

## Evaluation of the Level of HBV Antibody Titer after HBV Vaccination among Children in Tehran, Iran

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**Background and Aims:** Hepatitis B infection is a serious public health problem worldwide. It has been shown that the levels of antibody to hepatitis B surface antigen (anti-HBs) decrease after vaccination. The main objective of this study was to assess the level of anti-HBs among children after primary vaccination against hepatitis B virus (HBV) in Tehran, Iran.

**Methods:** The study was conducted in four selected healthcare centers in Tehran during a 6-month period from September 2005 to March 2006 in Tehran. Blood samples collected from 165 healthy, 1- to 5-year-old children who had been vaccinated against HBV were tested for anti-HBs using enzyme-linked immunosorbent assay (ELISA).

**Results:** Approximately 47.9 % of the cases were male. Among the cases, the minimum and maximum titers of hepatitis B surface antibodies (HBsAb) were zero and 1000 m IU, respectively. The mean level of HBsAb titer in this study was 232.64 m IU, with a standard deviation of 278.711 m IU.

**Conclusions:** The results showed that HBsAb titer may decrease over time after vaccination. Finally, along with prevention and control strategies, ongoing investigation and monitoring of antibody levels against HBV in children and other age ranges is recommended.

**Keywords:** HBV Antibody, Vaccination, Children, Iran

### Introduction

Hepatitis B virus (HBV) infection is one of the most common infectious diseases worldwide (1, 2). Around 2-4% of Iranians are chronic carriers of HBV and approximately 35-40% of them have been exposed to HBV. Moreover, HBV is the most frequent cause of end-stage liver disease in this country (3, 4).

The global prevalence of HBV carriers varies widely, from high (10-20%) in Southeast Asia and China, to intermediate (2-7%) in the Mediterranean region, Japan, Central Asia, and the Middle East, and low (< 2%) in the United States, Canada, Western Europe, and Australia (5). The prevalence of hepatitis B surface antigen (HBsAg) in Iran varies from 1.07% in Shiraz to 8.96% in Toiserkan (4). However, the global prevalence is lower than 3% (intermediate) (6). HBsAg occurs in all age ranges in the country (7). The transmission pattern of hepatitis B is mixed and has an intermediate endemicity in Iran (8). Vaccination during the first year of life has proven to be the best method of prevention against HBV infection (9, 10).

Despite the availability of an effective vaccine, hepatitis B continues to be a significant health problem, and more than 100 million hepatitis B carriers have been reported worldwide (11). Infection occurs early in life in highly endemic areas because of the high incidence of both vertical and horizontal transmission (12). Hepatitis B vaccination strategies may vary from country to country depending on HBV endemicity, the predominant modes of transmission of infection, the age of infection, and available healthcare resources (13). Despite the availability of effective vaccines for almost two

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decades, infection with hepatitis B virus remains a major problem in many nations, including Iran. One of the causes of this problem, in our opinion, may be the lack of a follow-up system after vaccination in the country. In addition, the level of antibody declines with time, especially during the first year of vaccination. Some risk factors, such as genetic determination or obesity, may reduce the immune system response to HBV. Accordingly, continuous assessment of HBV antibody titer is crucial for understanding the immunity levels of children in the country (14-16).

This study was designed to evaluate and test Iranian national system of vaccination for HBV and to examine the effectiveness of the vaccines used in Iranian healthcare centers in a randomized study.

## Materials and Methods

This research is a cross-sectional study and was conducted in four selected healthcare centers in Tehran during a 6-month period from September 2005 to March 2006. The study sample included 165 HBsAg negative children aged from 1

$$n = \frac{Z^2 \times P(1-P)}{d^2}$$

to over 5 years old as calculated below:

where  $P = 0.94\%$  and  $d = 0.18$ .

Epidemiological data were obtained using a questionnaire including age; sex; weight; history of hepatitis in parents, brothers or sisters; site of vaccination; and date of vaccination. After obtaining approval from the health authorities, the director and designated data collection team at each healthcare center were trained on the details of conducting interviews, filling out questionnaires, and obtaining blood samples. The families were contacted at healthcare centers, and every parent signed a consent form. The blood samples (2 ml each) were obtained from the participants and sent to the laboratory of the Blood Transfusion Organization of the Islamic Republic of Iran (state of Tehran) at the end of each day. Antibodies to hepatitis B surface antigen (anti-HBs) were measured using enzyme-linked immunosorbent assay (ELISA). The anti-HBs titers were reported in international units (IU) per milliliter. The optic density (OD) method was used with IU concentrations of 0, 10, 100, 500,

and 1000. Titer of hepatitis B surface antibody (HBsAb)  $\geq 10$  MIU/mL was defined as a positive serum sample. Results were recorded and collected, and then all data were fed into an access data bank. Statistical analyses were carried out with SPSS version 13.0 software (17).

## Results

One hundred sixty-five patients participated in this study; 47.9 % were male and 52.1% were female. The weight of children ranged from 8 to 22 kgs with a mean of 13.97 kgs. Figure 1 shows the distribution of HBsAb titers among different weight groups of children. The age of children ranged from 1.5 to 5 years. The mean age was 3.22 years. Figure

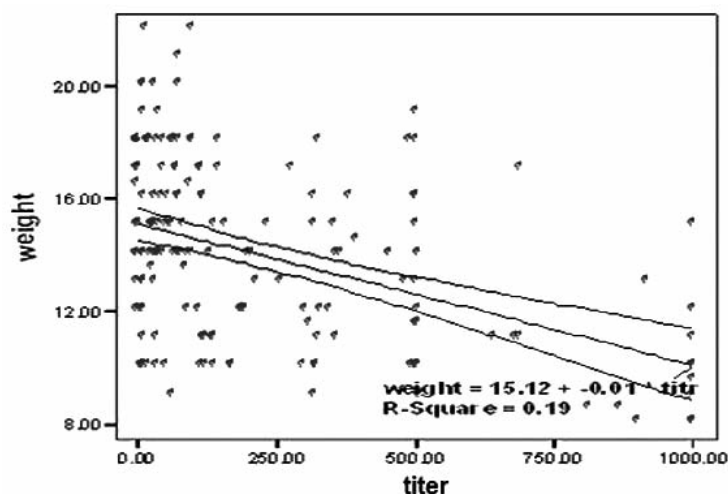


Figure 1. Distribution of HBsAb titers (m IU) among different weight groups of children.

