This cross-sectional descriptive study was conducted on 53 HBsAg-positive mothers in Khorasan Razavi province, Iran: A Case Study of Khorasan Razavi Province, Iran

Reza Ahmadi, Bahman Aghcheli, Ali Mohammad Hosseinpour, Shabnam Niroumand, Zeinolabedin Mohammadi, Nafiseh Afsharsafavi, Saied Ghorbani

1Infectious Disease Research Center, Gonabad University of Medical Sciences, Gonabad, Iran
2Department of Microbiology, Faculty of Medicine, Golestan University of Medical Sciences, Gorgan, Iran
3Department of HIV, STI, and Hepatitis Care and Prevention, Mashhad University of Medical Sciences, Mashhad, Iran
4Department of Bacteriology and Virology, Schlooh of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
5Mashhad University of Medical Sciences, Mashhad, Iran
6Department of Family Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
7Department of Bacteriology and Virology, Schlooh of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

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*Corresponding Author:
Bahman Aghcheli,
Email: b.aghcheli2011@gmail.com
Nafiseh Afsharsafavi,
Email: Afsharsafavi971@mums.ac.ir
Saied Ghorbani,
Email: vets.ghorbani@gmail.com

These authors contributed equally to this work.

Abstract

Background: Viral infections have been a major public health concern in recent years. Viral hepatitis B virus (HBV) is one of the serious healthcare system issues in Iran. Family transmission of HBV in pregnant women is a major cause of the high prevalence of HBV infection in neonates and related persons. The expanded program on immunization (EPI) was the main way to prevent this infection.

Objectives: This study aimed to estimate the effectiveness of the hepatitis B vaccine in infants born to HBsAg-positive mothers in Khorasan Razavi province.

Materials and Methods: This cross-sectional descriptive study was conducted on 53 HBsAg-positive women between March 2017 and April 2019 in Khorasan Razavi province, Iran. The enzyme-linked immunosorbent assay (ELISA) was employed to conduct screenings for HBsAg in children. Risk factors for HBV infection were investigated using medical records and structured questionnaires.

Results: The prevalence of HBsAg positivity was 1.2% (1/83) among children aged 1-3 years old. All children received three doses of HBV vaccine according to the HBV immunization program. The positive hepatitis B surface antibody (HBsAb) test among children under study was 80.7% (n=67).

Conclusion: The results indicated a low prevalence of hepatitis B infection among infants and children born to HBsAg-positive mothers (1.2); however, protective anti-HBs levels were reported in 80.7% (<95%) of the children. It appears that the efficiency level of the hepatitis B vaccination procedure was not sufficient in this study. Overall, revaccination is recommended for children who are anti-HBs-negative or not protected.

Keywords: Prevalence, Hepatitis B Virus, HBsAg, Children

Background

Hepatitis B virus (HBV) infection has been supposed to be a major public health issue that imposes a financial burden on the health system and economy of the societies. The virus has been considered one of the most common causes of human carcinogenesis. Overall, approximately 2 billion individuals possess serological proof indicating past or ongoing HBV infection, with 1.5 million new cases of infection each year. In the HBV endemic area, the main route of transmission is the maternal-infant perinatal transmission, while in low endemic areas, mother-infant transmission leads to about one-third of chronic infections. The use of contaminated needles, particularly among injecting drug users and sexual transmission, is the most common inter-human transmission route infection in these settings. The prevalence of hepatitis B in different parts of Iran has been estimated to be 0.87 to 8.86%. Newborns to HBsAg-positive mothers are at a higher risk of HBV infection, and viremia in these mothers is indicative of vertical HBV transmission. The two main ways for maternal transmission of hepatitis B virus infection include horizontal (from mother to newborn child in household activities or taking care of a baby) and vertical transmission (prenatal contact with body fluids and blood, especially during vaginal delivery and sexual activity).
Studies have indicated that in Iran, the primary method of viral transmission is through horizontal transmission, which is largely attributed to asymptomatic chronic carriers. Since 1993, the HBV vaccination program has been implemented in Iran for newborns. Based on guidelines, all pregnant women should undergo testing for HBsAg. In HBsAg-positive pregnant mothers, it is recommended that their newborn child be vaccinated against HBV and receive hepatitis B immunoglobulin (HBIG). Despite relatively wide coverage of vaccination against HBV and confirmed effectiveness in vaccination programs, the disease remains a worldwide health concern, and new cases of disease incidence and also mortality have been reported. Additionally, the efficacy of the hepatitis B vaccination procedure in neonates with chronic hepatitis B parents still remains disputable.

