



Intrahepatic cholestasis

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INTRODUCTION

Intrahepatic cholestasis also known as Obstetric cholestasis affects 0.7% of pregnancies in multiethnic population and 1.2 to 1.5 % of women of Indian Asian origin.¹ The disease is characterized by unexplained reversible pruritis beginning in the second or third trimester with elevated liver function test /bile acid in absence of other systemic or other hepatobiliary disorders.²

AETIOLOGY:

The etiology of obstetric cholestasis is multifactorial which could be genetic, environmental and hormonal.

1. **HORMONAL:** The cholestatic effect is because of estradiol and progesterone metabolites during pregnancy.
2. **GENETIC:** Genetic mutations in bile transporter gene as found in Familial intrahepatic cholestasis 3 or recurrent familial intrahepatic cholestasis are also implicated.
3. **ENVIRONMENTAL:** It includes dietary factors, excess erucic acid from rapeseed oil, selenium deficiency and pesticides.

RISK FACTORS:

A personal and family history is an independent risk factor with a recurrence risk from 40 to 92%. Multifetal gestation and hepatitis C positivity are also found in some.³

DIAGNOSIS:**SYMPTOMS AND SIGNS:**

The pruritus generally involves palms and soles and is typically worse at night. Dermatographia artefacta (skin trauma after intense itching) is not specific for obstetric cholestasis and can also be found in eczema, prurigo or atopic eruption of pregnancy.⁴ Other symptoms include pale stools, dark urine and jaundice.

LAB PARAMETERS;

1. LFT: Transaminases (SGOT/SGPT) and gamma glutamyl transferase are raised and occasionally bilirubin is also raised. Alkaline phosphatase is placental in origin hence not used in diagnosis. Upper limit of pregnancy ranges should be used.

2. BILE ACID:

Bile acids rise after meals and fasting gives a lower value hence random sample is a better option. Bile acid level above 10 micro mol/l are considered pathological and value above 40 micro/l are considered severe form of the disease.⁵

Liver enzyme	Non-pregnant	Pregnant	1st trimester	2nd trimester	3rd trimester
ALT (IU/L)	0-40	-	6-32	6-32	6-32
AST(IU/L)	7-40	-	10-28	11-29	11-30
Bilirubin (µmol/L)	0-17	-	4-16	3-13	3-14
,yGT (IU/L)	11-50	-	5-37	5-43	3-41
ALP (IU/L)	30-130	-	32-100	43-135	133-418
Bile acids (µmol/L)	0-14	0-14	-	-	-

Typical reference range of Liver Enzymes by trimester.⁶

3. Prothrombin time for associated coagulation defects.

COMPLICATIONS:

MATERNAL- Vitamin K deficiency and post-partum hemorrhage.

FETAL- Prematurity, meconium-stained liquor, fetal distress and still birth.

MANAGEMENT**SURVEILLANCE DURING PREGNANCY:**

1. MATERNAL

LFT should be monitored weekly. Abnormal rise in LFT despite treatment warrants other diagnosis.

Bile acids weekly for surveillance and risk of fetal morbidity is increased by 1-2% for each additional unit of rise. No cut off levels has been defined in literature as fetal deaths have been documented at lower levels also.⁷

2.FETAL:

Ultrasound, color doppler and NST are not reliable for predicting fetal prognosis. Continuous fetal monitoring for patients in labor. Poor outcome of fetus can be predicted by biochemical results but the decision of delivery should not be solely based on them.⁸

MANAGEMENT OF PRURITUS:

1.Topical emollients, Cholestyramine, S adenosylmethionine are not of any proven benefit.

2.Antihistaminic taken at night time may provide some relief.

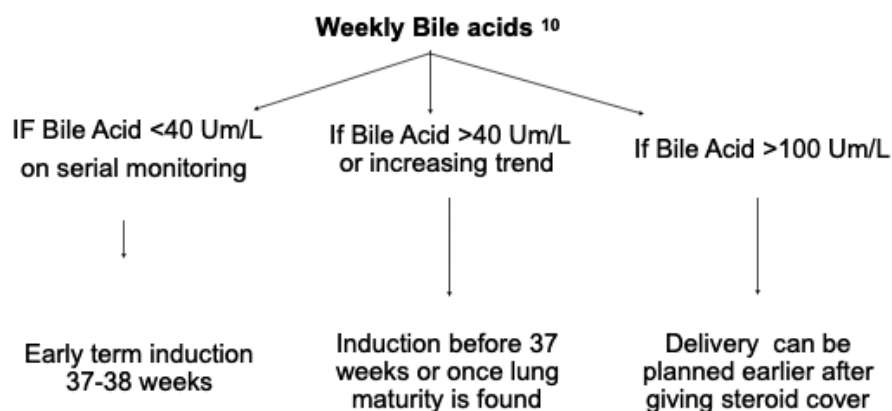
3. UDCA displaces hydrophobic bile salt from the bile pool and protect the hepatocyte from damage and enhance bile acid clearance across placenta from the fetus and hence cardioprotective. UDCA reduces pruritus but its effect on fetal outcome remains unclear. It is given at the starting dose of 10 to 15 mg/kg /day to a max of 25 mg/kg/day.⁹

4 Vitamin K at a dose of 5 to 10 mg/day should be used when prothrombin time is prolonged specially the water-soluble type. Vitamin K becomes deficient specially with biliary obstruction but regular use of water-soluble vitamin K can cause kernicterus, hemolytic anemia and hyperbilirubinemia in neonate.

5. Dexamethasone only for lung maturity.

6. Rifampicin under trial.

Timing of Delivery



Post Natal follow up: Resolution of pruritus and normalization of LFT after delivery is essential to establish the diagnosis.

Contraception: Estrogen containing pills to be avoided.

Conclusion:

Obstetric cholestasis has been associated with still birth, meconium aspiration syndrome, prematurity, PPH hence once diagnosed strict maternal and fetal surveillance is required.

SUMMARY:

- Obstetric cholestasis is unexplained pruritus without rash during pregnancy with deranged LFT and Bile acid.
- Pregnancies are high risk due to associated still birth.
- Bile acid above 40 micro/l warrant termination.
- Recurrence rate is 45- 90%

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