

Estimation of Anti-HBs Titer in Health Care Professionals of a Tertiary Care Centre of Southern Assam

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ABSTRACT

Background- Due to occupational exposure to blood, body fluids and sharps, the health care professionals are at increased risk of contracting the Hepatitis B virus infection than general population. To combat this, all the health care professionals must be immunized with protective level of anti-HBs but anti-HBs titer gradually wanes with passage of time and may be influenced by gender, smoking or chewing tobacco, diabetes mellitus etc. This study was thus carried out to find the percentage of health care professionals with protective titer of anti-HBs and find the association (if any) of low anti-HBs titer and factors like gender, smoking, diabetes mellitus and time elapsed post vaccination.

Method- This cross-sectional study has been carried out with proper ethical clearance from May 2018- September 2019 in Serology section of VRDL under Department of Microbiology in a Medical College of Southern Assam on serum samples collected from 150 health care professionals vaccinated with 3 doses of recombinant HBsAg vaccine atleast 5 years back. Anti-HBs IgG concentration was measured by conventional ELISA in multistandard mode.

Result- Out of 150 participants, 95 were males and 55 were females. 27 participants smoked/chewed tobacco, 8 had diabetes mellitus. Booster dose was received by 23. Protective level of anti-HBs IgG (>10 IU/ml) was found in 66% (98/150) of HCP only. Low anti-HBs titer has been found to be significantly associated with Diabetes mellitus ($p=0.03$) and passage of

more than 10 years post primary vaccination ($p=0.005$) but no significant association has been found with gender, smoking and history of blood transfusion.

Conclusion- HBsAg vaccine doesn't impart everlasting protection. So, all HCP, especially those with co-morbidities should get their anti-HBs titer estimated after vaccination to check out for adequate seroconversion and attainment of protective titer. If found inadequate, they should go for repeat vaccination /booster doses.

Key Words- Healthcare professionals, Vaccinated, Anti HBs IgG, Assam

INTRODUCTION

According to the World health Organization (WHO) approximately 240 million people are chronically infected with malady of HBV infection and more than 7,80,000 die every year due to its wide spectrum consequences [1]. India is considered to have intermediate level of HBV endemicity with a prevalence rate of 2-8% [2]. The number of HBsAg carriers in India has been estimated to be over 50 million. Every year, one million Indians are at risk for HBV and about 1,00,000 die from HBV infection [3]. Due to occupational exposure to blood, body fluids and sharps, the health care professionals are at 2-4 times increased risk of contracting the Hepatitis B virus infection than general population [4]. Throughout the world, millions of healthcare professionals work in health

institutions and it is estimated that 600,000 to 800,000 cut and puncture injuries occur among them per year, of which approximately 50% are not registered. The annual proportion of health-care workers exposed to blood-borne pathogens was 5.9% for HBV, corresponding to about 66,000 HBV infections in health-care workers worldwide [5]. In developing regions, 40%-65% of HBV infections in health-care workers occurred due to per-cutaneous occupational exposure. In contrast, the fraction of HBV was less than 10%, in developed regions, largely because of immunization and post-exposure prophylaxis [5]. Although most of the HBV infections in healthcare workers are attributed to per-cutaneous exposure, in many studies, most infected HCWs could not recall any overt per-cutaneous injury [6]. In addition, HBV has been demonstrated to survive in dried blood, at room temperature, on environmental surfaces, for at least one week. Thus, HBV infections that occur in HCWs with no history of exposure might have resulted from direct or indirect blood or body fluid exposures that inoculated HBV into the mucosal surfaces or cutaneous scratches and other lesions [7] contains the highest HBV titers of all body fluids and is the most important vehicle of transmission in the healthcare settings. HBsAg is also found in several other body fluids, including breast milk, bile, cerebrospinal fluid, feces, nasopharyngeal washings, saliva, semen, sweat, and synovial fluid. However, most body fluids are not efficient vehicles of transmission because they contain low quantities of infectious HBV, despite the presence of HBsAg [8]. Therefore, avoiding occupational blood exposure is the primary preventive means for the transmission of HBV. To combat the high risk of HBV infection among HCWs, routine pre-exposure vaccination of HCWs against Hepatitis B and the use of universal precautions to prevent exposure to blood and potentially infectious body fluids have been recommended in many countries as the main stay of prevention [9]. The risk of HBV

in an unvaccinated person after a single episode of needle prick injury ranges from 6 – 30% [10] and even 0.00001ml of blood can transmit HBV. Reports from India indicate that only 16-60% of HCWs have received complete HBV immunization. Paramedics have a higher risk of HBV/HCV transmission and receive HBV vaccination less often than doctors [11].

Hepatitis B vaccine provides protection against infection with HBV by producing immunity or antibodies to the surface protein or outer coat of the virus.

Recently, third generation vaccines produced in mammalian Chinese Hamster Ovary (CHO) cells [12] have been shown to induce an immune response, which occurs earlier and is stronger. Even in many so called “non-responders” to S protein a protective immune response was induced.

