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Viral hepatitis B in pregnancy: A review of its burden, vertical transmission and neonatal prophylaxis

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ABSTRACT

Chronic hepatitis B infection represents a high society burden due to its high morbidity and mortality rate, especially infections acquired by vertical transmission. This review's purpose is to update information regarding acute and chronic evolution and management of hepatitis B during pregnancy, vertical transmission, and prophylaxis of HBV infection. The database of PubMed was searched for literature reviews, guidelines, and research articles in English, regarding pregnancy and HBV infection from 2015 to October 2021. Pregnancy may have a serious impact on the natural evolution of chronic HBV in cases of advanced disease or liver fibrosis. Management of these patients include periodical monitoring and antiviral therapy during pregnancy. Alanine amino transferase (ALT) flares can occur during pregnancy or more often after birth, being related to the specific immune changes in pregnant women. The most important impact of HBV infection on pregnancy outcomes is represented by vertical transmission. Almost 90% of the infants infected at birth will develop chronic HBV infection out of which 25-40% will develop specific complications. Almost 9% of the newborns of positive HBsAg mothers acquire HBV infection despite standard immunoprophylaxis with hepatitis B vaccine and hepatitis B immune globulin. Failure of immunoprophylaxis can have a higher rate due to elevated levels of HBV DNA during pregnancy, that can be lowered by prophylactic antiviral administration from 28-32 weeks, during pregnancy. Screening every pregnant woman for HBsAg is a good practice measure, which should be standard, among the universal hepatitis B vaccination, in order to achieve a reduction of HBV infection prevalence.

Keywords: viral hepatitis B, pregnancy, neonate, transmission, prophylaxis

INTRODUCTION

Hepatitis B virus (HBV) is a small, enveloped double-stranded, hepatotropic DNA virus, which can lead to an acute or a persistent and chronic infection. It has a parenteral transmission route through percutaneous and mucosal exposure to the blood or bodily fluids of an infected individual, most common through injection drug use, sexual intercourse, or childbirth. It represents a highly infectious virus which can remain viable for up to seven days on different surfaces, in absence of proper disinfection [1,2,3].

In 2015, approximately 3.5% of the population were chronically infected with HBV, with a decreasing incidence due to vaccination and antiviral therapy. Chronic HBV represents a high society burden due to liver inflammation and fibro-genic process-

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es, leading from liver fibrosis and cirrhosis to decompensated liver disease and/or hepatocellular carcinoma. Among the VHB carriers, almost 25-40% develop complications, requesting hospital admissions and expensive treatment [1].

ACUTE INFECTION

Hepatitis B virus induces cell mediated destruction of infected cells leading to liver inflammation, symptoms, and resolution of illness, and also manifests pro-oncogenic effect upon hepatocytes. Acute VHB infection is usually asymptomatic but may lead to general manifestations such as anorexia, fatigue, malaise and gastrointestinal signs and symptoms like nausea, vomiting, jaundice and abdominal pain. In pregnant women differential diagnosis must include hyperemesis gravidarum, pre-eclampsia, HELLP syndrome (hemolysis, elevated liver enzyme, and low platelet), as well as acute fatty liver of pregnancy, which can mimic acute VHB signs and symptoms. In up to 90-95% of the infected adults, spontaneous resolution of illness occurs by 3-4 months, while 5-10% will develop chronic infection [2,4]. In rare cases it may lead to severe manifestations such as hepatic encephalopathy and coagulopathy, signs of fulminant hepatitis, making necessary hospitalization, primarily supportive treatment and antivirals to prevent progression to acute liver failure. Antiviral therapy is rarely necessary because almost 95% of the infected adults will have a complete spontaneous recovery, including seroconversion to anti-HBs [5].

The course and management of acute HBV infection as well as the incidence of fulminant hepatitis in pregnancy do not differ from those of the general population. Nevertheless sero-clearance of Ag HBs in pregnancy looks to be delayed and lower compared to non-pregnant patients, showing that pregnancy could be a risk factor of developing HBV chronic infection [4,6].

CHRONIC INFECTION

HBV chronic infection is defined as the persistence of AgHBs in the serum for more than 6 months from the infection. Persistent infection is frequently involving young and/or immunocompromised individuals, therefore 90% of infected neonates, 25-50% of infected children and 5-10% of infected adults will develop chronic HBV infection. Up to 40% of chronic infections progress to cirrhosis, in absence of suitable treatment, leading to a high risk of developing complications of liver fibrosis, such as ascites, jaundice, esophageal varices with or without hemorrhage and hepatic encephalopathy or hepatocellular carcinoma [2,7,8,9].

