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Chapter

Level of Antibody Response against Hepatitis B Virus after Vaccination and Seroprevalence of HBV in Children Addis Ababa, Ethiopia

Habtamu Biazin Kebede and Seifegebriel Teshome

Abstract

Approximately 2 billion people worldwide are infected with HBV and more than 240 million are chronic carriers. The World Health Organization officially launched the introduction of the hepatitis B vaccine for children in 1980. Since then, different countries have determined the level of response to the vaccine. Since the introduction of the vaccine in Ethiopia in 2007, there have been few studies evaluating the antibody response to the HBV vaccine. Therefore, the purpose of this study is to determine the HBV antibody response after hepatitis B vaccination and to evaluate the HBV seroprevalence of children in Addis Ababa, Ethiopia. A cross-sectional study was conducted using a multistage probability sampling technique. Four hundred and fifty children between the ages of five and eight living in Addis Ababa were enrolled. Socio-demographic characteristics were obtained through a structured questionnaire and three to four ml of blood was collected from each child. ELISA was performed to determine antibody levels against HBV. The average age is seven + one (SD) years. Anti-HBs were detected in 54.3% (208/450) of children, and girls 98 (54.7%) had a slightly higher level of protection than boys 110 did (53.9%). The overall coverage rate of the vaccine in this study was 85.1%. The proportion of children with protective levels (> 10 mIU / ml of anti-HBs antibodies) decreased with increasing age of the children: 5, 6, 7 and 8 years were 52.6%, 60%, 43.5% and 37.1%, respectively. The seroprevalence rate for HBsAg is 0.4% and the seroprevalence rate for anti-HBc is 5.6%. Age and antibody response level were negatively correlated ($p = 0.001$), while gender and history of HBV infection were not significantly correlated. Age was also significantly correlated with anti-HBc seropositivity ($p = 0.003$). HBV vaccine coverage for children is high, but the antibody response to the vaccine appears to be low. The seropositivity rate for the virus is also very low. Low levels of response to the vaccine should be a problem. For unresponsive children, revaccination or booster doses should be considered. More research needs to be done.

Keywords: HBV, antibody response level, vaccination status, HBsAg, Anti HBsAg, Anti HBc

1. Introduction

Hepatitis B virus (HBV) infection is a serious global health concern. Around two billion people have been infected with HBV worldwide, and more than 257 million people are currently living with hepatitis B virus infection [1]. There are an estimated 600,000 deaths annually from complications of HBV-related liver diseases [2]. The highest numbers of HBsAg carriers are found in developing countries with limited medical facilities. Endemicity levels of chronic HBV infection are classified as high (>8%), intermediate (2-8%), or low (<2%). Based on this classification, sub-Saharan African countries including Ethiopia are considered regions of high endemicity [1].

HBV infection can be prevented by using the HBV vaccine. HBV vaccine has been commercially avail- able since the 1980s. In 1991, WHO recommended the integration of the HBV vaccine into the national immunization programs and by the end of 2005, the vaccine coverage was 82.3% globally [3, 4]. Hepatitis B vaccine for infants had been introduced in 183 countries by the end of 2013. In 2007, almost all sub-Saharan African countries had Hepatitis B vaccination in their national program [5]. HBV vaccine was introduced into the Ethiopian Expanded Program of Immunization (EPI) in 2007 and national coverage had reached 86% by 2015 [6].

Immune response to the vaccine can be determined by measuring the concentration of antibodies against the HBsAg. Anti-HBs in vaccinated children decline with time, especially during the first few years of vaccination. Most children produce a high concentration of antibodies following vaccination; however, few children can have low or no response to the vaccine. The reason for this low or no response against the HBV vaccine is not well known. However, the site of injection and modes of administration are thought to be critical factors in achieving an optimal response [7]. Data on the level of immune responses against HBV vaccine in Ethiopia is very limited. This study was conducted to contribute to the base- line data needed for further monitoring of HBV vaccination effectiveness in Ethiopia and provides information on the level of immune responses against HBV vaccine among children in Addis Ababa.

2. Patients and methods

2.1 Study area and period

The study was conducted in Addis Ababa, which is the capital city of Ethiopia from April 2016 to May 2017. A total number of 450 children (5-8 years old) were recruited.

2.2 Study design

A prospective cross-sectional study design was used. Healthy appearing 5-8 years old children were included in the study following their parents' consent. Vaccination status was used to include and exclude participants.

