SURVEY OF HEPATITIS B SURFACE ANTIBODY CONCENTRATION IN PATIENTS EXAMINED AND TREATED AT THE CENTER FOR TROPICAL DISEASES-BACH MAI HOSPITAL

Nguyen Van Dung[1], Truong Thai Phuong[2], Nguyen Vu Hong Van[3], Le Thi Huyen[4], Nguyen Thi Lan Anh[5]

Summary

Objectives: Survey of anti-HBs concentration in patients examined and treated at the Center for Tropical Diseases - Bach Mai Hospital from April 2012 to July 2020.

Subjects: 1. 024 patients who tested negative for HBsAg and were tested for anti-HBs were examined and treated at the Center for Tropical Diseases - Bach Mai Hospital from April 2012 to July 2020; selected by convenience sampling technique.

Methods: Cross-sectional descriptive study.

Results and conclusion: A total of 1024 patientsincluding 708 positive anti-HBs patients (69.1%) with an average anti-HBs concentration of 356.1 ± 400.6 IU/mL, and 90.7% with anti-HBs levels ≥ 10 IU/mL in which 18.6% of patients have anti-HBs levels ≥ 1000 IU/mL, there was no significant difference in anti-HBs levels between male and female. Among 163 patients with a history of hepatitis B vaccination, 78.5% of patients were anti-HBspositive. Of the 268 tested foranti-HBc total, the positive anti-HBc total rate was 22.1% (17 patients) out of 77 negative anti-HBs patient.

Keywords: *Hepatitis B virus infection, HBV, anti-HBs.*

INTRODUCTION

Hepatitis B virus (HBV) has genetic material as DNA and a member of the Hepadnaviridae family. HBV infection can be acute, with complete clearance of the virus after 6 months, or chronic infection with a positive HBsAg test lasting for more than 6 months. Anti-HBs antibody is virus-neutralizing antibody, and in cases of acute HBV infection cured, antibodies persist for life and provide protection. In cases of chronic HBV infection, the body does not make anti-HBs. Simultaneously, the presence of anti-HBs assesses the response to HBV vaccination, which is the result of activation of the human immune system by HBsAg[1]. HBV infection can be prevented with a vaccine[2]. The most commonly used HBV vaccines in the world are recombinant HBsAg antigens and require periodic booster shots to maintain anti-HBs protection at 10 IU/mL. High-risk patients, such as healthcare workers, living with someone with a chronic infection should have an antibody levels of 100 IU/mL[3].

Vietnam is a high rate of HBV infectioncountry with the rate of positive HBsAg people being 8%, the main mode of infection is mother-child transmission, the main route of infection is mother-child transmission. Vaccine against

1: Center for Tropical Diseases - Bach Mai Hospital
2: Microbiology Department - Bach Mai Hospital
3: General medicine Department - Tam Anh Hospital
4: National Hospital of Tropical Diseases
5: National Institute of Hygiene and Epidemiology

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Responsibility for the scientific content of article: *Nguyen Van Dung, Center for Tropical Diseases - Bach Mai Hospital*

Email: dungaids2003@yahoo. com

HBV infection has been implemented in the Expanded Program on Immunization for children under 5 years old nationwide since 2002, early vaccination after birth was implemented in 2003. Due to the implementation of HBV vaccination, the positive HBsAg rate in children under 5 years old has decreased. Children outside the age of expanded vaccination and adults, the HBV vaccine is a service vaccine, must pay the cost. Vaccination needs to be repeated periodically to generate sufficient protective antibody levels. These issues will greatly affect the proportion of adults with protective levels of anti-HBs. Viet Nam is moving towards reducing the prevalence of HBV infection by 2030 and reducing the burden of disease caused by the progressive pathological consequences of chronic HBV infection, so that anti-HBs antibody response in populations may need attention. Thus, anti-HBs that appear after natural HBV infection or HBV vaccination is the result of activation of the body's immune system by HBsAg. Therefore, the study was conducted to evaluate the rate of anti-HBs antibody response in patients who came for examination and treatment at the Center for Tropical Diseases - Bach Mai Hospital from April 2012 to July 2020.

MATERIAL AND METHODS

Research design: NCross-sectional descriptive study.

Study participant: Patients were examined and treated at the Tropical for Diseases Center - Bach Mai Hospital from April 2012 to July 2020.

Inclusion criteria: Patients who were examined and treated at the Center for Tropical Diseases - Bach Mai Hospital have negative HBsAg test results and are tested for anti-HBs.

