

Original Research Article

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Study of Hepatitis B Surface Antibody Titres in Female Medical Students Post Vaccination

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ABSTRACT

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Hepatitis B viral infection is a major health problem worldwide. New cases can be prevented by immunization with hepatitis B vaccine containing the genetically engineered surface antigen. Values of ≥ 10 IU/ml are considered protective. However a small percentage of individuals fail to develop these levels. Such non responders are at risk of acquiring Hepatitis B virus infection. This is of concern especially in health care personnel. The study comprised of 100 female medical students from Mallareddy Medical College for Women, Suraram who completed the standard 3 dose course of vaccination. Their serum antibody levels were estimated quantitatively by ELISA technique. Information about Their height, weight, associated medical problems was documented. The data was analysed according to body mass index, age, and associated conditions. Though all of them showed protective levels, two of them had levels at borderline, 10 IU/ml. such individuals are considered to be hypo responders (10-100IU/ml). Those individuals should be given a booster dose and antibody levels estimated again to assess the efficacy of the booster dose.

Introduction

Hepatitis B viral infection is a serious liver infection caused by hepatitis B virus (HBV) that can lead to liver failure, cirrhosis or cancer of liver. According to WHO (World Health Organization), about 1/3 of the world's population (2 billion) has been infected with HBV, and 400 million people are chronically infected and are at risk of severe disease and death (Lai *et al.*, 2003; Kao *et al.*, 2005). Hepatitis B viral infection is a major health problem in India as there are 40 million estimated carriers (Pankaj Puri, 2014). The virus is transmitted through blood, and body

fluids of infected persons, unprotected sex and use of unsterile injections. Health care workers (HCW) are at a greater risk of acquiring Hepatitis B infection due to high frequency of exposure to blood and body fluids and the high contagiousness of HBV (Lai *et al.*, 2003; Kao *et al.*, 2005).

The Hepatitis B viral infection can be controlled by immunization, interrupting routes of transmission, and treating the infected patients (Kao *et al.*, 2005). Vaccination is an easy and cost effective

measure to prevent disease and infection. Recombinant Hepatitis B vaccine containing surface antigen is safe and effective against Hepatitis B infection.

In addition, vaccination eliminates the incidences of persistent HBV infection and chronic liver disease and diminishes the pool of chronic carriers, thus limiting transmission of infection to susceptible contacts. Recombinant Hepatitis B vaccine is known as the world's first "anti-cancer vaccine" by world health organization as it is effective in preventing HBV infection and liver cancer (World Health Organization Hepatitis B fact sheet, 2010).

Hepatitis B surface antibody (HBsAb) levels correlate with the immunity to HBV and levels of anti-HBs antibody are related to the number of doses of vaccine administered (Kubba *et al.*, 2003; Lin *et al.*, 2011).

A complete standard course of vaccination schedule consists of 3 doses (0 month, 1 month, 6 month). Each dose contains 1ml of recombinant Hepatitis B vaccine (Gene vac) given deep intramuscularly. A 3-dose course induces protective antibody concentrations in 95% of healthy infants, children, and adolescents and in 90% of healthy adults (Assad *et al.*, 1999; Venters *et al.*, 2004).

Vaccine efficacy studies have demonstrated virtually complete protection against acute and chronic hepatitis B in immunocompetent people, with post-immunization anti-HBs levels of ≥ 10 mIU/mL. Therefore, seroprotection against HBV infection was defined as having an anti-HBs level of ≥ 10 mIU/mL after having received a complete immunization schedule (Elke Leuridan *et al.*, 2011). Duration of protective efficacy can last many years and post vaccination immunological memory remains intact for much longer time (Gilca *et al.*, 2012). Almost

5-10% of vaccinees do not respond to these conventional vaccines (non-responders: HBsAbs < 10 IU/L after 3 doses of conventional vaccine) (Kubbu *et al.*, 2003). Vaccination failure depends on age, obesity, smoking, male gender, and immune suppression (Kwon *et al.*, 2011). The response rates are also lower in immune compromised patients, such as transplant recipients, patients receiving chemotherapy and those with end-stage liver disease. Patients with chronic kidney disease should be vaccinated early in the course of their disease, before the renal disease progresses, to ensure optimal response to vaccination (Perillo *et al.*, 2006).

