NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Intrahepatic Cholestasis of Pregnancy (ICP) or Obstetric Cholestasis (OC)

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Intrahepatic Cholestasis of Pregnancy (ICP) or Obstetric Cholestasis (OC)

Prevalence is influenced by genetic and environmental aspects.

In the UK ICP affects 7:1000 pregnancies – it is more common in Indian – Asian or Pakistani – Asian women where it affects 12-15:1000.

It is characterised by the presence of an itch with no visible rash and raised bile acid concentration of 19 micro mol/L or more.

The onset of symptoms is most common in the 3rd trimester but can be earlier in pregnancy.

Important points to remember:

- Alternative diagnosis (such as pre eclampsia) should always be considered before a diagnosis of ICP is made
- It is possible for other conditions to co-exist
- Pruritis and raised bile acid concentrations should return to normal after birth (persistently elevated levels may point to other diagnosis such as non alcoholic fatty liver)
- Around 25% of pregnant women develop itching – the majority of these do not have and do not develop ICP

Diagnosis

If a woman phones the maternity unit reporting itching in pregnancy, she should be invited in for assessment and consideration of blood tests. This should be at a convenient time but will usually be within 2-3 days.

A structured history and examination should be taken to consider other potential diagnosis ie pre eclampsia, drug reactions, allergic reactions and urticaria.

Raised Bile acid concentration of **19 micromol /L** or more supports a diagnosis of ICP

In women with persistent itch, normal skin and normal blood results an initial diagnosis of gestational pruritus should be considered.

ICP can develop in these women up to 15 weeks after a diagnosis of gestational pruritis – if itching continues, they should be offered review and repeated LFTs and bile acids should be taken. The timing of these should be individualised but could correlate with normal scheduled care. They may need to be more frequent later in the 3rd trimester when a ICP diagnosis may alter care.

Women with itch, raised transaminases and normal bile acids should not be given a diagnosis of ICP

Although the routine use of other investigations such as the liver screen and liver ultrasound is no longer routinely recommended additional investigations (including for Hepatitis C) should be considered in women with elevated transaminases, early onset ICP in the first or second trimester, a rapidly progressive biochemical picture, any features of liver failure or evidence of acute infection of if resolution does not occur after birth.

If the itch and biochemical abnormality starts in the 1st or 2nd trimester (especially the 1st) – this is more likely to be secondary to a genetic predisposition or alternative or additional diagnosis. Referral to a hepatologist should be considered.

Dark urine and pale stools are rare

Jaundice is rare (<1%)

Steatorrhea may occur – this can be associated with malabsorption of vitamin K

Be aware:

- Women with ICP have a higher chance of developing PET or GDM (additional testing for GDM based on a diagnosis of ICP alone is not currently recommended)
- ICP is not associated with fetal growth restriction – growth scans are not beneficial unless there are other obstetric concerns

Management

No treatment will improve pregnancy outcome or bile acid concentrations

Drug	**Action**	**Recommended**
Topical Emollients – Aqueous creams +/- menthol	may relieve some discomfort caused by itch	yes
Antihistamines - Chlorphenamine	Sedating antihistamine – relief may be more from sedating effect	yes
Ursodeoxycholic Acid (UCDA)	In some women with BA >40 who are 34-36 weeks – UCDA may offer some benefit in reducing late preterm birth. Does not reduce adverse perinatal outcomes.	Do not routinely offer for purpose of reducing adverse perinatal outcomes If being used – refer to

	Only very small reduction in itch	BNF dosing guidelines
Vitamin K (menadiol sodium phosphate 10mg day)		Only consider in women with steatorrhea who have had a coagulation assessment

Risk of Stillbirth

Risk of stillbirth is only increased above population rate once Bile acid concentrations are 100 micromol/L or more.

It is thought to be caused by an acute fetal anoxic event possibly due to fetal arrhythmia or acute placental vessel spasm.

The risk of stillbirth twin pregnancies is higher than with singleton pregnancies.

