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**Dr. Shan Damrolien**  
Assistant Professor of  
Microbiology Department,  
Regional Institute of Medical  
Science, Lamphelpat, Imphal  
West Manipur, India

**Dr. Yumlembam Bishwabati Devi**  
Microbiology Department,  
Regional Institute of Medical  
Science, Lamphelpat, Imphal  
West Manipur, India

**Dr. Khuraijam Ranjana Devi**  
Microbiology Department,  
Regional Institute of Medical  
Science, Lamphelpat, Imphal  
West Manipur, India

**Dr. Robert Sawian**  
Microbiology Department,  
Regional Institute of Medical  
Science, Lamphelpat, Imphal  
West Manipur, India

**Corresponding Author:**  
**Dr. Shan Damrolien**  
Assistant Professor of  
Microbiology Department,  
Regional Institute of Medical  
Science, Lamphelpat, Imphal  
West Manipur, India

## Seroconversion among healthcare workers vaccinated with hepatitis B vaccine of RIMS Hospital, Imphal, Manipur

**Dr. Shan Damrolien, Dr. Yumlembam Bishwabati Devi, Dr. Khuraijam  
Ranjana Devi and Dr. Robert Sawian**

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### Abstract

Hepatitis B, caused by hepatitis B virus (HBV) is a vaccine preventable disease. Health care workers are at high risk of HBV infection due to their exposure to infectious materials. Anti-hepatitis B surface antigen antibody (Anti HBs) titre of 10 IU/mL indicates protection.

**Aims:** To determine the antibody titre among health care workers of RIMS Hospital, Imphal.

**Settings and Design:** Cross-sectional study

**Methods and Material:** Blood samples were collected from 164 health care workers vaccinated with hepatitis B vaccine and anti HBs titre was estimated by ELISA.

Statistical analysis used: Descriptive and inferential statistics. The quantitative variables were expressed as mean and standard deviation while categorical variables were expressed as percentage. Odds ratio was used for calculation of protective antibody titre. Association between antibody titres and time since vaccination was analysed using Pearson correlation.

**Results:** Protective titre seen in 130(79.26%) participants while non-protective titre is seen in 34(20.73%) participants. While only 15.57% of fully vaccinated individuals have non-protective anti HBs titre, 40% of partially vaccinated HCWs do not have protective titre.

**Conclusions:** Completion of a three-dose series of hepatitis B vaccine is important to achieve seroconversion. A second series of vaccine may be recommended for seroconversion failure after the first series of vaccine followed by re-testing of anti Hbs titre. Booster dose is not recommended for seroconverted individuals with low antibody titre.

**Keywords:** Hepatitis B, vaccination, AntiHBs antibody titre, healthcare workers

### Introduction

Hepatitis B virus (HBV), a DNA virus known to cause both acute and chronic liver disease is transmissible from person to person.<sup>1</sup> Routes of transmission include vertical (mother to child or generation to generation through close contact and sanitary habits), early life horizontal transmission (through bites, lesions, and sanitary habits), and adult horizontal transmission (through sexual contact, intravenous drug use, and medical procedure exposure) and are evident to varying degrees in every country. It has been estimated that there are 350 million chronic hepatitis B virus (HBV) carriers worldwide<sup>[2]</sup>. The prevalence of chronic HBV infection continues to be highly variable, ranging over 10% in some Asian and Western Pacific countries to under 0.5% in the United States and northern European countries<sup>[3]</sup>. India accounts for 10-15% of entire pool of Hepatitis B carriers in the world<sup>[4]</sup>. There are varying reports of HBsAg positivity in India ranging from 2-4.7%<sup>[5]</sup>. People who develop chronic HBV infection are at an increased risk for hepato-cellular carcinoma, cirrhosis and death<sup>[6]</sup>.

Health care workers (HCWs) are at significant risk of contracting the virus because of their frequent exposure with patients and/or infective materials from patients. Hepatitis B vaccine is one of the recommended vaccines for HCWs<sup>[7]</sup>. A 3 intramuscular doses regimen (0,1 and 6) is usually followed. However, antibody titre of 10 IU/ml or more is considered protective. This study aims to determine the antibody titre among HCWs of RIMS Hospital, Imphal.

### Materials and Methods

A cross-sectional study was conducted by the Department of Microbiology at Regional

Institute of Medical Sciences, Imphal, Manipur for a period of five months from May 2020 to February 2021. The protocol was approved by Institutional Ethics Committee. Written informed consent was obtained from all the subjects. Doctors, nurses, medical students, interns, postgraduates, nursing students, technicians, and housekeeping staffs who have been vaccinated irrespective of the number of doses received were included in the study. Exclusion criteria include un-vaccinated HCWs and those who refused to give consent. A proforma was given to all subjects to capture the demographic details like age, gender, occupation, body mass index (BMI), and hepatitis B vaccination status. Under strict aseptic precautions, 3 ml of venous blood collected from all eligible subjects in plain vials were sent to department of Microbiology. Serum separation was performed by centrifugation of the blood sample at 3000 rpm for 5 minutes at room temperature. Serum thus separated was stored at -80°C until further analysis. The quantification of serum anti-HBs level was done by Enzyme Linked Immunosorbent Assay technique using a commercially available kit (Dia. Pro Diagnostic Bioprobes HBsAb) strictly adhering to the manufacturer’s protocol. Descriptive and inferential statistics were used to analyse the data. The quantitative variables age and time since vaccination were expressed as mean and standard deviation while categorical variables, namely, gender and occupation, were expressed as percentage. Odds ratio was used for calculation of protective antibody titre. Association between antibody titres and time since vaccination was analysed using Pearson correlation. Statistical Package for Social Sciences (SPSS) Version 21.0, manufactured by International Business Management (IBM) Corporation, was used for statistical analysis.  $p < 0.05$  value was considered statistically significant.

