

Antibody to Hepatitis B Surface Antigen in Vaccinated Healthcare Workers in a Tertiary Care Centre – A Descriptive Study from South Kerala

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ABSTRACT

BACKGROUND

Hepatitis B virus (HBV) has long been recognized as a work-related hazard for health-care personnel (HCP). HCPs are all paid and unpaid persons giving health care or working or training in health-care settings, who have reasonably expected risks for exposure to infectious materials. Post-vaccination serological testing is suggested 4 to 8 weeks after completion of the primary course in all health care workers. If the anti - HBs levels are less than 10 mIU / ml 4 - 8 weeks after the third dose of vaccine, the person's serum has to be tested for markers of HBV. The objective of the study was to evaluate the immune response after hepatitis B vaccination in health care workers.

METHODS

This study was a cross-sectional study that was conducted for a period of one year (January 2016 – December 2016). In this study, blood samples of 211 HCP were collected and sera were tested for quantitative anti - HBs level using anti - HBs EIA kit (Diapros, Italy).

RESULTS

75.83 % of HCP were completely vaccinated and 24.17 % did not complete the three-dose regimen. 91.87 % of completely vaccinated HCP had an anti- HBs titre of more than 10mIU/ml while 80.39 % of incompletely vaccinated HCP had protective antibody levels. 71.42 % of males and 90.35 % of females had protective antibody titre. The housekeeping staff were the most protected (100 %) while doctors were the least protected (54.54 %). Among the different vaccine, compliant subgroups 85.96 % of HCP who were completely vaccinated and had not taken booster dose had protective antibody titre even after five years where as 90.47 % of HCP who were completely vaccinated and had taken a booster dose and had protective antibody titre even after 5 years. It was also noted that 95.23 % of HCP who were vaccinated before the age of 20 had a protective antibody titre while only 70.58 % of those who got vaccinated after the age of forty had a protective antibody titre.

CONCLUSIONS

The records, if possible retrievable electronic records, should be maintained in health care centers as a reference in case of occupational exposure or for other purposes.

KEYWORDS

Hepatitis B, Anti HBs, Health Care Personnel

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BACKGROUND

Hepatitis B virus (HBV) has long been recognized as an occupational risk for health-care personnel (HCP).¹ The virus remains infectious for prolonged periods on environmental surfaces and is transmissible in the absence of visible blood.¹ HCPs are all paid and unpaid persons giving health care, or working or training in health-care settings, who have fairly expected risks for exposure to infectious materials, as well as blood or body fluids, contaminated medical supplies, and equipment, or contaminated environmental surfaces.

Children and adults with anti-HBs level ≥ 10 mIU / ml one to two months after receiving 3 doses of hepatitis B vaccine are termed as seroprotected or vaccine responders.² The immunological memory lasts more than the antibody levels and provides long-term immunity following hepatitis B vaccination. Testing and booster doses are not required in such vaccine non-responders.^{3,4} Testing is recommended 4 to 8 weeks after completion of the primary course in all healthcare workers if adequate levels of anti-HBs (≥ 10 mIU / ml) are not achieved in serological tests 4 to 8 weeks. After the 3rd dose, the possibility of HBV infection should be investigated by serological marker tests.

It is advisable to give a complete 3 dose series of HBV vaccine again followed by anti HBs testing one to two months after the third dose for that HCP with anti - HBS < 10 mIU / ml after completing the primary series rather than testing after each additional dose. To document the HCP's vaccine response status for future exposures, anti-HBs testing should be performed 1 – 2 months after the last dose of vaccine.

The objective of the study was to evaluate the immune response after hepatitis B vaccination in health care workers.

METHODS

This study was a cross-sectional study that was conducted for a period of one year (January 2016 – December 2016) to evaluate the immune response after hepatitis B vaccination in health care workers done in a tertiary care center in South Kerala. The study was started after getting clearance from the Institutional ethics committee (IEC No 05 / 2 / 2015 / MCT dated 27 / 11 / 2015).

The study population included doctors, nurses, lab technicians and housekeeping staff who have been vaccinated against hepatitis B with the protocol of three doses (0 – 1 - 6 schedule) and defaulted after one or two doses.

The exclusion criteria included the following:

1. Chronic liver disease.
2. Prolonged steroid therapy or immunosuppression.
3. Known nonresponse to an adequate series of HBV vaccination.
4. Renal failure requiring dialysis.
5. Hematopoietic cell or solid organ transplant.
6. Human immunodeficiency virus (HIV) infection.

