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STUDY OF ANTI-HBS ANTIBODY TITER AND ASSOCIATED FACTORS AMONG HEALTHCARE STAFF VACCINATED AGAINST HEPATITIS B MORE THAN TEN YEARS IN HOSPITALS OF JAHROM IN 2016

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ABSTRACT

Aim: Hepatitis B virus (HBV) is one of the major causes of viral hepatitis, cirrhosis and hepatocellular carcinoma throughout the world. Medical and paramedical professional staff members are at risk of contracting the virus. Study of vaccination and antibody titer in these people is very important in controlling the virus.
Material and Method: This cross-sectional study was conducted in 2016 on 229 staff working at the hospitals of Jahrom in Iran, all of which were completely vaccinated with recombinant hepatitis B vaccine more than 10 years. Blood samples were taken from individuals and serum anti-HBs titer was measured by ELISA assay. Titer over 10 Iu/ml was considered as a positive. Data were analyzed using SPSS 16 software via descriptive statistics, ANOVA, Pearson correlation coefficient and Multiple Linear Regression at the significant level of 0.05.
Results: The mean anti-HBs titer was obtained 457.24± 382.41 (95% CI; 407.45-507.04). The anti-HBs titer was <10mIu/Ml in 8 patients (3.5%) and ≥10mIu/Ml in 221 patients (96.5%). There was no significant relationship among anti-HBs titer and factors of gender, occupational groups, marital status, needle stick, BMI and underlying diseases such as diabetes, kidney and liver failures. However, history of receiving last dose of vaccine and older age were negative predictive factors for anti-HBs titer (p-value <0.05).
Discussion: The immunogenicity rate of hepatitis B vaccine within 10 years and over after primary vaccination was 96.5% and given the 33.6% history of needle stick in study staffs, none of the participants reported clinical symptoms consistent with hepatitis B infection in the years after vaccination. Therefore, continuation of vaccination against hepatitis B in the expanded program of immunization in Iran is the best practice of HBV infection control.

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Introduction

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Hepatitis B virus (HBV) is one of the major causes of viral hepatitis, cirrhosis and hepatocellular carcinoma throughout the world. The virus is introduced as second hazardous carcinogen in the world after smoking, and 37% of the world population is infected with the Hepatitis B virus [1]. It is estimated that about 2 to 3 percent of the Iranian population is carrying the virus, and approximately 300 thousand cases are suffering chronic liver disease, cirrhosis and hepatocellular carcinoma [2].
According to statistics released by Iranian Ministry of Health, 72% of patients with hepatocellular carcinoma and 84% of patients with cirrhosis in Iran have had a history of hepatitis B infection [3).
There are various routes of HBV transmission, whose the most important one in the world and Iran is transmission from mother to child during childbirth; other cases include sexual contact, family contact, intravenous unsanitary injection, and transmission in medical and health centers [4, 5].
One of the most common routes of HBV transmission in health centers is through wounds caused by a needle infected with the blood of patients with positive HBsAg [6].
The prevalence of HBV infections in medical staff has been reported 1% per year [7]. On the other hand, the risk of HBV transmission from health workers to population is high, which is not only a public health problem but also is a legal issue [8, 9].
The most effective way to prevent contracting the disease is vaccination with the recombinant vaccine. The strategy for vaccination against HBV is adapted based on geographical and epidemiological differences of hepatitis B infection. According to the World Health Organization, all infants and high-risk groups such as health workers, intravenous drug users, persons with multiple sexual partners, gay men, care staff working with mental retardation, prisoners and guards, family contacts of chronic carriers or those with acute hepatitis B infection should receive three doses of hepatitis B vaccine that can generate protective antibodies in 85% of healthy persons [10].
American Centers for Disease Control and Prevention (CDC) has reported that 100 to 200 healthcare staff die annually due to complications of occupational hepatitis B. Following the increase in incidence of hepatitis B in these individuals, Board of Workers announced viral hepatitis as an occupational hazard [11].
In Iran, different reports have been presented on the immunogenicity rate of vaccine. The durability of the immune responses after HBV vaccination is an important issue for decision making to prescribe a booster dose [12].
Given that many healthcare staff after receiving three doses of vaccine are unaware of the immune response outcome and appropriate response may not occur in all recipients, this study therefore was conducted to assess anti-HBs titers among staff working at hospitals of Jahrom, who had spent more than 10 years since their last vaccination.

