

ASSESSING SERO-PROTECTIVE LEVELS OF ANTI-HBS TITER IN PRE-VACCINATED DENTAL STUDENTS AND DENTAL PROFESSIONALS AT BAHRIA UNIVERSITY MEDICAL & DENTAL COLLEGE (BUMDC), KARACHI

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ABSTRACT

Dentists are always at a high risk of exposure to Hepatitis B virus (HBV). Therefore assessing their immunity is of utmost concern. Sero-conversion rates reported after Hepatitis B virus (HBV) vaccination globally range from 85–90%. Triple-course vaccine might sometimes fail to raise antibody titers.

Our study aims to determine the percentage of dental students and professionals who have received recombinant HBV vaccine, the percentage of those vaccinated individuals who possess Anti-HBs titer within the required protective range and the attitude of vaccinated dental students and professionals towards confirming their post-vaccination antibody titer.

The status of vaccination and attitude towards checking post-vaccination antibody titer were assessed through self-administered questionnaires. Blood tests were drawn for checking Anti-HBs titer of 101 vaccinated subjects including dental students, practicing dentists/ faculty and paramedics. Sero-protective range $\geq 10\text{mIU/ml}$ was termed reactive. Association of immune response with gender and year of study/ profession were assessed.

Out of 158 participants, 112 (70.9%) had completed vaccination course. Post-vaccination antibody titer was checked by 29 (25.8%) out of 112 participants. 72 (71.3%) out of 101 (who agreed to check their anti-HBs titer) vaccinated participants had reactive anti-HBs titer i.e $>10\text{mIU/ml}$, whereas 29 (28.7%) had non-reactive anti-HBs titer after receiving routine HBV vaccination. 18(58.1%) out of 31 males and 54 (77.1%) out of 70 females showed reactive titer. p value was found significant ($p = 0.032$)

Considerable rate of failure in maintaining acceptable titer levels following routine vaccination against HBV was found. Therefore, determining Anti-HBs titer after vaccination is recommended. The antibody titer of dental students and professionals should be checked after vaccination. It is of prime importance for all dental schools, medical and dental staff to conduct talks and create awareness about hepatitis B infection.

Key Words: HBV, Triple- course vaccination, sero- protection, Anti-HBs Titer, reactive, non-reactive, 10mIU/ml .

INTRODUCTION

Hepatitis B is a viral infection that infects the liver and can cause both acute and chronic disease.¹ Approximately, 780, 000 persons expire annually from

hepatitis B infection, 650,000 from liver cirrhosis and hepato-carcinoma due to chronic hepatitis B infection and 130,000 from acute hepatitis B infection.¹ There is a higher risk of liver-related death associated with HBV than hepatitis C virus.² Healthcare workers including dentists are always at a high risk of exposure to contaminated blood and body fluids like saliva. In dental setting, the most common mode of transmission from infected patient to dentist is from needle stick injuries

Vaccination against hepatitis B is known since 1982.³ Occasionally, Hepatitis B vaccine fails to produce adequate seroprotection.^{4,5} A number of factors might be responsible to influence the immune-competency and vaccine efficacy⁶ like stress⁷, age⁸, excessive body mass index⁸, chronic diseases and smoking.⁹ Rise in antibody

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titer usually occurs after primary vaccination but in most cases titer fails to rise either due to inappropriate vaccination or failure in immune response.¹⁰ A booster dose should be recommended for immune-compromised patients, based on serological monitoring.¹¹ Age and gender have been shown to have negative⁹ as well as positive¹² effects on Anti HBs levels. The duration passed since receiving the last dose of vaccine is anticipated perhaps associated with decreased levels of Anti –HBs titers.¹³

Recommended Anti-HBs titer to Hepatitis B surface antigen is ≥ 10 mIU/ml which is considered as protective immunity.¹⁴ No infection is being observed in patients with titer ≥ 100 mIU/ml.¹⁵ Mostly triple-course vaccination therapy of 10 μ g or 20 μ g recombinant HBs Ag evokes 90 % to 98% sero- protection among healthy individuals.¹⁵

In Pakistan, few researches that have been conducted regarding HBV vaccination status and levels of antibody titre in healthcare workers had revealed a lack of 100% vaccination and positive immune response.^{16,17}

The aims of the study were to assess the percentage of dental students and professionals who are vaccinated against HBV; to find the percentage of vaccinated subjects who checked their post-vaccination antibody titre, and to find the percentage of vaccinated subjects who have the anti-HBs titre within the required protective range.

