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Elimination of Vertical Transmission of Hepatitis B in Africa: A Review of Available Tools and New Opportunities

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Abstract

Purpose—This review article focuses on the prevention of vertical transmission of hepatitis B virus (HBV) among pregnant women living in sub-Saharan Africa (SSA), where disease is endemic and maternal HBV seroprevalence is estimated to be >8%. Available interventions that have been studied in low-income and middle-income countries (LMIC) are compared in terms of efficacy and real-world effectiveness. Global disease elimination targets, barriers to HBV prevention efforts, and critical research gaps are discussed.

Methods—A PUBMED literature search in February 2018 identified relevant studies of interventions to reduce or prevent the transmission of hepatitis B virus during pregnancy or the peripartum period. Studies were included if they focused on interventions that are currently available or could be made available in SSA. Trials conducted in SSA and other low-income countries were prioritized although interventions in middle and high-income countries were included.

Findings—Among 127 studies and reports included in the review, 60 included data from SSA. The most cost-effective intervention to reduce HBV infection rates in SSA is timely birth dose vaccination followed by completion of the 3-dose infant vaccine series. The identification and treatment of pregnant women with elevated HBV viral load to further reduce the risk of vertical transmission in SSA shows promise but efficacy and safety trials in Africa are lacking.

Implications—Scale up of currently available tools is required to reach HBV disease elimination goals in SSA. Many countries in SSA are in the process of rolling out national birth dose vaccination campaigns; this provides an opportunity to evaluate and improve processes in order to expand coverage. Early antenatal care, promotion of facility deliveries and increased awareness of

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HBV prevention are also key components of prevention success. Future studies in SSA should identity an “HBV prevention package” that is effective, safe and feasible and can be administered in antenatal clinic and tailored to vertical transmission risk.

Keywords

hepatitis B virus (HBV) infection; hepatitis B antiviral therapy; sub-Saharan Africa (SSA); vertical HBV transmission; hepatitis B in pregnancy

Introduction

There are 257 million people living with chronic hepatitis B virus (HBV) infection worldwide and 88% of them reside in sub-Saharan Africa (SSA).[1–7] Viral hepatitis was the 7th leading cause of global mortality in 2015 and deaths caused by viral hepatitis surpassed the number of deaths caused by HIV, tuberculosis and malaria infection. [7] If current trends continue, an estimated 63 million new cases of HBV will occur between 2015-2030, and the World Health Organization (WHO) has set a goal of disease elimination. Reaching this ambitious goal by 2030 will require a significant scale up of prevention and treatment efforts in SSA with a focus on efforts to prevent transmission of HBV during pregnancy and the peripartum period.[8–12] Vertical transmission is a key factor driving endemic HBV infection rates in SSA.[13]

Chronic active HBV infection is usually asymptomatic and only 9% of infected persons worldwide are aware of their infection.[14] Routine screening in antenatal clinic consists of testing for the presence of HBV surface antigen (HBsAg) but screening is not consistently performed among pregnant women in SSA.[15] Similar to other viral infections in pregnancy, the risk of vertical transmission of HBV is directly correlated with the maternal viral load titer. Studies have documented that women with HBV DNA levels >200,000 IU/mL (10^6 copies/mL) have higher risk of vertical transmission.[16] Infectiousness is also predicted by positive maternal HBV e antigen (HBeAg) serostatus which correlates with elevated HBV DNA levels (ranging from 2,000 IU/mL to >200,000 IU/mL).[5,17]

Vertical transmission of HBV is mucosal and caused by perinatal exposure to infected maternal blood and body fluids at the time of delivery. Transplacental transmission and transmission via breastfeeding are rare. Routine cesarean delivery is not recommended for the sole purpose of reducing the risk of vertical transmission to HBV-exposed infants, but data are limited. [18–20] A potential association between HBV infection and preterm delivery requires further validation.[21]

