

Immunologic Response to Hepatitis B Vaccine in Health Care Workers: A Screening Program and Evaluation of Some Host-Related Factors Role

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Abstract: Problem statement: To evaluation the immunologic response to hepatitis B vaccine in health care's workers and effects of host-related factors? **Approach:** In a cross sectional descriptive analytic study carried out on the medical staff of Tabriz Shahid Madani Hospital in 2009-2010, we evaluated the immunologic response of the staff to vaccination against Hepatitis B and factors affecting it. **Results:** The mean antibody titer in the studied medical staff was 366.76 ± 169.714 IU L⁻¹. 2.05% were in "no response" group, 1.46% in "Low response" group and 96.49% in "Good response" group. **Conclusion:** Immunological response in the smoking staff was significantly less ($p < 0.001$) but no significant difference was observed in the response between genders ($p = 0.127$) and no case of hyperlipidemia was reported. There was a significant reverse linear relation between age and antibody titer in the studied staff ($p = 0.003$, $R = 0.162$) but no significant linear relation was observed between weight, height and BMI and antibody titer.

Key words: Hepatitis B vaccines, occupational diseases, prevention and control, linear relation, antibody titer, factors affecting, immunologic response, analytic study, host-related factors

INTRODUCTION

Hepatitis B Virus (HBV) infection represents a major health problem, with 2 billion people infected worldwide and more than 400 million chronic carriers of HBV. Globally it causes about 1.2 million deaths per year due to various complications including chronic hepatitis, cirrhosis and liver cancer (Hou *et al.*, 2005; Lavanchy, 2004; Michielsen *et al.*, 2005; Seeger and Mason, 2000).

Hepatitis B comprises one of the major health problems worldwide (Perez *et al.*, 1998). Infection with hepatitis B virus has become a vaccine-preventable disease (Leroux-Roels *et al.*, 2001). Vaccination against Hepatitis B Virus infection (HBV) is safe and effective; however, vaccine-induced antibody level wanes over time (Hennig *et al.*, 2008). Health Care Workers (HCW) are a group at risk for Hepatitis B Virus (HBV) infection (Oliveira *et al.*, 1995). Protection against hepatitis B virus infection by vaccination is considered to be an important preventive measure for health care workers (Rachiotis *et al.*, 2005). Hepatitis B vaccination is recommended for all Health Care

Workers (HCW) at risk of exposure to infectious body fluids (Williams *et al.*, 2001). Health care workers' immunization against hepatitis B is an essential measure to avoid occupational transmission of hepatitis B virus at primary health care centers (Garcia and Facchini, 2008). The overall serum protection rate was 97.5 and 46.7% of the sample responded showing titers of over 100 mIU ML⁻¹ (Perez *et al.*, 1998). Hepatitis B vaccine is a vaccine developed for the prevention of hepatitis B virus infection. The vaccine contains one of the viral envelope proteins, Hepatitis B surface antigen (HBsAg). It is produced by yeast cells, into which the genetic code for HBsAg has been inserted. A course of three vaccine injections are given with the second injection at least one month after the first dose and the third injection given six months after the first dose. Afterward an immune system antibody to HBsAg is established in the bloodstream. The protective antibody is known as anti-HBsAg. This antibody and immune system memory then provide immunity to hepatitis B infection. The first vaccine became available in 1981 (Hou *et al.*, 2005). The aim of this study was evaluation

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the immunologic response to hepatitis B vaccine in health care workers and effects of some host-related factors.

MATERIALS AND METHODS

In a cross sectional descriptive analytic study carried out on the medical staff of Tabriz Shahid Madani Hospital in 2009-2010, we evaluated the immunologic response of the staff to vaccination against Hepatitis B and factors affecting it.

Medical staff is routinely vaccinated against hepatitis B and therefore antibody titration is essential to insure appropriate immunity.

The studied medical staffs are vaccinated by hepatitis B vaccine with following properties (entitled EUVAX B, met the WHO requirements, made in Korea, LG life sciences company) for three doses (0, 1 and 6 months) and antibody was titrated three months after vaccination. All utilized vaccines were from one brand and all tests were performed in one laboratory.

ELISA test was used to evaluate the samples used kit in this study was the Anti-HBs kit, made by ROCHE Company entitled "COBAS". Methods of this kit was ELISA, in which ELISA micro plates in this method ELISA micro plates are covered by antigen S so that after adding serum containing antibodies against antigen S, antigens would bind with antibodies. In the next step, antigen S conjugated with peroxidase enzyme is added which attaches to the part of the antibodies not bound to antigens. Later, adding chromogene and substrate dyes the solution whose color can be read by ELISA reader.

After performing tests and reading the plates by ELISA reader, standard curves were provided using standard samples. Later using these curves, the concentration of antibodies in the tested sample were calculated. Based on the instructions of the kit manufacturer, antibody level less than 10 units per mL was considered negative and amounts higher as positive.

