Practical approach to liver diseases in pregnancy

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Structure of this presentation

• The Liver in Normal Pregnancy

• Liver Diseases/Dysfunction Specific to Pregnancy

• Incidental Liver Disease during Pregnancy

• Pregnancy in patients with Chronic Liver Disease

• A Practical Approach to Liver Disease in Pregnancy
The Liver in Normal Pregnancy

- **Physical Examination**
  - Spider naevi, Palmar erythema
  - Liver palpation difficult, but palpable liver abnormal

- **Ultrasound Examination**
  - Biliary tract normal
  - Fasting Gall Bladder volume increased

- **Liver Function Tests**
  - Serum albumin *lower*
  - Serum alkaline phosphatase 2-4 times *higher*
  - Serum GGT lower & 5’Nucleotidase slightly *higher*
  - Serum bilirubin, ALT, AST, Bile acids within *normal* range
Liver Disease/Dysfunction Specific to Pregnancy

- Hyperemesis Gravidarum
- Severe Pre-eclampsia
- HELLP syndrome
- Intra-hepatic Cholestasis of Pregnancy (IHCP)
- Acute Fatty Liver of Pregnancy (AFLP)

(All tend to recur in subsequent pregnancies)
Incidental Liver Disease during Pregnancy

- Viral Hepatitis
- Gallbladder disease & Cholelithiasis
- Thrombotic disease – Budd-Chiari syndrome
- Drug toxicity

Pregnancy in patients with Chronic Liver Disease

- Auto-immune hepatitis
- Cirrhosis
- Non-cirrhotic portal hypertension
- Wilson’s disease
- Liver transplantation
Hyperemesis & Liver Dysfunction

- Severe nausea & vomiting in 1st Trimester - sometimes continues into 2nd Trimester
- Tends to recur in pregnancies
- Biochemical hyperthyroidism
- Elevated bilirubin & transaminases (ALT rises more than AST; usually not over 200 units)
- Need to exclude other causes of liver dysfunction & failure
- Otherwise supportive treatment and self limiting
Severe Preeclampsia and HELLP syndrome

- Hypertension (BP>140/90 mm Hg) with Proteinuria = Preeclampsia

- Hepatic dysfunction (Transaminitis) is a sign of Severe PE and indication to deliver. Bilirubin is usually normal.

- Subcapsular bleeding and stretching of liver capsule and epigastric pain is a sign of impending eclampsia.

- HELLP (Hemolysis, Elevated Liver enzymes & Low Platelets) is a variety of severe PE.
Intrahepatic cholestasis of Pregnancy (IHCP) aka Obstetric Cholestasis (OC)

- Presents with generalized pruritus without a rash
- 10% may have jaundice, dark urine and pale stools
- Usually in second half of pregnancy
- Elevated Transaminases &/or bile acids
- Hep C is commoner
- Increased risk of IUD after 37W (unknown cause)
- Increased risk of Preterm Labour and meconium stained amniotic fluid
- Increased risk of post-partum haemorrhage (PPH)
- 90% risk of recurrence in subsequent pregnancy
Intrahepatic cholestasis of Pregnancy (IHCP) aka Obstetric Cholestasis (OC)

- Ursodeoxycholic acid (UDCA) 500 mg BD (up to 2 G/day)
  - causes symptomatic improvement and reduction of AST/ALT/Bile acids
- Anti Histamines like cetirizine sometimes help with symptoms
- Vitamin K 10 mg orally daily for a week before delivery
- Dexamethasone, Cholestyramine not useful
- Close fetal monitoring
- Deliver at 38 wks
Acute Fatty Liver of Pregnancy (AFLP)

• Usually in 3rd Trimester
• Rare (1:13000)
• Can lead to hepatic failure, encephalopathy and mortality
• Typically present with nausea, vomiting, malaise & jaundice
• Often associated pre-eclampsia
• Lab changes:
  – Elevated WBC
  – Decreased Glucose
  – Elevated Transaminases & Bilirubin
  – Elevated Uric Acid
  – Decreased Platelets
  – Elevated Ammonia
  – Prolonged INR
Acute Fatty Liver of Pregnancy (AFLP)

