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Factors Influencing Immunologic Response to Hepatitis B Vaccine in Medical Students – A Cross-Sectional Study

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Abstract : Hepatitis B (Hep B) vaccine is essential for humans as a preventive measure, particularly for medical students who are at high risk due to their clinical training. After HBV immunization, various factors may influence the levels of hepatitis surface antibodies (HBs Ab) in students, which can be considered inadequate for sufficient protection (<10 m IU/ml) against Hepatitis. This study aimed to quantify Hepatitis B antibody titres to surface antigen in medical students and identify any factors involved in protection. A total of 115 medical students, both male and female, were included in the study. Descriptive data, including age, BMI, vaccine details, and diseases, were collected from the participants. Blood samples were collected after informed consent was obtained from the students. All students received two doses of the vaccine, with the assay period being five months after the second dose. The antibody titer was measured by Enzyme-Linked Immunosorbent Assay (ELISA). The data were analyzed using descriptive and Chi-square analysis through SPSS 15 software. The study included 115 medical students aged 18 to 24 years, with a mean age of 19.83 years. The post-vaccination antibody titres were 89.6% in >100 m IU/ml, 9.6% in 10-100 m IU/ml, and 0.9% in <10 m IU/ml, with one participant noted for having falling protective titres. This study evidenced that measuring the titer for anti-HBs response in vaccinated students can determine their level of protection. Most of the students were protected after vaccination, although one participant displayed low levels of anti-HBs. The collected information from the participant's factors was not associated with the falling titer, which may be related to individual immune function.

Keywords: Hepatitis, HBs Ab, Vaccine, HBs Ag, Titer

Introduction

Globally, hepatitis B virus (HBV) constitutes a significant portion of viral hepatitis cases. HBV is a prevalent infectious disease among healthcare workers (HCWs), leading to considerable morbidity and

mortality. According to the World Health Organization (WHO), approximately 350 million people are infected with HBV worldwide . In India, chronic HBV infection affects about 50 million individuals . Healthcare workers and medical students, who frequently come into contact with patients, are at a high risk of HBV infection due to occupational exposure . The Hepatitis B vaccine is part of the routine childhood immunization program in most Indian states. Vaccination schemes and health education must be robustly communicated to high-risk populations, including healthcare workers (HCWs). Hepatitis B vaccination in HCWs is a crucial element of the WHO's Elimination Strategy for Hepatitis B from 2016 to 2021 . Available since 1982, HBV vaccines are effective in preventing infection if administered before or immediately after exposure . Therefore, all HCWs should receive the HBV vaccine as a routine occupational safety measure . Plotkin stated that vaccine-induced seroprotection is a useful surrogate for its efficacy, suggesting that measuring anti-HBs antibody titers is essential to determine the protection status of healthcare students. According to Schillie et al., the Centers for Disease Control and Prevention (CDC) guidelines recommend measuring anti-HBs titer 1–2 months after the last vaccine dose. Given the high risk of contracting the disease among HCWs and medical professional students, admissions to medical colleges in Tamil Nadu mandate hepatitis B vaccination. It is crucial to confirm the HBs Ab titer after vaccination to ensure successful immunization. This study aims to investigate the HBs Ab titer levels in first-year medical students with available vaccination and any factors influencing the response to the HBV vaccine. The aim is to quantify HBs Ab titer by Enzyme-Linked Immunosorbent Assay (ELISA) in medical students. Additionally, the study seeks to assess HBs Ab titer levels concerning associated factors such as gender, BMI, post-immunization duration, and other health conditions (e.g., thyroid dysfunction, diabetes, tonsillitis, epilepsy, surgeries, and dental problems).

METHODS AND MATERIALS

This cross-sectional study was conducted in the department of microbiology at Swamy Vivekanandha Medical College Hospital and Research Institute (SVMCH & RI) in South India. The proposal was approved from our Institutional Ethical Committee (IEC-SVMCH & RI). The population involved in this study included 1st year medical students above 18 years old who gave written informed consent and students who were not interested to participate, were excluded from the study. The medical students who partially and fully completed hepatitis B vaccine doses will be enrolled for this study in SVMCH & RI. A total of 115 medical students were participated in this study and the descriptive data's were collected from the participants. Based on the information given by the participants data's were analysed. The data's included age, sex, height, weight, BMI, vaccination details and any other diseases. The exclusion criteria were unvaccinated and those with a past history of viral infection (Hep B), or those on prolonged steroid therapy. After getting informed consent and descriptive data's, blood sample were collected from the participant aseptically by venipuncture. The serum sample was separated and stored in eppendorf tubes in deep freezer (-80°C) until HBs Ab titer assay was done through quantitative

ELISA (Dia. Bro, Italy) according to the kit insert methods and quantified through ELISA reader (Rayto). The correlates of protection (CoP) is defined as the presence of HBs Ab titer ≥10 m IU/ml. The HBs Ab titer values<10 m IU/ ml was considered asinadequate.The data were analysed using Microsoft Excel and SPSS 15. Descriptive data'swere expressed using frequencies and percentages. Chi-square test was used to find the any association between antibody titer, gender and BMI.

