

## Original Research Article

# A cross-sectional study of post-vaccination anti-HBs titer and knowledge of hepatitis B infection amongst medical students in a metropolitan city

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### ABSTRACT

**Background:** Medical students are at risk of acquiring hepatitis B virus infection due to occupational contact with patients' blood or other body fluids. This study was conducted to determine knowledge of hepatitis B virus infection and anti-HBS antibody titer amongst medical students.

**Methods:** This cross-sectional observational study was conducted on medical students who satisfied the intake criteria and gave written informed consent to participate in the study. After Institutional Ethics Committee clearance, written informed consent was obtained and a structured, pre-validated questionnaire (pre-test) was administered to the participants. After an educational session, an identical questionnaire was administered (post-test). For determining anti-HBs titer (vaccinated participants) and HBsAg (non-vaccinated participants), blood was aseptically collected by cubital venepuncture. HBsAg and anti-HBs antibody levels were determined by immuno-chromatographic assay and enzyme-linked immunosorbent assay, respectively.

**Results:** 140 healthy, HBsAg-negative medical students (79 males; 61 females) participated in the present study. There was increased median correct response in the post-test with increased minimum and first quartile. 91 (65%) who were vaccinated against Hepatitis B were enrolled for anti-HBs titer estimation. There was no significant gender difference in mean antibody titer. 19 (20.9%) had inadequate levels of anti-HBS antibodies. 50% seroconversion was seen after single dose of hepatitis B vaccine.

**Conclusions:** It is essential to delve into the logistic aspects of evaluating all medical students for hepatitis B infection, procuring and offering free vaccination and assessing anti-HBS titer of vaccinated individuals.

**Keywords:** Anti-HBs titer, HBsAg, Hepatitis B infection, Hepatitis B vaccine

### INTRODUCTION

Hepatitis B virus (HBV) infection is one of the major infectious diseases without seasonal distribution.<sup>1</sup> Medical students are at risk of acquiring HBV infection due to contact with patients' blood or other body fluids in healthcare or laboratory settings.<sup>2</sup> In the state of Maharashtra, 85% of medical students are admitted to the

Bachelor of Medicine, Bachelor of Surgery (MBBS) course from various parts of Maharashtra while 15% are admitted through All-India quota. Hepatitis B vaccine is administered under the routine child immunization programme of many Indian states but vaccination coverage is not uniform nationwide. As a consequence, some medical students are either not vaccinated or incompletely vaccinated against hepatitis B infection.

Alternatively, if completely vaccinated (primary vaccination) some students do not take booster dose, leading to inadequate protective titer of anti-HBs antibodies and may harbour a false sense of having immunological protection against Hepatitis B infection. In addition to this, till second year of the MBBS course, the students are not aware about Hepatitis B infection. Individuals who were born before the introduction of routine hepatitis B vaccination are unimmunised, even if they are immunised they are not aware of their anti-HBs antibody titer, the risk of transmission and other high risk procedures that transmit HBV infection. The objective of this study was to assess the level of knowledge of hepatitis B infection amongst medical students and to determine their post-vaccination anti-HBS antibody titer.

## METHODS

This cross-sectional study was conducted in a metropolitan medical college in the State of Maharashtra in Western India. The population under study included healthy, HBsAg-negative medical students from 2nd year MBBS onwards, of either sex, aged above 18 years who gave written informed consent to participate in the study. Those with immune-compromised states or conditions; those on corticosteroids or similar immunosuppressive medications for any reason were excluded from the study. First-year medical students were excluded from the study because hepatitis B and universal safety precaution was not part of their curriculum.

**Knowledge of hepatitis B:** After obtaining clearance from Institutional Ethics Committee, prospective participants were told about the study, its benefits and possible side-effects. After obtaining written informed consent, their demographic and Hepatitis B vaccination profiles were recorded. A structured, pre-validated questionnaire was administered to the participants before they attended a lecture and video session (pre-test). After the educational session, an identical questionnaire was administered (post-test). One mark was given for each correct response and zero mark for each incorrect response.

**HBsAg test and anti-HBs titer:** 5 ml of blood was collected aseptically by cubital venepuncture for determining anti-HBs titer of participants who gave a history of complete or incomplete vaccination. Using the same method, similar quantity of blood was collected for testing Hepatitis B surface antigen (HBsAg) in non-vaccinated participants. HBsAg was tested by immunochromatographic rapid screening (Aspen Laboratories Pvt. Ltd., G.T. Karnal Road, Delhi-110033, India).