After getting the informed consent, the subjects were requested to fill up a questionnaire giving their personal, health, and HBV vaccine details. Blood samples were collected from 211 HCW and serum was stored at below-20° C until an anti-HBs test was undertaken. Commercially available anti-HBs EIA kit (DIA.PRO, ITALY) was used for quantitative assay of anti - HBs (IgG). The assay was performed as per the manufacturer's instructions. Anti - HBs positive subjects were defined as those having anti-HBs levels equal to or more than 10 mIU / ml, while anti - HBs negative subjects were those having anti-HBs levels of less than 10 mIU / ml.

HBV vaccine compliant subjects were defined as those who were administered with minimum of three doses of HBV vaccine, at a schedule of 0, 1, and 6 months intramuscularly with a dose of 20 micrograms of HBsAg (hepatitis B surface Antigen) i.e. completed minimum primary vaccination. They were further subdivided into groups as (i) Primary vaccinated < 5 years: Subjects who received primary vaccination and duration from last vaccine dose were five years or less on the date of enrolment for the study, (ii) Non-booster group or Primary vaccination > 5 years :- Primary vaccinated subjects where time gap from last vaccine dose and date of enrolment of the study was more than five years and they have not taken booster dose of vaccine (iii) Booster group-who received booster dose after five years or more of primary vaccination.

Statistical Analysis

Data was entered in Microsoft Excel, data cleaning done and completeness checked. The data was analyzed by SPSS version 23. The Anti HBS titre was expressed in mIU / ml using mean and Standard deviation. The qualitative variables were expressed in percentage.

RESULTS

Blood samples obtained from 211 health care personnel of a tertiary care center in South Kerala were tested for Anti HBs antibody. Among them, 75.83 % were completely vaccinated and 24.17 % did not complete the three-dose regimen. 91.87 % of completely vaccinated HCP had an anti-HBs titre of more than 10mIU/ml while 80.39 % of incompletely vaccinated HCP had protective antibody levels (Table 1). 71.42 % of males and 90.35 % of females had protective antibody titre (Table 2). The housekeeping staff was the most protected (100 %) while doctors were the least protected (54.54 %) (Table 3). Among the different vaccine compliant subgroups, 85.96 % of HCP who were completely vaccinated and had not taken booster dose had protective antibody titre even after five years whereas 90.47 % of HCP who were completely vaccinated and had taken a booster dose had protective antibody titre after 5 years (Table 4). It was also noted that 95.23 % of HCP who got vaccinated before the age of 20 had a protective antibody titre while only 70.58 % of those who got vaccinated after the age of forty had a protective antibody titre (Table 5).

Vaccination Status	Total		HCP with Positive anti HBs Levels (>10 mIU/ml)		HCP with Negative anti HBs Levels (<10 mIU/ml)	
	Number	%	Number	%	Number	%
Complete	160	75.83	147	91.87	13	8.12
Incomplete	51	24.17	41	80.39	10	19.60
Total	211		188	89.09	23	10.90

Table 1. Distribution of Anti HBs Levels in HCP

Gender	Total	Anti HBs Levels>10 mIU/ml		Anti HBs Levels<10 mIU/ml	
		Number	Percentage	Number	Percentage
Male	14	10	71.42	4	28.57
Female	197	178	90.35	19	9.64
Total	211	188	89.09	23	10.90

Table 2. Anti HBs Status According to Gender

Category of HCP	Anti HBs Levels>10mIU/ml		Anti HBs Levels<10 mIU/ml		Total
	Number	Percentage	Number	Percentage	
Doctors	6	54.54	5	45.45	11
Lab technician	13	81.25	3	18.75	16
Nurses	159	91.9	14	8.09	173
House keeping	11	100	0	0	11
Total	189	89.57	22	10.42	211

Table 3. Anti HBs Status in Different Categories of HCP

Vaccine Compliant Subgroups	Anti HBs Levels>10 mIU/ml		Anti HBs Levels<10 mIU/ml		Total
	Number	%	Number	%	
Fully vaccinated (non-booster) <5 years	60	98.36	1	1.63	61
Fully vaccinated (non-booster) >5 years	49	85.96	8	14.03	57
Fully vaccinated (booster taken) >5 years	38	90.47	4	9.52	42
Total	147	91.87	13	8.12	160

Table 4. Anti HBs Status in Various Vaccine Compliant Subgroups

Age of Vaccination	Number	Anti HBs Levels >10 mIU/ml		Anti HBs Levels<10 mIU/ml	
		Number	Percentage	Number	Percentage
<20 years	105	100	95.23	5	4.76
21-40 years	89	76	85.39	13	14.60
>41 years	17	12	70.58	5	29.41
Total	211	188		23	