Materials and methods

This cross-sectional study was carried out on 229 staff working at the hospitals of Jahrom in 2016. Inclusion criteria were the cases with three doses of hepatitis B vaccine (both regular and irregular), elapsing duration of 10 years or more after receiving the last dose of hepatitis B vaccine and satisfaction to participate in the study.
The serum level of anti-HBs was tittered using Microwen ELISA kit through enzyme immunoassay method on solid medium and using marked enzyme. Also at sampling, information on age, gender, marital status, occupational groups, history of smoking, underlying diseases like diabetes, kidney and liver disease, asthma, blood pressure, BMI (body mass index), history of contamination with hypodermic needles and blood transfusions as well as the intervals between immunization sessions were collected from each person. Data were analyzed using SPSS 16 software via descriptive statistics, ANOVA, Pearson correlation coefficient and Multiple Linear Regression at the significant level of 0.05. To analyze the results based on available resources, antibody levels higher than 10mIu/Ml were considered as sufficient response to hepatitis B vaccine and antibody levels lower than 10mIu/Ml were considered inadequate response to the vaccine. In addition, the first group was divided into two groups of low responder (10-100mIu/Ml) and high responder (over 100mIu/Ml) [12-15].
Adherence to ethical principles and declaration of Helsinki was considered at all stages of the project and all information related to the subjects was kept confidential by the investigators. The Ethics Committee of Jahrom University of Medical Sciences approved this project (code of IR.JUMS.REC.1395.114).

Results

Of 229 people studied, 198 patients (86.5%) were female and the rest were male, including 140 (61.1%) nurses, 22.7% operating room personnel, 7.4% service staffs, 7% midwives and 1.7% physicians. 82.5% of participants were married with a mean age of 36.67 ±6.46 years (ranging from 28 to 58 years). The mean BMI of personnel under study was 25.02±3.50 (ranging from 18 to 35). 86.9% of them had received three doses of the vaccine regularly as zero, one and six months. In conjunction with the antibody serum level and interval of last vaccination, 182 (79.5%) between 10 and 12 years, 36 (15.7%) between 13 and 15 years and 11 (4.8%) 16 or more years had elapsed from the last dose of vaccine; 77 of staff (33.6%) had a history of needle stick and 19 (8.3%) were suffering from underlying diseases such as diabetes and kidney and liver failures. None of the participants reported clinical symptoms consistent with hepatitis B infection in the years after vaccination.

The anti-HBs titer in 8 patients (3.5%) was <10mIu/Ml (non-responder) and in 221 patients (96.5%) was ≥10mIu/Ml (responder). The latter group based on the Anti-HBS level was divided into two groups, including 174 (76%) with antibody level over 100mIu/Ml (good responder) and 47 (20.5%) with antibody levels of 10-100mIu/Ml (low responder) (Figure 1).
The mean antibody titer in individuals with a history of 10-12 years of receiving the last dose of vaccine was 487.57± 392.63, in individuals with a history of 13-15 years of receiving the last dose of vaccine was 339.81± 393.74 and in individuals with a history of over 16 years of receiving the last dose of vaccine was 163.39± 116.37. This difference was statistically significant (p-value = .013) (Table 1 and Figure 2).
The analysis performed using Pearson correlation coefficient showed a significant relationship between anti-HBs titer and history of receiving the last dose of vaccine (p-value = 0.001, r = -0.21) (Figure 3).
In the present study, Multiple Linear Regression indicated no association between anti-HBs titer and variables of gender, occupational groups, marital status, and history of needle stick, BMI and underlying diseases such as diabetes, kidney and liver failures. But the history of receiving the last dose of vaccine and older age were negative predictive factors for anti-HBs titer. Thus, the level of antibody titer was reduced by 35.16 mIu/Ml with increasing one year of receiving the last dose of vaccine (p-value = 0.001). Also per one year increase in age, the level of antibody titer was reduced by 9.58 mIu/Ml (p-value = 0.014).

