Part I: Liver Disease in Pregnancy
(Jaundice in Pregnancy)

Part II: respiratory disease in pregnancy

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Objectives:

- Understand the different disease of liver that can affect pregnant women
- How to manage a pregnant woman with liver disease
- How to reduce vertical transmission of viral hepatitis
- How to deal with common respiratory problems during pregnancy including the new world wide infection with Corona Virus (COVID-19)
### Table 6.8.1 Normal ranges for liver enzymes in non-pregnant and pregnant populations

<table>
<thead>
<tr>
<th>Liver enzyme</th>
<th>Non-pregnant</th>
<th>Trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1st</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>7–40</td>
<td>10–28</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>0–40</td>
<td>6–32</td>
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<tr>
<td>Bilirubin (µmol/L)</td>
<td>0–17</td>
<td>4–16</td>
</tr>
<tr>
<td>Gamma GT (IU/L)</td>
<td>11–50</td>
<td>5–37</td>
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<tr>
<td>Alkaline phosphatase (IU/L)</td>
<td>30–130</td>
<td>32–100</td>
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</table>

- ALT, alanine transaminase; AST, aspartamine transaminase; GT, glutamyl transpeptidase.
Obstetric Cholestasis:

- Cholestasis is an impairment of bile flow which may clinically present with fatigue, pruritus and, in its most overt form, jaundice.
- Obstetric cholestasis is an uncommon condition, specific to pregnancy.
- Aetiology relate to genetic predisposition to the cholestatic effect of estrogen (Increased estrogen levels lead to increased cholesterol secretion and supersaturation of bile).
- The importance of this condition is its association with sudden IUFD, mostly at term.
Presentation

- It is most commonly present in the third trimester at around 32 weeks.
- Itching can vary from mild to intense and persistent, affecting the whole body particularly the palms & soles.
- There is no rash.
- Hepatic transaminases are only mildly elevated. Bile acids may be elevated.
- There may be associated dark urine, pale stool, steatorrhea & malaise.
differential diagnosis include:

- extrahepatic obstruction with gall stones
- acute & chronic viral hepatitis
- primary biliary cirrhosis
- chronic active hepatitis.
- Pre-eclampsia
- HELLP syndrome
- Acute fatty liver of pregnancy
- Sepsis
- Drug-induced hepatitis
Investigations should include:

- LFT
- Serum Bile acids
- Full blood count
- Clotting profile
- Renal function
- serology for hepatitis A, B, C, Ebstien-Bar virus & cytomegalovirus
- liver autoantibodies (anti- mitochondrial antibodies, & anti-smooth muscle antibody).
- liver ultrasound & ultrasound for fetal growth & amniotic fluid
Complications:

- postpartum haemorrhage
- premature labour
- meconium-stained liquor
- fetal distress in labour
- intra-uterine death.
Management:

- Pruritus may be troublesome and is thought to result from elevated serum bile salts.
- Control of pruritis: a combination of antihistamines & emollients, if no response ursodeoxycholic acid used.
- Vitamin K (water soluble form) should be given to the mother from the time of diagnosis to reduce the risk of postpartum haemorrhage.
- LFT & clotting time should be monitored regularly.

- Fetal surveillance with CTG & ultrasound.

- Delivery should be induced at 37-38 weeks.
- Following delivery, LFT returns to normal. Should be monitored at 6 weeks postpartum.
- Symptoms may recur with estrogen containing oral contraceptives which should be avoided.
- Recurrence in subsequent pregnancy is very high.
Acute Fatty Liver of pregnancy:

- AFLP is closely related to pre-eclampsia (genetic defect in fatty acid oxidation).

- presents in the third trimester with abdominal pain, nausea, vomiting, anorexia & jaundice.

- aetiology is unknown but histologically perilobular fatty infiltration of liver cells is noted.
Following the onset, there is a rapidly worsening cascade of problems.

- markedly deranged LFT, renal impairment, raised uric acid, raised white blood cells, hypoglycaemia & coagulopathy.

- Perinatal & maternal mortality & morbidity are increased. Maternal death result from hepatic encephalopathy or overwhelming haemorrhage.
Management:

- Relies on early diagnosis.
- Intensive care unit & multidisciplinary team.
- Delivery should be expedited, this will be by CS under GA, following correction of hypoglycaemia or coagulopathy with 50% dextrose, vitamin K, fresh frozen plasma & platelets.
- Management after delivery is conservative. Referral to liver unit is indicated if liver function still abnormal or there are features of hepatic encephalopathy.
Viral Hepatitis & Pregnancy:

- Most common cause of jaundice in pregnancy.
- None of the hepatitis viruses are known to be teratogenic.
- The course of most viral hepatitis infections is unaltered by pregnancy except with hepatitis E which exhibit markedly increased fatality rates.
HBsAg Endemicity

- >8% - High
- 2-7% - Intermediate
- <2% - Low
Treatment:

- may benefit from pharmacologic therapy for chronic HBV and chronic HCV infections.
- Interferon does not have an adverse effect on the embryo or fetus while the use of ribavirin during pregnancy is contraindicated.
- **Post-exposure Prophylaxis** for Susceptible Pregnant Women: HBV immunoglobulin, HAV vaccine, and HBV vaccine are approved for use during pregnancy.
Vertical Transmission:

- HAV is not transmitted to the fetus in utero but may be transmitted to the neonate during delivery or during the postpartum period (fecal-oral route).