The likelihood of developing chronic HBV infection is inversely proportional to age at the time of HBV exposure. [7,16,20,22–28] Ninety percent of HBV-exposed neonates will develop chronic infection, compared to 5-10% of HBV-exposed adults. Interventions to prevent HBV vertical transmission are highly cost-effective since they reduce both short-term adverse outcomes and long-term morbidity and mortality.[29,30] The long term outcomes of chronic HBV infection include cirrhosis, end stage liver disease (ESLD) and hepatocellular carcinoma (HCC). [31] The risk of HCC after perinatal HBV infection is 5% per decade – 100 times higher than the risk of HCC following horizontal transmission later in life.[32] Medical

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and surgical management options for ESLD and HCC in SSA are limited; this strengthens the rationale to allocate resources to disease prevention efforts. [33,34] HIV/HBV coinfection is important as well since an estimated 18 million women in SSA are living with HIV and most are of childbearing age. [35,36] Adults with HIV have elevated risk of acquiring HBV and HIV/HBV co-infected patients have more rapid progression of liver disease to fibrosis and cirrhosis. [37] Most pregnancy outcomes in women treated for HIV/HBV coinfection are reassuring to date, and coinfection does not appear to increase the risk of vertical HIV transmission.[38,39]

Fewer than 1% of pregnant women worldwide and very few women in sub-Saharan Africa are offered targeted antiviral therapy for HBV infection during pregnancy. [40,41] Several first-line antiretroviral therapy regimens used in SSA have dual activity against HIV and HBV viruses (including tenofovir, lamivudine and emtricitabine). [42]Although antiretroviral medications may be available free of charge through international and national HIV programs in SSA (such as the US Presidents Emergency Plan for AIDS Relief or PEPFAR), there is no equivalent program to cover the expense of antiviral therapy for HBV.

Fortunately, highly effective tools to prevent the vertical transmission of HBV with a long track record of safe administration in pregnant women and neonates are available. Low awareness about HBV prevalence and prevention interventions among providers and the general public in SSA limits uptake.[43,44] This review will focus on the HBV prevention options that are available in SSA – namely, HBV vaccination and HBV-targeted antiviral therapy.[45–50] Gaps in knowledge and research priorities necessary to reach vertical transmission HBV elimination goals in SSA will also be discussed.

Methods

A full PUBMED search on February 19, 2018 was conducted to identify relevant human studies of interventions to reduce or prevent the transmission of hepatitis B virus during pregnancy or the peripartum period. The terms or keywords used in the search were “hepatitis B antiviral pregnancy”, “prevention of vertical transmission of hepatitis B”, “mother to child hepatitis B prevention”, “hepatitis B birth dose vaccination”, “hepatitis B infant vaccination”, “hepatitis B immunoglobulin” or “HBIG”, or “HBV therapy in pregnancy”. Studies conducted in Africa or other low-income countries were prioritized for inclusion although studies of HBV prevention interventions in middle and high-income countries were included when relevant. Only articles written in English were reviewed. Studies of interventions to prevent horizontal transmission or the prevention of hepatitis B in adults were excluded. Articles were reviewed to address thematic areas of interest.

Results

Overall the search yielded a total of 4543 reports of which 127 were relevant and reviewed for this publication. Sixty reports focused on or included data from countries in SSA. We address ten thematic questions in the sections below.

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HBV Testing Strategies in Pregnant Women and Infants in SSA

When women are screened for hepatitis B infection during pregnancy in SSA, serologic testing for HBsAg is performed. However, since few pregnant women (0-20%) are routinely tested for hepatitis B in SSA, cross-sectional studies are used to document regional HBsAg prevalence. [51–53] Given the expense and expertise required for quantitative molecular diagnostic testing, HBeAg is the only available measure of infectiousness for most HBV-positive pregnant women in SSA. The feasibility of rapid antenatal HBV testing is under investigation.[54]

