



## Hbs ANTIBODY LEVELS AMONG MEDICAL INTERNS OF A TERTIARY CARE HOSPITAL IN PUDUCHERRY

### Microbiology

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### ABSTRACT

**Background:** Health care workers particularly medical students are at high risk of acquiring HBV infection. Though a universal vaccination programme to combat the infection is available, many medical students remain non-vaccinated, incompletely vaccinated or unaware of their post vaccination status. Thus, there is a need to document the compliance and effectiveness of Hepatitis B vaccination among the medical interns.

**Objective:** The present study was undertaken to analyze Hepatitis B vaccination status & prevalence of protective antibody titre among medical interns.

**Materials & methods:** A cross sectional study on 70 vaccinated medical interns (1-3doses) was carried out at a tertiary care hospital at Puducherry. Single blood samples were drawn and anti HBs titres were recoded using Enzyme linked fluorescent assay (ELFA). Statistical analysis was done using SPSS 20.0.

**Results:** 57% of the medical interns had completed 3 doses, while 19% received 2 doses and 24% received only a single dose. 72.8% were good responders while 15.7% were non-responders to the vaccination.

**Conclusion:** The compliance to complete immunization was found to be low; implementation of active follow-up with reminders to complete vaccination and post vaccination estimation of titres should be made mandatory at institutional level. A further assessment is essential on the need for booster dose and management of post exposure prophylaxis.

### KEYWORDS

Hepatitis B antibody, Hepatitis B vaccine, Medical Interns

### INTRODUCTION

Hepatitis B Virus (HBV) infection is a global public health problem and the tenth leading cause of deaths globally. According to an estimate, nearly 2 billion of the population is infected with HBV worldwide that results in 350 million chronic cases and 2 million annual deaths.<sup>[1]</sup> HBV is a major cause of acute hepatitis, cirrhosis of liver and hepatocellular carcinoma. At least one million people die annually from HBV related liver disease.<sup>[2]</sup> This is a significant health problem in India too.<sup>[3]</sup>

Prevention of HBV is a public health priority and immunization with hepatitis B vaccine is the most effective means of preventing hepatitis B infection and its consequences.<sup>[4]</sup> Health care workers are at particularly high risk of acquiring HBV infection.<sup>[5]</sup> Hence vaccination is deemed mandatory for all health care workers. The rate of successful vaccination i.e. acquiring protective levels of HBs antibody (>10 IU) is about 90% among healthy individuals.<sup>[6,7]</sup> This means that there will be a small group of non-responders to HBV vaccine who are at risk of infection.

Various studies have shown that prevalence of non-responsiveness to the initial 3-dose regimen ranges between 10 and 15%.<sup>[8]</sup> These individuals will require additional and/or higher doses of vaccine for achieving protection. Unless the antibody titer is checked after the primary course of vaccination, these individuals will be in the mistaken notion that they are protected against HBV.

This important aspect of checking for protection after vaccination is often not realized by even the high-risk group of medical professionals.<sup>[9]</sup>

The present study was undertaken to analyze Hepatitis B vaccination status and prevalence of protective antibody titers among medical Interns, since there is limited literature from the country, regarding this.

### MATERIALS AND METHODS:

This is a cross-sectional study carried out between June-July 2016 at a tertiary care hospital after obtaining institutional ethical clearance (PIMS Institute Ethics Committee). The medical interns who were present during the study were requested to participate in the study through a participant information sheet. The questionnaire consisting of personal details such as age, sex; vaccination details like number of doses, year of vaccination, testing for post vaccination anti-HBs levels,

booster dose and exposure to infection (through needle prick, direct contact; etc.) were documented.

**Inclusion criteria:** Medical interns who have received at least one dose of Hepatitis B vaccination.

**Exclusion criteria:** Unvaccinated individuals.

Blood samples of 3 ml quantity were collected after obtaining informed consent from 70 vaccinated (1-3 doses) subjects who agreed to participate in the study. The samples were then centrifuged and serum was separated and stored at -20°C till testing. All the subjects were tested using the commercially available anti-HBs kit (VIDAS Anti-HBs Total II(AHBS), Belgium). It is an automated quantitative test for immuno-enzymatic detection of antibodies to hepatitis B surface antigen in plasma using the Enzyme Linked Fluorescent Assay (ELFA) method.

