WOMEN'S HEALTH AND PAEDIATRICS

MATERNITY UNIT

Intrahepatic Cholestasis of Pregnancy Guideline

Amendments			
Version	Date	Comments	Approved by
1	April 2020		
2	May 202	Tracked changes made from original verison (V1) after circulation for comments	

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Target audience: All health professionals within the maternity services
Equality impact assessment: Perinatal Governance Guideline Group

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Contents

Abbreviations

BA Bile Acids
cCTG Computerised Cardiotocograph
FHR Fetal heart rate
ICP Intrahepatic Cholestasis of Pregnancy (Obstetric Cholestasis)
LFT's Liver Function Tests
MAC Maternity Assessment Centre
USS Ultrasound scan

MAC - Management of Intrahepatic Cholestasis of Pregnancy (ICP)

Present with: -

- Intense itching affecting the limbs and trunk, but classically affecting the palms and/or soles which is worse at night
- Usually develops during the second half of the pregnancy
- There is no associated rash, but excoriations can be present
- Insomnia is common
- Dark urine
- Pale stools
- Malabsorption of fat (Steatorrhea)
- Jaundice is rare
- After delivery symptoms usually resolve within 48hrs. LFT's may take 4-6 weeks to recover

Check LFT's and BA (gold topped bottle)

If BA and LFTs normal – discharge to routine care pathway

- Woman to contact Planned Care if ongoing itching after 7 days
- repeat LFTs and BA every 7-14 days

- If BA>10micromol/L +/-abnormal LFT's, typical history, no other clinical features for liver disease, then make diagnosis of ICP.
- No additional investigations needed

- Weekly BA and LFT's once OC confirmed in planned care
- Arrange Cons ANC at 36weeks to decide on timing of IOL
- Offer treatment with antihistamines and topical emollients (see ICP guideline for further details)

If BA normal and LFT's raised arrange investigations for liver pathology: -

- Viral screen – Hep A, B, C
- Epstein Barr Virus
- Cytomegalovirus
- Liver autoimmune screen (anti-smooth muscle antibody and anti-mitochondrial antibody
- Liver USS

If ALT >200iu/L or BA >100micromol/L require same day review in MAC

Check clotting if ALT >200iu/L, dark urine, pale stools, steatorrhea, early onset ICP (<24 weeks) or suspicion of HELLP/AFLP

Timing of IOL: -

- BA <40micromol/L – offer IOL at 40 weeks
- BA 40-100micromol/L initiate birth at 38 weeks
- BA >100micromol/L – individual plan, initiate birth at 37weeks.
- Consider early delivery from 34 weeks where there are additional co-morbidities e.g. GDM, Multiple pregnancy, PET

Intrahepatic Cholestasis of Pregnancy Guideline

1.0 Introduction

Intrahepatic Cholestasis of Pregnancy (ICP) is a multifactorial condition of pregnancy characterised by an intense pruritus (itch), in the absence of a skin rash with abnormal liver function tests, neither of which have an alternative cause and both of which resolve after birth.

It affects 0.7% of women in the general population but increases to 1.2 -1.5% of Asian population and 2.4% in Chilean women.

Genetic and environmental factors influence the prevalence worldwide.

2.0 Presenting signs and symptoms

Women with ICP may present with a combination of the following: -

- Intense itching affecting the limbs and trunk, but classically affecting the palms and/or soles which is worse at night
- ICP usually starts from 28 weeks onwards but can start as early as the first trimester
- There is no associated rash, but abrasions from intense scratching can be present
- Insomnia is common
- Dark urine
- Pale stools
- Malabsorption of fat (Steatorrhea)
- Jaundice is rare

The pruritus is caused by excess bile acids in circulation, which stimulate nerve endings.

Itching in pregnancy is common and usually not due to ICP (3 out of 4 women will not have ICP).

Women with GDM, previous history of contraceptive pill induced cholestasis or ICP in a previous pregnancy or multiple pregnancy are at an increased risk of developing ICP.

