

# Outcomes from a Canadian Public Health Prenatal Screening Program for Hepatitis B

1997-2004

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## ABSTRACT

**Background:** Without appropriate prophylaxis, the rate of vertical transmission of hepatitis B virus (HBV) can be as high as 95%. Alberta's provincial prenatal program screens all pregnant women for HBV, and provides prophylaxis to infants born to HBV-infected women. Canadian data on the outcomes of such programs are limited.

**Methods:** We conducted a retrospective review of data from pregnant Albertan women who were Hepatitis B Surface Antigen (HBsAg) positive from 1997-2004. We describe the frequency of hepatitis B immunoglobulin (HBIG) and vaccine administration, follow-up serology and pregnancy outcomes.

**Results:** In total, 1,485 HBsAg-positive pregnant women were identified; an average of 186 women annually (range: 125-216). Of the 980 infants eligible to have completed prophylaxis and serological follow-up, 82.0% were appropriately immunized and serologically tested, 11.3% had complete immunization but no serology testing and 6.6% were incompletely immunized. Of infants with complete immunization and follow-up, 3.7% failed to mount an immune response and 2.1% were infected.

**Conclusion:** A high proportion of infants born to carrier mothers are receiving appropriate post-natal prophylaxis in Alberta. Future research should examine maternal factors that may increase the vertical transmission of HBV.

**MeSH terms:** Hepatitis B virus; immunization; serologic tests; prenatal care; vertical transmission

*La traduction du résumé se trouve à la fin de l'article.*

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Without appropriate prophylaxis, approximately 95% of infants born to Hepatitis B virus (HBV) chronic carrier mothers (i.e., Hepatitis B Surface Antigen (HBsAg) positive) become infected with HBV.<sup>1</sup> The majority of these infected infants become chronic carriers themselves and face significant risk for future active hepatitis, liver cirrhosis, and hepatocellular carcinoma.<sup>2</sup> Passive-active immunoprophylaxis commenced immediately after birth can reduce the rate of vertical transmission by more than 90%.<sup>3,4</sup>

Canada is a low endemicity country for HBV infection; prevalence estimates of chronic HBV in Canada range from 0.5% to 2%, with the majority of these infections occurring among Aboriginal, Asian and injection drug use populations.<sup>5-7</sup> In 1985, a centralized program of HBV screening for all pregnant women was introduced in the province of Alberta. The coverage of this program is high and approximately 40,000 women are screened annually.<sup>5</sup> Any infant born to an HBsAg-positive mother is to be administered hepatitis B immunoglobulin (HBIG), three doses of HBV vaccine and post-immunization serology testing.

It is unclear to what extent appropriate postpartum prophylaxis is taking place in Alberta and there are limited Canadian data on outcomes of such prenatal HBV programs. In order to address these issues, we performed a retrospective review of women found to be HBsAg positive upon prenatal screening from 1997-2004. The goals of this research were to determine the proportion of infants from infected mothers receiving postpartum HBIG and HBV vaccination and to examine the serological outcomes of the infants.

## METHODS

### Description of the provincial program

As part of routine prenatal care, all pregnant women are screened for HBV using HBsAg serology. All provincial samples are tested at a central location. If a prenatal specimen tests HBsAg positive, the results are reported to: 1) the submitting physician, 2) Alberta Health and Wellness (AHW), the provincial government public health office, and 3) the Regional Health Authority (RHA). AHW sends a follow-up letter to both the submitting physician and

the appropriate regional medical officer of health to notify them of the need to arrange appropriate postpartum immunoprophylaxis. Immunoprophylaxis consists of the administration of 0.5 mL HBIG and first dose of the Recombivax HB (0.5mL) vaccine as soon as possible after delivery. Two additional doses of the Recombivax HB are to be administered at 1-2 months and 6 months of age. In addition, post-immunization serology testing (HBsAg; anti-HBsAg) is recommended at approximately one year of age. If the infant tests negative to HBsAg and anti-HBsAg, additional doses of vaccine and follow-up serology are recommended. The province monitors compliance with these protocols through communications with the RHAs and reminder letters to physicians. Information concerning HBV prophylaxis and follow-up is reported to AHW and included in the Provincial Prenatal HBV Registry.