Results

The study participants from 1st MBBS students of SVMCH & RI in total of 115 participant with 66.1% female and 33.9% male population. All the participants were received two vaccinations and after that five months interval at the time of sample collection.The participantsdescriptivecharacteristic such as age, BMI and anti-HBs Ag (HBs Ab) was shown in Table.1.

Descriptive Factor	N	Minimum	Maximum	Mean	Std. Deviation
Age	115	18	24	19.83	1.03
BMI (Kg/m^2)	115	15.61	33.78	22.27	4.32
HBsAb	115	9.80	345.75	268.28	90.18

Table.1. Descriptive baseline characteristics

The mean age of the participant's was 19.83 ±1.034, BMI 22.27±4.32 and HBs Ab titer 268.28 ±90.18 m IU/ml. There was one participant displayed levels of HBs Ab titer below <10 IU/L, 9.6% (11) in >10-100mIU/ml, and 89.6% (103) in > 100 m IU/ml (Figure1).

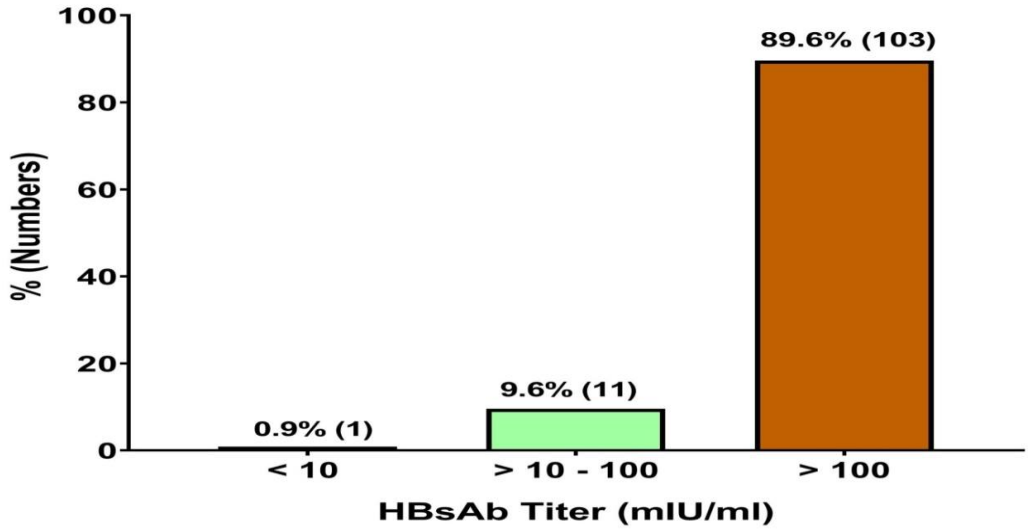

Figure 1. HBsAb titer distribution in the students

Further the HBs Ab titer was correlated with gender and found that one male (0.9%) participants with < 10 m IU/ml, 4 (3.4%) in >10-100 m IU/ml, and 34 (29.6%) in > 100 m IU/ml. In female participants was about 7 (6.1%) in >10-100 m IU/ml, and 69 (60%) in > 100 m IU/ml. There was no statistical difference in gender with HBs Ab titer (Table 2).

Gender	**< 10 (mIU/ml)**		**> 10 – 100 (mIU/ml)**		**> 100 (mIU/ml)**		P value
	Numbers	**(%)**	Numbers	**(%)**	Numbers	**(%)**	
Male	1	0.9	4	3.4	34	29.6	0.365
Female	0	0	7	6.1	69	60	

Table.2. Students post vaccination HBsAb titer associated with Gender (N=115). The data's were analyzed by Pearson Chi-Square (X^2) test there was no significant between male and female HBsAb titer.

BMI (Kg/m^2)	**< 10 (mIU/ml)**		**> 10 – 100 (mIU/ml)**		**> 100 (mIU/ml)**	
	Numbers	%	Numbers	%	Numbers	%
< 18.5 Underweight	0	0	2	1.7	22	19.1
18.5–24.9 Normal	1	0.9	6	5.2	58	50.4
> 25 Overweight and Obese	0	0	3	2.6	23	20

Table.3. Students post vaccination HBsAb titer associated with BMI (N=115)

BMI association with HBs Ab titer for underweight was shown that 2 (1.7%) in >10-100 m IU/ml, and 22 (19.1%) in > 100 m IU/ml. In normal BMI, one participant (0.9%) were found < 10 IU/L, 6 (5.2%) in >10-100 m IU/ml, and 58 (50.4%) in > 100 m IU/ml. Overweight and obese BMI, 3 (2.6%) in >10-100 m IU/ml, and 23 (20%) in > 100 m IU/ml (Table 3).

