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Research Article

Hepatitis B Virus Infection Prevention in Pregnant Women in Sub-Saharan Africa

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Abstract:

Context: The hepatitis B virus (HBV) is a highly infectious virus that spreads through blood and other infected fluids such as semen. Individuals can be infected with the virus through sexual contact, by sharing needles or by a needle accident, by getting a body piercing or tattooing, and prenatally or at birth, if the mother is infected with the virus.

Evidence Acquisition: We searched medical databases (PubMed and Scopus) from January 2000 to January 2015.

Results: Based on our results, the transmission of HBV from the infected mother to her child during pregnancy is a critical way for the acquisition of the virus. The routine vaccination of neonates and the use of immunoglobulin at birth are very effective for the prevention of infection when a mother is infected. Also, the treatment of the infected mother to decrease the viral load is another preventive method for the protection of her child.

Conclusions: Our study showed that routine vaccination in children and screening of pregnant women for HBV infection and then preventative strategies for neonates are the most important routes for minimizing the transmission of infection from mother to child.

Keywords: Hepatitis B; infection; Pregnancy; Prevention, transmission route.

1.0 Introduction

Infection with the hepatitis B virus (HBV) remains a global health problem despite successful vaccination programs. Hepatitis B virus (HBV) infection causes approximately 900,000 deaths per year globally,[1] and is the most important single risk factor for hepatocellular carcinoma (HCC) [2]. Whereas 3.6% of the global population is affected by chronic HBV infection, defined as a single positive HBV surface antigen (HBsAg) by the World Health Organization (WHO), most countries in sub-Saharan Africa (SSA) have a prevalence above 8% [1,3]. Mother-to-child transmission can occur during pregnancy and at birth. The mother-to-child transmission is responsible for about one-third of chronic HBV infections in the world [4,5]. Screening of all pregnant women for HBV infection enables Physicians to perform infant post-exposure prophylaxis and also treat the infected mother with specific antiviral drugs, which are the most important strategies for reducing the transmission rates and the global burden of a new HBV infection (1, 2, 6]. When a pregnant woman is referred for the first prenatal visit, the physician will give her a series of routine blood tests, including one test for the presence of the hepatitis B surface antigen (HBsAg), which can cause severe liver damage and hepatocellular carcinoma when the child becomes infected during infancy.[3,7] If the mother is infected, the physician will recommend a dose of hepatitis B immunoglobulin (HBIG) for her baby immediately after birth to protect her child from infection in the short term [4,6,7]. Neonates should also receive the first dose of the HBV vaccine within 12 hours of birth to be able to receive the second and third doses of this vaccine at a regular time [8]. All three doses are necessary for lifelong protection against HBV infection, and the Centers for Disease Control and Prevention (CDC) recommends that all babies receive them [3,9]. Together, the antibodies and the HBV vaccine are about 90% effective for the prevention of HBV infection in babies [2,10]. Cesarean sections and vaginal deliveries are safe for the HBV-infected mothers. A mother who is infected with HBV can breastfeed her infant, but she should protect her nipples from cracking and bleeding [8,9,10] There are many reports about the rate of the transmission of HBV infection during pregnancy and also understanding the mechanisms of the transmission of the infection from mother to child [11]. All these studies have sought to implement policies on maternal screening and infant follow-up as well as mechanisms to minimize the transmission rate [1,2,9].

The human HBV is the prototype member of the family Hepadnaviridae, which includes a variety of similar avian and mammalian viruses. The mature infectious HBV particle, originally called a “Dane particle”, consists of a nucleocapsid core enclosed in a

glycolipid envelope [12]. The nucleocapsid comprises partially double-stranded circular DNA attached to endogenous polymerase and an icosahedral capsid, while the envelope is made of a lipid bilayer bearing three different surface proteins [7]. The three viral surface proteins large (LHB), middle (MHB), and small (SHB) constitute the HBV surface antigen (HBsAg) [13]. It is a multifunctional glycoprotein and the major antigen of the viral envelope, responsible for eliciting humoral and cellular immune responses during infection [10,14]. HBsAg isoforms are involved in many biological functions during HBV infection—from initial and specific viral attachment to the hepatocytes to establishing chronic infection with their immunomodulatory properties [2,8]. The genetic variability of domains encoding HBsAg isoforms is responsible for their altered synthesis and presentation. Based on accumulated evidence, this may play a role in the pathogenesis of specific liver conditions [15].

