Worcestershire Acute Hospitals NHS Trust

Cholestasis in pregnancy

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Approved by:	Maternity Governance Meeting/ MSC	
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Key Amendments

Date	Amendments	Approved by
October 2021	Changes of the guideline have been made with regards to the timing of IOL for women with OC. The dosing of Urso has also been changed to 500mg BD in line with the TOG article (current RCOG guideline being updated). Recognition of 'off-label' prescribing of treatments for this indication (however recognised as standard treatment by RCOG)	Obstetrics Governance/ MSC

Background
Cholestasis in pregnancy usually presents in the third trimester. It affects 0.7% of pregnancies (1.2-1.55 in women of Asian origin) and it is most common in Northern Europe and South America.

It is also more common in older women, women with multiple pregnancy, following IVF treatment and in those with a history of gallstones, hepatitis C infection or with a sister affected by the condition.

Obstetric cholestasis is a multifactorial condition of pregnancy characterised by intense pruritus in the absence of a skin rash. It is associated with elevated maternal serum bile acid concentrations with or without deranged liver function tests. Neither of these have an alternative cause and both remit following delivery. Pruritus involving the palms and soles of the feet is particularly suggestive.

The clinical importance of obstetric cholestasis lies in the potential fetal risks. These may include spontaneous prematurity, iatrogenic prematurity, fetal distress, passage of meconium and intrauterine death. In a hospital setting the additional risk of stillbirth in association with obstetric cholestasis above that of the general population has not been determined but is likely to be small.

There can also be significant maternal morbidity in association with the intense pruritus and consequent sleep deprivation.

Women who have had previous cholestasis in pregnancy are at a high risk of developing cholestasis in a subsequent pregnancy (45-90%).

The patients covered by this guideline are women presenting with itching primarily on the hands and feet (although it may be generalised) with no rash after 24+0 completed weeks gestation.

It is rare for cholestasis to present under 24/40 (80% present after 30 weeks). However, there are case reports of onset in the first trimester, and of earlier onset in women with multifetal pregnancy. If the symptoms are classical then consideration should be given to the diagnosis and investigations performed as appropriate.

NB: Women who have had previous cholestasis of pregnancy do not require routine bloods.
Only investigate if symptoms occur.

Diagnosis and Treatment
See Appendix 1

Antenatal Fetal Monitoring

Poor outcome cannot be predicted by biochemical results and delivery decisions should not be based on results alone.

None of the fetal monitoring modalities (CTG/USS/Doppler) are reliable in predicting or preventing fetal death in obstetric cholestasis. Placental insufficiency, IUGR or oligohydramnios are not features of the disease and umbilical artery Doppler assessment of uterine, umbilical or fetal cerebral arteries are not different when compared with other pregnancies.

If fetal movements and fetal growth according to customised growth chart are satisfactory, additional fetal monitoring by CTG/ USS/ Doppler is not recommended in obstetric cholestasis.

Continous fetal heart rate monitoring is recommended in labour.

Timing of delivery

While it is certain that delivery at 37 weeks of gestation will prevent a stillbirth beyond that gestation, it is not known how high the risk of such a stillbirth might be. The widely adopted practice of offering delivery at 37 weeks of gestation, or at diagnosis if this is after 37 weeks of gestation, is not evidence based. Therefore, the iatrogenic consequences of elective delivery must be considered. Elective early delivery results in increased respiratory morbidity compared with later delivery. There is also compelling evidence that early term delivery (37-38+6 weeks) increases the risk of behavioural issues, poorer cognitive development and poorer educational performance in childhood when compared to delivery after 39 weeks (Murray et al 2017, Bentley et al 2016)
The risk of admission to a special care baby unit following an elective caesarean section is 7–11% at 37 weeks of gestation, 6% at 38 weeks of gestation and 1.5% at 39 weeks of gestation. Data in obstetric cholestasis pregnancy suggest that the risks may be similar.

