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Assessing the impact of the routine childhood hepatitis B immunization program and the need for hepatitis B vaccine birth dose in Sierra Leone, 2018

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Abstract

Sierra Leone is highly endemic for hepatitis B virus (HBV) infection and thus recommends three doses of hepatitis B vaccine (HepB3) from 6 weeks of age but does not recommend a birth dose (HepB-BD) to prevent mother-to-child transmission (MTCT). We evaluated impact of the existing HepB3 schedule and risk for MTCT of HBV. We conducted a community-based serosurvey among 4–30-month-olds, their mothers, and 5–9-year-olds in three districts in Sierra Leone. Participants had an HBV surface antigen (HBsAg) rapid test; all HBsAg-positive and one HBsAg-negative mother per cluster were tested for HBV markers. We collected children's HepB3 vaccination history. Among 1889 children aged 4–30 months, HepB3 coverage was 85% and 20 (1·3% [95% CI 0·8–2·0]) were HBsAg-positive, of whom 70% had received HepB3. Among 2025 children aged 5–9 years, HepB3 coverage was 77% and 32 (1·6% [1·1–2·3]) were HBsAg-positive, of whom 56% had received HepB3. Of 1776 mothers, 169 (9·8% [8·1–11·7]) were HBsAg-positive. HBsAg prevalence was 5·9% among children of HBsAg-positive mothers compared to 0·7% among children of HBsAg-negative mothers (adjusted OR = 10·6 [2·8–40·8]). HBsAg positivity in children was associated with maternal HBsAg ($p = 0·026$), HBV e antigen ($p < 0·001$), and HBV DNA levels ≥ 200 000 IU/mL ($p < 0·001$). HBsAg prevalence was lower among children than mothers, for whom HepB was not available, suggesting routine infant HepB vaccination has lowered HBV burden. Since HBsAg positivity in children was strongly associated with maternal HBV infection and most of the HBsAg-positive children in the survey received HepB3, HepB-BD may prevent MTCT and chronic HBV infection.

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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.

Keywords

Hepatitis B; Vaccination; Immunisation; Vaccine preventable diseases; Sierra Leone; Mother-to-child transmission

1. Introduction

In 2015, an estimated 257 million people worldwide were living with chronic hepatitis B virus (HBV) infection, with the highest prevalence in the African (6·1%) and Western Pacific (6·2%) regions [1]. The risk of developing chronic HBV infection is inversely related to the age of acquisition of infection; up to 90% of infants infected at birth will develop a chronic infection [2]. Among those chronically infected, up to 25% will develop cirrhosis or liver cancer [2]. In areas with intermediate or high HBV population prevalence (hepatitis B surface antigen [HBsAg] > 2%), most chronic infections are attributable to mother-to-child transmission (MTCT) and early childhood transmission [3]. MTCT is more frequent among infants born to women with HBV e antigen (HBeAg) or high HBV DNA levels [4-5]. In Africa, 3–29% of HBV-infected pregnant women are HBeAg-positive; based on the results of limited studies, approximately 38% of babies born to HBeAg-positive mothers become chronically infected [6-7]. Maternal HBeAg expression in Africa is lower than reported elsewhere; in contrast, in the Western Pacific region, 32–46% of mothers are HBeAg-positive and 70–100% of their babies become infected in the absence of vaccination [7-9]. HBV genotype may play a role as different genotypes predominate in different regions [10]. However, information on MTCT risk for HBV genotypes in West Africa (E and A_3) is scarce.

The World Health Organization (WHO) recommends children receive a hepatitis B vaccine birth dose (HepB-BD), preferably within 24 h of birth, followed by two or three doses of hepatitis B vaccine (HepB) to prevent MTCT and horizontal HBV transmission [3]. All African countries have introduced three doses of HepB (HepB3), but only a few provide a HepB-BD [6]. In 2016, all WHO Member States endorsed the Global Health Sector Strategy on Viral Hepatitis targets to reduce global HBV incidence by 30% (equivalent to ≤ 1% HBsAg prevalence among 5 year-olds) by 2020 and by 95% (≤ 0·1% HBsAg prevalence among 5 year-olds) by 2030 [11]. Sierra Leone is considered highly endemic (≥ 8% HBsAg prevalence) for HBV infection [12], but little is known about HBsAg prevalence among children or the risk of MTCT. From the published literature, HBsAg prevalence was 18% among 66 unvaccinated school children in Freetown, 6% among 302 pregnant women of middle and high socio-economic class in Freetown, and 11% among 179 pregnant women in rural or *peri*-urban locations [13-15]. Sierra Leone introduced HepB in 2007 for infants aged 6, 10, and 14 weeks, and national HepB3 coverage has exceeded 80% since 2009 [16]. However, the routine vaccination schedule does not include a HepB-BD.

