

## **Which Newborns Missed the Hepatitis B Birth Dose vaccination?**

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### **Abstract**

**Background:** In the 2002, the Advisory Committee on Immunization Practices (ACIP) indicated a preference for administering the first dose of hepatitis B vaccine for all infants soon after birth and before hospital discharge (birth dose). In 2005, the ACIP recommended the first dose of hepatitis B vaccine at birth routinely for all infants, to improve prevention of perinatal and early childhood hepatitis B virus (HBV) transmission.

**Objective:** Assess the prevalence of infants who missed the hepatitis B birth dose vaccination. Identify socio-demographic factors associated with non-receipt of the birth dose among infants in the United States.

**Methods:** A cross-sectional prevalence study was conducted for non-receipt of the hepatitis B birth dose vaccination among 17,053 infants in the 2009 National Immunization Survey (NIS). Multivariable logistic regression analysis was applied to determine factors independently associated with not receiving the birth dose of hepatitis B vaccine.

**Results:** Infants whose parents refused or delayed at least one vaccination were significantly less likely to receive the birth dose of hepatitis B vaccine compared to infants whose parents did not (adjusted Risk Ratio (RR) with 95% Confidence Interval 1.11(1.04, 1.19)). Lack of health insurance for infants was also significantly associated with non-receipt of the birth dose hepatitis B vaccine (adjusted RR 1.18 (1.08, 1.28)). Infants residing in state without a universal supply policy for hepatitis B were significantly more likely to not receive the hepatitis B birth dose (adjusted RR 1.19 (1.11, 1.29)).

**Conclusions:** Infants without health insurance, residing in states having not universal hepatitis B vaccine supply policy, and whose parent refused or delayed at least one vaccination were modifiable factors significantly associated with not receiving the birth dose of hepatitis B vaccination. Educating infants' parents and their providers on best vaccine practices will warrant increasing the hepatitis B birth dose vaccination rate in the US.

**Key words:** Hepatitis B vaccine, birth dose, universal supply policy, infants, ACIP recommendations.

## 1. Introduction

In 1991, the Advisory Committee on Immunization Practices (ACIP) first recommended hepatitis B vaccination for all infants regardless of the hepatitis B surface antigen (HBsAg) status of the mother, and hepatitis B vaccine was incorporated into the routine childhood vaccination schedule. The first dose could be administered during the newborn period, preferably before the infant was discharged from the hospital, but no later than when the infant was 2 months of age [1]. In 2002, the ACIP expressed a preference for administering the first dose of hepatitis B vaccine soon after birth and before hospital discharge [2]. In order to accelerate progress toward elimination of hepatitis B virus (HBV) transmission in the United States, on December 23, 2005, the ACIP recommended a “birth dose” of hepatitis B vaccination for all infants prior to discharge from the birthing hospital, ideally within 12 hours of birth, as a “safety net” for prevention of perinatal and early childhood HBV infection. The recommendations were supplemented with strategies for implementation including: 1) establishing hospital standing orders for administration of hepatitis B vaccination beginning at birth; and 2) instituting delivery hospital policies and procedures and case management programs to improve identification of and administration of immunoprophylaxis to infants born to mothers who are HBsAg positive and to mothers with unknown HBsAg status at the time of delivery [3].

Hepatitis B birth dose vaccination is a critical step in preventing perinatal HBV infection. The risk for chronic infection is greatest among infants and young children; approximately 90% of infants and 30% of children before age 5 years who acquire HBV infection become chronic carriers. An estimated 25% of those who become chronically infected during childhood will die of liver failure secondary to chronic active hepatitis, cirrhosis, or primary hepatocellular carcinoma [4]. The birth dose of hepatitis B vaccine is the most effective initial measure to prevent HBV infection and its consequences [3]. Completion of the hepatitis B vaccine series alone, when started within the first day of life, prevents 70% - 95% of perinatal HBV infections, as well as early childhood HBV infections acquired from HBV-infected household contacts [3].

A birth dose of hepatitis B vaccine provides a safety net against errors in maternal hepatitis B testing, reporting, and exposure to HBV infected household contacts. Recent data suggest that approximately 50% of expected births to HBsAg-positive women may be identified, even when maternal HBsAg testing does occur. In this setting, infants born of HBsAg-positive mothers may not receive postexposure immunoprophylaxis [5]. Infants born of women with unknown HBsAg status at the time of delivery also may miss receiving hepatitis B vaccine at birth because of delays in testing [6]. Routine hepatitis B vaccination at birth ensures some protection for these infants.