- The risk of HBV vertical transmission is 10% in mothers with negative HBeAg and positive HBsAb while it is 90% in those with positive HBeAg. Neonatal HBV infection increase with increasing gestation.

- Universal screening of pregnant women for HBsAg is performed to reduce perinatal transmission of hepatitis B virus.
Neonatal prophylaxis: Infants of HBsAg-positive mothers should receive hepatitis B immune globulin immunoprophylaxis at birth and hepatitis B vaccine at one week, one month and six months after birth.

This regimen reduces the incidence of hepatitis B virus vertical transmission to zero to 3%.
Delivery by cesarean section is not recommended.

Intrapartum fetal scalp electrode & fetal blood sampling should be avoided.
If instrumental delivery is needed, forceps rather than ventouse is appropriate.

With appropriate hepatitis B immunoprophylaxis, breast-feeding poses no additional risk for maternal to child transmission.
Gallstones

- The prevalence in pregnancy is around 19% in multiparous women & 8% in nulliparous women. Acute cholecystitis is much less common, occurring in around 0.1% of pregnant women.

- The aetiology: increased estrogen levels lead to increased cholesterol secretion and supersaturation of bile, and increased progesterone levels cause a decrease in small intestinal motility.

- Conservative medical management is recommended initially, especially during the first and third trimesters, in which surgical intervention may confer a risk of miscarriage or premature labour, respectively.

- Medical management involves intravenous fluids, correction of electrolytes, bowel rest, pain management and broad-spectrum antibiotics.

- Relapse rates (40–90%) are high during pregnancy and surgical intervention may be warranted, preferentially performed (open or laparoscopic cholecystectomy) in the second trimester.
Abnormal liver function tests in pregnancy

**Differential diagnosis:**

<table>
<thead>
<tr>
<th>1st Trimester</th>
<th>2nd Trimester</th>
<th>3rd Trimester</th>
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<tbody>
<tr>
<td>• Hyperemesis gravidarum</td>
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<td>• Acute viral hepatitis</td>
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<td></td>
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<tr>
<td>• Preexisting liver disorders</td>
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<tr>
<td>• Cholelithiasis</td>
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<tr>
<td>• Cholestasis of pregnancy</td>
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<tr>
<td>• Liver involvement in pre-eclampsia</td>
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<tr>
<td>• HELLP</td>
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<tr>
<td>• AFLP</td>
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<tr>
<td>• Liver haematoma</td>
<td></td>
<td></td>
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<tr>
<td>• Budd-Chiari syndrome</td>
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**Investigation:**

| • UEC |
| • HAV, HBV, HCV, EBV, CMV, HSV, (HEV) etc |
| • Autoimmune serology |
| • Chronic HCV, HBV |
| • Past history/antenatal LFTs |
| • US—structural changes |
| • History of alcohol/insulin resistance |
| • Upper abdominal US |
| • Bile acids/no RUQ pain |
| • Pre-eclampsia features—transaminase rise to fivefold |
| • Microangiopathic haemolytic anaemia/thrombocytopenia/pre-eclampsia features |
| • Encephalopathy/DIC/low BSL |
| • US or CT liver. Large rise in transaminases |
| • Doppler ultrasound/ascites |
Respiratory Disease in Pregnancy
Physiological changes in pregnancy

- Dyspnea is experienced by approximately half of all pregnant women by 20 weeks gestation because of high progesterone levels which acts via the Hypothalamus to increase respiratory drive.

- Anatomically, the lower chest wall circumference increases by 5-7 cm, the diaphragm is elevated 4-5 cm by term & the costal angle widens. These changes occur due to the pressure from the expanding uterus & the relaxation of thoracic ligaments.
Respiratory infection

- Pregnancy is a significant risk factor for the development of severe respiratory disease attributable to viral infection.
- A seasonal flu vaccine is recommended in pregnancy.
- Viral pneumonia follows a more complicated course in pregnancy and women often decompensate more quickly.
- Prompt treatment and early involvement of respiratory and infectious disease specialists in addition to the intensive care is essential.
- Bacterial pneumonia should be treated with penicillin or cephalosporins usually the first choice, and erythromycin used if atypical organisms are suspected.
Pneumonia: warning signs

- Respiratory rate > 30/minute.
- Hypoxaemia; pO2 < 7.9 kPa on room air. (n. > 10.5 kPa)
- Acidosis; pH < 7.3. (n. 7.35-7.45)
- Hypotension.
- Disseminated intravascular coagulation.
- Elevated blood urea.
- Evidence of multiple organ failure.
Coronavirus (COVID-19) Infection in Pregnancy

- Pregnant women do not appear to be more susceptible to the consequences of infection with COVID-19 than the general population.

