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REVIEW ARTICLE

Gastrointestinal and Other Hepatic Disorders in Pregnancy (Related Liver Disorders), Dysfunction in Pregnancy

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Abstract:

One of the least studied motifs in the field of obstetrics is liver complaint during gestation, which creates a challenge for both gynecologists and hepatologists. Roughly 3 of pregnant women are affected by some form of liver complaint during gestation. Some of these conditions can be fatal for both the mama and child. In addition, 3 types of liver complaints need to be discerned during gestation. One type is liver complaint directly related to gestation, which can do at a specific time during gestation. Another type is a liver complaint not related to gestation, which can do at any time, similar to viral-or medicine- convinced hepatitis. Likewise, gestation can do in women with pre-existing liver complaints. It's essential that the clinicians are familiar with this complaint so they can respond instantly and appropriately in all of these situations, especially when emergency delivery is demanded and must not be held up.

Keywords: Pregnancy, Liver, Pregnant women, Hepatitis

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Introduction

The most common cause of liver dysfunction in pregnancy is pregnancy-related liver disorders, which affect up to 3% of pregnant women. When they are severe, they are linked with considerable morbidity and mortality in both the mother and the child [1-5]. To facilitate effective care, a rapid evaluation is required to distinguish them from non-pregnancy-related liver dysfunction [4].

Hepatitis

Viral hepatitis is the most common type of liver disease globally, and it usually affects women of childbearing age, either as an acute infection or as a chronic condition, and it can have severe consequences for both the mother and the fetus [4,6,7].

Hepatitis A Virus

It is a small, non-enveloped RNA virus transmitted by feco-oral transmission. It is not associated with chronic infection, and the incubation period is 2-7 days. It does not usually cause major maternal or neonatal morbidity [3,8]. Acute infection in the third trimester is linked with pre-term labor. In utero transmission is rare and causes fetal meconium peritonitis in the first trimester and asymptomatic infection/self-limiting neonatal cholestasis in the third trimester. Vaccination is recommended for women at risk and Supportive treatment in acute infection [9].

Hepatitis B Virus

It is a double-stranded DNA virus with 8 known serotypes. The virus is transmitted through unprotected sex and intravenous drug use in low prevalence areas, and mother to child transmission in high prevalence areas. It can present as an acute or chronic infection. All pregnant women should be screened for the hepatitis B virus. Vaccination should be administered to anti-HBsAg-negative women who are at high risk. Pregnancy does not affect the course of acute or chronic infection. There is no link to congenital malformations or stillbirth. Supportive treatment in acute infection and nucleoside analogs can be used in fulminant infection or long-term severe infection. There is limited evidence for antiviral agents in pregnancy and no evidence to support routine elective cesarean section. Although the virus is present in breast milk, breastfeeding does not enhance the risk of transmission. HBV vaccine and immunoglobulin should be given to infants.

Hepatitis C Virus

It is an RNA virus with six known genotypes. The blood-borne virus is most commonly acquired through intravenous drug use in adults and mother-to-child transmission in children. HIV co-infection increases the risk of mother-to-child transmission. Acute or chronic infection can occur [10,11]. High-risk women must be screened. Pregnancy does not affect the course of infection. It is linked with an increased risk of intrahepatic cholestasis of pregnancy. There is no association with congenital malformations or stillbirth. Antiviral therapy is not recommended during pregnancy due to the risk of teratogenicity. There is no evidence to support the use of an elective cesarean section. HCV viremia, prolonged rupture of membranes (>6 hours), and intrapartum exposure to maternal blood are associated with mother-to-child transmission. Use fetal scalp electrodes and avoid prolonged rupture of membranes. Although the virus is present in breast milk, breastfeeding does not enhance the risk of transmission [6].

Hepatitis E Virus

It is an RNA virus. The route of transmission is unclear but most likely water-borne. Although it usually produces acute self-limiting hepatitis, pregnant women are more susceptible to infection and have a higher risk of fulminant hepatic failure. The rate of maternal mortality is up to 26%. Mother-to-child transmission may occur in utero or directly. Transmission in the third trimester is linked with a risk of neonatal hepatic necrosis and neonatal death. Not linked with chronic infection, congenital malformation, or stillbirth. It is associated with pre-term delivery, and management is supportive.