In sub-Saharan Africa (SSA) including Ghana, most infections occur at birth or during early childhood, 30%-50% of all cirrhosis-related deaths can be attributed to chronic HBV infection [12,16]. In 2016, the World Health Organization (WHO) started to advocate for the elimination of viral hepatitis as a public health problem [4, 16]. Specific objectives include the diagnosis of 90% of all individuals with chronic HBV infection, and the treatment of 80% of eligible individuals by 2030 [9,17]. In order to inform global resource allocation strategies, this research aimed to review the prevalence of Hepatitis B and ways to prevent this infection from mother to child [18].

2.0 Materials and Methods:

This review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guide-line. A search algorithm with the terms “HBV”, “Hepatitis B” and “liver infections” was developed in a PubMeb and Google Scholar database on the 10th of January, 2024 to scout for articles published between 2015 to 2020. Firstly, all studies, in all English language, published between 2015 and 2020 settings were eligible and considered. A total of 150 journal research articles were initially obtained and 30 of them were selected for the report because they involved some subjects of interest. A search through the reference list of the selected articles provided additional references about the HBV in relation to hosts, virulence, pathogenicity, clinical signs, disease burden, treatment, control and threat to the immunocompromised population.

3.0 Results

3.1 Prevalence of HBV infections in Sub-saharan Africa (SSA)

Approximately a chronic HBV infection in Africa (estimated prevalence: 6.1%, 95% confidence interval [Cl] A recent systematic review of the global prevalence of HBV infection showed high estimates across SSA: chronic HBV infection is hyper-endemic (>8% HBsAg-positivity in the general population) in parts of SSA, including most countries in-West and Central Africa. Other countries, mainly in southern and Eastern Africa, are considered areas of intermediate endemicity (2%-8%), while Egypt and Morocco have a low endemicity level (<2%) [5,18]. Most HBV-infected persons were born before HBV vaccine was available and widely used: although HBV vaccination is available since 1982, HBV immunization programs started only in the early 2000s in most of the African countries" [16,17]. Worldwide, the estimated prevalence of chronic HBV infection among children under five years was 1.3% in 2015, compared with 4.7% in the pre-vaccine era. However, the prevalence in young children remains above 3% in SSA, where the implementation of the birth-dose vaccine, a fundamental part of prevention of mother-to-child HBV transmission, has been very limited to date [1,3,19].

Whereas early studies suggested a high variation in HBV prevalence estimates between countries and sub-groups of the population in SSA, these findings can often be explained by methodological differences7-10. A recent meta-analysis of 44 studies in Cameroon highlighted the stability of HBV prevalence across different sub-populations, despite a certain degree of heterogeneity between studies. The overall pooled seroprevalence was 11.2% (95% CI 9.7- 12.8%), and the estimate remained above 10% after the exclusion of studies in populations previously considered as high-risk (10.6%, 95% CI 8.6-12.6%)[11, 20,23]. In line with these findings, recent data from Senegal showed similar HBV prevalence estimates across different populations, including blood donors (17%), prison inmates (14%), military staff (14%) and HIV-infected persons (12%) 12-15. Considering the consistent results from recent studies across SSA, WHO now recommends HBsAg testing at least once in the general population of this region. An estimated 2.7 million (interquartile range 1.8-3.9) of the 36.7 million persons living with HIV are co-infected with HBV, of whom 71% live in SSA16. HIV infection accelerates the progression of HBV-related liver disease and increases liver-related mortality17. In contrast to the situation in high-income countries, most persons acquire HBV during early childhood in SSA, long before being infected with HIV. Therefore, HBV prevalence among HIV-infected individuals is generally similar to estimates from the general population.

