UH Sussex Intrahepatic Cholestasis of Pregnancy (ICP) Guideline	
Summary statement: How does the document support patient care?	By providing evidence based guidance for staff in the maternity unit on the diagnosis and management of intrahepatic cholestasis of pregnancy (ICP).
Staff/stakeholders involved in development:	Leads for Maternity Risk Management (Obstetric and Midwifery), Labour Ward Leads (Obstetric and Midwifery), Joint Obstetric Guidelines Group.
Division:	Women and Children's
Department:	Maternity
Responsible Person:	Chief of Service
Author:	Obstetric Consultant
For use by:	Obstetric Medical staff and Midwives
Purpose:	To provide clinical guidance for staff on the diagnosis and management of ICP.
This document supports:	RCOG 2022 Green top guideline No 43
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Version	Date	Author	Status	Comment
1.0	April 2023	Sophia Stone, Obstetric Consultant (SRH&WH) Jo Sinclair, Obstetric Consultant (RSCH&PRH)	Archived	New merged UH Sussex Maternity guideline replacing: • MP021 Obstetric Cholestasis (legacy East) • CG1102 Intrahepatic Cholestasis of Pregnancy (legacy West)
1.1	September 2023	CE Team	Live	Merged approval from Legacy East.

The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician.
If in doubt contact a senior colleague or expert.

Contents

Intrahepatic Cholestasis of Pregnancy Guideline

1.0 Aim

The aim of this guideline is to provide evidence based guidance for staff in the diagnosis and management of intrahepatic cholestasis of pregnancy (ICP).

2.0 Scope

- Obstetricians
- Midwives

3.0 Responsibilities

Midwives and Obstetricians have a responsibility to:

- To access, read, understand and follow this guidance.
- To use their professional judgement in application of this guideline.

Management have a responsibility to:

- To ensure the guideline is reviewed as required in line with Trust and National recommendations.
- To ensure the guideline is accessible to all relevant staff.

4.0 Abbreviations used in the guideline

ICP - Intrahepatic Cholestasis of Pregnancy	**OC -** Obstetric Cholestasis
LFTs - Liver Function Tests	**IOL -** Induction of Labour
AST - Aspartate aminotransferase	**ALT -** Alanine Aminotransferase
PEP - Polymorphic Eruption of Pregnancy	**LKM -** Liver-Kidney Microsomal
DAU - Day Assessment Unit	**URSO -** Ursodeoxycholic acid
COCP - Combined Oral Contraceptive Pill	**INR -** International Normalisation Ratio
BA - Bile Acids	

5.0 Introduction

In the UK, Intrahepatic cholestasis of pregnancy (ICP) affects 0.7% of pregnancies in multi-ethnic populations, and 1.2%–1.5% of women/people of Indian-Asian or Pakistani-Asian

origin. The prevalence is affected by many variables including genetics, racial background and environmental factors.

The aetiology is still unknown and is likely to be multifactorial. There is a **high recurrence rate** in future pregnancies of between 45-90%.

Characteristics of ICP include pruritus (itching) in the absence of a rash, and deranged liver function tests (LFTs) and/or raised bile acids (BA), which resolve spontaneously after birth and which have no alternative cause.

In a meta-analysis of adverse perinatal outcomes of ICP with biochemical markers, in singleton pregnancies, stillbirth was associated with maximum total bile acid concentration, especially over 100 micromol/L. In pregnancies with co-morbidities that themselves may impact on pregnancy outcome (such as multifetal, diabetic, pre-eclamptic pregnancies), these must be taken into account when considering risks and care options.

Bile acid concentrations are not associated with intensity of itching. Other liver blood tests, such as alanine transaminase or aspartate transaminase are not associated with pregnancy outcome. In light of this, the consensus is now that the diagnosis of ICP requires elevated maternal bile acid concentrations, and that pregnant women and people with itching and isolated raised transaminases alone (with normal bile acid concentrations) should not be given a diagnosis of ICP. This is supported by the recent systematic review described above, in which there was no association between abnormal maternal and birthing parent transaminase concentrations and stillbirth.

6.0 Diagnosis

The diagnosis of ICP should be considered in pregnant women and people 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 bile acids resolve after birth.

Offer repeat liver function tests and bile acid measurement (depending on gestation and clinical context) in women/people with normal blood results whose itch persists, and no other cause is apparent.

