Aneurin Bevan University Health Board

GUIDELINE FOR INTRAHEPATIC CHOLESTASIS (ICP)IN PREGNANCY

N.B. Staff should be discouraged from printing this document. This is to avoid the risk of out-of-date printed versions of the document. The Intranet should be referred to for the current version of the document

Owner: Maternity Services

Aims

To provide support for clinical decision making with respect to patients with intrahepatic cholestasis in pregnancy (ICP).

Objectives

To standardise care for patients attending with intrahepatic cholestasis in pregnancy.

To provide high quality and evidence-based care to patients with ICP.

Scope

This guideline applies to all clinicians working within maternity services.

Roles and Responsibilities

The maternity management team will be responsible for the dissemination and implementation of the guidance.

Resources

No additional resources will be needed. As currently happens, a screening assessment in the form of initial blood investigations could be completed by the community midwife, DAU midwife or triage midwife depending on the clinical situation. Abnormal results should then trigger review by a doctor in the obstetric triage unit where the patient can be discussed with the on-call Consultant if needed.

Training

Staff will access appropriate training where provided. Training needs will be identified through appraisal and clinical supervision.

Standards for Health Services Wales

This section should outline how the proposal contributes to compliance with the Standards for Health Services Wales and should also indicate to which Standards this area of activity is linked.

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Equality

The document promotes assessment of patients on an individual basis taking onto account risk factors for the condition.

Audit

Compliance with the recommended management pathway should be audited regularly to ensure high quality patient care.

Review

Review policy document 3 years after publication.

Introduction

Abbreviations

ICP	Intrahepatic cholestasis in pregnancy
ALT	alanine aminotransferase
LFT	liver function test
UDCA	ursodeoxycholic acid
BA	bile acid
CTG	cardiotocography
CMV	cytomegalovirus
EBV	Epstein-Barr virus
FBC	Full blood count

Background

Intrahepatic cholestasis of pregnancy is a multifactorial condition. It is characterised by pruritus in the absence of a primary skin condition, with abnormal maternal bile acid concentrations.

The onset of ICP is most common in the third trimester but can be earlier in pregnancy.[4]

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Pruritus and raised bile acid concentrations should return to normal after birth.

Early onset ICP is when ICP happens in first and second trimester

The care of women and pregnant people with ICP is driven by the potential increased risk of stillbirth.

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.[2, 3]

TABLE 1. Terminology for pregnant women with itching of normal skin

Diagnosis	Clinical features
Gestational pruritus	Itching and peak bile acid concentrations <19 micromol/L[a]
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

Note: Peak bile acid concentrations refer to the highest bile acid 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.[10]

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 19micromol/L or more.
- The diagnosis is more likely if it is confirmed that itching and raised bile acids resolve after birth
- 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
- Offer repeat liver function tests and bile acid measurement (depending on gestation and clinical context) in women with normal blood results whose itch persists, and no other cause is apparent

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- Women and pregnant people with gestational pruritus may develop ICP up to 15weeks after initial presentation
- 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
- In clinical practice, diagnoses should be reconsidered if the clinical presentation changes

Investigations
Perform Bile acid and liver function tests

Additional laboratory and/or imaging investigations are not recommended in every woman, but could be considered on an individual basis.

Additional investigations are viral screening, autoimmune testing and Liver ultrasound.

Consider antenatal testing only if there are atypical clinical symptoms, presence of relevant comorbidities, or early onset severe ICP.

Consider postnatal investigations in women in whom resolution of abnormal liver function tests is delayed or does not occur

Consider discussing the care of women with severe, very early or atypical presentation of what appears to be ICP with a hepatologist

Maternal Morbidity

Symptom of itching can be severe, may fluctuate and may markedly affect sleep
Women with ICP may have a higher chance of developing pre-eclampsia or gestational diabetes.
They should have blood pressure and urine monitoring, and testing for gestational diabetes according to national guidance

Risk of stillbirth

National UK stillbirth rate 0.29%
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 100micromol/L or more:

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• In women with peak bile acids 19–39micromol/L and no other risk factors, advise them that the risk of stillbirth is similar to the background risk. Stillbirth rate 0.13%
• In women with peak bile acids 40–99micromol/L and no other risk factors, advise them that the risk of stillbirth is similar to the background risk until 38–39weeks' gestation. Stillbirth rate 0.28%

• In women with peak bile acids 100micromol/L or more, advise them that the risk of stillbirth is higher than the background risk. Stillbirth rate 3.44%

- 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

Perinatal Morbidity

- Women with moderate or severe ICP that they have a higher chance of both spontaneous and iatrogenic preterm birth
- Women with moderate or severe ICP that they have an increased chance of having meconium-stained amniotic fluid during labour and birth
- Women with moderate or severe ICP that their baby is more likely to receive neonatal care

Monitoring

Women should be under consultant led care

All women with itch and an initial raised bile acid level, should have a second bile acid measurement repeated around 1week later before any diagnostic or care decisions are determined

- Mild ICP with peak bile acids 19–39micromol/L, they could have weekly testing as they approach 38weeks' gestation in order to inform timing of birth.
- Moderate ICP with peak bile acid 40–99micromol/L, especially if they are approaching 35weeks' gestation, weekly testing should be considered, as timing of birth may be influenced if levels rise to 100micromol/L or more.