Chronic Liver Disease and Portal Hypertension

Women with severe chronic liver disease and cirrhosis frequently have anovulatory menstrual cycles or are amenorrheic, and therefore are unlikely to conceive. In pregnant women with noncirrhotic portal hypertension aggravated by physiologic increases in circulating blood volume, portal hypertension, ascites, and compensatory dilatation of submucosal esophageal veins connecting the portal circulation to the azygos vein might occur. These esophageal venous collaterals can become engorged during pregnancy due to normal circulatory changes, such as increased blood flow and compression of the inferior vena cava by the growing uterus, and can be detected on endoscopy even if there are no pathologic causes of portal hypertension. The latter type of enlarged veins does not bleed spontaneously. In those with underlying portal hypertension, normal pregnancy-related increases in maternal blood volume appear to increase the risk of variceal bleeding (Figure 1) [10,12,13].

Esophageal variceal bleeding has been documented in 18% to 32% of cirrhotic pregnant women, as well as 50% of those with known portal hypertension and 78% of those with pre-existing varices. According to reports published between 1950 and 1980, in addition to variceal bleeding, women with chronic liver disease and portal hypertension who become pregnant are at an increased risk of death, hepatic decompensation, splenic artery rupture, and uterine hemorrhage. Preeclampsia, pre-term delivery, low birth weight, and neonatal mortality appear to be considerably increased by cirrhosis.

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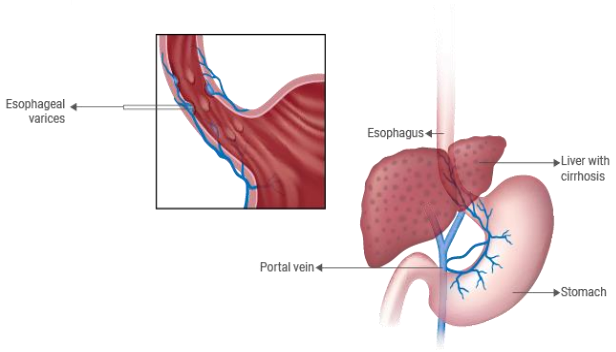

Figure 1: Esophageal Varices

Management

Although no trials of its safety and efficacy in this setting have been done, endoscopic band ligation is widely considered as the appropriate initial therapy for variceal bleeding in pregnant women. Infusions of the somatostatin analog octreotide, which is efficacious in non-pregnant individuals, are also employed. Infusions of vasopressin and octreotide have the potential to cause uterine ischemia and premature labor. When variceal bleeding cannot be controlled by other means, a transjugular intrahepatic portosystemic shunt may be indicated, despite the risks of associated radiation exposure.

β-Adrenergic receptor antagonists are tocolytic; however, they do not repress normal labor in pregnant women who have been on medication for a long time. Beta-blockers have not been formally tested as a main prophylactic against variceal bleeding in pregnant women. To reduce the risk of bleeding from varices during pregnancy, some authors recommend prophylactic band ligation, portosystemic shunt procedures, and cesarean section. Liver transplantation is the only treatment option for severe hepatic decompensation during pregnancy [14]. During pregnancy, orthotopic liver transplantation has been successfully performed. The MELD score can help in predicting clinical decompensation in a cirrhotic woman during gestation.

Wilson's Disease

Wilson's disease is a rare genetic autosomal recessive disorder of copper metabolism and is characterized by copper accumulation in the liver and other organs (Figure 2). This results in cirrhosis, liver failure, psychiatric and neurological problems. Wilson disease is associated with amenorrhea and infertility in women of childbearing age.

Management

Treatment to eliminate excess copper from affected individuals may result in the resumption of ovulatory cycles and eventual pregnancy. Pregnant patients must remain on medication to treat Wilson disease as discontinuation of treatment can result in abrupt copper release, hemolysis, acute liver failure, and death. Although d-penicillamine has been used successfully during pregnancy at dosages required for copper chelation, it is likely teratogenic in humans. Trientine is also teratogenic in animals but appears to be safe in humans as a copper overload therapy. Because zinc salts like zinc acetate do not appear to be teratogenic, some experts recommend using zinc during pregnancy as a treatment for Wilson's disease.

