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Evaluation of Efficacy of Hepatitis B Vaccine 20 Years Post Compulsory Vaccination

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Abstract

The length of protection after a first round of hepatitis B vaccination in children and adolescents is unknown. After vaccination, the levels of hepatitis B surface antibody titre (HBs Ab) have been shown to decrease over time. Protective antibodies created by the Hepatitis B virus (HBV) vaccine last for a long time after primary immunization, however there is evidence that the ability to preserve immunological memory declines as time passes following vaccination. The goal of this study was to see how long protective antibody levels lasted after a basic course of hepatitis B vaccination in people at the age of 20. The HBsAb levels of 100 vaccinated subjects (aged 20 years) were evaluated using an enzyme-linked immunosorbent test in a cross-sectional study. Hepatitis B seroprotection rate (anti HBsAb ≥ 10 IU/L) among vaccinated subjects was 62% ranging from (11 to 538.3) with geometric mean titre (81.5± 117.28), while 38% of subjects showed non- protective antibodies (anti HBsAb < 10 IU/L) ranging from (0.8 to 9.5) with geometric mean titre (4.29 ± 2.40). The geometric mean titer of HBsAb levels was found to be dropping. The findings revealed a downward trend in HBsAb titers in our region 20 years following hepatitis B virus immunization. More research is needed to determine whether a booster dosage is required in persons who might catch hepatitis B virus infection due to their risky work.

Keywords: Hepatitis B virus, Hepatitis B vaccine, Hepatitis B surface Ab titre, Hepatitis B surface antigen.

1. Introduction

Hepatitis B is a global health issue, particularly in developing countries. The hepatitis B virus has infected an estimated one-third around the world. Around 350-400 million people are suffering from HBV throughout the rest of their lives, and 0.5 percent of them seroconvert from HBsAg to HBsAb (anti-HBs) [1]. Hepatitis B

infection can lead to liver cirrhosis and the development of hepatocellular carcinoma (HCC). There are different dermatologic, cardiac, articular, neurologic, hematologic, and gastrointestinal (GI) tract symptoms, as well as glomerulonephritis and polyarteritis nodosa [1]. Hepatitis B prevention relies heavily on the hepatitis B vaccine. The World Health Organization (WHO) proposed that universal childhood immunization be implemented worldwide in 1992, and by the end of 2012, 181 nations had done so [2]. More than 95 percent of newborns, children, and young people have protective antibody levels after receiving the entire immunization series [3]. The durability of hepatitis B surface antibody (anti-HBs) and, as a result, protection against infection and carrier state is determined by the peak anti-HBs concentration obtained after primary immunization. Anti-HBs, on the other hand, deteriorate rapidly after immunization [4]. Hepatitis B virus (HBV) infection is relatively endemic in Egypt, with 4% of the population displaying indications of chronic HBV infection [5].

The HBV vaccination program in Egypt began in 1992 with a vaccine schedule of 2, 4, and 6 months of age, with no systematic HBsAg screening of pregnant women [6]. Despite the fact that there have been no sero-surveys among children born since the vaccine was introduced in Egypt, the discovery of acute disease transmission in these cohorts shows that HBV transmission is ongoing, and a more in-depth evaluation of the immunization program is required [7]. Safe and efficient hepatitis B vaccines have been commercially marketed since 1982, and recombinant DNA vaccines have steadily replaced plasma-derived immunizations. The World Health Organization first addressed hepatitis B vaccine policy gaps in 1992, when it suggested that all countries incorporate hepatitis B immunization in their national children's immunization programs [8]. After decades of use, the duration of protection from hepatitis B vaccination remains uncertain, as does the question of whether a supplemental dose is ever required. The basic requirement for immunity was a sufficient concentration of HBsAb in serum; higher levels of antibody production meant better immunity. Values of fewer than 10 IU/L of hepatitis B surface antigen (HBsAg) were assumed to indicate protective immunity against chronic HBV infection [9]. Serologic testing should be done 1–2 months following the final dose of vaccine to determine the vaccine's effectiveness and the necessity for revaccination. Serologic testing after vaccination should be done using a method that allows the protective level of anti-HBs (10 mIU/mL) to be determined [10]. The rapid decline in anti-HBsAb levels in children and teenagers raises the question of whether vaccine-induced immunity can be maintained in this age range [11]. HBV infection is more likely to occur as a result of increased sexual engagement and risky behavior. Vaccine-induced immunity should so be maintained all the way through puberty and beyond. An additional dose of the vaccine may be required if HBV immunity is lost during this time [12]. Anti-HBs concentrations drop significantly following primary hepatitis B immunisation for the first year and then slowly after that: 15–50% of children who respond to a primary 3-dose vaccination series with anti-HBs concentrations of 10 mIU/mL have low or undetectable anti-HBs concentrations 5–15 years after vaccination; anti-HBs concentrations decline to 10 mIU/mL in 7–50% of adult vaccinees within 5 years after vaccination, and in 30–60% within 9–11 years [13]. After the main immunization course, the higher the vaccine-induced anti-HB [14]. The present study aimed to examine how long protective antibody levels lasted after a basic course of hepatitis B vaccination in people at the age of 20.

