CLINICAL PRACTICE GUIDELINE

Cholestasis in pregnancy

This document should be read in conjunction with the Disclaimer

Contents

MFAU QRG: Suspected cholestasis

Criteria for referral

All women equal to or more than 20 weeks gestation experiencing intense pruritis (usually of hands and feet) in the absence of a skin rash.

Assessment

1. Document a maternal history. Note where pruritis is felt. When did the pruritis commence? Is it worst at night? Is a rash present? Note other symptoms e.g. steatorrhea, jaundice, malaise.
2. Record baseline maternal observations – temperature, pulse, blood pressure and urinalysis.
3. Perform an abdominal palpation, noting:
    - Fundal height
    - Lie and presentation (as appropriate for gestation)
    - Uterine tenderness/irritability/fetal activity
4. Assess fetal wellbeing
    - Auscultate the fetal heart rate
    - Perform a CTG if more than 30 weeks gestation
    - Arrange an ultrasound for biophysical profile and fetal wellbeing
5. Investigations
    - Serum Bile Acid levels, preferably fasting levels
    - Full blood picture
    - Liver function tests
    - Coagulation screen (if abnormal liver function)
    - Viral screen for hepatitis A,B and C, Epstein Barr and cytomegalovirus
    - Liver autoimmune screen for chronic hepatitis and primary biliary cirrhosis
    - Liver ultrasound

Management

Obstetric cholestasis not confirmed:

1. Discuss signs of cholestasis.
2. Advise women to report persistent symptoms.
3. Provide treatment options for pruritis e.g. calamine lotion and anti-histamines.
4. Inform women how to decrease skin irritants.

5. Review by the Obstetric Team Registrar or Labour and Birth Suite Registrar prior to discharge.
6. Ensure a management plan is documented prior to discharge.
7. Arrange a follow-up antenatal appointment.

MFAU QRG: Confirmed cholestasis

Criteria for referral

Diagnosis confirmed by:

- Clinical features
- Exclusion of other forms of liver disease or cholestasis
- Laboratory findings

Key points

1. The frequency of assessment in MFAU may change according to the maternal and fetal condition.
2. All assessments, test results and treatments are recorded on the MR226 Multiple Visit Record Sheet.
3. Where possible arrange assessment when the woman's Obstetric Team is rostered on duty for the Labour and Birth Suite.

Management

1. Check and record the maternal temperature, pulse, blood pressure respiration rate and $SA0_2$ and urinalysis.
2. Perform an abdominal palpation. Note:
    - Fundal height
    - Lie and presentation (depending on gestation)
    - Uterine activity
3. Perform blood tests
    - Liver function tests (LFTS) – **weekly**
    - Coagulation studies – order if the woman has abnormal LFTs.
4. Assessment of fetal wellbeing

Ultrasound assessment

- Perform a baseline ultrasound
- Perform an ultrasound 3 weekly for growth and well-being

More frequent assessment will depend on the maternal and fetal clinical condition.

Ultrasound is not a reliable tool for prediction of fetal death in obstetric cholestasis.

Cardiotocography (CTG) monitoring

- Weekly monitoring 30 - 34 weeks gestation
- Bi-weekly monitoring after 34 weeks gestation
- Monitoring prior to 30 weeks gestation is at the discretion of the Team Consultant

Fetal monitoring has not been shown to be predictive of fetal death.

