

## **Bile acids or total bile salts:**

### **A. For Diagnosis:**

#### **I. Pregnancy – suspect intrahepatic Cholestasis of Pregnancy (ICP):**

- In ICP, bile acids may increase before derangement in other liver function tests and not uncommonly LFTs including GGT may not be raised and if any, only mild. In some cases, even bile acids may not be elevated thus ICP remains a diagnosis of exclusion. Its value does not correlate well with pruritus severity.
- The pregnancy related liver condition that might simulate ICP in terms of biochemical/haematological picture is hyperemesis gravidarum (mildly raised aminotransferase, normal bilirubin, urate, platelet, coagulation profile, blood pressure, and urine protein). However, vomiting will be the presenting feature and not commonly present during 3rd trimester. In that respect, bile acid test availability is not urgent. Presence of features like low platelet, very high transaminases, hypertension, proteinuria etc. should sway the lead maternity caregiver in looking at other pregnancy related complications.
- ICP is associated with increased risk of stillbirth, premature delivery (especially iatrogenic) and meconium passage. If the patient presented with otherwise unexplained pruritus (with or without mildly raised transaminases) AND close to or beyond gestational week 37wks, there is a point in offering it urgently (within 24hours turnaround time) – as, if bile acid is raised especially if significantly so, it might sway the lead maternity caregiver/obstetrician to consider arrangement for delivery to reduce risk of still birth. The cut point of 40 umol/L (or above 4 x Upper Reference Limit for that laboratory) is often quoted as a level that requires serious consideration but it doesn't necessarily mean that a level between 16 to 39 umol/L (where  $\leq 15$  umol/L is the reference interval) is at much reduced risk. The association of increase risk of fetal compromise with serum bile acid level is suspected and possibly a continuum but there is no robust assessment to confirm this relationship thus far. Furthermore, the exact risk of still birth especially in the modern day's hospital setting is not well defined.

**REQUEST FOR URGENT BILE ACIDS (i.e. require <24 hours turnaround time) must come with approval from an Obstetricians /Maternal-Fetal Medicine or Obstetric Physician Senior Medical Officer**

In occasional patients, bile acids level may lag behind pruritus onset by several days to weeks thus repeat testing is advisable in suspicious cases. In patients with persistent pruritus and normal biochemistry tests (including bile acids and transaminases), UK NICE guideline recommend repeat biochemistry tests in 1-2 weeks – out of hours availability is not necessary

#### **II. Non-pregnant patients**

- a. In differential diagnosis of Hyperbilirubinaemia. Its level is expected to be raised in hepatic causes of Hyperbilirubinaemia but is normal in haemolytic disease and in Hyperbilirubinaemia due to specific defects of bilirubin metabolism e.g. Gilbert and Dubin-Johnson syndromes. Out of hours availability is generally not necessary (unless with prior discussion with chemical pathologist)
- b. Bile acids can be a sensitive marker of hepatic damage especially for those with otherwise normal conventional liver biochemical tests, in conditions like compensated cirrhosis, porto-systemic shunting and organic solvent induced hepatotoxicity. It is not specific for any particular kinds of liver diseases and its levels are not distinctive enough to distinguish different stages of chronic liver disease to guide decisions about liver biopsy or treatment.
- c. Bile acids can also be raised in non-hepatobiliary conditions including chronic renal failure, medication induced (cyclosporine, isoniazid, methotrexate, rifampicin) and intestinal blind loop syndrome or multiple small bowel resections. Fusidic acid can induce positive analytical interference

### **B. For Monitoring**

- Once ICP is diagnosed, NICE guideline considers it reasonable to repeat LFT weekly (there was no particular mentioning of bile acids). Out of hours availability is unnecessary
- Ursodeoxycholic acid (UDCA) improves pruritus and liver functions but there are no robust data to suggest its protection against still birth or safety to fetus or neonate (this 2011 NICE guideline is due to renewal soon). If the patient is on UDCA, monitoring of bile acid is reasonable but out of hours availability is not necessary

- Bile acids has been proposed as one of the markers for treatment monitoring of interferon therapy in chronic Hep C patients or ursodeoxycholic acid therapy in cholestatic liver diseases. Out of hours availability is generally not necessary (unless with prior discussion with chemical pathologist)

*References:*

1. UK NICE guidelines – Royal College of Obstetricians and Gynaecologists Green-top guideline no.43 April 2011 “Obstetric Cholestasis”
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3. Schiff ER, Sorrell MF, Maddrey WC (eds). Schiff's diseases of the Liver. 9th edition (2003) Chapter 7A: Evaluation of the liver: Laboratory tests. Lippincott Williams & Wilkins, Philadelphia
4. Walker IAL, Nelson-Piercy C, Williamson C. Role of bile acid measurement in pregnancy. Ann Clin Biochem 2002; 39:105-113
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