3.2 HBV Molecular Virology and Genetic Variability

The organization of the HBV genome includes four partially overlapping open reading frames (ORFs): S, P, C, and X [1,8]. The S ORF is composed of pre-S1, pre-S2, and S genes and is responsible for the synthesis of three surface proteins including in the HBsAg [17]. The longest P ORF encodes the viral enzyme essential for the viral life cycle—HBV polymerase [1,18]. The whole C ORF, including the pre-C and C regions, is translated into the precursor protein, which yields the hepatitis B e protein (HBeAg), a soluble antigen [19]. The C region encodes the hepatitis B core antigen (HBcAg) or C protein, representing the viral capsid’s primary structural protein [7]. Soon after its discovery in the 1960s, it became evident that the newly recognized hepatitis virus was highly

variable [20]. Ten serotypes (also known as HBsAg subtypes) were identified based on the amino acid variability of the HBsAg [8]. In the 1980s, HBV genotypes were recognized based on a sequence divergence of more than 8% over the entire genome. Thus far, 10 HBV genotypes (A–J) have been identified [9]. For isolates of genotypes A, B, C, D, and E, based on a genome sequence divergence of 4% to 8%, an additional classification of sub-genotypes was introduced, and so far, more than 40 have been recognized [9,10]. The genotypes, sub-genotypes, and serotypes have distinct geographical distributions. HBV genotypes and serotypes result from the evolutionary drift of the viral genome as a consequence of a long-term adaptation of the virus to genetic determinants of different host populations [18,21]. On the other hand, HBV is a virus prone to variability that arises spontaneously due to its unique life cycle [20]. The reasons for this spontaneous variability lie in an error-prone viral reverse transcriptase and a very high replication rate [15,22]. The estimated mutation frequency of HBV is approximately 10-fold higher than for other DNA viruses (1.4 to 3.2 × 10−5 substitutions/site/year) [11]. Accordingly, HBV exists as a quasi-species population whose composition is determined by the host immune response and antiviral therapy or vaccination. HBV also plays a role in natural infection with the hepatitis D virus (HDV). HDV is a satellite virus that does not code envelope glycoproteins but depends on HBsAg to form complete virions and, hence, can infect humans only as a co-infection or a superinfection with HBV [23]. Its genome, a single-stranded RNA, is associated with two isoforms of the hepatitis delta antigen—small (S-HDAg) and large (L-HDAg)—to form ribonucleoprotein (RNP). HDV RNA has >70% internal base pairing, enabling folding into a partially double-stranded rod-like structure. HDV virion assembly depends on the interaction of RNP with HBsAg isoforms [12].

Transmission

Mother-to-child transmission occurs in 5% - 15% of infants in the absence of specific prophylaxis [4,19,24]. The rate of infection in neonates is associated with the viral load in mothers and having a positive test for e antigen (HBeAg). In mothers who are seropositive for both HBsAg and HBeAg, vertical transmission can occur at an approximate rate of 90% [3,7,20]. In women with acute hepatitis B, vertical transmission happens in up to 10% of neonates when infection arises in the first trimester of pregnancy and in 80% - 90% of neonates when acute infection occurs in the third trimester. It has been reported that mothers with HBV DNA levels ≥ 106 copies/mL (> 200,000 IU/mL) are at greatest risk for the transmission of HBV to their infants [25].

Prevention

Centre for Disease Control (CDC) recommended the Advisory Committee on Immunization Practices (ACIP) and all healthcare professionals administer the HBV vaccine to all newborns before hospital discharge to protect them against HBV infection. Additionally, they should find all infants whose mothers are HBsAg positive or have unknown HBsAg status to administer appropriate prophylaxis to their infants [22,26].