METHODOLOGY

A cross-sectional study was conducted at Bahria University Medical and Dental College during 2016-2017. The study included dental students of 1st, 2nd, 3rd and final year, practicing dentists/ dental teaching faculty and paramedics. All subjects were Pakistani, comprising of both genders, varying ages (18-45 years), varied socio-economic status and assigned posts. The research proposal was approved by Ethical Research Committee BUMDC on 16th February, 2016. Funds were approved by the Office of Research, Innovation and Commercialization (ORIC) for examining anti-HBs titers of the vaccinated individuals at Agha Khan Hospital Laboratory. Informed consent was taken from the participants.

Self-administered questionnaires were distributed among 240 subjects comprising of questions on demographic data, professional status (student/dental teaching faculty/practicing dentists/paramedics), vaccination status including triple-course vaccination regime and checking post vaccination immune response. All the subjects participated and returned the filled questionnaires. Participants who had received complete primary vaccination scheduled at 0,1 and 6 months were considered vaccinated, whereas those who didn't receive vaccination or had not completed

vaccination course(one or two doses) were considered non-vaccinated.

Blood samples of 101 participants were drawn after taking their consent and sent to the Agha Khan Hospital Laboratory for the assessment and evaluation of Anti-HBs Titer. The state of immunity having Anti-HBs titer greater than 10mIU/ml was considered reactive immune response, whereas less than 10mIU/ml was considered non-reactive. The inclusion criteria for serological investigation was completion of appropriate triple-course vaccination and duration of one month after last vaccine dose.

STATISTICAL ANALYSIS

Data and the results of Anti HBs titer were entered in FOX-Pro software program-statistical package for social sciences SPSS version 16 for analysis. The rates of good immune responses allocated as reactive were recorded and the probable association between sero-protection and the gender was statistically assessed by Chi-square test. Level of significance was set at 5%.

RESULTS

A total of 240 questionnaires were distributed among dental students, faculty/practicing dentists and paramedics out of which 158 responses were received (response rate: 65.8%). Out of 158 participants, 112 had completed vaccination while remaining 46 participants either didn't receive any dose, had incomplete vaccina-

TABLE 1: DEMOGRAPHIC CHARACTERISTICS OF STUDY PARTICIPANTS

Variable (Gender)	Number	(%)
Male	39	25
Female	119	75
Year of Study		
1st Year	33	20.9
2nd Year	25	15.8
3rd Year	25	15.8
4th Year	17	10.8
Faculty and Paramedic Staff	58	36.7

TABLE 2: VACCINATION STATUS AGAINST HEPATITIS B

Responses	Are you vaccinated against Hepatitis B?	
	Number	(%)
Yes (completed course)	112	70.90
Did not complete course	12	7.60
No	14	8.90
I don't remember	20	12.70

TABLE 3: ATTITUDE TOWARDS CHECKING POST-VACCINATION ANTIBODY TITER

Res- ponses	Did you check Anti-HBs titer levels after full course of vaccination?	
	Number (112)	(%)
Yes	29	25.8
No	83	74.1

tion or couldn't recall their vaccination status. (Table 2) Among vaccinated respondents, 29 (25.8%) agreed having their anti-HBs titer checked after receiving vaccination.(Table 3).

Seventy two out of 101 vaccinated subjects who gave blood samples for serological testing showed sero-protection against HBV while remaining 29 showed lack of sero-protection against HBV. Eighteen out of 31 males and 54 out of 70 females showed reactive titer >10mIU/ml with a significant difference between genders (p-value=0.032). Eighteen students of 1st year BDS showed positive immune response while 8 showed no immune response. In 2nd year BDS, 7 showed positive immune response while 3 showed no immune response. In 3rd year BDS, 13 students gave positive immune response and 6 gave negative immune response. Out of 23 final year students, 22 showed positive immune response while 1 showed negative immune response. Out of 23 dentists and paramedics, 12 had positive immune response and 11 had negative immune response .The p value was found significant (P=0.032).

DISCUSSION

The percentage of vaccinated subjects in this study was 70.9%. This is lower than Canadian dentists (90.6%)¹⁸, English dentists (97%)¹⁹, German (74%)²⁰, Iranian dentists (87.9%)²¹ and higher than those of Japanese (64.3%)²², Italian dentists (56.2%)²³ and Health care workers in a tertiary hospital in Pakistan (53%).¹⁶ The reason behind the fact is that in this study the participants are not only the dentists but also the students and paramedic staff.

