

## HBV Vaccination Status and Response to Hepatitis B Vaccine Among Iranian Dentists, Correlation With Risk Factors and Preventive Measures

Nafiseh Momeni <sup>1</sup>; Mohammad Sadegh Ahmad Akhoundi <sup>1,2</sup>; Seyed Moayed Alavian <sup>3</sup>; Ahmad Reza Shamshiri <sup>4</sup>; Mehdy Norouzi <sup>5</sup>; Nima Mahboobi <sup>1</sup>; Nilufar Moosavi <sup>1</sup>; Seyed Mohammad Jazayeri <sup>5,\*</sup>

<sup>1</sup>Dental Research Center, Dentistry Research Institute, Tehran University of Medical Sciences, Tehran, IR Iran

<sup>2</sup>Orthodontic Department, Faculty of Dentistry, Tehran University of Medical Sciences, Tehran, IR Iran

<sup>3</sup>Middle East Liver Diseases Center (MELD Center), Tehran, IR Iran

<sup>4</sup>Research Center for Caries Prevention, Dentistry Research Institute, Department of Community Oral Health, Tehran University of Medical Sciences, Tehran, IR Iran

<sup>5</sup>Hepatitis B Molecular Laboratory, Department of Virology, School of Public Health, Tehran University of Medical Sciences, Tehran, IR Iran

\*Corresponding Author: Seyed Mohammad Jazayeri, Hepatitis B Molecular Laboratory, Department of Virology, School of Public Health, Tehran University of Medical Sciences, P. O. Box: 14155-6446, Tehran, IR Iran. Tel/Fax: +98-2188992660, E-mail: jazayerism@tums.ac.ir

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**Background:** Studies showed that HBV vaccination and consequent level of antibody are not completely adequate among dentists despite performance of highly exposure prone procedures.

**Objectives:** The objectives of the study were to evaluate the levels of responsiveness to HBV vaccine and to determine the occupational factors associated among dental staff.

**Materials and Methods:** In total, 1612 dental health care workers were recruited. The level of anti-HBs was tested using a commercially enzyme-linked immunosorbent assay (ELISA). Data on demographic, risk factors associated with dental practice and level of protective procedures and occupational exposure aspects were collected through self-reported questionnaires.

**Results:** Of 1538 vaccinated individuals, 55 (3.7%), 126 (8.4%) and 1309 (87.9%) had received one, two and full three doses of vaccine, respectively. One-hundred-seventy-six (11.5%) were nonimmune (anti-HBs < 10 IU/mL) and 1362 (88.5%) were immune (anti-HBs > 10 IU/mL). 392/542 (72.3%) of dentists who received their third dose of vaccination less than five years before the commencement of study were completely immune compared to those who had completed all three recommended doses in a longer period (308/491, 64.3%) ( $P = 0.001$ ). Fifty-eight (3.59%) of participants did not receive any HBV vaccine at all; however, they had positive results for anti-HBs, indicating a past HBV infection. Statistically, the levels of anti-HBs were significantly associated with gender, age, duration of dental practice engagement and regularly use of mask, glasses and shield.

**Conclusions:** Since dental care workers have a high risk of exposure to hepatitis virus, they should be advised to receive hepatitis B vaccine and it should be confirmed if they have acquired immunity to HBV by testing the level of anti-HBs.

**Keywords:** Hepatitis B Vaccines; Dentists; Infection Control

### 1. Background

Health care workers (HCWs) are at the front line for acquiring blood-borne viruses (hepatitis B virus, HBV; hepatitis C virus, HCV and human immunodeficiency virus, HIV) infections. The worldwide HBV infection rate is higher in dentists than other blood borne viruses like HCV and HIV. HBsAg prevalence among dentists reported to be 0.6% in the USA (1), 2.4% in Malaysia (2) and 13% in Korea (3). Likewise, among health care workers, dentists experience the highest chance of HBV infection and HBV incidences increase with duration of clinical experience of dentistry (4, 5). On the other hand, past (anti-HBc positivity) or present (HBsAg positivity) HBV infection rate in dentists are usually higher than the general population, regardless of HBV endemicity in those area (6).

Among blood-borne viruses, an immunoprophylactic vaccine is only available for HBV. Despite being effective in decreasing the HBV prevalence, the Extended Program on Immunization (EPI) only targeted newborns and adults in general populations, as well as high-risk groups, including dentists. However, dental health care workers are not fully covered by HBV immunization programs. Estimated of a 100-fold reduction in the incidence of HBV infection in vaccinated individuals compared to non-vaccinated individuals, regardless of the vaccine response (7), indicates that dental care workers should be advised to receive hepatitis B vaccine and it should be confirmed if they have acquired immunity to HBV by testing the level of anti-HBs (1, 4, 5, 8-10).