Chronic HBV infection is characterized by 4 phases defined by the dynamic interaction between cellular immune response and viral replication. The first phase, previously named immune tolerant, is more frequent and prolonged in perinatally infected individuals and characterized by positive HBeAg, normal ALT levels and high levels of HBV DNA, meaning that these patients are highly contagious but there is no liver necroinflammation or fibrosis. The second phase or previously named immune active, consists of positive HBeAg, high HBV DNA levels and elevated ALT levels, moderate/severe liver necroinflammation and progression of fibrosis, and is more frequently and rapidly reached by individuals infected in their adulthood. Phase three, HBeAg negative chronic infection or previously known as inactive carrier phase is characterized by seroconversion to anti HBe, low or undetectable HBV DNA and normal ALT levels, low fibrosis and inflammatory activity, low risk of progression towards cirrhosis and hepatocellular carcinoma, and 1-3% chance of spontaneous anti HBs seroconversion. The fourth phase known as HBeAg negative chronic hepatitis B is defined by anti HBe, moderate to severe liver inflammation and fibrosis, and has low rates of spontaneous disease remission [5,10,11,12].

Every pregnant woman tested positive for HBsAg in the early pregnancy should be assessed for phase of infection and monitored for progression, either forward or backward, between phases. HBV course of progression is complicated and usually takes a long period of time before developing clinical symptoms or severe complications, not commonly encountered in childbearing age women. Therefore, the main concern regarding chronic HBV infection during pregnancy is represented by vertical transmission, without excluding the possible maternal risks and complications. High risk patients such as cirrhotic pregnant women should be identified and properly managed because of the higher prevalence of severe complications leading to death compared with pregnant women without cirrhosis or non-pregnant women with cirrhosis [4].

Pregnancy is characterized by an immune alteration state to avoid fetal allograft rejection, characterized by the suppression of Th1 response and stimulating Th2 immunity, which leads to an impaired immune reaction to HBV and stimulates viral activity and reduction of CD8 T cells. These immune changes, which are reversible in the postpartum period, may be responsible for increased HBV replication and ALT elevated levels during pregnancy and postpartum period [4].

Researchers developed many studies to evaluate the triggers of chronic hepatitis B flares and also the appropriate assessment and treatment but there

are different results due to the lack of consensus regarding hepatitis flare definition. It is generally accepted that hepatitis flare is represented by a raise of ALT levels, usually asymptomatic or accompanied by mild and self-limited symptoms, but in rare cases it can lead to hepatic decompensation [4]. Giles et al. [13] considered hepatitis flare as the raise of ALT levels twice the upper normal limit (ULN), Chang et al. [14] defined it as ALT levels 5 times higher than the upper limit of normal (ULN; 19 U/l) or third times higher than the baseline, whichever was higher, while Kushner et al. [15] and Liu et al. [16] described flare as ALT levels twice higher than ULN, with ULN defined as 19 U/l vs 40 U/l. According to these studies the risk of hepatitis B flare in pregnant patients not using antivirals was between 1.6 and 14% during pregnancy and 3.5-50% in the postpartum period, which varies depending on diagnostic criteria and as a result of unadjusted normal level of ALT [4,13,16]. Normal level of ALT was defined in 2018 by the American Association for the Study of Liver disease as 35 U/l for males and 25 U/l for females [11]. Hepatitis flare had a greater rate in postpartum period comparing with pregnancy period, regardless of antiviral treatment. [4]. According to a retrospective study comparing pregnant women which interrupted antiviral therapy short before getting pregnant or in the early pregnancy, with those continuing the treatment, there were reported more hepatitis flares among the first group studied [17]. It appears that flare risk increased postpartum in patients interrupting antiviral therapy immediately after giving birth, hence most guidelines recommend discontinuing HBV treatment within 3 months of delivery [4].

