Immune Response to Hepatitis B Vaccine in Health Care Workers in Tertiary Care Hospital in South India

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ABSTRACT:
Background: Hepatitis B is one of the most prevalent infectious diseases in the world. Health care workers (HCWs) are at high risk of contracting Hepatitis B virus (HBV) infection. HBV vaccination followed by confirmation of vaccine response aids to reduce the risk of attaining the Hepatitis B infection and decreasing the chances of the spread of the infection from Health care workers into the society.

Aim: The aim of the study is to evaluate hepatitis B virus (HBV) immunization status and anti-HBs titre among HCWs.

Materials and methods: This is a cross-sectional study conducted at the Apollo Institute of Medical Sciences and Research, Hyderabad. 200 Health care workers from different sections who were completely vaccinated with HBV vaccine were included in the study. With due consent, blood samples were collected and tested for antibody to Hepatitis B surface antigen by Chemiluminescent Microparticle Immunoassay from May 2014 to June 2014. Titre ≥10 mIU/mL was considered to be seroprotective.

Statistical analysis: Statistical analysis of data was done in SPSS version 23 and p-value of <0.01 was considered statistically highly significant.

Result: Among 200 HCWs included in the study, 167 (83.5%) were identified as responders to the HBV vaccine and 33 (16.5%) were non-responders. The anti-HBs titres were found to decline with increasing age due to waning immunity. Other risk factors found to be associated with low anti-HBs titres were sex, time since last dose of vaccine and poor life style habits.

Conclusion: All HCWs should receive three doses of the vaccine and be monitored for their immune status 6–8 weeks post vaccination and after every five years. Boosters should be administered to those who lack protective level of anti-HBs antibody.

Key words: Health care workers, Antibody to Hepatitis B surface antigen, Hepatitis B virus, Chemiluminescent Microparticle Immunoassay

INTRODUCTION
Hepatitis B is a serious infectious disease of the liver which affects millions of people worldwide. It is important cause of morbidity and mortality from sequelae which include chronic hepatitis, cirrhosis and primary liver cancer. India has intermediate endemicity of HBV infection, with Hepatitis B surface antigen (HBs Ag) prevalence between 2% and 7%.

Blood contains the highest HBV titres of all body fluids and is the most important vehicle of transmission in the health care setting. 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. Hepatitis B vaccines have proved to be safe, highly immunogenic, and effective in preventing acute and chronic disease.

Post vaccination serologic testing for antibody to hepatitis B surface antigen (Anti-HBs Ab) is recommended 1–2 months after the last vaccine dose for healthcare workers (HCWs) who are at risk for occupational exposures. Studies have demonstrated that HBV vaccine induced protection persists for at least 11 years and booster vaccination for immune competent adults is not recommended for long-term protection. Anti-HBs Ab titres of >10 mIU/mL is considered protective. Anti-HBs titres decline overtime. Immunocompromised patients and high risk groups such as health care workers, should be monitored and a booster vaccinatin is recommended if their anti-HBs Ab levels decrease below 10 mIU/mL. Completely vaccinated HCWs with anti-HBs titres <10 mIU/mL should receive 3 additional doses of Hepatitis B vaccine (with higher dosage of 40µg compared to routine dose of 10µg), followed by anti-HBs testing 1–2 months after the last dose.

Possibilities of non-response to Hepatitis B vaccination might be multifactorial which include increasing age, smoking, obesity, gender and genetic factors. In present study we evaluated hepatitis B immunization status among different categories of HCWs and estimated anti-HBs Ab titres in vaccinated HCWs. This strategy will ensure safety at work place by reducing...
nosocomial transmission and will have cost effective impact at individual and national level, which is much desired in resource limited country like India.

MATERIALS AND METHODS
This cross-sectional study was conducted at Apollo Institute of Medical Sciences and Research, Hyderabad during May and June 2014. The study was approved by the institutional ethics committee. Participants were explained about the study and asked to complete an informed consent form and a questionnaire that included questions on demographics, health history and data related to HBV immunization.

HCWs with history of completed HBV vaccination from different sections of the healthcare setup were included in this study. The subjects included doctors, nurses, technicians, house-keeping staff and medical students.

Inclusion criteria: HCWs with history of completed HBV vaccination from different sections of the healthcare setup were included in this study. The subjects included doctors, nurses, technicians, house-keeping staff and medical students.

Exclusion criteria: HCWs not vaccinated or incompletely vaccinated against Hepatitis B. Interval between last dose of HBV vaccine and sampling was less than 1 month. Health care workers less than 18 yrs and more than 60 yrs age

Quantitative determination of Anti-HBs Ab levels was done by Chemiluminescent Microparticle Immunoassay (ARCHITECT- Abbott Ireland Diagnostic division) using commercial kits. Statistical analysis of data was done in SPSS version 23 and p-value of <0.01 was considered statistically highly significant.

RESULTS
Out of the 354 HCWs included, thirty one subjects did not complete the questionnaire and twenty six were lost to follow up, thereby leaving 297 HCWs. Out of 297 HCWs, 200 participants (18-60 yrs of age) who had received three doses of HBV vaccine according to the standard protocol and the last dose was more than one month from the time of sampling, were eligible to participate in the study. Of the 297 HCWs included, 200 (67.4%) were vaccinated, 66 (22.2%) were unvaccinated and 31 (10.4%) were partially vaccinated. 26 out of 31 partially vaccinated subjects had missed their third dose. Total of 200 health care workers were included in the study. Out of these 141(70.5%) were females and 59(29.5%) males. The median age of study subjects was 27.08 years (range 18-60 years) with 20-30 years being most common age group. Study population includes 26(13%) doctors, 23(11.55%) medical students, 87(43.55%) nurses, 24(12%) technical staff and 40(20%) housekeeping staff.

