



Review

A reduction in chronic hepatitis B virus infection prevalence among children in Vietnam demonstrates the importance of vaccination



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ABSTRACT

Background: Vietnam has high endemic hepatitis B virus infection with >8% of adults estimated to have chronic infection. Hepatitis B vaccine was first introduced in the national childhood immunization program in 1997 in high-risk areas, expanded nationwide in 2002, and included birth dose vaccination in 2003. This survey aimed to assess the impact of Vietnam's vaccination programme by estimating the prevalence of hepatitis B surface antigen (HBsAg) among children born during 2000–2008.

Methods: This nationally representative cross-sectional survey sampled children based on a stratified three-stage cluster design. Demographic and vaccination data were collected along with a whole blood specimen that was collected and interpreted in the field with a point-of-care HBsAg test.

Results: A total of 6,949 children were included in the survey analyses. The overall HBsAg prevalence among surveyed children was 2.70% (95% confidence interval (CI): 2.20–3.30). However, HBsAg prevalence was significantly higher among children born in 2000–2003 (3.64%) compared to children born 2007–2008 (1.64%) (prevalence ratio (PR): 2.22, CI: 1.55–3.18)). Among all children included in the survey, unadjusted HBsAg prevalence among children with ≥ 3 doses of hepatitis B vaccine including a birth dose (1.75%) was significantly lower than among children with ≥ 3 doses of hepatitis B vaccine but lacked a birth dose (2.98%) (PR: 1.71, CI: 1.00–2.91) and significantly lower than among unvaccinated children (3.47%) (PR: 1.99, CI: 1.15–3.45). Infants receiving hepatitis B vaccine >7 days after birth had significantly higher HBsAg prevalence (3.20%) than those vaccinated 0–1 day after birth (1.52%) (PR: 2.09, CI: 1.27–3.46).

Conclusion: Childhood chronic HBV infection prevalence has been markedly reduced in Vietnam due to vaccination. Further strengthening of timely birth dose vaccination will be important for reducing chronic HBV infection prevalence of under 5 children to <1%, a national and Western Pacific regional hepatitis B control goal.

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1. Introduction

Hepatitis B virus (HBV) infection is highly endemic in Vietnam with an estimated chronic infection prevalence among adults of 8–20% [1–4]. A survey in two districts in Thanh Hoa Province in 1998 showed prevalence of HBsAg, a marker for chronic HBV infection, to be 12% among infants, 18% among children (4–5 years), 20% among adolescents (14–15 years), and 19% among adults (25–39 years) [5]. HBV is a known carcinogen and the high prevalence of chronic HBV infection is an important contributing factor to liver cancer and cirrhosis, which is the most common cause of cancer death in Vietnam [6–8].

Like other countries in South East and Eastern Asia, the primary routes of HBV transmission in Vietnam are from mother-to-child or from close contacts during early childhood [9]. Hepatitis B vaccine is highly effective in preventing both perinatally and horizontally acquired chronic HBV infection [10–12]. Therefore, to reduce chronic HBV infection prevalence and protect children from infection, Vietnam introduced hepatitis B vaccine in the national immunization program in 1997 in selected areas. Infant hepatitis B vaccination program was expanded nationwide in 2002 and a monovalent hepatitis B vaccine birth dose was introduced in 2003 with financial support from the GAVI Alliance; the birth dose was initially recommended to be given within 7 days after birth; in 2002, it was recommended to be given within 3 days after birth, and in 2006 it was recommended to be given within 24 h after birth, the birth dose was given at health facilities only. Since 2010, the subsequent hepatitis B doses are given as part of a pentavalent DPT-Hib-Hepatitis B vaccine schedule at ages 2, 3, and 4 months, parents were requested to bring their child to commune health center and outreach points (for hard to reach areas only) for vaccination.

Three-dose hepatitis B vaccine coverage has increased substantially over time from 24% in 2000 to >90% every year starting in 2004 [13,14]. Additionally, birth dose coverage rapidly reached nearly 60% within 2 years after birth dose introduction in 2003. However, birth dose coverage declined dramatically to 29% in 2007 and 26% in 2008 following media reports of alleged adverse events following hepatitis B birth-dose administration [13,14].

To evaluate the impact of the hepatitis B vaccination program, a survey was conducted to look at chronic HBV infection prevalence among children born in three time periods representing different hepatitis B immunization programmatic strategies and performance: the first period (2000–2003) represents a phased introduction of hepatitis B vaccine with low birth dose coverage; the second period represents high birth dose coverage and high three dose hepatitis B vaccine coverage (2004–2006); and the third period (2007–2008) represents a decrease in birth dose coverage after the media reports of alleged adverse events.

2. Methods

2.1. Study population and design

The survey was designed to estimate HBsAg prevalence among a nationally representative sample of children born in three birth cohort groups: 2000–2003, 2004–2006, and 2007–2008. Expected prevalence was assumed to be 8%, 2%, and 4% and the desired precision of $\pm 2\%$, $\pm 1\%$, and $\pm 1\%$, respectively. The greater sample size in the younger cohorts was based on a desire to have a more precise measure relating to the most recent programmatic activities. A design effect of 2 and non-response rate of 20% was assumed for all 3 cohorts. Resulting sample size was 1696 for the 2000–2003 cohort, 1807 for the 2004–2006 cohort, 3540 for the 2007–2008 cohort and total sample size of 7044.

2.2. Sampling method and enrollment

This cross-sectional survey sampled children using a stratified three-stage cluster design. The district-level coverage of birth-dose given within 24 h in 2006 was used as a stratification variable. All 684 districts in the country were stratified into four strata of timely birth dose coverage: $\geq 50\%$, 25–49%; 10–24%; and $<10\%$. Ninety-eight primary sampling units (districts) were allocated to the four strata based on the population size of each; specifically, 63, 16, 6, and 13 districts were selected in the $\geq 50\%$, 25–49%; 10–24%; and $<10\%$ birth dose coverage categories, respectively. Two communes were randomly selected from each selected district. Nine children born in years 2000–2003, nine children born in years 2004–2006, and 18 children born in years 2007–2008 were randomly selected from commune lists. District health staff and commune leaders were informed of the survey site selection in advance; parents received a letter requesting them to bring selected children and vaccination records to a designated commune health post on the survey day.

2.3. Individual-level data: questionnaire, specimen collection and testing

A questionnaire was administered to the child's caregiver to collect basic socio-demographic information and vaccination history of the child. The Alere Determine™ HBsAg rapid assay test was used to detect HBsAg in whole blood specimens obtained from children [15]. Procedures were followed according to the package insert, including (1) obtaining approximately 50 microlitres of whole blood using a finger-prick, (2) immediately applying the whole blood specimen to the test strip, (3) visually reading and recording the results of the test strip after 15 min, and (4) confirming the test results by having a supervisor re-read the strip within 24 h.

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