



# Titres of Antibodies to Hepatitis B Surface Antigen following Hepatitis B Vaccination among Medical Students

Alisha <sup>a</sup><sup>o</sup>, T. A. Dhanalakshmi <sup>a</sup><sup>#</sup> and D. Venkatesha <sup>b</sup><sup>†</sup>

<sup>a</sup> Adichunchanagiri Institute of Medical Sciences (AIMS), B. G. Nagara, Nagamangala Taluk, Mandya District, Karnataka-571448, India.

<sup>b</sup> Department of Microbiology, Adichunchanagiri Institute of Medical Sciences, B. G. Nagara, Nagamangala Taluk, Mandya District, Karnataka-571448, India.

## Authors' contributions

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## ABSTRACT

**Aim:** To estimate antibody titres to Hepatitis B surface antigen (HBsAg) among vaccinated medical students.

**Study Design:** Cross sectional study

**Place and Duration of Study:** Study was done in the Department of Microbiology, Adichunchanagiri Institute of Medical Sciences, B.G. Nagara between October 2019 to November 2019.

**Methodology:** Study included 281 medical students who had taken three doses of Hepatitis B vaccination. Informed consent and Institutional Ethical clearance was obtained. Under aseptic precautions, 5 ml of venous blood was collected and serum was separated by centrifugation at 3000 rpm for 5 min. Serum were stored at -20<sup>o</sup> C. Antibodies to Hepatitis B surface antigen were estimated by Electro Chemiluminescence method (Anti-HBs G2 Elecsys cobas e 100- Roche Diagnostics India Pvt. Ltd.) as per manufacturer's instruction using quality controls.

<sup>o</sup>House Surgeon;

<sup>#</sup>Professor of Microbiology;

<sup>†</sup>Professor and Head;

\*Corresponding author: E-mail: dhanupavan6@gmail.com;

**Results:** In the present study, 98.9% of students had Anti HBs antibody titres >10mIU/ml. Only one (1.1%) student had titre <10mIU/ml. Seventy (77.8%) students had antibody titres >1000 mIU/ml and 15 (16.7%) had antibody levels >100≤1000 mIU/ml. Higher seroconversion rates were noted among female students (100%) but was not statistically significant (P value=0.34)

**Conclusion:** Except for one, all other study participants were found to have protective antibody titres. Vaccination cards containing the vaccination details and the antibody titres should be made available to all medical students to guide infection control practices in case of accidental exposure.

*Keywords: HBV; medical students; vaccination; antibody titres; hepatitis B surface antigen.*

## 1. INTRODUCTION

Hepatitis B virus (HBV) infections are a major serious public health problem worldwide. India belongs to intermediate endemicity zone [1]. Significant number of deaths have been reported due to complications such as chronic hepatitis, cirrhosis and hepatocellular carcinoma [2]. Health care workers (HCWs) including medical students are at high risk of acquiring the infection because of repeated occupational exposure to potentially infectious body fluids in health care or laboratory settings [1,3]. Vaccination is the best effective strategy in prevention and control of HBV infection [2]. Antibody to Hepatitis B surface antigen (Anti HBs) levels >10mIU/ml is considered as protective immunity [4]. Studies done in various parts of the world have reported 12-21% non-responders (antibodies levels <10mIU/ml) to HBV vaccine [5]. Non-responders are at more risk of acquiring infection because of false sense of security after vaccination [6].

Given the high prevalence of HBV infection and its life threatening sequelae, the medical students who are at high risk of acquiring infection, and considering the nonresponse rates observed following primary Hepatitis B vaccination, it becomes very essential to check for antibody titres following vaccination among the medical students so that effective infection control measures and post exposure prophylaxis can be planned in case of non-responders. With this background the present study was carried out to estimate the levels of antibodies to Hepatitis B surface antigen following hepatitis B vaccination among medical students.

## 2. MATERIALS AND METHODS

The present cross sectional study was carried out in the department of Microbiology of tertiary care teaching hospital over duration of 2 months (October 2019 and November 2019).

### 2.1 Sample Size Calculation

Using the formula for infinite population, ( $N = Z^2 pq/d^2$ ), assuming vaccination rate of 59%, confidence interval-95%, power-90% and 10 % non-response rate, the sample size arrived at 297. But only 281 students met our inclusion criteria and were included for the study [1].

### 2.2 Inclusion Criteria

Medical students belonging to phase 2 and Phase 3 MBBS, who had completed 3 doses of hepatitis B vaccination (0,1 and 6 schedule) and who had taken the last dose within 6 months at the time of sample collection were included in the study [6-9].

### 2.3 Exclusion Criteria

Medical students who were Hepatitis B positive, or had history of immunodeficient status, who were on immunosuppressive drugs or who had taken last dose of hepatitis B vaccination beyond 6 months at the time of sample collection were excluded from the study [3,4].

Medical students were explained regarding the objectives and implications of the study. Demographic details were obtained from students. Under aseptic precautions, 5 ml of venous blood was collected and serum was separated by centrifugation at 3000 rpm for 5 min. Serum were stored at -20<sup>0</sup> C. Antibodies to Hepatitis B surface antigen were estimated by Electro Chemiluminescence method (Anti-HBs G2 Elecsys cobas e 100- Roche Diagnostics India Pvt. Ltd) as per manufacturer's instruction using quality controls. Following operational definitions were used:

1. Students who had taken 3 doses of HBV vaccine at 0, 1 and 6 months interval were considered as completely vaccinated.

2. Students with antibody titres  $\geq 10$  mIU/ml were considered as responders
3. Students with antibody titres  $< 10$  mIU/ml were considered as non-responders.

