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Evaluation of the Effectiveness of Hepatitis B Vaccination in Children Aged 1 to 14 Years in Sulaimani City

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Abstract

Background and objectives: Hepatitis-B virus is one of the most serious and prevalent health problems. Vaccination against Hepatitis-B virus is the most effective way of preventing infection and transmission of the virus. The aim of this study was to assess the effectiveness of hepatitis-B virus vaccination among children in Sulaimani city **Methods:** A cross-sectional study was performed on 384 children aged between 1 and 14 years who received the scheduled 3 doses of hepatitis B virus vaccine in infancy period. Blood samples were taken from all children, and the sera were tested for antibody to hepatitis B surface antigen, antibody to hepatitis B core antigen, and hepatitis B surface antigen using enzyme-linked immunosorbent assay **Results:** Hepatitis B surface antigen and total antibody to hepatitis B core antigen were negative in all children involved in the study whereas antibody to hepatitis B surface antigen was positive (antibody to hepatitis B surface antigen $\geq$ 10 mIU/mL) in 256 (66.7%) and negative (antibody to hepatitis B surface antigen $<$ 10 mIU/mL) in 128 (33.3%) children; (77.3%) of children in the age group 1-5 years were positive for antibody to hepatitis B surface antigen, while the percentage was less (66.7%) in the age group 6-10 years and least (57.9%) in the age group 11-14 years, these differences in the age groups were statistically significant, p value $<$0.02. **Conclusions:** Universal Hepatitis B virus vaccination program provided protection to nearly two thirds of children in Sulaimani city, Kurdistan Region, Iraq, and seronegative antibody to hepatitis B surface antigen exists in different age groups of the vaccinated children.

Keywords: Hepatitis B virus; Vaccination; Sulaimani City; Antibody to hepatitis B surface antigen.

Introduction

Hepatitis B virus (HBV) is one of the most serious and prevalent health problems, affecting more than 2 billion people worldwide[1]. People with hepatitis B are at increased risk of developing hepatic decompensation, cirrhosis, and hepatocellular carcinoma. The estimated worldwide mortality is 0.5 to 1.2 million deaths a year[2]. In 1981, the first hepatitis B vaccine was approved in the United States. It was prepared from the plasma of hepatitis B surface antigen (HBsAg) carriers and was capable of stimulating the production of antibodies against HBsAg[3]. Although highly effective vaccines against hepatitis B virus have been available since 1982, there are still more than 350 million chronic carriers, 75% of whom reside in the Asia Pacific region[4]. The current hepatitis B vaccines are not produced from live viruses; rather they are genetically engineered and manufactured from noninfectious, recombinant DNA for HBsAg[5]. Administration of hepatitis B vaccine to all newborns has been recommended in order to prevent chronic hepatitis B virus (HBV) infection, and the associated disease burden[6]. Vaccination against HBV is the most effective way of preventing infection and transmission of the virus. It has been routinely performed for newborns and high-risk groups since 2001 in Iraq[7].

Hepatitis B virus vaccination at birth prevents perinatal and early childhood infection and is expected to provide protection throughout adolescence and young adulthood, when the chances of exposure to the virus are accentuated due to risky practices, including sexual activity and injectable drug use[8].

In the primary three doses course of immunization (0, 1, 6-month schedule), the first two doses usually suffice to initiate antibody to hepatitis B surface antigen (anti-HBs) production and to prime the immune system for a

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secondary response to antigen. The third dose stimulates this secondary response, anti-HBs titers are higher than those achieved after the first two doses and the antibodies appear in the blood more rapidly[9].

The strength of the immune response following administration of HBsAg, which is the basis of immunization against hepatitis B, has historically been assessed by measuring antibodies against HBsAg[10].

The aim of this study was to assess the effectiveness of HBV vaccination among children in Sulaimani city after primary vaccination with 3 doses during infancy; the response to HBV vaccination was evaluated by measuring the following HBV serum markers: anti-HBs, HBsAg, and antibody to hepatitis B core antigen (anti-HBc).

