

## ORIGINAL ARTICLE

# EFFICACY OF HBIG AND VACCINE IN INFANTS OF HBSAG POSITIVE CARRIER MOTHERS

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### Abstract

**Background-**Neonates born to HBsAg positive mothers are at high risk of hepatitis B virus (HBV) infection. The aim of this study was to evaluate the efficacy of hepatitis B immunoglobulin and HBV vaccine in these infants.

**Methods-**From September 1998 to September 2000, 103 infants born to HBsAg and HBeAg positive mothers were followed. All infants received HBIG and the first dose of vaccine at birth and the second and third doses of vaccine at 1.5 and 9 months of age, respectively. Post-vaccination tests were performed on 93 infants at 12 to 15 months of age. Data were then analyzed by the Chi-square and Fisher exact tests.

**Results-**Nine mothers (9.7%) were HBeAg positive. Fifty-nine (63.4%) infants were anti-HBs positive. The differences between the rate of anti-HBs were not significant in either sex ( $p=0.64$ ). An antibody titer of more than 100 IU/mL was defined as responder and seen in 41 (48.8%) infants who were born to HBsAg-positive mothers, significantly higher than infants of HbeAg positive mothers ( $p=0.0062$ ). HBsAg was positive in 3 (3.6%) infants born to HBeAg negative mothers, significantly lower than the incidence of HBsAg positivity (33.3%) in infants born to HBeAg positive mothers ( $p=0.011$ ). Seventeen infants (18.3%) were poor responders and 34 (36.6%) were non-responders.

**Conclusion-**In this study children who were poor or non-responders to HBV vaccination in these groups of children are relatively high and additional doses of the vaccine were required for satisfactory immunization. Some of these infants may become chronic carriers. Postvaccination testing is necessary.

**Keywords** • Hepatitis B virus (HBV) • transmission • neonate • HBV vaccine • hepatitis B immunoglobulin (HBIG)

### Introduction

One of the most important routes of hepatitis B virus transmission (HBV) is from asymptomatic carrier mothers to their infants.<sup>1,2</sup> This mode of transmission may occur transplacentally at the time or shortly after delivery.<sup>2-4</sup> The rate of perinatal infection can be as high as 90%, especially if the mother is HBeAg or HBV DNA positive. More than 90% of infected infants appear to become chronic carriers.<sup>1-5</sup>

Infected children have a 25% or greater chance to die from primary hepatocellular carcinoma or

liver cirrhosis.<sup>2</sup> To eliminate the risk of perinatal transmission of HBsAg from mothers to their infants, a program of combined active and passive immunization has been established.<sup>1-5</sup> Infants who are born to HBsAg positive mothers are immunized at birth with hepatitis B immunoglobulin (HBIG) and HBV vaccine, and then subsequent hepatitis B vaccination at 1.5 and 9 months of age. The effectiveness of HBIG and HBV vaccine vary in various parts of the world.<sup>6-10</sup> In Iran, there are few reports about the extent of effectiveness of HBIG and HBV vaccine in infants born to HBsAg positive mothers. Taking into consideration the fact that more than 3% of the general population in Iran are HBV carriers<sup>11</sup>, we conducted the present study to evaluate the efficacy of HBIG and

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## Efficacy of HBIG and Vaccine in Infants of HBsAg Carrier Mothers

**Table 1.** Postvaccination testing of infants born to HBsAg and HBeAg positive mothers.

	Non-responder (%)	Poor responder (%)	Well responder (%)	Total (%)
Infants of HBeAg- mothers	31 (36.9)	12 (14.3)	41 (48.8)	84 (90.3)
Infants of HBeAg+ mothers	3 (33.3)	5 (55.6)	1 (11.1)	9 (9.7)
Total	34 (36.6)	17 (18.3)	42 (45.1)	93 (100)

hepatitis B vaccine in infants born to HBV carrier mothers in Babol, northern Iran.

### Materials and Methods

This study was conducted on 103 (52.7% were females) infants born to HBsAg positive mothers who had been screened at the first antenatal visit during 1998-2000. All pregnant women were also tested for HBsAg and HBeAg in the third trimester of pregnancy. At the time of delivery, 0.5 mL of HBIG (Pharmacia & Upjohn, Sweden) and HBV vaccine (Heberbiovac HB, Cuba) were injected in the gluteal muscle of the neonates, separately. The second and third doses of the vaccine were given at 1.5 and 9 months of age (according to Iran's Ministry of Health Expanded Program on Immunization). Postvaccination testing (HBsAg, anti-HBs) was performed between 12 and 15 months of age on 93 infants. The remaining 10 cases did not return. An antibody titer equal to or greater than 100 IU/mL was considered as responders and that between 10 and 99 IU/mL was as poor responders. Non-responders were those with titers lesser than 10 IU/mL. Proportions were analyzed by the Chi-square and Fisher exact tests.