If resolution of itching is associated with normalisation of bile acids and liver function tests during pregnancy, the diagnosis of ICP is unlikely to be correct.

7.0 History and examination

If a diagnosis of ICP is suspected, carry out a structured history and examination, so that other causes of itching and liver dysfunction can be excluded.

Presence of a skin rash may be diagnostic of Polymorphic Eruption of Pregnancy (PEP) or Pemphigoid Gestationis, and these women/people should be referred or treated as appropriate.

8.0 Investigations

Bile acid (BA) measurement: raised peak random total bile acid concentration of 19 micromol/L or more is indicative of ICP.

Women and people with a typical picture of ICP do not need to routinely undergo the investigations (hepatitis serology and liver ultrasound) for other causes of liver disease.

However, these additional investigations (including viral and autoimmune screen and liver ultrasound), should be considered in women and people and pregnant people with an atypical or uncertain picture of ICP. This may include women and people with markedly elevated transaminases, early onset of ICP in the first or second trimester, a rapidly progressive biochemical picture, any features of liver failure or evidence of acute infection, or if resolution does not occur after birth. Consider discussing the care of women and people with severe, very early or atypical presentation of what appears to be ICP with a hepatologist.

Confirm the diagnosis of ICP in the postnatal period at least 4 weeks after birth, with resolution of itching and liver function tests returning to normal (including bile acids).

9.0 Discussion of maternal and perinatal risks

Maternal and birthing parent:

- Advise women and people with ICP that the predominant symptom is itching. This can be severe, may fluctuate and may markedly affect sleep.
- Women and people with ICP may have a higher chance of developing pre-eclampsia (OR 3.7) or gestational diabetes (OR 2.4). They should have blood pressure and urine monitoring, and testing for gestational diabetes according to national guidance.

Fetal:

- Stillbirth:
  Advise pregnant women and people 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:
  - In women and people with peak bile acids 19–39 micromol/L and no other risk factors, advise them that the risk of stillbirth is similar to the background risk.
  - In women and people with peak bile acids 40–99 micromol/L and no other risk factors, advise them that the risk of stillbirth is similar to the background risk until 38–39 weeks' gestation.

    - In women and people with peak bile acids 100 micromol/L or more, advise them that the risk of stillbirth is higher than the background risk.
- Advise pregnant women and people with ICP that the presence of risk factors or co-morbidities (such as gestational diabetes and/or pre-eclampsia and/or multi-fetal pregnancy) appear to increase the risk of stillbirth and may influence decision-making around timing of planned birth.
- Advise pregnant women and people with moderate or severe ICP that they have a higher chance of both spontaneous and iatrogenic preterm birth.
- Advise pregnant women and people with moderate or severe ICP that they have an increased chance of having meconium stained amniotic fluid during labour and birth.
- Advise women and people pregnant with moderate or severe ICP that their baby is more likely to receive neonatal care.

10.0 Management of ICP

10.1 Antenatal Care

- Pregnant women and people with ICP should receive the RCOG patient information leaflet: obstetric cholestasis / ICP once the diagnosis has been made.
- Pregnant women and people with ICP should be under consultant led care and should be managed within the Day Assessment Unit (DAU).
- BA & LFTs should be measured weekly in the majority until birth.
- Pregnant women and people should be checked regularly for other conditions that may alter LFTs such as pre-eclampsia, with on-going management dependent on the diagnosis.
- Ultrasound and regular antenatal CTG monitoring are not routinely indicated in pregnant women and people with ICP alone and are not reliable predictors of fetal morbidity.
- Advise women and people with ICP alone to monitor fetal movements and present for immediate assessment if they have concerns.

10.2 Drug treatment

- Advise pregnant women and people that there are no treatments that improve pregnancy outcome (or reduce BA concentration) and treatments to improve maternal itching are of limited benefit.
- Topical emollient, Aqueous Cream with menthol 1% (RSCH &PRH) or Levomethol 1% in Aqueous Cream (SRH & WH), for relief of pruritus may benefit some pregnant women and people.
- Antihistamine agents such as chlorphenamine may be considered.
- Ursodeoxycholic acid (URSO) has been shown not to improve symptomatic pruritus and should not be prescribed routinely. It may have a place in management of pregnant women and people with severe, very early onset ICP and individualised decision made for its use by senior obstetrician in discussion with maternal and birthing medicine. (The commonly used dosage is 250mg four times a day orally).