To evaluate the impact of the existing HepB3 schedule and the risk of MTCT of HBV, we conducted a community-based HBV sero-survey in three districts in Sierra Leone among children aged 4–30 months and their mothers, and children aged 5–9 years.

2. Methods

2.1. Survey participants and design

We included children aged 4–30 months and their mothers, and children aged 5–9 years living in Bo, Bombali, and Western Area Urban districts, which represent 32% of the national population and are located in three of the country's five provinces [17]. We set a 4-month lower age limit for the younger children to minimize potential false HBsAg positives due to transient positivity in some infants born to HBV-infected mothers or following HepB vaccination, and a 24-month upper limit in accordance with the U.S. Centers for Disease Control and Prevention (CDC) case definition of perinatal HBV infection [18]. Delays between household enumeration and serosurvey implementation led to some eligible children at pre-selected households aging out; therefore, we expanded the upper limit to 30 months to be able to meet our minimum sample size. Children aged 5–9 years (born between 2009 and 2013), who would have completed the highest risk period for developing chronic HBV infection, were included to permit a more complete estimation of HBV burden.

The estimated sample size needed for each age group of children was 1901 assuming HBsAg seroprevalence of 1%, desired precision of ± 0·75%, design effect of 1·4, and 2-sided 95% confidence interval (95% CI). Given the average household size of 4·6 persons and a birth rate of 29·5 per 1000 population, we estimated 1 in 5 households had a 4–30-month-old and 1 in 2 households had a 5–9-year-old. Assuming 25% nonresponse for the 4–30-month-old group, we estimated 2544 households should be visited, and 15% nonresponse for the 5–9-year-old group, we estimated 2332 households should be visited to achieve the desired sample size for each group.

We selected 212 out of 3900 Enumeration Areas (EAs; the lowest administrative unit used in the 2015 Census) in the three districts based on probability proportional to the number of households per EA, stratified by district [17]. In each selected EA, all households were listed to identify those with age-eligible children. Then using the lists of eligible households, we randomly selected 12 households identified as having a 4–30-month-old and 11 households identified as having 5–9-year-old per EA. Household selection for each age group was done independently; some overlap occurred where households had children in both age groups. If multiple children belonging to the same age group were present, one was randomly selected to participate. Mothers of recruited 4–30-month-olds were invited to participate. Households that did not participate were not replaced. After obtaining guardian consent and assent from children aged 5–9 years, all participants were tested for HBsAg using a rapid test (Alere Determine™). For each EA, we collected venous blood from all consenting mothers who tested positive for HBsAg by rapid test and the first HBsAg-negative mother that consented to provide blood. We also collected information on basic demographics, children's hepatitis B vaccination history, and potential exposures to HBV. We recorded hepatitis B vaccination history per the child's vaccination card, or if unavailable, per guardian verbal report. The serosurvey protocol was reviewed by the U.S. Centers for Disease Control and Prevention under human research protection procedures and was approved by the Sierra Leonean Ethical Review Board.

2.2. Specimen collection and testing

We conducted the Alere Determine™ HBsAg rapid test (Abbott Laboratories, IL; sensitivity: 95–100%, specificity: 96–100%) following the manufacturer's instructions, using capillary blood from a finger prick (or heel stick for infants < 6 months old) [19-20]. If invalid, we repeated the test on a second sample. We informed participants or their parents of their results, and if positive, referred them to their local health facility to seek care. We collected venous blood (5 mL) from consenting mothers per WHO guidelines [21], centrifuged the blood at 2000 g to collect serum, and stored the serum at 2–15 °C in a portable vehicle-based cooler until it was transferred to −20 °C at the end of each day. CDC (Atlanta) tested all serum samples, following the manufacturer's instructions, for total antibody to HBV core antigen (total anti-HBc) (VITROS Anti-HBc assay [Ortho-Clinical Diagnostics, NY; sensitivity: 92%, specificity: 100%]), HBsAg (VITROS HBsAg Test [Ortho Clinical Diagnostics, NJ; sensitivity: 90%, specificity: 100%]), and HBeAg (VITROS HBeAg Test [Ortho Clinical Diagnostics, NJ; sensitivity: 99%; specificity: 99%]). When discordant results were obtained with Alere and VITROS HBsAg tests, we tested the samples using the ARCHITECT HBsAg Test (Abbott Laboratories, IL; sensitivity: 99%, specificity: 100%). We extracted total nucleic acid using the MagNA Pure 96 DNA and viral NA kit (Roche Diagnostics, IN) according to the manufacturer's instructions. HBV DNA was quantified as described (Limit of Detection [LOD]: 250 IU/mL, specificity: 100%) [22]. We used Sanger sequencing of the HBV S-gene to genotype HBV DNA-positive samples as described [23]. For samples with discordant serological and HBV DNA results, we re-tested the samples for HBV DNA using the COBAS test (Roche Diagnostics, IN; LOD: 20 IU/mL, specificity: 100%).

