letter in *appendix 1* to the woman's GP and advise her to have her LFTs and bile acids checked at her 6 week postnatal check.
- Bile acids and LFTs should be checked weekly. This can be arranged via the Antenatal Assessment Unit (AAU).
- There is **no** association with fetal growth restriction – serial scans are not indicated (unless there are other clinical indications).
- There is **no** role for electronic fetal monitoring (CTG) until in labour (unless there are other clinical indications).
- Enquire about fetal movements at each visit as per local guidance. See also *Guideline for the management of Reduced Fetal Movements*.
- Discuss Induction of Labour (IOL). There is no evidence to suggest that operative or instrumental delivery is increased following IOL in women with obstetric cholestasis.
    - If bile acids < 40mmol/L offer IOL from 38 weeks
    - If bile acids > 40mmol/L at any point offer IOL from 37 weeks as the risk of adverse fetal outcome is higher
    - If bile acids > 100mmol/L or not responding to treatment earlier IOL may be considered
    - Inform the patient of the risks of admission to neonatal unit due to early delivery. Other risks include Transient Tachypnoea of Newborn (TTN) and neonatal jaundice

2.6. Drug Therapy

- **Aqueous cream with menthol** topically can relieve itching
- **Topical emollients** are safe and may offer some relief to some patients

- **Chlorphenamine** 4mg TDS orally may relieve itching, patients should be warned about its sedating effects.
- **Water Soluble Vitamin K** (Menadiol sodium phosphate) 10mg OD orally from 32 weeks can be considered in women with steatorrhoea or prolonged prothrombin time to reduce the risk of postpartum haemorrhage. Data regarding this practice is limited.
- **Ursodeoxycholic Acid (UDCA)** can reduce serum bile acids. It is extensively used 'off licence' for obstetric cholestasis, with no reported adverse maternal or fetal effects. Patients should be consented for off-licence use. It reduces serum bile acids and helps relieve pruritus.

  Starting dose: Ursodeoxycholic Acid 300mg TDS Orally
  Maximum dose: Ursodeoxycholic Acid 600mg QDS Orally

  Increase UDCA weekly following blood tests (LFTs, bile acids) if bile acids not responding OR >40mmol/L.
- **Rifampicin.** Can be added when UDCA is at maximum dose and patient is not responding (bile acids > 40mmol/L despite UDCA). Do not start if ALT >200IU/L. Works synergistically with UDCA to help reduce serum bile acid levels – UDCA must therefore be continued. Rifampicin may produce a reddish colouration of the urine, sweat, sputum and tears (Soft contact lenses have been permanently stained), and the patient should be forewarned of this, as well as the risk of hepatic dysfunction.

  The decision to prescribe rifampicin must be made by a consultant obstetrician only. Due to limited evidence for use, rifampicin is considered a last line agent for the management of refractory cases of obstetric cholestasis.

  Weekly LFTs are essential when on rifampicin due to risk of hepatic dysfunction.

  Rifampicin should be discontinued if LFTs worsen following commencement of drug.

  Starting dose: Rifampicin 150mg BD Orally
  Maximum dose: Rifampicin 300mg BD Orally
- **General Advice** is to wear loose cotton clothing which allows the skin to breathe. Avoid hot baths and showers and putting strongly perfumed products on the skin.
- **Patient Information** Patients can find support from various online websites. Recommended ones include:

  www.icpsupport.org
  www.britishlivertrust.org.uk and search cholestasis of pregnancy
  www.rcog.org.uk and search patient information leaflets for OC

2.7. Management of Delivery

- Delivery on the consultant led Delivery Unit (DU) is recommended

- Advise continuous electronic fetal monitoring due to higher risk of fetal heart rate abnormalities in labour.
- Be aware of higher rates of meconium staining of amniotic fluid especially at early gestations.
- Routine coagulation screen to be performed in labour/prior to an elective LSCS if abnormal LFTs
- Advise active management of 3rd stage of labour due to higher risk of postpartum haemorrhage secondary to liver dysfunction and possible vitamin K deficiency.