HBV Vaccine Products for Neonates and Infants

The first commercially available HBV vaccine was a plasma-derived product that was approved in 1981. Within 10 years, this formulation was replaced by a yeast-derived, recombinant DNA HBV vaccine product that remains in use today.[55,56] There are several HBV vaccine products currently available for pediatric populations in SSA; all contain 5-10 micrograms of HBV surface antigen (HBsAg) in a 0.5 mL standard volume dose. Any licensed and approved vaccine for HBV can be used interchangeably in national vaccination programs. In SSA, administration of a monovalent form of the HBV vaccine is recommended at birth for all infants (birth dose vaccine), followed by HBV vaccination as part of a pentavalent combination vaccine (HBV/DTP/Hib) at 6, 10 and 14 weeks of age. Three or four vaccines are required to complete the HBV series (four if the birth dose is followed by the 3-dose pentavalent series). Although most HBV vaccines have a long shelf life (up to 4 years), current cold-chain requirements mandate transportation and storage of vaccine at 2-8° C. This can be a challenge in areas of SSA with a lack of consistent electrical supply. Specific vaccine storage details are available in the product package insert and a recent WHO report focused on HBV prevention includes practical details for national HBV vaccination programs in low and middle-income countries (LMIC).[14]

HBV Vaccine Immunogenicity, Duration of Protection and Safety

Fortunately, pediatric HBV vaccination is highly immunogenic and vaccine series completion alone prevents 80-95% of vertical HBV transmission. Most healthy infants (>96%) have evidence of protective immunity upon completion of the primary series.[57,58] Protection is more limited without vaccine series completion. The standard definition of protective immunity is detectable antibody (HBsAb) levels >10 mIU/mL at 9 months of age (1-2 months after the last dose). According to the WHO, preterm, low birthweight infants (<2000 grams) are recommended to receive birth dose vaccination followed by the 3 dose pentavalent series, and serologic response rates are excellent.[59] Although US recommendations for low birthweight infants are similar for HBV-exposed infants (or if maternal status is unknown), CDC recommends HBV vaccination starting at 4 weeks of age among infants who are not HBV-exposed.[60]

Infants with HIV-infection appear to develop lower antibody levels in response to HBV vaccine but vaccination recommendations are unchanged.[61] Studies show that the duration of the protective response after completion of the primary HBV vaccine series is long lasting (>20-30 years), in areas of both high and low endemnicity.[13,14,62–65] A booster dose of HBV is not recommended, but since 5% of infants do not respond to vaccine, a search for

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underlying immunologic or genetic differences in this group is ongoing.[66] HBV vaccination is safe for use in infants and children with serious adverse events (anaphylaxis) occurring in fewer than 1.1 per million vaccinations.[67]

HBV Vaccine Timing

The ideal timing of HBV vaccination to prevent vertical transmission is at birth.[13,68] Receipt of the initial pentavalent vaccine at 6 weeks of age leaves an HBV-exposed neonate with inadequate protection for weeks and many infants in SSA have delayed initiation of the series, which prolongs the risk period.[47] Although many studies have shown efficacy of the monovalent birth dose HBV vaccine, only one controlled, non-randomized, vaccine effectiveness trial compared infection rates among infants who did and did not receive birth dose vaccination.[69] In Cote d'Ivoire, Ekra and colleagues compared HBV infection rates among 4600 infants vaccinated at 0, 6, and 14 weeks of age to those vaccinated at 6, 10, and 14 weeks of age.[70] Infection rates at 9 months of age were 0.5% in both groups, but in the subgroup of 41 infants born to HBeAg+ mothers, the infection rate was 38% in the birth dose group and 59% in the group with series initiation at 6 weeks. (p=−.18) It is not clear why the infection rate was elevated in both groups despite vaccination and study findings have not been replicated.

The initiation of HBV vaccination at birth vs. 6 weeks has been the subject of controversy for national programs in SSA. Although studies in Uganda (where birth dose HBV vaccine is not available) have shown efficacy of vaccine series initiation at 6 weeks, large scale HBV elimination in SSA depends on increasing access to birth dose vaccine. [71–74] In one model, 50% of new chronic cases of HBV worldwide in 2030 will have been acquired by vertical transmission.[75] A population-based, cross-sectional study of children in the Amazon region documented the impact of a birth dose vaccine program established in 2001.[76] The rate of chronic HBV infection decreased to 0.5% and receipt of the birth dose decreased the risk of HBV infection by 95%. A similar rate of chronic HBV infection (0.4%) was noted in Israeli children following nationwide adoption of the birth dose vaccine in 1992.[77] In Indonesia, low coverage of the birth dose vaccine was cited as one explanation for persistent pediatric HBV infection rates (seroprevalence as high as 6%) despite adoption of universal HBV vaccination starting at birth in 1997.[78] Randomized or other well-designed studies comparing HBV transmission rates with vaccine initiation at birth vs. 6 weeks are lacking.

