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Isolated hepatic disease rarely occurs during pregnancy. A number of associations between hepatic dysfunction and pregnancy exist. Acute viral hepatitis is most common cause of jaundice in pregnancy. The course of acute hepatitis is not affected in pregnancy however hepatitis E virus is associated with increased complications especially in the third trimester of gestation. Women with chronic liver disease exhibit higher risk of fetal loss during pregnancy. Pre-eclampsia associated with HELPP syndrome results in increased maternal and fetal mortality. The liver serves multiple functions: the biotransformation of insoluble compounds (e.g., drugs, toxins, bilirubin), the metabolism and excretion of cholesterol and bilirubin, the production of plasma proteins (e.g. albumin, coagulation factors, alpha- and beta-globulins, transferrin, haptoglobin), and the metabolism of amino acids, carbohydrates and lipids. No single liver function test is available to quantify liver disease. Increased level of AST and ALT determine liver cell necrosis, while synthetic function is quantified by determining albumin level and prothrombin time. Cholestasis and biliary obstruction are evaluated by measuring alkaline phosphatase, bilirubin, 5 - nucleotidase or gamma glutamyl transpeptidase levels¹. In normal pregnancies, increased ALP (up to 3-4 times) is secondary to placental ALP²⁻⁵.

PREGNANCY IN WOMEN WITH PRE-EXISTENT CHRONIC LIVER DISEASE

Cirrhosis and Pregnancy

Cirrhosis is often associated with amenorrhea and infertility. Still if women who do conceive with decompensated cirrhosis have increased risk of serious complication during pregnancy.

15-20% suffer spontaneous abortion. There is an increased risk of premature birth or stillbirth. There are also chances of the liver failure during pregnancy. Bleeding from esophageal varices is probably the biggest pregnancy-related health risk, which is most common during second trimester. So all women with cirrhosis who want to conceive should be evaluated before conceiving and should be put on betablocker, keeping in mind all the risk of beta-blocker to fetus or shunt procedure may be considered.

Chronic Hepatitis B and Pregnancy

Women with chronic hepatitis B do quite well during pregnancy as there is no flare up of disease. Transmission of hepatitis B virus to the fetus during pregnancy is rare because placenta is a very efficient barrier. But if blood leaks into fetus it may cause direct transmission of hepatitis B virus. However, perinatal transmission (during child birth) is very common. It occurs in 90% of these cases if mother is HBsAg and/or HBV DNA positive^{2,10}. The transmission is similar regardless of the mode of delivery. Universal vaccination of all newborns whose mothers are HBsAg +ve, with both the hepatitis B immune globulin (HBIG) shot and the hepatitis B vaccine within 24 hours of birth is now mandatory. This prevents transmission of HBV to infant in approx. 80-90% of the time. Mothers are advised to avoid breastfeeding if they are infectious, even though this mode of transmission is not considered very likely. If the mother has bleeding nipples, the risk of transmission increases. Infact, universal screening of pregnant women for HBsAg is now performed to reduce perinatal transmission of hepatitis B virus¹⁰. Treatment of a pregnant woman with actively infectious chronic hepatitis B should be avoided as medications are teratogenic.

Chronic Hepatitis C and Pregnancy

Women with chronic hepatitis C have normal pregnancy unless the disease has not progressed to decompensated cirrhosis. Transmission of the hepatitis C virus to the newborn is very uncommon. (only 4-7% of the time). Transmission may increase if the woman is HIV +ve or there is presence of high hepatitis C virus load. Invasive procedures like amniocentesis or fetal blood monitoring via scalp vein catheter should be avoided as they increased the risk of transmission. Transmission to the infant is determined by presence of anti-HCV Ab at > 18 months of age due to passive transfer of the antibody from mother during childbirth which will remain till 18 months of age. Detectable levels of HCVRNA is tested after the infant is 2 months of the age. (confirmed at least twice additionally at intervals of 3-4 months apart. Breastfeeding is considered safe unless nipples are traumatized or cracked. Most of the time children cleared HCV spontaneously by 2 years of age. Treatment of mother with hepatitis C should be delayed until after delivery as all drugs are teratogenic.