For a Pregnant Woman with a Positive HBsAg test in Her Prenatal Records, the Physician Must do the following:

- *Give her a test again to verify that the testing date is during this pregnancy not a previous one.*
- *Put a copy of the original HBsAg laboratory report into the infant and pregnant woman's laboratory records.*
- *If the pregnant woman is HBsAg positive, alert the nursery staff to the fact that the newborn is at high risk for HBV infection and will need post-exposure prophylaxis (both HBIG and HBV vaccine).*

The neonate should receive HBIG (0.5 mL, IM) and single-antigen HBV vaccine (0.5 mL, IM) at separate injection sites within 12 hours of birth. Any infant with a weight < 2 kg (4.4 lb) whose mother is HBsAg positive should receive the first dose of the HBV vaccine and HBIG within 12 hours of birth. This dose of the HBV vaccine should not be counted as the first dose in the vaccine series. Healthcare practitioners must reinitiate the full series of the HBV vaccine at age 1 - 2 months. Inform the medical team of the newborn's birth on the importance of additional on-time vaccination and post-vaccination testing of the infant for HBsAg and antibody to HBsAg after the completion of the HBV vaccine series. The medical team should recommend the following items to the mother (1, 2, 3, 20, 26]:

- *She can breastfeed her infant after delivery, even before the HBV vaccine and HBIG are given.*
- *It is critical for her infant to complete the full HBV vaccine series on the recommended schedule.*
- *Blood samples should be obtained from her child after the completion of at least three doses of the HBV vaccine series at age 9 - 18 months to determine if the child has developed a protective immune response to vaccination or needs additional management.*
- *The mother needs to know about the routes of HBV transmission and protection and the need for testing as well as the vaccination of susceptible sexual and household contacts and needle-sharing contacts.*
- *She needs to undergo a medical evaluation for chronic hepatitis B aimed at determining whether she is a candidate for antiviral therapy.*

There is evidence that antiretroviral drugs such as Lamivudine, Tenofovir, and Telbivudine can prevent vertical transmission when administered to women with a high HBV viral load in the third trimester (23,27]. It has been reported that mothers who have a viral load of more than HBV DNA levels ≥ 106 copies/mL are at the greatest risk for the transmission of HBV to their infants. Therefore,

the physician should recommend they take anti-viral drugs such as Tenofovir during the third trimester to minimize the risk of the transmission of the infection to their child [27].

For the Newborn of a Mother with Unknown HBsAg Status, Do the Following [19,20,22]:

- Administer a dose of the HBV vaccine (0.5 mL, IM) within 12 hours of birth. The physician should not wait for the test results to return before giving this dose of vaccine.
- Confirm that the laboratory has received the blood sample for the mother's HBsAg test. If the nursery does not receive the report of the mother's HBsAg test at the expected time, call the laboratory for the result.
- If the laboratory test shows that the mother is positive for HBsAg, the physician should administer HBIG (0.5 mL, IM) to the newborn baby. It should be injected during the first week after the birth. If more than 7 days have elapsed since birth, administering HBIG to the newborn has little benefit.
- If the newborn and mother should be discharged, you must take all contact information (i.e. addresses, telephone numbers, and emergency contacts) for follow-up.

3.4.1 For a Pregnant Woman Who Does not Have an HBsAg Lab Report in Her Prenatal Record, Do the following:

Carry out a repeat blood test for HBsAg if the pregnant woman has a negative test for HBsAg during a prenatal visit but is at risk for acquiring the HBV infection during this pregnancy because, for instance, she currently uses or has recently used injection drugs; she has an HBsAg-positive sex partner; or she is on evaluation or treatment for a sexually transmitted disease or another risk factor for the HBV infection (1, 2, 10). 3.2.3. For the Newborn of an HBsAg-Negative Mother, Do the Following:

a) Administer a dose of the HBV vaccine (0.5 mL, IM) before hospital discharge to all newborns weighing ≥ 2 kg at birth.