Out of 200 vaccinated HCWs, 33(16.5%) were non-responders (anti-HBs titres <10mIU/ml of blood) and 167(83.5%) were responders (anti-HBs titres ≥10mIU/ml of blood). Anti-HBs response was good among female HCWs compared to male (P value = 0.009). HCWs were categorised based on age into three groups: ≤ 30, 31-45 and 46-60 yrs. Anti-HBs titres was found to be low in middle age group (Figure-1; P value <0.01). The percentage of responders and non-responders in various occupational groups is depicted in figure-2. HBV vaccine protection rate was found to be higher among nursing staff and the housekeeping workers, followed by doctors (P value = 0.018) (figure-2).

Subjects were divided into three groups based on the time from last dose of vaccine. Group A <5 years post vaccination, Group B 5-10 years post vaccination and Group C >10 yrs post vaccination. Out of the 200 HCWs, 135 had received vaccination <5 years ago, 46 were vaccinated 5-10 years ago and 19 were vaccinated >10 years before the study. Protective titres of anti-HBs Ab (≥10 mIU/mL) were seen in 100% of the cases in the first group (<5 years since vaccination) and 56.5% and 31.5% in the other two groups, respectively (Figure-3; P-value <0.01).

Fig. 1: Anti-HBs response based on age
Fig. 2: Anti-HBs status in different categories of HCWs

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Responder N (%)</th>
<th>Non-responder N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical students</td>
<td>21 (10.5%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Doctors</td>
<td>21 (10.5%)</td>
<td>5 (2.5%)</td>
</tr>
<tr>
<td>Housekeeping</td>
<td>35 (17.5%)</td>
<td>5 (2.5%)</td>
</tr>
<tr>
<td>Nurses</td>
<td>76 (38%)</td>
<td>11 (5.5%)</td>
</tr>
<tr>
<td>Technical staff</td>
<td>14 (7%)</td>
<td>10 (5%)</td>
</tr>
<tr>
<td>Total</td>
<td>167 (83.5%)</td>
<td>33 (16.5%)</td>
</tr>
</tbody>
</table>

Figure 3: Anti-HBs status of HCWs in relation to time since vaccination

DISCUSSION

In present study out of 297 HCWs, 67.4% were completely vaccinated, 10.4% were partially vaccinated and 22.2% were unvaccinated. This observation suggests need for adequate vaccine coverage in high risk groups by creating awareness and formulating good vaccination policies.

In our study out of 200 health care workers (HCW) who participated, 16.5% were non-responders and 83.5% were responders. The percentage of non-responders in present study (16.5%) is in corroboration with previous studies on HCWs from different parts of world like Saberifiroozi M et al (12.7%) \(^7\), Averhoff F et al (12%) \(^9\), Platkov E et al (13.5%) \(^14\) and Zeeshan M et al (14%) \(^16\). Percentage of non-responders in present study (16.5%) was not in corroboration with other recent studies in India by Thomas RJ et al (1.1%) \(^20\) and Sarwat F et al (65%) \(^21\). Higher rate of non-responder in present study compared to study by Thomas RJ et al (1.1%) \(^20\) could be due to non exclusion of non-genetic risk factors like smoking, obesity, chronic medical conditions, malnutrition and stress. These non-genetic risk factors have been implicated as possible cause for non-response \(^7\).

The percentage of male non-responders (27.1%) was more than female counterparts (12%) and similar findings were reported in other studies \(^11\). The reason for increased nonresponsiveness in males could be life style factors. Immune response was found to be highest in younger HCWs (< 30 years), which started to decline with increasing age (P-value: 0.009) and similar observation was made in other studies \(^16\). This observation suggests that with increasing age the rate of seroprotective antibody response to vaccination decreases.

The category of HCWs in whom the anti-HBs titres were >10 mIU/ml and provided protection was the nursing staff and the housekeeping workers, followed by doctors. Poor response in doctors could have been due to more time since vaccination (>10yrs) compared to nurses and housekeeping workers. Poor response in technical staff might be because of high age at vaccination (> 40 years) wherein rate of seroconversion to vaccine is less.

Protective titres of anti-HBs Ab (≥10 mIU/mL) were seen in 100% of the cases in the group A (<5 years since vaccination) and 56.5% and 31.5% in the other two groups, respectively. Seroprotection rates must have decreased significantly with increasing time from last vaccination due to waning anti-HBs titre over time. This finding is in concordance with Sukriti et al \(^17\) and Mahawal et al \(^18\).

As part of present study, we have educated our HCWs regarding the importance of screening for anti-HBs titres to decrease the risk of HBV infection and also identified sections of the HCWs that had not been vaccinated previously despite being at a high risk of contracting the infection.
There is need for educational and training programmes, well formulated policies for HBV vaccination and screening for anti-HBs titres for various categories of HCWs in order to further decrease the risk of HBV infection. Hospital waste management is an important aspect in preventing the infection which should not be overlooked.

**CONCLUSION**

We conclude from the present study that in all health care institutions, personnel responsible for infection prevention and control should identify the staff whose work-related activities involve exposure to blood or other potentially infectious body fluids in a health-care, laboratory, public safety, or institutional setting (including employees, students, attending clinicians, emergency medical technicians, nurses and housekeeping etc.); provide education to staff to encourage HBV vaccination; and implement active follow-up, with reminders to track completion of the vaccine series. Post-vaccination estimation of titres 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 should be given additional doses.

Currently, the Occupational Safety and Health Administration (OSHA) has mandated that health care workers be educated about the vaccine and that employers offer it free of charge.

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**Conflict of interest:** No conflict of interest to declare.

**REFERENCES**