2.3 Sample size determination and sampling technique

The required samples size for this study was calculated using 50% of prevalence in vaccine response using the following formula:

$$n = \frac{\left(\frac{Z\alpha}{2}\right)^2 pq}{d^2} \quad (1)$$

where, n = sample size
q = 1 – p
p = proportion
Z = confidence interval.
Using confidence interval of 95%, Z = 1.96

$$N = \frac{(1.96)^2 * 0.5 * 0.5}{(0.5)^2} = 385 \quad (2)$$

The total number of the samples with 10% non- respondents should come to 424. However, just to be safe we collected 450 samples.

2.4 Data collection

There was a structured questionnaire to collect all relevant information about the study participants. After the participant's family agreed to take part in the study, they signed an in- formed consent form. 3-4 ml of blood sample was collected from each child and the serum was separated and stored at -20°C until further use.

2.5 Ethical clearance

Ethical clearance was obtained from the AHRI/ALERT Research Ethics Review Committee and the department of ethical research committee. A support letter was obtained from the Addis Ababa Health Bureau and from the health bureaus of each sub city. Written informed consent was obtained from each participant's parent or guardian before enrollment.

2.6 Data analysis and interpretation

SPSS Software statistical package version 20.0 was used to analyze the data. Association was determined by Chi-square test. P-values less than 0.05 were considered as statistically significant.

2.7 Serological assays

Serum level HBsAg, anti-HBc, and anti-HBsAg were determined using sandwich ELISA, where antigens/monoclonal antibodies were used both for capture and detection. All ELISA experiments were performed using BIO-RAD, Monolisa ELISA test kits, France. The test kits have a high sensitivity and specificity and each test procedure was undertaken according to the manufacturer's instruction based on standard operating procedures.

2.8 Operational definitions

Hepatitis B virus*:* A DNA virus that attacks the liver and can cause both acute and chronic disease.

HBsAg*:* It is the surface antigen of the hepatitis B virus. It indicates the presence of active hepatitis B infection.

Anti-HBsAg*:* An antibody that is produced against HBV infection or vaccination.

Anti-HBsAg: An antibody that indicates previous or ongoing infection with the hepatitis B virus in an undefined period.

3. Results

3.1 Socio-demographic characteristics

The mean age of the study participants was 7 ± 1 (SD) years. Among these, 244 (54.2%) were male and 383 (85.1%) had been vaccinated. Forty-nine (10.9%) children had a history of infectious disease, fifteen (3.3%) had a history of noninfectious disease, while three (0.7%) were HIV positive (**Table 1**).

Characteristics	Categories	Number (n)	Percentage
Sex	Male	204	54.2
	Female	206	45.8
Age	5	95	21.1
	6	130	28.9
	7	124	27.6
	8	101	22.4
Place of birth	Urban	422	93.8
	Rural	28	6.2
Sub city	Gulele	45	10
	Kirkos	92	20.4
	Lideta	313	69.5
History of previous disease status	Yes	66	14.7
	No	384	85.3
	Infectious	49	10.9
Disease type	Non Infectious	15	3.3
	Immunocompromised	3	0.7
	None	383	85.1
Vaccination status	Vaccinated for HBV	383	85.1
	Non vaccinated for HBV	67	14.9

Table 1.
Socio demographic characteristics of children between the age of 5 and 8 years old in Addis Ababa Ethiopia.

Vaccination status	Sex				Total	P value
	Male		Female			
	Frequency	%	Frequency	%		
Vaccinated	204	83.6	179	86.9	383	0.33
Non-vaccinated	40	16.4	27	13.1	67	
Total	244	100	306	100	450	

Table 2.
The coverage of hepatitis B vaccination among 5-8 year-old children in Addis Ababa.

3.2 Vaccination status

383 (85.1%) out of 450 children had received HBV vaccination, of which 99.2% (380/383) of them had received the complete three doses of the vaccination. Only two (0.8%) children among the vaccinated had taken just two doses of the vaccine. There was no one who took only a single dose of the vaccine. The proportion of girls vaccinated (86.9%) is slightly higher than of boys (83.6%) as tabulated in **Table 2**.

3.3 Level of anti HBsAg Ab

Anti-HBsAg concentration > 10mIU/ml was observed in 214 (47.6%) children, six of whom were unvaccinated. Among the 383 vaccinated children, 208 (54.3%) had a protective level of antibody concentration (anti-HBsAg concentration of >10mIU/ml), while the remaining 47.3% did not. Among 67 unvaccinated children, 61 (91%) had anti HBsAg <10mIU/ml. From the three HIV infected participants, two of them were vaccinated. However, they did not have protective level antibody response (anti-HBsAg <10mIU/ml) (**Figure 1**).

