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Assessment of the Effectiveness of Hepatitis B Vaccination among Vaccinated Infants after the first dose

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الملخص:

خلفية: التهاب الكبد الفيروسي البائي هو سبب شائع لعدوي التهاب الكبد الفيروسي، ومنذ بداية برنامج التطعيمات وبرامج الوقاية المختلفة فإن عدد الدول التي كانت مصنفة سابقاً أنها من الدول عالية الانتشار الآن أصبح معدل الانتشار فيها اقل من 8٪. **الهدف**: من هذه الدراسة هو تقويم فاعلية اللقاح ضد فيروس التهاب الكبد البائي واستجابة الأطفال بعد الجرعة الأولي في مدينة بنغازي عام 2022. **المنهجية:** أجريت دراسة وصفية للتصميم المقطعي في مراكز التطعيم ببنغازي، جمعت عينة دم من 43 طفلاً، وأخذت العينة أثناء زيارة عيادات التطعيم أو العيادات الخارجية. قدرت الأجسام المضادة ضد فيروس التهاب الكبد البائي بواسطة اختبار الأليزاELISA . **النتائج:** تراوحت أعمار الأطفال بين شهر إلى شهرين. كان متوسط عيار الأجسام المضادة بعد تلقي جرعة صفرية 18.9 (± 23.6) وحدة دولية / لتر. كان عدد الأطفال الوقائيين 29 من 43 (67.4٪) بجرعة صفرية. **الخلاصة:** أظهرت هذه الدراسة أن جرعة الولادة (جرعة صفر) أعطت مستوى وقائي جيد للرضع حيث كانت الحماية المصلية 67.4٪ بعد هذه الجرعة.

الكلمات المفتاحية: لقاح التهاب الكبد B، عيار مضاد لـ HBs، ELISA، حماية مصلية.

Abstract

Background: Hepatitis B virus is a common cause of viral hepatitis infection. Since the impact of immunization and other prevention programs, the number of countries previously categorized as high prevalence is now estimated to have a population seroprevalence below 8%. **Aim**: This study was done to evaluate the vaccine efficacy and measure the response of children to the vaccine after the first dose of the HBV vaccine in Benghazi-2022. Subjects and **Methods**: A descriptive study of a cross-sectional design was conducted in Benghazi vaccination centers; blood samples were collected from 43 children, and the samples were taken during vaccination visits or at OPD clinics. Anti-HBs titer was estimated by ELISA. **Results**: The ages of the infants in the study ranged from 1-2 months. The mean Anti-HBs titer after receiving zero doses was 18.9 (±23.6) IU/L. The number of protective children was 29 out of 43 (67.4%) at zero doses. **Conclusion:** This study showed that the birth dose (zero dose) gave a good protective level in infants as seroprotection was 67.4% after this dose.

Keywords: Hepatitis B vaccine, Anti-HBs titer, ELISA, seroprotection.

1. INTRODUCTION

The Hepatitis B virus is a common cause of viral hepatitis infection. Chronic HBV infection is a global major public health problem. Approximately two billion people worldwide have been infected with HBV, which is 33% of the world population and between 350-400 million among them are chronically infected, which represents about 5% of the population (1, 2). About four million new infections occur each year according to WHO 2019, HBV kills one to two million people every year because of its complications such as hepatocellular carcinoma and cirrhosis (1). WHO estimates that 296 million people were living with chronic hepatitis B infection in 2019, with about 1.5 million new infections each year [(4)].

Globally, it has been estimated that 45% of the world's population lives in an area of high endemicity [(17)]. There is evidence to suggest that vertical transmission is more common in Asia than in Africa, where a greater proportion of women are highly infectious at childbearing age. The universal infant vaccination was implemented early in these countries and screening of pregnant mothers helps in the reduction of vertical transmission and reduction of hepatitis B disease & its complications [(13)].

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Most infections worldwide are acquired through vertical transmission at birth, also through horizontal transmission to/between young children, sexual contact between adults, injecting drug use [(14)], contaminated blood or blood products and unsafe medical practices [(15,16)].

Since the impact of immunization and other prevention programs, the number of countries previously categorized as high prevalence is now estimated to have a population seroprevalence below 8 % [(5)]. Vaccination against hepatitis B is the key preventive step in eliminating the infection and it has been proven to be a powerful and useful method for preventing HB infection and giving good protection for infants and children [(1,3)]. WHO recommended that all infants receive the HBV vaccine as soon as possible after birth- within 24 hours- even in low-endemicity countries. The birth dose (zero dose) of the HBV vaccine is a monovalent HBV vaccine containing only HBsAg and it is required for effective post-exposure immunoprophylaxis to prevent prenatal HBV infection, especially for an infant born to an HBsAg-positive mother [(11)].