After delivery symptoms usually resolve within 48hrs. LFT's may take 4-6 weeks to recover

3.0 Risks

3.1 Maternal

There may be increased incidence of: -

- Post-partum haemorrhage; this is due to abnormalities of bile acid metabolism, leading to disturbance of absorption of fat-soluble vitamins, especially vitamin K
- High recurrence risk in a future pregnancy

3.2 Fetal

Women with BA of less than 40micromol/L can be reassured their risk of fetal complications is no higher than the background population.

In cases with BA 40-100micromol/L there is an increase in the incidence of meconium and preterm birth. Reassuringly, the latest evidence does not suggest there is an increased stillbirth risk in this group.

Women with BA>100micromol/L need individual counselling as there is an increase in adverse perinatal outcomes in later pregnancy.

4.0 Diagnosis of ICP

In the context of a suggestive history, ICP can be diagnosed on the basis of a BA level >10micromol/L.

If the history is suggestive of ICP: -

- Obtain liver function tests (LFTs) and bile acids (BA) in a gold topped bottle
- Pregnancy specific ranges should be used for all tests
- The normal pregnancy ranges:
    - ALT is <32iu/L (Abnormal LFT defined as ALT >32iu/L or other parameters as defined as Berkshire Surrey Pathology Services Reports)
    - The range of BA in pregnancy is 0-14micromol/L.
      Berkshire Surrey Pathology Service laboratory reporting range is 0-10micromoll/L, therefore anything above 10micromol/L would give a diagnosis of ICP

4.1 Management of ICP (see flowchart at start of guideline)

<u>BA and LFT within normal range</u>

- Discharge to routine care pathway
- Advise woman to contact Planned care if significant ongoing itch after 1 week.
- If itching continues repeat LFTs and BA levels every 7-14 days.

<u>BA >10micromol/L (+/- abnormal LFT's)</u>

- In the absence of no other concerning features for liver disease (LFTs not grossly abnormal, no evidence of PET, no jaundice or paint) give a diagnosis of ICP
- Arrange Consultant Obstetrician ANC appoint at 36 weeks to discuss IOL
- Offer treatment with antihistamines and topical emollients

<u>BA normal and LFTs abnormal</u>

Obstetrician to arrange investigations for liver pathology:

- Viral screen Hepatitis A, B, and C)
- Epstein Barr virus
- Cytomegalovirus
- Liver autoimmune screen for Chronic Active Hepatitis and Primary biliary cirrhosis (anti smooth muscle antibody and anti-mitochondrial antibody)
- Liver ultrasound

Remember the need to consider other important causes of abnormal LFTs:

HELLP syndrome (associated with severe pre-eclampsia) and/or acute fatty liver of pregnancy (AFLP) are important to exclude and prompt URGENT review in MAC

4.2 HELLP

Variant of severe PET

Incidence in PET pregnancies is 5-20% (many more women with PET 20-50% have mild abnormalities of liver enzymes without full blown HELLP.

Women often present with severe epigastric pain, nausea and vomiting and hypertension with/without proteinuria, AKI, placental abruption

Haemolysis on a blood smear, rarely enough to cause severe anaemia, platelets are often <100x10^9/L or falling, elevated ALT

4.3 AFLP

1 in 7,000 -1 in 20,000

Women often feel generally unwell and can have nausea and vomiting

May present with drowsiness, encephalopathy and jaundice

ALT and bilirubin often grossly abnormal and also renal dysfunction and DIC

5.0 Drug Management

Drug treatments that should be offered to women include:

5.1 Topical emollients

Topical emollients like Diprobase, Balneum Plus, Calamine lotion and aqueous cream with menthol can be offered as may provide temporary relief of symptoms. These topical emollients are safe but their efficacy is unknown. There are no trial data to support or refute their use.

5.2 Vitamin K

Routine Vitamin K replacement is not indicated. Selected cases with clinical evidence of malabsorption or a prolonged PT on clotting studies may benefit from Vitamin K (10mg, od, water soluble)

Neonatal vitamin K should be given as per routine care.

