MEDICAL MANAGEMENT OF JAUNDICE IN PREGNANCY

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• Mind constricts (No relaxation, full of anxiety & fear)
• Heart dilates (Cardiomyopathy)
• Kidney porous (Proteinuria)
• Blood toxic (Toxaemia)
• Body bloaty (Oedema)
• Liver fatty (Acute fatty liver - Jaundice)

This is the pregnancy
Now our topic of discussion is
Jaundice in pregnancy
This jaundice in pregnancy is described by two ways –

A. Jaundice caused by pregnancy (unique to pregnancy)
B. Jaundice can occur in pregnancy (intercurrent illness)
# Causes of jaundice during pregnancy

<table>
<thead>
<tr>
<th>Jaundice unique to pregnancy</th>
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<tbody>
<tr>
<td>- Intrahepatic cholestasis</td>
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<tr>
<td>- Acute fatty liver</td>
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<tr>
<td>- Severe pre eclampsia &amp; eclampsia</td>
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<tr>
<td>- HELLP syndrome</td>
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<tr>
<td>- Severe hyperemesis gravidarum</td>
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<td>- Endotoxic shock</td>
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<table>
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<tr>
<th>Intercurrent illness</th>
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<tbody>
<tr>
<td>- Viral hepatitis</td>
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<tr>
<td>- Drug induced – INH, phenothiazines</td>
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<tr>
<td>- Cholelithiasis</td>
</tr>
<tr>
<td>- Haemolytic jaundice – incompatible blood transfusion</td>
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<tr>
<td>- Auto immune hepatitis</td>
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<tr>
<td>- CLD</td>
</tr>
<tr>
<td>- Malaria</td>
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<tr>
<td>- Hepatic neoplasm</td>
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<td>- Pancreatitis</td>
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</table>
Why this is concern?

- Jaundice ➔ High risk condition
- Pregnancy ➔ Vulnerable situation
- Risky + Vulnerable ➔ Red alert situation
Why in pregnancy jaundice occurs?

- Humoral change?
- Placental hormones?
- Auto immune mechanism?
- Uterine stretching?
We are swimming in the sea of ‘enigma’

We are searching in the dark with a beam of light
Intra hepatic cholestasis of pregnancy (ICP/IHCP)

- Syn: Obstetric hepatosis
  Icterus graviderum

- What is ICP?
  - Reversible
  - 3rd trimester
  - Resolve after delivery

- Incidence – 0.5 – 1.8% of pregnancy

- Etiology – Unknown
  - Dominance inheritance
  - Prevalence in certain population i.e., Chile
  - Family clusters
  - Circulating hormones in pregnancy
  - OCP
Intra hepatic cholestasis of pregnancy (ICP/IHCP) – Cont’d

- **Pathology:**
  
  Impairment of the movement of the microvilli in biliary canaliculi
  
  Stasis of biliary flow
Pathogenesis

Pre existing covert defect of bile transport

OCP

Circulating hormones in last trimester

Overt defect of bile transport

Cholestasis
Clinical feature

• First - pruritus – 80%; begins with palm & sole

• Then - Jaundice – 20%; after 2 weeks of pruritus
Pruritus & Jaundice

- First jaundice, then pruritus – Acute hepatitis
- Jaundice & pruritus simultaneously – Obstructive jaundice
- First pruritus then jaundice –
  1. Jaundice 2 weeks after pruritus – ICP
  2. Jaundice months after pruritus – PBC
Investigations

• Bilirubin – elevated not more than 5 mg/dl
• Transaminase – 2-10 folds
• Alkaline phosphatase – 4 folds
• Bile salt ↑
Treatment

- **Strategy** –
  - Reducing symptoms in the mother
  - To provide an adequate obstetric care
  - To prevent fetal distress or sudden fetal death

- **Treatment design** –
  - General care of the mother –
    - Adequate rest
    - Low fat diet
    - Parenteral supplementation of vitamin K
  - Specific treatment –
    - Diphenhydramin
    - Ursodeoxycholic acid (UDCA) 300 mg twice a day
Treatment (Cont’d)

- Other emerging drugs:
  - Dexamethasone
  - Phenobarbital
  - S-Adenosylmethionine

- Care to the fetus:
  - Close fetal monitoring
  - Nonstress testing
  - Search for meconium - if suspected fetal distress
  - Elective delivery at 37 weeks
Outcome

- No increase in maternal mortality
- May be associated with –
  - Prematurity
  - Foetal distress
  - Perinatal death
- Resolves after delivery
- Recur in the subsequent pregnancies
Acute Fatty Liver of pregnancy

- Architecture intact
- Lobules swollen
- Fatty infiltration of hepatocytes
- Ballooning of hepatocytes
Acute fatty liver of pregnancy (AFLP) (Cont’d)

- First identified by Sheehan in 1940

- Earlier terminology:
  - Acute yellow atrophy of pregnancy
  - Acute obstetric fatty metamorphosis of liver
Acute fatty liver of pregnancy (AFLP) (Cont’d)

- **Etiology:** Not known precisely
  - Genetic relation
  - Biochemical Relation: Associated with **Glu474Gln** mutation in the long-chain 3-hydroxy acyl-coenzyme A dehydrogenase (LCHAD).
  