Management of pregnant patients with HBV chronic infection is individualized according to phase of infection, hepatic fibrosis stage, flares, and viral replication. In women undergoing antiviral therapy which plan to or get pregnant, careful consideration on whether to continue the treatment or switch it to tenofovir disoproxil fumarate (TDF) should be made. Therefore, in early pregnancy HBsAg, HBeAg, HBV DNA, ALT levels and hepatic fibrosis stage should be determined. Patients experiencing mild-moderate disease, with fibrosis stage defined between 0 and 2, without treatment should be evaluated every 3 months for ALT flare and HBV DNA and referred to a gastrointestinal/liver specialist regarding antiviral therapy if ALT flare is discovered. In case of HBV DNA levels > 200,000 IU/ml guidelines recommend vertical transmission prophylaxis started between 28 and 32 weeks of gestation, with TDF representing the first treatment line. In women with mild to moderate disease undergoing antiviral therapy prior to pregnancy with adefovir or entecavir, they must be replaced by TDF and continue monitoring every 3 months. Pregnant patients with advanced disease, defined as hepatic fibrosis stage 3-4, should be careful monitored every 1-2 months, antiviral treatment should be continued with TDF or initiated as soon as possible, and a superior digestive endoscopy should pe performed to rule out varices and portal hypertensive gastropathy, which can be aggravated by labor efforts [5,18]. ALT levels should be monitored the first 6 months, monthly or every 3 months, after delivery or antiviral prophylactic therapy discontinuation [4].

DIAGNOSIS

The serological marker of acute or chronic hepatitis B is represented by the surface antigen (HBsAg). Early acute infection is defined by the single presence of HBsAg and while the infection progresses antibodies against core antigen (HBcAg) start forming, initially IgM anti HBc, followed by the appearance of IgG anti HBc and the seroconversion to antibodies against surface antigen (anti HBs). Therefor an individual recovered after an acute infection will be immune throughout anti HBs and IgG anti HBc. Protective anti HBs concentration is considered to be over 10 IU/ml achieved either after recovery after acute illness, either by vaccination, in which case only anti HBs will be encountered. If HBsAg persists over a period of 6 months the infection becomes chronic and has a natural course described by the presence or absence of "e" or precore antigen (HBeAg) and levels of ALT and HBV DNA. HBeAg can be detected in persons with acute or chronic HBV infection and its presence correlates with viral replication and high infectivity. Antibody to "e" antigen(anti-HBe) is associated with the loss of replicating virus, is produced by the immune system temporarily during acute HBV infection and reversion to HBeAg positivity can occur during chronic infection. Chronic infection with HBsAg-negative phase, also known as occult HBV infection is characterized by serum positive anti-HBc, with or without detectable antibodies to HBsAg (anti-HBs) and can lead to HBV reactivation in case of immunosuppression [1,3,5,6,19].

All pregnant women should be routinely tested for HBsAg at the first prenatal visit, and all patients with hepatitis B should also be tested for hepatitis D virus (HDV) as well as for HIV infection. Investigations should also include the assessment of liver functions [19].

VERTICAL TRANSMISSION

Chronic HBV infection is estimated to affect >350 million people worldwide and serves as a major cause of morbidity and mortality due to cirrhosis

and hepatocellular carcinoma. In high endemic areas such as Africa and Asia perinatal and early childhood transmission are accountable for most of the chronic infections, being responsible for 1/3 of the infections among areas with low endemicity, where most of infections are transmitted horizontally, through sexual behavior and intravenous drug use. Nowadays the main transmission route of HBV is mother to child transmission (MTCT), accounting for near 50% of the number of worldwide patients [4,20,21,22].

Approximately 90% of the infected newborns have the risk to develop chronic HBV infection, hence vertical transmission prophylaxis has been recognized as the most important phase for prevention [21].

Acute HBV infection acquired early in pregnancy has a 10% potential transmission rate, while the risk of MTCT increases to nearly 60% if the infection occurs at or near the time of delivery [4]. The rate of vertical transmission regarding chronic carriers was estimated as high as 85% in women HBeAg positive, and around 30% in HBeAg negative cases, in the absence of neonatal immunoprophylaxis. After introduction of postexposure prophylaxis, represented by hepatitis B vaccine and hepatitis B immune globulin (HBIG) administered in the first 24 hours after birth, followed by completion of the HepB vaccine series, the rate of infected infants is estimated between 0.7 and 1.1%. Infants born from mothers with high HBV DNA levels > 10^6 IU/ml or HBeAg positive, have a greater risk, between 9 and 39%, of acquiring HBV chronic infection despite suitable prophylaxis [3,4].