For this evaluation, infants were considered to have completed immunoprophylaxis if they had received HBIG, three doses of HBV vaccine and post-vaccination serology, regardless of the timing of the vaccine doses or serology testing.

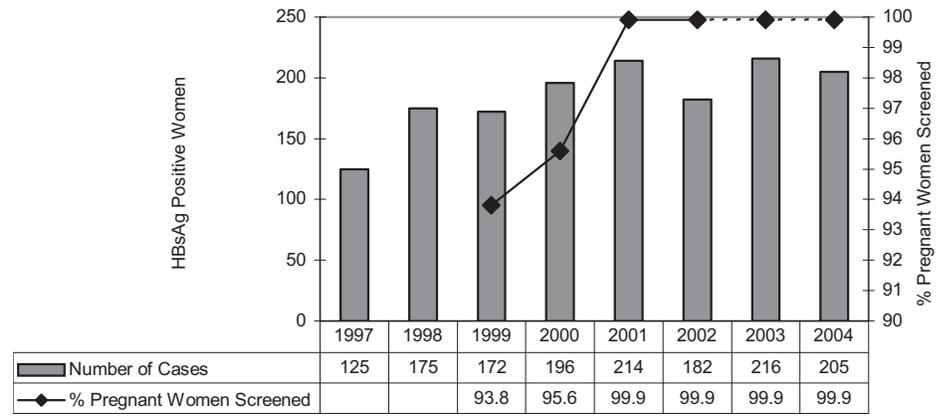
**Analyses**

Data were gathered from the Prenatal HBV Registry for all pregnant women who submitted routine prenatal blood samples from January 1, 1997 until December 16, 2004, and tested positive for HBsAg. Information extracted from the database included maternal age, infant date of birth, reason for pregnancy loss, and provincial region. Any missing information on infant vaccine or serological status was gathered from the reporting regions as required. This review was conducted for the purposes of a provincial program evaluation; only routinely collected data were analyzed.

Comparisons between groups were made using t-tests for continuous variables and Chi-square tests (or Fisher's exact tests) for categorical variables. Data cleaning and statistical analyses were done using Excel (Microsoft Corporation, Redmond, WA, USA) and STATA version 8 (Statacorp, College Station, TX, USA).

**RESULTS**

In total, 1,485 pregnant women were included in the Alberta Prenatal HBV



**Figure 1.** HBsAg-positive women identified and proportion of pregnant women \*† screened for hepatitis B surface antigen: Alberta, 1997-2004

\* Data on the proportion of women screened in 1997 and 1998 was not available to the authors; data for 2002-2004 are estimates.

† Pregnant women are defined as those registered with the Alberta Health Care Insurance Plan and receiving prenatal care. Percentage of Pregnant Women Screened.

Source for 1999-2001 data: Alberta Bloodborne Pathogens Surveillance Working Group. Alberta Bloodborne Pathogens Surveillance Report. Edmonton, AB: Alberta Health and Wellness, 2003.