In non-responders revaccination should be done according to the recommended schedule, therefore there is a need to estimate antibody levels. Approximately 50% of non-responders develop protective levels after 3 additional doses (MMWR, 2001; 50 No. RR-11).

Post vaccination testing for HBsAb is indicated for HCWs and should be conducted 1-2 months after the third dose (MMWR, 2011; 60 No. RR-7). HCWs with a reduced immune response to HBV vaccine in a high disease-prevalent population are at greater risk. Therefore, it is crucial to check post-vaccination HBsAb in all the HCWs. This strategy will ensure safety at work by reducing nosocomial transmission and will have a cost effective impact at an individual as well as a national level, which is very much desired in a resource-limited country (Zeeshan *et al.*, 2007).

There are few studies regarding seroconversion in medical students following vaccination. Many students do not have their antibody levels checked and may be under false impression that they are protected against HBV. The aim of this study is to detect the level of the antibodies against

HBsAg in the medical students, to identify non responders and suggest revaccination and to analyze the factors responsible for non-responsiveness.

Materials and Methods

This is a retrospective study for quantitative estimation of the HBsAb in medical students of 2nd and 3rd year MBBS of Malla Reddy Medical College for Women, Suraram. The participants received 1ml of recombinant Hepatitis B vaccine (Gene vac) deep intramuscularly at 0, 1, 6 months intervals as prescribed.

The study was approved by the institutional ethics committee. Participants were explained about the study and asked to complete an informed consent form and questionnaire that included questions on health history and data related to HBV immunization. Their age, height, weight, duration of post vaccination period and any other medical problem is documented. Body mass index (BMI) was calculated from height and weight.

Inclusion criteria: Medical students of 2nd and 3rd year MBBS who had completed the 3 dose standard regimen of hepatitis B vaccine and the time lapse of their last dose of vaccine was more than one month from time of sampling were included in the study.

Exclusion criteria: Students who had not completed the 3 dose standard regimen of hepatitis B vaccine (incompletely vaccinated) or not vaccinated at all were excluded from the study.

Out of the 300 female medical students included, 250 (83.3%) were vaccinated and 50 (16.6 %) were partially vaccinated. Of 250 students 102 volunteered to participate in the study during this period. The study was of 2 months duration during August and September 2016.

Sample collection and processing: 3ml of whole blood is collected from the participants by venipuncture in vacutainer tubes without anticoagulant, and serum is separated. Serum was preserved at 2-4 °C or frozen when more than 1 week storage is needed. All the samples collected were tested in batches.

Hepatitis B antibody estimation was done quantitatively by ELISA (Enzyme Linked Immunosorbent Assay) using commercial kits (DIAPRO- Sachina Diagnostics) in microbiology laboratory, Malla Reddy Narayana Multi Speciality Hospital to which the medical college is attached. Results were interpreted according to manufacturer's instruction. Data obtained was compiled, compared and analyzed using appropriate statistical methods.

Results and Discussion

The median age of study subjects was 20 years (range 18-22 years) with 20 years being most common age group (Table 1).

Study population includes 74 (72.5%) 2nd year MBBS students, 28 (27.4%) 3rd year MBBS students. Time lapse from last dose of vaccine to sample collection ranges from 6 to 15 months. Accordingly subjects were divided into two groups, Group I comprising participants with less than 7 months of post vaccination duration, Group II 8-15 months of post vaccination duration. We found no significant relation between time lapse since the last dose of vaccination (p value is 0.345). Body mass indices were calculated and participants were grouped into very severely underweight, severely underweight, underweight, normal, overweight, obese class I according to The International classification by WHO 2004 and correlated with the Ab titres (Fig. 1). There was no significant relation between BMI and Ab titres (p value 0.19). In the study sample, there were no non-

responders (anti-HBs titres < 10 mIU/ml of blood), 2 (2%) were hypo responders (anti-HBs titres 10-100 mIU/ml of blood) with 10 and 10.37 mIU/ml respectively and 100 (98%) were good responders (anti-HBs titres > 100 mIU/ml of blood) (Table 3).