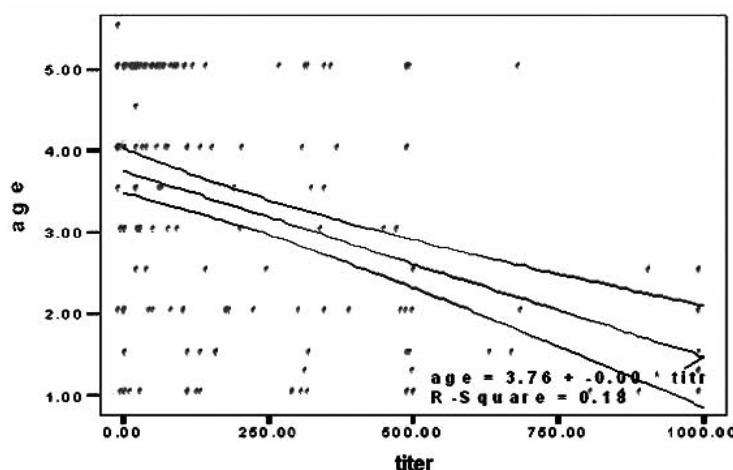
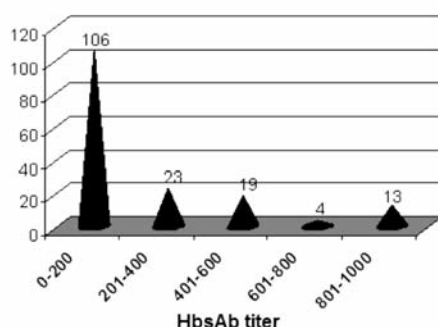


Figure 2. Distribution of HBsAb titers (m IU) among different age groups of children.

2 shows distribution of HBsAb titers among different age groups of children.

The minimum and maximum titers of HBsAb among participants were 0 and 1000 m IU, respectively. The mean of HBsAb in this study was 232.64 m IU, with a standard deviation of 278.711 m IU. Fifteen children (9.1%) had an HBsAb titer under 10 m IU, and 150 (90.9 %) had a titer level



**Figure 3.** Distribution of HBsAb titers (m IU) among the study children (n = 165), all of whom were vaccinated against HBV.

over 10 m IU. Figure 3 shows the distribution of HBsAb titers among the study children, all of whom were vaccinated against HBV.

We performed a t-test to examine the relationship between sex and titer of anti-HBV antibody (above and below 10 m IU). The relationship was not statistically significant, with a P-value above 0.05. To evaluate the relationship between child's weight and the efficacy of the HBV vaccination, a Pearson correlation test between weight and HBsAb titer was performed. The results revealed that increased weight was significantly correlated with lower HBsAb titer ( $P = 0.0134$  and  $R = 0.442$ ).

## Discussion

HBV infection and its complication is currently a major issue in medicine worldwide. Because of the nonspecific and mild clinical presentation, hepatitis B may be difficult to recognize, especially in children. HBV vaccination is the most effective and routine type of prophylaxis for HBV around the world (17, 18). Universal vaccination of all neonates against hepatitis B virus has been implemented in the Islamic Republic of Iran since 1993 (19).

Children are one of the at-risk populations for HBV infection. Consequently, measurement of

immunologic response to vaccination will help us create and implement effective vaccination programs and compare them with international standards as part of infection prevention and control strategies for at-risk populations (18, 20, 21).

This study was performed to evaluate the efficacy of HBV vaccination in Iranian children. A comparison of the present findings can be made with the results of other studies on the efficacy and immunogenicity of the HBV vaccine. In our study, 90.9% of children had HBsAb in protective ranges (higher than 10 m IU). The efficacy of HBV vaccination in similar studies was 100% in Peru (18), 88% in India (20), and 83.5% in Yemen (21).

In our study, sex and HBsAb titer were not significantly related, but a negative relationship between weight and HBsAb titer was observed. However, this correlation could be biased because antibody titer could have decreased over time after vaccination.

The present study has some limitations. The sample size was small. The infants were taken into the study when they attended the well-baby clinic for routine immunization. This resulted in the wide range for the age groups (1-5 years). The anti-HBs levels in the mothers were not estimated; hence, the effect of a mother's antibodies on the immunization of the child could not be evaluated. We did not check the hepatitis B core antibody and liver function tests. Doing so would have increased the cost and limited the study to a comparatively smaller size.

Finally, a booster vaccination must be advised at a point later in time when majority of vaccines begin to lose their protective value. Further studies that assess the protective levels of children are needed to measure whether the immunologic memory of the HBV vaccine will persist and protect against significant breakthrough infections over time.

In conclusion, the results showed that HBsAb titer may decrease over time after vaccination. Finally, along with prevention and control strategies, ongoing investigation and monitoring of antibody levels against HBV in children and other age ranges is recommended.

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