2.3. Statistical analysis

We analyzed the data in SAS v9·4 (Cary, NC, USA) and present summary statistics describing participant characteristics. We calculated estimates of HBsAg seroprevalence and vaccine coverage (reported as card documented, verbal report, or combined) using methods that accounted for the two-stage cluster design with application of calculated sampling weights and adjustment for EA response rates (proportion tested or with vaccination history, respectively). We then calculated Wilson 95% CIs for each estimate and used Rao-Scott second-order Chi-square test to assess differences in seroprevalence by participant characteristics. We fitted multivariate logistic regression models with a predetermined set of potentially relevant variables (district of residence, sex, maternal education level, maternal age, maternal ethnicity, hepatitis B vaccination history, and circumcision) to evaluate their relationship with HBsAg prevalence; then calculated odds ratios (OR), Wilson 95% CIs, and Wald p-values. We present summary statistics describing the distribution of HBV markers among mothers and the relationship of those markers to HBsAg positivity in children. We fitted univariate logistic regression models to evaluate the relationship between maternal HBV markers and HBsAg positivity in their children and presented ORs, Wilson 95% CIs, and Wald p-values.

3. Results

During November 7–December 18, 2018, survey teams enrolled 1889 children aged 4–30 months from 2243 households (84%), 1776 of their mothers (94%; n = 1776/1889), and 2025 children aged 5–9 years old from 2364 households (85%). Approximately 5% of households refused and 10% could not be located. Among children aged 4–30 months, 53% were male, 53% lived in Western Area Urban, 25% in Bo, and 22% in Bombali (Table 1). The median age was 17 months (interquartile range [IQR] 11–23 months). According to their guardian, 86% were born at a public health facility, 9% were born at home, and a skilled birth attendant (SBA; defined as a midwife, physician, obstetrician, nurse, or other healthcare professional that was present during the birth) was present at 98% of births (Table 1). Among mothers of 4–30-month-olds, the median age was 26 years (IQR 22–31 years). Forty-one percent of mothers had never attended school (Table 1). Among children aged 5–9 years, 49% were male, 54% lived in Western Area Urban, 23% in Bo, and 23% in Bombali (Table 1). The median age was 7 years (IQR 6–8 years). According to their guardian, 81% were born at a public health facility, 13% were born at home, and an SBA was present at 94% of births (Table 1).

We determined hepatitis B immunization history from children's immunization cards for 70% (n = 1332/1889) of the 4–30-month-olds and 22% (n = 437/2025) of the 5–9-year-olds and from guardian report for 26% (n = 489) of 4–30-month-olds and 66% (n = 1346) of 5–9-year-olds. No information on hepatitis B vaccination history (defined as no vaccination card and unknown history from guardian) was available for 4% (n = 68) of the 4–30-month-olds and 12% (n = 242) of the 5–9-year-olds. HepB3 coverage based on card or verbal report was 85% (95% CI 82–87) among children aged 4–30 months and 77% (95% CI 72–81) among children aged 5–9 years (Table 2).

HBsAg prevalence was 1·3% (95% CI 0·8–2·0) among children aged 4–30 months, 9·8% (95% CI 8·1–11·7) among their mothers, and 1·6% (95% CI 1·1–2·3) among children aged 5–9 years. There was no difference in HBsAg prevalence between the two age groups of children (p = 0·476). Children from both age groups were enrolled from 384 households; of these children, four 4–30-month-olds and seven 5–9-year-olds were HBsAg-positive, none from the same household. For both age groups, HBsAg prevalence did not differ by sex, district of residence, HepB3 receipt, blood transfusion, or circumcision, and additionally for the younger children, maternal age, education, or religion did not affect the HBsAg prevalence (Table 3). HBsAg prevalence among those who received no doses of HepB was higher (5·7% for 4–30-month-olds and 3·7% for 5–9-year-olds) than among those who received the recommended three doses (1% for 4–30-month-olds and 1·3% for 5–9-year-olds). HBsAg positivity decreased with each additional HepB dose received; however, these differences were not statistically significant due to the small number of unvaccinated children (Table 3). For children aged 4–30 months, HBsAg prevalence was 5·9% among those with HBsAg-positive mothers and 0·7% for those with HBsAg-negative mothers (p = 0·024; Table 3). Maternal HBsAg positivity remained a significant independent predictor of HBV infection in the child when adjusted for the child's sex, district of residence, HepB3 receipt, circumcision, and maternal age, education, and religion (AOR: 10·6 [95% CI 2·7–40·8]; p < 0·001). Of 20 HBsAg-positive children aged 4–30 months, 70% (n = 14) received

HepB3—11 card-confirmed and three by verbal report—and mother–child paired HBsAg rapid test results were available for 16. Of these 16 children, 10 (63%) had HBsAg-positive mothers. Of the 32 HBsAg-positive children aged 5–9 years, 56% (n = 18) received HepB3—five card-confirmed and 13 by verbal report.