When the mother is HBsAg negative, but the infant is exposed to HBV postnatally from another family member or caregiver, transmission may also occur in infancy. Household exposure has been the source of HBV infection in up to two-thirds of childhood cases. Most such infections can be prevented by hepatitis B vaccination prior to hospital discharge [7]. In addition, multiple studies indicate that children who received the first dose of hepatitis B vaccine during their first month of life (usually the birth dose) were more likely to complete the hepatitis B vaccine series and other important immunizations [8-9].

According to the 2006-2009 vaccination coverage reports from the Centers for Disease Control and Prevention (CDC), the percentage of infants who missed the birth dose of hepatitis B vaccination ranged from 39.2% to 49.9% [10]. Identification of risk factors for missing the birth dose of hepatitis B vaccine is needed in the efforts to improve birth dose uptake. Giraudon et al. described factors associated with incomplete hepatitis B vaccination series of babies [11]. Risk factors for missing the hepatitis B birth

dose vaccination have been examined for Arizona and Colorado [12-13]. However, socio-demographic factors associated with non-receipt of birth dose hepatitis B vaccine among infants at a national level have not been fully described.

## 2. Methods and materials

### 2.1. Survey design and data collection

National Immunization Survey (NIS) data collected in 2009 were used for this study. The NIS is conducted annually by the CDC to obtain national, state, and selected urban-area estimates of vaccination coverage for the U.S. non-institutionalized population of children age 19-35 months [14]. The NIS is a random-digit-dialed survey of households with age-eligible children, with a follow-up check of provider records to obtain vaccination history. Data for 17,053 infants who had adequate provider information were analyzed. In 2009 the NIS overall household response rate based on the Council of American Survey and Research Organizations (CASRO) guidelines was 63.8%. Adequate provider information was defined as sufficient vaccination history obtained from the providers to determine whether the infants were up-to-date according to the recommended vaccination schedule; the proportion of infants with a completed household interview and adequate provider information from the 2009 NIS was 68.7%.

### 2.2. Definitions and variables of interest

According to the CDC operational definitions for the Healthy People 2020 objective, the hepatitis B birth dose vaccination was defined as the 1st dose of hepatitis B vaccine given to a newborn zero (0) to three (3) days between birth date and date of vaccination [15].

In the US, state vaccine financing policy has been self-reported by the state immunization program to the National Immunization Program, CDC [16-18]. According to the policy in place for 2009, this study categorized the states as having a universal supply policy for hepatitis B vaccine or not; universal supply policy provides hepatitis B vaccine at no cost to all vaccination providers and for all children. For 2009, states in this category were Alaska, New Hampshire, New Mexico, Rhode Island, Vermont, Washington, Connecticut, Hawaii, Idaho, Maine, Massachusetts, Nevada, North Carolina, North Dakota, South Dakota, Wisconsin, and Wyoming.

In the 2009 NIS, parents of children were classified as refusing or delaying at least one vaccination if they answered affirmatively to either one or both of the two questions: (1) “Has there ever been a time when you refused or decided not to get a vaccination for the child?” (2) “Has there ever been a time when you delayed or put off getting a vaccination for the child?” [19].

Infants were defined as having health insurance if they were covered through the parent’s employer or union; Medicaid; S-CHIP; Indian Health Service; Military Health Care, Tricare, Champus, or Champ-VA; Other Health Insurance or Health Care Plan.

Other socio-demographic factors related to infants, family, mother, and vaccination provider available in the NIS were examined in both bivariable and multivariable logistic regression analyses. The following factors have previously been found to be associated with infant vaccination coverage in the United States [20-22]: infant race/ethnicity (non-Hispanic white only, non-Hispanic black only, Hispanic, non-Hispanic other), first born status (yes vs. no), and number of siblings (0 vs.  $\geq 1$ ); family poverty status (at or above vs. below poverty level), and locality (urban, suburban, rural); mother’s education level ( $\leq 12$  years vs.  $> 12$  years), marital status (married vs. not married), and age ( $\leq 29$  years vs.  $\geq 30$  years); number (1 vs.  $\geq 2$ ) and type (public, private, other) of vaccination providers; and survey interview language (English, Spanish, or other).