- Transmission: Expert opinion is that the fetus is unlikely to be exposed during pregnancy.

- Effect on the mother/symptoms: The large majority of women will experience only mild or moderate cold/flu like symptoms. Cough, fever and shortness of breath are other relevant symptoms.

- Effect on the fetus: no increased risk of miscarriage or early pregnancy loss in relation to COVID-19, no congenital effects of the virus on fetal development.
Attendance for routine antenatal care in women with suspected or confirmed COVID-19: should be delayed until after the recommended period of isolation.

Women attending for intrapartum care with suspected/confirmed COVID-19 and no/mild symptoms: encouraged to remain at home (self-isolating) in early (latent phase) labour.

When attend the maternity unit, settled in an isolation room, a full maternal and fetal assessment should be conducted to include:

- Assessment of the severity of COVID-19 symptoms should follow a multi-disciplinary team approach including an infectious diseases or medical specialist.
- Maternal observations including temperature, respiratory rate and oxygen saturations.
- Confirmation of the onset of labour.
- Electronic fetal monitoring using cardiotocograph (CTG).

If the woman has signs of sepsis, investigate & treat but also consider active COVID-19 as a cause of sepsis.
Mode of birth should not be influenced by the presence of COVID-19, unless the woman’s respiratory condition demands urgent delivery.

There is no evidence that epidural or spinal analgesia or anaesthesia is contraindicated in the presence of coronaviruses.

Epidural analgesia should therefore be recommended before, or early in labour, to women with suspected/confirmed COVID-19 to minimise the need for general anaesthesia if urgent delivery is needed, and because there is a risk that use of Entonox may increase aerosolisation and spread of the virus.

• If Entonox is used then the breathing system must contain a filter to prevent contamination with the virus.
In case of deterioration in the woman’s symptoms, make an individual assessment regarding the risks and benefits of continuing the labour, versus proceeding to emergency caesarean birth if this is likely to assist efforts to resuscitate the mother.

There is no evidence to suggest that steroids for fetal lung maturation, when they would usually be offered, cause any harm in the context of COVID-19.
Asthma in Pregnancy

- The prevalence of asthma in pregnancy is about 3–12 per cent.

Effect of pregnancy on asthma severity:

- Asthma remains stable in one-third of women, worsens in another third and improves in the remaining third.

- Most episodes occur between 24 and 36 weeks of pregnancy.

- The potential benefit of pregnancy-induced immune system modulation & progesterone-mediated bronchodilatation may be opposed by the reluctance of patient & physician to treat asthma for the fear of harming the fetus through drug exposure.
The effect of asthma on pregnancy:

- Severe & poorly controlled asthma have a detrimental effect on pregnancy including:
  - intrauterine growth restriction
  - hypertensive disorders
  - preterm labour
  - intrauterine fetal death.
Labour and delivery: are not usually affected by asthma and attacks are uncommon in labour.

Postpartum, there is no increased risk of exacerbations and those whose asthma deteriorated during pregnancy have usually returned to pre-pregnancy levels by three months after birth.
Management of asthma in pregnancy:

- Same as in non-pregnant patient. Prevention is the key & known triggers of exacerbations should be avoided.

- Short-acting & long-acting beta2-agonists, inhaled steroids & theophylline can be used in pregnancy. These drugs will suffice for mild to moderate asthmatics.

- Epinephrine should be avoided in the pregnant patient. It can lead to possible congenital malformations, fetal tachycardia, and vasoconstriction of the uteroplacental circulation.
Women with more severe asthma who have stabilized on leukotriene receptor antagonist may continue them through out pregnancy.

Prednisolone is the oral steroid of choice in pregnancy, as 88% of it is metabolized by the placenta, limiting fetal exposure. The teratogenic risk & possible harmful fetal effects of maternal steroid treatment remain an area of controversy.
Managing pregnancy in asthmatic patients:

- For those with poorly controlled or severe asthma, care should be multidisciplinary.
- Baseline investigations, such as peak flow measurements should be obtained at booking.
- Medical treatment should be optimized, with repeated reassurance about the use of necessary drugs in pregnancy.
- Women taking Prednisolone should be screened for glucose intolerance.
Labour & delivery:

- Parenteral steroid cover may be needed for those who are on regular steroids.

- Regular medications should be continued throughout labour.

- Bronchoconstrictors, such as ergometrine or prostaglandin F2α, should be avoided.

- Adequate hydration is important.

- Regional anaesthesia favoured over general, to decrease the risk of bronchospasm, provide adequate pain relief and to reduce oxygen consumption and minute ventilation.
Breast feeding is not contraindicated with any of the medications used although high-dose oral steroid use (≥ 40 mg per day) carries a risk of neonatal adrenal suppression.