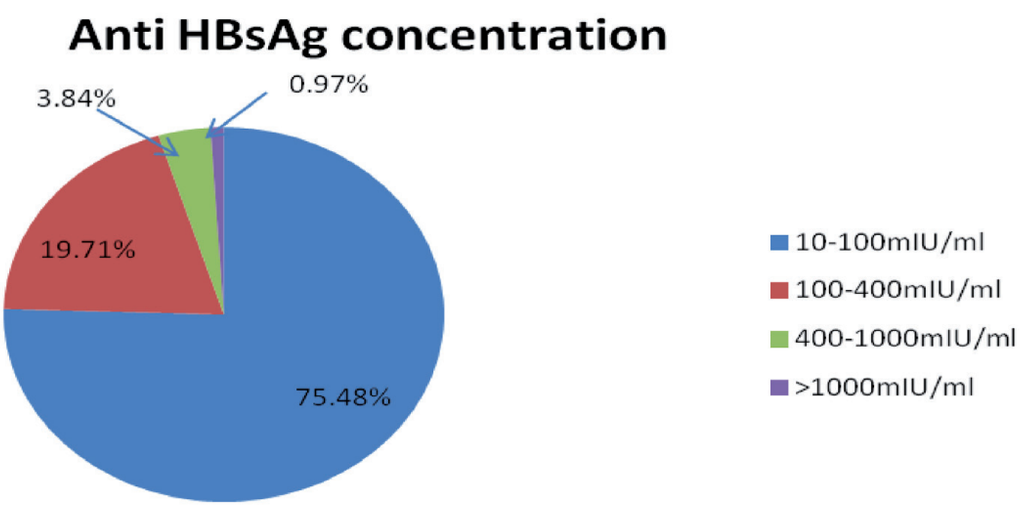


Figure 1.
Antibody response against hepatitis B vaccine in children between 5 and 8 years, Addis Ababa Ethiopia.

Variables	Categories	Number (n)	Percent (%)	P value
Sex	Male	15(244)	6.1	0.551
	Female	10(196)	4.9	
Vaccination status	Vaccinated	10(383)	2.6	0.000
	Not vaccinated	15(67)	22.4	
Age	5	4(95)	4.2	0.03
	6	3(130)	2.3	
	7	5(124)	4.0	
	8	13(101)	12.9	
Previous disease status	Yes	5(66)	7.6	0.438
	No	20(384)	5.2	

Table 3.
Seroprevalence of anti-HBc in 5-8 years old children in Addis Ababa, 2016-2017.

Anti-HBsAg concentration by age: A protective level antibody response against HBV vaccine was observed in 52.6%, 60%, 43.5% and 37.1% of children at the ages of 5, 6, 7, and 8, respectively. There was a significant association between age and the concentration of anti-HBsAg ($p = 0.001$). The levels of antibody concentration decreased as the age of the participant increased.

Seroprevalence of hepatitis B: From 450 children, only two (0.4%) were positive for HBsAg and 25 (5.6%) were positive for anti-HBc. 1 child (0.2%) was positive for both HBsAg and anti-HBc (**Table 3**). The two children who were positive for HBsAg were females, 5 years old, asymptomatic, and vaccinated for HBV.

Among anti-HBc positive children, 15 (6.1%) were male while 10 (4.9%) were female. There was no significant association between sex and anti-HBcAb ($p = 0.551$). Ten (2.6%) of anti-HBc positive children had received vaccination prior to this study. Among non-vaccinated children in this study, 15 (22.4%) were anti-HBc positive. There was a negative correlation between vaccination status and anti- HBc positivity ($p = 0.000$).

The seroprevalence of anti-HBc was 4.2%, 2.3%, 4% and 12.9% in 5, 6, 7 and 8 year old children, respectively. Age was significantly associated with anti- HBc seroprevalence ($p = 0.03$).

4. Discussion

The primary goal of vaccination against HBV is to generate an effective antibody response against the virus. The efficacy of HBV vaccine has not been determined in Ethiopia since its introduction in 2007. HBV vaccine coverage rate observed (85.1%) in our study is comparable with the estimated (86%) national coverage reported in 2015 [6]. Evidence has shown that the immune response against the vaccine decreases with increasing age. Our study observed a similar association between age and immune response against HBV vaccine.

In this study, 54.3% of vaccinated children had protective antibody response, as well as was obtained with low seroprevalence of HBsAg and anti-HBc of 0.4% and 5.6%, respectively. This result is comparable with a study conducted in Yemen and in Iran, where 54.8% and 56.3% of the children had protective antibody responses, respectively [8, 9].