The factors association of HBs Ab titer was shown in table 4. There was no statistical difference in BMI and factors associated for HBs Ab (Thyroid dysfunction, diabetes, tonsillitis, epilepsy, any surgery and dental problem).

Diseases	**< 10 (mIU/ml)**		**> 10 – 100 (mIU/ml)**		**> 100 (mIU/ml)**	
	Numbers	%	Numbers	%	Numbers	%
No Diseases (n=110)	1	0.9	9	7.8	93	80.9
Thyroid Dysfunction (n=2)	0	0	0	0	2	1.7
Diabetes (n=1)	0	0	0	0	1	0.9
Tonsillitis (n=1)	0	0	0	0	1	0.9
Epilepsy (n=1)	0	0	0	0	1	0.9
Surgery (n=3)	0	0	1	0.9	2	1.7
Dental Problem (n=4)	0	0	1	0.9	3	2.6

Table 4: Association of HBsAb titer with risk factors (n=115).

Discussion

Infection with HBV is measured as a serious health issues in developing nations that can lead to hepatocellular carcinoma, chronic liver cirrhosis, and liver failure(11).Clinical stage medical professionals are considered as a high risk for HBV infection(12,13). Since they can come across occupational exposure such as blood and body fluids in their training programs(14). Less vaccination coverage for HBV among medical professions, a high rate of accidental exposure and the relative inexperience can increase the risk of transmission of viruses(15). HBV immunization coverage in Somalia among medical students was tremendously low (2.8%) that indicating the urgency for increased

vaccination in this population(16). In the present study, we evaluated HBs Ab titer in 115 medical students after two completed vaccine schedule for HBV.

There are a proportion of vaccines who are nonresponders, and unable to generate sufficient immunological response and need to be identified for additional doses. In our study, 1 (0.9%) of subjects were non-responders. Hep B vaccine in India was introduced in the national immunization programme (NIP) in 2002 and extent up by 2011(17). The HBs Ab titer is equal or > than 10 m IU/L after completing the vaccination has protective in HBV infection(18). In the western Amazon identified as a high-endemic HBV area, here children's completed 32% of HBV vaccine had anti-HBs < 10 IU/L. An extra dose for vaccine schedule for later years of childhood may be considered to ensure HBV protection in endemic area (19).

Studies showed that vaccination is efficient in protecting against HBV about 90%–95% of adults (20). Globally, immune response after primary vaccination against Hep B has been found to be 55%–100%(21). Hepatitis B booster doses are administered after first vaccination series and then to be offer rapid protective immunity against HBV infection. However, taking booster dose without confirming the HBs Ab titer was not advisable, the responders to boosters differ by age and population for the primary hepatitis B vaccine(10) and suggested that those with anti-HBs Ab titer < 10 m IU/ml after first vaccination, further a secondary and tertiary doses has to be given. Those with titer >10 m IU/ml following revaccination are protected for life(5).We could not associate gender, other diseases such as thyroid dysfunction, diabetes, tonsillitis, epilepsy, any surgery and dental problem with titer < 10 m IU/ml in our study. For immunogenicity the inverse relation with age goes there was a decline in immunogenicity after vaccination. The protective level of anti-HBs antibodies was observed even after 22 years of first doses(22). For nonresponders, the recommendation is revaccination with full-course of vaccine(5). Once the vaccination schedule was completed and HBs Ab to be checked and documented.This could be made a mandatory need for all HCWs. Even after completion of vaccination there was a no follow up, therefore, instead of asking vaccination certificate against HBV, the mandatory HBs Ab titer documentation for students and HCWs to prevent from HBV infections.

Limitation and future recommendations

The limitation of the study was the participants received only two vaccine doses. Further studies are encouraged to establish after completion of the third and booster doses and need to test their HBs Ab titer for the confirmation of immune protection against HBV. The rate of HBs Ab titer decline is unforeseeable, but need to be checked frequently. HCWs have to receive a booster dose and the HBs Ab titer falls less than10 m IU/ml.

Conclusion

In the present study, one participant was found to have inadequate HBs Ab titer. Therefore, all persons vaccinated against Hepatitis B should have an assessment of their immunity, soon after vaccination in order to confirm their immunity and allow correct planning of further doses. Preventing Hepatitis B infection averts the development of complications including chronic disease and liver

cancer. This study also recommends the quantification of HBs Ab in the HCWs and need for initiating awareness program for immunisation against HBV in medical professionals.

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