We tested serum samples from 137 of the 169 HBsAg-positive mothers (82%) and 200 HBsAg-negative mothers using the HBsAg rapid test. Two of the HBsAg-negative mothers based on rapid test results were HBsAg-positive by the VITROS and ARCHITECT HBsAg assays, resulting in a total of 139 HBsAg-positive and 198 HBsAg-negative maternal serum samples. Among 139 HBsAg-positive mothers, 99% were total anti-HBc positive, 9% (n = 13) were HBeAg-positive, 91% (n = 126) had detectable HBV DNA, among whom 17% (n = 23) had HBV DNA levels ≥ 20,000 IU/mL and 9% (n = 12) had HBV DNA levels ≥ 200,000 IU/mL (the recommended threshold for antiviral treatment to prevent MTCT) [24], and all sequenced samples belonged to genotype E (Table 4). Of the 23 mothers with HBV DNA levels ≥ 20,000 IU/mL, 12 were HBeAg-positive. HBeAg positivity was strongly associated with HBV DNA levels ≥ 200,000 IU/mL (OR 23·1 [95% CI 9·0–59·7], p < 0·0001). Of the 13 HBeAg-positive mothers, 77% (n = 10) had HBV DNA levels ≥ 200,000 IU/mL. In contrast, although 90% (n = 113) of the 126 HBeAg-negative mothers had detectable HBV DNA, only 2% (n = 2) had HBV DNA levels ≥ 200,000 IU/mL. Among the 139 HBsAg-positive mothers who provided blood samples, eight (6%) had a HBsAg-positive child aged 4–30 months. Of the 13 HBsAg/HBeAg-positive mothers, seven (54%) had a HBsAg-positive child. In contrast, only one (0·8%) of the 126 HBsAg-positive/HBeAg-negative mothers had a HBsAg-positive child (Table 4). Fifty-eight percent of mothers with HBV DNA levels ≥ 200,000 IU/mL (n = 7/12) had a HBsAg-positive child (Table 4). This increased to 75% (n = 6/8) in mothers with HBV DNA levels > $1x10^8$ IU/mL, all of whom were HBeAg-positive. Among mothers with HBV DNA levels < 200,000 IU/mL, 0·8% (n = 1/124) had a HBsAg-positive child. The mother of this HBsAg-positive child was HBeAg-negative with < 316 IU/mL HBV DNA at the time of testing. The presence of either HBsAg, HBeAg, or HBV DNA levels ≥ 200,000 IU/mL in maternal serum was associated with HBsAg positivity in the child (Table 5). Among 198 HBsAg-negative mothers, 69% (n = 137) were total anti-HBc positive, 5% (n = 10) had detectable HBV DNA (range 250–12,589 HBV DNA IU/mL), and of the nine sequenced samples, eight belonged to genotype E and one to genotype A2. Of the 198 HBsAg-negative mothers, two had an HBsAg-positive child (both had card confirmed receipt of 3 doses of HepB); one mother was total anti-HBc positive, and neither had detectable HBV DNA at the time of testing. All mothers were asked if anyone living in the household had HBV. Thirteen mothers replied in the affirmative; however, none of the participating children from those households tested positive for HBsAg.

4. Discussion

High HBsAg prevalence (9·8%) among mothers and total anti-HBc prevalence (69%; indicative of previous HBV infection) among HBsAg-negative mothers confirm the high endemicity of HBV infection in Sierra Leone. These results, which are similar to previous HBsAg prevalence estimates among women of childbearing age in Sierra Leone (6·3%-11·2%) and West Africa (6·3%–16·2%) and total anti-HBc prevalence estimates in

