Intrahepatic Cholestasis of Pregnancy Guideline

TARGET AUDIENCE	Primary and Secondary Care. Obstetric Lanarkshire Service: Obstetricians and Midwives..
PATIENT GROUP	Women's Services Directorate.

Clinical Guidelines Summary

PURPOSE OF THE GUIDELINE

The purpose of this guideline is the management of women diagnosed with Intrahepatic Cholestasis of Pregnancy.

This guidance is not for use in multiple pregnancies or pregnancies with fetal abnormalities. This guidance should be used in conjunction with the Holistic Antenatal Pathway when risk assessing women for risk of FGR at each clinical encounter.

This guidance is relevant for:

- All pregnant women booked for antenatal care in NHS Lanarkshire (NHSL)
- University Hospital Maternity services and Day-care units across NHSL
- All midwifery and medical staff providing antenatal care in NHSL
- All ultra-sonographers working within maternity services in NHSL

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Background

Intrahepatic cholestasis (ICP) is a condition of pregnancy characterised by pruritus (itching), in the absence of skin rash, with abnormal bile acids, which both resolve after birth.

Pruritus is a common feature of pregnancy, affecting around 25% of women. The incidence of ICP is much lower - 0.7% (1.2% to 1.5% Indian/Pakistani) [1]

For ICP typically the soles of feet and palms of hands are affected. Other features can be abnormal LFTs, pale stool, dark urine and jaundice.

RISK FACTORS

- ethnicity
- personal/ family history
- multiple pregnancy
- Hepatitis C
- Gallstones
- Male fetus
- >35 years' old

POTENTIAL ASSOCIATED COMPLICATIONS OF ICP

Increased risks compared to the general population (background population risk % in brackets) [1]

- PET 12.2% (3.4%)
- GDM 13.2% (5.9%)
- pre-term birth (spontaneous or iatrogenic)
- meconium 15% (but no increases risk aspiration)
- malabsorption of Vitamin K; consider if steatorrhea
- jaundice <1% - usually mild
- Future hepatobiliary disease 15% (6.3%)

DIAGNOSIS/ TESTING

- *Bile Acids (BA) >19 positive for ICP and treatment should be considered*

Severity of ICP (Bile Acids)	Risk of stillbirth	Absolute number stillbirth	Extra testing/ care
Mild (19-39)	0.29% (background)	3/2310	Weekly BA/LFT from 38/40
Moderate (40-99)	0.72%	4/1412	Weekly BA/LFT from 35/40
Severe (>100)	3.44%	18/524	Weekly BA/LFT from diagnosis CTG in labour

- LFTs - ALP is elevated in pregnancy. Abnormal LFTs do not reflect risk of fetal demise. Other causes of abnormal LFT's such as PET/AFLP must be excluded prior to diagnosis of ICP.
- Consider liver screen (Hep A, B, C, Epstein Barr virus and CMV, anti-smooth muscle and antimitochondrial antibodies) and ultrasound based on LFT's and additional symptoms
- Coagulation screen - only if evidence of fat malabsorption
- Additional testing is NOT recommended unless atypical symptoms, early onset, rapid deterioration or no resolution after 6 weeks' post-partum. In these cases, investigate with liver screen as above

TREATMENT

Therapy may involve a combination of Ursodeoxycholic Acid, antihistamine and emollients.

Appendix 1 lists additional therapies that may be considered on an individual basis and only on the advice of a senior Obstetrician.

Ursodeoxycholic Acid (UCDA)

- Off license use, and there is no strong data to suggest it reduces risk of adverse perinatal events. May help relieve some pruritus and improve LFT's in some patients.
- Stop after delivery
- May protect hepatocyte membrane from toxicity caused by bile acid and protect fetal cardiomyocytes (demonstrated in rat studies)

Ursodeoxycholic acid available strengths

- Tablets: 150mg, 300mg
- Capsules: 250mg
- Suspension: 250mg/5ml
- Suggested starting dose, aiming to give 8-9mg/kg, this can be increased to a maximum of 16mg/kg.