However, in other areas, higher proportions of children were reported with protective level antibody responses in comparison to our study. Studies con- ducted in different areas of Iran observed that 78% of 5-10 years old children [10], 84% of 5 to 7 years old children [11], and 87.6% of under 7 years old children [12] had a protective level antibody response against HBV. A study that was conducted in Spain also revealed that 85% of children at the age of seven had protective level antibody response to the vaccine [13]. The difference in these countries could be attributed to differences in dose, vaccine type, and vaccination route.

In contrast to our study, a lower proportion of children with protective level antibody responses were observed in other studies. For example, in a study conducted in Egypt, 39.3% of the children (6-12 years old) had protective level antibody responses [14]. In addition, in different areas of Iran, only 47.9% of 10-11 year old children [15], 48% of 7 to 9 year old children [16], and 30% of the 8 months to 15-year-old children [17] had between ages of 8 months and 15 years had protective level antibody responses against HBV vaccine. These differences may be due to sampling difference, type of vaccine, and different age for vaccine administration.

Seroprevalence of HBsAg among vaccinated children varies in different countries ranging from 0 to 2.5%. Seroprevalence of HBsAg was 1.8% in Yemen [8], 0.13% in Nepal [18], 2.3% in Papua New Guinea [19], 0.77% in Eastern China [20],

2.5% in northwest China [21], while it was 0.4% in our study. This difference in seroprevalence of HBV infection could be attributed to the difference in vaccine coverage and difference in vaccination schedule.

In our study, seroprevalence of anti-HBc was 5.6%, which is lower than anti-HBc seroprevalence observed in studies conducted in Gambia (17.7%) [22], China (14.1%) [21] and Iran (7.5%) [23]. These discrepancies in anti-HBc seroprevalence could be attributed to age difference, race, prevalence of HBV, and immune response level.

Nowadays, mutant hepatitis B viruses are spreading globally. Vaccination regime and vaccine type should also be considered when we administer the vaccine to the child. High seroprevalence of anti- HBc in vaccinated children may indicate the presence of an occult HBV infection, which is a concern for everyone that needs to be addressed [24].

4.1 Limitations of the study

Some children did not come with their vaccination card. Therefore, we had to use the words of their parents/guardians as evidence for vaccination, which is not always reliable. Other serological markers of active HBV infection, like HBeAg, were not examined in this study. Further, there was an unequal number of vaccinated and non-vaccinated children and the study design did not account for occult infections.

5. Conclusion and recommendation

The vaccine coverage observed in this study is similar to that of the national estimate in 2014. However, less than half of the children had a protective level of anti- body response against HBV vaccine. Further, a negative association between anti-HBsAg antibody concentration and age was observed. Serological markers for hepatitis B virus were low: 0.4% for HBsAg and 5.6% of anti-HBc.

Persistence of anti-HBs antibodies is necessary for the long-term protection against hepatitis B virus infection. Even if different factors can contribute to low antibody response against the vaccine, we need to follow up children after vaccination, in order to see the effect of the vaccine in producing the desired response over time.

Finally, further studies should be undertaken to determine the duration of antibody response against HBV vaccine that may help in which years the vaccine response becomes less and less. For those who did not respond to the vaccine, booster doses should be given to enhance immunological responses to the vaccine. This can be important to elevate the vaccine response. Follow up is needed for those children who are administered with booster doses to evaluate response against the vaccine in those children.

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Conflict of interest

There was no conflict of interest among the authors or with any other parties.

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References

[1] WHO. Fact sheets, Hepatitis B. Accessed on October 9, 2018. Available from: URL: http://www.who.int/news-room/fact-sheets/detail/hepatitis-b. 2018.

[2] Gao S, Duan ZP, Coffin CS. Clinical relevance of hepatitis B virus variants. World J Hepatol. 2015;**7**(8):1086-1096

[3] WHO. Global Alert and Response. Hepatitis B. Prevention and treatment. Accessed by July 2, 2015. Available from: URL: http://www.who.int/csr/disease/hepatitis/ whocdscsrlyo20022/ en/index5.html 2002.

[4] WHO. Global immunization coverage. www.who.int/immunization/newsroom/ Global_immunization data October 2006.pdf.

[5] Françoisa G, Dochezb C, Mphahlelec MJ, Burnettd R, VanHala G, Meheus A. Hepatitis B vaccination in Africa: mission accomplished? The South Afri J Epid and Infect. 2008;**23**(1):24-28

[6] Ethiopia: WHO and UNICEF estimate of immunization coverage: 2015 revision, Available onURL:http//www.data.unicef.org. Accessed on July 2016.

