Clinical Guideline

INTRAHEPATIC CHOLESTASIS OF PREGNANCY (ICP)

SETTING Women's & Children's Services / Maternity

FOR STAFF Midwifery & obstetric staff

PATIENTS Women and pregnant people who have obstetric cholestasis

Introduction

In England, intrahepatic cholestasis of pregnancy (ICP) affects 0.7% of pregnancies in multi-ethnic populations. The incidence is greater (1.2-1.5%) in Indian and Pakistani ethnic groups.

Intrahepatic cholestasis of pregnancy is a multifactorial condition of pregnancy characterised by intense pruritus in the absence of a skin rash, with abnormal liver function tests (LFTs), neither of which have an alternative cause and both of which settle following delivery. It presents most commonly in the third trimester but can occur earlier in pregnancy. Around 25% of women and pregnant people develop itching in pregnancy, the majority of whom do not have or develop ICP.

The clinical importance of ICP lies in the potential fetal risks, which may include spontaneous prematurity, iatrogenic prematurity and intrauterine death. There can also be significant maternal morbidity secondary to the intense pruritus, consequent sleep deprivation, and anxiety.

Diagnosis: Clinical presentation + Bile Acids (BA) ≥ 19micromol/L

1. Clinical presentation: pruritus in pregnancy with normal appearance of skin. The pruritus of ICP is typically worse at night, is often widespread and likely to involve the palms of the hands and/or the soles of the feet.

2. Abnormal bile acids: Raised peak random total bile acids ≥19 micromol/L. There is poor correlation between severity of itch and level of bile acids.

- Liver function tests, such as ALT may be raised above the normal level for pregnancy. They do not appear to reflect risk of fetal demise or adverse pregnancy outcome, however, and intrahepatic cholestasis of pregnancy should not be diagnosed with itching and isolated raised ALT.

- If ICP is suspected, a structured history and systematic examination should be performed to exclude other causes of itching and liver dysfunction. Other causes of abnormal LFTs and pruritus include skin conditions such as eczema, atopic eruptions of pregnancy, prescription or recreational drug intake, allergies, infections, autoimmune causes, gall stones, pre-eclampsia and acute fatty liver of pregnancy.

Additional laboratory and/or imaging investigations are not recommended in every woman

Indications for additional liver screen investigation include:

1. if the itch is associated with atypical clinical symptoms (features of liver failure or evidence of acute infection)
2. relevant co-morbidities

3. in the case of early onset severe ICP (markedly elevated transaminases, onset in 1st or 2nd trimester, rapidly progressive biochemical picture).

Women with severe, very early, or atypical presentation of ICP should be discussed with a hepatologist. Women who develop pruritis and liver function or BA abnormalities in first or second trimester are more likely to have an underlying genetic pre-disposition or an alternative or additional diagnosis.

Clinicians should be aware that skin conditions causing itching (e.g. eczema) and ICP can co-exist.

In case of clinical symptoms but normal blood test results and no other apparent cause, offer repeat LFTs and BA weekly with the community midwife as ICP can develop up to 15 weeks after the onset of symptoms.

It is common for pruritis and biochemical abnormalities to fluctuate throughout pregnancy with ICP, however, if they resolve completely the original diagnosis may be re-considered. Transient liver function test abnormalities have many causes, including drug reactions and non-specific viral illnesses. In discussion with the woman or pregnant person, care may return to normal with decisions on timing of birth based on usual obstetric practice.

Monitoring of obstetric cholestasis

Women diagnosed with intrahepatic cholestasis of pregnancy should attend day assessment unit weekly for monitoring.

Women and clinicians should be aware of a higher chance of developing pre-eclampsia or gestational diabetes.

Management of all women with bile acids greater than 40mmol/l and/or significantly elevated ALT should be discussed with a senior obstetrician (ST6 or above).

For mild or moderate ICP (BA <100micromol/L):

- a consultant clinic appointment should be made at 37 weeks.
- If an appropriate ANC appointment is not available, the woman or pregnant person should be seen in DAU at the same gestation by consultant or senior registrar (ST6 or above), to discuss risks, management and timing of delivery as per table below.
- A cervical assessment (bishop score) should be performed before discussing with the team to help plan the management.

Women with severe ICP (BA ≥100micromol/L):

- should be seen by a senior obstetrician in DAU within 48 hours of diagnosis. At this review the management and timing of delivery should be discussed with the consultant / senior registrar.