West Africa, reflect the high HBV disease burden in this region and the ongoing MTCT risk [6,13-14,25]. HBsAg prevalence among children aged 4–30 months (1·3%) and 5–9 years (1·6%) was much lower compared to the mothers (9·8%)—for whom hepatitis B vaccine would not have been available; it was also lower than the previous estimate (18·2%) among children before HepB introduction [3,15]. Given the relatively high HepB3 coverage (>75%) in children and the much lower HBsAg prevalence among children than among mothers, these results suggest it is likely that routine infant HepB vaccination has substantially lowered HBV burden among children in Sierra Leone. Furthermore, the observations that HBsAg positivity in young children was strongly associated with having a mother with active HBV infection, that both age groups of children had similar HBsAg prevalence, and that > 70% of HBsAg-positive children aged 4–30 months old received HepB3, supports the conclusion that most of the residual infections that continue to occur among children are likely acquired at birth or prior to receipt of the first dose of HepB. Thus, Sierra Leone may consider introducing the HepB-BD to prevent MTCT of HBV and chronic HBV infections occurring before the first dose of HepB. The introduction of HepB-BD could also help Sierra Leone towards reaching the global hepatitis B elimination (HBsAg ≤ 0·1%) target by 2030 [11,26].

Preventing HBV infection in newborns is important as at this age HBV infection is much more likely to become chronic and lead to premature death [3]. When provided within 24 h after birth followed by at least two additional doses, HepB is approximately 90% effective at preventing perinatal HBV infection [3]. Thus, WHO recommends that all infants (including low birth weight and premature infants) receive their first HepB dose as soon as possible after birth, ideally within 24 h, followed by 2 or 3 additional doses [3]. China, Thailand, and Taiwan achieved < 1% HBsAg prevalence among children when high universal HepB3 and HepB-BD coverage was achieved [27-29].

The reported high SBA (> 95%) and health facility births (> 80%) in this serosurvey, higher than those reported in Multiple Indicator Cluster Survey (MICS; 82% and 77%, respectively), suggest HepB-BD introduction is feasible and high timely coverage could be achieved, which together with completion of the HepB3 vaccination series is the most effective strategy to prevent HBV infection [30]. In the context of intermediate (2–8%) or high (≥ 8%) chronic HBV infection population prevalence, such as in Sierra Leone, where MTCT and early childhood transmission are the main routes of infection, universal HepB-BD vaccination is a proven cost-effective strategy [31]. Other control strategies, such as screening pregnant women to provide hepatitis B immunoglobulin (HBIG) within 12 h of birth for children born to HBsAg-positive mothers and/or antivirals to pregnant women that meet WHO criteria for treatment, are best considered once high vaccination coverage has been achieved and where additional resources are available to manage and sustain HBV screening and treatment programs [11,32]

HepB3 coverage was relatively high (> 75%) among enrolled children and similar to estimates reported in the Demographic and Health Survey (78% among children aged 12–23 months; 2013) and the MICS (85% for children aged 12–23 months; 2017) [30,33], which are also community-based surveys, but lower than the WUENIC (90%) and country reported (94%) estimates for 2018 [16]. Our estimates suggest HepB3 coverage is below the global

targets of 90%. Thus, increasing coverage to > 90% would further reduce HBsAg prevalence among children [34].

Most HBsAg-positive mothers (91%) had detectable HBV DNA and thus could potentially transmit HBV; however, HBeAg prevalence was low (9%) similar to other estimates in West Africa (11%–29%) [6-7]. Among children for whom information on maternal HBV infection markers was available, the main risk factors for chronic HBV infection were their mother being HBsAg-positive, HBeAg-positive, or having high levels of HBV DNA, as has been shown previously [4-5,35]. We found more children (54%) were HBsAg-positive if their mothers were HBeAg-positive than had been previously reported (38%) by a *meta*-analysis of less robust studies conducted in the region, suggesting MTCT of HBV among HBeAg-positive mothers continues to be an important route of transmission in Africa [7].

HBV genotype E predominated in the survey and is the predominant genotype in West Africa [10]. Long-term cohort studies in The Gambia found that HBV genotype E infections were characterized by a shorter duration of viremia, which may reflect the lower proportion of women who are HBeAg-positive in the region [36]. However, low HBeAg-positivity could also be due to lower test sensitivity [37]. The same studies found that > 50% of those with severe disease were attributable to having a HBsAg-positive mother, highlighting the importance of preventing MTCT in the region to reduce HBV-related severe liver disease [36].

Among HBsAg-negative mothers, we identified ten potential occult HBV infections with detectable HBV DNA levels > 250 IU/mL. These were most likely due to the HBsAg concentrations being below the limit of detection of the VITROS HBsAg Test. The clinical and epidemiological significance of these types of infections is unclear but may have potential implications for the blood transfusion services and screening of pregnant women [38].