- Supportive treatment & stabilization
- Delivery
- Usually recovery of liver function occurs within a week following delivery
- Baby may have LCHAD (Long-chain 3-Hydroxy Acyl Co-enzyme A Dehydrogenase deficiency) and mother may be a carrier
- Risk of recurrence in next pregnancy
<table>
<thead>
<tr>
<th>Disease</th>
<th>Trimester</th>
<th>Laboratory studies</th>
<th>Differential diagnosis</th>
<th>Prognosis</th>
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</thead>
<tbody>
<tr>
<td>Hyperemesis gravidarum</td>
<td>1</td>
<td>Mean ALT: 45 may be normal or &gt;500</td>
<td>Gastroenteritis, cholecystitis, hepatitis, peptic ulcer disease, pancreatitis, appendicitis, diabetic ketoacidosis, hyperthyroidism, drug toxicity</td>
<td>No maternal or fetal mortality; may recur with subsequent pregnancies</td>
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<tr>
<td>HELLP syndrome</td>
<td>2</td>
<td>AST &gt; 70, marked elevations in the setting of hepatic infarction</td>
<td>Acute fatty liver of pregnancy, gastroenteritis, hepatitis, appendicitis, cholelithiasis, immune thrombocytopenia, hemolytic uremic syndrome</td>
<td>Maternal mortality is low, but complication rates are high; fetal mortality may be as high as 35%; recurs in 3 to 27% of subsequent pregnancies</td>
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<tr>
<td>Intrahepatic cholestasis of pregnancy</td>
<td>3</td>
<td>ALT/AST are usually &lt;500; occasionally they are &gt;1000</td>
<td>Cholelithiasis, viral hepatitis, primary biliary cirrhosis, drug hepatotoxicity, urinary tract infection. Urinary tract infection or other sepsis may either cause or worsen cholestasis.</td>
<td>No maternal mortality; associated with premature delivery and stillbirth (fetal mortality 1 to 2%); recurs in 60 to 70% of subsequent pregnancies</td>
</tr>
<tr>
<td>Acute fatty liver of pregnancy</td>
<td>PP</td>
<td>Modest elevations, up to 500 int. unit/L</td>
<td>HELLP syndrome, drug toxicity, fulminant viral hepatitis</td>
<td>Maternal and fetal mortality is low if prompt stabilization and delivery; recurrence may be seen in subsequent pregnancies</td>
</tr>
</tbody>
</table>
Laboratory work-up of icteric pregnant patient

- FBC
- LFT – Bilirubin, AST, ALT, GGT
- Fasting glucose
- PT/PTT
- Viral Hepatitis screen (screen for Hep A,B,C,E. HSV, CMV,EBV)
- Autoimmune Hepatitis screen
- Hepato-biliary ultrasound
Algorithm for elevated ALT

HBsAg (+)  
No  → Rule out viral hepatitis*  

Yes  

Passive and active immunoprophylaxis of newborn

ALT ≤ 1,000 U per L  
Review clinical context

ALT > 1,000 U per L  
Exclude
Toxins (e.g., acetaminophen overdose), hypotensive episode, liver infarction or rupture

Fever, leukocytosis, RUQ pain with or without jaundice

Preeclampsia associated with hemolysis, DIC, thrombocytopenia

Associated renal failure, hypoglycemia, DIC

No  
Exclude medications, hyperemesis gravidarum

Yes  
Consider HELLP syndrome

Consider acute fatty liver of pregnancy

Exclude cholelithiasis or liver abscess

Attempt prompt delivery
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<th>SCREENING</th>
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<tbody>
<tr>
<td><strong>VIRAL HEPATITIS</strong></td>
</tr>
<tr>
<td>Hep A IgM</td>
</tr>
<tr>
<td>Hep B S Ag</td>
</tr>
<tr>
<td>Hep B Core Ab</td>
</tr>
<tr>
<td>Hep C Ab</td>
</tr>
<tr>
<td>Hep E IgM</td>
</tr>
<tr>
<td>CMV IgM</td>
</tr>
<tr>
<td>HSV IgM</td>
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<tr>
<td>EBV IgM</td>
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Viral Hepatitis in Pregnancy

• Commonest cause of Jaundice in Pregnancy

• Course of most Viral Hepatitis (A, B,C,D) unaffected by pregnancy

• Hep C carriers have higher risk of IHCP

• Hep E and Disseminated HSV run a more severe course in pregnancy. Acute liver failure & Maternal mortality 10-20% in Hep E and nearly 50% in disseminated herpes simplex.
## Vertical transmission in Viral Hepatitis

<table>
<thead>
<tr>
<th>Hep A</th>
<th>No increased fetal risk. Transmission at birth possible but rare.</th>
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<td></td>
<td>If mother has active Hep A in labor, non-specific IgG for baby.</td>
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<tr>
<th>Hep B</th>
<th>In acute Hep B 10% risk in 1(^{st}) TM and 90% in 3(^{rd}) TM. For chronic Hep B 90% risk if Hep e Ag positive.</th>
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<td>Lamivudine to mother if HepB DNA load high to reduce vertical transmission. Combined HBIG and Hep B vaccine immunoprophylaxis at birth. 93% effective. BF safe.</td>
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<tr>
<th>Hep C</th>
<th>Transmission risk low if mother has low viral count. Risk higher if co-infection with HIV.</th>
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<td>Mode of delivery or BF does not influence risk of transmission.</td>
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<th>Hep E</th>
<th>Premature labour in 66% &amp; vertical transmission in 33%.</th>
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<td>Affected babies (1/3(^{rd})) have high neonatal mortality (33%).</td>
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Cholestasis during pregnancy

Assessed by elevated 5’nucleotidase, GGT and Bilirubin
ALP not useful unless more than 4 times elevated

Fever, leukocytosis, RUQ pain
with or without jaundice

No

Exclude drug-induced liver disease

New onset pruritus

Intrahepatic cholestasis of pregnancy

Yes

RUQ ultrasound examination

Exclude cholelithiasis or liver abscess
Women with Liver Transplant

- Pregnancy outcome worse if conceive within 2Y of transplant.
- Higher risk of miscarriage, CMV infection, preterm labor, preclampsia, IUGR.
- Cyclosporin, Tacrolimus, Azathioprine should not be stopped.
- Deterioration of Liver function suggests graft rejection (but could be due to IHCP or Preeclampsia).
- NIPT results may be inconclusive.
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Thank you for your warm invitation and kind attention.