### 2.4 Statistical Analysis

Data was entered into MS Excel and analysed using SPSS software. Categorical variables were expressed as proportions. Significance of categorical variables was tested by Chi-Square test. *P* value less than 0.05 was considered as statistically significant.

### 3. RESULTS

Out of 281 students, 90 (32.3%) had taken the last dose of vaccination within the last six months. Female (67.8%) students constituted

majority of study population (61) and males constituted 32.2% (29). Table 1 shows the age distribution of study population.

Table 1 shows that majority of students belonged to 20 and 21 years age group (33.3% and 28.9% respectively). Table 2 shows the immune response observed among study group.

Table 2 shows that 89(98.9%) of students were responders and one student (1.1%) was a non-responder. All female participants were responders (100%). Table 3 shows the antibody titres observed among study population.

Table 3 shows that, 70 (77.8%) students had antibody titres  $> 1000$  mIU/ml and 15 (16.7%) students had antibody levels  $> 100 \leq 1000$  mIU/ml.

**Table 1. Age distribution of students involved in study**

Age in years	Number of students (%)
19	11 (12.2)
20	30 (33.3)
21	26 (28.9)
22	17 (18.9)
23	3 (3.3)
24	2 (2.2)
26	1 (1.1)
Total	90 (100)

**Table 2. Immune response noted in study participants**

Immune Status	Male No (%)	Female No (%)	Total No (%)	$\chi^2$	<i>P</i> value
Completed three doses of vaccination, last dose taken within last six months	29 (32.2)	61 (67.8)	90 (100)	2.127	0.34
Responder	28 (96.6)	61 (100)	89 (98.9)		
Non responder	1 (3.4)	0	1 (1.1)		

**Table 3. Antibody titre categories and influence of gender on vaccine response**

Response level (mIU/ml)	Total No (%)	Gender		$\chi^2$	<i>P</i> value
		Male No (%)	Female No (%)		
$< 10$	1 (1.1)	1 (3.4)	0 (0)	5.825	0.12
$> 10 \leq 100$	4 (4.4)	3 (10.3)	1 (1.6)		
$> 100 \leq 1000$	15 (16.7)	4 (13.8)	11 (18.0)		
$> 1000$	70 (77.8)	21 (72.4)	49 (80.3)		
Total	90 (100)	29 (100)	61 (100)		

#### 4. DISCUSSION

In the present study, 98.9% of students had Anti HBs antibody titres >10mIU/ml and were responders. Similar findings were reported by others [2,4,6]. Only one student was found to be a non-responder with titre <10mIU/ml. This is in concordance with study by Babbikar et al. [10] Higher non-responder rates were observed in other studies [3,4,11]. In the present study higher seroconversion rates and titres were noted more among female students (Table 2 and 3). However, there was no significant statistical differences ( $P$  value=0.34,  $P$ =0.12 respectively) observed between the genders with respect to seroconversion rates and the antibody titres. These findings are in concordance with the observations seen in other studies [2-4,8,11]. Immune responses to vaccine depends on gender and age. Younger age and female gender mount better immune response. The smoking habits and genetic factors in male may be the probable reasons for poor immune response among males. As majority of study participants belonged to similar age group (19 to 22 years) (Table 1), the influence of age on immune response could not be evaluated in the present study.

Strengths of the study: The present study will guide the vaccination strategies and programmes of the institution as further immunization with second series of vaccination is advised for non-responders. Based on the results of the study, the hospital infection control activities regarding counselling of non-responders about standard precautions and in case of accidental needle stick injuries, the type post exposure prophylaxis can be determined. The study ensures the safety of medical students at workplace and thus, help in decreasing the occupational and nosocomial transmission of HBV infection.

The following are the limitations of the study. The recommended time for post vaccination antibody titre testing is 1 to 2 months of receiving the last dose of primary vaccination, but we included up to 6 months after the final dose of vaccine. We could not match the participant for confounding factors. Screening of participants for Hepatitis B surface antigen and antibodies to Hepatitis B core antigen was not carried out because of resource constraints. Because of non-random selection of participants and relatively small sample size, the results of the study cannot be generalized. The other problem encountered in the study is that, many students were not having

clear cut information about their vaccination in childhood under universal immunization programme. The possibility of non-responders to primary vaccination could not be excluded as childhood vaccination records were not available. There are some reports that the protection afforded by primary HBV vaccination during infancy would last at least for 22 years and that immune memory may be lost with ageing because of immature immune system at the time of primary vaccination in infancy [12]. There is an uncertainty regarding the duration of protection beyond 30 years after primary HBV vaccination. We suggest large scale long term prospective studies to determine the persistence of immunological memory beyond 30 years following primary vaccination so that guidelines can be decided on when to consider either booster dose or revaccination of health care workers.

#### 5. CONCLUSION

Vaccination is the best effective strategy to prevent occupationally acquired HBV infection and its complication among medical students. Except for one, all other study participants were found to have protective antibody titres. Vaccination cards containing the vaccination details and the antibody titres should be made available to all medical students to guide infection control practices in case of accidental exposure.

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#### ETHICAL APPROVAL AND CONSENT

Institutional ethical committee clearance and written informed consent from students were obtained before the study.

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#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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