Pregnancy and Liver Disease

Gastro Foundation Fellow Weekend 2020

Bilal Bobat
Liver Unit WDGMC
Pregnancy and Liver Disease

- Normal Changes
- Changes that Mimic Liver Disease
Any Change in Bilirubin or the Transaminases need to be investigated
INR Measured as Normal

### Table 2. Typical reference ranges for liver enzymes, by trimester.

<table>
<thead>
<tr>
<th>Liver enzyme</th>
<th>Non-pregnant</th>
<th>Pregnant</th>
<th>1st trimester</th>
<th>2nd trimester</th>
<th>3rd trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (IU/L)</td>
<td>0-40</td>
<td>-</td>
<td>6-32</td>
<td>6-32</td>
<td>6-32</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>7-40</td>
<td>-</td>
<td>10-28</td>
<td>11-29</td>
<td>11-30</td>
</tr>
<tr>
<td>Bilirubin (µmol/L)</td>
<td>0-17</td>
<td>-</td>
<td>4-16</td>
<td>3-13</td>
<td>3-14</td>
</tr>
<tr>
<td>γGT (IU/L)</td>
<td>11-50</td>
<td>-</td>
<td>5-37</td>
<td>5-43</td>
<td>3-41</td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td>30-130</td>
<td>-</td>
<td>32-100</td>
<td>43-135</td>
<td>133-418</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>35-46</td>
<td>28-37</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bile acids (µmol/L)</td>
<td>0-14</td>
<td>0-14</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Haemoglobin (g/L)</td>
<td>-</td>
<td>110-135</td>
<td>103-130</td>
<td>100-130</td>
<td></td>
</tr>
<tr>
<td>Platelets (10^3/ml)</td>
<td>212-135</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

ALT, alanine transaminase; AST, aspartate transaminase; INR, international normalized ratio.

Modified (with permission) from Walker I, Chappell LC, Williamson C “Abnormal Liver function tests in pregnancy” *BMJ* 2013 Oct 25:34.

Pregnancy and liver Disease, Westbrook R
Dusheiko G *J Hepatol.* 2016 Apr;64(4):933-45.

ACG Clinical Guideline: Liver Disease and Pregnancy Tran, Tram T; Ahn, Joseph; Reau, Nancy S
Liver Disease in Pregnancy

Pregnancy Related

- Hyperemesis Gravidarum
- Intrahepatic Cholestasis
- Hypertensive Related Liver Disease
- AFLP

Non-Pregnancy Related

Coincidental

- AIH
- Viral
- DILI

Pre-existing Liver Conditions

- Cirrhosis
- Portal Hypertension
- Post Liver Transplant
Work Up

- History & Examination
- Ultrasound Modality of choice
- Teratogenicity >100Rad
- CT Abd 3.5Rad
- Gadolinium not recommended
- Endoscopy Safe
Hyperemesis Gravidarum

• Severe Form of Nausea and Vomiting

• Intractable vomiting with Dehydration, Ketosis, LOW >5%

• HCG

• Vit B6/Doxylamine

What is the Duchess of Cambridge's condition? Kate suffers from extreme morning sickness that strikes just 1% of pregnant women and can be DEADLY

• Hyperemesis Gravidarum is excessive nausea and vomiting during pregnancy
• Unlike regular morning sickness, it doesn't fade away with time, experts claim
• Some women are sick many times a day and can't keep food or drink down
Intrahepatic Cholestasis of Pregnancy

- Reversible Cholestasis
- Multiple Pregnancies
- UDCA 10-15mg/kg
- tsBA >40=↑Foetal Risk
- Abn Bile Transport Receptors
- Deliver at 37 weeks
- Later Sequelae
Hypertensive Liver Disease

- Pre-Eclampsia
  - De Novo Hypertension after 20 weeks with Proteinuria
  - Severe when other maternal organ involvement or foetal distress

- HELLP

- Hepatic Rupture/Infarction/Haematoma
  - 50% Mortality
Acute Fatty Liver of Pregnancy

- Abnormality Mitochondrial Beta Fatty Acid Oxidation
- Supportive Management
- Prompt Delivery

Table 4. Swansea criteria for diagnosis of acute fatty liver of pregnancy

<table>
<thead>
<tr>
<th>Six or more criteria required in the absence of another cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
</tr>
<tr>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Polydipsia/polyuria</td>
</tr>
<tr>
<td>Encephalopathy</td>
</tr>
<tr>
<td>Elevated bilirubin</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
</tr>
<tr>
<td>Elevated urea</td>
</tr>
<tr>
<td>Leucocytosis</td>
</tr>
<tr>
<td>Ascites or bright liver on ultrasound scan</td>
</tr>
<tr>
<td>Elevated transaminases (AST or ALT)</td>
</tr>
<tr>
<td>Elevated ammonia</td>
</tr>
<tr>
<td>Renal impairment; creatinine</td>
</tr>
<tr>
<td>Coagulopathy; prothrombin time</td>
</tr>
<tr>
<td>Microvesicular steatosis on liver biopsy</td>
</tr>
</tbody>
</table>

ALT, alanine transaminase; APPT, activated partial thromboplastin time; AST, aspartate transaminase.
# Pregnancy Related Liver Disease