### 2.3. Statistical methods

All of the analyses in this study were conducted with SUDAAN 10.0.1 [23], which properly accounts for the survey sampling design, weighting process, stratification, correlated observations, and clustering. The prevalence rate of missing the hepatitis B birth dose vaccine was estimated using categorical data analysis in each category by the selected socio-demographic factors; weighted prevalence rates with 95% confidence interval (CI) were obtained; P-value of the Chi-square test was used to evaluate the association of each factor with missing the hepatitis B birth dose.

Bivariable logistic regression analyses were conducted for each of the socio-demographic factors as mentioned in section 2.2, with significance status evaluated by Wald Chi-square test, factors with P-value < 0.25 were entered into the multivariable logistic model. Backward multivariable logistic regression [24] was adopted to acquire the final model which comprises the independent factors for missing the hepatitis B birth dose vaccination. The Hosmer-Lemeshow goodness-of-fit Wald-F test was applied to evaluate the final multivariable logistic model [23]. Multicollinearity was assessed for all the factors in the final multivariable logistic regression model [25]. Model adjusted risk ratios (risk of missing the hepatitis B birth dose vaccination in the one category of the factor compared to the risk in the reference category for the same factor) were estimated for each of the factors in the final model.

## 3. Results

### 3.1. Prevalence of missing the hepatitis B birth dose vaccination.

Prevalence rates and 95% confidence intervals for missing the birth dose of hepatitis B vaccine in each category by the selected socio-demographic characteristics are presented in Table 1. In 2009, an estimated 1.6 million infants (39.2%) missed the birth dose of hepatitis B vaccine. Prevalence rates by selected factor ranged from 30.8% to 42.7%. The 3 characteristics with the highest prevalence rates were receiving vaccines from a private provider (42.7%); uninsured (42.5%); and having only 1 vaccination provider (42.5%). Among infants who do not reside in a state with a universal hepatitis B vaccine supply policy, 40.1% missed the hepatitis B vaccine birth dose. The difference in prevalence rates among all categories of each factor were significant (P-value < 0.05) for 8 out of the 9 selected socio-demographic characteristics, except for child's first born status.

### 3.2. Factors associated with missing the hepatitis B birth dose vaccination (multivariable model results).

Infants whose parents refused or delayed at least one vaccination were significantly less likely to receive the birth dose of hepatitis B vaccine compared to infants whose parents did not refuse or delay (adjusted Risk Ratio (RR) with 95% Confidence Interval 1.11(1.04, 1.19)) (Table 2). Lack of health insurance for infants also was significantly associated with missing the birth dose of hepatitis B vaccine (adjusted RR 1.18 (1.08, 1.28)). Infants residing in state without a universal supply policy for hepatitis B were more likely not to receive the hepatitis B birth dose vaccine (adjusted RR 1.19 (1.11, 1.29)). Other factors significantly associated with infants missing the hepatitis B birth dose vaccine included having a married mother (adjusted RR 1.19), and having only one vaccination provider (adjusted RR 1.20). The multicollinearity tolerance values for all of the 9 significant factors in the final model ranged from 81% to 99%, suggesting that there was little multicollinearity in the final model. The P-value of Hosmer-Lemeshow Wald F goodness-of-fit test was 0.67, and thus the final model was a good fit to the 2009 NIS data.

#### 4. Discussion

To our knowledge, this is the first study using a representative national survey (NIS) to identify factors associated with missing the hepatitis B birth dose vaccination. The consistent results obtained from the bivariable and multivariable analyses shown that the conclusions are reliable. The most important potential limitation of this study was that in 2009 the NIS was a random-digit-dial residential landline telephone survey susceptible to lack of representativeness of the sample data due to non-response and exclusion of households with only wireless telephone service. Bias from an incomplete sample frame and nonresponse could remain after weighting adjustments. A recent study [27] indicated that the total survey error in the NIS might be quite small, with mean 1.7% (95% CI: 1.71%, 1.74%), and would likely not have changed the conclusions in this study.

Infants without health insurance, residing in states that did not have a universal hepatitis B vaccine supply policy, and whose parent refused or delayed at least one vaccination were modifiable factors significantly associated with not receiving the birth dose of hepatitis B vaccine. Educating infants' parents and their providers on best vaccine practices will warrant increasing the hepatitis B birth dose vaccination rate in the US.

