

PATTERN OF RESPONSES TO HEPATITIS B VIRUS VACCINE IN BASRAH, IRAQ

Firas T. Mansour¹, Hassan J. Hasony²**ABSTRACT**

A serological study was carried out in Basrah governorate, southern Iraq, from October 2004 to the end of September 2006 aimed at estimating the prevalence of HBs-antibody among four groups of individuals: Children under 15 years of age, medical personnel, barbers and unvaccinated adults, to determine HBV vaccination coverage in our area, also to evaluate the duration of vaccine induced immunity and the rate of waning immunity as well as the determination of the proportion of hepatitis type B among the other causes of hepatitis occurring in the community. A total of 762 individuals were included in the study from whom blood samples were collected. The overall vaccination coverage among the study population was 62.9% leaving 37.1% unvaccinated. An enzyme-linked Immunosorbent assay (ELISA) was used for the determination of anti-HBs-IgG antibody, showed a prevalence of 71.2%, 66.7%, 51.4%, and 8.7% for barbers, medical personnel (occupational exposure), children under 15 years of age and unvaccinated adults respectively. There was a clear effect for the number of vaccine doses administered on the levels of seroconversion, with no significant differences in antibody associated with sex or geographical distribution of vaccinees, but there was a difference in relation to occupation. There was a significant decline in the levels of antibody overtime post vaccination and the losses of protective levels of antibodies were quite evident by 3-4 years post the primary vaccine doses which stress the need for booster doses. In the primary vaccination schedule the time interval of 5-6 months between the 2nd and 3rd vaccine doses is suitable for better responses to HBV vaccine. The proportion of icteric HB was 14.7% while 85.3% was due to other hepatitis causes, and the rate of hepatitis B among individuals with no history of hepatitis was 2.6% referring to the subclinical cases.

INTRODUCTION

Hepatitis B virus (HBV) is one of the most widespread infectious agent and causes millions of hepatitis cases and deaths each year.^[1] It is estimated that approximately 2 billions persons world wide have been exposed to the virus and approximately 350 million persons are chronically infected carriers to HBV;^[2,3] the total population of the world is approximately 6 billions, therefore about 5% of the world population are persistently infected with HBV.^[4] All of these chronic carriers of the virus are at 100-200 times the risk of non carriers of developing hepatocellular carcinoma,^[4,5] a disease that kills about one million person each year.^[6] Chronically it occurs in 90% of patients with perinatal transmission and in 5-10% when HBV is acquired during adulthood.^[7] Vaccination is the most important tool for hepatitis B prevention. It provides 90% protection to neonates whose mothers are HBV carriers when given as soon as possible.^[8] Since 1991, WHO has called for all countries to include hepatitis B vaccine into their national immunization programs.^[6] By March 2002, 16 countries have included HBV vaccine in their national programmes including most countries in Eastern and south east Asia, the Pacific Island, Australia, north and south America, western Europe and middle east.^[6] However, because of hepatitis B vaccine prices, many low income

countries in sub-Saharan Africa, the Indian sub-continent and in newly independent states do not use the vaccine.

The present study aimed on estimating HBs-antibody prevalence among 4 groups of individuals (children under 15 years of age, medical personnel, barbers and unvaccinated adults), estimation of HBV vaccination coverage in our area, evaluation of the duration of vaccine induced immunity and the rate of waning immunity as well as the estimation of the proportion of type B viral hepatitis among the other causes of hepatitis occurring in the community of Basrah.

MATERIALS AND METHODS

A total of 762 individuals have been included in the study from whom blood samples were collected (446 males and 316 females). For epidemiological purposes, study population was divided into 4 groups:

- *Children under 15 years of age (432:217 males and 195 females) at different immunization status or unvaccinated for various reasons. The obtained informations were based on each child vaccination card and school vaccination booklet records beside the parents interview. This group is considered as a representative for the general population obtained from the areas*

of Abu-Alkhasib with population of 167720 with target population eligible for vaccination of 67088; Al-Zubair (population: 501108, target 120443) and city center (population 397757, target 159102) where the target population estimated as 40% of the total population in each setting (Basrah health authorities; 2000 census).