5.3 Antihistamines

Antihistamines like Chlorphenamine may provide some night-time sedation but tend not to make a significant impact on the pruritus.

5.4 Ursodeoxycholic acid (UDCA)

Routine use of UDCA is not indicated. There may still be a role for a trial of therapy (this is at the discretion of a senior clinician after discussion with the woman) in selected cases (atypical / early onset disease intractable itch) - suggested started dose is 500mg BD and increase to 500mg TDS.

UDCA may enhance bile acid clearance across the placenta and protect the hepatocyte membrane from bile acid toxicity.

The PITCH[11] study was a large RCT of UDCA for women with ICP and demonstrated that this appeared to be safe but had no significant impact on fetal or maternal outcomes. It was not effective in reducing a composite of adverse perinatal outcomes. It had no clinically meaningful effect on maternal itch symptoms, did not reduce maternal bile acid concentration, there was a

small reduction in ALT but this is of uncertain significance in improving pruritus, protection against stillbirth and safety to the fetus and the neonate.

Rifampicin may also be considered following a referral and review in the Obstetric Medicine Clinic.

6.0 Monitoring in pregnancy

- Weekly BA and LFTs and antenatal check with ongoing itching or confirmed diagnosis
- This can be arranged through Planned Care
- Routine clotting not indicated (check clotting if ALT >200iu/L, dark urine, pale stools, steatorrhoea, early onset ICP (24 weeks) or suspicion of HELLP/AFLP)
- If there are no clinical concerns, a referral should be made to an Obstetric Antenatal Clinic at 36 weeks for IOL to be discussed
- If the ALT is >200iu or BA>100µmmol/L then this should prompt a same day review in MAC
- Early onset ICP (< 24 weeks gestation) or abnormal clotting and arrange review in the Obstetric Medicine Clinic (refer via BadgerNet on asp-tr.antenatalclinic.nhs.net)
- Routine CTG monitoring is not indicated (no evidence of any benefit)
- Routine growth scans are not indicated (no evidence of any benefit)
- Scan or cCTG should be undertaken for the usual clinical indications (pain, RFM, concern about fetal size etc.)

7.0 Timing and place of delivery

For women with confirmed ICP advise birth on Labour Ward with continuous CTG.

Use the highest recorded BA level to guide timing of birth **not** the most recent value.

BA <40micromol/L:

- Women with ICP and BA values less than 40micromol/L can be reassured that they have the same risk of stillbirth as the general population.
- Offer induction at 40 weeks in this group on the basis that timely detection of an acute BA rise may be more challenging in very late pregnancy

BA 40-100micromol/L:

- Women with BA levels of 40-100micromol/L have a small increase in stillbirth risk in late pregnancy
- Initiate birth at 38 weeks

BA >100micromol/L:

- Women with severe ICP (>100µmmol/L) need an individual plan for the timing of birth
- Initiate birth at 37 weeks.
- In cases with additional comorbidities (metabolic syndromes, GDM, PET, multiple pregnancy) consider early birth from 34 weeks gestation after Consultant review

8.0 Postnatal

- Advise women to contact GP to arrange repeat LFT at 10-14 days postnatal
- If these remain abnormal, GP to repeat at 6 week postnatal check
- Avoid oestrogen-based contraception
- Advise women there is a high risk of recurrence in subsequent pregnancies (60%) and that the onset of itching symptoms should prompt testing

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EQUALITY IMPACT ASSESSMENT

Equality Impact Assessment Summary

Name and title: Obstetric Cholestasis Guideline

Background • Clinical midwifery managers • Consultant obstetrician
Methodology • This guideline will be applied to all women who are pregnant • The guideline was informed by NICE and RCOG guidance • The guideline was reviewed by the multidisciplinary team
Key Findings • This guidance ensures that any woman who has concerns regarding fetal movements receives evidence based care that involves the multidisciplinary team.Describe the results of the assessment
Conclusion • This guideline will ensure that all pregnant women who have concerns regarding fetal movement receive a multidisciplinary evidence based approach to their care.
Recommendations • The guidance should be updated three yearly or as when new evidence is discovered