	Peak Bild Acid Level	Prevelance of Still birth (95% CI)	Hazard Ratio (95% CI)
Background Stillbirth Rate >28weeks		0.29%	
Mild ICP	19-39 micromol/L	0.13% (0.02-0.38%)	Referent
Moderate ICP	40-99 micromol/L	0.28 (0.08-0.72%)	2.35 (0.52-10.50)
Severe ICP	>100 micromol/L	3.44% (2.05-5.37%)	30.50 (8.83-105.30)

Table confers risk of stillbirth correlating to bile acid levels up to a gestation of 39 weeks. No evidence is available for risk of stillbirth beyond 39 weeks.

Monitoring

Women should be reviewed within a consultant led maternity unit due to the increased risk of pregnancy complications.

Maternal itch is poorly correlated to the BA and LFT levels.

All women with an itch and initial raised bile acid level, should have a second measurement repeated around 1 week later before any diagnostic or care decisions are made – it is common for women with BA levels >100micromol/L and 40-100micromol/L to have subsequent BA levels that are much lower.

Subsequent frequency of monitoring should be individualised depending on the impact that the result may have on future care but the table below may be a guide.

Classification:

Bile Acid Level (micromole/L)	Classification	Monitoring Frequency
19-39	Mild	Weekly BA levels from 35-40 weeks in order to inform timing of birth
40-99	Moderate	Weekly BA levels from 32-38 weeks – timing of birth will be influenced if levels increase over 100
100 or more	Severe	Routine testing of BA may not be routinely required

At every monitoring appointment for ICP, monitoring for signs of pre eclampsia should also be performed (BP, urinalysis, routine assessment of fetal wellbeing).

Advise women that CTG and fetal USS do not predict or prevent stillbirth in ICP.

Advise women with ICP to monitor fetal movements and present for immediate assessment if they are concerned.

Timing of Birth

Bile Acid Level*(micromol/L)	**Classification**	**Recommendation**
19-39	Mild	Consider planned birth by 40 weeks or ongoing AN care according to national guidelines (no increase in SB risk secondary to ICP)
40-99	Moderate (with no other risk factors)	Consider planned birth at 38-39 weeks (risk of SB is the same as background risk until 38-39 weeks)
100 or more	Severe	Consider planned birth at 35-36 weeks due to increased risk of stillbirth
40 + with comorbidities	Women with comorbidities such as GDM, pre eclampsia and multiple	Individualised plan from consultant determining

	pregnancy have increased risk of stillbirth	timing of birth

*** Timing of delivery should be based on peak bile acid concentration**

Mode of birth should be based on usual obstetric or medical indications.

Labour

Offer continuous CTG to women with peak Bile acids of 100micromol/L or more.

The presence of co – morbidities may influence the use of continuous CTG in women with peak Bile Acids below 100 – but in isolation bile acids below 100 is not an indication for a continuous CTG.

Meconium stained liquor is more common in moderate and severe ICP and if present may necessitate continuous CTG monitoring.

Offer women with uncomplicated ICP standard analgesia and anaesthesia options for birth.

There is no increased risk of post partum haemorrhage associated with uncomplicated ICP.

Post Natal Follow Up

Advise women that itching and raised bile acids should resolve after birth.

Follow up should be arranged for at least 4 weeks after delivery. The woman's discharge letter should include advice to the GP to ensure resolution of itch and recheck LFTs and Bile acid levels at the 6 week postnatal check.

If symptoms or blood abnormalities persist beyond 6 weeks post partum, other diagnosis should be considered and a referral to a hepatologist may be required.

Advice for the future

ICP does not influence their choice of contraception or hormone replacement therapy. (Combined hormonal contraception can be used provided there is no history of contraception related cholestasis. Symptoms and blood tests should be back to normal before considering starting).

For women with ICP and previous cholestasis secondary to COC advise them to use progestogen only or non hormonal methods.

Women with a history of ICP have an increased chance of recurrence of ICP in future pregnancies.

Perform a baseline LFT and Bile acid concentration with the booking bloods.

They should then only be repeated if clinically indicated.

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