Vertical transmission can occur in utero, during labor and delivery or after birth. Intrauterine transmission of HBV is considered to be the most important reason for immunoprophylaxis failure in preventing MTCT, and it is highly associated with raised serum HBV DNA levels and HBeAg positive status in pregnant women [23]. The exact mechanism of intrauterine transmission of HBV has not been yet established, but there were a series of hypothesis raised such as: 1. placental barrier breakage which usually occurs in conditions of placenta damage caused by contraction of the uterine muscle such as threatened abortion or preterm birth, hypothesis sustained by the identification of HBV in the endothelial cells of villous vessels and the trophoblasts; 2) invasive procedures into the uterus like amniocentesis or chorionic villus sampling may increase the risk of transmission when HBV viral load >7 log 10 IU/ml [24]; 3. genetic transmission refers to the possibility of germ cells like sperm and oocytes being infected by HBV and transferring the virus to the embryo [3,4,21].

Intrapartum transmission, represents the most important route of vertical transmission which occurs during childbirth. During labor, contractions of the uterus can cause placental damage resulting in microperfusion of maternal blood into the fetal circulating system. During vaginal delivery, newborns can be exposed to or even swallow vaginal secretions and maternal blood, while during a caesarean section (CS) infants get in contact with a high amount of maternal blood [21,25]. Many studies show that elective cesarean, performed before the onset of labor or rupture of the membranes, lowers the risk of MTCT comparing with vaginal delivery, by preventing microperfusion during contractions and exposure to vaginal secretions, especially in pregnant women with high viral load and/or positive HBeAg [25-29]. However, bearing in mind the raised morbidity and mortality of a CS compared with vaginal delivery, the use of postpartum immunoprophylaxis and prophylactic antiviral therapy during the last trimester used for HBV DNA > 200,000 IU/ml, Australia-New Zeeland (RANZCOG) and Center for Disease Control (CDC) guidelines outline that caesarean section should be reserved for usual obstetric indications [3,30,31]. The risk of MTCT transmission may increase during labor and delivery with the use of invasive procedures such as internal monitoring, episiotomy and operative vaginal delivery [24]. However, due to the availability of neonatal immunoprophylaxis, following regular obstetric practices is recommended, except invasive procedures such as fetal scalp electrodes and fetal scalp blood sampling in labor, that should be avoided [24,30].

Puerperal transmission refers to HBV infection as a result to contact with maternal breast milk, body fluids, blood or other close contacts between newborns and mothers after delivery. Researchers proved no difference in rate of infection between breastfed and formula fed vaccinated infants, encouraging breastfeeding the newborns, as long as they receive immunoprophylaxis at birth [24,31].

VERTICAL TRANSMISSION PROPHYLAXIS

HBV infections acquired at birth or in the first 5 year of life lead to the most HBV-associated deaths among adults. WHO and Global Health Sector Strategy call for the elimination of viral hepatitis as a public health threat by 2030 (defined as a 90% reduction in incidence of new infections and a 65% reduction in mortality).This target requires a reduction in the prevalence of hepatitis B surface antigen (HBsAg) to below 0.1% in children 5 years of age, which can be achieved through universal immunization of newborns against hepatitis B and other interventions to prevent mother-to-child transmission of HBV [32]. Universal hepatitis B vaccination of all newborns provides a critical safeguard and

prevents infection among infants born to HBsAg-positive mothers not identified prenatally [3].

For the target to be achieved it is important that routine testing for HBsAg to be offered to every pregnant woman at the first checkup meeting [3,32]. According to RANZCOG guidelines, routine HBsAg testing should be offered regardless of previous testing or vaccination [30]. Pregnant women at risk for HBV infection during pregnancy (e.g., been evaluated or treated for an STI, having more than one sex partner during the previous 6 months, having had an HBsAg-positive sex partner or recent or current injection-drug use) should be vaccinated. If HBV vaccination during pregnancy is not available or not accepted by the patient, screening should be repeated in late pregnancy [3]. In case of a positive result, the patient should be referred to an infectious disease consultant, hepatologist or gastroenterologist for further blood tests, such as HBeAg, antiHBe and HBV DNA level and liver function tests, to identify patients who can benefit from administration of antiviral therapy and pregnancies with an increased risk of neonatal prophylaxis failure [30,33]. High viral loads during pregnancy increase the risk of vertical transmission despite proper administration of active and passive immunoprophylaxis. Therefore women with HBV DNA level > 200,000 IU/ml (equivalent to 106 copies/ml or 6 log 10 copies/ml), should start antiviral therapy at 28-32 weeks of gestation to reduce the rates of perinatal HBV transmission [3,34-36]. In cases in which antenatal HBV DNA testing is not available, WHO recommends HBeAg testing and using as an alternative to HBV DNA testing to determine eligibility for antiviral prophylaxis to prevent MTCT [32]. According to NICE guidelines antiviral therapy should be started in the third trimester if HBV DNA > 107 IU/ml [37].