**Results**

Out of 164 participants, 73(44.5%) were males and 91(55.5%) were females. Mean age is 32.96 years. Non responders (<10 mIU/mL) constituted 20.73% (n=34) out of which 13(38.23 %) were males and 21(61.76%) were females. 41(25%) HCWs were low responders (10-100 mIU/mL) out of which 18 (43.9%) were males and 23 (56.09%) were females. Significant responders (>100 mIU/mL) constituted 54.26 % (n=89) of which 42 (47.19%) were males and 47(52.8%) are females. Protective titre seen

in 130(79.26%) participants. Non protective titre is seen in 34(20.73%) participants (Table 1).

**Table 1**

Category	N	Male	Female
Non responders	34(20.73%)	13(38.23%)	21(61.76%)
Low responders	41(25%)	18(43.9%)	23(56.09%)
Significant responders	89(54.26%)	42(47.19%)	47(52.8%)
Non protective titre	34(20.73%)	13(38.23%)	21(61.76%)
Protective titre	130(79.26%)	61(46.92%)	69(53.07%)

58.33% (14) out of 24 recipients of single dose vaccine have non-protective titre. 11 HCWs received 2 doses of vaccine and all 11 have protective titre. Of 129 participants who received three or more doses of vaccine, 15.50% (20) of them have non-protective titre and 84.49% (109) have protective titre (Table 2).

**Table 2**

No. of doses	N	Non protective titre	Protective titre
One dose	24(14.63%)	14(58.33%)	10(41.67%)
Two doses	11(6.7%)	0(0%)	11(100%)
Three or more doses	129(78.65%)	20(15.50%)	109(84.49%)

**Table 3**

No. of doses	n	Non responders	Low responders	Significant responders
One	24(14.63%)	14(58.33%)	7(29%)	3(12.5%)
Two	11(6.7%)	0(0%)	32(27.27%)	8(72.72%)
Three or more	129(78.65%)	20(15.50%)	31(24.03%)	78(60.46%)

34.14% (56), 33.53% (55) and 32.31% (53) participants received last dose of hepatitis B vaccine within last 5 years, 5-10 years and more than 10 years respectively. Among those who received last vaccine dose within 5 years, 12.5% (7) have non-protective titre whereas 87.5% (49) have protective titre. 20% (11/55) participants receiving last dose 5-10 years ago have non-protective titre while 80% (44) have protective titre. Lastly, among the 53 HCWs who received last dose of vaccine more than 10 years ago, 30.01% (16) of them have non-protective titre while 69.81% (37) have protective titres (Table 4). The subjects with duration of vaccination ≤ 5 years were 2.3 times protected compared to those with more than 5 years which was calculated using odds ratio.

**Table 4**

Time since last dose	n	Non protective titre	Protective titre	Low responders	Significant responders
<5 years	56(34.14%)	7(12.5%)	49(87.5%)	8(14.28%)	41(73.21%)
5-10 years	55(33.53%)	11(20%)	44(80%)	16(29.09%)	28(50.9%)
>10 years	53(32.31%)	16(30.01%)	37(69.81%)	17(32.07%)	20(37.73%)

**Discussion**

Our study showed 79.26% protective and 20.73% non-protective titres of anti-HBs antibodies respectively among vaccinated participants (HCWs) irrespective of the duration of vaccination. Prevalence of 80.6% protective titre among vaccinated health care workers, which is similar to our study is reported [7]. Iftekhar W *et al*, reported higher prevalence of 89% in a sample size of 56 subjects [8]. 84.49% of HCWs who are completely vaccinated are found to have protective titre irrespective of the duration of vaccination which is lower compared to a study by Lakshmi *et al*, where 93.5% of completely vaccinated subjects have protective titre. This can be explained by the fact that almost one third of

our study subjects received vaccine more than ten years ago. 58.33% of participants who have received only one dose of hepatitis B vaccine have non-protective anti-HBs titre, whereas, only 15.5% non-protective titre is found among those who have been completely vaccinated. Considering the time since vaccination, our study reports protective titre in 87.5%, 80% and 69.81% of participants who received vaccine within last 5 years, 5-10 years and more than 10 years, respectively. Similarly, one study reported protective titre in 88.5%, 84.5% and 58% of subjects within 5 years, 5 to 10 years and more than 10 years of vaccination [10]. Another study reported 92.5% and 83.3% protective titre within 5 years and more than five years, respectively [11].

Pearson correlation indicates negative association of the anti-HBs titres as the time progressed. The titre decreases progressively over time in our study similar to other studies<sup>[10, 12]</sup>. However, it is still debateable whether or not people with low antibody titres require booster dose. Based on current scientific evidence, booster vaccination against hepatitis B for immunocompetent children and adults is not recommended for long-term protection<sup>[13]</sup>.

### Conclusion

We conclude that incomplete vaccination is the major reason resulting in non-protective anti HBs antibody titres. Therefore, completion of a full three dose series is paramount to ensure protection against HBV, especially among high-risk population. Furthermore, we recommend revaccination with a second three-dose series for persons who failed to mount protective titre after the first series of vaccination followed by re-testing of antibody titre to establish non-responsiveness and if non-responsive, alternate protective methods can be adopted. Finally, booster dose is not recommended after seroconversion.

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