Serum was obtained after centrifugation from the samples and stored at -80°C prior to testing. Anti-HBs antibody levels were determined in the serum samples using enzyme-linked immunosorbent assay (ELISA), as per protocol recommended by the manufacturer (Medical Biological Services s.r.l., Opera, Milano, Italy). Anti-HBs antibody titer more than or equal to 10 IU per litre of

serum was considered to be sero-protective and labelled as “adequate titer” for the purpose of this study.<sup>3</sup>

## Operational definitions

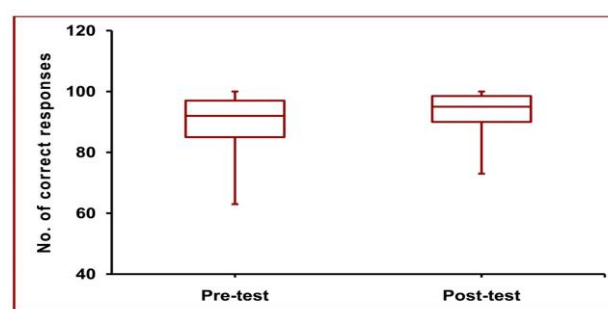
Participants who received three or more doses of Hepatitis B vaccine were considered to be “complete” vaccinated, while those who had received only one or two doses of this vaccine were termed “incomplete” vaccinated. Those who had not received even a single dose of Hepatitis B vaccine were labelled as “non-vaccinated”. When participants reported that they did not know if they had received the vaccine or they did not know the number of doses received, their vaccination status was deemed to be “unknown”. Participants who had taken complete primary vaccination followed by booster dose after 5 years of “complete” vaccination were considered as “booster dose” vaccinated.

## Statistical analysis

The correct responses in the pre- and post-tests were tabulated. Categorical data were presented as frequencies and percentages and continuous data as Mean and Standard deviation (SD). EpiInfo Version 7.2 (public domain software from the Centers for Disease Control and Prevention, Atlanta, Georgia, USA) was used to calculate paired Student’s t-test, Karl Pearson’s Chi-square test (with Mantel-Haenszel correction, where applicable) and Odds Ratio. Statistical significance was taken as p-value<0.05. Percentage distribution was determined for categorical variables, while mean and standard deviation (SD) was calculated for continuous variables. The confidence interval (CI) was stated in the range of [Mean - 2 \* (Standard Error)] to [Mean + 2 \* (Standard Error)].

## RESULTS

A total of 140 students had given written informed consent for participating in the study, of which, only 100 submitted completed pre- and post-test questionnaires. The causes for attrition of 40 students were not completing either pre- or post-test questionnaire and attending the lecture and video session but not filling up the questionnaire.



**Figure 1: Box plot depicting correct responses in pre- and post-tests.**

The box plot (Figure 1) depicts increased median correct responses in the post-test with increased minimum and first quartile, but the maximum correct response in both pre- and post-tests is 100. However, there was no significant difference in correct responses in the pre- and post-test, except for question No. 12 (increased risk of

hepatitis B due to medical or dental procedure), question No. 13 (air-borne transmission of hepatitis B) and question No. 14 (sexual transmission) (Table 1). Majority of students were aware about the vaccination and route of transmission of viruses and clinical presentation associated with HBV infection.

**Table 1: Analysis of correct responses in pre-and post-tests.**

Topic of question	Pre-test (n=100)	Post-test (n=100)	Paired t test (p value)
Hep B vaccination protects from hep B infection	99	100	0.3197
Necessity of anti-HbS titer estimation	90	97	0.1666
Doses of hep-B vaccine for adequate protection	94	99	0.1323
Whether booster dose is required	97	99	0.3197
Whether Hep-B vaccine prevents hepatic cancer	84	96	0.0003
Hep-B is caused by a virus	100	100	0.312
Hep-B is spread by mosquitoes	98	98	0.319
Hep-B is spread through close personal contact	86	93	0.08
Hep-B is spread by sharing injecting equipments	99	99	0.319
Hep-B can be transferred from mother to foetus	97	99	0.319
Hep-B is spread through blood-to-blood contact	98	98	0.158
Medical/dental procedure increases risk of hep-B	83	87	0.033 *
Air-borne transmission of hepatitis B	89	95	0.024 *
Sexual transmission of hepatitis B	65	78	0.021 *
Hepatitis B transmitted by unsterile tattooing	93	94	0.319
Symptoms appear soon after infection	87	88	0.13
Hepatitis B can lead to cirrhosis	92	92	1
Hepatitis B increases risk of liver cancer	95	95	0.56
Person infected with hep-B can be asymptomatic	95	95	0.134
Hep-B +ve persons should not work in health care	75	80	0.79
Hep-B test is done before marriage	69	73	0.25
Pharmaceutical treatment available for the hep-B?	63	83	3.01
Hep-B +ve persons should restrict alcohol intake	90	92	0.4