Autoimmune Liver Diseases

Women are more likely than men to have autoimmune diseases of various types, including autoimmune hepatitis.

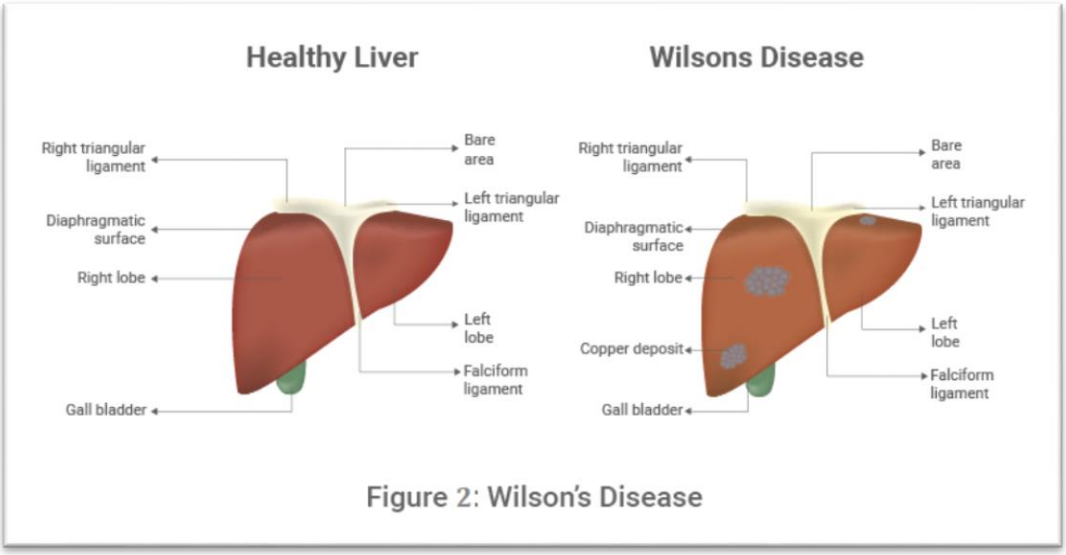

Figure 2: Wilson's Disease

Autoimmune Hepatitis (AIH)

Autoimmune hepatitis may present as hepatitis (acute, chronic) or even cirrhosis. It is characterized by hepatocellular inflammation and necrosis and mostly affects women (3:1 female to male preponderance). There are two presentation peaks (10-30 years and 40-50 years). Fatigue, myalgia, pruritus, nausea, anorexia, and upper abdominal pain are common symptoms of AIH **(Figure 3)**.

Types

AIH has divided into three subtypes: types I, II, and III. Anti-nuclear antibodies or anti-smooth muscle antibodies characterize AIH type I, which is the most common subtype. Unlike type II, which primarily affects children and young women, it affects people of all ages. Anti-liver kidney microsomal antibodies (LKM1, 3-4 %) and seronegativity for

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ANA and SMA characterize Type II. Type II is linked with a more severe phenotype and an increased risk of extrahepatic autoimmune disease. Anti-soluble liver antigen and liver-pancreas antibodies are present in Type III patients. It can account for up to 30% of AIH.

Classic (type I) autoimmune hepatitis in women usually presents around the time of menarche but is often associated with amenorrhea. When women with autoimmune hepatitis become pregnant, they have higher chances of spontaneous abortion and pre-term delivery.

Management

Patients who are affected may experience disease flare-ups throughout pregnancy and after delivery. As a result, women with autoimmune hepatitis who become pregnant should continue to take immunosuppressive drugs. The doses of azathioprine used in normal treatment regimens are not believed to be teratogenic. Patients with autoimmune hepatitis should be closely monitored during pregnancy and after delivery.

