HYWEL DDA UNIVERSITY HEALTH BOARD

Management of Intrahepatic Cholestasis of Pregnancy (ICP) Guideline

Guideline information

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Clinical

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Summary of document:
Clinical guideline to provide evidence based management of women with Intrahepatic Cholestasis of Pregnancy.

Scope:
The guidance uses the term “woman” (pronouns she or her) or Mother to describe individuals whose sex assigned at birth was female, whether they identify as female, male or non-binary. It is important to acknowledge it is not only people who identify as women for whom it is necessary to access women’s health and reproductive services. Therefore, this should include people who do not identify themselves as women but who are pregnant or have recently given birth. Obstetric and midwifery services and delivery of care must therefore be appropriate, inclusive and sensitive to the needs of those individuals whose gender identify does not align with the sex that they were assigned at birth.

This guideline summarises the evidence regarding the diagnosis, and the maternal and fetal risks of intrahepatic cholestasis of pregnancy (ICP), previously called obstetric cholestasis. It provides guidance regarding the different care options available. These should be considered in conjunction with the wishes of the woman, as part of shared and informed decision-making.

To be read in conjunction with:
667 Induction of Labour Guideline (opens in a new tab)
813 Continuous Intrapartum Fetal Monitoring Guideline (opens in a new tab)
621 Hypertensive Disorders in Pregnancy guideline (opens in a new tab)
632 Care of women with Diabetes in pregnancy guideline (opens in a new tab)

Patient information:
https://www.rcog.org.uk/media/xzwha1lm/intrahepatic-cholestasis-ofpregnancy-patient-information-leaflet.pdf

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Reviews and updates:
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New guideline 22.8.2022

Keywords
ICP Intrahepatic Cholestasis pregnancy

Glossary of terms

ICP	Intrahepatic Cholestasis of Pregnancy (old term: Obstetric Cholestasis).
BA	Bile Acids
ALT	Alanine Aminotrasnferase
AST	Aspartate Transaminase
CTG	Cardiotocography
CEFM	Continuous Electronic Fetal Monitoring
UDCA	Ursodeoxycholic Acid

LFT	Liver Functions Test
UK-MEC	UK- Medical Eligibility Criteria for contraception use
HRT	Hormone Replacement Therapy
RCT	Randomised Controlled Trial

Contents

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Aim

To give guidance to obstetricians and midwives on the management of women with ICP

Objectives

The aim of this document will be achieved by the following objectives:

- Provide a clear pathway for the management of women who are diagnosed with ICP based on the latest available evidence

Introduction

- In the UK, ICP affects 0.7% of pregnancies in multi-ethnic populations, and 1.2%–1.5% of women of Indian-Asian or Pakistani-Asian origin.
- It is a multifactorial condition. It is characterised by pruritus in the absence of a primary skin condition, with abnormal maternal BA (Bile Acids) concentrations. The onset of symptoms is most common in the third trimester, but can be earlier in pregnancy. Alternative diagnoses (such as pre-eclampsia) should always be considered before a diagnosis of ICP is made; it is also possible for other conditions to co-exist. Pruritus and raised BA concentrations should return to normal after birth.
- There are no clinical features or laboratory patterns that are unique to ICP, as other conditions can cause itching, or raised BA concentrations in pregnancy. Around 25% of pregnant women develop itching the majority of these do not have and do not develop ICP.
- BA concentrations are not associated with intensity of itching. Other liver blood tests, such as ALT or AST are not associated with pregnancy outcome. In light of this, the consensus is now that the diagnosis of ICP requires elevated maternal BA concentrations, and that women with itching and isolated raised transaminases alone (with normal BA concentrations) should not be given a diagnosis of ICP.

Terminologies to describe the condition

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

- **Peak bile acid concentrations** refer to the highest BA concentration recorded during a woman's pregnancy. Thus a woman's diagnosis may progress in severity during pregnancy.
- The upper limit of normal bile acid concentrations in pregnancy is 18 micromol/L.

