

## Original article

# Evaluate the Effectiveness of Infant Vaccination in Adulthood

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### Abstract

**Introduction:** Viral hepatitis is one of the causes of premature death in world peoples, according to WHO reports, five percentage of people are carrier, lethal from this disease is 1%, therefore about 1-1.5 million people each year die from complications of this disease. This disease varies from an acute to chronic illness. The aim of this study was to determine the level of anti-HBs Ag (hepatitis B surface antigen) in vaccinated children that born in Abarkouh city in 1992 in order to evaluation of the efficacy childhood hepatitis B vaccination in adults .

**Materials and Methods:** We measured anti-HBs Ag concentration in blood sera of 102 adult peoples than 600 new born children that vaccinated in 1992. Five milliliters (5ml) of blood sample was taken from 102 cases (33 male and 69 female).

**Results:** All blood samples were analyzed for anti-HBs Ag by ELISA method. 94 out of 102 samples (92.2%) showed anti-HBs Ag concentrations higher than 30 Iu/ml (positive) and, 4 out of 102 samples (3.9%) showed anti-HBs Ag concentrations less than 10 Iu/ml (negative), 4 out of 102 samples (3.9%) showed anti-HBs Ag concentrations between 10-30 Iu/ml (border line) considered immune after 20 year after the third dose of the vaccination. Non significant association in males and females (93.9% vs.97.1%) ( $P=0.390$ ,  $df= 1$ ,  $\chi^2=0.555$ )

**Conclusion:** our results reinforce the importance of hepatitis B vaccine in new born and efficacy of HBV vaccination in Abarkuh (Yazd province) is in the WHO standards.

**Keywords:** Hepatitis B Vaccine, Children, Anti-HBs Ag

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## Introduction

Hepatitis B virus (HBV) is a double strand, enveloped DNA virus of the hepadnaviridae family, which replicates in the liver and causes hepatic dysfunction <sup>[1,2]</sup>.

Hepatitis B virus have four genes (ORF), S gene coded protein S, a coating antigen, E gene codes E protein, a Core protein, P gene codes DNA polymerase and X gene codes proteins that delivers virus in to the host cells. S and e proteins are structural protein and X protein is DNA polymerase that control viral replication. X protein is associated with liver cancer. The main proteins that found in HBV infection are surface antigens (Hbs Ag), core proteins (HbcAg) and protein e (Hbe Ag) <sup>[3,6]</sup>.

The HBV chronic hepatitis that arises from HBV infectious can lead to cirrhosis and death, also HBV infection is a risk factor in 60-80% of liver cancer (HCC) in the world <sup>[6]</sup>.

Hepatitis B virus infection is one of the most common diseases in the world, the incidence of the disease has varied from 10-20% South Asia, China , 2-7% in the Mediterranean region, Japan and Central Asia, and less than 2 percent in United States, Canada, Western Europe and Australia. The estimated of that more than 35 percent of Iranians have been exposed to HBV, prevalence of hepatitis B in Iran is varied from the range of 1.7% to over 5% in Sistan and Baluchistan, but the mean of incidence is less than 3% <sup>[3]</sup>.

The first hepatitis B vaccine identified in the United States in 1981 that prepared from the plasma of carriers of HBV infection and able

to stimulate the immune system to produce antibodies against HBs Ag. Current vaccine is not produce from live virus but also produces by genetic engineering that a DNA recombinant plasmid delivers HBs Ag gene in to the *Saccharomyces cerevisiae*, then HBs Ag proteins will purified after cell lysis.

Hepatitis B vaccination is the most effective way to control HBV infection and its transmission, which can be done in three stages over a regular period (0, 1 ,8 months) <sup>[8]</sup>. The first two doses of vaccine adequate for stimulate of the immune system to produce Anti-HBs Ag in secondary response. Third dose stimulates secondary response and antibody (Anti-HBS) rapid rise in blood. The strength of the immune response is evaluated by measuring of antibodies against HBs Ag <sup>[9]</sup>.