The main aim of this study was to assess the effectiveness of the hepatitis B vaccination procedure in children born to HBsAg-positive mothers in Mashhad. The results provide updated data and valuable information regarding the effective implementation of vaccination programs and prevention strategies against HBV infection in Iran.

Materials and Methods

Research Methodology and Participants

This cross-sectional study was performed using the records of all pregnant mothers during 2017-2019 in a university-affiliated hospital in Mashhad, northeast Iran. All children received three doses of HBV vaccine according to the HBV immunization program. In addition, the information available in the city’s health center was carefully examined, and a list of HBsAg-positive mothers during pregnancy was prepared. Data obtained from the participants included demographic characteristics, medical history, and vaccinations. Researchers explained the research procedure and the objectives to invited parents’ under study.

Data Collection and Serological Tests

After consulting and obtaining the mother’s consent and completing the questionnaire, the children were referred to the laboratory to obtain a blood sample. All participants signed an informed consent form before participating in the study. This hospital-based survey included 53 HBV-positive mothers with at least one child less than 3 years of age from which 30 have more than one child. The sera separated from the blood of these children were stored at -20 °C, and keeping the cold chain, they were transferred to the department laboratory of the Mashhad University of Medical Sciences for performing relevant tests. All samples were analyzed to detect the presence of hepatitis B serological markers, including anti-HBs and HBsAg. The enzyme-linked immunosorbent assay (ELISA) was performed in duplicate for all samples. Then, anti-HBs were titrated based on IU/mL, and hepatitis B surface antibody (HBsAb) levels ≥ 10 IU/L were considered protective against HBV infection.

Statistical Analysis

Descriptive analyses were done, and results were depicted with proportions and frequency. Categorical variables were compared between groups using the chi-square test, and a binary logistic regression model was utilized to establish the relationship between the dependent and independent variables. A P value ≤ 0.05 indicated statistical significance. The data were analyzed using SPSS16 software (SPSS Inc., Chicago, IL, USA).

Results

A total of 83 children were included in this study, and the subject group consisted of 49 (59.0%) males and 34 (41.0%) females. In addition, most of the children were 2-3 years old (with an average age of 28 ± 6.62 months) and lived in low-income families (53.0%). All children received three doses of the hepatitis B vaccine (10 μg/dose). The results indicated no significant relationship between any of the factors such as gender, delivery type, paternal HBsAb, maternal HBsAg, children’s age, and socioeconomic status in received and non-received groups of HBIG based on statistical analyses (Table 1).

In this study, 82 children tested negative for HBsAg, and HBV infection was present in 1.2% (1/83) of children. The positive HBsAb test among children under study

Table 1. Some Criteria in Neonate Born to HBsAg-positive Mothers

<table>
<thead>
<tr>
<th>Variables</th>
<th>HBIG</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>38 (59.4)</td>
<td>11 (57.9)</td>
</tr>
<tr>
<td>Female</td>
<td>26 (40.6)</td>
<td>8 (42.1)</td>
</tr>
<tr>
<td>Delivery type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cesarean section</td>
<td>26 (40.6)</td>
<td>4 (21.1)</td>
</tr>
<tr>
<td>NVD</td>
<td>38 (59.4)</td>
<td>15 (78.9)</td>
</tr>
<tr>
<td>HBsAb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>50 (78.1)</td>
<td>17 (89.5)</td>
</tr>
<tr>
<td>Negative</td>
<td>14 (21.9)</td>
<td>2 (10.5)</td>
</tr>
<tr>
<td>HBsAg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>0 (0.0)</td>
<td>1 (5.3)</td>
</tr>
<tr>
<td>Negative</td>
<td>64 (100)</td>
<td>18 (94.7)</td>
</tr>
<tr>
<td>Children age (y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>11 (17.2)</td>
<td>6 (31.6)</td>
</tr>
<tr>
<td>2-3</td>
<td>53 (82.8)</td>
<td>13 (68.4)</td>
</tr>
<tr>
<td>Socio-economic Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>32 (50)</td>
<td>11 (57.9)</td>
</tr>
<tr>
<td>Moderate</td>
<td>27 (42.2)</td>
<td>8 (42.1)</td>
</tr>
<tr>
<td>High</td>
<td>5 (7.8)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

Note: HBIG: Hepatitis B immunoglobulin; NVD: Normal vaginal delivery.
was 80.7% (n = 67). In contrast, in 19.3% (n = 16) of the children, the level of anti-HB antibodies was found to be less than 10 IU/mL. All the studied children had received three doses (at birth, 1 month, and 6 month) of the vaccine according to the routine vaccination schedule. Overall, 77.1% (64/83) of subjects received HBIG, regardless of the mother’s HBeAg status at birth.