An information leaflet about obstetric cholestasis should be given to the women once the diagnosis has been confirmed. They should also be advised to reduce fatty food and alcohol intake.

Maternal wellbeing:

- Monitoring should include blood pressure measurement, urinalysis and blood tests (FBC, LFT, and bile acids).

- Coagulation testing is no longer recommended routinely for women and birthing people with uncomplicated ICP whether mild, moderate or severe. Coagulation testing should now only be carried out if there is another condition that may alter the coagulation pathway such as fatty liver), or evidence of reduced absorption of dietary fats (e.g.steatorrhoea).
- Bile acid measurements can be taken at a convenient time, and do not need to be performed fasting.

Fetal wellbeing should be assessed by:

1. Inquiring about fetal movements
2. Measuring symphysial fundal height
3. Auscultation of fetal heart beat

CTG and AFI should be offered:

1. Where there is concern regarding fetal wellbeing
2. When the bile acids are greater than 40mmol/l at ≥38 weeks
3. When bile acids are 100micromol/L or more at ≥ 28 weeks gestation
4. On maternal request

There is an increased risk of stillbirth with obstetric cholestasis. The cause of stillbirth is not hypoxia or placental insufficiency. It is thought that bile acids may cause an acute fetal anoxic event possibly due to fetal arrhythmia or acute placental vessel spasm. CTG and AFI are unlikely to be a useful monitoring tool. CTG and AFI can be offered for maternal reassurance, where there is concern about fetal wellbeing, or at maternal request but women should be advised that these tests do not provide any prediction of perinatal outcome.

Timing of delivery:

Considerations when planning timing of delivery:

1. Poor perinatal outcome such as stillbirth has greater correlation with severely elevated Bile acid (greater than 100micromol/l).
2. Presence of additional risk factors or co-morbidities (such as gestational diabetes and/or pre-eclampsia and/or multiple pregnancy) increase the risk of stillbirth and may influence decision about timing of birth.

Terminology	Peak bile acid concentrations	Prevalence of stillbirth (with 95% CI)	Advice for women	Timing of Induction of labour
Mild ICP	19-39µmol/L	0.13% (0.02 to 0.38%)	If no other RF, risk of stillbirth is similar to background risk	40 weeks or earlier if another indication
Moderate ICP	40-99µmol/L	0.28% (0.08 to 0.72%)	Risk of stillbirth is similar to background until 38-39/40 Higher chance spontaneous and iatrogenic preterm birth, meconium stained liquor and NICU admission.	38-39 weeks
Severe ICP	≥100µmol/L	3.44% (2.05 to 5.37%)	Risk of stillbirth is higher than background. Higher chance of both spontaneous and iatrogenic preterm birth, meconium stained liquor and NICU admission	35-36 weeks

The above factors should be discussed with women and pregnant people along with the inability to predict stillbirth if pregnancy continues and explanation that fetal ultrasound and cCTG do not predict or prevent stillbirth in ICP.

Induction of labour should be considered as detailed in the table above. The risk of stillbirth should be weighed against the increased maternal and perinatal morbidity.

Intrapartum care:

Peak bile acids ≥100micromol/L: Offer continuous electronic fetal monitoring in labour

Peak BA 40-100micromol/L: Benefit of CTG is uncertain. Shared decision making around monitoring in labour should be based on co-morbidities and maternal preference.
Peak BA <40micromol/L and no risk factors: Intrapartum care can follow standard national and local guidelines.

Medical management:

Drug treatment can reduce maternal itching and discomfort, but there is no evidence for improvement in bile acid concentrations or perinatal outcomes.

1. **Topical emollients**: Topical emollients such as aqueous cream with menthol, calamine lotion, Balneum or Diprobase may provide partial symptomatic relief to some women.

2. **Antihistamines** eg. Chlorphenamine. Effectiveness is uncertain but may be beneficial especially at night in relation to its sedative action. Harmful effects have not been reported with use for other conditions.

3. **Ursodeoxycholic acid (UDCA):** Consider for women with moderate to severe OC (BA >40micromol/L). Do not routinely offer UDCA to reduce adverse perinatal outcomes for women with mild ICP. Ursodeoxycholic acid (8-12mg / Kg in 2-3 divided doses) improves pruritus and liver function in some women with obstetric cholestasis. There is no reduction in stillbirth or spontaneous birth <34 weeks in women prescribed UDCA versus placebo, although there may be a small reduction in spontaneous pre-term birth under 37 weeks.

