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Jaundice in pregnancy

Jaundice in pregnancy, whilst relatively rare, has potentially serious consequences for maternal and fetal health. It can be caused by pregnancy or occur intercurrently. Causes of jaundice specific to pregnancy include:

- Pre-eclampsia associated with HELLP syndrome (= haemolysis, elevated liver enzymes and low platelet count).
- Acute fatty liver of pregnancy.
- Hyperemesis gravidarum.
- Intrahepatic cholestasis of pregnancy.

The presenting clinical features of liver disease in pregnancy are often nonspecific and consist of jaundice, nausea, vomiting and abdominal pain. All liver diseases occurring during pregnancy can lead to increased maternal and fetal morbidity and mortality^[1].

Acute viral hepatitis^[2]

Viral hepatitis is the most common cause of jaundice in pregnancy with infections due to hepatitis A, hepatitis B, hepatitis C, hepatitis D and hepatitis E viruses.

The incidence of hepatitis in pregnancy varies greatly around the world; in developed countries the incidence is around 0.1%, whilst in developing countries it can range from 3-20% or higher.

• Hepatitis A is most prevalent in developing countries. 1:1,000 pregnant women are infected with acute hepatitis A virus (HAV). The disease is mostly self-limited, with mortality of 0.3% to 0.6%.

- Hepatitis B affects more than 250 million individuals worldwide and is the most common cause of chronic hepatitis worldwide. Sixty-five million women of childbearing age are infected with chronic hepatitis B virus (HBV). About 800,000 to 1.4 million people are infected with HBV in the USA. There is a 0.7% to 0.9% prevalence of chronic HBV infection among pregnant women in the USA.
- Hepatitis C virus (HCV) affects more than 170 million people worldwide. About 8% of pregnant women are infected with HCV. The estimated prevalence of antenatal HCV infection in the USA is 1% to 2.5%.
- Hepatitis D virus (HDV) affects 15-20 million people worldwide with HBV carriers. New studies estimate the prevalence of hepatitis D to be closer to 62-72 million. The prevalence of HDV in the USA is estimated to range from 2% to 50%, depending on the patient population. The prevalence of HDV in a study in Pakistan revealed an estimated 20.63% in pregnant women with chronic HBV infection.
- Hepatitis E virus (HEV) affects about 20.1 million new infections. HEV infection is prevalent in developing countries. The course of most viral hepatitis infections is unaltered by pregnancy – the exception is hepatitis E, where pregnant women who contract the disease exhibit fatality rates of 10–20%.

Hepatitis A

See the separate Hepatitis A article for further information.

- Isolate the infected patient to prevent spread.
- Symptomatic treatment includes maintenance of adequate hydration and nutrition.
- Pregnant women exposed to the virus can be given immune globulin within two weeks of exposure, together with vaccine.
- It is not clear if the virus is transmitted from mother to baby but, if the illness has occurred in the final month of pregnancy, the neonate should receive immune globulin.

Hepatitis B

See the separate Hepatitis B article for further information.

- This is the most common cause of acute viral hepatitis in pregnancy and can occur in acute, subclinical or chronic form.
- The presence of HBeAg is associated with a very high risk of neonatal infection.
- All women should now be offered hepatitis B screening as part of routine antenatal screening.
- Infants of HBsAg-positive women should receive hepatitis B immune globulin immunoprophylaxis at birth and hepatitis B vaccine at 1 week, 1 month and 6 months of age. This regime reduces the incidence of hepatitis B vertical transmission to less than 3%.
- The prevalence of neonatal infection depends on the time during gestation that maternal infection takes place: rare in the first trimester, 6% in the second trimester and 67% of those in the third trimester.

Hepatitis C

See the separate Hepatitis C article for further information.

- No therapy has been shown to influence the neonatal transmission of HCV.
- Interferon should not be used during pregnancy because of possible adverse effects on the fetus.

Hepatitis D

This develops as a co-infection with hepatitis B. When present, it increases the incidence of acute hepatic failure.

Hepatitis E

- This is rare in the developed world but, in developing countries (where it is more common), it is responsible for a high level of fulminant hepatic failure and mortality in pregnant women.
- In India it appears to be associated with a higher maternal mortality rate and worse obstetric and fetal outcomes compared with other causes of acute viral hepatitis in pregnancy.

Cholelithiasis in pregnancy

Symptomatic gallstone disease occurs in approximately 1 in 2,000 pregnancies^[3].

Pregnancy alters bile composition and gallbladder emptying slows in the second trimester, increasing the risk of gallstones.

Individual risk factors are multiparity and previous gallbladder disease.

Presentation

Symptoms are similar in pregnant and non-pregnant women:

- Pain in the right upper quadrant or epigastrium, peaking at 12-24 hours.
- Pain may radiate towards the back and there may be epigastric or right upper-quadrant tenderness. Murphy's sign (right-sided tenderness at the tip of the 9th costal cartilage as the patient breathes in) is much less common in pregnancy.