Discussion

Despite the comprehensive vaccination program in many countries, especially in developed countries, the prevalence of hepatitis B infection poses a significant health concern.\textsuperscript{15} Hepatitis B vaccination strategies may differ depending on HBV status, transmission routes, age of infection, and healthcare status of the region in different countries.\textsuperscript{16-18} The most effective method for preventing the perinatal transmission of HBV is believed to be through both the active and passive immunization of children born to HBsAg-positive mothers. The HBV infection rate among newborns from HBsAg-positive mothers is a valuable factor in estimating the effectiveness of vaccination programs.\textsuperscript{19, 20}

In this study, the prevalence of HBsAg and anti-HBs in infants born to HBsAg-positive mothers was 1.2% and 80.7%, respectively. A total of 19.3% of the patients lacked immunity against HBV infection. This indicates that the efficacy of the hepatitis B vaccine in this study is inadequate. In a study in Babol, which was conducted on 93 children born to HBsAg-negative and HBsAg-positive mothers, the prevalence rate of HBsAg was 6.4%.\textsuperscript{21} The other study in Iran indicated that the prevalence rates of anti-HBc, anti-HBs, and HBsAg in 60 infants who received HBIG and hepatitis B vaccine are 38.7%, 85.7%, and 3.6%, respectively.\textsuperscript{22}

A study conducted by Moradi et al in Bandar-e Turkmen demonstrated the effectiveness of the HBV vaccination program in Iran’s region. Most of the children (97.88%) displayed positive immune responses after receiving three doses of the vaccine.\textsuperscript{23} The current study indicated a lower prevalence of HBsAg positivity compared to other cities such as Guangdong (7.69%),\textsuperscript{24} Shaanxi (7.07%),\textsuperscript{25} Anhui (10.39%),\textsuperscript{26} Zhejiang (5.88%),\textsuperscript{27} Fujian (11.39%),\textsuperscript{28} Tianjin (3.77%),\textsuperscript{29} Yunnan (3.28%),\textsuperscript{30} Liaoning (3.08%),\textsuperscript{31} Xinjiang (4.43%),\textsuperscript{32} and Sichuan (4.24%).\textsuperscript{33} These remarkable differences could be attributed to the level of awareness, public health education, socioeconomic status, and infection prevention practices of the community.\textsuperscript{34-38} However, it is noteworthy that Iran has been supposed to be an intermediate endemic region for HBV infection.\textsuperscript{39}

In this survey, the level of immunity (the rate of anti-HBs-positive cases) was reported in 80.7% of the infants with HBsAg-positive mothers. There are discrepancies in the reports on the efficacy of HBV vaccination in Iranian children. Some studies reported low or insufficient immune response to HBV standard vaccination.\textsuperscript{40-48} but in other studies, vaccination was found to be more efficient.\textsuperscript{49, 50} The current investigation did not find a notable correlation between HBV infection and the sociodemographic characteristics of the subjects being examined. These findings align with a study conducted in Ghana.\textsuperscript{51}

On the other hand, other studies in Uganda, Congo, and Ethiopia found significant associations between HBV infection and sociodemographic factors such as age, occupation, and marital status among pregnant women population.\textsuperscript{52-56} Variations could have occurred due to disparities in sampling techniques and laboratory protocols. Several studies indicated that the likelihood of HBV infection is 11 times higher for mothers with over four children compared to those with just one child.\textsuperscript{1}

Sex workers and women with multiple sexual partners may be exposed to unsafe sex. Previous studies have indicated that various factors, including the method of delivery (cesarean or vaginal), particularly surgical procedures and blood transfusions, have the potential to present risks for HBV transmission.\textsuperscript{52, 56, 57} Despite the use of immunoprophylaxis, newborns who become chronic carriers of HBV, may have mutated viruses (vaccine-escape virus mutants).\textsuperscript{58-61} It is important to identify and closely monitor children who have been infected for an extended period. Intrauterine transmission is an important reason for the failure of immunoprophylaxis and cannot be prevented by the HBV vaccine or HBIG administered at birth.\textsuperscript{62-64}

