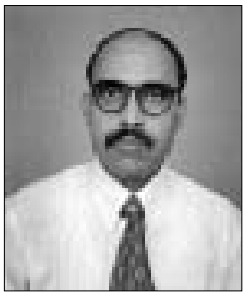

Viral Hepatitis in Pregnancy

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ABSTRACT

Viral hepatitis in pregnancy deserves special attention because it is likely to affect the health of both mother and infant in addition to influencing the parturition. Proper knowledge of this will help in preventing the maternal and perinatal mortality.

This may be acute or chronic and may be due to HAV, HBV, HCV, HDV, HEV or even due to herpes virus and CMV. Of these, only HEV has an increased predilection for pregnant women and the outcome can also be fatal for the mother (ALF) and the child (premature delivery, abortion and fetal abnormality). HAV, HBV, and HCV do not alter the course of pregnancy nor their course is altered by it (pregnancy). Vertical transmission to the infant is common in HBV and less often on HCV. HIV co-infection and the high viral load in the mother is a major determinant of this. Human hyperimmune globulin and vaccine to the pregnant mother alongwith Lamivudine therapy in late pregnancy prevent the vertical transmission of HBV effectively. Caesarian section with an intention to reduce transmission is no more advisable. Though HAV and HBV may cause premature labour, no significant fetal abnormality is noticed. Management of the hepatitis is similar as in non-pregnant state. Of the specific antivirals, only Lamivudine is safe in pregnancy.

Finally, breast-feeding is not contraindicated in any of the viral hepatitis except in HBV infection when it can still be advised with adequate immunoprophylaxis of the mother and the infant.

Viral Hepatitis is a major health concern affecting millions of people worldwide. In pregnancy, viral hepatitis assumes special importance. In addition to the morbidity and mortality in mother it influences the process of parturition and is also likely to be transmitted to the fetus.

Viral hepatitis can be acute or chronic and can be due to the hepatotropic viruses (A, B, C, D, E) or non-hepatotropic viruses (Herpes and cytomegalovirus). The clinical picture, prognosis and management depends a lot on the abovementioned factors.

The prevalence of viral hepatitis in pregnancy has been showed differently by different groups. Khuroo, et al showed the %age of pregnants among sporadic AVH women of child bearing age to be 28.7%,[1] but later in 2003 they found this to be 18.4% [2] and Tsega, et al [3] had found this to be 48%. In all these studies, most of these cases were in their third trimester. Aetiologically most of these are due to HEV followed by NonA-E, HBV, HAV and HCV.[1-3] Only HEV has an increased attack rate in pregnant women.[2]

CLINICAL FEATURES

Acute Viral Hepatitis

It is the result of parenteral or enteral exposure to a hepatotropic virus. After a variable gap (called incubation period) the virus spreads from the point of entry to hepatocytes and excites a host immune response, which in almost every type of acute hepatitis is the cause of liver cell injury. Damaged hepatocytes release enzymes (AST and ALT) into the blood which becomes abnormal one week before and peaks approximately one week after the symptoms develop. All persons exposed to hepatitis virus do not develop clinically apparent disease; only a small percent have severe grade symptoms resulting in fulminant hepatic failure and the rests have a milder acute hepatitis. Persons with clinical viral hepatitis initially have nonspecific complaints viz: fatigue, malaise, anorexia, headache, myalgias and low grade fever. If the illness resolves before there is sufficient liver cell injury to cause jaundice, it may be mistaken for flu-like viral syndrome or even for the normal physiological effects of pregnancy itself. There is jaundice and invariably hepatomegaly. Splenomegaly is present

only in ten percent of cases. Coagulopathy and encephalopathy are seen in rare situations of fulminant hepatic failure, which simulates a situation of acute fatty liver of pregnancy.

Chronic Viral Hepatitis

In most affected individuals, it is asymptomatic either indefinitely or until there is sufficient damage to develop end stage liver disease. Some persons experience periodic clinical exacerbations that resemble mild, moderate or even severe acute viral hepatitis. So, many cases of chronic viral hepatitis, therefore, are diagnosed after serum ALT/AST levels are noted to be abnormal. This commonly occurs when an apparently healthy young woman becomes pregnant and consults an obstetrician. Results of other lab tests are usually normal unless there is cirrhosis. Physical examination also may be normal or the patient may have subtle findings consistent with early cirrhosis. Examination of the abdomen is difficult and may be ambiguous in the later stage of pregnancy when the liver and spleen are not palpable and the patients often have physiologic palmar erythema. In the minority of cases who develop end-stage liver disease, clinical features of liver failure are mistaken for hepatic complication of pregnancy. It is uncommon for women with significant pre-existing liver disease to become pregnant.

HEPATITIS A VIRUS (HAV)

The affection of this virus has no special predilection in pregnancy nor the course of disease is affected by pregnancy. The presentation, diagnosis and management are no different than in nonpregnant women.[4] Intrauterine[5,6] and perinatal transmission[7] have been reported. However, maternal HAV infection during pregnancy is not associated with fetal loss or developmental abnormalities. Passive immunization with pooled human serum immunoglobulin, 3 to 6 months before, or within 2 weeks after exposure to HAV attenuates or prevents HAV in 85 to 95% of cases. The IG and the vaccine both are safe in pregnant women.