  *(LCHAD is a fatty acid β oxidation enzyme)*
Patogenesis

Mutation of the LCHAD

Mutant LCHAD is ineffective

No β oxidation of fatty acid

Accumulation of fat in liver
- **Incidence:** Rare, 0.01% pregnancies (1 in 10,000)
- **Risk factors:**
  - Age: Mean 26 (16-39)
  - Primipara (67%)
  - Onset week of pregnancy: 28-38 (33%)
  - Male baby (60%)
  - Twin pregnancies
  - Pre eclampsia
## Clinical features

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Vomiting</td>
<td>80%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>52%</td>
</tr>
<tr>
<td>Jaundice</td>
<td>93%</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>87%</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>80%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>60%</td>
</tr>
<tr>
<td>Ascites</td>
<td>47%</td>
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</tbody>
</table>
Laboratory findings

- Transaminase level increased 1-5 folds
- Alkaline phosphatase increased 2-8 times
- WBC > 15,000
- Platelets < 1,00,000
- Hypoglycemia
- Decreased clotting factors
- S.creatinine raised
- **Histopathology (liver biopsy is not indicated for diagnosis):**
  - *In contrast with viral hepatitis & other common causes of fulminant hepatic failure, necrosis of hepatocytes is always minor*
Complications

- Cerebral oedema
- Renal failure (60%)
- Hypoglycemia (53%)
- Infections (45%)
- GI hemorrhage (35%)
- Coagulopathy (30%)
- Fetal death
- Severe PPH
Management:
- Delivery & supportive care

Outcome:
- Maternal & fetal mortality approximately 20%
- Normal liver functions return soon after delivery
- Usually does not recur in subsequent pregnancies
HELLP

- Haemolysis
- Elevated liver enzymes
- Low Platelet
RBC in HELLP Syndrome
Liver in HELLP Syndrome
HELLP syndrome (Cont’d)

- 1st diagnosed by Weinstein in 1982
- Evolution of the syndrome:
  - In 19th century – very unusual varieties of severe pre eclampsia with complicated progress
  - Today – HELLP syndrome (Association of characteristic hepatic & Haematologic disorder)
Possible etiology

1. Increase in volume?
2. Fetal decidual cell?
3. Vasospasm?
4. Deficient vascular repair?
5. Idiopathic?
Pathogenesis

Above causal agents

Vasculo-endothelial disorder

Platelet Aggregation/Consumption

Fibrin Activation/Consumption

Selective organic ischemia/Insufficiency

Variable manifestation
Diagnosis

- Mid – II trimester
- 1st days postpartum
- Antepartum diagnosis is made in 70% between 27 & 37 weeks of gestation
Criteria for establishing the diagnosis

- **Haemolysis** –
  - Abnormal peripheral blood smear
  - Elevated bilirubin > 1.2 mg/dl
- **Elevated liver enzymes** –
  - SGOT > 72 IU/L
  - LDH > 600 IU/L
- **Low platelets** –
  - Platelet count < 100 X 10^3 / mm^3
- Hypertensive woman
- Epigastric & / or right hypochondrial pain
- Nausea, vomiting
- Positive investigation

Right diagnosis of HELLP
Classification of the HELLP syndrome

- A. On the basis of the platelet count
- B. On the basis of expression
A. On the basis of the platelet count

- **Class 1** – Platelet count < 50,000 / mm$^3$

- **Class 2** – Platelet count between 50,000 / mm$^3$ to 1,00,000/ mm$^3$

- **Class 3** – Platelet count between 1,00,000 / mm$^3$ to 1,50,000/ mm$^3$
B. On the basis of expression

- **Complete HELLP –**
  - Microangiopathic haemolytic anaemia in woman with severe pre eclampsia
  - LDH ≥ 600 IU/L
  - SGOT ≥ 70 IU/L
  - Thrombocytopenia < 1,00,000/ mm$^3$

- **Partial HELLP –**
  - One or two of the above
Differential diagnosis of the HELLP syndrome

- Thrombotic microangiopathies
- Fibrinogen consumption disorders
- Connective tissue disorders
- Primary renal disease
Risk factors for maternal morbidity

Clinical
- Epigastric pain
- Nausea
- Vomiting
- Eclampsia
- Severe hypertension
- Abruptio placenta

Laboratory
- Platelets < 50000
- LDH > 1400 IU/L
- CPK > 200 IU/L
- ALT > 100 IU/L
- AST > 150 IU/L
- Creatinine > 1.0
Management