Management

Obstructive jaundice requires surgical intervention, usually via laparoscopic cholecystectomy. There is an associated fetal loss of approximately 6%.

Chronic liver disease

Chronic liver disease in pregnancy is associated with an increased risk of fetal loss:

- In patients with primary biliary cirrhosis (PBC), ursodeoxycholic acid can be safely continued. Cholestasis may worsen during pregnancy with PBC^[4].
- Infants of patients with marked hyperbilirubinaemia during pregnancy may require exchange transfusion at birth.

Autoimmune hepatitis^[5]

Autoimmune hepatitis (AIH) in pregnancy is associated with an increased risk of fetal complications and maternal complications. However, data show that the number of pregnancies reported in women with AIH is becoming more frequent due to better clinical management and highquality prenatal and antenatal care. Currently, pregnancy and childbirth in AIH appear to be safe for both mother and child. Azathioprine treatment has been used during pregnancy.

Pre-eclamptic liver disease and HELLP

See the separate HELLP Syndrome article for further details.

This complicates 3-10% of pre-eclamptic pregnancies and the risk of recurrence in future pregnancies is 3-4%.

The most effective treatment for HELLP is prompt delivery.

Acute fatty liver of pregnancy^[6]

Epidemiology

- It is a rare condition with a prevalence of 0.005-0.01%.
- Acute fatty liver of pregnancy (AFLP) tends to occur in late pregnancy.
- Risk factors include first pregnancies, pre-eclampsia, twin pregnancies and male fetuses.
- It may be associated with a mutant gene producing a defect in mitochondrial fatty acid oxidation and infants born to mothers with AFLP should be screened for defects in this system.

Presentation

This usually presents acutely with nausea, vomiting and abdominal pain, fevers, headache and pruritus, beginning typically at about 35 weeks of gestation but can occur much earlier. It may also appear immediately after delivery. Jaundice appears soon after onset of symptoms and can become intense in a large proportion of patients. Fulminant liver failure may follow.

Investigations

- The white cell count is often elevated. There may also be neutrophilia and thrombocytopenia.
- Liver transaminases are moderately high.
- Raised serum bilirubin.
- Abnormal clotting with coagulopathy (prolongation of prothrombin and partial thromboplastin times with depression of fibrinogen levels).

Biopsy would be diagnostic but coagulation problems often preclude it. CT/MRI scanning may show reduced attenuation in the liver.

Management

Consider early delivery, as the condition usually resolves afterwards with complete recovery. Supportive ITU care is frequently required.

Complications

AFLP is a life-threatening condition. To date, there are no reports of spontaneous remission of AFL prior to delivery of the infant. The characteristic course is progression to acute liver failure within one or two weeks, which is characterised by increasing jaundice, hypoglycaemia, development of coagulopathy, ascites/pleural effusions, encephalopathy and acute kidney failure in up to 90% of affected women.

Intrahepatic cholestasis of pregnancy

Intrahepatic cholestasis is defined as pruritus with elevated serum bile acids occurring in the second half of pregnancy, which resolves after delivery.

See also the separate Obstetric Cholestasis article.

Epidemiology

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ICP incidence rate is between 0.2% to 2% of pregnancies ^[7]. It is more common in South American and northern European continents. Research has described ICP in 0.2% to 0.3% of pregnancies in the USA.

Presentation

The main symptom is pruritus, especially of the palms and soles, which is followed by generalised symptoms. This usually occurs from week 25 of gestation.

Jaundice is uncommon. However, when present, it arises 2-4 weeks after the onset of pruritus.

Investigations

- Aminotransferase activity can be increased by 20 times the normal level.
- Raised gamma-glutamyltransferase activity is unusual but is indicative of MDR3 mutation or underlying liver disease unrelated to pregnancy. The key diagnostic test is a fasting serum bile acid concentration of greater than 10 mmol/L.

Management

Ursodeoxycholic acid is the mainstay of medical management, but it has not been shown to reduce adverse perinatal outcomes in women with ICP. Therefore, some call for its routine use for this condition be reconsidered^[8]

Complications

Maternal morbidity results from pruritus and insomnia. The importance of this disorder is the effects on the fetus which can lead to prematurity, perinatal death, fetal distress and stillbirth. ICP often recurs in subsequent pregnancies^[9].

Further reading

- Ibrahimi S, Mroue AA, Francois E, et al; Jaundice in a pregnant woman. Acta Gastroenterol Belg. 2017 Jul-Sep;80(3):422-424.
- Gupta A, Tiwari P, Sachdeva P; A Case of Dubin-Johnson Syndrome in Pregnancy. Cureus. 2019 Feb 11;11(2):e4048. doi: 10.7759/cureus.4048.

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Authored by:	Peer Reviewed by: Dr Colin Tidy, MRCGP	
Originally Published:	Next review date:	Document ID:
20/11/2023	27/09/2021	doc_743

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