5. Arrange medical review.

Abnormal results

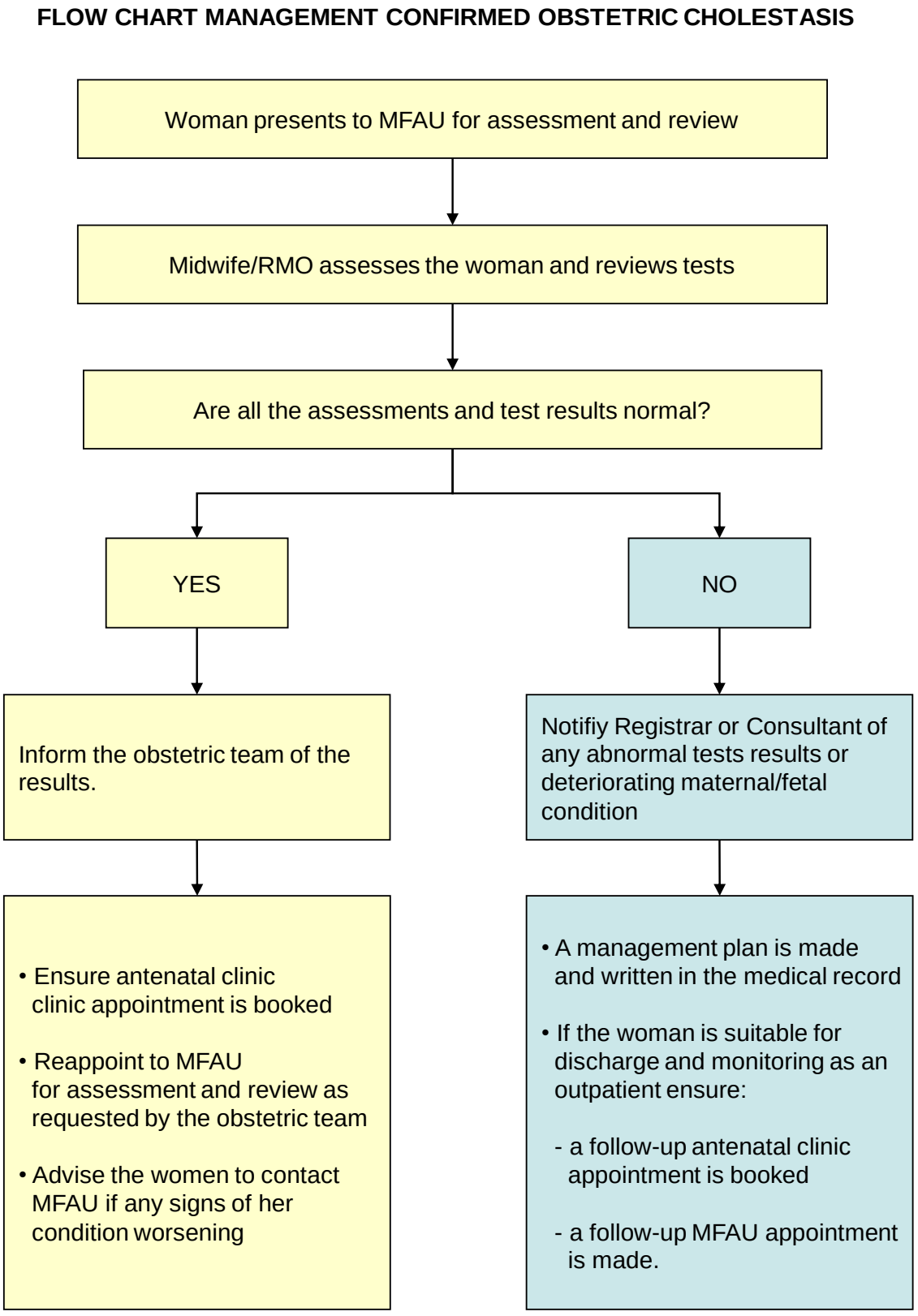
- Inform the Senior Registrar or Consultant immediately of any abnormal results
  - Non reassuring FHR pattern
  - Abnormal ultrasound findings
  - Maternal reporting of a reduction in fetal activity
  - Maternal reporting of worsening pruritis, despite treatment
  - Abnormal and/or deteriorating blood results
  - Increased uterine activity
- Document a medical plan in the woman's medical records e.g. 'MR226 Maternal Fetal Assessment Outpatient' and the MR004 'Obstetric Special Instruction Sheet'.
- Arrange a follow-up antenatal clinic appointment in 1-2 weeks.
- Arrange a follow-up MFAU appointment and monitoring as discussed with the Senior Registrar and Consultant.

  The frequency of appointments depends on the maternal/fetal condition, and is adjusted accordingly.

Normal results

- Inform the Obstetric team of the test results and maternal/fetal condition.
- Reappoint to MFAU for assessment if requested by the obstetric team prior to the antenatal clinic appointment. Clinic appointments are generally made 2 weekly if normal results.

Flowchart for confirmed obstetric cholestasis



Cholestasis in pregnancy

Background

Obstetric cholestasis is a multifactorial condition of pregnancy characterised by pruritus in the absence of skin rash with abnormal liver function tests (LFTs) neither of which has an alternative cause and both of which resolve after birth. Most authorities accept elevations of any of a wide range of LFTs beyond pregnancy specific normal ranges. Investigations to exclude other causes of pruritus and of abnormal LFTs should be performed.

The clinical importance of obstetric cholestasis is 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 pruritis and consequent sleep deprivation.