The overall seroconversion rate (anti-HBs \geq 10 mIU/mL) was 100%, there were no non-responders (anti-HBs titres < 10 mIU/ml of blood). 100 (98%) were good responders

(anti-HBs titres > 100 mIU/ml of blood). 2 (2%) were hypo responders (anti-HBs titres 10-100 mIU/ml of blood) with 10 mIU/ml in Group I and 10.37 mIU/ml in Group II respectively. Among good responders 3 had titers > 500 mIU/mL, 92 had titers 400-500 mIU/mL, 8 had titers 100-400 mIU/mL. Out of 102 participants, 39 had received prior (childhood) vaccination, 20 in group I and 24 in group II (Table 4).

Table.1 Age and number of participants

Age (yrs)	No of participants (Female)
18-20	70
21-22	32
Total	102

Table.2 HBsAb response in two groups of participants

Groups	No of Participants (female)	Mean HBsAb titre (mIU/ml)
I - less than 7 months of post vaccination period	48	417.81
II - 8-15 months of post vaccination period	54	426.54

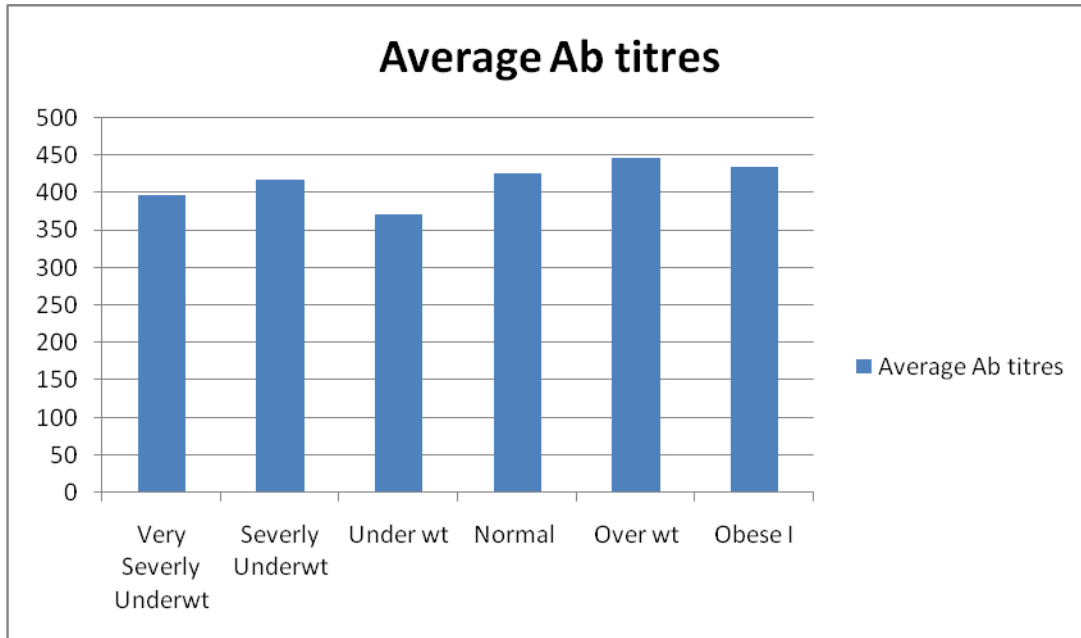
Table.3 Distribution of antibody levels in the study group

Ab titres	No of participants
0-9	0
10-99	2
100-399	8
400-499	89
\geq 500	3

Table.4 Number of subjects with and without prior (childhood) vaccination and their average antibody titres