RESULTS

This study was carried out on 341 people from the medical staff and HBsAg titers were measured after three dose vaccination (0, 1 and 6 months), the following results were obtained.

126 people (37%) from the studied staff were male and 215 people (63%) female. Demographic data of the studied medical staff are presented in Table 1.

Table 1: Demographic factors of health care workers

	Sex		P_value
	Male	Female	
Age (year)	34 ± 9	30 ± 6	<0.001
Length (m)	1.71 ± 0.07	1.60 ± 0.06	<0.001
Weight (Kg)	74 ± 12	62 ± 11	<0.001
BMI	25.55 ± 4.02	24.13 ± 3.86	0.002
Smoker	15	1	<0.001
HLP	30	10	<0.001

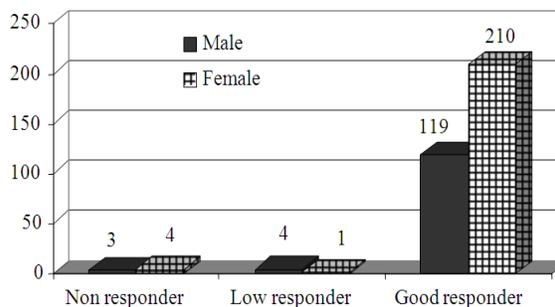


Fig. 1: Response to vaccination in studied health workers between two sexes (P = 0.127)

The mean antibody titer in the studied medical staff was 366.76 ± 169.714 IU L⁻¹ in the range of 1-1000 IU L⁻¹ and median of 382 IU L⁻¹.

Antibody titer of the studied staff according to gender, smoking and hyperlipidemia are presented in Table 2.

Dividing the antibody titer into three groups of "no response" (Titer < 10 IU L⁻¹), "Low response" (Titer 10-100 IU L⁻¹) and "Good response" (Titer > 100 IU L⁻¹) revealed that from 341 studied staff, 7 people (2.05%) were in "no response" group, 5 people (1.46%) in "Low response" group and 329 people (96.49%) in "Good response" group.

Response of the staff according to gender, smoking and hyperlipidemia are presented in Fig. 1-3 which shows that response in the smoking staff was significantly less (p < 0.001) but no significant difference was observed in the response between genders (p = 0.127) and no case of hyperlipidemia was reported.

There was a significant reverse linear relation between age and antibody titer in the studied staff and antibody titer decreased significantly as age increased (p = 0.003, R = -0.162) but no significant linear relation was observed between weight, height and BMI and antibody titer.

Table 2: Antibody titer of health care workers at the base of sex, smoking and hyperlipidemia

		Titer antibody (IU/L)							P_Value
		Mean ± Std	Median	Percentile 05	Percentile 25	Percentile 75	Percentile 95	Percentile 99	
Sex	male	385 ± 176	419	50	270	491	607	995	0.130
	Female	356 ± 165	370	100	220	485	602	734	
Smoking	No	368 ± 168	382	100	236	485	605	787	0.541
	Yes	341 ± 207	398	2	95	496	-	-	
Hyperlipidemia	Yes	382 ± 177	414	12	263	480	605	-	0.555
	No	365 ± 169	380	100	230	488	606	749	

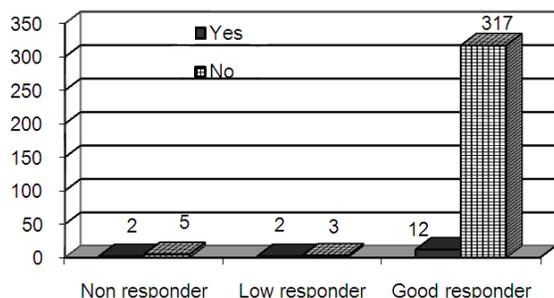


Fig. 2: Repose to Vaccination in studied health workers in smokers and nonsmokers (P<0.001)

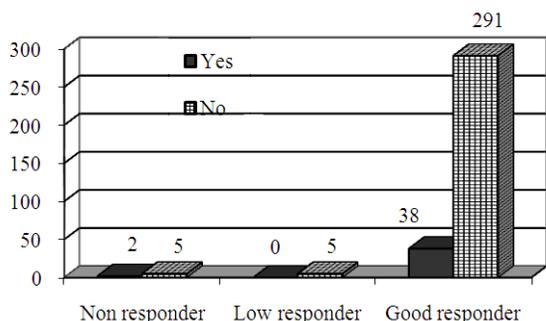


Fig. 3: Repose to Vaccination in studied health workers by HLP (P=0.571)

DISCUSSION

Hepatitis B is one of the important vocational diseases threatening medical staff. The main prevention method is vaccination against hepatitis B and maintaining appropriate immunity. High immunity level of the staff working in hospitals and other health centers can reduce hepatitis B infection among personnel. In this study we evaluated vaccination and immunity status in the personnel working in Shahid Madani Hospital.