Reports from different countries indicated that HBV vaccine coverage rate in dental health care workers ranged between 26% and 96.6% (8, 9). In Iran, this coverage rate ranged between 74.8% and 94.9%; on average 70% of dentists care workers received at least one dose of HBV vaccine (11). As it shown, the reported response to HBV vaccine has not been reached 100% among dentists. Response to HBV vaccine (i.e. anti-HBs levels > 10 IU/mL) between Iranian dental workers has been studied extensively and 89.2% to 94.4% of dentists showed reasonable levels of anti-HBs following one to three doses of HBV vaccine (11-14). In the largest Iranian survey, of 598 participants, 35 (5.9%) were nonimmune (anti-HBs < 10 IU/L), 101 (16.9%) were relatively immune (anti-HBs > 10-99 IU/L) and 462 (77.3%) were completely immune (anti-HBs > 100 IU/L) (14).

## 2. Objectives

The objectives of the present study were to assess the HBV vaccine coverage and investigate the responsiveness to HBV vaccine as well as socio-demographic data, health-related and occupational factors and other correlates of vaccine responsiveness in Iranian dentists and dental staff.

## 3. Materials and Methods

This was a cross-sectional survey of dentists attending the 51st annual international congress of Iranian dental association held on 10 to 13 May 2011. Announcements were given at the time of meeting registration and before the scientific sessions. Individuals who met our inclusion criteria and willingness to give blood samples and knowing their vaccination history were recruited. An informed consent was obtained from all enrolled participants and a questionnaire was distributed to collect data. At a special booth in the conference building, potential participants gave oral consent and completed the questionnaire.

The purpose of the study and questionnaire was explained to all participants. The items on the questionnaire included: 1) demographic information, such as age, gender and marital status; 2) occupational information, comprising years of dental practice and place of practice and 3) vaccination data, which included the number of doses, time interval between doses, last dose date and checking the titer of antibody after vaccination. Among 1665 participants, history of immunization was extracted for 1612 individuals; hence 53 cases were excluded from the study. Ten millimeters of blood was obtained from each participant at the congress site. Blood samples were collected by peripheral venipuncture from all dentists. The samples were tested for antibodies against hepatitis B (anti-HBs) and anti-HBc using commercially available enzyme linked immunosorbent assays (ELISA) (M.B.S S.R.L. kit M.B.S. s.r.l. Medical Biological Service.

Italy). Anti-HBs were measured in IU/mL, and the results were classified into two groups as follows: 1) titers below 10 IU/L as no immunity and 2) titers above 10 IU/mL as complete immunity.

Data was analyzed using the Statistical Package for Social Sciences (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0, Armonk, NY: IBM Corp). All statistical comparisons were performed by simple and multiple linear regression analyses on logarithm (base 10) of the anti-HBs antibody values.  $P < 0.05$  was considered as statistically significant.

## 4. Results

### 4.1. General Characteristics

1612 participants including 1300 (80.7%) general practitioner, 155 (9.6%) students, 120 (7.4%) specialists and 37 (2.3%) clinical dental assistants were studied (Table 1). The subjects comprised 1058 (65.6%) males and 554 (34.4%) females with a mean age of 40.4 years (range 19-75 years, results not shown). The number of years in practice ranged from 0 to 55 years (excluding students) with a median of 15 years (results not shown). The demographic characteristics of the study sample according to job classifications are shown in Table 1.

### 4.2. Vaccination Status

Of total 1538 vaccinated individuals, 176 (11.5%) were nonimmune (anti-HBs < 10 IU/mL) and 1362 (88.5%) were immune (anti-HBs > 10 IU/mL) regardless of the number of doses and time after the last dose and time intervals between doses. No significant associations were found between the levels of anti-HBs and the kind of dental job (Table 2). According to subjects' reports, 55 (3.7%), 126 (8.4%) and 1309 (87.9%) had received one, two and full three doses of vaccine, respectively (See Table 1 for more details). Fifty-eight (3.59%) of participants did not receive any HBV vaccine at all; however, they had positive results for anti-HBs, indicating a past HBV infection. Data was missing for 16 individuals.