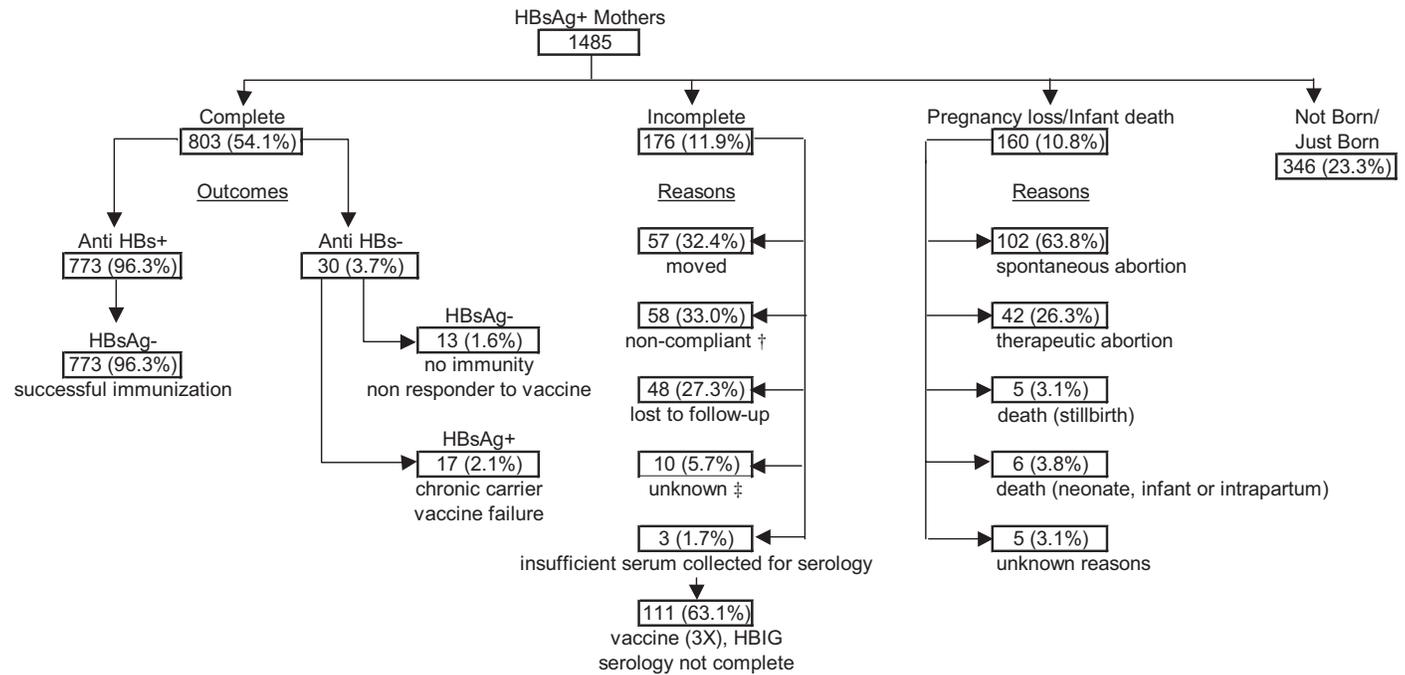
Registry from January 1, 1997 to December 14, 2004. The average age was 30.4 years (range: 15-46 years). On average, 186 (range: 125-216) HBsAg positive women were identified each year (Figure 1).

Of the 1,485 women in the registry, 23.3% (n=346) had yet to give birth or their infants had not completed the 18 months of follow-up for appropriate serology to have taken place (Figure 2). Another 10.8% (n=160) of the mothers evaluated had lost their pregnancy, had a stillbirth or the neonate/infant had died. The most common reason for this loss was spontaneous abortion (63.8%; n=102), which was not significantly higher than age-specific provincial rates. The proportion of therapeutic abortions reported among women in our database was significantly lower than the provincial rate for all age categories (data not shown).

In total, 979 mothers in the registry had live births and were eligible to have had complete immunoprophylaxis and serological follow-up for their infants. Of these, the majority was from the two largest cities in Alberta: Edmonton (38.5%) and Calgary (52.4%). In total, 82.0% (n=803) had complete prophylaxis and serological follow-up performed on their infants (note that one mother had twins, therefore the number of infants is 804). Of all infants

with complete prophylaxis and follow-up, 88.7% (713/804) had HBIG and 83.0% (667/804) had the first dose of vaccine administered on their day of birth. Three infants had not received HBIG by the second day of life (range for these three infants: 3-28 days) and nine infants had not received their first vaccine dose by the second day of life (range: 3-28 days). On average, the second dose was administered at 2.1 months of age (range: 0.5-7.8 months) and the third dose was administered at 6.7 months of age (range: 2.8-18.1 months).

The remaining 18.0% (n=176) of eligible mothers had incomplete prophylaxis or follow-up for reasons such as the mother had moved outside of the province (n=57), non-compliance (n=58) and lost to follow-up (n=48). Of these incomplete cases, the majority (63.1% (n=111)) had HBIG and three vaccine doses administered, however there was no record of adequate serological follow-up testing being performed. Of those who moved, only 33.3% (n=19) had received three vaccine doses and none had received serological follow-up. Among the non-compliant group, the majority (91.4%) had received three vaccine doses, but none had serological testing. Among those infants lost to follow-up, 64.6% had received three vaccine doses but no follow-up serology.