Exclusion criteri: Patients who have a positive HBsAg test.

Place and duration of the study: The Tropical for Diseases Center - Bach Mai Hospital from April 2012 to July 2020.

Sample size and sampling methods: Convenience sampling, all patients eligible for study.

Specimens: Venous blood samples are tested as indicated, including HBsAg, anti-HBs and anti-HBc total.

Test technique: Qualitative HBsAg, anti-HBc total, and quantitative anti-HBs tests were performed at the Department of Medical Microbiology - Bach Mai Hospital.

Data processing and analysis: Data were entered according to EpiData 3.1 program and analyzed by medical statistical method on Stata 15.0 software.

RESULTS

All 1024 patients in this study were examined and treated in the Center for Tropical Diseases - Bach Mai Hospital, tested negative for HBsAg and assigned to test anti-HBs.

Table 1. Demographic characteristics

Characteristics		n (%)	Characteristics		n (%)
Sex	Male	492 (48.1)	Job	Worker	73 (7.1)
	Female	532 (51.9)		Farmer	373 (36.4)
	Total	**1024 (100)**		Office worker	111 (10.9)
Living area	City, town	288 (28.1)		Student	113 (11.1)
	Countryside	680 (66.4)		Businessmen	75 (7.3)
	Mountains	56 (5.5)		Retire	79 (7.7)
	Total	**1024 (100)**		Teacher	37 (3.6)
History of HBV vaccination	Yes	163 (15.9)		Housewife	27 (2.6)
	No	812 (79.3)		Driver	20 (2.0)
	Unclear	49 (4.8)		Other	116 (11.3)
	Total	**1024 (100)**		**Total**	**1024 (100)**
Age (year)	Age group: < 18	55 (5.4)	Reason for medical examin-ation	Other medical examination	583 (57.0)
	Age group: 18 - < 30	164 (16.0)		Periodic health examination	359 (35.0)
	Age group: 30 - < 49	446 (43.6)			65 (6.3)
	Age group: 49	359 (35.1)		Have symptoms	17 (1.7)
	Total	**1024 (100)**		Other	1024 (100)
	Mean ± SD: 42.8 ± 16.1			Total	
	Min - Max: 4 - 89				

(Mean: mean, SD: standard deviation, min: minimum value, max: maximum value)

In our study, female patients accounted for 51.9 %, the mean age was 42.8 ± 16.1 (age), the most common age was between 30 and 49 years old. The patient's occupation is very diverse, such as farmer, worker, student, etc. Most patients lived in rural areas, accounted for 66.4%, the majority of patients came to the center for other diseases accounted for 57%, 35% of patients had health examination and only 15.9% of patients remembered the history of vaccination against hepatitis B virus.

Table 2. Anti-HBs results and history of vaccination against hepatitis B virus

Anti-HBs	History of vaccination againsthepatitis B virus			
	Yes (n = 163)	**No (n = 812)**	**Unclear (n = 49)**	**Total (n = 1.024)**
Anti-HBs positive				
Ratio (n/%)	128 (78,5)	547 (67.4)	33 (67. 4)	708 (69.1)
Average anti-HBs levels	520.8 ± 512.5 (0.2 - 3884)	317.6 ± 361.4 (0.2 - 1000)	355.2 ± 374.4 (6.1 - 1000)	356.1 ± 400.6 (0.2 - 38884)
Rate of anti-HBs>10 IU/mL (%)	93.0	89.9	93.9	90.7

Anti-HBs	History of vaccination againsthepatitis B virus			
	Yes (n = 163)	No (n = 812)	Unclear (n = 49)	Total (n = 1.024)
Anti-HBs negative				
Ratio (n/%)	35 (21.5)	265 (32. 6)	16 (32.6)	316 (30.9)

According to table 2, 708 patients (69.1%) in total 1024 patients of study were positive anti-HBs. The prevalence of antibodies in the vaccinated and unvaccinated groups was 78.5% and 67.4%, respectively.