- Medical personnels (57:30 males and 27 females). This occupational group were interviewed for their duration of occupation, history of needle stick injuries, blood transfusion, surgical procedures and occurrence of previous jaundice.
- Barbers (66: all were males), asked for duration of occupation, history of razor cut, exposure to customers blood sheds.
- Group of adults (unvaccinated group) including 112 males and 94 females. This group was divided into two subgroups:

The first, randomly selected with no history of clinical hepatitis or exposure to any risk factor(s) and the second were selected on the basis of occurrence of hepatitis infections and exposure to risk factor(s) such as blood transfusion, surgical procedure, needle stick injuries. These informations were collected on special questionnaire form to cover the relevant data. The study was carried out from October 2004 to the end of September 2006. Hepatitis Bs-IgG antibody was measured by Enzyme-linked immunosorbent assay (ELISA) test using Bioelisa anti-HBs in a direct immunoenzymatic method (bioelisa kit, Spain) and the procedure was carried out as described by the manufacturers instructions. The results were expressed as Elisa titers which was converted into mIU/ml through the standard method

provided by the kit instructions (bioelisa, Spain).

RESULTS

Among 432 children of 1-15 years of age from various areas in Basrah city, 22% were covered with a single dose only of HBV vaccine (Table-1). Vaccination coverage with 2 and 3 doses (primary doses) of vaccine was 23.5% and 35.5% respectively. Only 7.2% had boosted with a 4th dose and the unvaccinated proportion of children at this age range accounted for 12%.

Table 1. Hepatitis B vaccination coverage among children in relation to vaccine doses.

Vaccine doses	Vaccination coverage No. (%)
1 dose	95 (22)
2 doses	100 (23.5)
3 doses	154 (35.5)
4d (booster)	31 (7.2)
Unvaccinated	52 (12)

The overall serologic profile to HBV in the study population is shown in table-2. The overall sereopositivity among unvaccinated individuals (natural exposure) was 8.4% compared to 3.8% among unvaccinated children which differ from that observed among risk groups (occupational); Barbers: 18.2% (30 had razor cut, 47 razor cut and exposed to customer's blood sheds, 6 none; these figures may overlaped); medical personnels: 23.1%. The susceptibility rate (as estimated from the number of seronegative) among unvaccinated children was 91.2% which was reduced to 37.4% by the introduction of HBV vaccine. Generally the susceptibility rates among vaccinated children, barbers, and medical personnel were 42%, 18.2% and 20.5% respectively.

Table 1b. The overall serological results to HBV in the study population

Vaccination status	Study group	No. tested sera	Serological results	
			Positive No. (%)	Negative No. (%)
Vaccinated	Children	380	220(57.9)	160(42.1)
	Adults	-	-	-
	Barbers	55	45(81.3)	10(18.2)
	Medical personnel	44	35(79.5)	9(20.5)
	Subtotal	479	300(62.6)	179(37.4)
Unvaccinated	Children	52	2(3.8)	50(96.2)
	Adults	207	18(8.4)	189(91.3)
	Barbers	11	2(18.2)	9(81.9)
	Medical personnel	13	3(23.1)	10(76.9)
	Subtotal	283	25(8.8)	258(91.2)

Table 2b. Occupational exposure to a risk factor(s).

Risk factor	Medicals (53)	Barbers (66)
Blood transfusion	10	6
Admitted to surgical procedure	4	3
Needle-stick injuries	25	-
Razor cut	2	30
Exposure to customer's blood shed	15	27

* These figures may overlapped.