\* Disclaimer: The findings and conclusions in this article are solely the responsibility of the authors and do not necessarily represent the official view of Centers for Disease Control and Prevention.

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**Table 1. Prevalence of missed hepatitis B birth dose vaccination\* by selected factors.**

Factors		Un-weighted sample size N (Weighted %)	Weighted prevalence % (95%CI <sup>†</sup> ) and significant level	
			% (95% CI <sup>†</sup> )	Chi-Square P-value
		17,053	39.2 (37.9, 40.6)	
Parent refused/delayed at least one vaccination	Yes	6,816 (38.6)	41.9 (39.9, 44.0)	< 0.01
	No	10,237 (61.4)	37.5 (35.8, 39.3)	
Health insurance status of child	Yes	14,467 (80.7)	38.4 (37.0, 39.9)	0.02
	No	2,586 (19.3)	42.5 (39.4, 45.6)	
Lived in a state with a hepatitis B vaccine supply policy	Yes	4,677 (14.3)	34.0 (31.8, 36.3)	< 0.01
	No	12,376 (85.7)	40.1 (38.6, 41.6)	
Mother's marital status	Yes	12,929 (67.4)	41.6 (40.0, 43.2)	< 0.01
	No	4,124 (32.6)	34.3 (31.8, 36.9)	
Vaccination provider type	All private	10,493 (62.1)	42.7 (41.0, 44.4)	< 0.01
	All public	1,771 (11.8)	36.8 (32.8, 41.1)	
	Other type	4,617 (26.1)	30.8 (28.2, 33.4)	
Location of household	Urban	7,181 (42.3)	39.6 (37.4, 41.8)	< 0.01
	Suburban	6,071 (41.1)	40.7 (38.6, 42.8)	
	Rural	3,801 (16.6)	34.6 (32.1, 37.2)	
Mother's age	≤ 29 years	5,824 (40.8)	36.0 (33.8, 38.3)	< 0.01
	≥ 30 years	11,229 (59.2)	41.4 (39.8, 43.1)	
Number of vaccination providers	1	11,117 (61.2)	42.5 (40.9, 44.1)	< 0.01
	≥ 2	5,893 (38.8)	33.8 (31.6, 36.1)	
Child first born status	Not	9,199 (53.8)	38.4 (36.6, 40.3)	0.22
	Yes	7,854 (46.2)	40.1 (38.2, 42.1)	

\* Hepatitis B birth dose vaccination was defined as the 1<sup>st</sup> dose of hepatitis B vaccine administered to a newborn zero (0) to three (3) days between birth date and date of vaccination.

† Confidence Interval.

**Table 2. Risk ratios for missing the hepatitis B birth dose vaccination\* among infants**

Factors	Comparison	Unadjusted risk ratios	Adjusted risk ratios
		% (95% CI <sup>†</sup> )	% (95% CI <sup>†</sup> )
Parent refused/delayed at least one vaccination	Yes vs. No	1.12(1.05, 1.20)	1.11 (1.04, 1.19)
Insurance status of child	No vs. Yes	1.10 (1.02, 1.20)	1.18 (1.08, 1.28)
Living in a state with a hepatitis B vaccine supply policy	No vs. Yes	1.19 (1.10, 1.28)	1.19 (1.11, 1.29)
Mother marital status	Yes vs. No	1.22 (1.12, 1.33)	1.19 (1.09, 1.31)
Vaccination provider type	All private vs. All public	1.16 (1.03, 1.31)	1.09 (0.96, 1.24)
Location of household	Urban vs. Rural	1.15 (1.05, 1.26)	1.13 (1.03, 1.24)
	Suburban vs. Rural	1.18 (1.08, 1.29)	1.12 (1.02, 1.23)
Mother's age	≥ 30 years vs. ≤ 29 years	1.15 (1.07, 1.24)	1.09 (1.00, 1.18)
Number of vaccination providers	1 vs. ≥2	1.26 (1.16, 1.36)	1.20 (1.11, 1.31)
First born status	Yes vs. No	1.05 (0.98, 1.12)	1.09 (1.02, 1.17)

\* Hepatitis B birth dose vaccination was defined as the 1<sup>st</sup> dose of hepatitis B vaccine administered to a newborn zero (0) to three (3) days between birth date and date of vaccination.

† Confidence Interval.