Approach to Elevated Liver Enzymes in Pregnancy

Rshmi Khurana
Director of Obstetric Medicine
Associate Professor of Medicine and Ob/Gyn
University of Alberta
Objectives

- To understand the types of liver diseases specific to pregnancy and how to recognize them
- Acquire an approach to their initial investigation and management
- Understand the role of the internist in the management of these patients
Outline

- Liver physiology and liver tests during pregnancy
- Key features of pregnancy specific causes
- Cases
- Review
R Khurana: Elevated Liver Enzymes in Pregnancy
Physiology

- **Increased**
  - Cholesterol, triglycerides
  - Alkaline phosphatase

- **Decreased**
  - Albumin
  - Bilirubin
  - GGT

- **Essentially unchanged**
  - ALT, AST
  - Bile Acids
Physiology

- **Biliary changes**
  - Reduced gallbladder motility
  - Increased lithogenicity of bile
Approach

- Same as in non-pregnant
  - Consider pre-existing disease

- In addition:
  - Consider trimester pregnancy
  - Associated symptoms (nausea/vomiting, itchy, headaches)
  - Prior pregnancy history
Timing

- **T1**: Hyperemesis
- **T2**: Cholestasis
- **T3**: Preeclampsia/HELLP
- **PP**: AFLP
Pattern Recognition

- Hyperemesis Gravidarum
  - Vomiting
- Intrahepatic cholestasis of pregnancy
  - Pruritus without rash
- Preeclampsia/HELLP
  - Hypertension, proteinuria
- Acute fatty liver of pregnancy
  - Liver dysfunction
Prospective study of liver dysfunction in pregnancy in Southwest Wales

142 women in 4377 deliveries over 15 months

- Not pregnancy specific: 31%
- Cholestasis: 16%
- Hyperemesis: 8%
- AFLP: 3%
- PEC/HELLP: 32%
- Unclear: 10%
Case 1

- 32 yo G1P0 at 32+ weeks, twin gestation
- Previously healthy
- 2-3 day nausea, vomiting, heartburn, anorexia
- 1 day jaundice, lethargy
- Brought in by husband for dehydration
Case 1

- BP 135/78, HR 107, O2 sat 98% on room air, afebrile
- Drowsy, GCS-14 (disoriented)
- No stigmata of chronic liver disease
- Gravid uterus
- Mild tenderness epigastrium
- Initial diagnosis: gastroenteritis, dehydration
- C/S - 2.2, given D50W
## Case 1 - Labs

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>141</td>
<td>AST</td>
<td>300</td>
</tr>
<tr>
<td>WBC</td>
<td>9.9</td>
<td>ALT</td>
<td>302</td>
</tr>
<tr>
<td>Platelets</td>
<td>128</td>
<td>LDH</td>
<td>480</td>
</tr>
<tr>
<td>Sodium</td>
<td>122</td>
<td>Bilirubin</td>
<td>142</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.5</td>
<td>INR</td>
<td>1.9</td>
</tr>
<tr>
<td>Chloride</td>
<td>90</td>
<td>PTT</td>
<td>58</td>
</tr>
<tr>
<td>Total CO2</td>
<td>17</td>
<td>Fibrinogen</td>
<td>1.7</td>
</tr>
<tr>
<td>Creatinine</td>
<td>196</td>
<td>Glucose</td>
<td>2.2</td>
</tr>
</tbody>
</table>
What is the most likely diagnosis?

- Acute viral hepatitis
- Intraheptic cholestasis of pregnancy
- Hyperemesis gravidarum
- Acute fatty liver of pregnancy
- Preeclampsia
Acute Fatty Liver of Pregnancy

- Acute fatty liver of pregnancy (AFLP) - different from fatty liver
- Rare condition (1 in 13000 deliveries)
- Presents after 20 weeks, usually 3rd trimester

Initial presentation:
- Nausea and vomiting in 75%
- Abdominal pain (epigastric) in 50%
- Anorexia, jaundice
- Some may initially only have laboratory abnormalities
Key Features of AFLP

- Modestly elevated AST/ALT (up to 1000)
- 70% have associated DIC
- 50% have signs of preeclampsia
- Liver dysfunction in AFLP vs PEC/HELLP
- Acute kidney injury common

Complications
- Bleeding
- Hypoglycemia
- Encephalopathy
- Ascites
- Infection
- Hypernatremia
AFLP Treatment

- Treatment: stabilize mother and deliver!
- Prognosis:
  - Maternal mortality under 10%
  - Usually no sequelae
  - Rarely need liver transplant
  - Recurrence risk unclear
- Association with L-CHAD (long-chain 3-hydroxyacyl CoA dehydrogenase) deficiency
Back to case...