Diagnosis

Diagnosis of cholestasis in pregnancy is confirmed by:

- clinical features
- exclusion of other forms of liver disease or cholestasis
- laboratory findings

Clinical features

- Pruritis without a rash – itching is classically on the palms and soles of the feet although it may be more widespread. The pruritis is worst at night[1], and women may exhibit dermatographia artefacts (skin trauma from intense scratching).[1, 2]
- malaise[2]
- steatorrhea with fat malabsorption[2]
- Jaundice - uncommon[2], but can occur in 10-15% of cases[1]

Exclude other causes

- Autoimmune hepatitis[1-3]
- Hepatitis A,B, C[2, 3] or E[1]
- Epstein Barr[1, 3]
- Cytomegalovirus[1, 3]
- Gall bladder disease[2]
- Liver disease e.g. cirrhosis, acute fatty liver[1, 3]
- Early HELLP syndrome or preeclampsia[1]
- Skin conditions e.g. eczema, pruritic eruption of pregnancy[3], scabies[1]

Laboratory tests

- Bile Acids – levels greater than 10µmol/L are a common diagnostic marker[4]
- Liver Function Tests (LFTs):
  - Aminotransferase (ALT, AST) activity can be raised by up to 20 times the normal level[5]
  - Gamma-glutamyl transferase activity is unusual but indicative of MDR3 gene mutation leading to increased bile acids, or of underlying liver disease.[5]
  - It is uncommon to have a raised serum bilirubin[3]

Antenatal management

Investigations

1. Fasting Serum Bile Acids – to make the diagnosis
2. LFTs –**weekly** once obstetric cholestasis is diagnosed
3. Full blood picture
4. Coagulation studies – may be ordered by the obstetric team if abnormal LFTs. Prolonged prothrombin times may reflect Vitamin K deficiency.[1]
5. Viral screen for hepatitis A, B and C, Epstein Barr and cytomegalovirus.
6. Liver autoimmune screen for chronic hepatitis and primary biliary cirrhosis.
7. Liver ultrasound

Fetal surveillance

Fetal surveillance (ultrasound and CTG monitoring) has not been shown to be predictive of fetal death in obstetric cholestasis.

The decision and frequency of ultrasound and CTG monitoring is at the discretion of the obstetric team.

Frequency of antenatal visits

Antenatal visits should be arranged 2nd weekly.

Timing of birth

Aim to deliver the woman between 37weeks [1, 2, 6, 7] and 38 weeks gestation, or earlier if there is sufficient risk for maternal morbidity or fetal compromise detected. Consider administration of corticosteroids if induction of labour is anticipated prior to 36+6 weeks gestation.

Treatment of maternal pruritis

1. The use of topical emollients e.g. calamine lotion may provide temporary relief of itching.[3] They are safe but their efficacy is unknown.
2. Offer advice to decrease skin irritation - wear cool loose cotton clothing, keep skin moisturised, cool baths/showers for comfort, use of cotton material where possible (e.g. bed linen).[8]
3. Encourage a low fat diet, and advise women to increase their water intake.[8]
4. Offer anti-histamines at night (beneficial for their sedative effect).[3, 9]
5. Offer Ursodeoxycholic acid (UDCA or URAO). Dosage required to attain effect on maternal pruritis and serum bile acids is from 10 to 15 mg/kg/day.[5, 10] Relief usually occurs in one to two weeks.[10]

Ursodeoxycholic acid (UDCA)

Ursodeoxycholic acid (UDCA) improves pruritus and liver function in women with obstetric cholestasis

Vitamin K supplementation

Obstetric cholestasis can lead to a reduction of circulating enerohepatic bile acids causing reduced absorption of fat-soluble vitamins. Vitamin K is a fat-soluble vitamin required for coagulation.[3]

A discussion should take place with the woman regarding the use of vitamin K.

Recommend daily supplementation of water soluble 5-10mg of Vitamin K orally to reduce the risk of post-partum haemorrhage (PPH).

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

Nutritional supplementation

Steatorrhea and fat malabsorption may lead to nutritional deficiency.[1]

Consider multivitamin supplementation. Consider referral to the dietician for information regarding a low fat diet.

Paediatric consultation

Arrange a paediatric consult if risk of pre-term birth is anticipated.

Labour and birth management

Maternal management

1. Arrange a blood group and hold, full blood picture, and LFTs on admission.
2. If LFTs are abnormal order a coagulation profile.
3. Monitor the fetal heart rate continuously with a CTG.
4. Anticipate the risk of meconium liquor and request a paediatrician at delivery as necessary.