In July 2016, the WHO announced its new Global Health Sector strategy on viral hepatitis in 2016-2020, outlining a plan to reduce transmission of all hepatitis viruses and their disease burden. This plan aimed for a 30% decline in new HBV infections and also in HBsAg prevalence in children of no more than 1% by 2020, and by the year 2030, a 90% decline in new

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infections with prevalence in children of no more than 0.1% [11,8].Hepatitis B in Libya remains a significant communicable disease because the estimated number of chronic HBsAg carriers in Libya is between 120,000 and 150,000 individuals, and infections have occurred mostly among high-risk behavior people [6,7]. According to the latest WHO data published in 2019 hepatitis B deaths in Libya reached 0.08% of total deaths and the prevalence of the disease was 2.2 % [4,6], therefore Libya is considered an area of intermediate endemicity for hepatitis B infection [6,7,9,10].

In Libya, the HBV vaccine was introduced into infant immunization schedules by the Ministry of Health in 1993. Subsequently, children born in 1991-92, and 1989-90 were vaccinated by the vaccination campaigns in 2005 and 2006 respectively. Vaccination schedules in Libya follow the recommendations of the WHO and the Advisory Committee on Immunization Practices (ACIPI2005): the zero dose at birth (monovalent), the first dose at 2 months, and the second dose at 4 months, the last dose at 6 month age (hexavalent); the duration of protection provided by the vaccine is unknown [5]. This study was done to evaluate the vaccine efficacy and measure the response of children to the vaccine after zero doses of the HBV vaccine.

2. SUBJECTS AND METHOD

Study design: This study was an observational descriptive study of cross-sectional design.

Study sample and settings:

The study populations were children from the city of Benghazi; a purposive sample of children included in this study who were vaccinated, or in their usual vaccination visit with hepatitis B vaccine according to the Libyan immunization schedules.

The study was conducted in four public vaccination centers randomly selected in Benghazi; Salawi, Benghazi Algadeda, Allethi Medical Center and the 23rd of July Clinic, in addition to Benghazi Children's Hospital. All parents gave informed consent regarding the study directly before enrollment.

The data was collected from the 1st of January to the 11th of April in 2021. Blood samples were collected in this study from 43 children at two months of age after receiving the zero dose and before taking the first dose. The response and concentrations of Anti-HBs titer were detected.

Laboratory Method

Sample collection: 43 blood samples (3-5ml) were collected by venipuncture in accordance with a standard medical technique.

Identifications Method: Enzyme Linked Immuno Sorbent Assay (ELISA). The study used the HBsAb ELISA Quantitative Kit, manufactured in CHINA.

Interpretation of Results and Quality Controls

The results were taken from the dual filter plate reader (Diareader), then the average read relative absorbance value (optical density) was calculated for each set of reference calibrators and samples from the print report of microplate reader, the absorbance (OD) for each calibration standard on the Y axis versus the corresponding anti-HBs concentration on the X axis was plotted on logarithmic paper and the standard curve through the plotted points was drawn(Figure1).

To determine the concentration of anti-HBs for an unknown, we located the OD for each unknown on the Y- axis of the graph, found the intersecting point on the standard curve, and read the concentration from the X-axis of the graph.

Table 1: Readings of optical density of our standards and kit standards

Standards	Mean OD (kit)	Mean OD (our results) Two reading
0 IU/L	0.05	0.111/0.052
10 IU/L	0.186	0.135/0.164
20 IU/L	0.380	0.284/0.341
40 IU/L	0.770	0.550/0.650
80 IU/L	1.42	0.902/1.00
160 IU/L	2.249	2.185/2.515

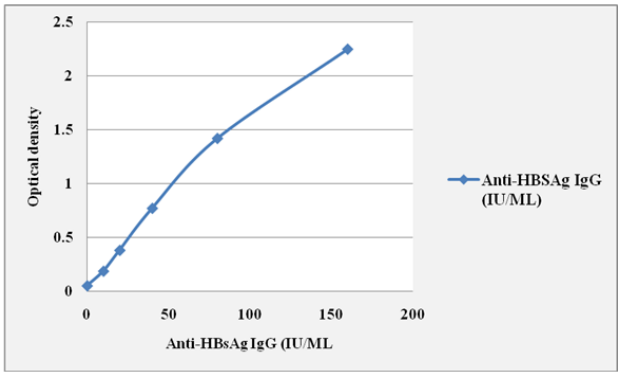


Figure 1: Optical density and anti-HBs Ag IgG

3. RESULTS

Statistical analysis of data:

Data from this study were entered into and analyzed using SPSS version 25 for Windows. Continuous variables were presented as means, standard deviations, minimum and maximum. Categorical data were presented as counts and percentages. Comparisons were done if needed using inferential tests such as the t-test for comparing means for continuous data. The chi-square test or Fischer`s exact was used for categorical outcomes as appropriate.