Hepatitis B is one of the threatening infectious diseases in the staff of the medical centers. Infection risk of the hepatitis B in the medical staff is four times

more compared to the normal adult population and the people who are not active in the field (Lavanchy, 2004).

Immunity level of the medical staff in our country has been reported to be 50-90% in the different studies carried out (Zali *et al.*, 1996). In a study carried out by Jack *et al.* (1999) in Gambia within seven years it was concluded that children having antibody titers higher than 10 units in mL were immune against hepatitis B at least within the study period (seven years), whereas children having lower levels of antibody (less than 10 units in mL) were infected by hepatitis B in the following years (Jack *et al.*, 1999).

Geometric mean titers of anti-HBs after vaccination were also higher in the females than in the males (257±19.7 Vs. 29±1.88 Miu mL⁻¹, P = 0.01, 1802±35.2 vs. 306±13.6 mIU mL⁻¹, P < or = 0.05, 6465±72 vs. 2142±73.6 mIU mL⁻¹, P < 0.05) (Thakur *et al.*, 2010).

In our study antibody titers in the studied males and females were 385±176 IU L⁻¹ and 385±176 IU L⁻¹ respectively (p = 0.130).

In a study carried out in the US, it was identified that hepatitis B vaccination was effective in 72% of nurses and 71% of the physicians (Beltrami *et al.*, 2000).

In 1991 in England almost 94% and in 1990 in another study ¾ of the people (75%) and half of the residents were vaccinated whereas in Berlin only were 74% of dentists and 63% of their residents were vaccinated (Martins and Barre, 2003).

The overall serum protection rate was 97.5 and 46.7% of the sample responded showing titers of over 100 mU mL⁻¹.

Anti-HBsAb titers were > 100 mLU mL⁻¹ in 211 subjects (62.2%), 10-100 mLU/mL in 85 (25.1%) and <10 mLU mL⁻¹ in 43 (12.7%) persons (Saberifiroozi *et al.*, 2006). The overall antibody response rate was 95% (Cockcroft *et al.*, 1990).

In our study, Anti-HBsAb titers were >100 mLU mL⁻¹ in 329 persons (96.49%), 10 - 100 mLU mL⁻¹ in 5 (1.46%) and < 10 mLU mL⁻¹ in 7 (2.05%) persons.

Compared to the above-mentioned studies, our study showed a better coverage.

Previous studies have shown that 5-15% of healthy people do not show a protective antibody response following hepatitis B vaccination.

9.5% were non-responders (Perera *et al.*, 2002). Duration of vaccination, sex and body mass index was not significantly associated with anti-HBs levels (Perera *et al.*, 2002).

The responders were significantly younger than the non-responders and had significantly lower values of body mass index (wt/ht²) (Cockcroft *et al.*, 1990).

In our study only 12 people from the studied sample had antibody titers less than 100 after vaccination.

Smoking and alcoholism were significantly correlated with unsatisfactory response (Thakur *et al.*, 2010).

Female sex, intramuscular vaccination, young age and being a non-smoker were associated with a higher response rate and a higher geometric mean anti-HBs titer than male sex, intradermal vaccination, old age and being a smoker (Struve *et al.*, 1992).

Stratifying by vaccine brand demonstrated that age (P = 0.01), body mass index (P < 0.01) and smoking status (P < 0.01) were associated with lacking anti-HBs only for Recombivax HB recipients; and gender (P = 0.03) was associated with lacking anti-HBs only for Engerix-B recipients (Wood *et al.*, 1993).

In our study there was a significant reverse linear relation between antibody titer and age of the patients (R = -0.162 and P= 0.003) whereas no significant difference was observed regarding weight (P = 0.764), height (P = 0.321) and BMI (P = 0.407). Also no significant relation was observed in antibody titers between smoking, non-smoking and hyperlipidemic people (P = 0.555).

In our study also antibody titer significantly decreased as the age of the patients increased. "No response" was observed in people below 25 years 0, 0.3% in the age range of 25-34, 0.9% in the age range of 35-49 and 0.9% in the age range of over 50.

Testing of blood for anti-HBs one month after vaccination is recommended to recognize non-responders as a booster dose will be beneficial in the majority of them (Perera *et al.*, 2002).

We recommend (a) post vaccination testing within 1-3 months to document immunity, (b) periodic anti-HBs monitoring and (c) booster vaccination to maintain protective titer levels.

CONCLUSION

From 341 studied people, seven (2.05%) showed no response to vaccination, five (1.46%) low response and 329 (96.49%) good response. In our study there

was a significant reverse linear relation between antibody titer and age whereas no significant relation was observed with weight, height and BMI. Also there was no significant relation regarding antibody titer with smoking, non-smoking and hyperlipidemic.

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