Primary Sclerosing Cholangitis (PSC)

It is a chronic inflammatory disease that affects the intrahepatic and extrahepatic bile ducts, causing scarring and blockage of the bile ducts. It can present with cirrhosis or liver failure. Symptoms are typical of cholestasis, including jaundice, chronic fatigue, pruritus, and malabsorption. Males are more likely than females to develop PSC (2:1 male to female preponderance), with a peak age of diagnosis between 20 and 30 years. Although there are no particular antibodies for PSC, peri-nuclear anti-neutrophil cytoplasmic antibodies are found in 80% of those affected, and anti-nuclear antibodies or anti-smooth muscle antibodies are found in 20% to 50% of those affected. PSC is associated with ulcerative colitis, and inflammatory bowel disease is present in up to 70% of cases. PSC is linked with increased risks of worsening liver function either during pregnancy or after delivery. Treatment with Ursodeoxycholic acid may help to reduce this risk. Nutrition should be optimized, and women should be encouraged to take vitamin supplements to avoid malabsorption, especially fat-soluble vitamins.

Primary Biliary Cholangitis (PBC)

It is an autoimmune disease characterized by the progressive destruction of small bile ducts resulting in cirrhosis. Although the symptoms are similar to those of PSC, PBC is a disease that primarily affects women (9:1 female to male preponderance). It usually appears in middle age (35-55 years); however, it can also be diagnosed in reproductive-age women. Extrahepatic autoimmune diseases are frequently associated with PBC, and up to 80% of people affected have another autoimmune disease. Antimitochondrial Antibodies (AMA) are found in 90-95% of patients with PBC. In up to 35% of cases, Anti-Nuclear Antibodies (ANA) are also positive. During pregnancy, women with PBC may suffer an increase in pruritus. Treatment with ursodeoxycholic acid can help with pruritus, while the safety of this therapy during pregnancy has not been proven. Maternal nutritional status should be optimized, and women should receive vitamin supplementation.

