THE PATHCARE NEWS

Hepatitis B and Pregnancy

Acute hepatitis B virus (HBV) infection

Acute viral hepatitis is the most common cause of jaundice in pregnancy. HBV infection during pregnancy is usually mild, not associated with increased mortality or teratogenicity, and should not prompt consideration of termination. Acute HBV infection may lead to perinatal transmission up to 60% if near time of delivery. If the mother remains HBsAg -positive or has detectable serum HBV DNA, the infant should receive HBV immune globulin in addition to the first dose of the hepatitis B vaccine at birth. Treatment is mainly supportive, but tenofovir disoproxil fumarate (300mg daily) – preferred – or lamivudine (100mg daily) are suitable if reduction of viral load is considered.

Chronic HBV infection

Effect on maternal disease

Pregnancy is associated with high levels of adrenal corticosteroids that may modulate immune responses. Thus the following may be seen in chronic HBV:

1. **Hepatic flares** (also in the postpartum period, and related to immune reconstitution during that period), especially in patients that are HBeAg-positive.
2. **Progression of liver disease:** this could be difficult to monitor as normal physiologic changes can mimic features of chronic liver disease. Decompensation can occur in severe flare setting.
3. **HBV DNA** levels usually remain stable.

Pregnancy outcomes

Some controversy exists on whether chronic HBV impacts the newborn. There are possible associations with gestational diabetes mellitus, risk of prematurity, lower birth weight and antepartum haemorrhage.

Women with **cirrhosis** have a significant risk for perinatal complications and poor maternal and fetal outcomes, e.g. intrauterine growth restriction, intrauterine infection, premature delivery and intrauterine fetal demise.

Management

Manage pregnant women in conjunction with a hepatologist.

Consider indications for treatment, duration of treatment, potential adverse effects, risk of drug resistance, accessibility and cost of antiviral agents.Some women with chronic HBV require antiviral therapy to prevent progression of liver disease (eg, those with immune-active hepatitis), while others may be observed.

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- **Indications for antiviral therapy** - The decision to initiate therapy while pregnant depends upon the presence or absence of cirrhosis, HBeAg, and hepatitis B e antibody (anti-HBe), as well as the HBV DNA and aminotransferase levels. (Therefore the viral load and liver function recommendations below).

The indications for antiviral therapy are generally the same as those for patients who are not pregnant; and which is as follows:

Who to treat

- All adults, adolescents and children with CHB and clinical evidence of compensated or decompensated cirrhosis, regardless of ALT levels, HBeAg status or HBV DNA levels.
- Adults with CHB who do not have clinical evidence of cirrhosis but aged more than 30 years AND with persistently abnormal ALT levels AND HBV DNA > 20 000 IU/mL, regardless of HBeAg status.
- Patients co-infected with HIV

Who not to treat but continue MONITORING:

- Defer treatment in persons **without** clinical evidence of cirrhosis AND with persistently normal ALT levels AND HBV DNA < 2000 IU/mL regardless of HBeAg status or age.
- Persons without cirrhosis aged less than 30 years with HBV DNA levels > 20 000 IU/mL BUT persistently normal ALT.
- HBeAg-negative persons without cirrhosis aged 30 or less, with HBV DNA that fluctuate between 2000 and 20 000 IU/mL OR who have intermittently abnormal ALT levels.

Some scenarios may differ. As examples:

- Although antiviral therapy is recommended for most patients with an ALT >2x the upper limit of normal, **women without evidence of cirrhosis may choose to defer therapy until after delivery if they have low viral loads and have mild disease activity** (eg, aminotransferase levels just above the treatment threshold).
- **Women with high viral loads should initiate therapy in the third trimester,** even if the aminotransferase levels are normal, to prevent transmission to their child.
- Monitoring women without indications for antiviral therapy - Women who are not on antiviral therapy during pregnancy should be monitored closely to evaluate for a flare. (every 3 months during pregnancy and for 6 months postpartum)
- HBV DNA should be tested concurrently or when there is ALT elevation. In addition, the HBV DNA should be measured at 26 to 28 weeks to determine if antiviral therapy should be offered to reduce the risk of mother-to-child transmission.
- **Women with cirrhosis** - The management of cirrhosis in a pregnant woman does not differ from that of non-pregnant patients. Obtain a hepatologist's input.