HEPATITIS B VIRUS (HBV)

HBV infection is no severer in pregnant women than in non-pregnant individuals,[8] although the disease may rarely be fatal in any affected person. Chronic HBV carriers usually have normal pregnancies, unless there is also severe chronic hepatitis or cirrhosis and associated complications.[9]

Ten percent of infants born to women with acute HBV infection during the first trimester of pregnancy are HBsAg positive at birth [10],and 80 to 90% of neonates become HBsAg positive without prophylactic therapy if acute maternal infection develops during the third trimester of pregnancy.[11]

The variable rate of vertical transmission is due to the fact that the placenta acts as an effective barrier to the spread of HBV infection; 85% of neonatal HBV infections are caused by intrapartum exposure to infectious blood and vaginal secretions, and the remaining 15% to hematogenous transplacental viral spread. In the absence of appropriate prophylaxis, 40% of the neonates of HBeAg-negative mothers and 90% of the neonates of HBeAg-positive mothers will develop chronic HBV infection.[12] This makes it mandatory to test HBsAg status of pregnant women.

The infants of potentially infectious mothers are treated with HBV human hyperimmune globulin (HBIG) 0.5ml IM at delivery and simultaneously inoculated with first three injections of HBV vaccine at birth (within 12 hrs.), 1 month and 6 months.

To prevent vertical transmission, pregnant women suspected of having been exposed to HBV infection should be treated with HBIG and inoculated with HBV vaccine; this therapy is safe and effective during pregnancy.[13] Use of Lamivudine from 28th week of gestation in a dose of 100mg/day PO has been safe and efficacious in preventing vertical transmission.[14] However, cesarean section does not show any extra reduction in the incidence of immunoprophylaxis failure in comparison to vaginal delivery.[15]

There is no increase in congenital malformations, stillbirths, abortions or intrauterine malnutrition in comparison to controls[8] even though HBV infection is associated with an increased incidence of prematurity.

HEPATITIS C VIRUS (HCV)

HCV infection during pregnancy does not interfere with normal pregnancy, unless the patient is having cirrhosis. Pregnancy also does not alter the natural course of the infection. Mother-to-infant transmission of HCV is uncommon(7%), except in HIV co-infection, where the neonatal infection rate approach 20%.[16] High maternal viremia, HIV co-infection, infantile hypoxia and intrapartum exposure to virus-contaminated maternal blood increased the risk of HCV transmission during vaginal deliveries[17]. However, in ten years follow up it has been shown that, vertically transmitted HCV rarely induce chronic hepatitis and most of the infants have good outcome.[18]

HEPATITIS D VIRUS (HDV)

Most patients with chronic HDV have hemophilia or a history of IVDU. Perinatal transmission of HDV is rare, and there is no documented case of vertical transmission of HDV in United States.[19]

HEPTITIS E VIRUS (HEV)

Unlike other hepatotropic viruses, HEV poses a significantly increased attack rate in pregnant women. Clinical illness develops in 70-80% of infected individuals and may be mild to severe. Fulminant hepatic failure occurs in upto 20% of pregnant patients but in nonpregnants it is only 1%.[1] Similarly, overall fatality rate of HEV is 0.5% to 4% , but in 2nd trimester it is 8.5% and in 3rd trimester it is 21%. The reason why this virus causes severe disease in pregnant women is unknown. An increased frequency of abortion and fetal complications also has been described, and vertical transmission has been reported.[20-22]

OTHER NON-HEPATOTROPIC VIRUS

Herpes simplex virus and Varicella zoster virus pose a threat to the mother and child. Most of them occur in the late second and third trimester with only half exhibiting characteristic mucocutaneous lesion.[23] Typical features on presentation include prodromal symptoms followed by fever, abdominal pain, nausea and vomiting and an absence of jaundice. Serology, culture or liver biopsy can establish the diagnosis. Maternal mortality rate approaches 40%.[23]

Cytomegalovirus hepatitis is rare during pregnancy. Typical features include fever and chills, abdominal pain, hepatomegaly, markedly raised transaminases and high percentage of circulating atypical lymphocytes.

ANTIVIRAL THERAPY

Acute hepatitis due to the hepatotropic viruses doesn't have any recommended specific antiviral therapy.

For chronic hepatitis due to HBV: *Interferon alpha* is not used possibly for lack of adequate controlled study even though reports of its use in HCV infection does not show significant fetal malformation.[24,25] The safety of *Adefovir Dipivoxil* in pregnancy has not been clearly established.[26] Only *Lamivudine* has been found to be safe and has been advocated in the usual oral dose of 100mg/day for use in pregnancy.[27]

For hepatitis due to non-hepatotropic viruses: Acyclovir is the drug of choice[28] for herpes virus and it is not shown to increase birth defects. Ganciclovir is helpful in the management of cytomegalovirus infection but its teratogenic effect has limited its use.

MULTIPLE VIRAL INFECTION

With multiple hepatitis virus infection the maternal mortality rate, incidence of pregnancy related morbidities are not altered, but incidences of premature rupture of membrane (PROM), premature delivery, fetal distress and neonatal asphyxia increase significantly as compared to single virus infection.[29]

BREAST FEEDING

Mothers with HAV have no restrictions concerning breast feeding.[30] Despite presence of HBV DNA in the breast milk of HBV infected mother, with appropriate immunoprophylaxis, including hepatitis immunoglobulin and hepatitis B vaccine, breast feeding of infants posses no additional risk for the transmission of the virus.[31] Even though HCV is isolated from breast milk, the risk of trnsmission during breast feeding is not known[30] .There are no contrindications to breast-feeding in HEV infection, although scrupulous hand washing is essential.[30]

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