\* Statistically significant

### **Hepatitis B vaccination and Anti-HBS titer**

140 healthy, HBsAg-negative, medical students (mean age=25.5 years) participated in the present study. 79 (56.42%) were males and 61 (43.57%) were females

(Table 2). The vaccination profile of participants (n=140) is depicted in Table 3. Out of 140 participants, 91 (65%) who were vaccinated against Hepatitis B were enrolled for anti-HBs titer estimation (Table 4). There was no significant gender difference amongst students who had adequate titer.

**Table 2: Gender-wise distribution of participants (n=140).**

Year	Males (n=79)	Females (n=61)	Chi <sup>2</sup> value	p value	Odds ratio
2 <sup>nd</sup> MBBS (n=22)	15	7	1.465	0.226	1.81
3 <sup>rd</sup> MBBS (n=38)	17	21	14.06	0.0002*	0.185
4 <sup>th</sup> MBBS (n=32)	16	16	0.697	0.404	0.714
Interns (n=26)	7	19	11.31	0.0008*	0.215
Residents (n=22)	14	8	0.551	0.458	1.427

\* Statistically significant

**Table 3: Vaccination profile of participants (n=140).**

Year	Vaccinated (n=79)	Non-vaccinated (n=61)	Chi <sup>2</sup> value	p value	Odds ratio
2 <sup>nd</sup> MBBS (n=22)	09	13	2.56	0.11	0.475
3 <sup>rd</sup> MBBS (n=38)	17	21	2.9	0.09	0.522
4 <sup>th</sup> MBBS (n=32)	17	15	0.184	0.668	0.841
Interns (n=26)	14	12	0.087	0.769	0.88
Residents (n=22)	22	0	18.11	0.00002 *	Undefined

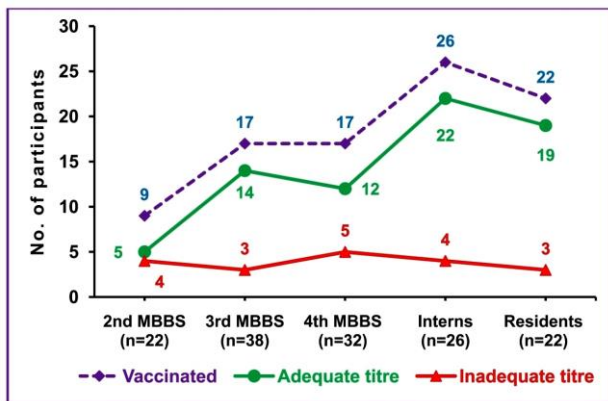
\* Statistically significant

19 participants (20.9%) had inadequate levels of anti-HBS antibodies. Only three participants had taken booster dose after 5 years of vaccination and all of them showed seroconversion indicating and emphasizing importance of booster dose in maintaining adequate Anti-HBS titer for protection against hepatitis B. 2 doses of vaccine can maintain the adequate level of titer in 19 (79.1%) of students. Participants who had single dose of vaccination showed 50% seroconversion (Table 4).

**Table 4: Vaccination profile of participants with adequate anti-HBS titer (n=72).**

Vaccination profile	Number	Percent
1 dose (n=08)	04	50.0
2 doses (n=24)	19	79.1
3 doses (n=53)	43	81.13
3 doses & booster (n=03)	03	100.0
Not known (n=03)	03	100.0

This finding may indicate a misleading interpretation due to inadequate sample size. Seven students out of 13, who had been vaccinated in childhood without any booster dose, had adequate level of antibodies. 13 students did not recollect their date of vaccination but had taken 3 doses of Hepatitis B vaccination and 10 of them had adequate level of antibodies and 3 of them had inadequate level of Anti HBS titer. The distribution of antibody titers in participants is depicted in Figure 2.