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- Severe ICP with peak bile acid 100micromol/L or more, further routine testing of bile acids might not impact on decision making and therefore may not be routinely required.

Fetal monitoring

Fetal ultrasound and/or cardiotocography (CTG) do not predict or prevent stillbirth in ICP

Advise women with ICP to monitor fetal movements and present for immediate assessment at their local maternity unit if they have any concerns

Treatments

1.Advise women that there are no treatments that improve pregnancy outcome (or raised bile acid concentrations) and treatments to improve maternal itching are of limited benefit.

2. Consider topical emollients such as aqueous cream (with or without menthol added) to ameliorate skin symptoms.

3. Consider antihistamine agents, such as chlorphenamine, particularly at night although the effectiveness of this treatment is uncertain in women with.

4. Other common antihistamine agents including loratadine and cetirizine are also used in pregnancy for other indications but do not have sedative side-effects

5. Ursodeoxycholic acid is not routinely offered for the purpose of reducing adverse perinatal outcomes in women with ICP.

6. 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

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Timing and Mode of Delivery

Mild ICP: Consider options of planned birth by 40weeks' gestation or ongoing antenatal care according to national guidance in women with mild ICP (peak bile acids 19–39micromol/L) and no other risk factors; advise women that the risk of stillbirth is similar to the background risk
Moderate ICP: Consider planned birth at 38–39weeks' gestation in women with moderate ICP with peak bile acids 40–99micromol/L and no other risk factors; advise them that the overall risk of stillbirth is similar to the background risk until 38–39weeks' gestation
Severe ICP: Consider planned birth at 35–36weeks' gestation in women with severe ICP with peak bile acids 100micromol/L or more; advise them that the risk of stillbirth is higher than the background risk

Advise women 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

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

Monitoring in labour

1. Offer continuous electronic fetal monitoring (CEFM) to women with peak bile acids 100 micromol/L or more.
2. There is insufficient evidence for or against CEFM in women with peak bile acids below 100micromol/L.
3. 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.
4. Advise women that meconium-stained liquor is more common in moderate and severe ICP, and that this will influence decision making around CEFM
5. Offer women with uncomplicated ICP standard analgesia and anaesthesia options for birth

Third stage of Labour

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There is no evidence of an increased risk of postpartum haemorrhage if they have uncomplicated

Postnatal management

1. For women who have uncomplicated ICP, follow-up should be arranged at least 4 weeks after birth to confirm resolution of ICP with GP/ MW. The healthcare professional should ensure that itching has resolved, and maternal bile acid concentrations and liver function tests have normalised.
2. Repeat Bile acid and liver function test in 4 weeks
3. 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.
4. Advise women that ICP itself does not influence their choice of contraception or hormone replacement therapy
5. For women with ICP and previous cholestasis secondary to combined hormonal (oestrogen-containing) contraception, advise them to use progestogen-only or non-hormonal methods.
6. Women should be advised that there is an increased risk of recurrence in subsequent pregnancies.
7. Perform a baseline liver function test and bile acid concentration with booking blood investigation

Further Information Clinical Documents

www.britishlivertrust.org.uk/liver-information/liver-conditions/icp/

References

Biccoca M.J., Sperling J.D., Chauhan S.P., Intrahepatic cholestasis of pregnancy: Review of six national and regional guidelines. *European Journal of Obstetrics and Gynaecology and Reproductive Biology*, 2018; 231: 180-187

Cui D., Zhong Y., Zhang L., Du, H., Bile acid levels and risk of adverse perinatal outcomes in intrahepatic cholestasis of pregnancy: A metaanalysis. *The Journal of Obstetrics and Gynaecology Research,* 2017; 49 (9): 1411-1420.

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Management of intrahepatic cholestasis of pregnancy. Published online February 14, 2019 http://dx.doi.org/10.1016/S0140-6736(18)32323-7. www.lancet.com

