# PREVALENCE OF SEROPOSITIVITY AGAINST HEPATITIS B VIRUS IN PREVIOUSLY IMMUNIZED ADOLESCENT CHILDREN

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**ABSTRACT**

**BACKGROUND**

Less is known regarding the duration and long term protection offered by Hepatitis B vaccination and whether there is a need for booster doses of hepatitis B vaccine. This study determines the level of antibodies to Hepatitis B surface antigen and analyses the prevalence of seropositivity.

**METHODS**

A total of 30 children in the age group of 10-15 years were included for anti-HBs titres assessment. All were vaccinated for hepatitis B (3 doses) during infancy.

**RESULTS**

Only 30% of the children had anti-HBs titres in the protective range, majority are between 10 and 100 mIU/mL. Remaining 70% of the children had anti-HBs titres in the subprotective range (less than 10 mIU/mL).

**CONCLUSION**

This small study warrants further research on the necessity of booster doses of Hepatitis B and seroprotective levels of titres in Indian population.

**KEYWORDS**

Hepatitis B Vaccine, Seropositivity, Adolescents.

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**INTRODUCTION:** India is a country with intermediate prevalence of Hepatitis B infection. The Hepatitis B virus apart from causing a serious infection which may be fatal also causes a chronic carrier state and also increases the risk of cirrhosis and hepatocellular carcinoma.[1] The Government of India with a view to bring down the incidence of this infection has introduced the Hepatitis B vaccine in the national immunisation schedule. There are around 110 countries which have included the vaccine in their vaccination schedules. The introduction of the vaccine has brought down the incidence of the disease and also the incidence of cirrhosis and hepatocellular carcinoma.

The longterm effects of the vaccination and the need for further boosters are still under study and various studies have given a wide range of results.[2,3,4,5,6,7] While some studies say the anamnestic response is good and rule out the need for boosters,[2,4,5,6] some have come out that the anamnestic response may not be so good in all the vaccines and stresses the need for pre-vaccination testing and booster doses.[7,8] There are no studies from India in this regard. This study tries to throw light on the protectiveness and seropositivity of the Hepatitis B vaccine in the Indian children aged 10–15 years who were vaccinated with the three primary doses of the vaccine before 1 year of age. This study may be a starting point for further studies in this regard from India.

**MATERIALS AND METHODS:** This descriptive, hospital-based study was done at PSG Hospitals, Coimbatore, India during September 2014 to August 2015. Institutional human ethics committee approved the study. Children aged 10-15 years who had received three hepatitis B vaccination doses before one year of age and who had records of the same were recruited for the study. Since this was a pilot study a convenient sample of 30 subjects were included for final analysis from 40 recruits. Records were verified for the immunisation status and confirmed. After getting proper consent for the study from the parent and obtaining assent from the children, 3 mL of blood sample was taken and anti-HBs levels were determined by Chemiluminescence immunoassay technique. Children with history of Hepatitis B infection, Hepatitis B infection in the parents, children with chronic renal failure on dialysis, history of blood transfusion and immunocompromised children status were excluded from study. A total of 30 samples were collected for study purpose. An anti-HBs level of ≥10 mIU/mL was considered to be a protective antibody level. Children with values <10 mIU/mL were considered to have inadequate antibody titres.

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Data were collected and stored in Microsoft Excel and results were given in proportions.

**RESULTS:** Out of the 30 subjects included in this study, 14 were males (table-1). The mean age was 12.2 years (Figure-1). Of the 30 subjects, 9 had anti-HBs levels greater than 10 mIU/mL (30%) out of which 5 had titres between 10 and 100 mIU/mL (Figure-2). These 30% are considered to be having protective titres. The rest 21 have titres less than 10 mIU/mL and are considered to have inadequate protective antibody levels (70%). One subject had a titre of 0 mIU/mL. Hence, among the study population of 30 children aged 10 to 15 years who were vaccinated for hepatitis B during infancy, only 30% had protective titres of anti-HBs antibody. Of the 9 subjects who had protective levels of anti-HBs antibody, 4 were males and 5 were females (Table 1). Of the protected, 1 was in the age group on 10–11 years, 4 between 11–12 years, one between 12–13 years, 2 between 14–15 years and one was between 15–16 years (Figure 2).

| Subjects (n=30) | Anti-HBs >10 mIU/mL | Anti-HBs <10 mIU/mL |
|---|---|---|
| Male (n=14) | 4 | 10 |
| Female (n=16) | 5 | 11 |

