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Research Article

# Serum Level of Anti-Hepatitis B Surface Antigen 18 Years after Vaccination in Students of Golestan University of Medical Sciences, Iran

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## ABSTRACT

**Background and objectives:** Hepatitis B virus (HBV) is one of the most common viral infections and amongst the top health priorities worldwide. Due to frequent exposure, medical students are at high risk of developing HBV infection. This study was conducted to evaluate serum level of anti-HBV surface antigen (HBsAg) 18 years after HBV vaccination in students of the Golestan University of Medical Sciences (Gorgan, Iran).

**Methods:** In this cross-sectional study, 241 students (18-20 years old, 137 women) who had been vaccinated at infancy were enrolled. After recording demographic data, blood sample was taken to measure HBsAg, HBs anti-body (HBs-Ab) and HBc antibody (total HBcAb) using commercial enzyme-linked immunosorbent assay kits. Data were analyzed by the chi-square test using SPSS 16 and at significance of 0.05.

**Results:** HBsAb titer of less than 10 mlU/ml was found in 167 (69.3%) participants (89 females and 78 males). Positive HBsAg and anti-HBcAb were not observed in the subjects. There was no significant relationship between antibody titer and sex, body mass index, place of residence and ethnicity (P>0.05).

**Conclusion:** The high number of medical students with seronegative antibody levels is a cause for concern. In this regard, more attention should be paid to high risk students in medical school of the Golestan Province.

**Keywords:** Hepatitis B virus, HBs antibody, vaccination.

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## INTRODUCTION

Hepatitis B infection is a major health problem worldwide (1). Around two billion people in the world have hepatitis B, and more than 350 million people suffer from chronic hepatitis B, who mostly live in the Southeast Asia (2, 3). Each year, at least 800,000 people die from hepatitis B virus (HBV) infection and its complications. The virus accounts for 70-80% of chronic hepatitis incidents, which are the most common cause of liver disease and the leading cause of HBV-associated mortality. This virus is also the most important cause of fulminant hepatitis in Iran (4). The World Health Organization (WHO) has categorized the world into three epidemiological regions in terms of HBV prevalence: prevalence of less than 2%, moderate prevalence (2–8%) and high prevalence (more than 8%) (5). The average prevalence of the disease is currently 2.2% in Iran; however, the Golestan Province has a higher prevalence rate (8.9%) compared to the national average rate in Iran (6).

Currently, the best way to control and prevent the disease is to use HBV vaccines (7). According to the WHO recommendation, all infants should receive hepatitis B vaccine right after birth, preferably within 24 hours. In Iran, the national hepatitis B vaccination program has been implemented since 1993 for infants and high-risk groups. Complete vaccination increases the antibody levels in over 95% of infants, children and adults (8). Immunity against this disease is assessed by measuring the serum level of antibody against the hepatitis B surface antigen (HBsAb). Values equal to or greater than 10 mlU/ml indicate immunity (7). Various studies have shown that the antibody titer decreases over time (9, 12-14). On the other hand, numerous studies have shown that 1-10% of apparently healthy individuals cannot produce antibodies at acceptable levels after vaccination, probably due to genetic factors, immunity suppression and certain diseases (10). Medical students are among the people at risk of developing hepatitis B infection. Needle stick injury and contact with patient's mucosal surfaces are the main routs of HBV transmission (11). Given the lack of knowledge about HBV immunity in medical students in the Golestan Province, this study was conducted to evaluate the level of immunity against HBV among 2018-intake medical students.

## MATERIALS AND METHODS

Based on previous data and considering a confidence interval of 95% and an accuracy of 0.06, the sample size of the present study was calculated as 238 individuals (10). Accordingly, this descriptive cross-sectional study was conducted on 241 (137 men and 104 women) aged 18-20 years who were studying medicine, dentistry, nursing, paramedicine and midwifery at the Golestan University of Medical Sciences, Gorgan, Iran. Informed written consent was obtained from the participants, and the study protocol was approved by the ethics committee of the university (ethics code: IR. GOMUS.REC.1397.089). Participants completed a data collection form on age, sex, place of residence, body mass index (BMI) and ethnicity.

Blood samples were taken from the volunteers and kept at -20 ºC after separating the serum. Each sample was tested for HBsAb, HBsAg and HBcAb (total) using commercial enzyme-linked immunosorbent assay kits (DIAPRO Inc., Italy). A serum level of HBsAb equal to or greater than 10 mlU/ml indicated immunity.