Anti-HBs estimation after vaccination is recommended for healthcare workers and public safety workers at high risk for continued percutaneous or mucosal exposure to blood or body fluids to guide post-exposure prophylaxis, chronic haemodialysis patients, HIV-infected persons, sex partners of HBs Ag-positive persons and other immune compromised persons and for follow-up [13]. Testing should be performed 1 month after administration of the last dose of the vaccine series using a method that allows determination of a protective concentration of anti-HBs.

PURPOSE OF THE STUDY

1. To find the percentage of health care professionals in a tertiary health care centre with protective titer of anti-HBs
2. To find the association (if any) of low anti-HBs titer and factors like gender, smoking, diabetes mellitus and time elapsed post vaccination.

MATERIALS & METHODS

This prospective cross-sectional study was carried out from May 2018-September 2019 in Serology section of the Viral Research Diagnostic Laboratory under

Department of Microbiology, in a tertiary care hospital of Southern Assam after obtaining Ethical clearance from the Institutional ethical Committee. Blood samples were collected after obtaining written consent from total 150 vaccinated health care workers in the age group of 24-65years (Inclusion-criteria-Health Care Professionals vaccinated with 3 doses of recombinant Hepatitis B vaccine at least 5 years back) in Clot activator vials and serum samples were preserved at -20°C until tested. Subsequently these serum samples were thawed and Anti-HBs IgG concentration was measured by conventional ELISA using HBsAb ELISA kit from Diapro Diagnostics Italy (CE-IVD approved). Quantitative ELISA was done in multistandard mode of ROBONIK ELISA reader using microwells plate coated with inactivated Hepatitis B surface antigens. Samples are pre-treated in the well with a specimen diluent able to block interference present in vaccinated individuals. In 1st 1 hour of incubation, the IgG antibodies are captured onto the coated wells at 37°C. After washing, during the 2nd hour of incubation the captured antibodies are detected by an HBsAg, labelled with peroxidase (HRP), that specifically binds the second available binding site of these antibodies. The enzyme specifically bound to wells, by acting on the substrate /chromogen mixture, generates an optical signal that is proportional to the amount of HBsAb in the sample and can be detected by an ELISA reader.

The amount of antibodies may be quantitated by means of a standard curve calibrated against the W.H.O reference preparation. Primary and secondary filters used are 450nm and 620nm respectively.

STATISTICAL ANALYSIS-

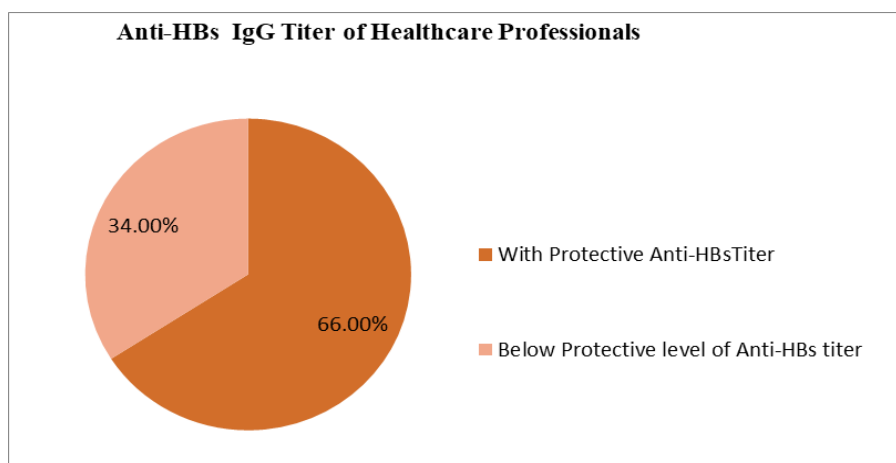
Statistical analysis of result and calculation for p value by obtaining chi square score was done by using online p value calculator from Statistical Package for the Social Sciences (SPSS) version 26. Association of factors with P value <0.05 has been considered significant.

RESULT

Out of 150 participants, 95 were males and 55 were females. Designation wise 37 were senior faculties, 41 were Junior Residents, 30 were Interns, 19 were nursing staffs and 23 were Lab technicians. 27 participants habitually smoked/chewed tobacco, 8 had diabetes mellitus. Booster dose was received by 23. Protective level of anti-HBs IgG(>10 IU/ml) was found in 66% (98/150) of HCP only. Based on peak concentration of anti-HBs, the vaccine recipients have been categorized into following 3 groups^[14] -

1. Non-responders with peak anti-HBs concentration < 10 IU/L
2. Low responders with peak anti-HBs concentration of 10-100 IU/L
3. Good responders with peak anti-HBs concentration > 100 IU/L

ANTI-HBs IgG TITER	NO. OF HEALTH CARE PROFESSIONALS
< 10 IU/mL	51
10-100 IU/mL	40
100- 500 IU/mL	59



GENDER	BELOW PROTECTIVE ANTIHBs IgG TITER	PROTECTIVE ANTI-HBs TITER IgG
MALE	34	61
FEMALE	18	37

OBSERVATION

Gender predilection of health care professionals has not been found to significantly associated with low anti-HBs titer ($p=0.704$). Below protective anti-HBs titer has been found to be significantly associated with Diabetes mellitus ($p=0.03$) and passage of more than 10 years post primary vaccination ($p=0.005$) but no significant association has been found with habit of smoking or chewing tobacco and history of blood transfusion.