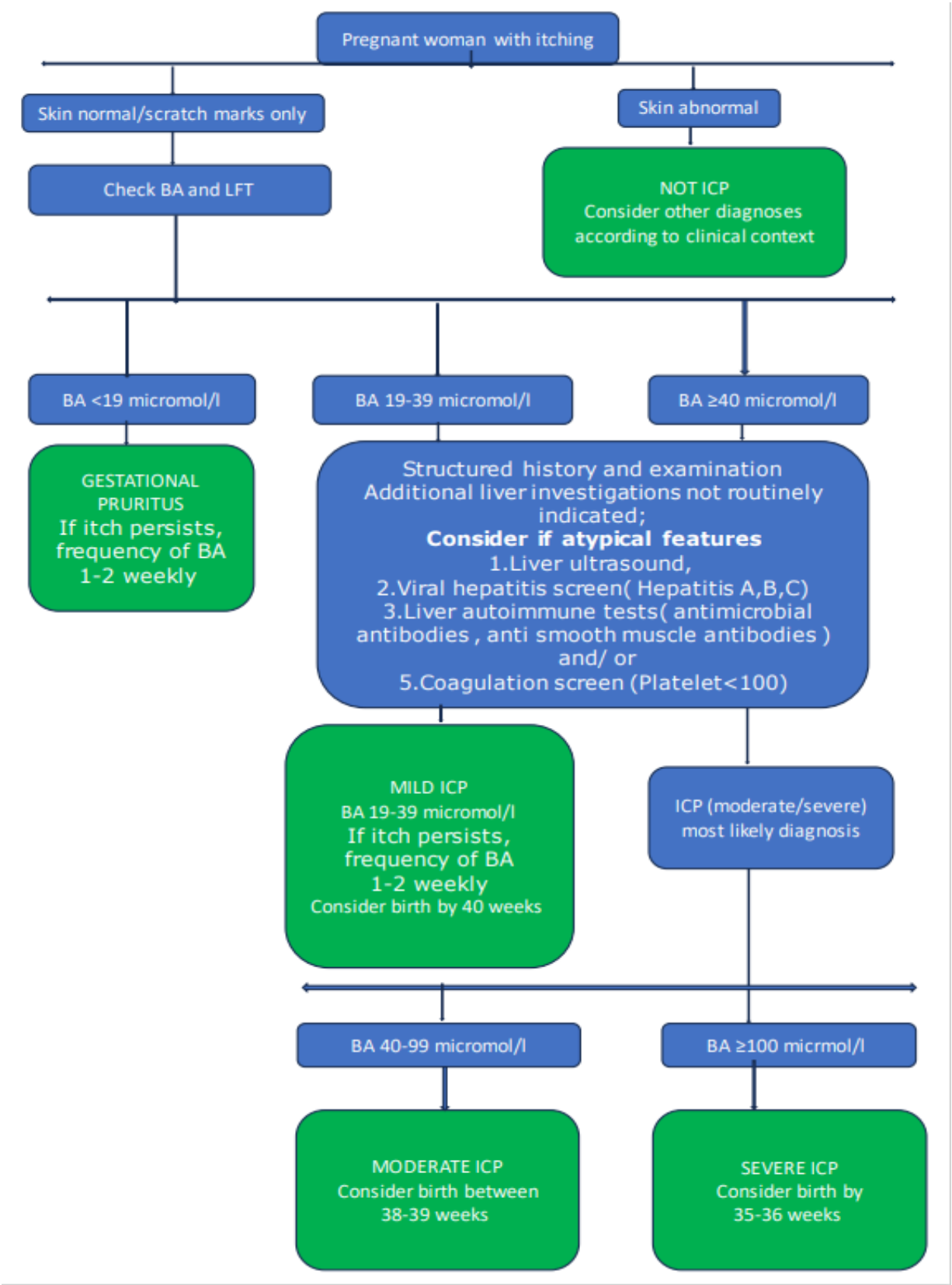
Herrera C.A. et al, Perinatal outcome associated with intrahepatic cholestasis of pregnancy. *Journal of maternal-fetal and neonatal medicine*, 2018; 31 (14): 1913-1920.

McIllvride S., Dixon P.H., Williamson C., Bile Acids and Gestation. *Molecular Aspects of Medicine*, 2017; 56: 90-100.

Obstetric Cholestasis: Greentop Guideline number 43, 2022 (09 th August), RCOG.

Turkmen G.G. et al, Low serum vitamin D level is associated with intrahepatic cholestasis of pregnancy. *The Journal of Obstetrics and Gynaecology Research,* 2018; 44 (9): 1712-1718.

Ovadia C, Seed PT, Sklavounos A, Geenes V, Di Ilio C, Chambers J, et al. Association of adverse perinatal outcomes of intrahepatic cholestasis of pregnancy with biochemical markers: results of aggregate and individual patient data meta-analyses. *Lancet*. 2019; **393**(10174): 899–909.


Pregnant woman with itching
Skin normal/scratch marks only
Skin abnormal
Check BA and LFT
NOT ICP
Consider other diagnoses according to clinical context
BA <19 micromol/l
BA 19-39 micromol/l
BA ≥40 micromol/l
GESTATIONAL PRURITUS
If itch persists, frequency of BA 1-2 weekly
Structured history and examination
Additional liver investigations not routinely indicated;
Consider if atypical features
1.Liver ultrasound,
2.Viral hepatitis screen(Hepatitis A,B,C)
3.Liver autoimmune tests(antimicrobial antibodies , anti smooth muscle antibodies)
and/ or
5.Coagulation screen (Platelet<100)
MILD ICP
BA 19-39 micromol/l
If itch persists, frequency of BA 1-2 weekly
Consider birth by 40 weeks
ICP (moderate/severe) most likely diagnosis
BA 40-99 micromol/l
BA ≥100 micrmol/l
MODERATE ICP
Consider birth between 38-39 weeks
SEVERE ICP
Consider birth by 35-36 weeks