The median of anti-HBs titer was 247 ranged between 0 and 1502. However, anti-HBs mean value was 12.96 (95% CI: 5.72-29.39) for those who did not receive HBV vaccine. Nevertheless, the mean anti-HBs titers were 24.89 (95% CI: 11.16-55.52), 100.32 (95% CI: 70.52-142.72) and 107.04 (95% CI: 96.82-118.33) for subjects who received one, two and three doses of vaccine, respectively ( $P$  values between 1 and 2; 2 and  $\geq 3$  doses: 0.006, and 0.98, respectively, results not shown). Therefore, no significant difference was found between antibody levels and receiving second or third doses of vaccine; whereas, this association was significant between individuals who received only one versus those who received the second dose.

Among total participants, 1033 who knew their exact

time of vaccination history, 542 (52.5%) mentioned that they received vaccination within the past five years, while others (491; 47.5%) reported having received the last dose of vaccine more than five years prior this study. 356/542 (65.7%) of dentists who had received their third dose of vaccination less than five years before the study were completely immune (anti-HBs > 100 IU/mL); this rate was significantly higher than individuals who had completed all three recommended doses in a period more than 5 years prior to the study 279/491 (56.8%) ( $P = 0.003$ ) (Table 1).

A significant relation was found between gender and anti-HBs antibody titer; females showed a higher level of anti-HBs ( $P = 0.022$ ), (Table 1). Accordingly, the median of

antibody titer was significantly higher in the age group < 45 years compared to the age group > 45 years ( $P < 0.001$ ). Furthermore, statistically significant associations were found between the median titer of anti-HBs following vaccination and duration of dental practice engagement ( $P < 0.001$ ) (Table 1).

Eighty-one (5%) of participants had positive results for anti-HBc, of whom 66 (81.4%) had a history of vaccination (results not shown); 55 (83.3%) had protective levels of anti-HBs ( $\geq 10$  IU/mL) and 11 (16.7%) had inadequate anti-HBs levels (< 10 IU/mL). Although 13 (16.5%) of anti-HBc positive dentists did not receive vaccine, seven had protective levels of anti-HBs and six had inadequate levels, indicating a possible past HBV infection.

**Table 1.** Distribution of Demographic Characteristics<sup>a</sup>

	Student (n = 155)	General Practitioner (n = 1300)	Specialist (n = 120)	Resident (n = 37)
<b>Age, y</b>	23.93 ± 3.61	42.47 ± 9.94	43.4 ± 10.53	28.78 ± 3.25
<b>Gender</b>				
Male	60 (38.71)	905 (69.62)	82 (68.33)	11 (29.73)
Female	95 (61.29)	395 (30.38)	38 (31.67)	26 (70.27)
<b>Hepatitis vaccination</b>				
No	13 (8.39)	38 (2.92)	8 (6.67)	0 (0)
Yes	142 (91.61)	1262 (97.08)	112 (93.33)	37 (100)
<b>Years from the last vaccination, y</b>				
No vaccination	13 (8.39)	38 (2.92)	8 (6.67)	0 (0)
≤ 5	98 (63.22)	408 (31.37)	28 (23.33)	14 (37.84)
> 5	11 (7.10)	429 (33.00)	41 (34.17)	17 (45.95)
Unknown	33 (21.29)	425 (32.69)	43 (35.83)	6 (16.21)
<b>Number of doses</b>				
None	13 (8.39)	38 (2.92)	8 (6.67)	0 (0.00)
One dose	15 (9.68)	37 (2.85)	3 (2.50)	0 (0.00)
Two doses	11 (7.10)	101 (7.77)	14 (11.67)	2 (5.41)
≥ 3 Doses	108 (69.68)	1093 (84.08)	91 (75.83)	35 (94.59)
Unknown	8 (5.15)	31 (2.38)	4 (3.33)	0 (0.00)
<b>Years of working</b>	0	15.55 ± 9.35	16.14 ± 9.02	7.54 ± 3.23
<b>Marital status</b>				
Single	134 (86.45)	230 (17.69)	19 (15.83)	17 (45.95)
Married	21 (13.55)	1070 (82.31)	101 (84.17)	20 (54.05)

<sup>a</sup> Data are presented as mean ± SD or No. (%).