***Table 1: Sex wise Distribution of Subjects and anti-HBs Titres***

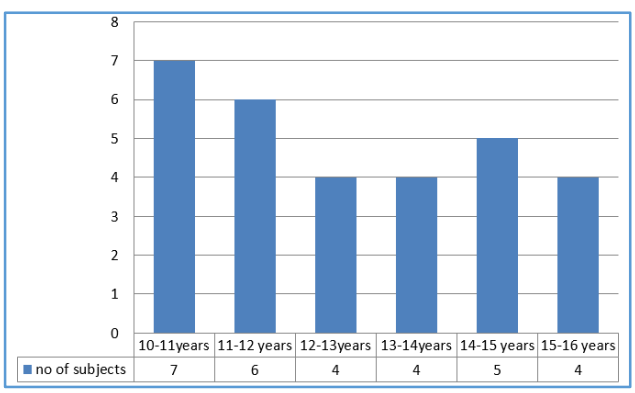


***Figure 1: Age wise Distribution of Subjects***

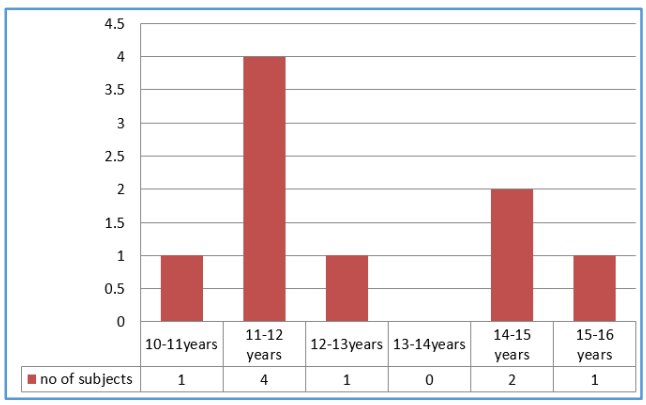


***Figure 2: Age wise Distribution of Protective anti-HBs titres (>10 mIU/mL)***

**DISCUSSION:** This study aimed at finding out the protectiveness against hepatitis B infection 10-15 years after complete vaccination and whether there is a need for further booster doses. Though there are only a very few studies available in this regard, none has come out from India. The studies from various regions have found out a variable percentage of protection by estimating the anti-HBs levels in the serum.[2,3,4,5,6,7] Since the vaccine failure has a genetic determinant also, it is necessary to know the protective levels of anti-HBs in Indian children ten years after completing the three doses of hepatitis B vaccine.

Our study has found that only 30% of the children who have completed the three doses of vaccine at infancy have protective titres of anti-HBs antibodies after 10 years of age. This is lower than the percentage of protection found in many studies.[2,4,5] Table-2 gives comparison of seroprotection against Hepatitis B across various countries.

| Sl. No. | Study done by | Place | Year | Age group | Protection percentage |
|---|---|---|---|---|---|
| 1 | Reza Norouzirad et al | Iran | 2011 | 1-18 years | 40.10% |
| 2 | Amy B. Middleman et al | Houston | 2011 | 16-19 years | 24% |
| 3 | E. Spada et al | Italy | 2014 | 10-17 years | 60.30% |
| 4 | Hiva Saffar et al | Iran | 2014 | 20 years | 42.60% |
| 5 | Paul K. S. Chan | China | 2010 | 17-23 years | 18.90% |
| 6 | Hammitt et al | Alaska | 2007 | 14-15 years | 5% |
| 7 | Present study | India | 2015 | 10-15 years | 30% |

***Table 2: Seroprotection against Hepatitis B 10 years after Primary Vaccination***

A study from Ahvaz city in Iran by Reza Norouzirad et al evaluated the anti-HBs levels in 840 healthy individuals in the age group between 1 and 18 years who were vaccinated during infancy.[2] The percentage of study group who had protective levels of anti-HBs (>10 mIU/mL) 1 year after vaccination was 90%. The average number of subjects having protective levels of antibody titres between 1 and 5 years was 72.1% which declined to 40.1% in the age group between 11 and 15 years. In another study among 420 healthy children aged 16 to 19 years in Houston metropolitan area by Amy B. Middleman et al, it was found that only 24% of the children had anti-HBs levels in the protective range

>10 mIU/mL.[3] But this study further checked the anamnestic response by giving one booster dose of Hepatitis B vaccine and re-checking antibody titres. 92% of children in the study group developed protective antibody titres after receiving one booster dose of the Hepatitis B vaccine. This study thus concluded that though the antibody levels were less, there was an intact immune memory which was responsible for the rapid response after receiving the booster dose of vaccination. The study also compared two groups of vaccinees – one in whom the first dose of Hepatitis B vaccine was given within 7 days and another group in whom the first dose was given after one month and found statistically significant variation in the baseline anti-HBs antibody values between the two groups with the early vaccinated group having decreased titres. This is of interest to us because many of our children are given the first dose of Hepatitis B vaccination at birth.

