Management of Hepatitis B Virus Infection During Pregnancy

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Introduction

Hepatitis B (HBV) is a partially double-stranded, circular DNA virus belonging to the *Hepadnaviridae* family. There are ten known genotypes (designated A to J) which vary in their geographical distribution. Genotypes A and D are the most prevalent genotypes detected in South Africa, while genotype A is the most prevalent in Kenya.

HBV is a global problem, especially in developing areas. It is most commonly spread by percutaneous or mucosal exposure to body fluids including blood, saliva, semen and vaginal fluid. HBV can survive for long periods of time on environmental surfaces. Approximately one-third of the world's population have been infected with HBV, with more than 250 million chronic infections. An estimated 2.5 million South Africans are chronically infected with hepatitis B virus.

The outcome of infection largely depends on the age of the patient when they are infected. In immunocompetent adults < 5% become chronic carriers, whereas > 90% of perinatally-infected infants will have chronic disease.

Despite the availability of an effective HBV vaccine, the rate of HBV-related hospitalisations, cancers and deaths continues to rise. Approximately 20% to 30% of patients with chronic infection will develop liver cirrhosis and hepatocellular carcinoma after an average of 3 decades, and an estimated 650 000 people die annually due to chronic hepatitis B infection.

Influence of HBV infection on pregnancy

Maternal infection with HBV has not been associated with increased foetal morbidity, including congenital abnormalities, and mortality.

In one case-control study chronic hepatitis B infection (CHB) was associated with an increased risk of gestational diabetes mellitus, threatened preterm labour and antepartum haemorrhage. These complications may be due to the increased levels of pro-inflammatory cytokines associated with CHB. However, these findings could not be confirmed in large population-based cohorts.

Liver cirrhosis in pregnancy has been associated with poor pregnancy outcomes, including a 15% chance of hepatic decompensation, and an increased risk of gestational hypertension, antepartum and postpartum haemorrhage, foetal death, prematurity and intra-uterine growth restriction.

Pregnancy does not typically cause worsening of liver disease in pregnant women, but rare cases of cholestasis and peripartum hepatitis flares have been described.
How is HBV transmitted from the mother to her child?

HBV can be transmitted from the mother to her child intra-uterine, during delivery and postpartum. Transmission during delivery is the main route of mother-to-child transmission (MTCT). Fortunately, administration of HBV vaccine and immunoglobulin (HBIG) to the neonate at birth can prevent infection in more than 90% of infants born to hepatitis B surface-antigen (HBsAg)-positive mothers. Transplacental transmission occurs much less frequently (< 5% of cases), but remains important as it cannot be prevented by the administration of HBV vaccine or HBIG to the neonate at birth. The precise mechanism of postpartum transmission is unclear, but involves close contact between the mother and her child. Breastfeeding is safe during this time, as several studies have shown that it carries no additional risk of transmission.

Risk of perinatal transmission of HBV

In the absence of immunoprophylaxis, 10%-40% of infants born to HBeAg-negative mothers, and 70%-90% of those born to HBeAg-positive mothers will be infected HBV during the peripartum period. Maternal serum HBV DNA level appears to be the most important independent viral risk factor for MTCT. Other risk factors include HBeAg status, amniocentesis, preterm premature rupture of membranes, prolonged uterine contractions during labour, and prior failure of immunoprophylaxis during a previous pregnancy.

How do I prevent mother-to-child transmission of HBV?

Immunoprophylaxis combined with vaccination, as recommended by the World Health Organisation, is the most effective strategy for preventing mother-to-child transmission of HBV, as peripartum transmission is the main route of MTCT. Hepatitis B immunoglobulin (HBIG) should be administered as a single intramuscular dose of 200 IU within 24 hours of delivery. Concurrently, the first dose of HBV vaccine should be given at a separate anatomical site (e.g. opposite arm or thigh). Three further doses of HBV vaccine are required at the regular intervals (6, 10 and 14 weeks), as recommended by the Expanded Programme on Immunisation (EPI SA). This schedule prevents perinatally-acquired CHB infection in up to 95% of cases. Factors that have been associated with the failure of this protocol include younger maternal age, high maternal HBV DNA viral load, HBeAg positivity, and if the infant received less than 3 doses of HBV vaccine.

As a high maternal HBV DNA viral load (> 10 IU/mL) is the single most important risk factor for MTCT, the addition of antiviral therapy during the last trimester of pregnancy will reduce maternal viraemia and consequently may reduce the risk of infection of the infant. Tenofovir disoproxil fumarate (TDF) is the antiviral of choice in pregnant women due to its high anti-HBV potency, high genetic barrier to resistance, and the significant safety data available from the treatment of HIV-infected pregnant women. Lamivudine and telbivudine have also been shown to be safe in pregnancy, but lamivudine monotherapy is not recommended due to its low genetic barrier to resistance, and telbivudine is not currently available in South Africa. Pegylated interferon α is contra-indicated during pregnancy. Antiviral therapy may be stopped 4 to 12 weeks after the birth, unless the patient meets the criteria for long-term treatment of chronic hepatitis B infection. These women should be monitored carefully for at least 6 months as hepatitis B flare-ups have been described after cessation of antiviral therapy.

Administration of hepatitis B immunoglobulin (HBIG) to the pregnant woman during the pregnancy is not effective in preventing MTCT and is therefore not currently recommended.
Can a mother with CHB breastfeed?

There is no additional risk for transmission of HBV through breastfeeding, provided that the infant received the correct course of post-exposure prophylaxis. There are currently no consensus guidelines regarding the continued use of antivirals during breastfeeding.

Follow-up of the infant

Infants should be followed up at 7–9 months of age, and tested for HBsAb to confirm protective immunity, and for HBsAg to determine whether post-exposure prophylaxis has failed to prevent transmission of HBV to the infant.

References:

- National Institute for Health and Care Excellence. Hepatitis B (chronic) - Diagnosis and management of chronic hepatitis B in children, young people and adults, June 2013. Available at: https://www.nice.org.uk/guidance/ch165