Two suggested models of fetal demise in intrahepatic cholestasis of pregnancy are consistent with evidence indicating that high bile acids contribute to the causes of adverse outcomes: increased bile acids are associated with fetal cardiac arrhythmia and placental vessel spasm. For women with bile acids more than or equal to 40 micromoles per litre, at any time during pregnancy, adverse outcomes showed a linear relationship with serum bile acid levels

Therefore:

- **If BA <40** there is no increased risk of adverse outcome and induction should be offered from 39 weeks
- **If BA >40** (at any time during pregnancy**)** there is an increased risk of adverse perinatal outcomes and IOL should be offered from 37 weeks after thorough counselling of the risks and benefits
- **If BA >100** (at any time during pregnancy) there is a significantly increased risk of adverse perinatal outcomes and IOL should be offered from 36 weeks after thorough counselling of the risks and benefits

Postnatal

LFT may take 10 days to return to normal post delivery and therefore should not be checked prior to this. Confirmation of the diagnosis relies on the postnatal resolution of symptoms and abnormal biochemistry. Postnatal review should therefore include checking LFT's and bile acids at 6 weeks post partum.

Women should be informed of the high recurrence rate in subsequent pregnancies (45-90%).

Women with a history of cholestasis should be advised to avoid the use of oestrogen containing contraception.

Appendix 1. Investigation and Management of Cholestasis in Pregnancy

Itching mainly on palm & sole with no rash after 24 weeks gestation

Also consider the diagnosis in women with classical symptoms prior to 24 weeks

Check Serum Bile acid & LFTs

Bile acids normal Alt/Ast normal

Pruritis persists
< 34 weeks repeat bloods fortnightly
>34 weeks repeat bloods weekly

Bile acids normal Alt/Ast raised

Exclude other causes.
Check:
- Hep A/B/C
- Antimitochondrial antibodies, smooth muscle antibodies, antinuclear antibodies
- Liver USS

Consider PET, HELLP, AFLP

Pruritis persists
< 34 weeks repeat bloods fortnightly
>34 weeks repeat bloods weekly

Bile acids raised And/or Alt/Ast raised

Exclude other causes.
Check:
- Hep A/B/C
- Antimitochondrial antibodies, smooth muscle antibodies, antinuclear antibodies
- Liver USS
- Coagulation studies if platelets deranged or steatorrhoea

Consider PET, HELLP, AFLP

If above investigations are negative diagnose ICP.
Transfer to consultant care

Consider treatments
Perform BA + LFT weekly in DAU until delivery

Treatment*

Chlorphenamine - 4mg 4-6 hrly maximum 24mg/24 hrs (can cause drowsiness)

Topical emollients such as aqueous cream with menthol PRN

Ursodeoxcholic acid (UDCA) 500mg BD increased to 4g/QDS

(Rifampicin may be used in severe cases at the discretion of the consultant)

Oral Vitamin K (Menadiol 10mg/OD) can be considered from 32 weeks in those with a prolonged PT time

BA <40 continue weekly BA and LFTs. Offer IOL from 39 weeks
BA >40 (at any time) recommend delivery at 37 weeks
BA >100 (at any time) recommend delivery at 36 weeks

*while these treatments are not specifically licensed for the treatment of cholestasis in pregnancy, they are recognised as standard treatments by RCOG

APPENDIX 1

Worcestershire NHS
Acute Hospitals NHS Trust

Maternity Day Assessment Unit
Obstetric Cholestasis Surveillance

Bile Acids 15 and above ± alt > 40

Patient details sticker

Blood for	Treatment Used	Treatment Used
▪ Hepatitis A☐ B☐ C☐ ▪ EBV/CMV ☐ ▪ Liver smooth muscle Antimitochondrial /Ab S	Aqueous cream with menthol ☐ Chlorphenamine 4 mgs ☐	Ursodeoxycholic acid (UDCA) (starting dose 500mg BD) ☐ Oral Vit K 10 mg/day (menadiol) from 32 wks ☐ If prothrombin time prolonged
▪ Liver U/S scan		

Liver Profiles							
Date							Non-pregnant values
T Protein							60-85 g/l
Albumin							35-55 g/l
Globulin							18-36 g/l
Bilirubin							2-17 umol/l
Alk. Phos							30-130 IU/l
GGT							0-30 U/l
ALT							>30 U/l
Bile acids							0-14 umol/l
Platelets							
Coagulation studies							
Prothrombin time							

Women who have had confirmed raised bile acids should have their LFT's checked at 6 weeks by GP and referral to physician if they remain raised.

Women should be advised to avoid oestrogen containing contraception.
Woman informed □

References

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