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The Evaluation Anti-HBsAb Titer Among University Students in Shiraz, 2019

Seyed Mohammad Ali Hashemi[1,2], Fatemeh Hashemzadeh[1], Helen Bahrampour[1], Fatemeh Nekooei[1], Negar Joharinia[1], Jamal Sarvari[1,3*]

1. *Department of Bacteriology & Virology, Shiraz University of Medical Sciences, Shiraz, Iran*
2. *Department of Microbiology, Golestan University of Medical Sciences, Gorgan, Iran*
3. *Gastroenterohepatology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran*

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ABSTRACT

Background: Regarding the availability of an effective vaccine against hepatitis B virus, global vaccination is the best cost-effective strategy to prevent HBV infection. However, some people may not respond to the vaccine or the titer of antibody decreases by time. Therefore, the present study aimed to determine the frequency of anti-HBs antibody (anti-HBsAb), among university students in Fars province, southern Iran.

Methods: In this cross-sectional study, 825 medical students were enrolled. Blood samples were taken from the subjects, and the serum separated and stored at – 20 ºC until use. Next, HBs Ab titer was measured by ELISA method.

Results: Out of 825 students 54% was male and 46% were female. The mean age of the students was 19.5±1.9. The titer of anti-HBsAb in 529 (64%) of subjects was lower than 10 mIU/mL. Significant relationship was observed between age and the titer of anti-HBsAb (P=0.001), although no significant relationship was observed between gender (P=0.19), history of blood transfusion (P=0.58) and the titer of anti-HBsAb.

Conclusion: Finding of this study showed that the titer of anti-HBsAb in more than half of students was lower than 10 mIU/mL and by time the anti-HBsAb titer decreased, indicating the necessity of measurement of anti-HBsAb titer in medical students.

Keywords: Hepatitis B virus, Antibody titer, Student, Shiraz

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Corresponding Information: **Jamal Sarvari,** Associate Professor, Department of Bacteriology & Virology, Shiraz University of Medical Sciences, Shiraz, Iran. Email: sarvarij@sums.ac.ir

Introduction

The hepatitis B virus (HBV)-related liver disease is a public health problem worldwide. HBV is classified in the Hepadnavirida family with an incomplete and circular DNA genome (1). The virus is transmitted through parenteral, sexual as well as vertically from mother to fetus (2). Due to the availability of an effective vaccine against the HBV as well as high cost of treatment for the health system, general vaccination is the best way to prevent the transmission of disease as an affordable and efficient strategy. However, some people may not respond to the vaccine or the titer of antibody decreases by time.

Following vaccination, antibodies are produced against a highly immunologic antigen, and the only serological index that appears after vaccination in the serum is anti-HBs Ab. In exposed subjected to the HBV, in addition to anti HBsAb, the anti- core antibody (anti-HBcAb) is also positive. The antibody titers created below the 10 IU/L indicate poor immunity, 10-100 IU/L as moderate

immunity and the titer higher than 100 IU/L is considered as good immunity (11). Various studies conducted in different countries show that after a full period of vaccination against the HBV, 5-15% of individuals do not produce enough antibodies. Moreover, the titer of Ab may decrease after vaccination; thereby reduce the rate of immunity against the virus by time (12). Various studies have shown that peoples who produced high level of Abs after vaccination may have longer immunity (13). Moreover, after vaccination, it is essential to investigate the immunological level, especially in people with the possibility of occupational exposure. Therefore, the present study aimed to determine the frequency of anti-HBs Ab among university students in Fars province, southern Iran.

Materials and Methods

Subjects and Sampling

In this cross-sectional study, 825 students from Shiraz University of Medical Sciences (Shiraz, Iran) were enrolled consecutively. The study performed from September 2019 to January 2020. A questionnaire containing questions about demographic and history of vaccination were filled by participants. Informed written consent was obtained from each participant, and the study was approved by Ethics Committee of Shiraz University of Medical Sciences (SUMS.MED.REC.1399.47). 5 mL blood sample were taken from each student, centrifuged and then the separated serum were stored at – 20°C until assay.

ELISA for the assay of anti HBs Ab

The anti-HBs Ab titer was measured using an ELISA commercial kit according to the manufacturer's protocol (DiaPro, Italy). The results were reported as quantitative with mIU/mL.

Statistical Analysis

The results of this study were analyzed using SPSS version 26 (SPSS Inc., Chicago, IL., USA) and Chi-squared test, and P-value<0.05 was considered as a significant level.

Results

Out of 825 students 54% was male and 46% were female. The mean age of the students was 19.5±1.9. The titer of anti-HBsAb in 529 (64%) of subjects was lower than 10 mIU/mL. A significant relationship was observed between age and the titer of anti-HBsAb (*P*=0.001), although no significant relationship was observed between gender (*P*=0.19), history of the blood transfusion (*P*=0.58) and the titer of anti-HBsAb.