2. Materials and Methods

This cross sectional study was carried out at Al-Azhar University Hospitals (El-Hussein and BAB El-Shaarea) during the period between December 2019 to June 2021 and was conducted on 100 basically healthy persons aged 20 years, All had received the three doses of the compulsory HBV vaccination during infancy documented by vaccination certificate or an official proof, The 100 healthy persons were selected from over 326 tested subjects who were enrolled from Hepato-gastroenterology and infectious diseases department and the study was approved by Ethical committee of faculty of medicine, Al-Azhar University while written informed consents were taken from all participants in the study, and also they were informed by any probable side effects that may happen to them. Inclusion criteria included persons aged 20 years old receiving a full vaccination course during infancy. Exclusion criteria included persons aged < OR > 20 years old, those who had taken a booster dose of HBV vaccine, those who have positive test results for HBsAg and/or hepatitis B core antibodies (HBcAb), persons with history of current or recent injection drug use, chronic illness, international travelers to countries with high levels of endemic HBV infection and high risky individuals as (sex partners of HBsAg-positive persons, sexually active persons, Human immunodeficiency virus infection, healthcare and public safety personnel, patients on chronic hemodialysis…… ETC),All the studied subjects were subjected to complete history taking, Clinical assessment stressing on information regarding date of birth, sex, health status, and dates of vaccinations were recorded, full general and abdominal examinations. Laboratory investigations were done and was including, complete blood count (CBC), liver enzymes (AST, ALT), S. Creatinine Abs, HIV Abs, random blood sugar, hepatitis B surface antibodies (anti-HBs) titer, total antibodies against HBV core antigen (anti-HBc), and HBV surface antigen. Also abdomin-pelvic ultrasonography was done to detect organomegaly, hidden malignancy or chronic diseases, Out of 326 persons 226 persons were excluded as follows; 40 persons were HCV positive, 20 persons were HBsAg positive, 7 persons were HbcAb positive, 5 persons were HIV positive, 10 persons had high random blood sugar,33 persons had taken abooster dose of HBV vaccine, 15 persons had hepatomegaly on ultrasound,17 persons had splenomegaly on ultrasound, 2 persons had pancytopenia, 50 persons were healthcare and public safety personnel, 5 persons had drug addiction, 10 persons had elevated liver enzymes, 3 persons with renal impairment and 9 persons with recurrent use of corticosteroids for controlling their diseases as bronchial asthma and rheumatoid arthritis. Finally, 100 persons were selected for the study.

2.2 Data management and statistical analysis

The data was coded, revised, and entered for statistical analysis using IBM SPSS version 20 of the Statistical Package for Social Science. Quantitative data with parametric distributions were presented as mean, standard deviations, and ranges, while quantitative data with non-parametric distributions were presented as median with inter quartile range (IQR). Chi-square test was applied to compare two groups with qualitative data, but when the projected count in any cell was less than 5, the Fisher exact test was used instead. The independent t-test was used to compare two groups with quantitative data and parametric distribution, and the Mann-Whitney test was used to compare two groups with quantitative data and non-parametric distribution. The confidence interval was set at 95%, while the acceptable margin of error was set at 5%. As a result, the following p-value was declared significant:

P > 0.05: Non-significant (NS)

P < 0.05: Significant (S)

P < 0.01: Highly significant (HS)

3. Results

Table 1 below shows that 57% of patients were females and 43% were males, mean of age was 20, mean of BMI was 22.86 with range from 18.6 to 28.6.