Status of vaccination	No	Average Ab titres
Prior Vaccination	44	422.61
No Prior Vaccination	58	421.13

Figure.1 Average Ab titres in different subject groups based on the BMI



This is a study exclusively on female medical students and highlights the seroconversion rates in this group. In many of the studies from India, health care personnel were assessed for their immune response after hepatitis B vaccination by estimating the antibody levels and detecting the non responders for further action. One such study by Sunita *et al.*, from Uttarakhand showed that there was 100% seroconversion by 8 weeks post vaccination with which our study is in concurrence. Another such study is by Bidhan Chakraborty *et al.*, (2011) from west Bengal. On the other hand, other studies from different parts of the world, like Thomas *et al.*, (2015); Averhoff *et al.*, (1998); Platkov *et al.*, (2001); Zeeshan *et al.*, (2007);

Chaturang *et al.*, (2013) and Sarwat *et al.*, (2014) showed different rates of seroconversion rates, 98.89%, 88%, 86.5%, 86%, 90.1% and 35% respectively.

The incidence of non responders was seen more in males in one study by Pavani *et al.*, (2015) 27.1% vs. 12% in male vs. females. Thomas *et al.*, (2015) found no statistical significant difference in the rates but found higher levels of antibody titers in females than in males and found association with low Body Mass Index. The same study found the occurrence of hyporesponders in 2 (0.43%) individuals as in our study. They concluded that gender and BMI levels might influence the levels of anti HBs titres (Table 2).

In present study 50 (16.6%) out of 300 medical students were partially or not vaccinated. This observation suggests that there is a need for adequate vaccine coverage in high risk groups by creating awareness and formulating good vaccination policies.

As part of present study, we have educated our medical students regarding the importance of screening for anti-HBs titers to decrease the risk of HBV infection and also identified the medical students that had not been vaccinated previously despite being at a high risk of contracting the infection.

In conclusion, the present study that in all medical colleges, students should be encouraged to take HB vaccination and active follow-ups should be done, with reminders to track completion of the vaccine series. Post-vaccination estimation of titers should be made mandatory in all healthcare institutions to assess the protection attained through the vaccine. Those who do not achieve the protective anti-HBsAb titres for the initial 3 dose vaccine regime should be either given a booster dose or repeat 3 dose vaccine regimens depending on their Ab titres and follow-ups should be done for estimation of Ab titres.

References

- Assad, S., Francis, A. 1999. Over a decade of experience with a yeast recombinant hepatitis B vaccine. *Vaccine*, 18: 57–67.
- Baddavithana, A.K., F. Noordeen, C.M. Mendis, A.M.S.B. Abeykoon. 2015. Sri Lanka, *J. Inf. Dis.*, vol. 5(1): 7-12
- Averhoff, F., Mahoney, F., Coleman, P., Schatz, G., Hurwitz, E., Margolis, H. 1998. Immunogenicity of Hepatitis B Vaccines. Implications for persons at occupational risk of hepatitis B virus infection. *Am. J. Prev. Med.*, 15(1): 1-8.
- Bidhan Chakraborty, Tanvir Bashar, Konok Roy, Rashed Noor, and M. Majibur Rahman. 2011. Persistence of Anti-HBs Antibody and Immunological Memory in Healthy Individuals Vaccinated With Hepatitis B Vaccine Stamford, *J. Microbiol.*, Vol. 1, Issue 1 ISSN: 2074-5356.
- Lin, C.C., C.Y. Yang, C.T. Shih, B.H. Chen, and Y.L. Huang. 2011. “Waning immunity and booster responses in nursing and medical technology students who had received plasma-derived or recombinant hepatitis B vaccine during infancy,” *The American J. Infect.*, vol.39, no.5, pp.408–414.
- Elke Leuridan and Pierre Van Damme. 2011. Hepatitis B and the Need for a Booster Dose, *Clin. Infect. Dis.*, 53(1): 68-75.
- Gilca, V., et al., 2012. Antibody persistence and the effect of a booster dose given 5, 10 or 15 years after vaccination with a recombinant hepatitis B vaccine. 52nd *Inter science Conference on Antimicrobial Agents and Chemotherapy*, San Francisco, abstract G-1047.
- Immunization of health-care personnel: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 2011;60 [No. RR-7]).
- Kao, J.H., Chenn, D.S. 2005. Hepatitis B vaccination: to boost or not to boost? *Lancet*, 366: 1337-1338
- Kubba, A.K., Taylor, P., Graneek, B., Strobel, S. 2003. Non-responders to hepatitis B vaccination: A review. *Commun. Dis. Public Health*, 6: 106–12.
- Kwon, S.Y., Lee, C.H. 2011. Epidemiology and prevention of hepatitis B virus infection. *Korean J. Hepatol.*, 17(2): 87-95.
- Lai, C.L., Ratziu, V., Yuen, M.F., Poynard, T. 2003. Viral hepatitis B. *Lancet*, 362: 2089-2094.