HBV Vaccine Coverage, Availability and Cost-effectiveness in SSA

The WHO has recommended universal HBV birth dose vaccination for all infants since 2009. [13](Figure 1) HBV vaccination within 24 hours of birth is also recommended as a key performance indicator for national immunization programs.[14] HBV birth dose vaccination has been supported by Gavi, the Vaccine Alliance, since 2000. Gavi recognizes HBV birth dose as a high-impact vaccination that should be included in SSA vaccination platforms. Despite these longstanding recommendations, coverage of the HBV birth dose vaccine in 2015 was only 38% worldwide and 10% in SSA.[50] Fewer than 100 (97) countries have adopted a policy of birth dose vaccination, and only 11 of 54 countries in SSA, although many are working towards adoption.[15,79] Rates of completion for the three dose pentavalent HBV-containing vaccine series are 87% worldwide and 76% in SSA.[15,47] Infant HBV

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vaccination rates in SSA are correlated with higher maternal age and education, urban residence and access to health care. [47,80]

The monovalent vaccine is quite affordable at 20 cents per dose, although country procurement costs and patient charges may be significantly higher. Gavi does not currently provide financial support for the birth dose vaccine as it does for the pentavalent vaccine. The cost-effectiveness of HBV prevention with vaccination is favorable, whether analyses include short-term outcomes of infection prevention in children or long-term outcomes of HBV-associated morbidity and mortality.[29,81,82] At an estimated cost of $15.5 million USD, scale up of HBV birth dose vaccination in South Africa was shown to be the most cost-effective intervention compared to several other intervention efforts modeled to reduce national viral hepatitis rates.[83]

Methods to improve HBV vaccine coverage in SSA

There are four critical barriers to wider implementation of the birth dose vaccine in SSA: 1) limited awareness of HBV prevalence and prevention interventions, 2) vaccine availability, 3) out-of-facility deliveries, and 4) cold-chain storage requirements.[84,85]

Training and supervision of healthcare workers to increase awareness about the importance of HBV birth dose, ensuring consistent vaccine supply and developing standing orders for birth dose vaccination in facilities significantly improved vaccine coverage in the Western Pacific. [86] Similarly, in China, birth dose coverage improved when facility delivery rates increased from 58% to 93% and access to vaccine was ensured. [87] In the Philippines, timely birth dose coverage was 40% in 2011 but private facilities had lower coverage rates compared to government facilities.[88] Since many health officials and antenatal providers in SSA have worked to promote facility deliveries in order to improve a variety of maternal and infant health incomes, facility delivery rates in most countries now approach 80%.[89,90] However, in regions where out-of-facility delivery rates remain high, innovative strategies to offer HBV birth dose vaccination have been developed.[91] One effective project in rural Asia provided regional and local health workers with mobile phones to track home deliveries; birth dose coverage in intervention districts was 57% compared to 20% in control districts.[92]

HBV monovalent vaccine is “relatively heat-stable” according to in-vivo and in-vitro studies. [14,93–95] This provides some indication that HBV vaccine may retain its potency in the absence of continuous cold-chain transport and storage. There are no thermostable HBV vaccine products available at present but ongoing studies are promising given the relevance of this challenge in SSA.[96–99]

Data from HBV birth dose national vaccination campaigns from outside SSA provide useful information for national programs that are in the process of adopting or rolling out their own birth dose vaccination programs (including Benin, Cameroon, Republic of the Congo, Cote d’Ivoire, Ethiopia, Ghana and Sierra Leone). [10,47] Published findings highlight the need to ensure consistent vaccine access, engage relevant clinical and public health partners in training opportunities, and conduct public awareness campaigns about the importance of HBV prevention efforts.