Table 1: Demographic data

		No
Sex	Female	57
	Male	43
Age	Mean ±SD	20.00
	Range	20
Body mass index (BMI)	Mean ±SD	22.86 ± (2.21)
	Range	18.6 - 28.6

Table 2: Laboratory data of the studied subjects

	Mini	**Max**	**Mean**	**SD**
AST (U/L) normal range = (10-40) U/L	10	40	24.39	8.67
ALT (U/L) normal range = (7-56) U/L	9	52	30.45	11.15
Creatinine (mg/dl) normal range= (0.5-1.4) mg/dl	0.4	1.3	0.82	0.25
Hemoglobin (g/dl) normal range= (13-18) g/dl	8.5	14.2	11.87	1.17
Platelets (x1000/ml) normal range= (150-450) ×1000/ml	166	428	286.89	76.53
WBCs (x1000/ml) normal range= (4-11) ×1000/ml	3.9	13	7.67	2.00
Random blood sugar (mg/dl) normal range = 80-140 (mg/dl)	79	139	104.79	16.82

Table 2 that mean of AST was 24.39 with range from 10 to 40, mean of ALT was 30.45 with range from 9 to 52, mean of creatinine was 0.82 with range from 0.4 to 1.3, mean of HB was 11.87 with range from 8.5 to 14.2, mean of WBCs was 7.67 with range from 3.9 to 13, mean of platelets was 286.89 with range from 166 to 428, mean of random blood sugar was 104.79 with range from 79 to 139.Table 3 shows that HIV Abs, HBsAg, HBcAb and HCVAbs of all subjects were negative.

Table 3: HIV Abs, HBsAg and HBcAb

		No	%
HIV Abs	Negative	100	100.0%
HBsAg	Negative	100	100.0%
HBc Ab (total)	Negative	100	100.0%
HCV Abs	Negative	100	100.0%

Table 4: HBsAb titre

		No	%	Mean± SD	Range
HBsAb titre (gr)	< than 10	38	38.0%	4.29±2.40	0.8-9.5
	≥ than 10	62	62.0%	81.5±117.28	11-538.3

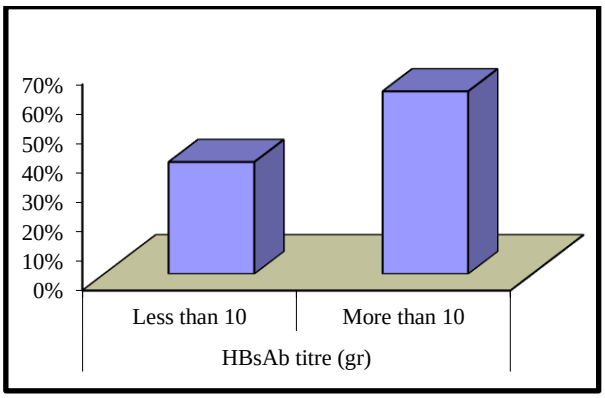

Figure (1): HBsAb titre of 38% of the subjects was less than 10 with mean 4.29 and range from 0.8 to 9.5, while 62% of the subjects show HBsAb titre more than 10 with mean 81.5 and range from 11 to 538.3.

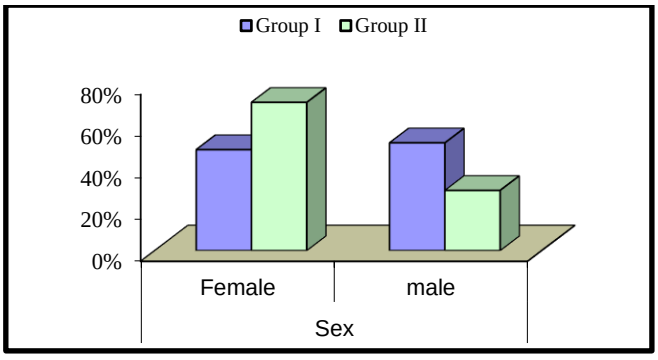

Figure (2): This figure reveals a statistically significant difference in sex regarding HBsAb titre in group II as females were significant more than males, No statistically significant difference in group I in comparison to group II with BMI.

Table (5): Comparison between HBsAb titre as regards demographic data

		HBsAb titre (gr)				Chi square test		
		Group I (≥10) (No.=62)		Group II (<10) (No.=38)				
		No	%	No	%	x^2	p value	
Sex	Female	30	48.3%	27	71.1%	9.562	0.008	S
	Male	32	51.7%	11	28.9%			
Age	Mean± SD	20.00		20.00		NA	NA	
Body mass index (BMI)	Mean± SD	22.40 ± (2.28)		23.60 ± (1.88)		-2.713	0.4	NS

4. Discussion

ELISA was used to test each person's serum samples for antibody against hepatitis B surface antigen (anti-HBs) titer, anti-HBc, and HBV surface antigen. If a person's HBsAb levels were equal to or greater than 10 IU/L, they were categorized as seropositive against HBV, and if their HBsAb levels were less than 10 IU/L, they were classified as seronegative.

Group I (seropositive): HBsAb levels ≥ 10 IU/L.
Group II (seronegative): HBsAb levels < 10 IU/L.

