Society for Maternal-Fetal Medicine (SMFM) Consult Series: #38: Hepatitis B in pregnancy screening, treatment, and prevention of vertical transmission

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Between 800,000-1.4 million people in the United States and more than 240 million people worldwide are infected with hepatitis B virus (HBV). Specific to pregnancy, an estimated prevalence of 0.7-0.9% for chronic hepatitis B infection among pregnant women in the United States has been reported, with >25,000 infants at risk for chronic infection born annually to these women. Vertical transmission of HBV from infected mothers to their fetuses or newborns, either in utero or peripartum, remains a major source of perpetuating the reservoir of chronically infected individuals globally. Universal screening for hepatitis B infection during pregnancy has been recommended for many years. Identification of pregnant women with chronic HBV infection through universal screening has had a major impact in decreasing the risk of neonatal infection. The purpose of this document is to aid clinicians in counseling their patients regarding perinatal risks and management options available to pregnant women with hepatitis B infection in the absence of coinfection with HIV. We recommend the following: (1) perform routine screening during pregnancy for HBV infection with maternal HBsAg testing (grade 1A); (2) administer hepatitis B vaccine and HBV immunoglobulin within 12 hours of birth to all newborns of HBsAg-positive mothers or those with unknown or undocumented HBsAg status, regardless of whether maternal antiviral therapy has been given during the pregnancy (grade 1A); (3) In pregnant women with HBV infection, we suggest HBV viral load testing in the third trimester (grade 2B); (4) in pregnant women with HBV infection and viral load >6-8 log 10 copies/mL, HBV-targeted maternal antiviral therapy should be considered for the purpose of decreasing the risk of intrauterine fetal infection (grade 2B); (5) in pregnant women with HBV infection who are candidates for maternal antiviral therapy, we suggest tenofovir as a first-line agent (grade 2B); (6) we recommend that women with HBV infection be encouraged to breast-feed as long as the infant receives immunoprophylaxis at birth (HBV vaccination and hepatitis B immunoglobulin) (grade 1C); (7) for HBV infected women who have an indication for genetic testing, invasive testing (eg amniocentesis or chorionic villus sampling) may be offered—counseling should include the fact that the risk for maternal-fetal transmission may increase with HBV viral load >7 log 10 IU/mL (grade 2C); and (8) we suggest cesarean delivery not be performed for the sole indication for reduction of vertical HBV transmission (grade 2C).

Key words: antiviral therapy, breast-feeding, chronic hepatitis, hepatitis B, immunoprophylaxis, vertical transmission, viral load

Introduction

Obstetric providers are challenged continuously with the evaluation of the potential benefits and harms of new diagnostic and therapeutic procedures or treatments for patients (mother and fetus), often in the setting of limited high-quality data (eg, from randomized clinical trials). The purpose of this document is to aid clinicians in counseling their patients regarding the risk and management options available after a positive hepatitis B surface antigen (HBsAg) test result.

What risks and potential impact does hepatitis B infection present during pregnancy?

Between 800,000-1.4 million people in the United States and >240 million people worldwide are infected with hepatitis B virus (HBV).[1] From a global public health perspective, chronic HBV infection is the major source of hepatocellular carcinoma, leading to 50% of cases worldwide and 80% in high-endemic areas for HBV. Specific to pregnancy, an estimated prevalence of 0.7-0.9% for chronic hepatitis B infection among pregnant women in the United States has been reported,[2,3] with >25,000 infants at risk for chronic infection born annually to these women.[4]

While transmission through sexual intercourse and intravenous drug abuse are the major risk factors for acquisition of hepatitis B among adults in the

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United States, perinatal transmission is responsible for up to 50% of HBV infection worldwide (Table 1). Vertical transmission of HBV from infected mothers to their fetuses or newborns, either in utero or peripartum, remains a major source of perpetuating the reservoir of chronically infected individuals globally. It has been demonstrated that prenatal risk factor–based screening alone will miss many chronic HBV infections among pregnant women, thereby missing the opportunity to interrupt perinatal transmission via established neonatal protocols.[1] For this reason, universal screening for hepatitis B infection during pregnancy at the first prenatal visit has been recommended for many years by both the American Congress of Obstetricians and Gynecologists and the US Preventative Services Task Force.[5,6]

