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Distribution of Anti-HBs Levels in Korean Adults

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Abstract

Exact titration of anti-HBs with mIU/mL unit is necessary in evaluating the success of HBV vaccination or in making a decision to increase the dose of HBV vaccination. Data of distribution of anti-HBs titers can contribute to cutting of public health costs by reducing unnecessary HBV booster doses. Moreover, anti-HBc is also an important marker for differentiation of vaccination-induced anti-HBs from infection-acquired anti-HBs. However, not much study about these subjects has been done in Korea. So we evaluated anti-HBs associated with anti-HBc and vaccination history. HBsAg and anti-HBs tests were done in 1,465 cases. The positive rates of HBsAg and anti-HBs were 4.5% and 74.6%, respectively. Anti-HBs positive rate was higher in the vaccinated group than that in the non-vaccinated group. The rates of anti-HBs positive cases with lower titers (10−<100 mIU/mL) were 31.9%, while cases with higher titers (≥100 mIU/mL) were 68.1%. This suggested about 70% of anti-HBs-positive Korean adults (about 53% of the general adult population) have long-lasting immunity against HBV infection and may not require booster doses of HBV vaccination for a long time. Anti-HBs titers in the vaccine-induced anti-HBs group were higher than those in the infection-acquired anti-HBs group. No statistical differences were noted between male and female or among age groups. 25.7% of the HBsAg (−)/anti-HBs (−) group showed anti-HBc positive and HBV-DNA was detected in 11.1% among HBsAg (−)/anti-HBs (−)/anti-HBcAb (+) cases. Further study about post vaccination anti-HBs titer decay in Korean should be performed to help cut vaccination costs.

Key Words: Anti-HBs, titration, HBsAg, anti-HBc, HBV-DNA, Korean

INTRODUCTION

Hepatitis B virus (HBV) vaccination has been available in Korea since 1983. Many studies on HBV vaccination and positive rates of anti-HBs in Koreans have been made since then. Positive rates of anti-HBs in Korean adults are known to be about 60−85%.[1-10]

Many of them were probably acquired from recovery of transient HBV infection because programmed HBV vaccination has been relatively thoroughly carried out under the age of 20, but not in most Korean adults. For the effective prevention of HBV infection or success of HBV vaccination, more than 10 mIU/mL unit of anti-HBs titer is required. Simple acquisition of positive or negative results is not enough to evaluate the immune status of vaccine candidates. However, studies about anti-HBs titers among Korean adults have been rare. A few studies were performed about anti-HBs titration associated with evaluation of HBV vaccination efficiencies. However, they did not use the exact titration of anti-HBs based on mIU/mL unit recommended by the World Health Organization (WHO), but on the calculation of radioimmunoassay (RIA) unit. Exact titration of anti-HBs with mIU/mL unit is necessary to evaluate the success of HBV vaccination or to determine the booster dose of HBV vaccination. Data of anti-HBs titers can contribute to cutting public health costs by reducing unnecessary HBV booster doses. Moreover, anti-HBc is also an important marker for differentiation of vaccination-induced anti-HBs from naturally-acquired anti-HBs. However, this has not been studied much in association with other HBV viral markers in Korea. So we evaluated the anti-HBc associated with anti-HBs and vaccine history. The purpose of this study was to investigate the status of anti-HBs titers in Korean adults associated with other HBV viral markers (HBsAg, anti-HBc, HBV-DNA) and HBV vaccination history, to provide guidance in HBV booster vaccination.

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MATERIALS AND METHODS

Surveillance of HBV vaccination history

We surveyed 1,465 persons visiting the health care center of Seoul Paik Hospital, from June to August 1998. The number of male and female subjects were 1,149 (78.4%) and 316 (21.6%) respectively. The age distribution was between 21 and 67. Among 1,465 persons, 754 persons replied to surveillance questions and they were classified into the vaccination surveillance group. Items of surveillance included history of HBV vaccination, number of doses administered and the interval between the last dose and time of anti-HBs test. We also asked about the type of regimen of HBV vaccination, but most people did not remember whether it was Hepavax, Hepax, or Engelix B etc. As a results, we excluded that item and only analyzed the inoculation of vaccine, the number of doses and intervals. Anyone being inoculated more than once was classified into the vaccinated group. According to the number of doses, they were divided into complete (3 or more) and incomplete (1 or 2) vaccine groups. Persons who did not receive any vaccine were classified in the non-vaccinated group.