Table 1. Demographic and other features of subjects and relative seropositivity to anti-HBsAb among university students in Shiraz

Variables	HBsAb titer			P value
	<10mIU/ml	HBs Ab Titer<100mIU/ml 10mIU/ml<	>100mIU/ml	
Sex				
Male (n=446)	17(3.81%)	146(32.73%)	283(63.45%)	P =0.19
Female (n=379)	24(6.34%)	109(28.76%)	246(64.9%)	
Age				
≥20 (n=708)	29(4.1%)	233(32.9%)	446(63%)	P=0.001
<20 (n=117)	12(10.26%)	22(18.8%)	83(70.94%)	
Majors				
Medical Student (n=233)	11(4.72%)	74(31.76%)	148(63.52%)	
Nursing (n=138)	10(7.25%)	30(21.74%)	98(71.01%)	
Laboratory Science (n=84)	6(7.14%)	18(21.43%)	60(71.43%)	
Anesthesia (n=53)	2(3.77%)	16(30.2%)	35(66.03%)	
Dentistry (n=51)	4(7.85%)	14(27.45%)	33(64.7%)	
Surgical Technologist (n=49)	3(6.12%)	11(22.45%)	35(71.43%)	-
EMT (n=44)	1(2.3%)	18(40.9%)	25(56.8%)	
Physical Therapy (n=35)	0(0.0%)	11(31.4%)	24(68.6%)	
Radiology Technologist (n=32)	3(9.37%)	10(31.25%)	19(59.3%)	
Midwifery (n=22)	0(0.0%)	6(27.3%)	16(72.7%)	
Occupational Therapy (n=22)	1(4.55%)	7(31.81%)	14(63.63%)	
Others major (n=62)	1(1.61%)	23(37%)	38(61.3%)	
Blood Transfusion (n=48)	2(4.17%)	16(33.33%)	30(62.5%)	P=0.58

EMT: Emergency medical technician

Discussion

Finding of this study showed that the titer of anti-HBsAb in 529 (64%) of subjects was lower than 10 mIU/mL. The significant relationship was observed between age and the titer of anti-HBsAb, although no significant relationship was observed between gender, history of the blood transfusion and the titer of anti-HBsAb.

The understanding of effective and safe vaccination of hepatitis B is one of the most significant developments in medical science in the twentieth century. One of the most important ways to prevent morbidity and mortality related to HBV is a vaccination for all newly born babies, and the population is at risk. Finding of this study showed that the titer of anti-HBsAb in more than half of students was lower than 10 mIU/mL and by time the anti-HBsAb titer was decreased, indicating the necessity of measurement of anti-HBsAb titer in medical students. Taiwan, which was an endemic area for chronic HBV infection and liver cancer, was the first place to start the child's general vaccination program in 1986 and recent studies have reported the efficacy of the long-term effect of this vaccination program in reducing liver cell carcinoma **(14)**. The general vaccination program for infants in Iran started in 1993 **(15)**. The routine program of neonatal and pediatric vaccination has significantly changed the epidemiology of HBV and has reduced the cancer of liver cells around the world **(12,16)**. Rad *et al.* investigated the titer of anti-HBsAb in subjects with the ages of 1 to 18 years old in Ahvaz and found that the anti-HBsAb titer ≥10 mIU/mL among the children with the age one and teenagers 18 years were % 90 and % 48.9 respectively. They showed that, there was a significant relationship between the reductions of antibody titers with age **(13)**. In a meta-analysis study Rezaei *et al.* showed that with age increase, the number of respondents in the vaccine was reduced significantly. (P = 0.001) There was no significant difference between the two groups in terms of gender, vaccines, ethnicity, and living place. Also, the meta-analysis was shown that based on Iranian research and other international research, there is no significant difference between the lacks of response to HBV vaccine **(12)**.

According to studies, although the rate of response to the vaccine varies from country to country, the rate of response to the vaccine in childhood is higher than in adulthood. Several factors have been mentioned in connection with the lack of response to vaccines and reducing the antibody titers in various studies. However, due to the decrease in antibody titers over time, it is necessary to inject a booster dose in individuals who are likely to have an occupational exposure to the virus. The results of our study showed that there was a significant relationship between age and antibody titer and with increasing age, antibody titer was decreased.

Moreover, a series of studies have shown that about 5% of individuals with a healthy immune system do not respond to vaccines after receiving regular vaccination periods and even after receiving booster doses **(11)**. The factors that might be related to lower rate of responsively to the vaccine include male gender, diabetes, chronic liver disease, genetics background and smoking **(23, 24)**. Other factors include vaccine storage, intervals time between injections and inappropriate concentration of injected vaccine **(11, 24)**. Moreover, another factor that is important in the efficacy of vaccines and the production of neutralizing antibodies is the nature of the vaccine, and there are several different strategies that might improve the effectiveness of the vaccine. In the second generation that produced in yeast a part of HBs antigen that plays an essential role in virus attachment is used for the stimulation of neutralizing antibodies **(21)**. The third generation of vaccines that produced in mammalian cells, increases the production of neutralizing antibodies in non-responder individuals **(25)**. It is also reported that using appropriate adjuvants can improve the effect of HBV vaccine and its response in these individuals **(26)**. Fabrizi *et al.* reported that using a higher dose of Timopentin as adjuvant can lead to an increase in the response rate to HBV vaccination **(27)**.

Conclusion

In conclusion, the results of this study indicated that by time, the level of immunity against hepatitis B virus is decreased. So it is necessary for high-risk groups including students of medical sciences, that the anti-HBsAb titer were examined, and if the titer was lower than 10 mIU/mL, the booster dose was recommended.

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