The prevalence of anti-HBs antibody among vaccinated children in relation to vaccine doses is presented in table-3. Single dose of vaccine confers immunity to 24.2% only, and coverage of vaccinees with 3 doses (primary doses)

increased the seropositivity to 82.5%. Booster dose(s) is required since the 4th dose increased the seropositivity to 90.3% among children group.

Table 3. Prevalence of anti HBs antibody among children in relation to vaccine doses.

Immunization doses	No. tested	Serological results	
		Positive n (%)	Negative n (%)
1 dose	95	23(24.3)	72(75.8)
2 doses	100	42(42)	58(58)
3 doses	154	127(82.5)	27(17.5)
4d (booster)	31	28(90.3)	3(9.7)
Unvaccinated	52	2(3.8)	50(96.2)
Total	432	222(51.4)	210(48.6)

Table-4 presents the pattern of waning immunity at different periods post vaccination which was done on 185/479 who had confirmed dates of vaccination by both the vaccination card and the school vaccination and health booklets where 94.6% of children sera posses the protective levels of antibody by 6 months

to 2 years post vaccination. This rate of seropositivity was declined to 87.9% by 3-4 years and reached the levels of seroconversion obtained by the initial doses (82.3%) by 5 years post vaccination. However, periods greater than 5 years left larger percentages of susceptible.

Table 4. The waning immunity over time-past vaccination

Intervals between vaccination and blood sampling (years)	No. tested	Serological results	
		Positive n (%)	Negative n (%)
6 months- 2 years	37	35(94.6)	2(5.4)
3-4	33	29(87.9)	4(12.1)
5-6	28	24(85.7)	4(14.3)
7-8	34	28(82.3)	6(17.7)
9-10	25	19(76)	6(24)
11-14	28	20(71.4)	8(28.6)
Total	185	155(83.8)	30(16.2)

Out of 283 unvaccinated individuals, only 107 gave a précised informations about the presence or absence of previous jaundice. The prevalence and proportion of viral hepatitis type B among unvaccinated adults with previous history of jaundice is presented in table-5. There was

significant differences ($P < 0.01$) in the prevalence of HBV between adults with previous history of jaundice (14.7%) and those with no history (2.3%) which represent the subclinical exposure and the causes of hepatitis accounted to 85.3%.

Table 5. The prevalence and proportion of HBV among unvaccinated with previous history of hepatitis.

History of hepatitis	No. tested	Serological results	
		Positive n (%)	Negative n (%)
Positive	68	10(14.7)	58(85.3)
Negative	39	1(2.6)	38(97.4)
Total	107	11(10.3)	96(89.7)

DISCUSSION

High vaccination coverage is the most important factor needed to interrupt HBV transmission; lack of hepatitis B vaccine was the factor most strongly associated with HB susceptibility. The overall vaccination coverage was 42.8% and the seropositivity of all vaccinated children (at least one dose) was 57.9%^[9] which is low that may be attributed to the inadequate vaccination schedule and the late introduction of HBV vaccine in the immunization program in Iraq beside the in availability of the vaccine to health authorities to do their jobs. Also there is no school based immunization schedule similar to that found in other countries.^[10,11] The results showed a clear effect for the vaccination to rise the immunity levels, but the overall immunity is inadequate to prevent HBV infections especially among those at risk. Experience from the USA suggested that the incidence of HB would decline rapidly if vaccination coverage kept high in order of 90%.^[12] Knowledge about the distribution of an infectious agent immunity in relation to age in a country is useful to determine the target population for an effective mass vaccination program. Among the occupational group (medical personnels and barbers) the distribution of antibody in different age groups is not significant, because the vaccination and natural infections is not limited to specific age which is in consistent with other studies.^[13] However, children group showed quite significant differences in the presence of anti-HBV antibodies in relation to age, a trend which was correlated to the vaccination time. The value of antibodies indicates high protective