Diagnosis of ICP

- The diagnosis of ICP should be considered in pregnant women who have itching in skin of normal appearance and raised peak random total bile acid concentration of 19 micromol/L or more.
- The diagnosis is more likely if it is confirmed that itching and raised BA resolve after birth
- Offer repeat LTFs and BA measurement (depending on gestation and clinical context) in women with normal blood results whose itch persists, and no other cause is apparent (Because women with gestational pruritus may develop ICP up to 15 weeks after initial presentation).
- If resolution of itching is associated with normalisation of BA and LFTs **during pregnancy**, the diagnosis of ICP is unlikely to be correct (In clinical practice, diagnoses should be reconsidered if the clinical presentation changes, other causes included drug reactions (e.g. to antibiotics or non-specific viral illnesses).
- Additional laboratory and/or imaging investigations are not recommended in every woman, but could be considered on an individual basis. Consider antenatal testing **only if** :-
  - Presence of relevant comorbidities.
  - Early onset severe ICP.
  - There are atypical clinical symptoms. These may include:
    1) Women with markedly elevated transaminases.
    2) Early onset of ICP in the first or second trimester.
    3) A rapidly progressive biochemical picture.
    4) Any features of liver failure.
    5) Evidence of acute infection.
    6) If resolution does not occur after birth.
- Consider discussing the care of women with severe, very early or atypical presentation of what appears to be ICP with a hepatologist.

Maternal and Perinatal Risks

- Advise women with isolated ICP and a singleton pregnancy that the risk of stillbirth only increases above population rate once their serum bile acid concentration is 100 micromol/L or more:
  7) In women with mild ICP and no other risk factors, advise them that the risk of stillbirth is similar to the background risk.
  8) In women with moderate ICP and no other risk factors, advise them that the risk of stillbirth is similar to the background risk until 38–39 weeks' gestation.
  9) In women with severe ICP, advise them that the risk of stillbirth is higher than the background risk

	Peak bile acid concentrations	**Prevalence of stillbirth**	**Absolute numbers of stillbirths**
National UK stillbirth rate from 28 weeks (2015)		**0.29%**	
Mild ICP	19–39 micromol/L	**0.13%** (0.02 0.38%	3/2310
Moderate ICP	40–99 micromol/L	**0.28%** (0.08 0.72%)	4/1412
Severe ICP	≥100 micromol/L	**3.44%** (2.05 5.37%)	18/524

- Advise women with ICP that the presence of risk factors or co-morbidities (such as gestational diabetes and/or pre-eclampsia and/ or multifetal pregnancy) appear to increase the risk of stillbirth and may influence decision-making around timing of planned birth.
- Advise women with ICP and a twin pregnancy that the risk of stillbirth is higher compared with a twin pregnancy without ICP (about 6 fold higher in one study).

Antenatal Care

- Women with ICP should be reviewed within a consultant-led maternity unit.
- For women with ICP, consider repeating LFTs and BA after 1 week, and then determine frequency on an individual basis
- If the woman has mild ICP, they could have weekly testing as they approach 38 weeks' gestation in order to inform timing of birth.
- If the woman has moderate ICP, especially if they are approaching 35 weeks' gestation, weekly testing should be considered, as timing of birth may be influenced if levels rise to 100 micromol/L or more.
- If the woman has severe ICP, further routine testing of bile acids might not impact on decision making and therefore may not be routinely required.
- Do not offer CTG nor USS to predict or prevent stillbirth in ICP.
- Advise women with ICP to monitor fetal movements and present for immediate assessment if they have any concerns (Recommended in Saving Babies' Lives Care Bundles version 2 (2019) for all pregnant women)

Treatment options:

- Advise women that there are no treatments that improve pregnancy outcome (or raised BA concentrations) and treatments to improve maternal itching are of limited benefit.
- Consider topical emollients such as aqueous cream (with or without menthol added) to ameliorate skin symptoms (Used in clinical practice, but not formally evaluated for evidence of benefit in reducing itching) Example: Dermacool 1% cream, twice per day.
- Consider antihistamine agents, such as chlorphenamine, particularly at night although the effectiveness of this treatment is uncertain in women with ICP. (Used in clinical practice, but not formally evaluated for evidence of benefit in reducing itching).
  Example: Chlorphenamine maleate (sedative) 4 mg PO every 4-6 hrs, max 24 mg/day.

  Or Loratadine (non-sedative) 10 mg PO OD.