Weight (Kg)	Total Daily Dose (mg)	Morning Dose (mg)	Evening Dose (mg)
< 45	Match dose to above strengths. If < 150mg per dose liquid will be required.		
45-50	400	150	250
50-69	450	150	300
60-69	550	250	300
70-79	600	300	300
80-89	700	300	400
90-99	750	250	500
100-109	900	400	500
110-134	1000	500	500

135 - 145	1250	500	750

Emollients

Symptomatic itch may be improved by Dermacool (Menthol in Aqueous cream 1%)

Antihistamines

- Chlorpheniramine (Piriton) 4mg tid or Promethazine (Phenergen) 25mg at night may help to relieve pruritus
- Antihistamines may also have a sedative effect which may help improve sleep
- Non-sedating antihistamines such as Loratidine and Cetirizine are safe use in pregnancy

MONITORING

- Women should attend their local Consultant led clinic for bloods and monitoring.
- LFT's should be checked every 1-2 weeks depending on gestation and severity of ICP. Consider alternative diagnosis if normalise or deteriorate quickly. Women with mild ICP should have weekly LFT's and bile acids from 38 weeks. Women with moderate ICP should have weekly LFT's and bile acids from 35 weeks. Women with severe ICP should have weekly LFT's and bile acids from diagnosis.
- USS for fetal growth every 4 weeks for mild/ moderate and every 2 weeks for severe (Although in GTG there are no recommendation for USS/ Antenatal CTG as there is no evidence to suggest they reduce stillbirth risk.)
- Offer continuous fetal monitoring in labour (not recommended unless severe disease)

TIMING OF DELIVERY

Singleton pregnancy

Recommended timing of delivery for women with ICP varies depending on peak bile acids levels to reduce risk of stillbirth. Mode of delivery guidance must be individualised to the Mother. ICP is not an indication of a CS. There is no increased risk of assisted/ operative births. [1]

Severity of ICP (Bile Acids)	Timing of delivery
Mild (19-39)	40/40
Moderate (40-99)	38-39/40
Severe (>100)	35-36/40

TWIN PREGNANCY

Management of Twin pregnancies with ICP is highly specialised and women should be reviewed urgently in the Multiple Pregnancies clinic for an individualised management plan.

If the patient is pregnant with a multiple pregnancy then the risk of stillbirth is higher, compared to a multiple pregnancy without ICP. [2]
Data for twins based on one retrospective cohort study in China, background stillbirth rate was 0.8% with an overall risk of 3.9% for twin pregnancies complicated with ICP. There is no further advice on timing of delivery for twin pregnancy.

Bile acid (classification ICP)	Stillbirth risk - Twin pregnancy.
19-39 (Mild)	3.3%
>40	5.1%

POSTPARTUM CARE

Ensure LFTs resolved 4-6 weeks postpartum, during the antenatal period this should be communicated with the GP by letter.

CONTRACEPTION

- COCP is UKMEC 2 (benefit outweighs risk) and can be started when itch and LFTs resolve. (unless previous contraceptive related cholestasis) [4]
- All other are UKMEC 1 (no risk).

HRT

- can be offered if no other contraindications.

Appendices

1. Governance information for Guidance document

Lead Author(s):	Dr E Jarvie/ Dr A Geraghty/ H Fulton
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Responsible Person (if different from lead author)	

CONSULTATION AND DISTRIBUTION RECORD	
Contributing Author / Authors	As above S Maharaj K Rogers for formatting as requested by CCCEG
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Distribution	All in Maternity

CHANGE RECORD

Date	Lead Author	Change	Version No.
October 2020	Dr F. Watson/S Maharaj/ H Fulton	First version	1
			2
			3
		.	4
			5

2.You can include additional appendices with complimentary information that doesn't fit into the main text of your guideline, but is crucial and supports its understanding.

e.g. supporting documents for implementation of guideline, patient information, specific monitoring requirements for secondary and primary care clinicians, dosing regimen/considerations according to weight and/or creatinine clearance