Table 3. Analysis of anti-HBs levels by age

	< 18 years old n (%)	18 - < 30 years old n (%)	30 - < 49 years old n (%)	≥ 49years old n (%)	Total n (%)
Anti-HBs antibody levels (IU/mL)					
0.17 - < 10	4 (12.5)	7 (7.0)	20 (6.3)	35 (13.5)	66 (9.3)
10 - < 100	7 (21.9)	28 (28.0)	84 (26.5)	108 (41.7)	227 (32.1)
100 - < 200	6 (18.7)	13 (13.0)	33 (10.4)	30 (11.6)	82 (11.6)
200 - < 1000	5 (15.6)	27 (27.0)	110 (34.7)	59 (22.8)	201 (28.4)
≥ 1000	10 (31.3)	25 (25.0)	70 (22.1)	27 (10.4)	132 (18.6)
Total	**32 (100)**	**100 (100)**	**317 (100)**	**259 (100)**	**708 (100)**
	< 18 years old n (%)	**18 - < 30 years old n (%)**	**30 - < 49 years old n (%)**	**≥ 49years old n (%)**	**Total n (%)**
Mean ± SD	539.9 ± 753.5	434.5 ± 411.0	403.2 ± 381.1	245.3 ± 327.2	356.1 ± 400.6
Min - Max	0.55 - 3884	0.19 - 1000	0.17 - 1001	0.25 - 1000	0.17 - 3884
History of vaccination against HBV					
Vaccination rate (%)	68.8	37.0	18.3	4.3	18.1

In 708 patients with positive anti-HBs, the average concentration was 356.1 ± 400.6 IU/mL, the highest was 3884 IU/mL. There were 90.7% patients with anti-HBs levels ≥ 10 IU/mL, 18.6% of which had levels ≥ 1000 IU/mL, only 9.3% had levels 10 IU/mL. The mean anti-HBs levels was highest in the age group < 19 years old (539.9 ± 753.5 IU/mL), the antibody levels gradually decreased with age.

Table 4. Analysis of anti-HBs levels by sex

Anti-HBs levels (IU/mL)	Male n (%)	Female n (%)	Total n (%)	P
0.17 - < 10	31 (8.8)	35 (9.8)	66 (9.3)	> 0.05
10 - < 100	123 (34.9)	104 (29.2)	227 (32.1)	
100 - < 200	39 (11.1)	43 (12.1)	82 (11.6)	
200 - < 1000	96 (27.3)	105 (29.5)	201 (28.4)	
≥ 1000	63 (17.9)	69 (19.4)	132 (18.6)	
Total	**352 (100)**	**356 (100)**	**708 (100)**	
Mean ± SD	343.8 ± 419.8	368.2 ± 380.8	356.1 ± 400.6	> 0.05
Min - Max	0.24 - 3884	0.17 - 1001	0.17 - 3884	

The average anti-HBs concentration of male is 343.8 ± 419.8 IU/mL and female's is 368.2 ± 380.8 IU/mL. There is no difference between male's and female's anti-HBs levels (> 0.05).

Table 5. Anti-HBs levels by Anti-HBc total

Anti-HBc Total		Anti-HBs		
		Positive	Negative	Total
Positive	n	130	17	147
	%	68.1	22.1	54.8
Negative	n	61	60	121
	%	31.9	77.9	45.2
Total	**n**	**191**	**77**	**268**
	%	**100**	**100**	**100**

There were 269 patients tested for anti-HBc total in 1024 patients of study. In 191 patients with anti-HBs positive, anti-HBc total were negative in 61 patients (31.9%). In 77 patients with anti-HBs negative, 17 patients had positive anti-HBc total (22.1%).

DISCUSSION

Chronic HBV infection is a major cause of cirrhosis and hepatocellular carcinoma. HBV vaccination is an effective method for preventing these infections and complications[4]. Anti-HBs is a serological marker that assesses immunity to HBV achieved through vaccination or resolved HBV. People with anti-HBs positive have immunity against HBV infection. This immunity is determined by the concentration of antibodies in the blood following an innate immune response to HBV or following vaccination[5]. 1024 patients in ours study were examined and treated at the Center for Tropical Diseases - Bach Mai Hospital between April 2012 and July 2020, the average age of patients was 42.8 ± 16.1 (years) in those, age from 30 to < 60 years old accounted for 64.3%, 78.7% of the patients in the study were aged > 30 years old, most of them lived in rural areas, the proportion of male was 48.1% and female was 51.9% (Table 1). The Center for Tropical Diseases - Bach Mai Hospital is mainly responsible for examining and treating for adult patients, so the number of children in our study is low, almost children follow their parents to the Center. In 1024 patients, 57% of patients were examined for other diseases and then were tested. There was only 35% patient with tests for HBsAg and anti-HBs belong to the periodical health examinations group (Table 1). Anti-HBs is an antibodies that neutralize the virus. This antibody is produced in people with acute HBV infection or is achieved through HBV vaccination. This study investigated anti-HBs levels in 1024 patients came to the Center for Tropical Diseases - Bach Mai Hospital, who had a negative HBsAg screening test, shows the prevalence of anti-HBs is 69.1%, the rate with protective antibody levels > 10 IU/mL is 90.7% (Table 2).