Patients and methods

A cross-sectional study was performed on children aged between 1 and 14 years who received the scheduled 3 doses of HBV vaccine in infancy period supervised by the health authority in Sulaimani City. The study extended for nearly one year from January 2017 till January 2018.

Children whose immunization status could not be verified or documented and those with partial immunization were excluded. The children with chronic illnesses and those on repeated blood transfusions were not excluded and were counted in the results. Serum samples were taken from 384 children enrolled in the study; stratified sampling method was used to select samples from 34 regions of Sulaimani city (according to the administrative divisions of the city). Sera then stored at -20°C prior to testing for anti-HBs (Foresight HBsAb EIA Test Kit /Acon Laboratories /USA), HBsAg (Foresight HBsAg EIA Test Kit /Acon Laboratories / USA), and anti-HBc (Foresight HBcAb EIA Test Kit /Acon Laboratories /USA) using enzyme-linked immunosorbent assay (ELISA) for all three HBV serological markers. Anti-HBs Abs cut-off of was 10mIU/mL, and results of anti-HBs Abs $\geq$ 10 mIU/mL were considered as positive and the child as immunized.

The laboratory tests were done in the General Public Laboratory/Sulaimani city. In addition to laboratory testing, the children's caregivers were interviewed to collect demographic data and information related to hepatitis B vaccination.

Statistical analysis was done using the Statistical Package for Social Science (SPSS, Chicago, Il, USA), version 16.

Approvals from scientific committee and ethical committee of Kurdistan Board for medical specialties were conducted before starting sample collection. Written informed consent was obtained from the children's caregivers

Results

The number of children enrolled in this study was 384, of which 199 (51.8%) were males and 185 (48.2%) were females. The children were divided into three age groups: 1-5 years, 6-10 years and 11-14 years, the numbers of children were 88, 189, and 107, respectively.

The upper limit of anti-HBs titers in all three age groups was >250 mIU/mL while the lower limit was 1.78 mIU/mL, 1.3 mIU/mL, and 1.5 mIU/mL for 1-5 years age group, 6-10 years age group, and 11-14 years age group respectively.

Most of the children have no chronic illnesses, with no family history of HBV infection, and did not receive blood previously, Table 1.

The results of laboratory testing of HBsAg and total anti-HBc were negative in all children involved in the study whereas anti-HBs was positive in 256 (66.7%) and negative in 128 (33.3%) children.

Upon comparison between children with protective anti-HBs (positive anti-HBs) and children with non-protective anti-HBs titer (negative Anti-HBs) there were no statistical differences between the two groups regarding the presence of chronic diseases, blood transfusion, and gender, Table 2.

The results revealed that (77.3%) of children in the age group 1-5 years were positive for anti-HBs, while the percentage was less (66.7%) in the age group 6-10 years and least (57.9%) in the age group 11-14 years; these differences in the age groups were statistically significant, p-value of 0.02, Table 2.

Table (1): Demographic data of children enrolled in the study

Variable		No.	%
Age	1 - 5 Year	88	22.9
	6 - 10 Year	189	49.2
	11 - 14 Year	107	27.9
Gender	Male	199	51.8
	Female	185	48.2
Chronic illness	Absent	371	96.6
	Thalassemia minor	5	1.3
	Thalassemia major	1	0.3
	Other*	7	1.8
Family history of HBV	Present	5	1.3
	Absent	379	98.7
Blood transfusion	Present	8	2.1
	Absent	376	97.9

* Hemophilia, G6PD deficiency, nephrotic syndrome, tetralogy of Fallot, asthma, epilepsy.

Table (2): Distribution of children according to their anti-HBs positivity

Variable		Protective anti HBs		P-value
		≥10mIU/ml	< 10mIU/ml	
Age	1 - 5 Year	68 (77.3%)	20 (22.7%)	0.02
	6 - 10 Year	126 (66.7%)	63 (33.3%)	
	11 - 14 Year	62 (57.9%)	45 (42.1%)	
Chronic illness	No	249 (67.1%)	122 (32.9%)	0.32
	Yes	7 (53.8%)	6 (46.2%)	
Blood transfusion	No	250 (66.5%)	126 (33.5%)	0.61
	Yes	6 (75.0%)	2 (25.0%)	
Gender	Male	133 (66.8%)	66 (33.2%)	0.94
	Female	123 (66.5%)	62 (33.5%)	

The results of the current study showed a significant negative correlation between the anti-HBs titers and the age of children as demonstrated in Figure 1.