Breastfeeding - Infants who received hepatitis B immune globulin (HBIG) and the first dose of hepatitis B vaccine at birth (within 12 hours) can be breastfed. However, it is i**mportant that the infant complete the hepatitis B vaccine series.** Mothers with chronic hepatitis B who are breastfeeding should also exercise care to **prevent bleeding from cracked nipples.**

Mother-to-Child-Transmission

Risk of transmission

The risk of mother-to-child transmission has been reported to be as high as 90 % without the use of active and passive immunization. Transmission can occur in utero, at birth, or after birth.

The risk of HBV transmission has been significantly reduced with the introduction of universal maternal HBV screening, hepatitis B vaccination of all newborns, and the use of prophylactic hepatitis B immune globulin (HBIG) for infants of HBsAg-positive mothers.

Most infections occur at birth when maternal secretions and blood in the birth canal come into contact with the infant's mucosal membranes. Transplacental transmission appears to cause only a minority of infections.

Risk factors for transmission

The most important risk factors for mother-to-child transmission, despite proper administration of prophylaxis (HBIG and first dose of hepatitis B vaccine given within 12 hours of birth, and completion of hepatitis B vaccine series), appear to be a positive HBeAg and/or a high HBV DNA level in the mother.

The benefit of cesarean delivery in protecting against transmission has not been clearly established. Thus, **the obstetrical approach should not be influenced by the HBV status of the mother.**

Children born to HBeAg-positive mothers remain at risk for HBV infection, even if they receive hepatitis B vaccination and HBIG.

The risk of HBV transmission is rare when maternal HBV DNA is <105 to 106 IU/mL.

Amniocentesis and other procedures

The risk of transmisison following amniocentesis appears to be low, particularly if the mother is HBeAg-negative with a low HBV viral load, and the procedure is done using a 22-gauge needle under continuous guidance. The effect of other invasive procedures during pregnancy (eg, chorionic villus sampling, cordocentesis, fetal surgery) on the risk of transmission is unknown.

Preterm premature rupture of membranes

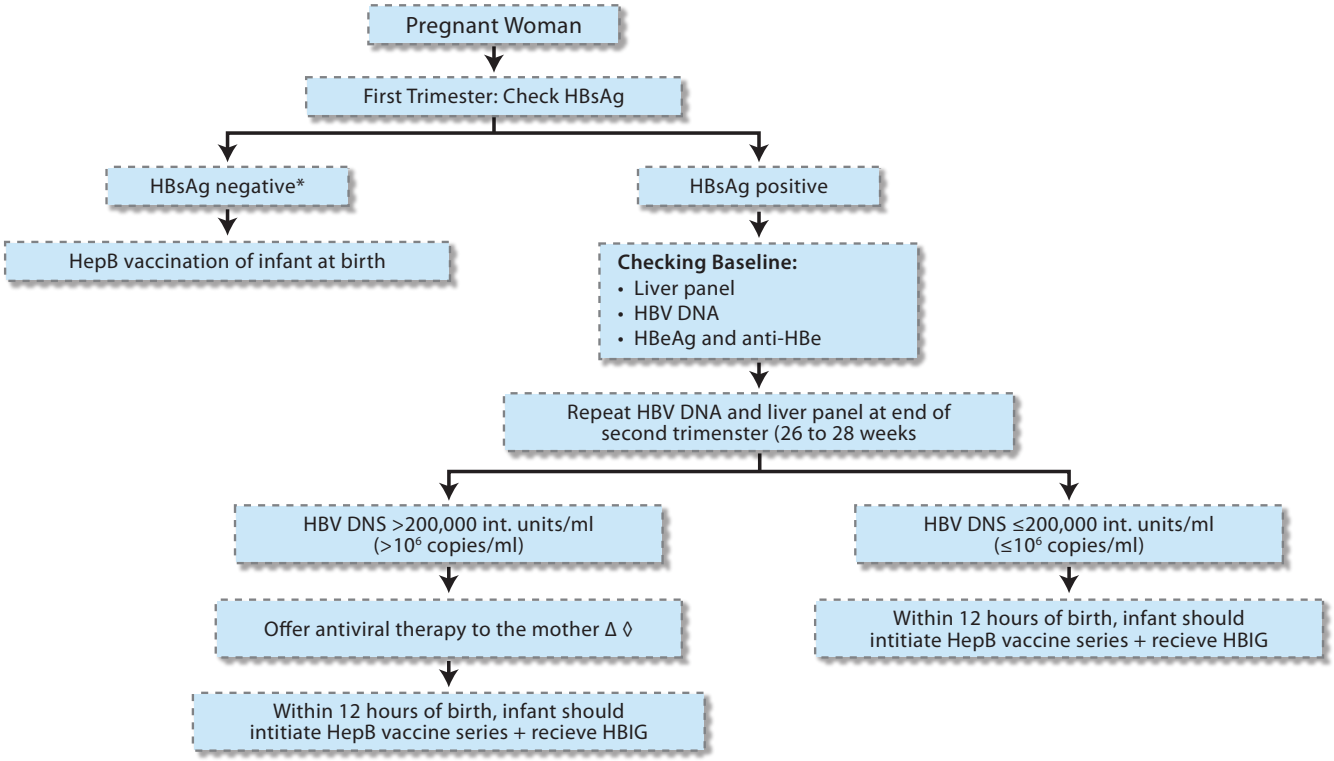
There are limited data that have examined preterm premature rupture of membranes as a risk factor for HBV transmission, and the available data are conflicting. As a result, management of such patients should not differ from that of women with chronic HBV without preterm premature rupture of membranes.

