ORIGINAL ARTICLE

Frequency to Anti-HBS Antibody Sero-Positivity (> 10 mIU/ml) in Children Aged 5-10 Years after Hepatitis B Vaccination in Infancy

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ABSTRACT

Objective: To determine the frequency of anti-Hepatitis B Surface antibody (anti-HBS antibody) seropositivity (≥ 10 mIU/ml) in 5-10 years old children after hepatitis B vaccination during infancy.

Study Design: Cross-sectional study.

Place and Duration of Study: This study was conducted in the Pediatrics Department, Combined Military Hospital (CMH) Rawalpindi, Pakistan from 16th May 2020 to 16th November 2020.

Methods: Patients aged 5-10 years, irrespective of gender, and who completed vaccination of hepatitis B during infancy were included in this study. Parents of patients who refused to consent and were without complete immunization of hepatitis B during infancy were excluded. Blood samples were taken for anti-HBS antibody titer. Patients with anti-HBS antibody levels ≥ 10 mIU/ml were considered to have a positive response to vaccination. The patients whose anti-HBS titer was < 10 mIU/ml were considered to have the negative response to immunization against hepatitis B. Data were entered using the proforma.

Results: A total of 343 cases were enrolled. The mean age was 7.46 ± 1.80 years (minimum was five and maximum was 10 years). About 47.8 % of cases had titer less than 10, 43.1 % had equal to or more than 10, and 9 % had Titer equal to or more than 100. 52.2 % had immune status positive, and 47.8 had negative status.

Conclusion: Although the majority of our cases were immune to HBV infection, the difference was only minor compared to the numbers in the non-immune group. After EPI vaccination, the immune status was found to be more retained in the females than in the males.

Keywords: *Children, Hepatitis B Vaccine, Hepatitis B Virus.*

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Introduction

Hepatitis B is an infection caused by hepatitis B virus (HBV), which primarily affects the liver and is potentially fatal. It can lead to chronic infection of the liver, cirrhosis, hepatocellular carcinoma, and death. This virus has affected approximately 257 million people globally and resulted in 887000 deaths due to its complications in 2015 alone.[1] The prevalence of HBV infection is variable throughout the world. However, one study determined that the prevalence of hepatitis B in children in Pakistan is 2.4% and 3.31.[2] Children, in contact the virus, are more prone to have a chronic disease as compared to adults1981. However, it was introduced. The first vaccine against hepatitis B was approved in the United States of America in

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Pakistan in 2009 in an extended program of immunization (EPI). Three doses are given to children in their first year of life at 6, 10, and 14 weeks of age.[3]

Hepatitis B vaccination is 95% effective against hepatitis B infection.[1] The response of the hepatitis B vaccine can be seen after 6-8 weeks of immunization, and the child is considered protected when he has anti-HBS levels $\geq$ 10 mIU/ml. However, few studies have shown that response of vaccination against hepatitis B diminished over time with only one-third of vaccinated children had anti-HBS antibody levels in protective range at the age of 15 years.[4]

Similarly, another study highlighted the fact that although the hepatitis B vaccine confers good protection, the factors leading to decreased immune response should be evaluated.[5,6] Some studies questioned the long-term protection from hepatitis B vaccination in infancy. There has been evidence of loss of anamnestic response with increasing age, and debate is ongoing about whether to have a booster dose during adulthood.[7] Another study conducted in Turkey titerto evaluate the immune response in 2-12 year old children showed that only 66.4% had protective antibody titers.[8]

Pakistan is one of the countries where hepatitis B virus infection is endemic. Vaccinations against hepatitis B started at a larger scale in neonates in Pakistan in 2009.[3] There are no studies available in Pakistan regarding the protective response of hepatitis B vaccination in children. As there is evidence of reduced immune response with progressing age, it is necessary to determine the immune response in Pakistani children.[9] Furthermore, it will help guide the booster dose requirement in adulthood.