**Table 2.** Association Between Anti-HBs Antibody Status and Demographic, Type of Dental Activity, Vaccination Details, Risk Factors and Using Protective Measures<sup>a</sup>

	Anti-HBs, IU/mL <sup>b</sup>	Regression Coefficient	95% CI	P Value
<b>Age</b>	-	-0.011	-0.015 – -0.007	< 0.001
<b>Job description</b>				
Student	234.26 ± 17.65	Ref.		
General practitioner	214.25 ± 5.48	0.0004	-0.147 – 0.148	0.996
Specialist	202.77 ± 11.51	0.069	-0.096 – 0.235	0.413
Dental assistant	190.02 ± 19.41	0.027	-0.262 – 0.316	0.853
<b>Time from last vaccination, y</b>				
≤ 5	254.58 ± 10.07	Ref.		
> 5	191.77 ± 7.97	-0.201	-0.309 – -0.094	< 0.001
No vaccination	147.34 ± 31.31	-0.981	-1.216 – -0.746	< 0.001
<b>Number of vaccine doses</b>				
None	147.34 ± 31.31	Ref.		
One dose	145.02 ± 22.38	0.283	-0.033 – 0.599	0.079
2 doses	238.22 ± 21.95	0.889	0.623 – 1.154	< 0.001
≥ 3 doses	220.03 ± 5.16	0.917	0.693 – 1.14	< 0.001
Unknown doses	180.57 ± 27.24	0.649	0.315 – 0.983	< 0.001
<b>Gender</b>				
Male	209.55 ± 5.81	Ref.		
Female	223.81 ± 8.43	0.106	1.874 – 0.197	0.022
<b>Working experience, y</b>	-	-0.011	-0.016 – -0.007	< 0.001
<b>Marital status</b>				
Single	227.86 ± 10.12	Ref.		
Married	210.31 ± 5.52	-0.075	-0.176 – 0.026	0.145
<b>History of needle stick</b>				
negative	215.84 ± 8.77	Ref.		
positive	213.24 ± 5.82	0.034	-0.059 – 0.127	0.468
<b>Number of needle stick</b>	-	0.007	-0.013 – 0.027	0.495
<b>Liver disease</b>				
negative	213.62 ± 4.90	Ref.		
positive	225.07 ± 21.15	-0.112	-0.28 – 0.055	0.188
<b>Sharp Trauma</b>				
negative	216.28 ± 5.00	Ref.		
positive	180.19 ± 18.16	-0.106	-0.324 – 0.112	0.34
<b>Sex contact</b>				
negative	214.52 ± 4.91	Ref.		
positive	218.18 ± 30.35	-0.115	-0.409 – 0.179	0.442
<b>History of transfusion</b>				
negative	216.94 ± 5.05	Ref.		
positive	178.00 ± 15.73	-0.234	-0.423 – -0.044	0.016
<b>History of hepatitis in parents</b>				
negative	214.42 ± 4.89	Ref.		
positive	226.29 ± 39.11	0.07	-0.258 – 0.397	0.676
<b>Gloves</b>				

Regular use of gloves	215.52 ± 4.94	0.15	-0.147 – 0.447	0.322
Irregular or never used	197.15 ± 25.02	Ref.		
<b>Mask</b>				
Regular use of mask	216.11 ± 5.00	0.192	-0.032 – 0.416	0.093
Irregular or never used	163.35 ± 17.50	Ref.		
<b>Glasses</b>				
Regular use of glasses	212.91 ± 5.36	0.075	-0.029 – 0.179	0.158
Irregular or never used	214.35 ± 10.74	Ref.		
<b>Shield</b>				
Regular use of shield	226.78 ± 8.27	0.072	-0.02 – 0.164	0.127
Irregular or never used	207.85 ± 6.27	Ref.		
<b>Smoking</b>				
Smoker	201.04 ± 10.31	-0.032	-0.164 – 0.101	0.64
Non-smoker	221.32 ± 6.26	Ref.		

<sup>a</sup> Abbreviation: CI, confidence interval, Ref., reference group.

<sup>b</sup> Data are presented as mean ± SE.

#### 4.3. Risk Factors and Anti-HBs Status

To determine possible risk factors and anti-HBs levels, no significant associations were found between levels of antibody titers and number of needle stick as well as other risk factors such as trauma, suspicious sexual contact and a history of liver disease (Table 2). However, a significant negative association was found between the history of transfusion and low levels of anti-HBs ( $P = 0.016$ ) (Table 2).

Of 1385 cases with known cigarette smoking history, there were 211 (15.2%) dentists who were smokers. The median of years for smoking was 14 and the median of pack-years of smoking was 3.75 (results not shown). However, there was no significant association between antibody titer and history, duration and pack-years of smoking ( $P = 0.1, 0.38$  and  $0.37$ , respectively).

