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Intrahepatic Cholestasis of Pregnancy (ICP) Guideline

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2	August 24	Helen Marx/Samantha Thalayasingam	Revised and updated guideline

AUTHORSHIP, RESPONSIBILITY AND REVIEW

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Job Title	Consultant Obstetrician	Review Date	August 2027

Disclaimer

When using this document please ensure that the version is the most up to date by checking the Obstetrics & Gynaecology Guidelines on WISDOM

PRINTED DOCUMENTS MUST NOT BE RELIED ON

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1. Definition

Intrahepatic cholestasis of pregnancy (ICP) is a multifactorial condition of pregnancy characterised by intense pruritus in the absence of a skin rash, with raised peak random total bile acid concentration of 19 micromol/L or more, which resolves following birth. Previously ICP was diagnosed in pregnant who developed itching together with elevation of any of a wide range of liver function tests beyond pregnancy-specific limits. However, most liver function tests do not reflect the risk of fetal demise and only maternal total bile acid concentrations have been shows to be associated with the risk of stillbirth. Women with isolated raised transaminases and normal bile acid concentrations should not be given a diagnosis of ICP.

Fetal complications include preterm birth, meconium-staining of amniotic fluid, neonatal unit admission and, in pregnant women with bile acid concentrations ≥100 micromol/L, intrauterine fetal death. Maternal complications include a risk of gestational diabetes and pre-eclampsia. There is also maternal morbidity in association with intense pruritus and consequent sleep deprivation.

These guidelines have been developed for Cwm Taf Morgannwg University Health Board, incorporating previous guidance from Cwm Taf University Health Board and RCOG guideline No. 43 “Intrahepatic cholestasis in pregnancy” *June 2022*. These guidelines replace any previous health board versions.

2. Risk Factors

The prevalence of intrahepatic cholestasis of pregnancy is approximately 0.7% in the UK (RCOG 2022). The following factors are associated with an increased risk:

Strong risk factors

- A personal or family history of Intrahepatic cholestasis of pregnancy
- Carriage of hepatitis C
- Presence of gallstones

Weak risk factors

- Chronic hepatitis B infection
- Multiple pregnancy
- Assisted reproduction

- Ethnicity (Women of Indian and Pakistani descent have a two-fold increase in risk)

Women with a previous history of ICP should have baseline bile acid concentrations and liver function tests at booking.

3. Presentation

ICP usually presents in the second trimester with history of pruritus. The following symptoms may be indicative of ICP:

- Unexplained pruritus, typically worse at night
- Usually no rash (excoriations only)
- Uncommonly - mild jaundice: Pale stools, Dark urine

4. Diagnosis

Pruritus in pregnancy is common (RCOG 2022), and can affect up to 25% of pregnancies, of which only a small proportion will have ICP. Itching that involves the palms and soles of the feet is particularly suggestive of ICP. Investigations to exclude other causes of pruritus should be performed, as well as bile acids concentration and liver function tests (LFTs).

The skin should be inspected, and care must be taken to differentiate skin trauma from intense scratching, which may be seen in intrahepatic cholestasis of pregnancy, from other common skin conditions such as eczema or atopic eruption of pregnancy (previously referred to as eczema of pregnancy, prurigo and pruritic folliculitis). If a rash is present, polymorphic eruption of pregnancy should be considered.

Diagnosis can be made by:

- Typical history of pruritus without rash (pruritus that involves the palms and soles of the feet is particularly suggestive).
- Elevated Bile Acids (>19 micromole/litre)
- Exclusion of other causes of abnormal liver function
- Postnatal resolution of symptoms and liver function tests (testing should occur at least 4 weeks postnatally)

Diagnosis	Clinical Features
Gestational pruritis	Itching and peak bile acid concentrations <19 micromol/L
Mild ICP	Itching and raised peak bile acid concentrations 19-39 micromol/L
Moderate ICP	Itching and raised peak bile acid concentrations 40-99 micromol/L
Severe ICP	Itching and raised peak bile acid concentrations ≥100 micromol/L

5. Investigations

1st line investigations:

- Exclude other causes of pruritus. Remember pruritus can precede elevation of bile acids.
- Bile acids
- Liver function tests

Other investigations are no longer routinely recommended. Consider further investigation if particularly elevated liver dysfunction, symptomatic of liver disease, steatorrhoea or if liver dysfunction persists postnatally:

- Coagulation profile
- Hepatitis C virology
- Liver and biliary tract ultrasound
- Full blood count
- Auto-antibody tests

Severe, early, or atypical cases of appears to be ICP should be discussed with a hepatologist.
Consider postnatal investigations in women who do not have resolution of abnormal liver function tests postnatally.