DISCUSSION

In this study conducted in the only tertiary health care centre of Southern Assam, 66% of the completely vaccinated healthcare professionals have been found to have protective anti-HBs titer. Similar estimate of protective antibody titer (67.92%) was found by Syed Rahamathulla *et al* [15] in a cross-sectional study carried out among 106 vaccinated doctors in Andhra Pradesh. Lakshmanan *et al* [14] from Agartala have found protective anti-HBs titer in 89% of the healthcare professionals, while Dr. V K Kataria *et al* [16] from New Delhi found that only 46.16% of the vaccinated healthcare professionals had protective antibody levels after 10years post HBsAg vaccination. Sarman Singh *et al* [8] in a study conducted on vaccinated healthcare professionals of AIIMS New Delhi found that 79% of them had protective antibody titer ($>10\text{IU/L}$). Studies carried out in South Indian states like that of T.V Rao *et al* [17] from Thrissur Kerala, Shruti Hegde *et al* [18] from Mangalore Karnataka and Reshmi Gopalkrishnan *et al* [9] from Calicut Kerala found protective anti-HBs titer in 89%, 92% and 100% of the completely vaccinated healthcare professionals respectively.

Presence of Diabetes mellitus in participating health care professionals has been significantly attributed to inadequate

level of antiHBs IgG in this study. This finding has been seconded by Lakshmanan *et al* [14] in their study conducted in Agartala Govt. Medical College.

Unlike the study of Shruti Hegde *et al* [18] in dental students of Mangalore and that of Syed Rahamathulla *et al* [15] in vaccinated doctors in Andhra Pradesh where male gender has been attributed to low anti-HBs titer, no such statistically significant gender predilection has been found with low anti HBs IgG in our study

Anti-HBs IgG titer has been said to wane with time elapsed after vaccination and so has been found in our study where passage of >10 years post vaccination has been found to have been significantly associated with inadequate protective anti-HBs. Similar observation has been made in the study of Dr V K Kataria *et al* [16] in their study on healthcare professionals from New Delhi.

The fact observed in this study that Smoking of tobacco is not significantly associated with low level of anti-HBs IgG has been in discordance with studies of Shruti Hegde *et al* [18] from Karnataka in South India and Lakshmanan *et al* [14] from Agartala in North east India as they have found smoking to be a significant attribute for low levels of anti-HBs IgG titer in medical students and health care workers respectively.

Though conducted in non-health care professional, Study by Amy B Middleman *et al* [19] in 420 subjects in the age group 16-19 years found that only 24% had protective anti-HBs titer after 5 years of vaccination but they did check the anamnestic response to find that the non-responders also developed protective anti-HBs titer after receiving a booster dose of the vaccine, proving that immune memory against recombinant HBsAg was intact leading to rapid rise in antibody response. This finding is at par with the views and opinions stated in the study of Lakshmanan *et al* [14] from Agartala that persistence of immunological memory remains intact for at least 10years. Thus, it reiterates the need

and enhancing role of booster dose of HBsAg vaccine

CONCLUSION

As this study brings to light that 34% of the completely vaccinated healthcare professionals of this tertiary care hospital lack protective anti-HBs titer, health care professionals must bear in mind that merely completing the primary schedule of recombinant HBsAg vaccination against Hepatitis-B doesn't impart them everlasting protection. So, they all, especially those with co-morbidities like Diabetes Mellitus should get their anti-HBs titer estimated 1 month after vaccination and follow up at intervals to check out adequate priming of immune system leading to seroconversion and attainment of protective titer. In order to verify the persistence and intactness of immune memory, anti-HBs titer should be estimated at least 5 years after completing the primary schedule if not done after one month of completing the primary vaccination schedule and if anti-HBs titer is found inadequate they should go for repeat vaccination or administration of booster doses. This study also calls for raising awareness and scaling up of complete HBsAg vaccination in healthcare professionals of tertiary care hospitals.

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Limitation

Involvement of the incompletely vaccinated or the recently vaccinated (at least 6 months back) health care professionals could have projected the exact scenario of seroconversion to protective IgG level. This study also could not follow up the non-responders to post booster dose anti-HBs IgG estimation to check out for the persistence of Immunological memory.

Conflict of Interest: None

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Ethical Approval: Approved

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