- In pregnant women and people with BA >40 micromol/L who are 34-36 weeks' gestation, URSO may offer some benefit in reducing late preterm birth but it is not clear that this reduction results in any benefit to the baby and nor prevent stillbirth.
- Other agents should not be offered for treatment of ICP outside of a research study or individualised specialist treatment.
- If the prothrombin time is elevated or if evidence of reduced absorption of dietary fats (eg steatorrhoea), consider 10mg water soluble vitamin K (menadiol sodium phosphate). Routine use of vitamin K is not indicated because most pregnant women and people with ICP will not have evidence of reduced fat absorption.
- Any pregnant women and people with total bile acids >100 micromol/l should have an urgent consultant review and a discussion regarding on-going management.
- Pregnant women and people with bile acids <100 micromol/l but are rapidly rising should also be discussed with a consultant.

10.3 Timing of birth/ Induction of Labour (IOL)

- Timing of birth should be planned by (or after discussion with) Consultant obstetrician taking into account co-morbidities and peak BA concentration.
- Consider planned birth at 38–39 weeks' gestation in women and people with moderate ICP with peak bile acids 40–99 micromol/L and no other risk factors; advise them that the overall risk of stillbirth is similar to the background risk until 38–39 weeks' gestation.
- Consider planned birth at 35–36 weeks' gestation in women and people with severe ICP with peak bile acids 100 micromol/L or more; advise them that the risk of stillbirth is higher than the background risk. Advise pregnant women and people that giving birth at a late preterm gestation will require their hospital stay to be lengthened to 3 days minimum to monitor their baby (WH&SRH see CG21010 Care of the late preterm newborn guideline).
- Advise pregnant women and people that the presence of co-morbidities (such as gestational diabetes, pre-eclampsia, multifetal pregnancy) appear to increase the risk of stillbirth and may influence decision-making around timing of planned birth.

10.4 Intrapartum care

- Advise pregnant women/people 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/person.
- Offer continuous electronic fetal monitoring (CEFM) to pregnant women/people with peak bile acids 100 micromol/L or more.
- There is insufficient evidence for or against CEFM in pregnant women/people with peak bile acids below 100 micromol/L. A shared decision can be made based on co-morbidities and preferences.
- Advise pregnant women/people that the presence of risk factors (such as gestational diabetes, pre-eclampsia, multi-fetal 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 pregnant women and people that meconium-stained liquor is more common in moderate and severe ICP, and that this will influence decision-making around CEFM.
- Offer pregnant women and people with uncomplicated ICP standard analgesia and anaesthesia options for birth.
- Advise pregnant women and people that there is no evidence of an increased risk of postpartum haemorrhage if they have uncomplicated ICP.

10.5 Postnatal care

- Inform women and people with ICP that the itch usually stops after birth and LFTs and BAs should return to normal within a few weeks.
- BAs and LFTs should be checked at 4 weeks post birth and the woman and people reviewed in a postnatal follow up appointment to ensure resolution of the symptoms and normalisation of blood results and hence confirmation of the diagnosis.
- Pregnant women and people with on-going abnormalities do not have ICP and should be investigated via the primary care practitioner for other causes of abnormal liver function.
- Pregnant women and people with previous ICP should be advised that ICP does not influence choice of contraception unless they have previously experienced cholestasis secondary to the combined oral contraceptive pill (COCP) - they should consider progesterone-only or non-hormonal methods.
- Women and people with previous ICP may have HRT if there are no other contraindications.

10.6 Subsequent pregnancies

- Pregnant women and people should be advised about the risk of recurrence in future pregnancies. Referral should be made for consultant led care if symptoms develop in subsequent pregnancies.
- **Perform a baseline liver function test and bile acid concentration with booking blood investigations in order to establish that these are normal.**

11.0 Audit

RCOG suggested audit questions:

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

12.0 Useful links

Information for healthcare professionals:

- Maternal use of medication in pregnancy (UK Teratology Information Service) Maternal exposure – UKTIS