Autoimmune Hepatitis (AIH) and Pregnancy

Severe AIH causes amenorrhea, so patient cannot become pregnant. However treatment with corticosteroids and azathioprine, menstrual cycles usually return to normal and pregnancy can occur with normal delivery. Flare-ups of AIH may occur during pregnancy but it is rare due to immunosuppressive effects of pregnancy. Infact, pregnancy may sometime cause remission of AIH. To avoid flaring up of AIH, low dose prednisone and azathioprine may be used but azathioprine should be discontinued as early as possible. Other medicines like ursodeoxycholic acid and cholestyramine are safe during pregnancy. Although rare, stillbirth and premature labor have been reported among women with AIH. Conservative management during pregnancy, which should include fluid and sodium restriction and the elimination of all unnecessary medications, enhances the likelihood of a normal delivery.

ALCOHOLIC LIVER DISEASE (ALD) AND PREGNANCY

Women with alcoholic liver disease are often infertile. Women with ALD who do become pregnant and continue to drink alcohol cause fetal alcohol syndrome in their infants. Infants with fetal alcohol syndrome have enlarged, scarred livers and elevated transaminase levels. Other abnormality often found in these newborns include mental retardation, delayed maturity and growth, defects in the skull, face and brain.

PRIMARY BILIARY CIRRHOSIS (PBC) AND PREGNANCY

Women with PBC usually have uneventful pregnancies and deliveries. But some have reported increase chances of complications like abortion, miscarriage and worsening liver function. These events occur in women with advance liver disease. Pruritus can worsen during pregnancy may be treated with cholestyramine. Ursodeoxycholic acid use to treat PBC is safe during pregnancy.

LIVER TUMORS AND PREGNANCY

Most liver tumors found in women who are of childbearing age are benign—like hepatic adenomas, focal nodular hyperplasia and hemangiomas. These tumor enlarge and rupture due to high level of estrogen, which can occur during pregnancy. Fortunately, such complications are rare. If rupture does occur, immediate treatment is surgery. Surgical resection of large liver tumor (greater than 5 cm) should be considered prior to becoming pregnant.

LIVER DISEASE THAT MAY DEVELOP DURING PREGNANCY

Viral hepatitis is the most common cause of jaundice in pregnancy.¹ Course of hepatitis infection (A, B, C and D) is unaffected by pregnancy^{2,3} however more severe course of viral hepatitis in pregnancy has been noted in hepatitis E and herpes simplex virus infection^{4-7, 12,13}.

Other causes of jaundice in pregnancy can be because of gallstones and medications. Gallstones commonly occurs during pregnancy because of change in bile composition predisposed to cholelithiasis^{8,9}. During second trimester, gallbladder emptying slows and there is a fall in bile salt pool leading to increase in biliary cholesterol resulting in lithogenic bile.

ACUTE VIRAL HEPATITIS AND PREGNANCY

Hepatitis A: Course of disease is not affected by pregnancy. Transmission to newborn is rare. When transmitted dose not cause any increased risk of miscarriage or fetal abnormalities.

Hepatitis B: Course of infection is not affected by pregnancy. Transmission of hepatitis B virus to the newborn commonly occur during childbirth when the baby passes through the birth canal. This happens approx. 10-20% of the time, in cases where the mother is HBsAb +ve and HBV DNA -ve during the third trimester. The risk of transmission increases to 90% if mother is HBsAg +ve and HBV DNA +ve^{2,10}. Therefore,

universal screening of pregnant women for HBsAg is performed to reduce the prenatal transmission of Hepatitis B viruses. Newborn infected with HBV usually have no symptoms, but they typically develop either chronic hepatitis B or become chronic carriers of the virus. Therefore, any newborn whose mother is HBsAg +ve should receive the hepatitis B immune globulin shot and hepatitis B vaccination. For women exposed to HBV during pregnancy, the immune globulin shot and hepatitis B vaccination — both of which have been shown to be safe and effective for pregnant women — should be obtained.

