Liver diseases in pregnancy

Soonthorn Chonprasertsuk, M.D., M.Sc.
Thammasat University
THASL meeting
March 23, 2012
Normal physiologic change of liver during pregnancy

- Increase plasma volume 50%
- Increase venous pressure
- Increase total cardiac output
- Unchanged hepatic blood flow
- Decreased blood pressure and systemic vascular resistance
- High estrogen level
  - Spider telangiectasia
  - Palmar erythema
## Liver function tests in normal pregnancy

<table>
<thead>
<tr>
<th></th>
<th>Non-pregnant</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; trimester</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; trimester</th>
<th>3&lt;sup&gt;rd&lt;/sup&gt; trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AST (U/L)</strong></td>
<td>7-40</td>
<td>10-28</td>
<td>11-29</td>
<td>11-30</td>
</tr>
<tr>
<td><strong>ALT (U/L)</strong></td>
<td>0-40</td>
<td>6-32</td>
<td>6-32</td>
<td>6-32</td>
</tr>
<tr>
<td><strong>Bilirubin(mg/dL)</strong></td>
<td>0-1</td>
<td>0.23-0.94</td>
<td>0.17-0.76</td>
<td>0.17-0.82</td>
</tr>
<tr>
<td><strong>GGT(U/L)</strong></td>
<td>11-50</td>
<td>5-37</td>
<td>5-43</td>
<td>5-41</td>
</tr>
<tr>
<td><strong>ALP (U/L)</strong></td>
<td>30-130</td>
<td>32-100</td>
<td>43-135</td>
<td>130-418</td>
</tr>
</tbody>
</table>

How to approach liver diseases in pregnancy

- Liver diseases unique to pregnancy
- Liver diseases coincident with pregnancy
- Chronic liver disease with pregnancy
Clinical clues may help to DDx

- Symptom and sign of chronic liver diseases
- Exclude common liver diseases
  - Any gestational ages
- Gestational age
- Clinical syndromes
  - Intractable vomiting
  - Pruritus
  - Hepatocellular dysfunction
  - Other organs involvement
# Liver diseases unique to pregnancy

<table>
<thead>
<tr>
<th>1\textsuperscript{st} trimester</th>
<th>2\textsuperscript{nd} trimester</th>
<th>3\textsuperscript{rd} trimester</th>
<th>Post partum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperemesis gravidarum (0.3-1%)</td>
<td>Intrahepatic cholestatic of pregnancy (0.1-1.3%)</td>
<td>Acute fatty liver of pregnancy (0.005-0.01%)</td>
<td>Pre-eclampsia/Eclamsia (5-7%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HELLP syndrome (0.2-0.6%)</td>
<td></td>
</tr>
</tbody>
</table>

(\%) = prevalence of disease
Hyperemesis gravidarum

- 1st trimester, week 4 – week 18
- 10% of cases persists throughout the pregnancy and resolve only after delivery

**Definition**
- Intractable vomiting
- Weight loss >5% pre-pregnant body weight
- Large ketonuria

**Cause:** abnormal gastric motility, hormonal factors, change in ANS
Hyperemesis gravidarum

- **Risk factors:**
  - Obesity, psychiatric illness, molar pregnancy, pre-existing diabetes, multiple pregnancies

- **Transient hyperthyroidism** 60% of cases - no treatment required

- **Liver involvement** 50% of cases
  - Increased aminotransferase (ALT > AST)
  - Aminotransferase x 2-20 ULN
  - Jaundice is rare

- **Relapse is common**
Hyperemesis gravidarum

- I.V. fluid (parenteral nutrition)
- Correct electrolyte imbalance
- Prevent Wernicke encephalopathy - Thiamine administration
- Small, frequent, high carbohydrate, and avoid high fat
- Promethazine, metoclopramide, ondansetron
- High dose hydrocortisone in severe cases
Intrahepatic cholestatic of pregnancy

- Typical onset at week 25\textsuperscript{th} of gestation
- Resolve after delivery and recur in subsequent pregnancy
- Pruritus palms and soles $\rightarrow$ generalized
- Steatorrhea, Fat soluble vitamin deficiency

**Causes**
- Mutation of ABCB4 of MDR3, ABCB11 of BSEP, ATP8B1 gene
- During pregnancy: estrogen inhibit BSEP, sulphated progesteron metabolite saturated hepatic transport system

**Risk factors:** cholestasis after taking oral contraceptive pill, FH of this condition
Intrahepatic cholestatic of pregnancy

Lab:
- Fasting serum bile acid level > 10 μmol/L
- AST (1-20X ULN)
- Jaundice 10-25%, after 2-4 weeks of the onset of pruritus

Complication: placental insufficiency → prematurity, perinatal death, fetal distress and stillbirth when serum bile acid > 40 μmol/L

Treatment:
- Vitamin K supplement
- Ursodeoxycholic acid 10-15 mg/kg.day
- Termination of pregnancy when serum bile acid >40 μmol/L
Acute fatty liver of pregnancy