Bile Acids processing in CTM

Bile acids are processed in Biochemistry at PCH on a Tuesday and Thursday pm. RGH send bile acids to PCH for processing. Bile acids are processed in POW on a daily basis. Results should be followed up by Maternity Day Assessment Unit.

If a woman has persistent unexplained itching but liver function tests (LFTs) and bile acids are normal, LFTs and/or bile acids should be monitored every 2 weeks until LFT/bile acids become abnormal, or symptoms stop. Seek specialist advice if the itch significantly worsens.

NB. ICP alone is not an obstetric emergency. Therefore, if a woman complains of itching in the absence of other symptoms (e.g. Altered fetal movements, it is perfectly acceptable to arrange an appointment via MDAU Monday to Friday. Urgent out of hours assessment is not required for itching alone.

6. Associated Risks

Fetal

- Spontaneous or iatrogenic prematurity
- Passage of meconium during labour and birth
- More likely to receive neonatal care
- Intrauterine death
    - Mild ICP (19-39 micromol/L) with no other risk factors: the risk of stillbirth is similar to the background risk.
    - Moderate ICP (40-99 micromol/L) with no other risk factors: the risk of stillbirth is similar to the background risk until 38-39 weeks gestation.
    - Severe ICP (≥100 micromol/L): the risk of stillbirth is higher than the background risk.
    - Women with ICP that have additional risk factors or comorbidities appear to increase the risk of stillbirth and may influence decision-making around timing of planned birth.
    - Women with ICP and a twin pregnancy have a risk of stillbirth that is higher compared to a twin pregnancy without ICP.

The pathophysiology of stillbirth in ICP is uncertain but it is thought that bile acids may cause an acute fetal anoxic event possibly due to fetal arrhythmia or acute placental vessel spasm.

Maternal

- Itching that can be severe, may fluctuate and cause sleep deprivation.
- Higher change of developing pre-eclampsia (OR 3.7) or gestational diabetes (OR 2.4) (RCOG 2022)

7. Monitoring of Intrahepatic cholestasis of pregnancy

Women diagnosed with Intrahepatic cholestasis of pregnancy should be transferred to consultant led care and advised to give birth in an Obstetric Unit.

***Maternal Monitoring*.**

- Repeat LFTs and bile acids after 1 week and then determine frequency on an individual basis.
  - Mild ICP (19-39micromol/L) – consider weekly testing around 38 weeks gestation.
  - Moderate ICP (40-99micromol/L) – consider weekly testing around 35 weeks gestation.
  - Severe ICP (≥100micromol/L) – further testing might not impact decision making, may not be routinely required.
- Regular BP and urinalysis
- Arrange OGTT

Reconsider diagnosis if itch and bile acids resolve – unlikely ICP.

(Clotting studies are no longer routinely recommended in uncomplicated ICP. Consider in cases with steatorrhoea or abnormal LFTs)

Fetal Monitoring.

- Maternal monitoring of movements
- Ultrasound and Cardiotocography are **not** reliable methods for preventing fetal death in ICP and are **not necessary** unless other indications for monitoring exists.
- Continuous fetal monitoring in labour should be offered if bile acids ≥100micromol/L (no evidence for or against continuous fetal monitoring in labour for women with peak bile acids <100micromol/L – individualise decision based on co-morbidities and preferences)

8. Treatment

Although there is no current evidence that any specific treatment improves either maternal symptoms or neonatal outcomes, the following may be considered (RCOG 2022) (UKTIS 2015).

- Topical emollients e.g. aqueous cream (with or without menthol added) – no known harmful effects, may relieve some discomfort.

- Antihistamines - e.g. chlorphenamine 4 mg TDS or promethazine 25 mg at night may help relieve pruritus and provide some sedation if needed (effectiveness uncertain)

Ursodeoxycholic acid:

Do NOT routinely offer ursodeoxycholic acid for the purpose of reducing adverse perinatal outcomes in women with ICP. Reduction in maternal itch not considered clinically relevant but can be considered for intractable symptoms. Ursodeoxycholic acid is not licensed for use in pregnancy. The usual dose is 8-12mg/kg per day in 2-3 divided doses. The drug is available as 150mg and 250mg capsules.

Vitamin K:

Consider 10mg daily vitamin K if there is a suspicion of reduced absorption of fats (e.g. steatorrhoea) and/or evidence of a prolonged prothrombin time (if coagulation studies are performed).

NB. Postnatal vitamin K must be offered to the babies in the usual way.