Table 5. Anti HBs Levels Depending on the Age of Primary Vaccination

DISCUSSION

In the present study, 75.83 % of HCP were fully vaccinated, and 24.17 % were partially vaccinated. A similar study done at New Delhi showed that only 55.4 % of HCP were fully vaccinated against HBV.⁵ A lower incidence of fully vaccinated HCP, 42.2 %, was also observed by Kumar et al.⁶

The percentage of male nonresponders (28.57 %) in the present study was more than females (9.64 %). Wood et al. reported a response rate of 18 % and 9 % respectively in male and female.⁷ According to various studies females are known to mount a better response. Hepatitis B vaccines are highly immunogenic, but have decreased immunogenicity associated with age, obesity, smoking, males, and chronic disease in older adults.

The category of HCPs in whom the anti-HBs titres were > 10 m IU / ml and provided protection was the housekeeping staff and nurses, followed by lab technicians and doctors. In a study done by Annapurna et al. protective titres of anti-HBs were 83.1 % in doctors, 85.5 % in nursing

staff, 88.8 % in technical staff, and 84.6 % in attendant staff.⁸ A study done by Pavani K et al. showed that the category of HCP in whom the anti-HBs titres were > 10 m IU / ml and provided protection was the nursing staff and the housekeeping workers, followed by doctors who are in concordance with the present study.⁹ In contrast to the present study, a study by Sarwat Fathima et al. showed that doctors were the most vaccinated and protected (86.3 %, 42 %) whereas the least vaccinated and protected were the paramedics (43 %, 35 %).¹⁰

The anti-HBs titre was significantly higher in those who had been vaccinated within the last 5 years. However, it was lower in patients vaccinated 5 years ago. A study in Iran showed that 89 % of subjects with complete vaccination less than five years achieved protective anti-HBs titres which are in concordance with the present study.¹¹ In another study protective titres of anti-HBsAb (≥ 10 m IU / mL) were seen in 100 % of the cases who were vaccinated less than 5 years ago.⁹ Similar findings were also seen in studies by Sukriti et al. and Mahawal et al.¹²

An inverse relation was observed concerning age and protective titres of anti-HBs which is consistent with the findings of Resende et al.¹³ Studies by Sukriti et al. and Mahawal et al. also showed decreased sero protection rates with increasing time from last vaccination.^{5,12} Studies by Locquet C et al. FismanDN et al. and Averhoff F et al. also showed the inverse relation of age at primary vaccination and anti-HBs positive status.^{14,15,16}

In the present study, 90.47 % of HCP who had taken booster dose of the vaccine had protective antibody titres. Most of the studies do not recommend booster injections of the vaccine, but a few advised one dose of the vaccine if the anti-HBs level is less than 10 mIU / ml after primary vaccination to provide a stronger antibody response and to delay the reduction in the protective role of the vaccine. In the study by Chadha and Arankalla, 34 HCW were monitored for the long-term presence of an anti-HBs antibody after primary series of vaccination and it was found on 10 years follow-up that one booster dose after 3 years was raised antibody levels from 19 % to 40 %.¹⁷

Hepatitis B Vaccine

There are 2 types of hepatitis B vaccines: plasma-derived and recombinant vaccines. There is no difference in antigenicity, effectiveness, thermal stability and duration of protection between the two. Plasma-derived vaccines are made from purified HBsAg obtained from the plasma of individuals with chronic HBV infection. HBsAg produced by yeast or mammalian cells by inserting HBsAg / pre HBsAg gene by plasmids is used in recombinant hepatitis B vaccines. The route of administration is intramuscular, that is, the anterolateral aspect of the thigh in children less than 2 years and deltoid in older children and adults. Hepatitis B vaccines have themselves proven to be safe in people of all ages.¹⁰ The most frequently reported side effects are pain at the injection site (3 % – 29 %) and temperature of > 99.9°F (> 37.7°C) (1 % – 6 %).²

The contraindication for the vaccines are the people with history of allergy to yeast or any other vaccine component,

those who had developed serious drug reactions after receiving the vaccine were denied for additional doses.² As with other vaccines, vaccination of persons with moderate or severe acute illness, with or without fever, should be deferred until the illness resolves.²

Vaccination is not contraindicated in persons with history of multiple sclerosis, Guillain-Barré Syndrome, autoimmune disease (e.g., systemic lupus erythematosus and rheumatoid arthritis), or other chronic diseases.² Hepatitis B vaccination is not contraindicated for pregnant or lactating women¹. The hepatitis B vaccine can be given at the same time as other vaccines, without interference from the antibody response to other vaccines. If an unanticipated delay occurs after the first dose, a second dose should be given as early as possible followed by a third dose in 2 months. If there is a delay in the third dose, it can be administered at any suitable time.