Antiviral drugs considered to be safe to use during pregnancy are TDF, Lamivudine (LAM) and Telbivudine (TBV). Reports show that birth defect risk in case of LAM and TDF use in pregnancy is comparable with the general population of pregnant women. Brown et al. [38] reported that LAM, TBV and TDF appear to be safe in pregnancy with no increased risk for maternal and fetal outcome. These three antivirals were not associated with fetal malformation and do not increase the risk of cesarean section, postpartum hemorrhage, preterm delivery, creatinine level or low Apgar score. Antiviral therapy improves HBV suppression, significantly reducing HBV DNA levels before delivery, therefore reducing MTCT in women with chronic HBV infection and high viral load compared to active and passive immunoprophylaxis alone [34,38]. While LAM and TBV have a low resistance barrier, being more likely to experience resistance, TDF represents the first line treatment due to its high resistance barrier and potent antiviral activity. Some studies show some cases of mild elevation of creatinine kinase level and myopathy in TBV treated patients, while some cases of renal toxicity and bone mineral density effect were reported as adverse effects of TDF [39,40-42]. However, no association between in utero exposure to TDF and infant growth was found [43]. Treatment with LAM, TBV, TDF for active CHB in early pregnancy appears to be safe and effective for controlling maternal disease as well as interrupting MTCT [39,44].

Breastfeeding is considered to be safe regarding HBV transmission in neonates receiving standard immunoprophylaxis. Most guidelines suggest that breastfeeding is not contraindicated in HBV positive mothers receiving treatment with LAM or TDF. Safety data in nursing mothers on TBV therapy is limited, such that an alternate drug should be administered. Antiviral therapy can be interrupted from delivery to 12 weeks postpartum, and a special attention should be given to the risk of postpartum flares during or after discontinuing antiviral drugs [3,30,32,34].

Counseling about the potential risk of HBV transmission associated with invasive procedures in HBsAg-positive women, particularly those with a high viral load (HBV DNA level > 200,000 IU/ml), should be given. Noninvasive prenatal test (NIPT) should be offered instead of invasive procedures whenever it is possible. In cases requiring invasive procedures, amniocentesis is probably safer than CVS, and transplacental amniocentesis should be avoided, if possible [11,24,30,36].

NHS guidelines recommend delaying artificial rupture of membranes as long as possible during labor, active labor management in case of spontaneous rupture of membranes and avoiding as much as possible fetal scalp electrodes and fetal blood sampling, in order to minimize the risk of vertical transmission [33].

ACTIVE AND PASSIVE IMMUNOPROPHYLAXIS

Active immunoprophylaxis is represented by hepatitis B vaccines which are available as single-antigen formula and in combination with other vaccines. Only single-antigen hepatitis B vaccine should be used for the birth dose, while the combination vaccines can be used to complete the vaccine series. The final dose in the series should not be administered before age 24 weeks [3,32,34].

Passive immunoprophylaxis, represented by HBIG, provides passively acquired antiHBs and temporary protection. These antibodies can be detected in the serum for 4-6 months after administration. HBIG is extracted from the plasma of donors with high concentration of anti HBs and is used as

an adjunct to hepatitis B vaccine birth dose for infants born to positive HBsAg mothers, to help decrease the rate of MTCT or as postexposure prophylaxis [34].

WHO and CDC guidelines recommend universal hepatitis B vaccination within 24 hours of birth for medically stable infants weighing ≥ 2,000 grams, followed by the next 2 doses at 1 and 6 months. Infants < 2,000 grams born from HBsAg negative mothers should be given the first vaccine dose at the time of hospital discharge or at age 1 month, even if they still weight < 2000 grams, followed by the rest of the vaccination scheme [3,32].