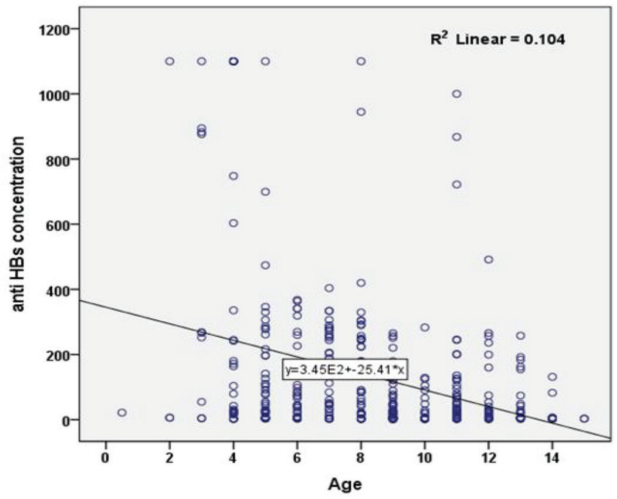

Figure (1): Correlation between ages of children and the titers of anti-HBs Abs in sera of the children (R=0.32).

Discussion

The results showed that none of 384 children enrolled in the current study has evidence of current or previous HBV infection. This perfect result in part reflects an effective vaccination program among children in Sulaimani city; however, sample size may be another factor for negative HBsAg and Anti-HBc. Moreover, HBV infections are, in general, less common among children than adults[11].

Similar to other studies, in our study the distribution of protective anti-HBs titers among males and females was statistically not significant[12-15].

Although all children involved in our study had received the standard vaccination schedule against HBV, only two thirds of them (66.7%) had protective anti-HBs levels (i.e. anti-HBs titer of 10 mIU/ml) while these antibodies had vanished in the remaining children (33.3%), comparable results were obtained by Amy B. et al[15] . Rezaei et al found that among 210 cases, 166 children (79%) had protective anti-HBs level[13].

We found a decline in anti-HBs titers in all age groups and its frequency was more in older children (protective antibody levels were detected in 77.3%, 66.7% and 57.9% of children in the age groups 1-5, 6-10 and 11-14 years, respectively), thus the older the child the more probability to be anti-HBs negative. The decline in antibody titers among the age group 11-14 years should pay attention to the susceptibility of acquiring infection due to risk factors in this age group.

A similar result was obtained by Aghakhani et al who detected protective antibody levels in 65% of children one year after vaccination, which declined significantly over time to 24% in 15 years after vaccination[15]. Gilca et al also found protective antibody levels in 88.2%, 86.4% and 76.7% of cases 5, 10 and 15 years after vaccination[17]. Generally, 3-30% of vaccinated individuals lose their protective anti-HBs titers five years after the hepatitis B vaccination[14]. The type of vaccine used, the amount of antigen delivered and the population immunized might account for the variability in the anti-HBs[18-21].

The results of our study revealed that the duration of protection reflected by the level of anti-HBs titer was dissimilar in different age groups, thus some children below five years who received the full HBV vaccination doses were negative for anti-HBs, while some children with older age groups were anti-HBs positive and vice versa, similar findings were recorded in previous studies[22-24].

Conclusions

In conclusion, universal Hepatitis B virus vaccination program provided protection to nearly two thirds of children in Sulaimani city, Kurdistan Region, Iraq, and seronegative anti-HBs exist in different age groups of the vaccinated children. There is a significant negative correlation between the anti-HBs titers and the age of children. Thus, as the children's age increases, the number of children with protective anti-HBs levels decreases. There is an urgent need to screen all children in Sulaimani city for anti-HBs titers and to provide those with negative titers with booster dose of HBV vaccine, while those with positive titers should be screened periodically for anti-HBs titers.

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