In Iran, vaccination against HBV has been routinely performed for all infants that were born to HBs Ag negative mothers and high-risk groups since 1992. The protective efficacy of hepatitis B vaccination is directly related to development of anti-HBs Ag, Anti-HBs Ag levels of 10 mIU/ml or higher are considered to be 100% protected against clinical illness and chronic infection. The vaccines produced by each manufacturer have been evaluated in clinical trials to determine the age-specific dose that achieves the maximum seroprotection rate <sup>[1]</sup>.

In Islamic republic of Iran the Hepatitis B vaccination began in 1992 as a national project. There are few studies focused on the

seropositive rate of protective antibody, named anti-HBs Ag, among adolescents in Iran [1]. The objective of the present study was to determine the level of Anti HBs Ag antibodies and immunity to hepatitis B infection in children who were vaccinated in 1992 and evaluate the effectiveness of infant vaccination in adulthood, To achieve the purpose of the study, anti-HBs Ag concentration in blood sera of vaccinated infants that vaccinated in 1992 were collected and analyzed.

### Materials and Methods

One-hundred and One children of Health people in Abarkouh city, Yazd province, Iran that were vaccinated against hepatitis B in 1992 by vaccine serial No.wva09028 were selected randomly by collection data from health network and use excel software.

The vaccine was administered intramuscularly in the anterolateral thigh. Cases that have been selected receive regular doses of the vaccine, also the cases that received a higher or a lower dose or vaccinated again in later years were excluded from project. A questionnaire was used to record demographic information from participants.

Twenty years after third dose vaccination, first Cases was examined by a physician to evaluate the clinical status, in laboratory 5ml of blood participants were obtained, then blood samples were collected in non-anticoagulant sterile tubes and centrifuged. Sera sample were stored at  $-70^{\circ}\text{C}$  until used. All blood samples were analyzed for anti-HBs Ag by ELISA method (enzyme-linked immune sorbet assay) using commercially kit according

to the manufacture's instruction (Delaware). Briefly, 50 $\mu\text{l}$  of standards, controls and each sample were added to the appropriated wells and in the same time 50 $\mu\text{l}$  of the enzyme conjugate reagent were added to each well and incubated at  $37^{\circ}\text{C}$  for 60 min. Micro titer plate was washed four times with wash buffer and one time with distilled water. 100 $\mu\text{l}$  TMB-substrate was added to each well and incubated at  $37^{\circ}\text{C}$  for 20 min and the reaction stopped by adding 100 $\mu\text{l}$  of stop solution. The absorbencies were read at 450nm wavelength with 620nm as reference. We considered cases as sera positive against hepatitis B if their anti-HBs Ag antibody concentration was equal or greater than 30 mIU/ml, and seronegative if anti-HBs Ag antibody concentration was less than 10 mIU/ml and borderline if their anti-HBs Ag antibody concentration was between 10-30 mIU/ml according to the Kit instruction (Delaware).

### Statistical analysis

The data of demographic variables and anti-HBs Ag concentration were transferred to SPSS software version 17. T-test and Pearson Chi-square test were used for data analysis. The  $p < 0.05$  was considered statistically significant.