Infants born to woman HBsAg positive or with HBsAg results during pregnancy not available but evidence suggesting maternal HBV infection (e.g., presence of HBV DNA, HBeAg-positive, or mother known to be chronically infected with HBV) should receive hepatitis B vaccine and hepatitis B immune globulin (HBIG) within 12 hours of birth, administered at different injection sites. For infants weighing < 2,000 grams the birth dose should not be taken into consideration as part of the vaccination series due to potentially reduced immunogenicity of the vaccine in these infants. Therefore 3 additional doses of vaccine (for a total of 4 doses) should be administered beginning when the infant reaches age 1 month. After completion of the vaccine series these infants should be tested for quantitative antiHBs and presence of HBsAg between 9 and 12 months. Testing should not be offered before age 9 months to avoid detecting passive antiHBs from HBIG administered at birth and to maximize the detection of late HBV infection. HBsAg negative with anti HBs > 10 IU/ml infants are protected while HBsAg positive infants should be referred for appropriate follow up. In case of HBsAg negative with anti HBs < 10IU/ml infants, they should be revaccinated with a single dose of hepatitis B vaccine and retested after 1-2 months. If antiHBs level remain < 10 IU/ml these infants should receive two additional doses to complete the second vaccination series, followed by postvaccination serologic testing after 1-2 months. Another option for infants HBsAg negative and antiHBs < 10 IU/ml after first vaccination series is to be revaccinated with a second, complete 3 dose series, followed by serologic testing after 1-2 months. If antiHBs remain < 10 IU/ml after administration of 2 complete vaccine series, there is no benefit in administering additional hepatitis B vaccine doses. Testing infants for anti HBc is not recommended because passively acquired antiHBc from HBsAg mothers might be detected in infants' serum for up to 24 months after birth [3,32].

Regarding infants born to mothers with unknown HBsAg status, weighing ≥ 2,000 grams, birth dose hepatitis B vaccine should be administered in the first 12 hours of life, and the mother should be tested as quick as possible for the presence of HBsAg. If this proves to be positive the infant should receive HBIG as quick as possible, no later than seven days after birth. If the mother's HBsAg status cannot be determined in the first 12 hour after birth, infants < 2,000 grams should receive hepatitis B vaccine and HBIG within 12 hours of birth, administered at different injection sites, and complete the vaccine series with three additional doses beginning at age 1 month [3].

Hepatitis B vaccine alone is 75% effective in preventing MTCT HBV transmission, while HBIG alone has a 71% effectiveness rate. The efficacy of active and passive immunoprophylaxis combined is 94% [3].

Postvaccination serologic testing revealing positive HBsAg infants define immunoprophylaxis failure. One of the risk factors is represented by a high maternal HBV DNA level during pregnancy among with the presence of HBeAg. Studies show that during pregnancy HBeAg has the ability to cross the placenta generating fetal HBV specific T cell tolerance to the virus and dysfunctional CD8 T cells. Therefore, the fetus may develop immune tolerance to HBV infection in utero and long-term exposure to HBV could be a cause of immunoprophylaxis failure [4].

CONCLUSIONS

Pregnancy seems to have, in general, a minimal influence on the natural course of HBV chronic infection. Acute infection, advanced disease or flares during pregnancy can benefit from antiviral therapy, TDF representing the first line drug, which appears to be safe during pregnancy.

Guidelines recommend routine screening of all pregnant women for HBsAg during the first checkup meeting. HBV DNA high levels or presence of HBeAg are associated with a high risk of immunoprophylaxis failure. Antiviral therapy should be started at 28-32 weeks if HBV DNA levels are above 200,000 UI/ml or HBeAg is present, according to WHO guidelines to reduce the risk of vertical transmission. In utero infection or placental transmission may also play an important role in immunoprophylaxis failure.

Universal hepatitis B vaccination in the first 24 hours after birth is recommended, while infants born to positive HBsAg mothers should receive the first vaccine dose among the HBIG as soon as possible, within 12 hours postpartum. Infants born to unknown HBsAg mothers should be treated as the ones born to positive mothers until further proof is acquired.

HBV should not alter the mode of delivery, and caesarean section should be performed for obstetric reasons only.

Breastfeeding has more benefits than risks, especially in neonates receiving standard immunoprophylaxis. Prophylactic antiviral therapy can be continued up to 3 months after giving birth, if chronic treatment is not required, and breastfeeding appears to be safe in mothers treated with TDF and LAM. Postpartum women should be closely monitored for ALT flares.

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