- Third trimester (some at the end of second trimester)

- Cause:
  - Inherited defect in mitochondrial fatty acid β-oxidation- long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency
  - Accumulation of 3-hydroxyacyl metabolites produced by the fetus or placenta → hepatotoxicity

- AST, ALT x2-20 ULN

- Increase bilirubin, increase uric acid, coaulopathy +/- DIC

- Renal dysfunction, metabolic acidosis, leukocytosis, anemia, and hyperammonemia

- Diabetic insipidus ** pathognomonic symptom
Acute fatty liver of pregnancy
Acute fatty liver of pregnancy

- Microvesicular steatosis in zone 3, sparing periportal area
- Testing of genetic variant of LCHAD
- Treatment
  - Termination of pregnancy
  - Steroid for 48 hours before delivery in case of preterm
- Serious fetal outcome
- Cholestatic phase up to 4 weeks postpartum
- Liver histology improvement within days to weeks after delivery
Acute fatty liver of pregnancy
Pre-eclampsia/eclampsia

- BP >140/90 mmHg + Proteinuria > 300 mg/day + edema (+ seizure or alteration of consciousness)

- Multi-organs involvement

- Cause:
  - Abnormal development of placental vasculature
  - Antiangiogenic factor
  - Endothelial dysfunction and activation of procoagulant factors

- RUQ pain or epigastrium pain - liver involvement

- Aminotransferase 10-20 X ULN

- High alkaline phosphatase, Mild elevation of total bilirubin

- Resolve within 2 week after delivery
HELPP syndrome

- **Hemolyis**
  - Microangiopathic hemolytic anemia

- **ELevated liver enzymes**
  - Transminitis

- **Low Platelet**
  - Accelerated destruction
HELLP syndrome

- Associated with severe pre-eclampsia 20%
- 3rd trimester, 30% of cases presented in postpartum period (up to 1 week)
- Subcapsular hematoma, Hepatic rupture, Hepatic infarction
- Clinical clues: Transminitis+ CBC (Low Hct, low PLT, MAHA) +/- pre-eclampsia
- Termination of pregnancy
  - Term > 34 weeks
  - Pre-term with multiorgan failure (DIC, AKI, Abruptio placentae) or fetal distress after 48-hr steroid
- Peak of Lab abnormalities in the first 48 hours and return to normal within 3-11 days

# Acute fatty liver vs pre-eclampsia/eclampsia

<table>
<thead>
<tr>
<th></th>
<th>Acute fatty liver</th>
<th>Pre-eclampsia/eclampsia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>50%</td>
<td>100%</td>
</tr>
<tr>
<td>Jaundice</td>
<td>100%</td>
<td>40%</td>
</tr>
<tr>
<td>Amino transferase</td>
<td>&lt;10</td>
<td>&gt;10</td>
</tr>
<tr>
<td>(x normal)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scans</td>
<td>Diffuse Change</td>
<td>Focal abnormalities</td>
</tr>
<tr>
<td>Liver biopsy</td>
<td>Microvesicular steatosis</td>
<td>Fibrin (perisinussoid)</td>
</tr>
<tr>
<td>Liver failure</td>
<td>Present</td>
<td>Absent</td>
</tr>
</tbody>
</table>

Modified from Sherlock’s diseases of the liver and biliary system 12\textsuperscript{th} edition. 2011
Liver diseases coincident with pregnancy
HEV

- The most prevalent viral cause of acute liver failure in pregnancy
- Endemic are in South Asia and Africa
- 2nd and 3rd trimester
- Maternal mortality rate 41-54% and fetal mortality rate 69%
- Treatment: supportive treatment

Pregnant women are more susceptible than general population

Maternal mortality 39%

Clinical clues:
- Raised aminotrasferase without jaundice (in early course)
- Leucopenia, thrombocytopenia, and coagulopathy
- Mucocutaneous lesion 50% of cases
HSV

- **Diagnosis**
  - Liver biopsy
  - CT scan: multiple low-density areas of necrosis

- **Treatment**
  - I.V. Aciclovir should not be delayed
Budd-Chiari syndrome

- Intrapartum → 2 months after post partum
- Immediate postpartum
- Underlying hypercoagulable state: primary antiphospholipid, factor V Leiden mutation
- Precipitate by relative protein S deficiency during pregnancy

Diagnosis
- USG
- CT

Treatment: anticoagulant
- Intrapartum Prefer LMWH
- Post partum: oral anticoagulant
Hepatic hemangioma and focal nodular hyperplasia

Hepatic hemangioma
- Usually asymptomatic if size < 5 cm
- Not progress during the course of pregnancy

Focal Nodula hyperplasia
- 2nd most common
- May increase in size during pregnancy
- Not contraindication for pregnancy
Hepatic adenoma

- Estrogen causes increasing size of hepatic adenoma
- Complication: hemorrhage, rupture, hemoperitoneum
- Prophylaxis:
  - Size > 5 cm → surgical resection before conception
  - Pregnancy should be avoided
Thank you