**Figure 2: Distribution of anti-HBS antibody titers in participants.**

**DISCUSSION**

In the present study, the mean correct response in the pre-test was 88.61 with SD of 10.98 (CI: 86.41-90.80), while that in the post-test was 92.61 with SD of 7.64 (CI: 91.08-94.13), indicating increase in correct responses in the post-test with reduced dispersion of scores, as compared to the pre-test.

A majority of participants had adequate level of knowledge at the pre-test stage. Significant improvement in post-test responses were observed for question No. 12 (p=0.033), question No. 13 (p=0.024), and question No. 14 (p=0.021) (Table 1).

A cross-sectional study conducted without educational intervention on 111 medical students in Cameroon, Africa, reported adequate knowledge of the risk factors for HBV infection and awareness about the availability of hepatitis B vaccine, but only 44.6% knew details about the vaccine.<sup>4</sup>

**Hepatitis B vaccination and Anti-HBS titer**

Out of 140 participants, 91 (65%) were vaccinated against Hepatitis B. Of these, 56 participants were completely vaccinated, 49 incompletely vaccinated and 35 were not vaccinated at all. The reasons for reduced percentage of complete vaccination (despite awareness) include lack of motivation, non-availability of free vaccine at institutional level, delayed implementation of Hepatitis B vaccination programme in national immunisation schedule and lack of awareness of the distributor of vaccine. The vaccination coverage is the highest amongst residents, followed by interns and final year students (Table 3).

Similar findings were reported by a Brazilian study, in which, the vaccination coverage showed an increasing trend from first-year students (26.0%) to sixth-year students (70.6%) and 48.9% had received 3 or more doses of hepatitis B vaccine, while 31.6% had received two or less doses.<sup>5</sup>

In an African study 18% were adequately vaccinated against HBV, 30.6% were inadequately vaccinated and 51.4% were not vaccinated.<sup>4</sup> Inadequate and non-

vaccination were ascribed to lack of money to pay for the vaccine, information about the vaccine and lack of motivation. Studies have reported varying levels of hepatitis B vaccine coverage - Nigerian medical students (47.7%), Nigerian dental students (37.9%), Palestinian medical students (76.8%) and interns (46.7%).<sup>2,6,7</sup>

Jachuk et al found that 75% of vaccinated individuals had protective seroconversion and that an additional 9% showed seroconversion after the 4<sup>th</sup> dose.<sup>8</sup> A study from Uttarakhand, India, has revealed 100% post-vaccination seroconversion, protective levels of antibody within 5 years of vaccination (88.236%) and even after ten years post-vaccination (85%).<sup>9</sup> A Catalonia-based study on 2,058 participants reported evidence of protective antibody levels in 92.2% within six months post-vaccination.<sup>10</sup>

In the present study, first-year medical students were excluded because hepatitis B and universal safety precaution was not part of their curriculum. However, a Syria-based study compared knowledge of hepatitis B among first and fifth year medical students and advocated routine evaluation of anti-HBS titer among medical students, incorporation of health education and safe clinical practices early in the medical curriculum, and provision of hepatitis B vaccine free of cost to all non-vaccinated clinical-year students and new students during first year of the medical course itself.<sup>11</sup>

The decline in seroconversion in childhood vaccination group in the present study is similar to the findings reported by an Indian study, which found protective antibody levels in 99.9% of participants one year post-vaccination, which decreased to 80.96% by 5 years post-vaccination and further, decreased to 46.16% in 10 years after vaccination. This study recommended the estimation of anti-HBS titer every 5-10 years after the last inoculation in high-risk groups, such as medical students.<sup>12</sup>

The limitation in the present study was that the exposure of participants to blood and body fluids was not studied.

## CONCLUSION

Assessment of cognitive domain revealed reasonably good scores in the pre-test, with improvement in the post-test. Despite high levels of awareness, the percentage of complete vaccination against hepatitis B was inadequate among the participants. It is necessary to include various aspects of universal biosafety precautions early in the MBBS course.

Moreover, this information needs to be reinforced periodically up to the level of interns and residents. Besides, it is necessary to explore the logistic aspects of evaluating all medical students for hepatitis B infection (anti-core antibodies /HbSAg titer), procuring and

offering free vaccination and assessing anti-HBS titer of vaccinated individuals.

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