### Results

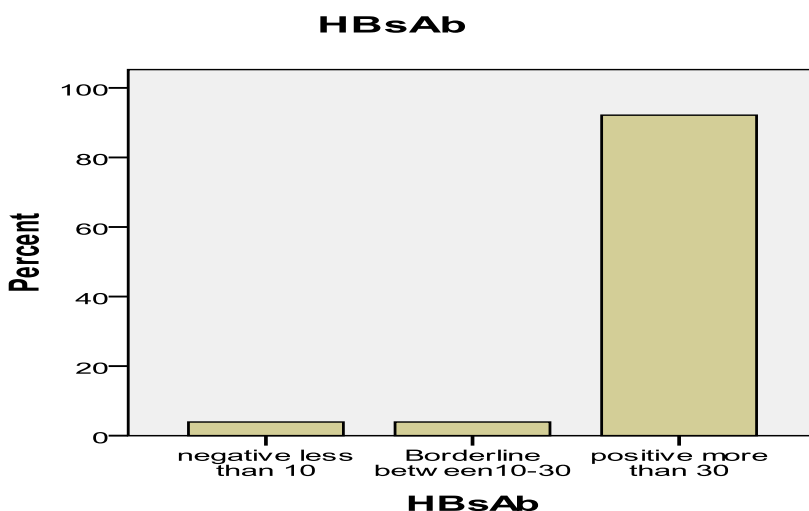
One-hundred and two participants, who gave consent for bleeding after twenty years vaccine administration, were 67.6% females and 32.4% males. The age range of the participants was from 19 to 21 years with a mean age of 20.43 years. 3.9% of them had anti-HBs Ag less than 10 mIU/ml and 3.9% of them had anti-HBs Ag

between 10- 30 mlu/ml and 92.2% of them had anti- HBs Ag more than 30mlu/ml

concentrations of antibody (Table 1 and Figure1).

**Table 1:** Comparison of antibody levels in vaccinated individuals

	Frequency	Percent	Valid Percent	Cumulative Percent
Less than 10 Iu/ml	4	3.9	3.9	3.9
Between 10-30 Iu/ml	4	3.9	3.9	7.8
More than 30 Iu/ml	94	92.2	92.2	100.0
Total	102	100.0	100.0	



**Figure 1:** Comparison of antibody levels in vaccinated individuals

The Statistical data analysis of antibody concentrations the two study groups (males and females) indicates that in male, 30 out of 33 samples (90.9%) showed anti-HBs Ag concentrations higher than 30 Iu/ml(positive), 2 out of 33 samples (6.1%) showed anti-HBs Ag concentrations less than 10 Iu/ml(negative), 1 out of 33 samples (3%) showed anti-HBs Ag concentrations between 10-30 Iu/ml(border

line) and in female, 64 out of 69 samples (92.8%) showed anti-HBs Ag concentrations higher than 30 Iu/ml(positive), 2 out of 69 samples (2.9%) showed anti-HBs Ag concentrations less than 10 Iu/ml(negative), 3 out of 69 samples (4.3%) showed anti-HBs Ag concentrations between 10-30 Iu/ml(border line) considered immune after 20 year after the third dose of the vaccination. Non-immune

participants were in males (6.1%) and females (2.9%) Table2.

There was no significant association in males and females (93.9% vs.97.1%) (P=0.390, df=1, ( $\chi^2=0.555$ )).

Table 2: The concentration of anti-HBs Ag in study group 20 years after vaccination

		Number of case with non-protective Immunity(anti-HBs Ag less than 10mIU/ml)	%	Number of case with Protective Immunity(anti-HBs Ag more than 10mIU/ml)	%	Total of case
Gender	Male	2	6.1	31	93.9	33
	Female	2	2.9	67	97.1	69
Total		4	3.9	98	96.1	102

As a result of "Figure 2" and "Table 2" anti-HBs Ag of more than 10 mIU/ml (protective)

after 20 year vaccine administration was seen in 93.9% of males and 97.1% of females.

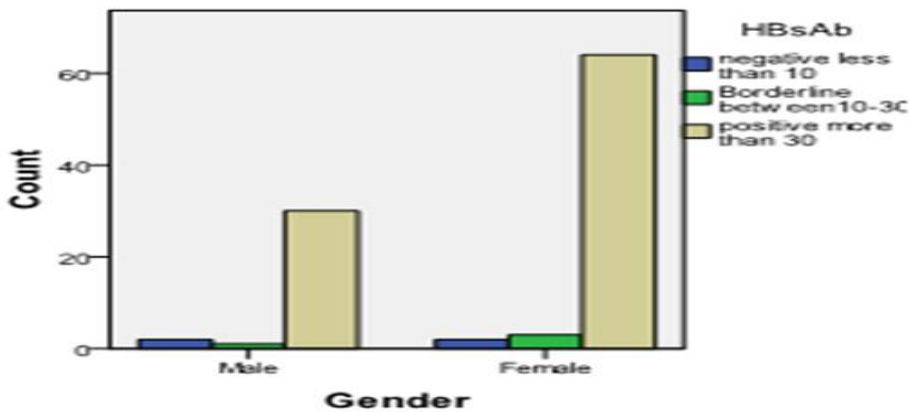


Figure 2: The concentration of anti-HBs Ag in study group 20 years after vaccination