- **Do not** routinely offer UDCA (Ursodeoxycholic Acid) for the purpose of reducing adverse perinatal outcomes in women with ICP. The largest RCT of UDCA showed no evidence of benefit. Only small group of women might benefit with reduction of itching (less than 5%).
  Example: Ursodeoxhcholic Acid 500 mg PO BD (may be increased to TDS)
- Consider maternal vitamin K treatment **only if** there appears to be reduced absorption of dietary fats (e.g. presence of steatorrhoea) and/or evidence of abnormal prothrombin time if coagulation studies are performed. (Extrapolation from other clinical scenarios where dietary fat absorption is impaired, but routine use in all women with ICP is lacking an evidence base). Menadiol, the water soluble version of vitamin K, is preferred over fat soluble preparations in intrahepatic cholestasis.

  Example: Menadiol Sodium Phosphate 10 mg PO OD from 32 weeks.

Timing and Mode of delivery

Advise women that ICP in itself does not impact their choice around mode of birth and that these decisions should be based on usual obstetric practice for that woman.

Severity	Timing of birth	Risk of stillbirth
Mild ICP without other risk factors	planned birth by 40 weeks' gestation or ongoing antenatal care according to national guidance	Similar to the background risk
Moderate ICP without other risk factors	planned birth at 38–39 weeks' gestation	similar to the background risk until 38–39 weeks' gestation
Severe ICP without other risk factors	planned birth at 35–36 weeks' gestation	Higher than the background risk (3.44%)
ICP with risk factors e.g. multifetal pregnancy, GDM or Pre-eclampsia.	Individualise	Higher than the background risk

Intrapartum Care

Place of birth:

- Offer continuous electronic fetal monitoring (CEFM) to women with severe ICP.
- Mild/Moderate ICP does not require CTG, therefore, birth in low risk setting is not contraindicated.
- Advise women that the presence of risk factors (such as gestational diabetes, pre-eclampsia, multifetal pregnancy) appear to increase the risk of adverse perinatal outcomes and that these conditions themselves may necessitate monitoring during birth or in conjunction with ICP may influence decision-making around monitoring in labour.
- Advise women that meconium-stained liquor is more common in moderate and severe ICP, and that this will influence decision-making around CEFM
- Offer women with uncomplicated ICP standard analgesia and anaesthesia options for birth
- Care of third stage should follow routine clinical practice (no evidence of an increased risk of postpartum haemorrhage if they have uncomplicated ICP)

Postpartum Care

- Follow-up should be arranged at least 4 weeks after birth to confirm resolution of ICP (resolution of itching and normalisation of LFT and BA)

- If itching or biochemical abnormalities persist beyond 6 weeks postpartum, consider other diagnoses depending upon the history and examination findings. Referral to a hepatologist may be required.
- Copper-bearing intra-uterine devices, levonorgestrel-releasing intrauterine systems, progestogen-only implant, progestogen-only injectable, and progestogen-only pill can be used without restriction in women with a history of ICP (UKMEC category 1).
- Combined hormonal contraception can be used in women with ICP (UKMEC 2) provided they do not also have a history of contraception related cholestasis. Resolution of itching and LFTs and BA concentrations returning to normal levels should be confirmed before commencing this method.
- Advise women to attend for review if recurrence of itch and abnormal LFTs occur while using combined hormonal contraception, this would give a diagnosis of contraceptive-related cholestasis (UKMEC 3) and alternative contraception options should be discussed.
- For women with an atypical presentation of ICP, atypical postnatal clinical course, where other diagnoses are suspected, or where itching and LFTs have not resolved, a personalised approach to contraceptive choice should be undertaken, with provision of information about avoidance of pregnancy with active liver disease.
- For menopausal women considering hormonal replacement therapy (HRT) it seems reasonable to offer the lower physiological dose of oestrogen found in HRT, with review of use if women develop itching or other signs of cholestasis.
- Advise women with a history of ICP that they have an increased chance of recurrence of ICP in subsequent pregnancies (precise magnitude of this is unclear).
- Perform a baseline LFTs and BA concentration with booking blood investigations **in the next pregnancy**.

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%)

These targets have been set in recognition of the need for individualised care particularly in women with comorbidities and atypical ICP.

Links and Support Groups

Information for healthcare professionals

Maternal use of medication in pregnancy (UK Teratology Information Service) (http://www.uktis.org/html/maternalexposure.html)
http://www.uktis.org/html/maternal_exposure.html

Information for women and families

Research based charity and support group ICP Support (http://www.icpsupport.org/)
RCOG. *Intrahepatic Cholestasis of Pregnancy*. Information for you (https://www.rcog.org.uk/for-the-public/)

Information for women and their families on use of medicines in pregnancy

http://www.medicinesinpregnancy.org/

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