In contrast to HBV acquisition in adulthood, which more commonly leads to acute resolved infection and immunity, perinatal/neonatal HBV is more likely to lead to chronic infection and its long-term disease risks. Chronic hepatitis B infection will develop in up to 90% of exposed neonates who do not receive appropriate immunoprophylaxis, in contrast to 10-25% of infected children and only 5-10% of exposed immunocompetent adults. Among all individuals with chronic HBV infection, regardless of the timing of infection, 20% will eventually die from complications of HBV infection including cirrhosis, end-stage liver disease, and liver cancer.[1]

With the exception of the major risk of perinatal transmission (see below), data are insufficient to suggest that acute or chronic HBV infection is associated with adverse pregnancy outcomes such as preterm birth, low birth weight, or gestational diabetes. However, cirrhosis due to chronic HBV may be associated with increased maternal and perinatal death, gestational hypertension, abruption, preterm birth, and fetal growth restriction.[7-13]

How are HBV-infected pregnant women identified and what have been traditional approaches to their pregnancies?

Identification of pregnant women with chronic HBV infection through universal screening has had a major impact in decreasing the risk of neonatal infection. Recent data demonstrate that 95% of pregnant women are currently screened prior to delivery for evidence of chronic HBV infection, with rates of perinatal transmission decreasing significantly over the past 2 decades.[14]

The presence of HBsAg in maternal blood more commonly represents chronic infection than acute infection. While some adults will be identified because of symptomatic illness, the vast majority of chronically infected adults are asymptomatic. The diagnosis of the chronic carrier state is confirmed with persistence of HBsAg and the absence of hepatitis B surface antibody (HBsAb), which is a neutralizing antibody that can be detected after HBV infection has been cleared. HBsAb and HBsAg essentially do not exist together. HBsAb is also detected after successful immunization with the HBV vaccine. **Therefore, we suggest performing routine screening during pregnancy for HBV infection with maternal HBsAg testing (GRADE 1A).** Hepatitis B core antibody, on the other hand, develops in the setting of natural infection, never from immunization, and persists regardless of whether the acute infection is cleared or becomes chronic (Table 2). It is emphasized strongly that pregnancy is not a contraindication to hepatitis B vaccination. Pregnant women who are identified as being at risk for HBV infection during pregnancy (eg, having >1 sex partner during the previous 6 months, been evaluated or treated for a sexually transmitted disease, recent or current injection drug use, or having had an HBsAg-positive sex partner) should be vaccinated.

The most common risk for perinatal HBV infection occurs when the infant comes into contact with infected vaginal blood and secretions at the time of delivery. Invasive procedures during labor and delivery (including internal monitors, episiotomy, and operative vaginal delivery) may theoretically increase the risk of transmission. However, the availability of neonatal HBV immunoprophylaxis is thought to ameliorate these risks, and current opinions do not support altering regular obstetric practices. Elective cesarean delivery has also been discussed as one way to reduce vertical transmission, but it is not recommended since available data are conflicting and of poor quality.[15] **We suggest cesarean delivery not be performed for the sole indication for reduction of vertical HBV transmission (GRADE 2C).** Similarly, in the setting of neonatal HBV immunoprophylaxis, breast-feeding is not contraindicated.[16] Studies have documented no difference in rates of infection between breast-fed and formula-fed vaccinated infants born to HBV-infected women, with rates in both groups between 0-5%.[17,18] **We recommend that women with HBV infection be encouraged to breast-feed as long as the infant receives immunoprophylaxis at birth (HBV vaccination and hepatitis B immunoglobulin) (GRADE 1C).**

TABLE 1
Risk factors for hepatitis B infection

Multiple sexual partners
Intravenous drug use
Household or sexual contacts of HBV carriers
Infants born to HBV-infected women
Patients and staff who work or live in an institutional setting
Hemodialysis patients
Health care workers with contact with patient blood
Persons born in countries with high HBV seroprevalence

HBV, hepatitis B virus.

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