2.8. Postnatal Management

2.8.1. Intramuscular (IM) Vitamin K is recommended for neonates. See also local guideline *Vitamin K (Konakion® MM) for Newborn Babies – A Guide for Hospital staff*.

2.8.2. Do not check LFTs on the postnatal ward unless there is another clinical reason to do so.

Therapy for OC should be discontinued at the time of birth.

Advise the patient to have her LFTs and bile acids checked in 6 weeks at her postnatal check with her GP. A letter should have already been sent to the GP from AAU.

2.8.3. Advise the patient that itching should resolve, and bile acids and LFTs should return to normal within 6 weeks.

2.8.4. Counsel the patient about the recurrence risk of 45-90% in subsequent pregnancies, and the increased incidence of 35% in family members (Geenes, 2014; RCOG, 2011).

2.8.5. Advise women that use of oestrogen-containing contraception such as the combined oral contraceptive (COC) pill may result in recurrence of cholestasis. The use of COC with a history of obstetric cholestasis is a UK Medical eligibility criteria category 2 (a condition where the advantages of using the method generally outweigh the theoretical or proven risks).

2.8.6. Advise women that they have a higher risk of hepatobiliary disease in later life (Williamson and Geenes, 2014).

2.9. Communication and Documentation

All women with learning disabilities, visual or hearing impairments or those whose first language is not English must be offered assistance with interpretation where applicable, and where appropriate a telephone interpreter must be used. It is paramount that clear channels of communication are maintained at all times between all staff, the women and their families. Once any decisions have been made/agreed, comprehensive and clear details must be given to the woman thereby confirming the wishes of the women and their families.

The contents of any leaflet issued must be explained in full at the time it is issued. All communication difficulties (including learning difficulties) and language barriers must be addressed as outlined in the previous paragraph at the time the leaflet is issued.

Ensure the provision and discussion of information of the risks and benefits with women during the antenatal, intrapartum and postnatal periods.

Staff should aim to foster a culturally sensitive care approach in accordance with the religious and cultural beliefs of the parents and families in our care.

3. Equality, Diversity and Human Rights Impact Assessment

This document has been equality impact assessed using the Trust's Equality Impact Assessment (EqIA) framework. The EqIA score fell into low priority; no significant issues in relation to equality, diversity, gender, colour, race or religion are identified as raising a concern.

4. Consultation, Approval and Ratification Process

This guideline has been approved and ratified in accordance with the agreed process. See: *Guideline for the Introduction or Re-approval of a Clinical Guideline for Obstetric Practice.*

5. Monitoring Compliance

This guideline will be audited in accordance with the Obstetric Directorate audit plan. The findings of the audit report will be presented to staff via the Obstetric Clinical Effectiveness Group and where appropriate an action plan will be developed and monitored at the Obstetric Clinical Effectiveness Group.

6. Trust associated documents

Guideline for the management of Reduced Fetal Movements

Vitamin K (Konakion® MM) for Newborn Babies – A Guide for Hospital staff.

7. References and bibliography

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8. Appendices

Appendix 1: Template letter to send to the GP
Appendix 2: Investigation and management algorithm

Appendix 1: Template letter to send to the GP

Date: Patient Details:

Dear Dr,

The above patient of yours has been diagnosed with obstetric cholestasis.

Her EDD =

Would you kindly repeat her LFT's and bile acids at her 6 week postnatal check-up.

If any of the above are abnormal please manage in accordance with your protocol.

Please note, in women diagnosed with obstetric cholestasis:

- Itching should resolve, and bile acids and LFTs should return to normal within 6 weeks.
- There is a recurrence risk of 45-90% in subsequent pregnancies, and an increased incidence of 35% in family members.
- Women that use oestrogen-containing contraception such as the combined oral contraceptive (COC) pill may result in recurrence of cholestasis. The use of COC with a history of obstetric cholestasis is a UK Medical eligibility criteria category 2.
- Women have a higher risk of hepatobiliary disease in later life.
- Children born to women with obstetric cholestasis are reported to have higher body mass index and dyslipidaemia at age 16.

Yours sincerely,

Midwife Antenatal Assessment Unit

Appendix 2: Investigation and management algorithm obstetric cholestasis