Methods

This cross-sectional study was conducted from 16th May 2020 to 16th November 2020 at the Pediatrics Department of Combined Military Hospital Rawalpindi, Pakistan, after taking permission from the hospital's Ethical Review Committee, held on 10th May 2020, vide Committee, held on 10th May 2020, vide permission letter serial no: 442. The sample size of 343 was calculated with a confidence interval of 95.0% and a 5.0% margin of error, taking anti-HBS antibody positivity to be 66.4%.

Patients aged 5-10 years, irrespective of gender and completed vaccination of hepatitis B during infancy, were included in the study. Parents of patients who refused to consent and were without complete vaccination of hepatitis B during infancy were excluded.

Blood samples were taken for anti-HBS antibody titer. Patients with anti-HBS antibody levels $\geq$ 10 mIU/ml were considered to have a positive response to vaccination. The patients whose anti-HBS titer was < 10 mIU/ml were considered to have the negative response to vaccination against hepatitis B. Data were entered using the proforma.

Data was entered, and analyses were done using SPSS version 20.0. Age and antibody titers were expressed as mean and SD. Categorical data such as gender was presented as frequency & percentage. *Chi-square* test was done to assess the relationship between advancing age and immune response positivity, and $P<0.05$ will be considered significant.

Results

A total of 343 patients were enrolled. The mean age was 7.46 ± 1.80 years. The mean Anti-HBS Titer was 24.03 ± 29.032. There were 184 (53.6%) males and 159 (46.4%) females. 191 (55.7%) had an age less than or equal to 7 years, and 152 (44.3%) had an age more than 7 years. (Table-1). 164 (47.8 %) had Titer less than 10, 148 (43.1%) had equal to or more than 10, and 31 (9%) had Titer equal to or more than 100. (Table-2). 179 (52.2%) had immune status positive and 164 (47.8%) had negative status. (Table-3). Stratification of immune status was done with regard to age groups and gender. *P*-values were found to be 0.883 and 0.000, and *Chi-Square* test values were 16.04 and 0.0015, respectively. Thus, the difference in immune status distribution between genders is statistically significant, while the distribution across the two age groups shows no significant difference. (Table-4).

Table-1: Gender and age distribution

Variables		Frequency (%)
Gender	Male	184 (53.6%)
	Female	159 (46.4%)
Age	Mean ±SD	7.46 ±1.80
	≤7 years	191 (55.7%)
	>7 years	152 (44.3%)

Table-2: Distribution of anti HBs titer group among study cases

Anti HBs titer groups (mIU/ml)	Frequency (%)
Less than 10	164 (47.8%)
Equal to or more than 10	148 (43.1%)
Equal to or more than 100	31 (9%)

Table-3: Distribution of immune status among study cases

Immune Status	Frequency (%)
No	164 (47.8%)
Yes	179 (52.2%)

Table-4: Stratification of immune status with regard to age groups and gender

		Immune status (anti HBs titer equal to or more than 10)		*Chi-Square* value	*P*-value
		Yes	No		
Gender	Male	69	115	16.04	0.002
	Female	95	64		
Age Group	Less than or equal to 7 years	92	99	0.0015	0.88
	More than 7 years	72	80		

Discussion

Hepatitis B is a widely spread contagiousdisease. An estimated 350 million chronic carriers of the hepatitis B virus (HBV) worldwide. The overall prevalence of chronic HBV infection ranges from high (>8%), intermediate (2-7%), and low (less than 2%) among different regions.[10] It is a hepatotropic virus that causes immunological anergy in humans and can cause a long-term infection.