9. Timing of Birth

- Seek consultant opinion if other complications present or twin pregnancy.
- Mild ICP (19-39 micromol/L) with no other risk factors: consider planned birth by 40 weeks gestation or ongoing antenatal care (risk of stillbirth is similar to the background risk)
- Moderate ICP (40-99 micromol/L) with no other risk factors: consider planned birth at 38-39 weeks gestation (overall risk of stillbirth is similar to the background risk until 38–39 weeks' gestation)
- Severe ICP (≥100 micromol/L): consider planned birth at 35-36 weeks gestation (risk of stillbirth is higher than the background risk

Other considerations around labour and birth:

- ICP does not impact choice around mode of birth and should be based on normal obstetric practices.
- Offer continuous fetal monitoring to women with peak bile acids ≥100micromol/L.
- Can have standard analgesia and anaesthesia options for birth.
- No evidence of an increased risk of postpartum haemorrhage if have uncomplicated ICP.

10. Post Natal Follow Up

- Postnatal resolution of symptoms and normalisation of LFTs can be crucial in confirming the diagnosis of ICP. The majority will stop itching in the first few hours or days after birth.
- LFTs and bile acids should be checked at least 4 weeks after birth to allow time for levels to return to a normal range.
- If the person is clinically unwell or other diagnoses are suspected then liver function testing should be repeated sooner, as clinically indicated.
- If, after 6 weeks, the results are still abnormal, seek specialist advice from appropriate specialist team (gastroenterology) and consider other diagnoses/investigations.
- Provide appropriate counselling to ensure that the mother has fully understood the implications of Intrahepatic cholestasis of pregnancy – these women should have baseline liver function tests and bile acid concentration testing with booking blood investigations.

11. Hormonal treatments (contraception/HRT)

- ICP alone should not influence the choice of contraception or hormone replacement therapy.
- For women with ICP and previous cholestasis secondary to combined hormonal contraception – advise them to use progestogen-only or non-hormonal methods.
- In women with previous ICP requesting HRT, consider offering if there are no other contraindications to use.

Guidance should be in line with UKMEC.

12. References

RCOG (2022) - Intrahepatic Cholestasis in Pregnancy. Green Top Guideline No 43. Published 09/08/2022. Available from https://www.rcog.org.uk/globalassets/documents/guidelines/gtg_43.pdf

UKTIS (2015) Treatment of Intrahepatic cholestasis of pregnancy. TOXBASE. UK Teratology Information Service. www.toxbase.org

British National Formulary (On-line). London: BMJ Group and pharmaceutical Press. http://www.medicinescomplete.com [Accessed on 08.06.20].