## Discussion

Effective vaccines against HB have become available in 1982. Their widespread use in many areas of the world has dramatically reduced the rate of HB. In Iran, in spite of the

availability of an effective vaccine and the incorporation of HBV in to the national infant vaccination program, now it is recommended

to be vaccinated high risk adults that were not vaccinated in infancy.

It is important to know the rate of protection of HB vaccination in adults. In this study, the concentrations of anti-HBs Ag after the 20 year determined and efficacy of vaccine was assessed. We defined anti-HBs Ag antibody concentration of 30 mIU/ml as the seropositive threshold and anti-HBs Ag antibody concentration between 10-30 mIU/ml as the borderline and anti-HBs Ag antibody concentration less than 10 mIU/ml as the negative as recommended by ELISA kit instruction. The findings showed that 3.9% of individuals had not protective anti-HBs Ag in serum after 20 year vaccination that recommended there is a need for again immunization to maintain protection in them.

Some studies showed that giving a booster dose of HB vaccine to persons who have been vaccinated and the concentration of anti-HBs Ag was below 10 mIU/ml could develop a rapid rise in anti-HBs Ag antibody<sup>[1]</sup>. In this research, 92.2% of the samples had anti-HBs Ag higher than 30 mIU/ml and 3.9% of the samples had anti-HBs Ag between 10- 30 mIU/ml in their serum after the 20 year of vaccine administer So that Protective antibody levels were 96.1%. The results indicated that the vaccine of HB is effective, for infant to increase the seropositive rate of anti-HBs Ag in adults that confirm the research that indicates passive-active immunoprophylaxis in high risk children was effective and it is proposed that all children born to HBs Ag positive mothers should be immunized against

HBV<sup>[7]</sup>. One report has revealed that vaccination at older ages was associated with persistence of higher anti-HBs Ag level<sup>[11]</sup>, which supported the effectiveness of vaccination in infants rather than younger age<sup>[1]</sup>. There was a good overall response rate of 93.8%, women responding better than men<sup>[13]</sup>.

In the study by Roome et al, Connecticut public safety personnel had been vaccinated using RecombivaxHB of 528 individuals, 11.9% were found to have no or inadequate levels of antibody. The frequency of inadequate level of antibody increased significantly with age, from 2.8% among those younger than 30 years to 42.1% among those older than 60 years<sup>[14]</sup>. A study which was carried out by Chen, demonstrated that after 1984 that the free HBV vaccination program in Taiwan has been provided to the newborns, the HBV infection rate and HBs Ag carriers rate decreased. This study demonstrated the protective of public HBV vaccination among university students older than 18 years of age<sup>[15]</sup>. It was also found that, there was not a significant difference between sex and anti-HBs Ag concentration<sup>[1, 15]</sup>. This means the percentage of male no responders are equal to female participants and anti-HBs Ag production is not affected by sexual factor such as feminine hormones that support our study. Another finding demonstrated the significant differences between age and antibody production. In other words, as age increased, the antibody production decreased. It is known that increasing age is associated with a decline in humeral and cellular immunity to vaccines

<sup>[16]</sup> so the vaccination in childhood is the better adulthood.

### Conclusion

The results reinforce the importance of HB vaccine in infants and suggest that three dose of HB vaccine is necessary to increase the seropositive rate of anti-HBs Ag in adults; in

addition vaccination procedure in Abarkouh city is acceptable.

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