4. **Oral Vitamin K:** Oral vitamin K (10 mg once daily) should be offered to women only if there is evidence of reduced absorption of dietary fats (eg. steatorrhoea) and/or abnormal prothrombin time on coagulation tests.

Postnatal care:

Advise women that itch usually resolves within the first few days after birth, and LFTS/BA should return to normal within a few weeks.
Re-check BA/LFTs at least 4 weeks after birth to confirm resolution. If BA/ LFT abnormalities and symptoms persist beyond 6 weeks, GP should consider investigating for other diagnoses and a referral to hepatology.

Discuss contraceptive use with all women during the antenatal and early postpartum period. Copper IUD, IUS, progesterone implant, injectable and pill can be used without restriction in women with a history of ICP. Combined hormonal contraception can be used providing there is no previous history of contraception related cholestasis, but itching and biochemical abnormalities should resolve before commencing this method.

Future pregnancy:

Women and people of reproductive age who have a pregnancy complicated by ICP have an increased chance of ICP in a future pregnancy. The magnitude of this is unclear.

In future pregnancies perform baseline LFTs and BA at booking to establish that they are normal at baseline. Repeat only if clinically indicated.

Authors
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Table

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AUTHORISING BODY	AN Working Party **March 2023**
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History of persistent pruritis in pregnancy without rash

GP/Midwife to check Liver Function Tests (LFT) and Bile Acids (BA)

Raised LFTs **or** BA

DAU MW assessment (1st presentation)

- BP & urinalysis.
- Check bile acid levels and LFTs.
- Initiate Intrahepatic Cholestasis of Pregnancy check list.
- Consultant led care.
- Book consultant ANC appointment for 37+ weeks if BA<100.
- If BA ≥100 Consultant/Senior registrar review within 48hours.

Medical review

- History and examination.
- If atypical, severe or early presentation- arrange investigations to exclude other causes of deranged LFTs (viral screen, liver USS, autoantibody screen.
- Consider coagulation screen only if failure of liver synthetic function or fat absorption is suspected.
- Offer emollients, UDCA (8-12mg/kg), antihistamine and vitamin K (if abnormal prothrombin time).
- Recommend continuous fetal monitoring in labour and an active 3rd stage if BA>40.

Normal blood results

Advise repeat LFTs and Bile Acids in a week if symptoms persist.

Surveillance

- Repeat LFTs, BA and BP, urinalysis weekly (chart results).
- Consultant review for timing of planned IOL as per guideline.
- CTG/AFI as indicated.

Induction of labour

- Perform FBC, U&Es, LFTs, and group and save on admission.
- Coagulation screen only necessary if failure of liver synthetic function or fat absorption is suspected.
- Consider increased fetal monitoring during induction of labour- 8 hourly CTG.

Post natal

- 28 days: postnatal LFTs and Bile Acids to be checked by midwife or GP.
- Consultant led care for subsequent pregnancies (high recurrence rate) with baseline LFTs / BA at booking.

Checklist

Intrahepatic Cholestasis of Pregnancy

Name

Date of Birth

Hospital Number

Gestation at diagnosis: _____/40

LFTs at diagnosis: ALT (>32) _____

Bile Acids (≥19) _____

Additional risk factors or co-morbidities: _____ **Consultant:** _____

Further investigation indicated (early, severe or atypical symptoms) Yes/No

VIRAL SCREEN: Date Sent : ___/___/___ Results _____
Acute Hepatitis Screen-Hep A B C and E, EBV, CMV (serology)

AUTO IMMUNE PROFILE Date Sent : ___/___/___ Results _____

LIVER SCAN Date : ___/___/___ Results _____

If indicated, other causes of abnormal LFTs to be excluded:
CLINIC APPOINTMENT MADE FOR 37/40 (BA<100) _____

Senior Registrar or Consultant review within 48 hours (BA≥100) _____

Weekly Bloods in DAU: FBC, LFTs, Bile Acids, U&Es

Chart weekly bloods in hand held notes and regular attenders' folder.

OFFER The Following:

Emollients
Antihistamine
UDCA (if BA>40) 8-12mg/kg in divided doses BD or TDS.
VITAMIN K If clotting abnormal (INR/PT)_____

CTG If: reduced Fetal movements / Bile Acids>40 / gestation >37 weeks / maternal request

PLANNED GESTATION AT DELIVERY /40