This study has some limitations, most of which are inherent to the cross-sectional survey design. First, since HBsAg prevalence among 4–30-month-olds could reflect both vertical and horizontal HBV transmission, the role of MTCT may be overestimated. However, since most children received HepB3, with the first dose given at 6 weeks of age, they would have had some protection reducing the contribution of horizontally acquired HBV infection. Second, maternal HBV markers were determined months after the birth of their child, and the findings might have been different than those obtained during their pregnancies, had they been done. Third, some information was not available, such as the characteristics of non-participating eligible households so we could not determine how they compared to enrolled households. We also did not test other household members to assess other potential routes of transmission. Fourth, it was not nationally representative; however, the three included districts account for 32% of the population and incorporate a large urban area with residents originating from many parts of the country. Fifth, since so few children reported receiving zero doses of HepB we were unable to assess the impact of receipt of different HepB doses in the multivariate model. Sixth, vaccination card retention was low among 5–9-year-olds, and the reliance on parental recall may have reduced the accuracy of these estimates. Finally, although the Alere Determine HBsAg rapid test has very good sensitivity,

we may have missed some children or mothers whose HBsAg levels were below the LOD for the test. However, the impact of this would have likely underestimated the level of HBV infection burden and the association of HBsAg positivity in young children with having a mother who had active HBV infection.

5. Conclusions

This survey provides important information on the impact of routine infant HepB vaccination and the ongoing risk of MTCT, particularly for infants whose mothers have high HBV DNA levels, which have rarely been documented in West Africa. The results of this study suggest that it is likely that routine infant HepB vaccination has substantially reduced HBV infection among children in Sierra Leone but that the prevalence of chronic HBV infection among mothers is high and, there remains an ongoing risk of MTCT. As HBsAg positivity in young children was strongly associated with having a mother who had active HBV infection and because > 70% of HBsAg positive children aged 4–30 months received HepB3, HepB-BD introduction may help prevent MTCT transmission and chronic HBV infections. This would help Sierra Leone towards achieving the global HBV elimination goal by 2030.

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Disclaimer

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Abbreviations:

HBV	hepatitis B virus
HBsAg	hepatitis B virus surface antigen
HepB	hepatitis B vaccine
HepB-BD	hepatitis B vaccine birth dose

HepB3	Three doses of hepatitis B vaccine
WHO	World Health Organization
WUENIC	WHO and UNICEF estimates of national immunization coverage
CI	Confidence interval
IU	International units
IQR	Interquartile range
HBeAg	hepatitis B virus e antigen
MTCT	Mother-to-child transmission
SBA	Skilled birth attendant
LOD	Limit of Detection
EA	Enumeration area
total anti-HBc	total antibodies to the hepatitis B virus core antigen
U.S. CDC	United States Centers for Disease Control and Prevention

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Table 1

Characteristics of children enrolled in the hepatitis B serosurvey — Sierra Leone, 2018.

	4–30 months old (N =1889)		5–9 years old (N = 2025)	
Variable	**No.**	**%**	**No.**	**%**
Sex				
Male	999	52·9	995	49·1
Female	890	47·1	1029	50·8
Unknown	–	–	1	0·1
District				
Western Area Urban	1004	53·1	1097	54·2
Bo	466	24·7	467	23·1
Bombali	419	22·2	461	22·7
Age (months)/(years)				
4–6 months /5 years	141	7·5	356	17·6
7–12 months/6 years	426	22·6	483	23·9
13–18 months/7 years	470	24·9	440	21·7
19–24 months/8 years	484	25·6	407	20·1
25–30 months/9 years	368	19·4	339	16·7
Skilled Birth Attendant present at birth				
Yes	1843	97·6	1899	93·8
No	44	2·3	79	3·9
Unknown	2	0·1	47	2·3
Location of birth				
Home	165	8·7	266	13·2
Public hospital	676	35·8	675	33·3
Public health center	568	30·1	592	29·2
Public health post	373	19·8	364	18·0
Private health facility	101	5·3	94	4·6
Unknown	6	0·3	34	1·7
Maternal age (years)				
15–20	207	11·0	..	..

Variable	4–30 months old (N =1889)		5–9 years old (N = 2025)	
	No.	%	No.	%
21–25	453	24·0	..	..
26–30	386	20·4	..	..
31–35	232	12·3	..	..
>35	146	7·7	..	..
Unknown	465	24·6	..	..
Maternal religion				
Islam	1217	64·4	..	..
Christian	558	29·5	..	..
Unknown	114	6·1	..	..
Maternal ethnicity				
Temne	608	32·2	..	..
Mende	534	28·3	..	..
Limba	193	10·2	..	..
Loko	120	6·3	..	..
Fullah	85	4·5	..	..
Mandingo	79	4·2	..	..
Other Sierra Leone or foreign	157	8·3	..	..
Unknown	113	6·0		
Maternal education (*highest level of school attended*)				
No school	767	40·6	..	..
Primary school	211	11·2	..	..
Junior school	339	17·9	..	..
Senior school	343	18·1	..	..
Vocational	62	3·3	..	..
Higher	53	2·8	..	..
Unknown	114	6·1	..	..