#### 4.4. Anti-HBs Status and Using Protecting Measures

Among participants, anti-HBs levels were not different according to consistent use of gloves ( $P = 0.322$ ; Table 2). On the other hand, anti-HBs levels for those who regularly used mask, glasses and shield were higher than those who used them irregularly or not at all, although they were not significant statistically ( $P = 0.093, 0.158$  and  $0.127$ , respectively; Table 2).

### 5. Discussion

This study was performed to determine the anti-HBs antibody titers of Iranian dental care workers and to investigate the possible correlation between demographic features as well as details of vaccination schedule with anti-HBs antibody titer in this population. Moreover, risk factors related to immune status of subjects together with protective measurement were considered in this investigation. Although the study sample was not selected

randomly, our sample size was the largest among Iranian researches. In the present investigation, 1538 HBV vaccine recipients were anti-HBs-positive, of whom 1362 (88.5%) subjects developed adequate levels of antibody to HBV infection and 176 (11.5%) were non-immune. A similar study on dentists in Iran showed that 69%-77% of participants were completely immune, while 17% were relatively immune and 6-13% were non-immune (12, 14). The number of those who had received their three recommended doses of vaccine was 1312 (87.9%). Furthermore, statistically significant correlations were found between the median titer of anti-HBs following vaccination and time after the last vaccine injection ( $P < 0.001$ ).

Regarding very low to moderate levels of anti-HBs ( $< 10-100$  IU/mL) in 481 (31.3%) participants, they are at increased risk for HBV infection (15-17). There are two possibilities: (i) decline in the antibody titer with the passage of time despite initial adequate levels of anti-HBs. In the present study, the difference between the times lasting from the third dose of vaccine was statistically significant ( $> 5$  years vs.  $< 5$  years). Similar studies showed that in individuals who respond adequately to vaccination, anti-HBs antibody levels decrease over time and may fall below protective levels. Basically, administering a booster dose of HBs Ag vaccine results in a vigorous anamnestic response, demonstrating that immune memory against HBV infection lasts longer than anti-HBs antibodies (18, 19). On the other hand, (ii) the other possibility is nonresponsiveness to the vaccine. Several factors were reported to influence the response to HBV vaccine in nonresponders such as genetic background, older age, obesity (20, 21) and smoking (9, 22). For those who do not respond to the primary vaccination series, an additional regimen of ordinary vaccines (either administration of a higher dose or a second course of three doses of HBV recombinant vaccine) usually gives rise to about

15% to 25% and 30% to 50% of responsiveness to one and three additional doses, respectively (23, 24). Likewise, still more than 50% of non-responders are not able to acquire protective levels of anti-HBs despite administration of at least two additional booster recombinant vaccines (25, 26). Alternate schedule includes intradermal vaccine administration (27) or third generation vaccines (that contained Pre-S1/Pre-S2 proteins through recombinant technology in mammalian cell lines) with higher immunogenicity and more seroconversion rate compared to the second generation vaccines (28, 29). Otherwise, for those persistent nonresponders, it is recommended to avoid EPP (exposure-prone procedures) and they should be noticed that they may be susceptible to HBV and that they should receive hepatitis B immune globulin (HBIG) following HBV exposure (30). We did not check anti-HBc status of participants, hence anti-HBs level in the study does not necessarily differentiate rising of antibody following vaccination or past infection with HBV.

In the present study, the rate of incomplete vaccinations was 13%, hence more efforts should be made to persuade all dentists to receive the three doses of vaccine. Unfortunately, as worldwide, no mandatory HBV vaccination program exists for dentists in Iran, which may cause a low rate of compliance in voluntary vaccination program(s) now available for HCWs at health offices. It is of some concern that dentists are willing to accept significant degree of personal risk, despite recorded danger from hepatitis B, either by failing to ensure immunization against hepatitis B or by failing to check the presence of hepatitis B antibodies following immunization.

In conclusion, HBV vaccine coverage and infection control measures were satisfactory among Iranian dental personnel in this study. Since dental care workers have a high risk of exposure to hepatitis virus, a compulsory vaccination for hepatitis B virus is desirable for all dental care workers.

### Authors' Contributions

Study concept and design: Ahmad Akhondi, Momeni, Jazayeri and Alavian. Sampling and executive procedure: Momeni, Ahmad Akhondi, Norouzi, Mahboobi, Moosavi and Jazayeri. Drafting of the manuscript: Momeni, Ahmad Akhondi and Jazayeri. Statistical analysis: Shamshiri.

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