Hepatitis C: Hepatitis C does not adversely affect the outcome of pregnancy. Course of hepatitis C is also not affected by pregnancy. The risk of transmission of HCV to the newborn is extremely low (0.18%)¹¹. This risk of transmission increases when there is coinfection with HIV. Unfortunately there is no protective vaccination available.

Hepatitis E: Hepatitis E virus is a water borne virus, occurs most commonly in third-world countries, and has a very severe course in the pregnant women. It results in fulminant hepatitis in 20% of pregnant women and 20% pregnant women who acquire this infection in third trimester die as a result. Hepatitis E also increases incidence of fetal complications and fetal death. At present there is no vaccination or treatment for hepatitis E virus.

OTHER NON-HEPATOTROPIC VIRUSES

Herpes simplex virus and varicella zoster virus pose a threat to both mother and child. Most of them occur in the late second and third trimester with only half having established characteristic mucocutaneous lesions¹⁵. Disseminated HSV infection is associated with prodromal systemic illness, vesicular skin rash, and leucopenia. Maternal and fetal mortality rate is 50% without treatment. Acyclovir effectively treats early disseminated HSV infection.

CHOLELITHIASIS IN PREGNANCY

Cholelithiasis is common in pregnancy (6%) because of changes in bile pool composition and slow emptying of gall bladder in second trimester. Symptoms of cholelithiasis are similar in pregnant and non-pregnant patient⁸. Ultrasound abdomen is most helpful in determining the presence of cholelithiasis⁸. Surgical treatment of biliary colic can be safely accomplished in second trimester¹. Surgery during first trimester may lead to spontaneous abortion. Surgery should be avoided in third trimester because of increase in size of uterus⁸.

PREGNANCY SPECIFIC LIVER DISEASE

Intrahepatic Cholestasis of Pregnancy

Intrahepatic cholestasis of pregnancy occurs in 0.01% of pregnancies. It mostly occurs in third trimester of gestation. Although it has been reported as early as 13 weeks of pregnancy. Pruritis, jaundice and steatorrhea is common presentation in these cases. Serum bilirubin is raised < 5 mg% and transaminase levels remain normal or slightly elevated. Ursodeoxycholic acid given at the doses of 15 mg/kg/day has been found useful in cholestasis of pregnancy. Cholestyramine binds bile acids and may improve pruritis; however, it may exacerbate steatorrhea. Intrahepatic cholestasis of pregnancy is associated with increased incidence of prematurity and perinatal mortality.

Preeclampsia

Liver dysfunction in preeclampsia is well recognized more so in HELLP syndrome (hemolysis, elevated liver enzymes and low platelet count). Pathophysiology in HELLP syndrome reflects that of preeclampsia, with microvascular damage, platelet activation and vasospasm. Histopathology of liver reveals periportal hemorrhage and fibrin deposition. Nitric acid metabolism may also contribute to preeclampsia and HELLP syndrome. The maternal mortality is 2% and perinatal mortality is 33% in these cases. Acute liver rupture and DIC is a common complication. The most effective treatment of HELLP syndrome is prompt delivery. Postpartum steroid therapy may help in improving platelets.

Acute Fatty Liver of Pregnancy

Acute fatty liver in pregnancy complicates third trimester and is commonly associated with eclampsia^{10,13}. Although rare it is a life threatening condition with an 18% maternal and 23% fetal mortality risk¹⁴. Symptoms associated with acute fatty liver of pregnancy include anorexia, nausea, emesis, abdominal pain, jaundice, headache and CNS disturbances^{10,14}. The laboratory abnormalities include moderate elevation of AST, ALT, usually < 1000 IU per L, prolongation of prothrombin time and partial thromboplastin time, decreased fibrinogen levels, renal failure, hypoglycemia and raised bilirubin level of 1-10 mg% . The treatment of acute fatty liver of pregnancy is expeditious delivery and intensive care. Patient usually improve promptly following delivery and in the absence of long chain 3 hydroxy acyl CoA dehydrogenase deficiency, the prognosis in pregnancies with acute fatty liver of pregnancy is good.

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