See also Clinical Guidelines, Obstetrics & Gynaecology:

- Labour: Meconium Stained Amniotic Fluid
- Labour: Neonatal Team Attendance at Birth
- Fetal Surveillance: Fetal Heart Rate Monitoring

Postnatal management

Counselling prior to discharge

Counselling prior to discharge should include the following:

- risk of reoccurrence in a subsequent pregnancy is 40-60%[10]
- reassurance about the lack of long term sequelae for mother and baby
- pruritis normally resolves within 48 hours of giving birth[3], however in some women it may last 4-8 weeks[1]
- women who have had a familial severe form of obstetric cholestasis are at risk for chronic liver disease and should have long term follow-up[10]
- female family members may have an increased chance of developing obstetric cholestasis
- the use of combined oral contraceptive pill postpartum should be avoided for life.[11] Low dose estrogens or progesterone –only pills are recommended.[1]
- Hormone Replacement Therapy is safe and appropriate for these women.

GP referral

- Ensure the GP is apprised of the woman's condition prior to discharge and a follow-up plan is in place.
- Arrange review by the GP in 2-4 weeks to check resolution of the woman's condition. Liver function tests are expected to normalise within a month of delivery.[9]
- Follow-up monitoring of LFTs should be deferred for at least 10 days after birth. In normal pregnancy the LFTs can normally increase in the postpartum period.[3]

References

1. Kondrackiene J, Kupcinskas L. Intrahepatic cholestasis of pregnancy - current achievements and unsolved problems. **World Journal of Gastroenterology**. 2008;14(38):5781-88.
2. Mays JK. The active management of intrahepatic cholestasis of pregnancy. **Current Opinion in Obstetrics and Gynecology**. 2010;22:100-3.
3. Royal College of Obstetricians and Gynaecologists. Obstetric cholestasis. **Green-Top Guideline No 43**. 2006.
4. Glantz A, Reilly SJ, Benthin L, et al. Intrahepatic Cholestasis of Pregnancy: Amelioration of Pruritis by UDCA Is Assoiciated with Decreased Progesterone Disulphates in Urine. **Hepatology**. 2008;47:544-51.
5. Joshi D, James A, Quaglia A, et al. Liver disease in pregnancy. **The Lancet**. 2010;375:594-605.
6. Greenes V, Williamson C. Intahepatic cholestasis of pregnancy. **World Journal of Gastroenterology**. 2009;15(17):2049-66.
7. Lee RH, Kwok KM, Ingles S, et al. Pregnancy Outcomes during an Era of Aggressive Management for Intrahepatic Cholestasis of Pregnancy. **American Journal of Perinatology**. 2008;25:341-45.
8. Nichols AA. Cholestasis of Pregnancy. A review of the evidence. **Journal of Perinatology and Neonatal Nursing**. 2005;19(3):217-25.
9. Saleh MM, Abdo KR. Intrahepatic Cholestasis of Pregnancy: Review of the Literature and Evaluation of Current Evidence. **Journal of Women's Health**. 2007;16(6):833-41.
10. Pathak B, Sheibani L, Lee RH. Cholestasis of Pregnancy. **Obstetrics and Gynecology Clinics of North America**. 2010;37:269-82.
11. Saleh MM, Abdo KR. Consensus on the management of obstetric cholestasis: National UK survey. **BJOG**. 2007;114:99-103.

Related WNHS policies, procedures and guidelines

KEMH Clinical Guidelines, Obstetrics & Gynaecology:

- Labour: Meconium Stained Amniotic Fluid
- Labour: Neonatal Team Attendance at Birth
- Fetal Surveillance: Fetal Heart Rate Monitoring

Keywords:	Cholestasis, liver disease, pruritis, bile acids, LFTs, fetal surveillance, delivery, vitamin K, ursodeoxycholic acid, CTG		
Document owner:	Obstetrics, Gynaecology & Imaging Directorate		
Author / Reviewer:	Head of Department, Obstetrics		
	June 2019: Evidence on this topic was reviewed and overall guidance remains unchanged. The two quick reference guides were merged into this document.		
Date first issued:	February 2008		
Reviewed:	; July 2014 (amended July 2016); June 2019	Next review date:	June 2022
Supersedes	**History**: In June 2019 amalgamated three individual guidelines on cholestasis dating from February 2008. **Supersedes**: 1. Cholestasis in Pregnancy (version last amended April 2016) 2. Cholestasis (Suspected): MFAU QRG (dated July 2014) 3. Cholestasis (Confirmed): MFAU QRG (dated July 2016)		
Endorsed by:	MSMSC (OOS approval- HoD Obstetrics, Coordinator of Midwifery, Midwifery Co-Director)	Date:	June 2019
NSQHS Standards (v2) applicable:	1 Governance, 4 Medication Safety, 8 Recognising & Responding to Acute Deterioration		
Printed or personally saved electronic copies of this document are considered uncontrolled. Access the current version from the WNHS website.			