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HBIG Efficacy and Availability in SSA

HBIG contains high levels of purified antibodies from plasma donors that are specific to the hepatitis B surface antigen (HBsAg). HBIG provides short-term protection for the HBV-exposed neonate for 3-6 months after delivery when provided along with birth dose vaccination. From an ethical perspective, HBIG should be available to HBV-exposed neonates in every country, but unfortunately, it is not widely available in SSA. Even if a local supply is identified, HBIG is rarely affordable at a cost up to several hundred dollars per dose. Safety concerns further limit the feasibility of HBIG administration in SSA.[14] Current evidence shows that HBIG provides protection for HBV-exposed infants that is additive to the protection afforded by the birth dose vaccine, particularly among women with an elevated HBV viral load.[68,69,100] However, studies also show minimal benefit of HBIG for HBV-exposed infants who are born to HBeAg negative women; additional study will be helpful in defining the precise role for HBIG in LMIC. [101–103] According to the WHO, the option of HBIG immunoprophylaxis in SSA has limited utility until cost, further efficacy and safety concerns are addressed. [13]

HBV Antiviral Treatment in Pregnancy to Reduce Vertical Transmission

The main causes of prophylaxis failure for vertical transmission are high maternal viral load or HBeAg positivity, in utero infection, escape mutants and the maternal immune status.[104] Of these, high maternal serum viral load (HBV DNA level > 200,000 IU/mL) appears to be the major cause of prophylaxis failure, with up to 3-9% of perinatal transmissions despite both active and passive immunization. [105]

Antiviral drugs are safe and effective in the third trimester to prevent intrauterine transmission of hepatitis B virus and are generally recommended for HBV infected pregnant women with high viral load, followed by neonatal HBV vaccination. [106,107] Most major international liver society guidelines recommend antiviral therapy for women at higher risk of vertical transmission of HBV with initiation during the 3rd trimester (28-32 weeks gestational age) and cessation during the postpartum period for women who do not meet criteria for continuation of therapy.[43] Antiviral therapies which have been used to decrease HBV DNA levels during late pregnancy include nucleotide/nucleoside analogue polymerase inhibitors: lamivudine, telbivudine, tenofovir and entecavir. Although lamivudine and tenofovir may be available at no cost to treat patients with HIV or HIV/HBV coinfection in SSA, no similar program covers the expense of these medications for adults with HBV monoinfection. Since antiviral therapy is necessary to reach elimination targets, increased global funding is needed to expand access to these medications.[10,83]

Lamivudine was the first antiviral drug used in HBV-infected mothers to lower vertical transmission rates. A nucleoside analogue and reverse transcriptase inhibitor, it can significantly reduce the HBV viral load. In 2014, 45 women in Ireland met criteria for lamivudine treatment, and no cases of perinatal transmission occurred in infants born to mothers who received treatment. [108] The study authors concluded that lamivudine therapy in highly viremic, HBV-infected pregnant women could help reduce the rate of vertical transmission. In 2011, a meta-analysis of randomized controlled trials including 1,693 HBV-

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infected mothers showed that lamivudine initiated at 28 weeks substantially reduced vertical HBV transmission compared to immunoprophylaxis with HBIG alone. [109]

Telbivudine has anti-HBV activity with no known fetal toxic effects. Wu and colleagues performed a prospective study of 450 HBeAg positive pregnant woman with 279 woman receiving telbivudine and 171 women participating as controls [110]. None of the infants whose mothers were given telbivudine tested positive for HBsAg at 6 months of age, compared to 14.7% of infants in the control group. The authors concluded that telbivudine was safe and significantly reduced vertical transmission of HBV.

One major drawback that complicates lamivudine and telbivudine use is HBV antiviral resistance. In contrast, tenofovir disoproxil fumarate (TDF), a nucleotide reverse transcriptase inhibitor, is a potent medication with minimal resistance and a favorable pregnancy safety profile. Tenofovir is the antiviral therapy of choice for HBV in pregnancy according to the American Association for the Study of Liver Diseases (AASLD).[111] Data are mixed about the efficacy of tenofovir in reducing vertical HBV transmission. A retrospective review of 48 women treated with tenofovir throughout pregnancy reported a vertical transmission rate of 0% with a spontaneous abortion rate of 6% in the first trimester [112]. Two large randomized controlled trials have studied the impact of tenofovir on vertical transmission of HBV. In the first trial in China involving HBeAg-positive women with an HBV DNA level > 200,000 IU/mL during the third trimester, the rate of vertical transmission was 5% among those who received tenofovir therapy compared to 18% among who received usual care without antiviral therapy.[113] In contrast, in the second, multicenter, double-blind clinical trial performed in Thailand, maternal tenofovir therapy in 331 HBEAg + pregnant women did not result in a significantly lower rate of HBV transmission compared to women who did not receive antiviral therapy (0% vs 2%, p=0.12) when provided in conjunction with HBIG immunoprophylaxis and HBV vaccination.[114] Findings from this study may not generalize to SSA where immunoprophylaxis is not consistently available. There is significant interest in the potential role of tenofovir alafenamide fumarate (TAF) therapy during pregnancy (a prodrug of tenofovir disoproxil fumarate with improved bone and renal safety profiles in adults) but studies have not yet been reported.