Dose	Routine dosing	Accelerated dosing
1	1st day of visit	1st day of visit
2	1-2 months after 1st dose	At least 1 month after 1st dose
3	4-6 months after 1st dose	At least 2 months after 2nd dose, at least 4 months after 1st dose

Table 6. Vaccine Sero Protection

The usual vaccination schedule provides an adequate protection level of anti-HBs in more than 90 % of adults. The antibody titre increase from 35 % after the first dose to greater than 90 % after the second dose and the third dose ensures long-term protection and increases the number of responders.

Duration of Protection

It is now believed that the hepatitis B vaccine offers indefinite protection. However, it was previously believed and suggested that vaccination would only provide effective coverage for five to seven years, but it was subsequently recognized that long-term immunity arises from the immunological memory that survives the loss of antibody levels, and hence subsequent testing and booster dosing is not required in immunocompetent individuals who have been vaccinated successfully.^{3,4}

Serological Testing Following Hepatitis B Vaccination

In the case of children born to mothers with chronic hepatitis B, Anti-HBs and HBsAg levels should be tested after 3 - 12 months of vaccination.

Other than the above mentioned, a serological test after vaccination is recommended 4 to 8 weeks after completing the primary course for people in the following categories:

- Those with a high risk of occupational exposure that is, health care employees who are frequently exposed to human tissue, blood, or body fluids
- People who are at risk of severe or complicated HBV disease that is, people with a weakened immune system and people with pre-existing liver disease unrelated to hepatitis B
- Those who may have a poor response to hepatitis B vaccination, that is, haemodialysis patients, people with

bleeding disorders who were vaccinated via the subcutaneous route.

- Partners and close contacts of hepatitis B infected people.

In the above-mentioned categories, if anti-HBs levels, 1 -2 months after primary vaccination is < 10 mIU / ml, the chance of HBV infection including chronic HBV should be suspected and all the serological markers should be checked. In selected cases, if indicated, HBV deoxyribonucleic acid (DNA) should be checked. If there are no markers for HBV infection, the person should be treated as a non-responder to hepatitis B vaccination.

Non-Responders to Primary Vaccination

A non-responder is a person without HBV infection who has a documented history of the age-appropriate primary course of the hepatitis B vaccine, but with an anti-HBs level < 10 mIU / mL. Persons who do not achieve protective levels after primary vaccination with no evidence of chronic HBV infection should receive additional doses.

A single booster dose (4th dose) of the vaccine can be given to confirm non-responder status. People who do not respond after receiving the booster / 4th dose (and for whom HBV infection has been excluded) should receive 2 doses of the hepatitis B vaccine at a one-month interval and be tested again at least 4 weeks after the last dose for anti-HBs levels. The booster / 4th dose received could be counted as the 1st of the 3 repetitive doses, as recommended for non-responders. A few studies have shown that protective levels of anti-HBs are achieved in non-responders with high dose or double dose for the fourth dose of vaccine. But the evidence for the above is not consistent.

If individuals at significant risk for hepatitis B (e.g., healthcare workers) have anti - HBs levels < 10 mIU / mL when tested, they should be given a single booster dose (4th dose) of the vaccine. If there is earlier evidence of the protective level of antibody, the chance of responding to a single booster dose is high. If the anti-HBs level is still < 10 mIU / ml, there is a chance for HBV infection and it should be looked for. If this is ruled out, the person should be treated as a non-responder to vaccinations. If the anti-HBs level is ≥ 10 mIU / ml, the person can be considered immune.

Persistent non-responders should be aware of their risk of acquiring hepatitis B infection and hence advised to reduce exposure. They should be given HBIG within 72 hours if suspected of exposure to HBV.

Immunocompetent adults and children with vaccine-induced anti-HBs levels of ≥ 10 mIU / ml 1 - 2 months after receiving a full hepatitis B vaccine series with more than or equal to 3 doses are considered sero protected and are called vaccine responders.² Long-term immunity after a hepatitis B vaccination is based on an immunological memory that survives the loss of antibody levels. As a result, immune-competent individuals who have been vaccinated successfully do not require subsequent testing and booster dosing.^{3,4} Post-vaccination serological testing is recommended 4 to 8 weeks after completing the basic course for all healthcare workers. If adequate anti-HBs levels

are not achieved in serological tests 4 to 8 weeks after the 3rd dose, the possibility of HBV infection should be investigated by tests for serological markers.