- Urgent C-section with transfusion support
- ICU post-partum
- Encephalopathy, ascites, evidence of DIC
- Gradual improvement
- Home 2 weeks later
Case 2

- A 25 yo G1 at 34 weeks
- Severe pruritus for a few weeks
- Otherwise healthy
- Can’t sleep!
- No rash, excoriations from scratching
Case 2

- Her lab tests are as follows:
  - ALT 320
  - AST 285
  - Bili 25
  - Alk Phos 200
  - GGT normal
  - Normal CBC, creat
  - Normal INR, PTT

- Internal Medicine consulted
What investigations do you want to order?

- Hepatitis C serology
- Bile acids
- Ultrasound of liver
- All of the above
IHCP – Key Features

- Intense pruritus worse at night
- Affects palms and soles
- No primary skin lesion
- Usually starts in the second trimester or later
- Jaundice uncommon (<10%)
- Genetic and hormonal factors important
ALT/AST modestly up or can reach 1000
GGT usually normal or minimally elevated
Increased bile acids diagnostic
  - Right clinical setting
  - Absence of other cause
INR normal unless vitamin K deficiency
IHCP - Risks

- **Maternal**
  - Sleep deprivation

- **Fetal**
  - Stillbirth
  - Preterm delivery
  - Meconium passage in utero

- Risks to fetus related to levels of bile acids
- Fetal monitoring not predictive of stillbirth
IHCP - Treatment

- Ursodeoxycholic acid
  - Improves pruritus
  - Reduces bile acids, liver enzymes
  - May benefit fetal outcomes

- Symptomatic
  - Topical creams with menthol
  - Sedating antihistamines

- Vitamin K

- Many patients delivered early (37 weeks)
IHCP - Long term prognosis

- Ensure normalization of liver enzymes and bile acids postpartum!
- High risk recurrence in subsequent pregnancies
- Some women may get cholestatic with OCP’s
Case 3

- 24yo G1P0 at 25 weeks
- 6 month visit to Pakistan to visit husband
- While in Pakistan
  - Intermittent diarrhea
  - Epigastric pain
  - Some pale stools and dark urine
  - Mild pruritus
- Walked off plane and mother noticed jaundice!
Case 3

#### May 24
- CBC - WBC 15.1, Hgb 133, plt 206
- ALT - 1091
- Creatinine 40
- Ferritin 86
- Ultrasound fetus - reassuring

#### May 27
- Albumin 29
- Alk phos 181
- AST 116
- Bili 92
- GGT 63
- Hep A, B, C negative
- HIV negative
- Normal INR, PTT
- Ultrasound - normal
Case 3

- **Further history**
  - No herbals, no vices,
  - Prenatal vitamins only
  - No headache, abdominal pain, visual complaints

- **Physical exam**
  - Blood pressure 124/62
  - Jaundiced
  - Otherwise unremarkable
What is the most likely diagnosis?

- Hyperemesis gravidarum
- Preeclampsia
- Cholestasis of pregnancy
- Acute fatty liver of pregnancy
- Non pregnancy related
<table>
<thead>
<tr>
<th>Lab</th>
<th>5/24</th>
<th>5/27</th>
<th>5/30</th>
<th>5/31</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT</td>
<td>1091</td>
<td></td>
<td>144</td>
<td>107</td>
</tr>
<tr>
<td>AST</td>
<td>116</td>
<td>59</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>GGT</td>
<td>63</td>
<td>73</td>
<td>76</td>
<td></td>
</tr>
<tr>
<td>Alk Phos</td>
<td>181</td>
<td>96</td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>Bili</td>
<td>92</td>
<td>90</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>Conj Bili</td>
<td>44</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bile Acids</td>
<td></td>
<td>135</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Further investigations

- Urine negative protein
- EBV, CMV serology indicative of past exposure
- Serum bile acids - 279
- Started on Ursodeoxycholic Acid
The answer!

- Hepatitis E IgM positive!
- Sample sent for Hepatitis E RNA - positive
- Liver enzymes and bile acids continued to improve
- Ursodiol tapered and discontinued as labs improved
- Off medications with normal tests by 34 weeks
- Spontaneous delivery of healthy baby girl
Hepatitis E

- Fecal oral transmission
- Most often in the developing world
- Usually self-limited acute infection
- Similar presentation to other acute viral hepatitis
- Can get prolonged cholestatic phase
- Fulminant hepatitis can occur in pregnancy
- 20% maternal mortality
Key Points

- **Hyperemesis gravidarum**
  - Nausea and vomiting
  - Onset 1st trimester
  - Modest increase ALT/AST (<200)

- **IHCP**
  - Pruritus, palms and soles
  - Onset 2nd or 3rd trimester
  - Elevated bile acids
Key Points

- **Preeclampsia**
  - Onset after 20 weeks
  - Usually hypertension, proteinuria
  - Can have temporary improvement, esp with steroids

- **Acute fatty liver of pregnancy**
  - Usually 3rd trimester
  - Liver synthetic dysfunction
  - Modest increase AST/ALT (usu <500)
  - Often acute kidney injury