Entecavir, another nucleoside analog that inhibits reverse transcription and DNA replication has an excellent resistance profile and comparable efficacy and safety with tenofovir for the treatment of HBV. However, data is limited about its efficacy in pregnancy to reduce vertical transmission.[115]

Combination Interventions to Reduce HBV Prevalence in SSA

Several models have been created to identify high impact interventions using current tools (single or in combination) to reach global HBV elimination goals. In a recent model by Nayagam and colleagues, worldwide scale up of birth dose vaccination prevented 18.7 million new cases of HBV by 2030, while scale up of pentavalent vaccine coverage without birth dose vaccine prevented 4.3 million new infections.[75] In another model, a package of interventions (population wide test and treat, peripartum antiviral therapy for HBeAg+ women, universal birth dose vaccination and series completion), reduced new chronic HBV infections worldwide by 90% and mortality by 65%. A response of this scale would be

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required in order to reach Global Health Sector Strategy targets for elimination goals.[10] (Figure 1) The study also enumerates the high cost of this intervention package ($5.5 billion/year) and some of the challenges of scale up in SSA where disease prevalence is high and public health resources are limited.

Studies have also compared the cost-effectiveness of various antenatal HBV prevention strategies: universal birth dose vaccination, universal infant vaccination starting at 6 weeks or maternal HBsAg screening with targeted birth dose vaccination for exposed infants. In Cameroon, universal HBV vaccination with birth dose may be the most effective strategy in terms of reducing pediatric HBV infection by age 10 at a willingness to pay threshold of $150. [46] Similarly, universal HBV vaccination with birth dose was the least costly HBV prevention option in a population in Thailand with maternal seroprevalence of 7%. [116] Provision of HBIG for infants born to HBV infected women in Thailand was cost-effective at a willingness-to-pay threshold of $1200.

An optimal package to prevent vertical HBV transmission in SSA includes the identification of pregnant women who are highly infectious since these women may transmit HBV vertically despite birth dose vaccination and HBIG. This risk averages 8.5% but can be as high as 30% among women with elevated HBV viral load. [16,24,117,118] Identification of these women during early antenatal care would allow time for providers to discuss the risks and benefits of maternal antiviral therapy during pregnancy.

Research Gaps in the Prevention of HBV Vertical Transmission in SSA

Research innovation is needed on several fronts simultaneously to launch new efforts to reach global HBV vertical elimination targets in SSA: diagnosis, vaccination and treatment[119] For diagnosis, universal screening for HBsAg in all pregnant women would increase the awareness of infection status in this key population. The development of rapid and affordable point-of-care diagnostic testing with excellent performance characteristics would also advance the field. Point-of-care HBeAg testing could be a useful strategy in SSA to determine treatment eligibility in ANC clinic. Another pragmatic goal would involve the incorporation of HBV testing into a single testing platform to facilitate the diagnosis of multiple infections at the time of the initial antenatal visit in SSA (HIV/HBV/Syphilis).

For vaccination, innovative implementation studies in SSA are needed to optimize facility delivery rates and maximize access to monovalent birth dose in any birth setting compared to initiation at 4-6 weeks. Additional studies to develop an effective and safe heat-stable HBV vaccine product are critical. National campaigns working on birth dose vaccination should reduce patient cost constraints as much as possible.