The persistence of HBsAb levels in people who were immunized against HBV in their first year of life was investigated in this study, which took place 20 years after Egypt initiated a nationwide HBV vaccination program in 1992. With age, vaccine induced HBsAb titers fall to low or undetectable levels, which could be a problem with HBV immunization.
In our study, Hepatitis B seroprotection rate (HBsAb ≥ 10 IU/L) among vaccinated subjects was 62% with mean titre (81.5±117.28); while 38% of subjects showed non- protective antibodies (HBsAb < 10 IU/L) with mean titre (4.29 ± 2.40). According to the results of seroprotective antibodies, our results were compatible with the following studies: Pileggi., (2014) [15] who revealed that after 18 years from the original vaccination, that over 25% of HBV vaccine recipients had an antiHBs titer of less than 10mIU/ml. This is consistent with the findings of Mackie et al., (2009) [16], who discovered that HBsAb levels decrease during the first few years after vaccination, and that by the age of 10 to 15, a third to half of vaccinated children may have titers of less than 10 IU/L. They also discovered that 67 percent of 5-year-olds, 52 percent of 9-year-olds, and 44 percent of 15-year-olds exhibited a mild response to boosters. Similarly, in an Egyptian study including 242 children, the effectiveness of immunisation was evaluated, Afifi. et al., (2009) [17] showed seroprotection rates of 84.3 percent at one year and 39.3 percent at 6 to 11 years after vaccination, respectively, in addition, Shamsizadeh et al., (2011) [18] reported a favourable response rate of 75.4 percent among children 5 years after HBV vaccination. However, our findings were contradictory with the following studies: Abolghasemi et al., (2009) [19] reported a positive response rate of 38 percent in students after 18 years of vaccination ,

while Jafarzadeh. et al., (2006) [20] showed 47.9% of children had protective anti-HBsAb levels 10 years after vaccination, Furthermore, Javad Hosseini et al., (2009) [21] found that HBsAb show protective levels in 29.2% of those pediatric patients 6 years following immunisation. Lin. et al., (2003) [22] found that HBsAb show protective levels in 47.5 percent at 6 to 7 years, and in 39 percent at 9 years following primary immunisation in an Egyptian study.

Differences in environmental and genetic factors, vaccine type and dose, age of initial vaccination, immunisation schedule, and vaccine administration intervals can be attributed to the declining trend in HBsAb levels reported in this study, as well as the wide range of results reported in other studies. Our findings revealed a potential drawback of HBV vaccination: vaccine-induced HBsAb levels may decline as persons age, Bialek et al., (2008) [23] similarly observed that protective HBsAb levels steadily fell after the last dose of vaccine in a series of trials among healthy children who had received a complete HBV immunisation program, Schonberger et al., (2013) [24] found that the frequency of children with seroprotective levels of HBsAb fell steadily from 71.1 percent at the age of 7 years to 37.4 percent at the age of 12 years. In cross-sectional research of 840 vaccinated children and adolescents, Norouairad. et al., (2014) [25], the results demonstrated a lowering tendency in HBsAb titres over time after hepatitis B virus vaccination and recommended the need for a booster dose,Aghakhani et al., (2011) [26] similarly found that the rate of anti-HBsAb persistence in vaccinated people reduced with age. In terms of the duration of immunity in children, Su. et al., (2007) [27] propose that universal vaccination of newborns between the ages of one and eleven years may ameliorate the endemic status of infection in normal individuals, Afifi. et al., (2009) [17] advised using hepatitis B vaccine booster for teenagers to raise the immunisation rate against HBV during maturity due to low levels of protective HBV antibodies during adolescence. Yuen et al., (2004) [28] revealed that HBV vaccine booster gives long-term immunity against HBV infection, hence determining HBsAb levels in children following immunisation is also advised. Indeed, several studies have found that despite childhood vaccination, the prevalence of HBV infection in vaccinees increased with age, and that both anti-HBs titer and anamnestic response declined with age. It is clearly time to clarify the long-term protection conferred by childhood vaccination, and to implement protective measures such as booster vaccine doses [29].

5. Conclusion

Around 62% of the vaccinated population had protective levels of HBsAb after 20 years after primary vaccination with recombinant HBV vaccine.

Recommendations

Measurement of HBsAb titre 2 months after the end of primary compulsory vaccination to determine who had protective level of antibodies and who do not have to revaccinate them.Long term study to detect hepatitis B surface antidody titre at 2,5,10,15 and 20 years old in an intimate follow up to determine the effectiveness of HBV vaccine at different age stages and the requirement of booster doses.

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