Based on the results, the subjects were divided into two groups of seropositive and seronegative. Data were analyzed with descriptive statistics using the Chi-square test. All statistical analyses were performed using SPSS 16 software and at significance level of 0.05.

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## RESULTS

All participants had received HBV vaccine during infancy according to the national vaccination program. Among the participants, 167 (69.3%) had HBsAb level of less than 10 mIU/ml and were therefore classified as susceptible, while only 74 (30.7%) subjects had antibody level of above 10 mIU/ml. The distribution of HBsAb titers relative to sex, place of residence, BMI and ethnicity is presented in table 1. There was no significant relationship between the variables and the HBsAb level (P>0.05). Furthermore, all participants had negative HBsAg and HBc Ab (in total).

**Table 1. Frequency distribution of HBsAb titers by sex, place of residence, BMI and ethnicity**

| Variable | | HBsAb < 10 (%) | HBsAb ≥ 10 (%) | Total | P-value |
|---|---|---|---|---|---|
| **Sex** | Male | 78 (75) | 26 (25) | 104 | 0.094 |
| | Female | 89 (65) | 48 (35) | 137 | |
| **Place of residence** | Urban | 148 (69.2) | 66 (30.8) | 214 | 0.898 |
| | Rural | 19 (70.4) | 8 (29.6) | 27 | |
| **BMI** | Underweight | 22 (68.8) | 10 (31.3) | 32 | 0.618 |
| | Normal | 101 (68.7) | 46 (31.3) | 147 | |
| | Overweight | 28 (70) | 12 (30) | 40 | |
| | Obese | 12 (87.5) | 2 (14.3) | 14 | |
| **Ethnicity** | Persian | 113 (68.9) | 51 (31.1) | 164 | 0.221 |
| | Turkman | 31 (63.3) | 18 (36.7) | 49 | |
| | Others | 23 (82.1) | ◦5 (17.9) | 28 | |

## DISCUSSION

The results of this study indicated that a high proportion of people who had received HBV vaccination according to the national vaccination program had low serum levels of HBsAb (less than 10 mIU/ml). Various studies have shown that vaccine-dependent antibody levels decrease or become immeasurable years after vaccination, which is consistent with this study (12-17). It seems that anti-HBsAb levels will drop in the first few years after vaccination, and one-third to half of the vaccinated children may have a titer of less than 10 IU/L at the age of 10 to 15 years (12, 13). Environmental factors, infant age, type and dose of vaccine and vaccination intervals in each country can affect the serum levels of antibodies and the level of serum protection in individuals (18). Some previous studies showed that despite the continuous decline, antibody levels can remain at a protective level for a long time (7, 18), which is inconsistent with this study. Other previous works have shown that 1-10% of apparently healthy individuals are unable to produce antibody after vaccination (10, 20). Results vary in this regard, which is most likely due to genetic factors and difference in geographical features (7, 10).

There was no significant relationship between gender and antibody titers, which is consistent with the results of previous studies (16, 20-22). However, some other studies reported a role for gender in increasing antibody titers (5, 10, 23-27). The inconsistency in the results could be due to the difference in study methods, antibody titer measurement, sample storage conditions before tests, sensitivity and specificity of kits used for the measurements, age of the study population and time of first vaccination. In our work, there was also no significant relationship between antibody level and place of

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residence, which is consistent with urban studies (28).

Considering the lack of an immune system response to HBV in some individuals and the decrease of vaccine-dependent antibody levels over time, the limitations of this study included the lack of knowledge of the immune response of participants after neonatal vaccination. One of the strengths of this study is the evaluation of markers of infection (anti-HBcAb and HBsAg) and the evaluation of antibodies (anti-HBsAb) in people with dispersed places of residency. Since HBsAg and HBcAb are markers of HBV infection, a negative result indicates no infection in our study subjects.

## CONCLUSION

Due to the low levels of immunity against HBV in two-thirds of our subjects, injection of a HBV vaccine in the non-immune group is recommended. In addition, because students in different medical fields are exposed to HBV, it seems necessary to evaluate HBsAb titer in all students upon admission to the university. It is also recommended to measure HBsAb titers several months after vaccination to evaluate the response to vaccine.

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## DECLARATIONS

### Funding

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### Ethics approvals and consent to participate

The study was approved by the ethics committee of Golestan University of Medical Sciences, Gorgan, Iran (ethics code: IR. GOMUS.REC.1397.089). A written informed consent was obtained from all subjects prior to participation.

### Conflict of interest

The author declares that there is no conflict of interest regarding publication of this article.

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