Children born to HBsAg-positive mothers may possess anti-HBc antibodies, which can persist for a prolonged period. However, if children who are 2 years old or above are found to have only anti-HBc antibodies, it could imply a past encounter with the virus.\textsuperscript{65} This study showed that serological testing can be useful to identify children who may need repeat vaccination (booster dose). It is recommended to consider administering HBIG to newborns whose biological fathers are HBsAg positive, employ intradermal vaccination, and actively search for cases in children who have received the HBV vaccine but have parents with HBsAg positive. Accordingly, it seems that we should pay more attention to other ways in addition to mother-to-child transmission (MTCT), including horizontal HBV transmission in the region.

There are many potential limitations to this study. First, this study was a hospital-based retrospective cross-sectional investigation, which may reflect selection bias as a potential limitation. Second, some laboratory tests, including the detection of HBV-DNA and HBcAb, were not evaluated. Third, follow-up analyses for MTCT and neonatal/maternal outcomes were not performed. Fourth, the study may have a limited number of participants, which could potentially restrict the generalizability of the results to a larger population. Future studies should consider a larger sample size from different provinces to
enhance the statistical power of the findings.

Despite lacking novelty, this article remains significant for assessing the vaccine’s effectiveness across various cities.

Conclusion
The results indicated a low occurrence of hepatitis B infection in children born to HBsAg-positive mothers (1.2%), but protective anti-HB levels were reported in 80.7% (<95%) of the children. It appears that the effectiveness of the hepatitis B vaccine in this study was not sufficient. Overall, the revaccination of these non-protected subjects is recommended.

Factors such as working at a healthcare facility, giving birth at home, being admitted to a hospital, having tattoos, sharing personal care items, lacking knowledge about HBV, and being HIV-positive contributed to the high prevalence of HBV infection among delivering mothers. It is crucial to administer the hepatitis B vaccine to all newborns within 24 hours after birth to prevent MTCT and its associated complications. Additionally, there is a need for health education and information dissemination about HBV, specifically targeting pregnant mothers and young women of child-bearing age, to reduce HBV infection and MTCT in Mashhad.

Additionally, we are more conscious of children who are chronically infected with HBV and require special medical care. We proposed to administer additional surveys applying molecular tests on a larger sample size to prevent any bias regarding limitations and different genetic backgrounds in various populations. With considerable effort, information sharing, and scientific support, we have contributed to the World Health Organization’s (WHO) slogan for impressive reduction in morbidity and mortality rate of HBV infection until 2030.

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Authors’ Contribution
Conceptualization: Nafiseh Alsharsafavi, Saeid Ghorbani.
Data curation: Reza Ahmadi, Bahman Aghcheli.
Formal analysis: Zeinolabedin Mohammadi.
Funding acquisition: Reza Ahmadi, Ali Mohammad Hosseinpour.
Investigation: Ali Mohammad Hosseinpour, Shabnam Niroumand.
Methodology: Reza Ahmadi, Bahman Aghcheli.
Project administration: Nafiseh Alsharsafavi, Saeid Ghorbani.
Resources: Nafiseh Alsharsafavi, Saeid Ghorbani.
Supervision: Nafiseh Alsharsafavi, Saeed Ghorbani.
Validation: Reza Ahmadi, Bahman Aghcheli.
Visualization: Saeid Ghorbani, Bahman Aghcheli.
Writing—original draft: Reza Ahmadi, Bahman Aghcheli, Ali Mohammad Hosseinpour, Shabnam Niroumand, Zeinolabedin Mohammadi, Nafiseh Alsharsafavi, Saeid Ghorbani.
Writing—review & editing: Nafiseh Alsharsafavi, Saeid Ghorbani.

Competing Interests
We disclose that there is no conflict of interests related to the publication of this article.

Data Availability Statement
Ask the corresponding author for permission to access the datasets examined in this study.

Ethical Approval
This study was approved by the Research Ethics Committee of Mashhad University of Medical Sciences (IR.MUMS.MEDICAL.REC.1398.334), and all steps of the study were performed following the Helsinki Declaration. Written informed consent was also obtained from all patients before they participated in the study.

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References


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