In terms of HBV therapy, there are many new exciting pharmacologic developments in the pipeline, including combination therapies and new life cycle targets. Each new antiviral therapy or strategy will require well-designed, prospective studies to determine drug safety and efficacy in pregnant women and infants exposed to antiviral medication in-utero.[41,120] In the meantime, studies in SSA documenting the efficacy and safety of tenofovir use in HBV-infected pregnant women are needed. Relevant questions for the use of tenofovir therapy during pregnancy include: participant selection (in the absence of routine virologic testing),

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duration of therapy, timing of cessation of therapy (to reduce postpartum disease flares), mode of delivery and breastfeeding safety.[121–123] Treatment outcomes for the newest formulation of tenofovir (tenofovir alafenamide or TAF) should also be investigated since, in non-pregnant adults, TAF has lower rates of bone and nephrotoxicity compared to tenofovir disopoxil. [43] Additional studies of cost effectiveness are needed to help prioritize prevention options. Since effective antiviral therapy is already available in much of SSA (but limited to those with HIV), pregnant women with HBV will need better access to affordable therapy if HBV "treatment as prevention" becomes standard of care. [124–126] Examples of successful HBV treatment programs in SSA already exist but expansion will be necessary if certain pregnant women become eligible for routine antiviral therapy in the future. [127]

Conclusions

HBV infection is endemic in SSA and a major cause of morbidity and mortality. New and ambitious elimination targets provide an ideal opportunity to focus resources on optimizing the prevention of HBV vertical transmission. Current prevention efforts in SSA require universal access to timely HBV vaccination at birth. Public health officials and providers in SSA must continue to work to develop effective national HBV elimination strategies that are well-resourced, sustainable, supported by the community and linked to other antenatal infection prevention efforts (such as HIV prevention). Models with SSA-specific data should be used to prioritize cost-effective intervention combinations and advocate for appropriate allocation of resources. The optimal antenatal HBV prevention package in SSA is yet to be defined but future research will define the efficacy, safety and feasibility of a package that may include universal antenatal testing, targeted antiviral therapy during pregnancy and provision of HBV vaccine starting with the birth dose for all infants.

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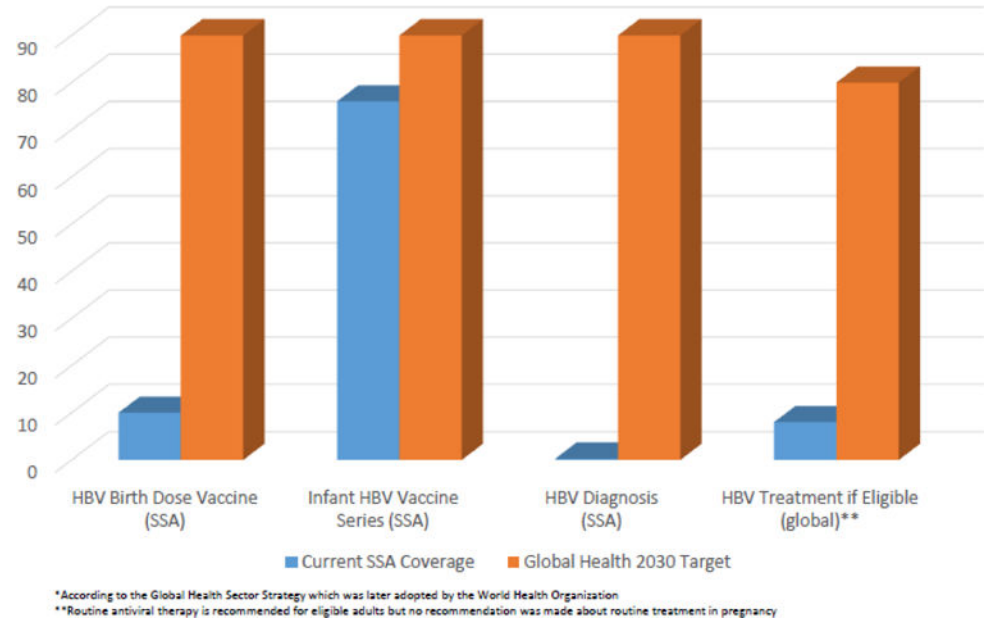

Figure 1.

Current Rates and 2030 Targets for HBV Elimination in sub-Saharan Africa *