13. Useful Links

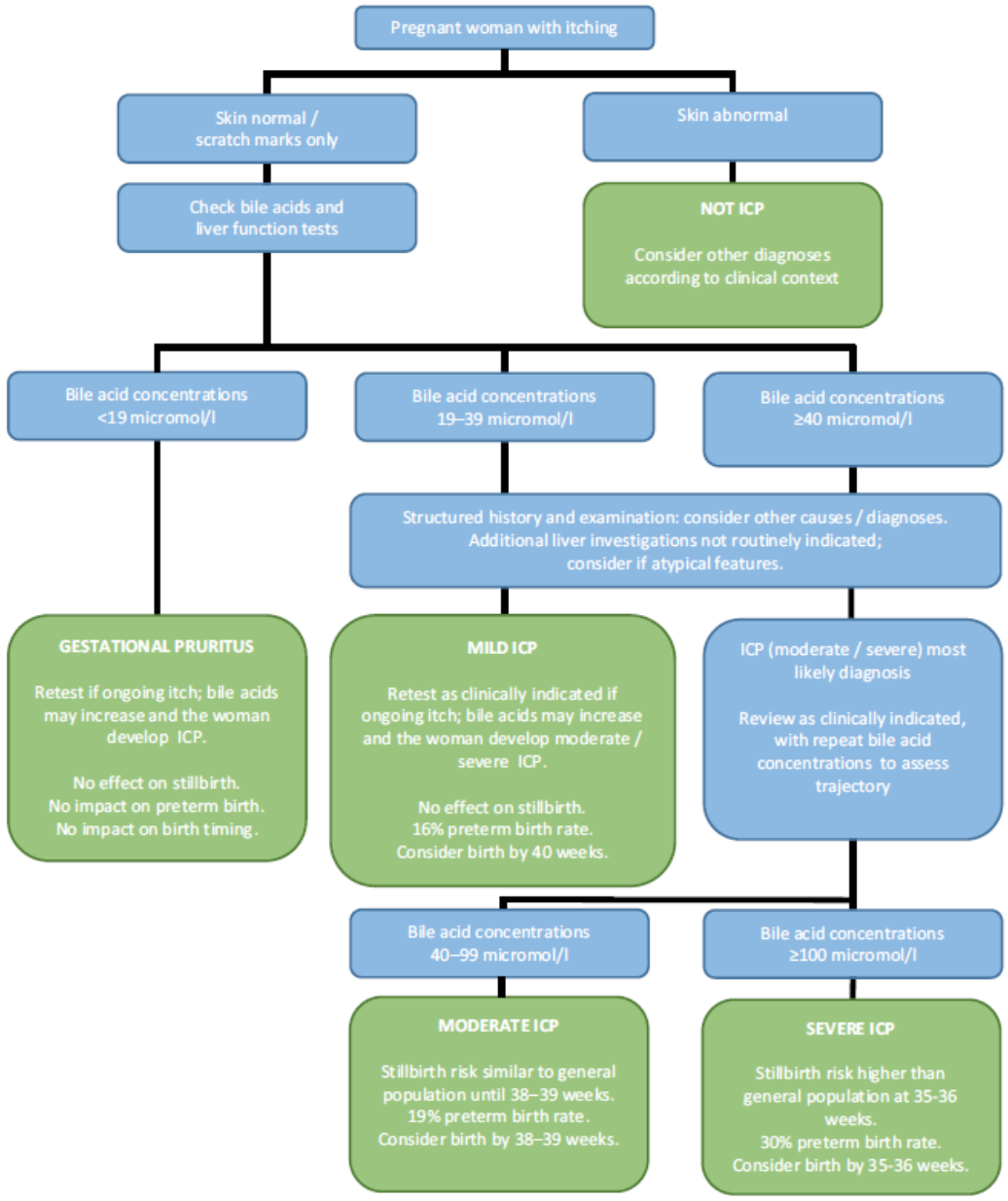
- RCOG Patient Information Leaflet https://www.rcog.org.uk/for-the-public/browse-all-patient-information-leaflets/intrahepatic-cholestasis-of-pregnancy-patient-information-leaflet/
- Intrahepatic Cholestasis in Pregnancy Support https://www.icpsupport.org/
- British Liver Trust https://britishlivertrust.org.uk/information-and-support/liver-conditions/intrahepatic-cholestasis-pregnancy/

14. Auditable Standards

- Proportion of women with raised bile acid concentrations offered timing of birth in line with RCOG Green-top Guideline. (>90%)
- Proportion of women with uncomplicated raised bile acid concentrations having additional investigations routinely performed. (<10%)
- Proportion of women with raised bile acid concentrations offered ursodeoxycholic acid in line with RCOG Green-top Guideline. (<5%)
- Proportion of women with severe ICP (peak bile acids ≥100 micromol/L) offered continuous electronic fetal monitoring during labour. (>90%)

Appendix 1

Flowchart for the care of pregnant women with itching



RCOG (2022) - Intrahepatic Cholestasis in Pregnancy. Green Top Guideline No 43

Appendix 2

Summary of care for pregnant women with itching and normal skin

	Otherwise uncomplicated low risk singleton pregnancy[a] Itching with normal skin/excoriations Peak total BA concentration, micromol/L			
	<19 micromol/L	**19–39 micromol/L**	**40–99 micromol/L**	**≥100 micromol/L**
Initial diagnosis	Pruritus gravidarum	Mild ICP	Moderate	Severe ICP
	Structured history and examination, no additional or alternative causes identified			
If itch persists, frequency of BA	1–2 weekly	1–2 weekly	1–2 weekly	Only if will impact care plans
Risk of stillbirth compared with general obstetric population [0.18–0.75]	Unchanged	Unchanged 0.13%	Unchanged until 39 weeks, 0.28%	Raised, 3.44%
Timing of mode of birth	No impact	Consider planned birth by 40 weeks	Consider planned birth at 38–39 weeks	Consider planned birth at 35–36 weeks
Preterm birth rate, spontaneous and iatrogenic	Unchanged	16%	19%	30%
Role for routine use of UDCA	No	No	No impact on stillbirth	No impact on stillbirth
Additional liver investigations[b]	Not indicated routinely. Consider for women with atypical features (e.g. early onset, marked tranaminitis, jaundice, fever, or in whom postpartum resolution does not occur)			

[a] For pregnancies with other obstetric or medical conditions, these should be taken into consideration when deciding management options.

[b] Such as liver ultrasound, viral hepatitis screen, liver autoimmune tests. ICP, intrahepatic cholestasis of pregnancy; UDCA, ursodeoxyxholic acid.

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