b) Give the mother an immunization record card bearing the date of the HBV vaccination. C. Advise the mother to complete the HBV vaccine series to protect her baby against the virus and remind her to bring the immunization record card each time she brings her baby to the clinic (1, 2, 18-20)

3.4.2 For the Newborn of a Mother with Unknown HBsAg Status, Do the Following:

a) Administer a dose of the HBV vaccine (0.5 mL, IM) within 12 hours of birth. The physician should not wait for the test results to return before giving this dose of vaccine.

b) Confirm that the laboratory has received the blood sample for the mother's HBsAg test. If the nursery does not receive the report of the mother's HBsAg test at the expected time, call the laboratory for the result. C. If the laboratory test shows that the mother is positive for HBsAg, the physician should administer HBIG (0.5 mL, IM) to the newborn. It should be injected during the first week after the birth. If more than 7 days have elapsed since birth, administering HBIG to the newborn has little benefit (19-22). D. If the newborn and mother should be discharged, you must take all contact information for follow-up (i.e. addresses, telephone numbers, and emergency contacts).

3.6 Post-Exposure Prophylaxis for Susceptible Pregnant Women

After exposure to persons with acute Hepatitis B: When exposure has happened because of sexual contact, within 14 days after the recent sexual contact, the physician should administer a course of the HBV vaccine as soon as possible [8,27]. In addition, the mother should receive one dose of HBIG at a dose of 0.06 mL/kg IM in the contralateral arm (14,28]. For prophylaxis after a percutaneous or mucous membrane injury, it is recommended that a second dose of HBIG be injected one month later.[29,30]

3.7 Recommended priority actions for the elimination of hepatitis B.

(Retrieved from: https://www.thelancet.com/journals/langas/home)

- Prevention of mother-to-child transmission (MTCT)
- Mandatory antenatal hepatitis B surface antigen (HBsAg) screening: screening tests using available laboratory infrastructures—eg, ELISA-based serology or point-of-care tests
- Initiation of tenofovir 300 mg daily at 28–32 weeks of pregnancy if hepatitis B virus (HBV) DNA concentration is higher than 200000 IU/mL to further reduce risk of perinatal transmission
- Real time quantitative PCR or in-house quantitative PCR to establish MTCT risk
- Hepatitis B e antigen (HBeAg) testing if quantitative HBV PCR not available
- If HBeAg and quantitative HBV PCR not available, treat pregnant women based on HBsAg positivity and refer for further assessment of whether antiviral therapy is needed after delivery
- Baby treated with HBV birth-dose vaccine within 24 h of birth
- Ensure full coverage of universal hepatitis B vaccination
- Identify high-risk groups, especially family members, household contacts, and sexual contacts for HBsAg screening, HBV vaccination, or linkage to care
- Use of affordable WHO prequalified point-of-care testing for HBV serology and HBV DNA concentration quantification to upscale identification of individuals infected with HBV
- Ensure that health-care workers are screened and vaccinated against HBV

- Establish pathways of linkage to care for individuals who are HBV monoinfected
- Ensure sustainable access to tenofovir for individuals who are HBV monoinfected

4.0 Conclusions

Universal screening of all pregnant women for HBV infection is the most important and effective factor for the prevention of the transmission of HBV infection from mother to child. Education about the importance of administering the birth dose of the vaccine within 12 hours of birth is vital. Using antiviral drugs such as Lamivudine, Tenofovir, and Telbivudine can prevent vertical transmission when administered to women with a high HBV viral load in the third trimester. Research is being carried out to develop a vaccine suitable for non-responders to the currently available vaccine

Credit authorship contribution statement

Sabastian Samuel Kwesi: Visualization, Analysis. Richard Sam Abakah: Methodology, Investigation. Writing – Editing, Investigation, Emmanuel Martin Obeng Bekoe: Review and editing, Cornellius Eshun: Formal analysis, Project administration.

Data availability

The data presented in this study are available upon request pending approval from the authors.

Additional information

No additional information is available for this paper.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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