HBV vaccination has been included in the National Expanded Program on Immunization in Vietnam since 2002 for children under 5 years old in order to induce an anti-HBs immune response to achieve the goal of reducing the HBV infection rate. Thus, people aged 30 years and over have not yet received the HBV vaccine from the Expanded Program on Immunization. Our study shows that the average anti-HBs concentration in the group of patients < 15 years old was 611 ± 908.3 IU/mL, then the anti-HBs concentration gradually decreased and the group of patients ≥ 60 years old was 193. 5 ± 286.4 IU/mL (Table 3). In another study by Le Dinh

Vinh Phuc in women between 20 and 35 years old, the average anti-HBs concentration in the group of patients from 20 to < 35 years old was 227.8 IU/mL, from 25 to < 30 years old was 242.6 IU/mL and, from 30 to 35 years old was 270.6 IU/mL[6]. When the body is exposed to HBV, the immune system is activated to produce antibodies called anti-HBs. The qualitative and quantitative testing of anti-HBs to be able to assess the body's ability to protect against the attack of HBV. In normal people, anti-HBs is obtained in acute HBV infection patients who clear the virus from the body. In these patients, the body has immunity against HBV and isn't reinfected HBV. A failed immune to HBsAg leads to chronic HBV infection. Anti-HBs is also achieved after HBV vaccination, and the body produces anti-HBs. In vaccinated individuals, in contrast, the immune response is usually not as strong as in natural HBV infection, and vaccine-induced antibodies are not long-lived but subside and can be detected after the last vaccination. Anti-HBs is produced in the vaccinated person, but it varies from person to person[5]. That explains why there are some people, even though they are fully vaccinated vaccination against HBV but isn't acquired anti-HBs[7]. Therefore, the anti-HBs test helps patients know whether they have protective antibodies against HBV or is vaccination effective. Research results of 163 patients with a history of vaccination HBV, 21.5% (35 patients) had negative anti-HBs (Table 2). It means, these patients are not immune to HBV. Over time, anti-HBs levels can gradually decrease and if the results are negative or the antibody levels are not protective enough, these patients need to be vaccinated again. To be able to know the exact concentration of anti-HBs in the body, we need to quantify anti-HBs1. Because when the level of anti-HBs is low, the ability to resist the attack of HBV is weak, it is difficult to protect patients from HBV reinfection. Not only HBsAg positive's patients are infected HBV, but also patients who have been infected with HBV and achieved seroclearance with HBsAg or are in occult HBV infection group, have negative HBsAg and negative anti-HBs. Initial screening for occult HBV infection in HBsAg negative patients should be tested for anti-HBc total. This is an antibody against the core antigen HBcAg, appears when the body is infected with HBV and isn't acquired after vaccination. A positive anti-HBc total shows the infected HBV before. According to table 5, in 268 patients tested for anti-HBc total, 147 patients were positive (54.9%), of which 17 patients were anti-HBs negative. Patients with HBsAg negative and anti-HBc total positive still remain at risk of HBV reactivation when receiving immunosuppressive therapies, even when anti-HBs is positive.

CONCLUSION

During the period from April 2012 to July 2020, the study selected 1024 patients who were examined and treated at the Center for Tropical Diseases - Bach Mai Hospital met the study criteria, have some conclusions.

In total 1024 patients, there were 708 patients (69.1%) with anti-HBs positive and the average anti-HBs concentration was 356.1 ± 400.6 IU/mL, with 90.7% of anti-HBs levels ≥ 10 IU/mL, in which 18.6% of patients had anti-HBs levels ≥ 1000 IU/mL. The average anti-HBs concentration was highest at the age of < 15 years old (611.3 ± 908.3 IU/mL) then the average concentration gradually decreased with age, anti-HBs levelsisn't different between male and female. Among 163 patients with a history of HBV vaccination, 78.5% of patients were positive anti-HBs. In 268 tested for anti-HBc total, there were 17 possitive patients, accounted for 22.1% in 77 anti-HBs negative patients

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