In this study, the attitude of dental students and professionals towards checking their post-vaccination antibody titer was poor as only 29 out of 112 (25.89%) vaccinated subjects checked for sero-protection after completing vaccination. However, studies conducted at India²⁴ and Bulgaria²⁵, only 1.41% (out of total 494 subjects) and 13.9% (out of 96 subjects) respectively, showed the attitudes of dental professionals to check their anti HB titer after vaccination. Thereby, after comparative analysis of different studies, it is stated that although the attitude percentage to check the anti HB titer in this study is low but it is far better than the attitude of the dental professionals in the former studies.^{24,25} Hence, health Care Professionals should do

post-vaccination serological testing 1-2 months after the final dose of vaccine is administered.²⁶

Findings of this study indicate sufficient sero-positivity among dental students and professionals with reactive HBs Ab titer in 71.2% subjects and non-reactive HBs Ab titer in 28.7%. The results of the previous studies reported 44%²⁸ failure to produce necessary immune response against HBs antigen, Talebi reported 63.7% failure¹³, Chan et al with 57.1% failure rate²⁹, Eshagh et al⁴ reported 67.8% (anti-HBs in 46% students < 100 mIU/ml and in 21.8% <10mIU/ml). This might be attributed to the fact that the former study⁴ categorized anti-HBs levels ranging between 10mIU/ml-100mIU/ml as positive but poor immune response. However, Estevez et al.⁸ Van Damme et al³⁰, Velu et al³¹ and Ramezani³² reported much lower rates of failure in producing immune response. This study concurs with study of Koff et al who reported higher level of HBs Ab in 67%.³³

According to a study, quality standards for hepatitis B vaccines require at least 95% sero-protection in vaccinated healthy adults, that is, >10mIU/ml, if measured 1-3 months after the administration of last dose of regime.³⁴

There was significant difference in reactivity of antibody titer between different groups (students and professionals) Despite of being a high-risk group, the dental professionals showed contrasting results. 52.1% had reactive titer, while 47.8% showed poor immune response, almost equal ratio in being sero and non-sero protective respectively. This might be attributed to the time that elapsed after the last dose (more than 5-10years) or any chronic infection that led to a decrease in antibody titer.^{32,35} Perhaps, some hadn't completed their vaccination regime or if they had, it might be the brand of vaccine that couldn't produce stable levels of Anti-HBs titers or could only produce antibodies within a period of 2 years, which is in harmony with research done by Eshagh.⁴

The present study showed sufficient anti-HBs titers among dental students who might have received appropriate vaccination regime just before joining the institute, that depicts short duration had passed since they had been immunized. The university encourages students to receive appropriate triple-course vaccine before joining the institute, which lowers the possibility of forgetting doses. On the other hand, the university does not forbid previously vaccinated students to receive it again, there is a probability for the students to have boosters. Hence, suffice immune response was certainly expected in this healthy young population.

The finding of this study concerning the positive association between gender and sero-protection was consistent with other studies.^{17,36,37} Though it should be also noted that females were 69% of the study which

might have masked the effects of the male gender on the findings. Male gender may be associated with non-response to hepatitis B vaccine. This is linked to sex hormones, androgen and estrogen and has been shown through researches done on animal models. X chromosome has more immunological genes compared to Y chromosome. Estrogen activates monocytes to secrete IL-10, which stimulates B cells to release IgG and IgM³⁸, while testosterone hampers the formation of IgG and IgM from B-cells, as well as inhibits monocytes.³⁹

This study was limited by some factors. The vaccination status was not verified by vaccination record cards and researchers relied largely on memory of participants. There was a fair chance that they didn't remember the exact vaccination times, and that whether they were completely vaccinated or not. Most factors affecting immune response to vaccine were not included such as age, stress, chronic diseases, smoking, BMI and time elapsed after last vaccine dose. The sample size for serological tests was also small as it was limited by funds.

CONCLUSION & RECOMMENDATIONS

Considerable rate of failure in maintaining acceptable titer levels following routine vaccination against HBV was found. Therefore, determining Anti-HBs titer after vaccination is recommended. The antibody titer of dental students and professionals should be checked after vaccination. It is of prime importance for all dental schools, medical and dental staff to conduct talks and create awareness about hepatitis B infection. The varying results of study highlight the need for strict monitoring of vaccination of dental students and professionals, especially those who are practicing dentistry. Sero-protection of students should be checked before they start working at dental OPD. The concerned regulatory bodies should also devise a strategy to keep a check on dental professionals nation-wide. Furthermore, a comprehensive study may be conducted in future encompassing the larger sample size and gradation of immune response.

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