Currently, 3.5% of the world's population has been infected with HBV on a long-term basis; despite the fact that the incidence of HBV infections is reduced as a result of vaccination and other measures, to a lesser extent, antiviral therapy used to reduce the load of infected individuals.[10,11]

Vaccine responses are strongly affected by age, especially in young children and the elderly. To counter the infection in newborns, they should be immunized as soon as possible after birth.[12,13]

The study was conducted on 343 cases. The mean age was 7.4606 ± 1.80741 years. The mean anti-HBs Titer was 24.0321 ± 29.03211 (the minimum was 3, and the maximum was 109). 47.8 % had a Titer less than 10, 43.1 % had a Titer equal to or more than 10, and 9 % had a Titer equal to or more than 100. 52.2 % had an immune status positive, and 47.8 had a negative status. Hepatitis B vaccination is 95% effective

against hepatitis B infection. In a study, 20634 tested individuals. The average age at the time of testing was 14.8 years. Average anti-HBs Ab levels decreased to 16.39 mIU/ml in the 15-20 year age group ($P < 0.001$). After 15 years, the proportion of unfavorable outcomes increased progressively ($P< 0.0001$) to 66.7 percent. After a booster dosage, 604 of 644 seronegative individuals (93.8 percent, 95 percent) became seropositive, according to anamnestic assessment response. HBs Ag was found in 91 of the 20,634 samples.[4]

Out of 170 students who were negative for both HBsAg titerand anti-HBs, 44 69 supplied blood samples after the first booster dosage. With anti-HBs levels of 10 mIU/mL in 14.5 percent and 10–100 mIU/mL in 29.0 percent, a three-dose booster was necessary to get 97.2 percent of these participants to achieve an anti-HBs titer > 100 ml U / mL.[7] Indeed, at the age of 15, up to half of the children who had been vaccinated at the time of birth had no anamnestic responses to booster vaccination.

In a study by Gold Y et al. had detectable antibody levels (HBsAb $\geq$ 10 mIU/ml) were seen in 94.0 (77.1%) children as compare to even a high antibody levels (HBsAb titer greater than100 mIU/ml) seen in 59.0 (48.4%) of the youngsters and 38 (22.9%) children had antibodies that were undetectable (HBsAb titer 10 mIU/ml). Once the children were placed in 3 groups based on how long it had been since they had been vaccinated, it showed that antibody levels decreased over time ($P<0.009$).[14] In another study, during the 30 years period, 243 people (56%) reacted to the initial primary series but did not receive any more doses, levels of Anti- HBs of less than 10miU/ml were found in 125 (51%) of the participants.[15]

In one study, Vaccine effectiveness against infection & carriage was 83.4 % and 96.5 %. When limited to primary responders, vaccine effectiveness against disease was similar (85.3%); however, there was a significant effect of maximum antibody concentration. With age, both vaccine effectiveness & anti-hepatitis B surface antibody levels decreased, resulting in 70.9 % (95 percent CI, 60.4 percent -80.5 percent) and 91.1 % vaccination efficacy for infection or carriage in individuals aged 20-24 years, (95% & 75.8 %) respectively. 15.0 years after primary vaccination, less than half of the individuals had detectable anti-HBs.[16]

In our study, immune status was stratified by age groups and gender. The *P*-values were found to be 0.883 and 0.000, respectively.

Conclusion

The majority of our cases were male, with a mean age of 7 years at the time of testing for the efficacy of HBV vaccination. Although the majority of our cases were immune to HBV infection, the difference was only minor compared to the numbers in the non-immune group. Immune status was not associated significantly with increasing age, but it was significant with gender. After EPI vaccination, immune status was found to be more retained in females than in males.Although positive immune status is lower in our age group than in the early years of life, as described in previous literature, the same decreasing trend was not observed in our age group.

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Authors Contribution

AZ: Idea conception, data collection, data analysis, manuscript writing and proofreading

ST: Study designing, data analysis, results and interpretation, manuscript writing and proofreading

AI: Data collection, manuscript writing and proofreading

GJ: Data collection, manuscript writing and proofreading

SH: Data collection, manuscript writing and proofreading

HS: Data collection, manuscript writing and proofreading