HCP with anti - HBs below 10 mIU / ml after receipt of the primary series should be re-vaccinated. For these HCPs, giving a second full 3-dose series on an appropriate schedule, followed by anti - HBs testing 1 - 2 months after the third dose, is usually more convenient than performing serologic testing after each additional vaccine dose. Anti-HBs testing should be performed 1 - 2 months after the last vaccine dose and the vaccine response status should be documented for future exposures.

CONCLUSIONS

All HCPs should adhere to infection control guidelines and follow standard precautions. The records, if possible retrievable electronic records should be maintained in health care centers as a reference in case of occupational exposure or for other purposes. A copy of the hepatitis B vaccination and anti-HBs test results should be provided to HCP and urged to keep them with their medical records so that they can be made readily available to future employers.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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REFERENCES

- [1] US Public Health Service. Updated U.S. Public Health Service guidelines for the management of occupational exposures to HBV, HCV and HIV and recommendations for post-exposure prophylaxis. *MMWR Recomm Rep* 2001;29:50(RR-11):1-52.
- [2] Mast EE, Weinbaum CM, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. *MMWR Recomm Rep* 2006;55(RR-16):1-33, quiz CE1-4.
- [3] Gabbuti A, Romanò L, Blanc P, et al. Long-term immunogenicity of hepatitis B vaccination in a cohort of Italian healthy adolescents. *Vaccine* 2007;25(16):3129-3132.
- [4] European Consensus Group on Hepatitis B Immunity. Are booster immunisations needed for lifelong hepatitis B immunity? *The Lancet* 2000;355(9203):561-565.
- [5] Sukriti, Pati NT, Sethi A, et al. Low level of awareness, vaccine coverage, and the need for booster among health care workers in tertiary care hospitals in India. *J Gastroenterol Hepatol* 2008;23(11):1710-1715.
- [6] Kumar KKA, Baghel PK, Shukla CB, et al. Prevalence of hepatitis B surface antigen among health care workers. *Indian J Comm Med* 2000;25(2):93-95.
- [7] Wood RC, MacDonald KL, White KE, et al. Risk factor for lack of detectable antibody following hepatitis B vaccination of Minnesota Health care workers. *JAMA* 1993;270(24):2935-2939.
- [8] Sajjan AG, Mangalgi SS. Awareness and practice of complete hepatitis b vaccination and anti-HBs testing in vaccinated health care workers. *Journal of Krishna Institute of Medical Sciences University* 2015;4(2):81-88.
- [9] Pavani K, SrinivasRao MS, Samhitha M, et al. Immune response to hepatitis b vaccine in health care workers in tertiary care hospital in south India. *Indian J Microbiol Res* 2015;2(4):210-213.
- [10] Sarwat F, Ajaz H, Ayesha A. Hepatitis B vaccination status of health care workers and their antiHBs titres - a cross sectional study. *Al Ameen J Med Sci* 2014;7(3):217-223.
- [11] Yoshida T, Saito I. Hepatitis B booster vaccination for healthcare workers. *The Lancet* 2000;355(9213):1464.
- [12] Mahawal BS, Bhai N, Kataria VK, et al. Estimation of anti HBs antibody titre in adults during 5-10 years period following three doses of vaccine. *IOSR Journal of Pharmacy and Biological Sciences* 2013;7(1):20-23.
- [13] Resende VL, Abreu MH, Paiva SM, et al. Concerns regarding hepatitis B vaccination and post-vaccination test among Brazilian dentists. *Virology* 2010;7(1):154. <https://doi.org/10.1186/1743-422X-7-154>.
- [14] Locquet C, Marande JL, Choudat D, et al. Hepatitis B vaccination in women healthcare workers: a seroepidemiological survey. *Eur J Epidemiol* 2007;22(2):113-119.
- [15] Fisman DN, Agrawal D, Leder K. The effect of age on immunologic response to recombinant hepatitis B vaccine: a meta-analysis. *Clin Infect Dis* 2002;35(11):1368-1375.
- [16] Averhoff F, Mahoney F, Coleman P, et al. Immunogenicity of Hepatitis B vaccines. Implications for persons at occupational risk of Hepatitis B virus infection. *Am J Prev Med* 1998;15(1):1-8.
- [17] Chadha MS, Arankalle VA. A ten-year serological follow-up of hepatitis B vaccine recipients. *Indian J Gastroenterol* 2000;19(4):168-171.