COMPLICATIONS OF PREGNANCY

CHOLESTASIS IN PREGNANCY

BACKGROUND INFORMATION

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, and women may exhibit dermatographia artefacts (skin trauma from intense scratching).
- Malaise
- Steatorrhea with fat malabsorption
- Jaundice - uncommon, but can occur in 10-15% of cases

EXCLUDE OTHER CAUSES

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

LABORATORY TESTS

- Bile Acids – levels greater than 10μmol/L are a common diagnostic marker
- Liver Function Tests (LFTs):
  - Aminotransferase (ALT, AST) activity can be raised by up to 20 times the normal level
  - Gamma-glutamyl transferase activity is unusual but indicative of MDR3 gene mutation leading to increased bile acids, or of underlying liver disease.
  - It is uncommon to have a raised serum bilirubin
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. 
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 ANTE NATAL VISITS
Antenatal visits should be arranged 2nd weekly.

TIMING OF DELIVERY
Aim to deliver the woman between 37 weeks 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 34 weeks gestation.

TREATMENT OF MATERNAL PRURITIS
1. The use of topical emollients e.g. calamine lotion may provide temporary relief of itching. 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).
3. Encourage a low fat diet, and advise women to increase their water intake.
4. Offer anti-histamines at night (beneficial for their sedative effect).
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. Relief usually occurs in one to two weeks.

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 enterohepatic bile acids causing reduced absorption of fat-soluble vitamins. Vitamin K is a fat-soluble vitamin required for coagulation. 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. 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.

INTRAPARTUM CTG
1. Monitor the fetal heart rate continuously with a CTG.
2. Anticipate the risk of meconium liquor and request a paediatrician at delivery as necessary.

Increased incidence of meconium liquor at delivery has been linked with obstetric cholestasis, and is more common in preterm than term pregnancies (25% versus 12%).

POSTNATAL MANAGEMENT

COUNSELLING PRIOR TO DISCHARGE
Counselling prior to discharge should include the following:

- risk of reoccurrence in a subsequent pregnancy is 40-60%
- reassurance about the lack of long term sequelae for mother and baby
- pruritis normally resolves within 48 hours of giving birth, however in some women it may last 4-8 weeks
- 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
- 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. Low dose estrogens or progesterone –only pills are recommended.
- 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.
- 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.
REFERENCES (STANDARDS)


15. Walker I, Chappell, LC., Williamson C. Abnormal liver function tests in pregnancy. BMJ. 2013;347

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