Discussion

The durability of the immune responses after HBV vaccination is not clear exactly [16]. The results of this study suggest that within 10 years after the completion of primary vaccination, 96.5% of hospital staff had immunogenicity of Anti-HBS (titer over 10mIu/Ml). However, 3.5% of people had no immunity against the virus (titer <10mIu/Ml).
In a study performed in hospitals of Tehran in Iran by Yadegari Nia et al. in 2010, the efficacy rate of hepatitis B vaccine has been reported 85.3%. The immunogenicity rate had no significant differences with age, gender, smoking, diabetes and the last time of vaccination. The last time of vaccination in this study was 6 years [10].
In another study carried out in the burn hospital of Yazd in Iran by Oliya et al. in 2011, 90.4% of people had a positive titer (>10 mIU: ml) and 9.6% had a negative titer (< 10 mIU: ml). Furthermore, no statistically significant relationship were between age, gender, interval between immunization sessions and anti-HBs titer (p-value <0.05). However, the association between history of receiving the last dose of vaccine and antibody titer was significant (p-value = 0.046) [17].
The immunity level of staff working in health centers in Iran has been reported between 50% and 90% in different studies [18, 19]. The immunity level of personnel in the hospitals of Jahrom in the present study was higher than other studies. This difference can be attributed to factors such as the type of kit used to measure the level of Anti-HBS, genetic, geographical and regional differences, as well as types or methods of vaccination.
In a study conducted by Kulendran et al. in 2013 among nurses at hospitals of Sri Lanka, failure rate of immune response in patients with three doses of hepatitis B vaccine has been reported 7.7% and immunogenicity rate had no relation with simultaneous disease (such as diabetes, asthma and hypertension). However, pregnancy had been significantly contributed to the disruption of immunization in patients who received only two doses of vaccine [20].
In another study by Zanetti conducted on 525 adolescents and young Italians in 2003, anti-HBs titer in 95% of cases has been reported desirable 7 years after receiving three doses of vaccine (<10 mIU: ml) [13]. In the present study, significant association was found beetween anti-HBs titer and age and duration of receiving the last dose of vaccine; this finding is in line with most studies in this area [12, 17, 21 and 22].
Given that the ability to create an effective and protective immune response after HB vaccine needs integration and coordination of action between T and B cells as well as macrophages [14], changes caused by humoral and cellular immune systems after aging reduce the effectiveness of HBV vaccine in elderly comparing young adults and children [23]. Concerning the history of receiving last dose of vaccine, results of a review article have expressed reduction in anti-HBs titer following increase in this time [15].
In the present study, anti-HBs titer was not associated with variables of history of alcohol use and smoking, blood transfusion history, and family history of hepatitis B. The lack of correlation could be due to the low number of samples with positive history of the variables mentioned.

Conclusion

The results of this study showed that within 10 years and over after the completion of the primary vaccination, 96.5% of hospital staff had immunogenicity level of Anti-HBS and given the 33.6% history of needle stick in study staff, none of the participants reported clinical symptoms consistent with hepatitis B infection in the years after vaccination. Therefore, continuation of vaccination against hepatitis B in the expanded program of immunization in Iran is the best practice of HBV infection control.

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Conflicts of Interest:
The authors declare no conflict of interest.

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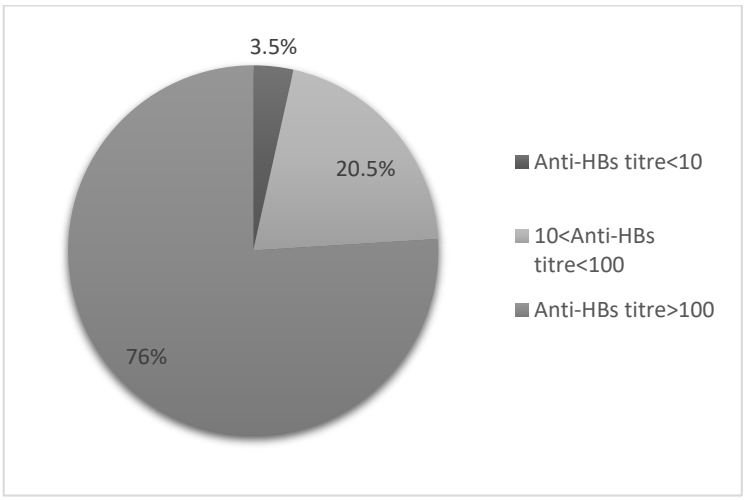