No. – number, % – percent.

Table 2

Hepatitis B vaccination status among children aged 4–30 months and 5–9-years in Bo, Bombali, and Western Area Urban—Sierra Leone, 2018.

	4–30-months old (n = 1821)		5–9-years old (n = 1783)	
Vaccine	**N**	**% (95% CI)**	**N**	**% (95% CI)**
HepB dose 1				
Vaccination card	1317	73·7 (70·6, 76·6)	426	26·0 (22·1, 30·3)
Verbal report	404	20·6 (17·7, 23·8)	1103	56·2 (50·0, 62·2)
Either source	1721	94·3 (92·0, 96·0)	1529	82·1 (77·4, 86·0)
HepB dose 2				
Vaccination card	1278	71·5 (68·3, 74·5)	415	25·4 (21·5, 29·7)
Verbal report	391	19·8 (16·9, 23·1)	1096	55·6 (49·5, 61·6)
Either source	1669	91·3 (88·9, 93·2)	1511	81·0 (76·3, 85·0)
HepB dose 3				
Vaccination card	1203	67·0 (63·6, 70·2)	388	24·2 (20·3, 28·4)
Verbal report	350	17·6 (14·9, 20·6)	1046	52·4 (46·4, 58·3)
Either source	1553	84·6 (81·6, 87·2)	1434	76·5 (71·8, 80·7)

Coverage estimates accounted for sampling weights and were adjusted for missing vaccination history. N – number; % – percent, 95% CIs – 95% confidence intervals, HepB – hepatitis B vaccine.

Table 3

Determinants of HBsAg prevalence among children aged 4–30 months and 5–9 years in Bo, Bombali, and Western Area Urban—Sierra Leone, 2018.

	4–30-month-olds				5–9-year-olds			
	No. tested	**No. HBsAg+**	**HBsAg prevalence (Wilson 95% CIs)**	**P-value**	**No. tested**	**No. HBsAg+**	**HBsAg prevalence (Wilson 95% CIs)**	**P-value**
Overall HBsAg prevalence	1887	20	1·3% (0·8, 2·0)		2022	32	1·6% (1·1, 2·3)	
Sex								
Male	997	13	1·7% (1·0, 3·1)		993	19	1·8% (1·1, 3·0)	
Female	890	7	0·7% (0·3, 1·8)	0·110	1028	13	1·3% (0·7, 2·4)	0·436
District								
Western Area Urban	1002	11	1·2% (0·6, 2·4)		1095	14	1·4% (0·8, 2·4)	
Bo	466	5	1·1% (0·5, 2·7)		466	11	2·0% (1·1, 3·7)	
Bombali	419	4	1·5% (0·6, 3·6)	0·916	461	7	1·3% (0·5, 3·1)	0·579
Received HepB [*]								
3 doses	1552	14	1·0% (0·5, 1·9)		1432	18	1·3% (0·8, 2·2)	
1 or 2 doses	167	3	2·3% (0·8, 7·0)		95	2	1·5% (0·3, 6·5)	
0 doses	25	1	5·7% (1·2, 23·0)		29	1	3·7% (0·7, 17·5)	
Unknown	143	2	1·6% (0·4, 5·9)	0·190	466	11	2·0% (1·1, 3·8)	0·531
Blood transfusion [ɣ]								
Yes	19	1	6·1% (1·2, 26·2)		77	1	1·3% (0·2, 7·0)	
No	1864	19	1·2% (0·7, 2·0)	0·417	1921	30	1·5% (1·0, 2·3)	0·862
Circumcision [ɣ]								
Yes	586	9	2·3% (1·1, 4·6)		955	18	1·8% (1·0, 2·9)	
No	1300	11	0·8% (0·4, 1·6)	0·115	1064	14	1·4% (0·8, 2·4)	0·540
Maternal age (years) [≠]								
15–25	660	9	1·2% (0·5, 2·6)		..	..	..	
>25	763	4	1·0% (0·4, 2·6)		..	..	..	
Unknown	351	3	1·6% (0·6, 4·5)	0·447	..	..	..	..
Maternal Education [≠ ɣ]								
None	766	5	1·2% (0·5, 2·7)		..	..	..	
Primary & Junior School	549	8	1·5% (0·7, 3·4)		..	..	..	