<table>
<thead>
<tr>
<th>Pattern of LFT changes</th>
<th>Likely diagnosis</th>
<th>Estimated proportion of pregnant women with abnormal LFTs that have each diagnosis*</th>
<th>Recommended additional investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ALT (1.5-8 fold)</td>
<td>Intrahepatic cholestasis of pregnancy (also known as obstetric cholestasis)</td>
<td>17%</td>
<td>Viral serology Anti-mitochondrial and anti-smooth muscle antibodies Abdominal USS</td>
</tr>
<tr>
<td>↑tBA (1.5-15 fold)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tBil usually normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑ALT (2-5 fold)</td>
<td>Pre-eclampsia with hepatic impairment</td>
<td>49%</td>
<td>↑BP in most Urinalysis for protein U&amp;E, creatinine ↓Platelets</td>
</tr>
<tr>
<td>tBA usually normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tBil usually normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑ALT (2-30 fold)</td>
<td>HELLP syndrome (haemolysis, elevated liver enzymes, and low platelets)</td>
<td>22%</td>
<td>↑BP in most Proteinuria in most ↑Creatinine ↓Platelets in all ↑LDH</td>
</tr>
<tr>
<td>↑tBA usually normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑tBil (1.5-10 fold)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑ALT (3-15 fold)</td>
<td>Acute fatty liver of pregnancy (AFLP)</td>
<td>4%</td>
<td>↑BP in most Proteinuria in most ↑Creatinine ↓Platelets ↑WBC ↓LDH</td>
</tr>
<tr>
<td>tBA usually normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑tBil (4-15 fold)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑ALT (2-5 fold)</td>
<td>Hyperemesis gravidarum</td>
<td>8%</td>
<td>↑Thyroxine, ↓TSH↑ Hyponatraemia Hypokalaemia</td>
</tr>
<tr>
<td>tBA usually normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tBil usually normal</td>
<td></td>
<td></td>
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### Table 3. Liver diseases unique to pregnancy

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Trimester</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>HG</td>
<td>First through 20 weeks</td>
<td>Supportive management</td>
</tr>
</tbody>
</table>
| IHCP              | Second/third       | Ursodeoxycholic acid 10–15mg/kg
Early delivery at 37 weeks |
| AFLP              | Third              | Women with AFLP should be delivered promptly
Infant should be monitored for manifestations of deficiency of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase including hypoketotic hypoglycemia and fatty liver |
| Eclampsia, preeclampsia | After 20 weeks   | After 36 weeks, women with severe preeclampsia should be delivered promptly |
| HELLP             | After 22 weeks     | Delivery after 34 weeks
Platelet transfusion to 40,000–50,000 cells/μl should be considered before delivery, especially if cesarean section is likely |
Pre-existing Liver Disease and Pregnancy

• Uncommon

• Maternal Mortality 10%

• Variceal Bleeding is the main driver
Pre-existing Liver Disease and Pregnancy

- Management still poorly defined
- Identify the at risk patient preconception
- Primary Prophylaxis
- Short 2nd stage of labour
Cholelithiasis

- Stone formation is accelerated by cholesterol supersaturation and GB hypo motility
- Cholecystitis 2nd most common surgical condition in pregnancy
- Complicated stone disease can lead to poor Maternal and foetal outcomes
- ERCP followed by Cholecystectomy
  - Maternal Complication rate of 4.3% and Foetal of 5.8%
Liver Masses

- FNH/Heamangiomas
- Hepatic Adenoma
Coincidental Liver Disease

- HAV, HEV, HSV - Increased Severity
- AIH - Flares
- PBC
Proposed algorithm for the risk assessment and reduction of HBV MTCT by expert consensus

Pregnant mothers with +ve HBV surface antigen

HBV DNA >200,000 IU/mL or previous child failed HBIG +ve HCV vaccine

- HBeAg +ve
  - HBV DNA >200,000 IU/mL
  - High risk for MTCT
    - 3TC or LdT during the 3rd trimester
    - Consider TDF for active CHB
    - Consider elective C-section if HBV DNA >20 million IU/mL at full term

HBV DNA ≤200,000 IU/mL, previous child had successful immunoprophylaxis

- HBeAg -ve
  - HBV DNA ≤200,000 IU/mL
  - Low risk for MTCT
    - All infants should receive HBIG +ve hepatitis B vaccine within 12 hours after birth, and two additional doses later

Threatened premature labor
Hepatitis C

- 3-10% Risk of Vertical Transmission
- Screen at risk Woman
- Avoid Invasive procedures
- Breastfeeding encouraged
Thank you

LIVER DISEASE IN PREGNANCY: WHAT’S NEW

<table>
<thead>
<tr>
<th>INCIDENCE</th>
<th>TRENDS</th>
<th>BY THE NUMBERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>3% – 5%</td>
<td>HELLP</td>
<td>100 µmol/L</td>
</tr>
<tr>
<td></td>
<td>ICP</td>
<td>bile acid level threshold for stillbirth in ICP</td>
</tr>
<tr>
<td></td>
<td>ACUTE HCV</td>
<td>200,000 IU/mL</td>
</tr>
<tr>
<td></td>
<td>NAFLD</td>
<td>5% rates of variceal hemorrhage in pregnant women</td>
</tr>
</tbody>
</table>

Liver enzyme abnormalities in pregnancy

HELPP: Most costly liver disease in pregnancy

ICP: Most common liver disease unique to pregnancy

ACUTE HCV: Rising incidence in childbearing women

NAFLD: Most common liver disease in childbearing women