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

- http://www.medicinesinpregnancy.org/

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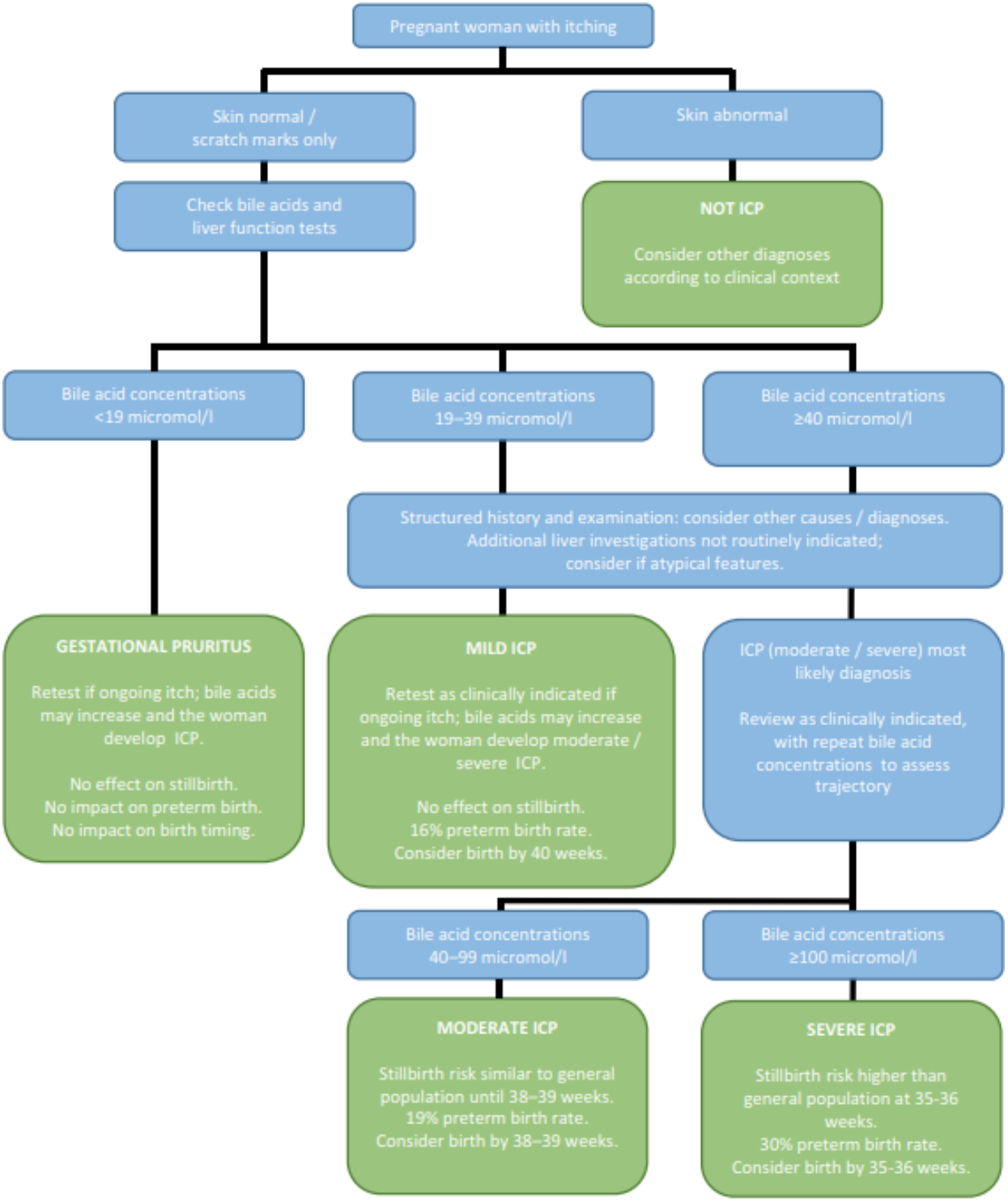
Appendix 1: Flowchart for care of pregnant women and people with itching



Figures above relate to singleton pregnancy with no other risk factors.

Comorbidities (particularly pre-eclampsia and diabetes) or other obstetric risk factors (such as multifetal pregnancy), are associated with increased risk of stillbirth and should be taken into consideration when planning management.

Additional liver investigations may be considered in women with atypical features (e.g. early onset, marked transaminitis, jaundice, fever, or in whom postpartum resolution does not occur). These investigations may include liver ultrasound, viral hepatitis screen, liver autoimmune tests, and/or coagulation screen.