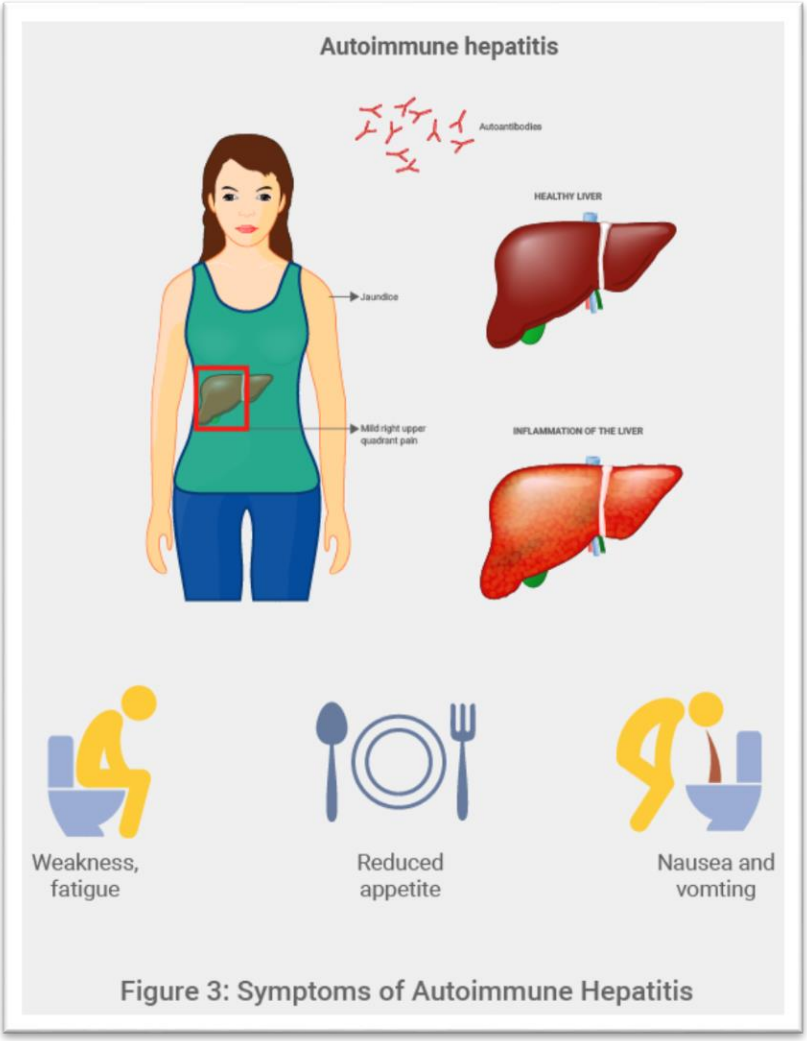

Figure 3: Symptoms of Autoimmune Hepatitis

Hepatic Tumors and Mass Lesions

During pregnancy, mass-like abnormalities of the hepatic parenchyma can be identified as an incidental finding on an ultrasound. Adenomas, focal nodular hyperplasia, and hemangiomas are common benign liver lesions in women of childbearing age. Hepatic adenomas are linked with the use of oral contraceptives and can enlarge during pregnancy, bleeding and rupturing into the abdominal cavity. Hemorrhage has also been reported in pregnant women with focal nodular hyperplasia and hemangiomas. Women who have a benign hepatic nodular defect should have a serial ultrasound evaluation to measure the size of the tumor and search for signs of intralesional hemorrhage. Hepatocellular

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carcinoma is generally exclusively found in adults with chronic liver disease; however, it can also appear in young people with chronic HBV infection without cirrhosis.

During pregnancy, at-risk patients should receive routine liver cancer screening. It's important to remember that maternal serum AFP levels are always slightly elevated during normal pregnancy, and they can rise even higher in cases of fetal Down syndrome, neural tube defects, and hydatidiform mole, lowering the positive predictive value for detecting hepatocellular carcinoma during pregnancy. Pregnant women have been observed to develop hepatic fibrolamellar carcinoma. Fibrolamellar carcinoma is a type of liver cancer that grows slowly and is most commonly encountered in young persons (median age, 25 years). Unlike conventional primary liver cancer, this neoplasm has no known link to cirrhosis or chronic liver disease, and it is not linked to elevated AFP levels in the blood. It is an aggressive neoplasm with a 5-year survival rate of less than 50%. In women of reproductive age, hepatic metastases from other malignancies are uncommon.

Pregnancy After Liver Transplantation

After a successful orthotopic liver transplant, women of reproductive age may become pregnant and deliver normal infants. Delaying pregnancy until the second year after transplantation may reduce the risk of pre-term. During pregnancy, transplant patients must continue immunosuppressive therapy, although their treatment may need to be modified. Many post-transplant immunosuppressive regimens contain mycophenolate mofetil, which is highly teratogenic and should be avoided by women of childbearing age who may become pregnant. Other immunosuppressive drugs' side effects, such as hypertension and hyperglycemia, have been linked to an increased risk of fetal distress and pre-eclampsia in pregnant liver transplant recipients. Organ rejection has caused pregnancy complications in a few cases.

Conclusion

Liver disease during pregnancy and pregnancy in women with liver disease is uncommon. However, because of the increased morbidity and mortality for both the mother and the baby, this is a clinically important patient group. The range of disease and its manifestations is vast, resulting in delays in diagnosis and treatment. Viral hepatitis is the most common type of liver disease and usually affects women of childbearing age, either as an acute infection or as a chronic condition, and it can have severe consequences for both the mother and the fetus. Esophageal variceal bleeding has been documented in cirrhotic pregnant women, those with known portal hypertension, and pre-existing varices. Wilson's disease is a rare genetic autosomal recessive disorder of copper metabolism and is associated with amenorrhea and infertility in women of childbearing age. Women are more likely than men to have autoimmune diseases of various types, including autoimmune hepatitis. During pregnancy, mass-like abnormalities of the hepatic parenchyma can be identified as an incidental finding on an ultrasound. Adenomas, focal nodular hyperplasia, and hemangiomas are common benign liver lesions in women of childbearing age. After a successful orthotopic liver transplant, women of reproductive age may become pregnant and deliver normal infants. Delaying pregnancy until the second year after transplantation may reduce the risk of pre-term.

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