- Chathuranga, L.S., F. Noordeen, A.M.S.B. Abeykoon. 2013. Immune response to hepatitis B vaccine in a group of health care workers in Sri Lanka, *Int. J. Infect. Dis.*
- Pankaj Puri. 2014. Tackling the Hepatitis B disease burden in India. *J. Clin. Exp. Hepatol.*, 4(4): 312-319.
- Pavani, K., Srinivas Rao, M.S., *et al.*, 2015. immune response to hepatitis b vaccine in health care workers in tertiary care hospital in south india *Indian J. Microbiol. Res.*, 2(4): 210-213.
- Perrillo, R., Nair, S. 2006. Hepatitis B and D. Chapter 75, pages: 1666-9: Feldman M, Friedman L S, Brandt LJ.(Eds): Sleisenger and Fordtran's Gastrointestinal and liver disease Pathophysiology / Diagnosis/ Management 8th Edition 2006 Saunders Elsevier Inc.
- Platkov, E., Shlyakhov, E., Glick, V., Khalemsky, S., Fischbein, A. 2001. Humoral immune response of hospital employees Induced by a recombinant Hepatitis B vaccine: 5 years after the primary standard immunization. *The J. Preventive Med.*, 9(3): 59-66.
- Thomas, R.J., *et al.*, 2015. Prevalence of non-responsiveness to an indigenous recombinant hepatitis B vaccine: A study among South Indian health care workers in a tertiary hospital, *J. Med. Microbiol.*, 33, Suppl S1:32-6
- Saberifiroozi, M., Gholamzadeh, S., Serati, A.R. 2006. The long-term immunity among health care workers vaccinated against hepatitis B virus in a large referral hospital in southern Iran. *Arch. Iran. Med.*, 9(3): 204-7.
- Sarwat, F., Ajaz, H. and Ayesha, A. 2014. Hepatitis B vaccination status of health care workers and their antiHBs titres - A cross sectional study. *Al Ameen J. Med. Sci.*, 7(3): 217-223.
- Sunita Tripathy., H.C. Sati, *et al.*, 2011. study of immune response after hepatitis b vaccination in medical students and health care workers ISSN- 0301-1216 *Indian J. Prev. Med.*, vol.42 no.3.
- The international classification of adult underweight, overweight and obesity according to BMI Adapted from WHO, 1995, WHO, 2000 and WHO 2004.
- Updated US Public Health Service guidelines for the management of occupational exposures to HBV, HCV, HIV and recommendations for post exposure prophylaxis, *MMWR*, 50: No. RR-11.
- Venters, C., Graham, W., Cassidy, W. 2004. Recombivax-HB: perspectives past, present and future. *Expert Rev. vaccines*, 3: 119–129.
- World Health Organization. 2008. Hepatitis B World Health Organization factsheets 2008. Geneva, World Health Organization, 2010.
- Zeeshan, M., Jabeen, K., Ali, A.N., *et al.*, 2007. 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.*, 7: 120.

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