[7] Franco E, Bagnato B, Marino MG, Meleleo C, Serino L, Zaratti L. Hepatitis B: Epidemiology and preven- tion in developing countries. World J Hepatol 2012; 4(3): 74-80.

[8] Al-Shamahy HA, Hanash SH, Rabbad IA, Al-Madhaji NM, Naser SM. Hepatitis B Vaccine Coverage and the Immune Response in Children under ten years old in Sana'a. Yemen: *SQU Med J*. 2011;**11**(1):77-82

[9] Norouzirad R, Shakurnia AH, Assarehzadegan MA, Serajian A, Khabazkhoob M. Serum Levels of Anti- Hepatitis B Surface Antibody among Vaccinated Population Aged 1 to 18 Years in Ahvaz City Southwest of Iran. Hepat Mon. 2014;**14**(1):1-5

[10] Rezaei M, Nooripoor S, Ghorbani R, Ramezanshams F, Mamishi S, Mahmoudi S. Seroprotection after hepatitis B vaccination in children aged 1 to 15 years in central province of Iran, Semnan. J PMH. 2014;**55**:1-3

[11] Yazdanpanah B, Safari M, Yazdanpanah S. Persistence of HBV Vac•cine's Protection and Response to Hepatitis B Booster Immuniza•tion in 5- to 7-Year-Old Children in the Kohgiloyeh and Boyerah•mad Province. Iran. Hepat Mon. 2010;**10**(1):17-21

[12] Esmaili M, Seyedkolal F. Evaluation of anti HBS levels in vacci•nated children against Hepatitis B, Amirkola Hospital, Babol. KAUMS J (FEYZ). 2003;**6**(4):45-49

[13] Gonzalez ML, Gonzalez JB, Salva F, Lardinois RA. 7-year follow-up of newborns vaccinated against hepatitis B. Vaccine. 1993;**11**:1033-1036

[14] Shaaban FA, Hassanin AI, Samy SM, Salama SI, Said ZN. Long term immunity to hepatitis B among a sample of fully vaccinated children in Cairo. Egypt. East Med Helth J. 2007;**13**(4):750-757

[15] Jafarzadeh A, Montazerifar SJ. Persistence of anti-HBs antibody and immunological memory in children vaccinated with hepatitis B vaccine at birth. J Ayub Med Coll Abbottabad. 2006;**18**:4-9

[16] Rafizade B, Kazemi AN, Amir Moghadami HR, MoosaviNasab N. Survey of Anti-HBs Serum Level in Vaccinated 7-9 Year-old Chil•dren in Zanjan City 2004. ZUMS J. 2004;**12**(47):49-55

[17] Aghakhani A, Banifazl M, Izadi N, McFarland W, Sofian M, Khadem-Sadegh A, et al. Persistence of an- tibody to hepatitis B surface antigen among vaccinated children in a low hepatitis B virus endemic area. World J Pediatr. *2011*;**7**(4):358-360

[18] Upreti SR, Gurung S, Patel M, Dixit SM, Krause LK, Shakya G, et al. Prevalence of chronic hepatitis B virus infection before and after implementation of a hepatitis B vaccination program among children in Nepal. Vaccine. 2014;**32**(34):4304-4309

[19] Kitau R, Datta SS, Minal K. Patel MK, Hennessey K, Wannemuehler K et al. Hepatitis B Surface Antigen Seroprevalence among Children in Papua New Guinea, 2012-2013. Am. J. Trop. Med. *Hyg* 2015;92(3): 501-506

[20] Huang P, Zhu LG, Zhu YF, Yue M, Su J, Zhu FC, et al. Seroepidemiology of hepatitis B virus infection and impact of vaccination. World J Gastroenterol. 2015;**21**(25):7842-7850

[21] Ji Z, Wang T, Shao Z, Huang D, Wang A, Guo Z et al. A Population-Based Study Examining Hepatitis B Virus Infection and Immunization Rates in Northwest China. PLoS ONE 2014: 9(5).

[22] Van der Sande MAB, Waight PA, Mendy M, Zaman S, Kaye S, Sam O et al Long-Term Protection against HBV Chronic Carriage of Gambian Adolescents Vaccinated in Infancy and Immune Response in HBV Booster Trial in Adolescence. PLoS ONE 2007; 2(8): e753.

[23] Jafarzadeh A, Montazerifar SJ. Persistence of anti-HBs antibody and immunological memory in children vaccinated with hepatitis B vaccine at birth. J Ayub Med Coll Abbottabad. 2006;**18**:4-9

[24] Zeinab NAS. An overview of occult hepatitis B virus infection. World J Gastroenterol. 2011;**17**(15):1927-1938