**Figure 2.** Outcomes of HBsAg-positive mothers identified through prenatal screening, Alberta: 1997-2004  
 Complete cases were defined as the infant having received HBIG, completed 3 doses of vaccine and completed follow-up serology  
 † includes 10 mothers who refused follow-up serology testing  
 ‡ includes 2 mothers with no info on their pregnancy outcome + 8 mothers with no known reason for their incomplete status  
 NOTE: One of the Complete Mothers had twins, therefore number of infants=804

Mothers of infants with complete immunoprophylaxis had a statistically significant older mean age (30.4 years vs. 29.0 years,  $p=0.01$ ) when compared to mothers of infants who had incomplete vaccination and follow-up (not including women who had moved away). No significant differences in month of infant birth or provincial region were noted.

In total, there were 980 infants eligible to have completed HBV vaccination and serological follow-up. Of these, 82.0% ( $n=804$ ) were appropriately immunized and serologically tested, 11.3% ( $n=111$ ) of infants were immunized but had no follow-up serology, and 6.6% ( $n=65$ ) were incompletely immunized. Of all babies with complete prophylaxis and follow-up ( $n=804$ ), 1.6% ( $n=13$ ) failed to mount an immune response and were not infected (anti-HBsAg and HBsAg negative), while 2.1% ( $n=17$ ) were infected (HBsAg-positive). Seven of the babies who were anti-HBsAg positive had initially been seronegative after three vaccine doses; they were administered a fourth dose of vaccine and subsequently seroconverted. Therefore, the proportion of infants who did not respond (i.e., anti-HBsAg and HBsAg negative) after HBIG and three vaccine doses was

2.5% (20/804). There were no significant differences in the timing of vaccine doses, maternal age, or provincial region between those infants who did and did not respond to the vaccine series.

### CONCLUSIONS

Prenatal HBV screening in Alberta identified 1,485 mothers as HBsAg positive from 1997-2004. Of 980 infants eligible to have completed postnatal HBV prophylaxis and follow-up, 82.0% were appropriately immunized and serologically tested. Of these infants, 3.7% failed to mount an immune response and 2.1% were infected.

The vast majority (93.4%) of infants born to HBsAg-positive women in Alberta had HBIG and three doses of vaccine. This is far higher than previous evaluations which reported three-dose vaccine coverage to be 59% in New York City<sup>8</sup> and 63% in Louisiana<sup>9</sup> and Ontario.<sup>10</sup> It is interesting to note that previous research in the mid-1980s from Alberta reported that 94% of infants born to carrier mothers had received appropriate vaccination, suggesting that the provincial prenatal screening and HBV prophylaxis program have consistently high uptake.<sup>11</sup> Despite this suc-

cess, improvements can be made to ensure that *all* children are appropriately vaccinated. Research by Kohn et al.<sup>9</sup> indicated that infants with incomplete vaccine series were nearly eight times more likely to become HBV carriers, and half as likely to have serological protection against HBV.

We were initially concerned about the apparent high rate of pregnancy loss and infant death of almost 11%. However, our prevalence of spontaneous abortion, therapeutic abortion and stillbirth were not significantly higher than the age-specific provincial rates. These data support the previously reported finding that HBV carrier status is not associated with adverse fetal or neonatal outcomes.<sup>12</sup>

In total, 12.1% of appropriately vaccinated infants did not have follow-up serology. The lack of serological follow-up is less of a concern than incomplete vaccination as it is estimated that the vast majority of infants will seroconvert after HBIG and three vaccine doses.<sup>1</sup> However an effort to ensure that all children are appropriately protected after immunization is worthwhile in order to provide appropriate care and follow-up for children who are HBV susceptible or carriers. Assuming that seroconversion rates are similar for children

with and without serological follow-up, it can be estimated that of the 111 infants who did not receive serological follow-up, 4 will have no antibody protection and 2 of these infants will become infected. These infants may not be receiving appropriate medical care and follow-up.