The assay principle combines an enzyme immunoassay sandwich method with a final fluorescent detection (ELFA). The Solid Phase Receptacle (SPR), coated with HBsAg subtype ad plasma (inactivated) and ay recombinant was inserted into the appropriated slot provided in the instrument. This serves as the solid phase. HBs total strip which consists of 10 wells covered with a labeled, foil seal were then inserted after checking the assay codes both on the strip as well as on the SPRs so that they match each other. 150µl of samples were used. The instrument performed the five reaction steps automatically. The reaction medium was cycled in and out of the SPR several times. Each step was followed by a wash cycle, which eliminates unbound components. The intensity of the fluorescence was proportional to the quantity of anti-HBs in the sample. At the end of the assay results were automatically calculated by the instrument in relation to the calibration curve stored in the memory and was then printed out.

### Statistics:

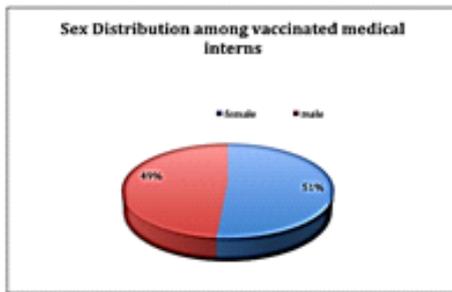
The data and results of anti-HBs titre test were entered in the spreadsheet of MS excel. Association between variables was tested using Chi-square test or Fishers Exact test. 95% confidence interval was estimated. p value less than 0.05 was considered as statistically significant. Statistical analysis was done using SPSS version 20.0.

### RESULTS:

Out of the 70 vaccinated medical interns who participated in the study,

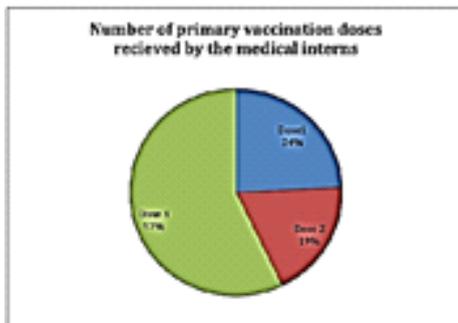
51% (36) were females and 49% (34) were males (Fig.1). The age distribution was in the range of 23 yrs to 25 yrs.

Figure 1



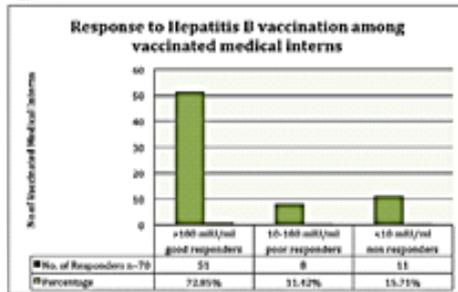
Among the 70 vaccinated medical interns, 57% had received 3 doses, 19% had received 2 doses while 24% received only a single dose. (Fig.2)

Figure 2



Out of the 70 vaccinated medical interns, 51 (72.85%) of the responders had a titre level above 100 mIU/ml and were considered to be good responders, 8 (11.42%) were poor responders with a titre level between 10- 100 mIU/ml and 11 (15.71%) were Non-responders with a titre level less than 10 mIU/ml. (Fig.3)

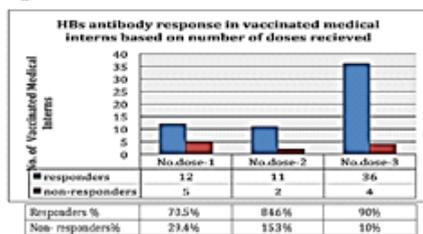
Figure 3



95% Confidence interval was calculated for both responders and non-responders. 84.3% of the interns were found to be responders with a lower limit of 75.8% and an upper limit of 92.8%, while 15.7% were non-responders with a lower limit of 7.2% and upper limit of 24.4%.