	4–30-month-olds				5–9-year-olds			
	No. tested	**No. HBsAg+**	**HBsAg prevalence (Wilson 95% CIs)**	**P-value**	**No. tested**	**No. HBsAg+**	**HBsAg prevalence (Wilson 95% CIs)**	**P-value**
Senior School & Higher	458	3	0·7% (0·2, 2·6)	0·634	..	..	..	..
Maternal religion ≠ ϒ								
Islam	1215	10	1·1% (0·5, 2·1)		..	..	..	
Christian	558	6	1·5% (0·7, 3·3)	0·567	..	..	..	..
Maternal HBsAg (Alere)≠								
Positive	169	10	5·9% (2·8, 11·8)		..	..	..	
Negative	1605	6	0·7% (0·3, 1·5)	0·024	..	..	..	..

No. – number, 95% CIs – 95% confidence intervals.

* Includes vaccination card documented and verbal report of hepatitis B containing vaccine receipt.

≠ Excludes 113 mothers (6%) that refused or were unable to participate.

ϒ Excludes unknown values. Unknown values were included in maternal age as they accounted for > 20% of the values, whereas for all other variables unknown values were < 5.

Table 4

Frequency of HBV markers (total anti-HBc, HBeAg, HBV DNA, and HBV genotype status) among HBsAg-positive mothers and the HBV infection status of their children by maternal HBV marker—Sierra Leone, 2018.

Maternal HBV Marker	HBsAg + mothers (N = 139) n (%)	Children (4–30-month olds)	
		HBsAg+ (N = 8) n (%)	HBsAg− (N = 131) n (%)
Total anti-HBc			
Positive	138 (99·0)	8 (5·8)	130 (94·2)
Negative	1 (1·0)	0 (0·0)	1 (100·0)
HBeAg			
Positive	13 (9·3)	7 (53·8)	6 (46·2)
Negative	126 (90·7)	1 (0·8)	125 (99·2)
HBV DNA levels (IU/mL) *			
<250	13 (9·4)	0 (0·0)	13 (100·0)
250-<2000	81 (58·3)	1 (1·2)	80 (98·8)
2000-<20,000	22 (15·8)	0 (0·0)	22 (100·0)
20,000-<200,000	11 (7·9)	0 (0·0)	11 (100·0)
≥200,000	12 (8.6)	7 (58·3)	5 (41·7)
HBV genotype	(n = 126)		
Unable to genotype	23 (18·3)	1 (4·3)	22 (95·7)
E	103 (81·7)	7 (6·8)	96 (93·2)

HBV – hepatitis B virus, HBsAg – hepatitis B surface antigen, No. – number, % – percent, total anti-HBc – total antibodies to hepatitis B virus core antigen, HBeAg – hepatitis B virus e antigen, IU/mL – International Units per milliliter. After being tested by the Alere Detrmine™ HBsAg rapid test, 137 HBsAg-positive and 200 HBsAg-negative mothers consented to provide blood samples which were then tested for anti-HBc, HBsAg, HBeAg, and HBV DNA on commercially available assays in the laboratory. HBsAg confirmatory testing identified 139 mothers of those who provided serum to be HBsAg-positive.

* Limit of detection is 250 IU/ml and the limit of quantification is 316 IU/ml.

Table 5

Association of maternal HBV markers (total-HBc, HBsAg, HBeAg, HBV DNA levels) with HBsAg positivity in the 4–30-month-olds—Sierra Leone, 2018.

Maternal HBV Marker	No. of mothers (N = 336)	No. of HBsAg+ 4–30-month olds (N = 10)	OR	95% CI	P value (Wald)
Total anti-HBc					
Negative	62	1	Ref		
Positive	274	9	1·4	0·5 – 4·1	0·494
HBsAg					
Negative	197	2	Ref		
Positive	139	8	2·4	1·1 – 5·3	0·026
HBeAg	(N = 335)				
Negative	322	3	Ref		
Positive	13	7	11·1	5·1 – 24·5	<0·001
HBV DNA levels * (IU/mL)					
<200,000	321	3	Ref		
≥200,000	12	7	12·2	5·5 – 27·4	<0·001

HBV – hepatitis B virus, HBsAg – hepatitis B surface antigen, No. – number, HBsAg+ – hepatitis B surface antigen positive, OR – odds ratio, 95% CI – 95% confidence interval, total anti-HBc – total antibodies to hepatitis B virus core antigen, HBeAg – hepatitis B virus e antigen, IU/mL – International Units per milliliter, Ref – reference. After being tested by the Alere Detrmine™ HBsAg rapid test, 137 HBsAg-positive and 200 HBsAg-negative mothers consented to provide blood samples which were then tested for anti-HBc, HBsAg, HBeAg, and HBV DNA on commercially available assays in the laboratory. HBsAg confirmatory testing identified 139 mothers of those who provided serum to be HBsAg-positive. Results presented include mother–child pairs where both have valid test results.

* Limit of detection is 250 IU/ml and the limit of quantification is 316 IU/ml.