Fig 1- Frequency percentage of subjects at different levels of anti-HBs titer

Table 1- The level of Anti-HBS among staffs working at hospitals of Jahrom in terms of the interval since the last dose of vaccine

Interval from the last dose of vaccine (year)	Median	Number (%)	Mean (anti-HBs)	Standard deviation	95% confidence interval for mean	Significance
10-12	352	182(79.5)	487.57	392.63	430.14-544.99	0.013
13-15	284	36(15.7)	393.74	339.81	278.77-508.72	
<16 years	173	11(4.8)	163.39	116.37	85.21-241-57	
		229(100)	457.24	382.41	407.45-507.04	

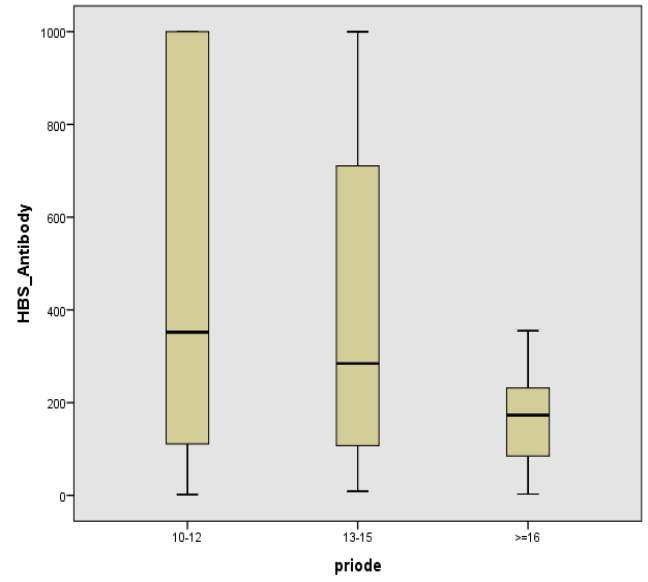

Fig 2- Anti-HBS levels in staffs working at hospitals of Jahrom in terms of interval since the last dose of vaccine (whiskers)

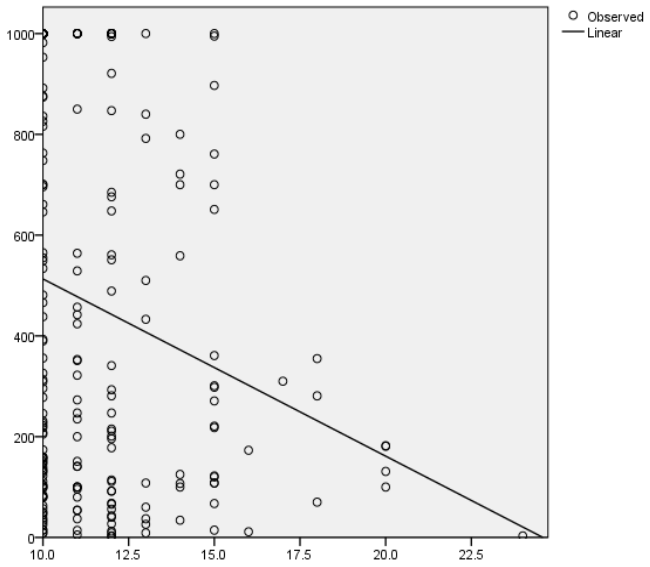

Fig 3- Correlation between antibody level against hepatitis B and history of vaccination among personnel of hospitals in Jahrom