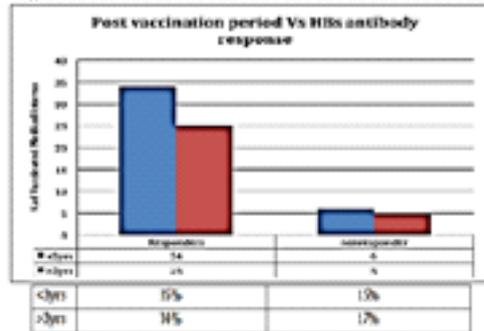
Figure 4 explains the HBs antibody response based on the number of doses. It was found that the association between number of doses and their antibody titre was not statistically significant. Fisher's exact test has a p value of 0.150. (Fig.4)

Figure 4



It was observed that, 31(77.5%) of individuals who received the vaccination 3 years ago and 20 (66.6%) of the individuals who were vaccinated prior to 3 years were good responders. The association between post vaccination period and response is not statistically significant (p=0.85). (Fig.5)

Figure 5



Among the 36 females, it was observed that 24 (66.6%) were good responders, 5 (13.8%) were poor responders while 7 (19.4%) were non-responders. Among the 34 males, it was observed that 27 (79.4%) were good responders, 3 (8.8%) were poor responders while 4 (11.7%) were non-responders. (Table 1)

Table 1:

VARIABLES	Good Responder	Poor Responder	Non-Responder	TOTAL	
Sex	Female	24 (66.6%)	5 (13.8%)	7 (19.4%)	36
	Male	27 (79.4%)	3 (8.8%)	4 (11.7%)	34
Duration Post Vaccination	<3 yrs	31 (77.5%)	3 (7.5%)	6 (15%)	40
	>3yrs	20 (66.6%)	5 (16.6%)	5 (16.6%)	30

**DISCUSSION:**

Blood from persons with HBV infection contains the highest Hepatitis B viral particles and is the most important vehicle of transmission in the health care setting. High prevalence rate of the infection in general population increases the risk of occupational exposure in HCW, which is 2-4 times higher than in general population [10]. The most important approach for prevention of occupational HBV infection is the use of Hepatitis B vaccine among HCW at risk.

In the present study, 70 medical interns who had been vaccinated with a single or all three doses were subjected to anti-HBs titre testing. In a study by Seddique et al, conducted at Iran, it was observed that 86.8% of HCW have been vaccinated against Hepatitis B of which complete vaccination (3 doses) was received by only 71.7% of them. [11] In the present study, 57% of the medical interns had completed the 3-dose course of vaccination, while 19% received 2 doses and 24% received only a single dose. This low compliance towards completion of the vaccination series could be due to lack of awareness or improper institutional follow-up. Therefore, implementation of active follow up with reminders to complete vaccination is needed among the study group.

Regarding the immune response developed among vaccinated medical interns, 72.8% were found to be good responders and 11.42% were poor responders.

The percentage of non-responders in the study (15.7%) is in corroboration with previous studies on HCW from different parts of the world like Saberifiroozim et al (12.7%), [12], Averhoff F et al (12%) [13], Platkov E et al (13.5%) [14] and Zeeshan M et al (14%) [15]. A small proportion of the individuals (11.11%) who completed the 3-dose course were found to be non-responders.

Unresponsiveness to the HB vaccine is attributed to a number of environmental and genetic factors, the most important ones being the halo type of HLA antigen and immunological tolerance. [16] Smoking, obesity, chronic medical conditions, male sex could be other factors responsible for the unresponsiveness (non-responders) to the vaccine. These non-responders require additional or higher doses of vaccine for achieving protection. Therefore, postvaccination estimation of titres should be made mandatory at institute level.

Among the vaccinated, 84% (11 out of 13 two doses) and 71% (12 out of 17 single doses) responded to Hepatitis B vaccination. This shows that even with incomplete vaccination, few have developed seroprotection, which may be due to individual immune response. Few of them may have received primary immunization in their childhood but these details were not documented due to their lack of knowledge

of their childhood immunization schedule. Educational and training programme along with well formulated policies for Hepatitis B vaccination and screening for antiHBs titres for medical interns should be implemented.

The association between number of doses and the antibody titre was found to be statistically insignificant which is in concurrence with the study conducted by Poongodi and Palaniappan.<sup>[17]</sup>

Current data shows that vaccine induced anti-HBs titre levels had no significant decline in association with post vaccine duration. Among the vaccinated interns, 85% (34 / 40) within 3 years of vaccination and 83% (25/ 30) more than 3 years of vaccination had antibody titre >10 mIU/ml . Studies have shown that protection is dependent on immune memory rather than declining anti-HBs responses. Following a complete course of vaccination, booster doses are not needed if initial response is good.<sup>[18]</sup> More studies are necessary to highlight the need for further line of action in the case of non-responders and management of post exposure prophylaxis highlighting the need and timing of booster dose.