A level of significance of less than 0.05 was assigned to judge any statistical significance. Tables and diagrams were exhibited as needed for data summary and results presentation.

43 children aged between 1-2 months who were 23 males and 20 females (very close gender distribution).

Table 2: Age by gender distribution of the sample

Gender	Age
	1-2 months
Male	23
Female	20
Total	43

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Anti-HBs titer according to dose and time since vaccination
Zero dose titer: The number of children in this study who received only the zero dose was 43 children and their anti-HB titer at the time of receiving the dose ranged between 6.09 -137. The mean titer was about 18.9 (±23.6) IU/L with a mode and median of about 10 IU/L.

Table 3: Anti-HBs titer by dose of the study sample

Statistic	Zero dose
N	43
Mean Anti-HBs titer	18.9
Minimum	6.09
Maximum	137.00

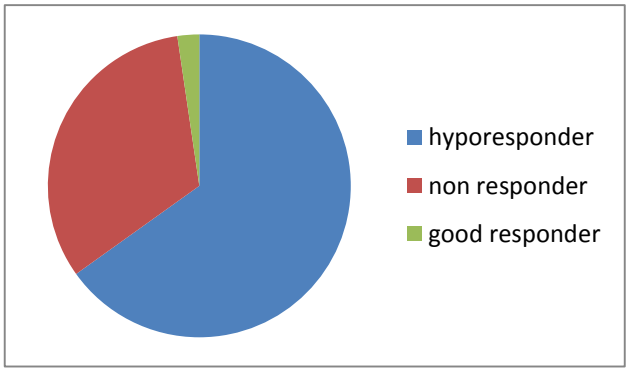


Figure 2: Distribution of the sample according to their response and time

Seroprotection of hepatitis B vaccine:

Seroprotection in different age groups was achieved when the titer of anti-HBs antibody ≥10 IU/L, and the distribution of seroprotection include the hypo responders and good responders in each age group.

The number of protective children is as follows: 29 out of 43 (67.4%) at zero doses.

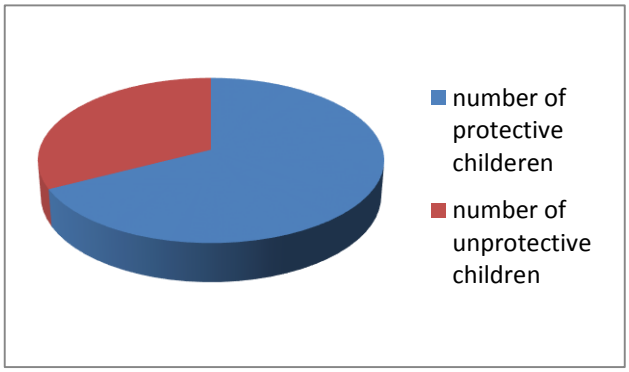


Figure 3: Seroprotection level after the zero dose of the hepatitis HB vaccine

4. DISCUSSION

The present study considers the effectiveness of the HBV vaccine among Libyan children, who all received the same recombinant HBV vaccine on the same schedule in different vaccination centers in Benghazi. The immunity derived from the HBV vaccine was assessed by measuring the antibodies in 43 children who were vaccinated in a routine vaccination program in Benghazi. The sample of the study was from an age group of 1-2 months represented by 43 children. According to several studies among healthy children who had received a complete hepatitis B immunization program, the protective titer of anti-HBs antibody > 5 years after the last dose was seen in 50-100% of individuals. It has been reported that the variability in the anti-HBs antibody might be due to the type of vaccine used, the amount of antigen delivered and the population immunized [(11)].

The seroprotective antibody levels ≥ 10 IU/L were estimated for those who had taken the zero dose before taking the second dose group (29 out of 43 children) showing the anti-HB level >10IU/L was 67.4%.

The American Advisory Committee on Immunization Practices (ACIPI2005) recommends an 8-week gap between the 2nd and 3rd doses of HB vaccination and the 1st and 3rd doses should be administered at least 16 weeks apart, which is the same as our vaccination program. It also recommended a birth dose which will give 70-95% seroprotection. These observations were included in our vaccination program which resulted in good seroprotection in the age group in our study.

Because specialized research is deficient on the zero dose, we compared our results to a study performed on children within the same age range in Egypt [(12)]; the seroprotective was 90.2% at <3 years where they had completed the vaccine dose in comparison to 67.4% at 1-2 months in our study.

5. CONCLUSION

In conclusion, the present study showed the birth dose (zero dose) gave a good protective level in infants as seroprotection was 67.4% after this dose.

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