- It needs multi disciplinary team –
  - Obstetrician
  - Internist
  - Neonatologist

- Management strategy –
  A. Management *before* labor & delivery
  B. Management *of* labor & delivery
  C. Management *after* labor & delivery
  D. Advice on *future* pregnancy
Management (Cont’d)

A. Management *before* labor & delivery –

1. Anticipate the diagnosis
2. Evaluate maternal condition –
   - Control of hypertension
   - Water & electrolyte balance
   - Prophylaxis of convulsion with MgSO$_4$
   - Hemotherapy
   - Be alert of multi organ failure
3. Evaluate fetal condition
Management (Cont’d)

B. Management of labor & delivery –
   - By obstetrician

C. Management after labor & delivery –
   - Intensive post partum treatment of the patient
   - Optimize perinatal care

D. Advice on future pregnancy
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<tr>
<th>Condition</th>
<th>Incidence</th>
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<tr>
<td>IHCP</td>
<td>0.5 – 1.8%</td>
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<tr>
<td>Acute fatty liver</td>
<td>0.01%</td>
</tr>
<tr>
<td>HELLP syndrome</td>
<td>4 – 12%</td>
</tr>
<tr>
<td>Acute Hepatitis</td>
<td>3 – 20%</td>
</tr>
<tr>
<td>Cholelithiasis</td>
<td>6 – 7%</td>
</tr>
<tr>
<td>Condition</td>
<td>Maternal Mortality Mother Risk</td>
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<td>-------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>IHCP</td>
<td>No increased risk</td>
</tr>
<tr>
<td>Acute fatty liver</td>
<td>18-20% maternal mortality</td>
</tr>
<tr>
<td>HELLP</td>
<td>2%</td>
</tr>
<tr>
<td>Pre eclampsia + AFL</td>
<td>Upto 85%</td>
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Acute viral hepatitis

- Commonest jaundice
- Hepatitis A, B, C, D & E
**Incidence**

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<tbody>
<tr>
<td>Developed countries</td>
<td>0.1%</td>
</tr>
<tr>
<td>Developing countries</td>
<td>3 – 20%</td>
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<tr>
<td>Acute hepatitis B</td>
<td>2 per 1000 pregnancies</td>
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<tr>
<td>Acute hepatitis C</td>
<td>1 per 1000 pregnancies</td>
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Clinical feature

- Fever
- Anorexia
- Nausea
- Vomiting
- Yellow discoloration
- Right upper quadrant tenderness
Laboratory findings

- ↑ Serum transaminase (200 - 2000 u/l)
- ↑ Plasma bilirubin
- Specific viral markers
Treatment

- Symptomatic & supportive:
  - Adequate rest
  - Nutrition - Diet rich in carbohydrate and adequate protein
  - Drugs - Neomycin, lactulose
  - Avoid - sedatives, narcotics etc
  - Prevention of complications
Treatment (cont’d)

- Immunization of the newborn:
  - Any potential for transmission of HBV at delivery is an indication for passive and active immunization of the newborn

No analogous treatment is available for hepatitis C
CHOLELITHIASIS & CHOLEDOCHOLITHIASIS IN PREGNANCY
Incidence: May affect 6-7% of pregnant women

Risk factors:
- Multiparity
- Previous gallbladder disease
Mechanism

- Altered composition of bile
- Slowing of gall bladder emptying

↑ Risk of gall stone
Clinical feature

- Symptoms similar to nonpregnant women
- Abdominal pain –
  - Right upper quadrant / Epigastric region
  - Peaking at 12 – 24 hours
  - Radiate towards the back
- Murphy's sign less common in pregnancy
- Jaundice in 5% occasions
Laboratory findings

- Similar to non-pregnant women
- USG- shows the stones in gall bladder or in ducts
Management

- Obstructive jaundice requires surgical intervention
# Outcome

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<tr>
<th>Uncomplicated cholecystectomy</th>
<th>5% fetal loss</th>
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<tr>
<td>With bile duct exploration especially with pancreatitis</td>
<td>15% maternal and 60% fetal mortality</td>
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Autoimmune hepatitis

- Can present with an acute attack
- Serum bilirubin increase is dependent upon type of disease
- Can be treated with azathioprine during pregnancy
- Usually, a favorable outcome in terms of mother and baby
Chronic liver disease in pregnancy

- Increased risk of fetal loss
- In PBC ursodeoxycholic acid can be safely continued
- Cholestasis may worsen during pregnancy with PBC
- Infants of patients with marked hyperbilirubinaemia during pregnancy may require exchange transfusion at birth
Conclusion

Pregnancy –
- The milestone of creation, thing is divine
- Sometimes complicates behind
- Patient should alert
- Doctor must vigilant
- Then comes to a nice end
Thank You