levels among the recently vaccinated children a finding that in consistent with other studies.^[14,15,16] The rate of susceptibility to HBV infections is greater than 50% among children over 7 years of age since the levels of antibody drops to a lower levels by 3-6 years postvaccination due to waning immunity overtime and most of our children are not boosted with the relevant booster doses required after a period to keep antibodies at their protective levels.^[15,16] These observation imply the urgent need for more than one booster dose to maintain the protective levels of anti-HBV antibodies over age. HBV antibody loses overtime significantly correlated with the number of vaccine doses given to the vaccinees and the time interval between the primary doses. Reported data from other studies are conflicting; some results showed a variable periods for vaccine induced antibody to persist, where in some other studies the immunologic memory against vaccination remain for 9 years and confer protection against HBV infection^[16] while other studies indicates a postimmunization antibody decline by 5 years.^[13] However, many authors agreed with our observed range of 3-6 years in a declined levels of HBs-antibody at various degree may reach the non-protective levels.^[14,16,18] On the other hand, the first two doses of HBV vaccine should be at least one month a part, but increasing the interval beyond one month add no immunologic advantage^[14,19] and the second and the third doses should be separated by 2 months, and interval of 4 months or more is optimal.^[18,19,20] Non-responder or poor

responders (with postvaccination antibody levels never exceed 10 mIU/ml or less than 100 mIU/ml respectively) to HBV vaccine was obtained in our study which is indicated by the presence of a fair number of vaccinees with low antibody levels after the primary vaccine doses. The administration of booster dose(s) to those with low antibody levels increased significantly the titer which stress the need for booster doses to maintain the protective levels of immunity and to cover the overtime loses of immunity. However, HBV antibody level among poor responders and non-responders can be increased up to 1000 mIU/ml after a 4th booster dose.^[21,22] These results are in agreement with other studies.^[23] The presence of HBs-antibody without immunization refer to natural exposure by different mode of HBV transmission as perinatal or occupational hazard of health workers and other risk groups.^[6] However, the present study showed that HBs-antibody prevalence among unvaccinated medical personnels is higher than that among the unvaccinated individuals in other groups, which indicates the impact of the occupational exposure on this group, considering that medical personnel as high risk group since the prevalence of HBV antibodies among unvaccinated was 23.1% which is relatively high. These results are in consistent with another study.^[24] Similarly, the unvaccinated barbers presented with high percentage of HBs-antibody (18.2%) which suggest that HBV infections constitute an occupational hazard for them. It was found that most of the studied barbers had been exposed to scissor cuts and accidental injuries by razors and become in contact with blood sheds. However, in a study in Turkey higher prevalence of anti-HBs-antibody among unvaccinated barbers that reach 39.8%.^[25] Once an immune response has been induced by vaccination, it can be stimulated by natural exposure to the virus, with an active increase in anti-HBs- antibody during the early phase of incubation period of the disease hence protection against clinical illness or development of the carrier status can be achieved. In endemic setting repeated exposure to HBV carriers could sustain or even boost HBV-antibody responses without any serological evidence of infections.^[26] The proportion of HBV infections among those with

previous history of icteric hepatitis was 14.7% leaving the major proportion to the other causes of hepatitis, possibly viral hepatitis type A which is more endemic in our area.^[27] The prevalence of anti-HBs-antibody among individuals reported no history of the occurrence of icteric hepatitis was 2.6% which represent the ordinary exposure to HBV and most of these infections were subclinical. However, exposure rate to HBV was reported to be up to 11.7% in some regions of Saudi Arabia^[28] which is almost in consistent with our figure.

In conclusion, despite the introduction of HBV vaccine and the presence of reasonable vaccination coverage in our community, still there were a fair number of susceptible to HBV infections and the occupational exposure can be considered as risk factor for medicals and barbers professions, where there was an indication for the overtime waning immunity post vaccination. Hence, the implementation of good follow-up and stressing on vaccination program to be achieved and monitored through serological surveys are highly recommended to maintain the protective levels of anti-HBV antibody.

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