In a study in Italy by E. Spada et al, 571 teenagers were included and their anti-HBs levels were tested at 10 and 17 years of age.[4] 60.3% of the subjects had protective antibody levels to HBsAg. Out of the remaining 227 subjects, 199 were administered a booster dose of Hepatitis B vaccine. The protective levels of antibody were found in 72.9% subjects at 17 years which included the persons who received the booster dose of the vaccine. Out of the 155 subjects who had anti-HBs levels <10 mIU/mL, 96 were given booster dose of the vaccine to which all except two responded. The remaining two subjects received also responded after three doses of the vaccine. This study also concludes that though the antibody titres may be less, the immune response is good after a booster dose.

Saffar et al conducted a study in Iran in which 176 individuals vaccinated for Hepatitis B at infancy were administered one booster dose of Hepatitis B vaccine at 20 years of age.[5] Pre-booster anti-HBs values and the pre and post booster cytokine values were taken. It was found that only 42.6% had protective pre-booster values of anti-HBs of more than 10 mIU/mL. Among the non-protected, the cytokine values showed a two-fold increase after a booster dose in around 80% of individuals confirming preserved cells mediate immunity.

The effect of giving three doses of boosters was studied in a study conducted in China by Paul K. S. Chan which found that out of 212 students aged 17 to 23 years, only 18.9% had protective anti-HBs titres. One month after a single booster, this went up to 85.5% and after three booster doses, this number reached 100% with 97.1% having anti-HBs titres above 100 mIU/mL.[6] This study demonstrates a declining immune memory in a substantial group of individuals and the requirement of three doses of booster vaccination to achieve protective antibody titres. This study recommends pre-booster testing of anti-HBs titres and vaccinate accordingly.

These studies give a wide range of protection against Hepatitis B infection and the durability of this anamnestic response is not completely understood. A variable proportion of the vaccinated persons over a period of time lose both the protective antibody titres and the anamnestic response. The 30% protective efficacy obtained in our study is line with that obtained in many of the studies. The low levels of protection in the present study may be due to genetically determined lack of response to vaccination or due to technical errors such as intragluteal injections and inappropriate storage conditions. Some of the studies have assessed the immune memory by giving a booster dose of Hepatitis B vaccine and found that most of the subjects had a good immune memory and responded very well to a single booster dose of the vaccine.

Interestingly, there is a study from Alaska which gives a considerably lower percentage of anamnestic response. This is particularly significant since this study included a significant number of American Indians along with Alaskan natives.

One of these studies included 37 children who were vaccinated with all three primary doses of Hepatitis B before 1 year and who had documented anti-HBs titres >10 mIU/mL before 18 months of age.[7] The anti-HBs levels of these subjects were done at 14 to 15 years of age and it was found that only 5% had protective levels of anti-HBs. The subjects with anti-HBs antibody levels <10 mIU/mL were boosted with a dose of vaccine and the titres of anti-HBs rechecked after 15 days. Anamnestic response to booster dose was only 51%.

The difference in the protective titre levels of antibodies in different populations studied, the waning of anamnestic response with age in certain populations and lack of studies in the Indian population warrants further studies in this regard. Our study gives a protective level of antibodies to HBs in only 30% of the studied subjects who completed three doses of Hepatitis B vaccine before one year of age. A larger study with a larger sample and also studies assessing the anamnestic response is required in Indian population to find out the necessity of booster doses in the general Indian population.

The study also exposes the need for testing anti-HBs titres and the need for booster doses of vaccination. If not possible in all, at least in the more vulnerable groups like health care workers and contacts of HBsAg positive individuals. First of this kind of study among south Indian population, estimating the protectiveness and seropositivity of the Hepatitis B vaccine is the major strength of this study. No estimation of HBsAg antigens and core antibodies levels and small number of subjects were limitations of the study.

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