Previous research would suggest that even when active-passive immunoprophylaxis is carried out appropriately, 1-5%<sup>3,13,14</sup> of infants are nonetheless infected due to numerous factors, including *in utero* infection<sup>15</sup> and high maternal viral load.<sup>16,17</sup> Our infection rate of 2.1% among vaccinated infants is similar to the proportion of infected infants identified annually in British Columbia (BC). Out of approximately 400 carrier women identified annually in BC, 3 (~0.75%) delivered infected infants in 2002 and 6 (~1.5%) in 2003.<sup>18</sup>

This review provides important information on prenatal screening and the subsequent prophylaxis of infants. The study was limited by the fact that several pertinent pieces of information, such as ethnicity, parity, and obstetrical factors, were not systematically recorded in the Alberta Prenatal HBV Registry. In addition, the interpretation of the data is limited as some infants were given a fourth dose of the vaccine if they failed to mount an immune response after the first three vaccine doses. Unfortunately, this information was not recorded systematically and therefore, our proportion of non-responders may overestimate the true effectiveness of a three-dose vaccine schedule as some of these infants may have received a fourth dose of vaccine.

Finally, the true effectiveness of this public health program cannot be fully interpreted due to incomplete information on numbers of infants born to women who did not have prenatal screening. However, available data suggest that this represents only a very small proportion of all pregnant women in Alberta. Annually in Alberta, there are approximately 52,000 pregnancies, 40,000 women undergoing prenatal testing and 37,000 live births.<sup>5,19</sup> The difference in these numbers is thought to be due in part to spontaneous abortions (~4,500 annually) and therapeutic abortions (~10,000 annually).<sup>19</sup>

Evaluation of the screening program indicates that the vast majority of infants born to HBsAg positive mothers are receiving

appropriate vaccination, however the level of serological follow-up could be improved. Although the level of vaccine failure in Alberta is similar to that found elsewhere, future research should be conducted to identify feasible methods to detect women at highest risk of transmitting HBV infection to their infants. If maternal markers, such as Hepatitis B e Antigen or viral load, can be used to identify these high-risk women, maternal prophylaxis, such as lamivudine, could be given during the last weeks of pregnancy<sup>20</sup> to reduce perinatal HBV transmission.

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## RÉSUMÉ

**Contexte :** Sans prophylaxie appropriée, le taux de transmission verticale du virus de l'hépatite B (VHB) peut atteindre 95 %. Dans le cadre du programme prénatal provincial de l'Alberta, toutes les femmes enceintes sont testées pour le VHB, et la prophylaxie est offerte aux nourrissons de femmes infectées par le virus. Les données canadiennes sur les résultats de tels programmes sont limitées.

**Méthode :** Nous avons mené une étude rétrospective auprès des femmes enceintes de l'Alberta qui étaient porteuses de l'antigène de surface de l'hépatite B (AgHBs) entre 1997 et 2004. Nous avons décrit la fréquence de l'administration de l'immunoglobuline anti-hépatite B (HBIG) et du vaccin contre le VHB, les résultats des tests sérologiques et les résultats de grossesse.

**Résultats :** Sur l'ensemble des femmes enceintes testées, 1 485 porteuses de l'AgHBs ont été identifiées, soit en moyenne 186 femmes par année (125 à 216). Des 980 nourrissons admissibles à la prophylaxie complète et au suivi sérologique, 82 % avaient reçu tous les vaccins ainsi que les tests sérologiques, 11,3 % avaient reçu les vaccins mais aucun test sérologique, et 6,6 % n'avaient pas été complètement immunisés. Sur les nourrissons immunisés et ayant fait l'objet d'un suivi sérologique, 3,7 % n'avaient pas manifesté de réponse immunitaire, et 2,1 % étaient infectés.

**Conclusion :** En Alberta, une proportion élevée de nourrissons de mères infectées par le VHB reçoit la prophylaxie postnatale appropriée. D'autres études sont nécessaires pour déterminer les facteurs maternels qui augmentent le risque de transmission du VHB de la mère à l'enfant.

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