Cesarean delivery

The benefit of cesarean delivery in protecting against HBV transmission has not been clearly established in well-conducted controlled trials. Thus, cesarean delivery should not be routinely recommended for carrier mothers for the purpose of reducing HBV transmission.

Prevention of mother-to-child transmission Algorithm from UpToDate:

Algorithm for hepatitis B virus during pregnancy



Anti-HBc: hepatitis B core antibody; anti-HBe: hepatitis Be antibody; anti-HBs: hepatitis B surface antibody; HBeAg: hepatitis B e antigen; HBIG: hepatitis B immune globulin; HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus.

* Check anti-HBs and anti-HBc if mother is at high risk for HBV infection (eg, injection drug user, sexual partner or household contact has chronic HBV). Mothers with no evidence of prior HBV infection (ie, negative for HBsAg, anti-HBs, and anti-HBc) should be vaccinated.

* Women whio have a high HBV DNA (>200,000 int. units/mL), elevated aminotransferase levels, and/or a positive HBeAg should be referref to a hepatologist to see if early initiation of antiviral medication is needed.

* Start at 28 to 30 weeek gestation. We prefer tenofovir disoproxil fumarate rather than other antiviral agents. Refer to the topic on Hepatitis B and pregnancy for a more detailes discussion of treatment .

* For those who continue antiviraltherapy after delivery, the pros and cons of breastfeeding must be discussed with the mother. Refer to the topic on Hepatitis B and pregnancy for more detailed discussions of breastfeeding.

Women who start antiviral therapy during pregnancy for the sole purpose of preventing mother-to-child transmission may stop antiviral therapy immediately after delivery, especially if they want to breastfeed.

Risk of teratogenicity

There are limited human data available on the risk of teratogenicity of antiviral agents used to treat HBV. Available animal and human data have found no evidence of teratogenicity for tenofovir disoproxil fumarate and telbivudine. Human studies also support the safety of lamivudine in pregnancy, although adverse events were observed in some animal studies. There are less safety data for tenofovir alafenamide, entecavir, or adefovir in pregnancy; thus, the risk of teratogenicity cannot be ruled out.

References

Lee, H; Lok, ASF. (2017) Hepatitis B and pregnancy, Mitty J, (Ed). *UpToDate.* Retrieval in October 2018, https://www.uptodate.com/contents/hepatitis-b-and-pregnancy.

Terrault, N.A., et.al. (2015). AASLD guidelines for treatment of chronic hepatitis B. *Hepatology*, p 1-23