### Results

HBeAg was positive in 9 mothers, whose mean±SD age was 25.6 ± 4.9 years in the last trimester of pregnancy.

Twenty-nine male (65.9%) and 30 (61.2%) female infants (total of 59 infants) were anti-HBs positive. The rate of seropositivity for anti-HBs did not differ in either sex (p=0.64). Among 84 infants of HBeAg negative mothers, 3(3.6%) were HBsAg positive, significantly lower than the incidence of HBsAg positivity (33.3%) observed in infants from HBeAg positive mothers (Fisher exact test, p=0.01).

Forty-one (48.8%) infants born to HBsAg positive mothers, were responders, which was significantly higher than the response of infants (11.1%) born to HBeAg positive mothers

(p=0.0062) (Table 1). Seventeen (18.3%) infants were poor responders and 35 (36.6%) infants were non-responders.

### Discussion

An important indication for passive or active immunization is for neonates born to HBsAg positive mothers.<sup>1-4</sup> It is necessary to test for evidence of adequate immunity in infants at 12 months of age.<sup>1</sup> It is important to identify children who need additional doses, because of the potential risk of transmission after the perinatal period from the mother or from other HBV-infected household members.<sup>1-4</sup> In the present study, the rate of non-responders in infants (36.6%) was similar to data obtained from other studies performed in Canada, France and India.<sup>12-14</sup>

Several studies revealed a much lower non-response rate than our results. A study performed by Gallo et al on 85 infants born to HBsAg positive mothers showed that, only two neonates (2.4%) were non-responders.<sup>15</sup> Poovorawan et al in 1997, reported a 3.8% non-responder rate in neonates born to HBeAg positive mothers<sup>16</sup>.

In a study conducted by Darmiani et al on 22 neonates of HBsAg positive mothers, the non-responder rate was zero.<sup>7</sup> These studies demonstrate that the rate of non-responders, in infants born to HBsAg positive mothers, is different in various parts of the world. An *in utero*-induced immune tolerance to low doses of HBsAg appears as the most plausible hypothesis to explain this unresponsiveness to the HBV vaccine.<sup>13</sup> In our study, 6 cases (6.5%) were chronic HBV carriers. In a study conducted by Roome et al (1994-1997), 1.3% of infants were HBsAg carriers.<sup>17</sup>

In another study performed in Taiwan, the HBsAg carrier rate in infants born to HBsAg positive mothers was 2.4%.<sup>8</sup> Chernesky et al in Canada and Yu et al in China, reported the rate of HBsAg carriers of infants born to HBsAg positive mothers to be 7.2% and 13.7%, respectively.<sup>12,18</sup> The study conducted by Zhu et al in China showed that 14.7% of infants became HBsAg carriers.<sup>19</sup> In Canada and China the prevalence of HBeAg

positive mothers was higher than that of our study.<sup>12,19</sup> The low prevalence of HBeAg in HBsAg positive mothers in Iran, may explain the low infection rate (9.7%) found in our study.

The presence of HBeAg seropositive mothers greatly increases the risk of infection in the newborn. This e-antigen is associated with a defective immune response to the hepatitis B virus, which permits continued replication of the virus in liver cells.<sup>20,4</sup> More than 40% of Chinese HBV carrier women are HBeAg-positive, so infection can occur *in utero*.<sup>2,19</sup> Infants who become chronic HBV carriers despite perfect immunoprophylaxis may be infected *in utero*, or their mothers might have a high virus load or might have been infected with vaccine-escape virus mutants.<sup>2-4</sup> Infected children should be identified and long-term management is needed. This infection may occur transplacentally, so HBIG and HBV vaccine cannot prevent the infection.

In conclusion, our study shows that serologic testing of infants is useful in the identification of children who might benefit from booster vaccination (non-responders, poor responders) and several chronic HBV infected children who need specialized medical care and follow-up.

### Acknowledgment

*We would like to thank Dr. Soleimani for performing the laboratory tests and Dr. Haji-Ahmadi for analyzing the data.*

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