#### REFERENCES:

1. Lavanch D. Hepatitis B virus epidemiology, disease burden, treatment and current and emerging prevention and control measures. *J viral Hepatic.* 2004;11:97–107. [PubMed]
2. Sun Z., Ming L., Zhu X., Lu J. Prevention and control of hepatitis B in China. *Journal of Medical Virology.* 2002; 67(3). www.ncbi.nlm.nih.gov
3. Sukriti , Pati NT, Sethi A, Agrawal K, Agrawal K, Kumar GT, Kumar M, Kaanan AT, Sarin SK. Low levels of awareness, vaccine coverage, and the need for boosters among health care workers in tertiary care hospitals in India. *Journal of Gastroenterology and Hepatology.* 2008. 23(11). www.ncbi.nlm.nih.gov
4. Park NH, Chung YH, Lee HS. Impact of vaccination on hepatitis B viral infections in Korea over a 25-year period. *Intervirology.* 2010;53:20–28. [PubMed]
5. Pathoumthong K, Khampanisong P, Quet F, Lathaphasavang V, Souvong V, Buisson Y. Vaccination status, knowledge and awareness towards hepatitis B among students of health professions in Vientiane, Lao PDR. *Vaccine.* 2014 Sep 3; 32(39) www.ncbi. nlm. nih. gov
6. R. Ananthanarayan, CK Jayaram Panikar."Hepatitis viruses". Textbook of Microbiology,9th ed. Hyderabad: Universities press, 2013. Pg 548
7. Frederica Chiara, Giovanni battista bartolucci, Margherita Cattail, Anna Piazza, Annamaria Nicolli, Alessandra Buja, Andrea Trevisan. Hepatitis B vaccination of adolescents: significance of non-protective antibodies. *Vaccine.* 2013 Dec 17; 32(1):62-8.
8. Thomas R J, Fletcher G J, Kirupakaran H, Chacko M P, Thenmozhi S, Eapen C E, Chandu G, Abraham P. Prevalence of non-responsiveness to an indigenous recombinant hepatitis B vaccine: A study among South Indian health care workers in a tertiary hospital. *Indian J Med Microbiol* 2015;33, Suppl S1:32-6
9. Al Ghamdi SS, Fallatah HI, Fetyani DM, Al-Mughales JA, Gelaidan AT. Long-term efficacy of the hepatitis B vaccine in a high-risk group. *J Med Virol.* 2013. 85(9):1518-22. www.ncbi.nlm.nih.gov
10. Singhal V, Bora D, Singh S, Prevalence of hepatitis B virus infection in Health care workers of tertiary care centre in India and their vaccination status. *J Vaccines Vacci* 2011;2:118.
11. Seddiqee Amini- Ranjbar, Mohammad Esmael Motlagh. Hepatitis B Vaccination Coverage Among Iranian Medical Students and Nursing Staff. *American Journal of Applied Sciences* 2008;5(6):747-749.
12. Mehdi S, Sakineh G, and Ali-Reza S. The long term immunity among health care workers vaccinated against Hepatitis B virus in large referral hospital in Southern Iran. *Arch Iran Med.* 2006;9(3):204-207.
13. 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; 15:1-8.
14. Platkov E, Shlyakhov E, Glick V, Khalemsky S, Fischbein A. Humoral immune response of hospital employees Induced by a recombinant Hepatitis B vaccine: 5 years after the primary standard immunization. *The Journal of Preventive Medicine.* 2001;9(3):59-66.
15. Zeeshan M, Jabeen K, Ali A N, Ali A W, Farooqui S Z, Mehrj V et al, " Evaluation of immune response to hepatitis B vaccine in health care workers at a tertiary care hospital in Pakistan: an observational prospective study." *BMC Infect Dis* 2007; 7:120. Doi: 10.1186/1471-2334-7-120.
16. Chisari FV, Ferrari C. Hepatitis B Virus immunopathogenesis. *Ann Rev Immunol* 1995;13:29-60.
17. Poongodi SL, Palaniappan N. Hepatitis B vaccination and immunity in health care workers- A long way to achieve. *International Journal of Basic Medical Science* 2012;3;93-97.
18. West DJ, Calandra GB. Vaccine induced Immunological Memory for hepatitis B surface antigen: implications for policy on booster vaccination. *Vaccine* 1996 Aug;14(11):1019-27.