HBsAg and anti-HBs with titration

HBsAg test and anti-HBs test with titration were performed in 1,465 specimens with microparticle enzyme immunoassay (Abbott, Chicago, IL, USA) using an AxSym analyzer. Samples with S/N (sample rate/index calibrator mean rate) values greater than or equal to 2.0 were considered positive in HBsAg test. In anti-HBs test, specimens with values greater than or equal to 10 mIU/mL were considered positive. Specimens with anti-HBs titers in the range of 10 to 100 mIU/mL were classified in the lower titer group and anti-HBs titers greater than 100 mIU/mL were classified in the higher titer group.

Anti-HBc study

Anti-HBc tests were performed in 351 specimens among the vaccination surveillance group with microparticle enzyme immunoassay (Abbott, Chicago, IL, USA) using an AxSym analyzer. Samples with S/C (sample to cut off ratio) values in the range of 0.000 to 1.000 were considered positive.

Liver function test and HBV DNA PCR study

Among anti-HBc positive cases, liver function test regarding alanine aminotransferase and aspartic aminotransferase (Beringer-Mannheim, GmbH, Mannheim, Germany) were performed and HBV-DNA polymerase chain reaction (PCR) tests (Roche Diagnostic System, Inc. Branchburg, NJ, USA) were performed in anti-HBs negative cases. Reference ranges of aminotransferase were between 0 to 40 mIU/mL. HBV-DNA PCR test was also done in two cases of HBsAg and anti-HBs co-positive specimens.

Statistical analysis

SPSS for Windows version 8.0 was used for statistical analysis. The unpaired student t-test, one way analysis of variance, or Mann-Whitney test was performed for comparison of variables between groups.

RESULTS

Patient distribution according to HBsAg and anti-HBs positivity (Table 1)

HBsAg and anti-HBs tests were done in 1,465 cases. The positive rate of HBsAg was 4.5% (66/1,465). There were two cases of HBsAg and anti-HBs co-positive cases, which showed negative results in HBV-DNA PCR test. The positive rate of anti-HBs was 74.6% (1,093/1,465). The number of HBsAg and anti-HBs co-negative cases were 308 (21%). The total number in the HBV vaccination surveillance group was 754 and the total number of vaccinated and non-vaccinated groups among these were 465 (61.7%) and 289 (38.3%), respectively. The proportions of HBsAg and anti-HBs positivity in the vaccination surveillance group were similar to those of the total study group. However, the positive rates of HBsAg (+)/anti-HBs (−) in the vaccinated group was 0.9% compared with a positive rate of 10.0% in the non-vaccinated group ($p<0.001$). Anti-HBs positive rates were 84.3% and 63.3% in the vaccinated and non-vaccinated groups, respectively ($p<0.001$). Anti-HBc tests were performed in 351 cases among the vaccination surveillance group. The proportions of HBsAg and anti-HBs positivity in this group were also similar to those in the total study group.

Table 1. Patient Distributions According to the HBsAg and Anti-HBs Positivity

HBsAg/anti-HBs Group	HBsAg (+)/ anti-HBs (+) No. (%)	HBsAg (+)/ anti-HBs (−) No. (%)	HBsAg (−)/ anti-HBs (+) No. (%)	HBsAg (−)/ anti-HBs (−) No. (%)	Total No. (%)
Total study group	2 (0.1)	64 (4.4)	1091 (74.5)	308 (21.0)	1465 (100.0)
Male	2 (0.2)	53 (4.6)	866 (75.4)	228 (19.8)	1149 (100.0)
Female	0 (0.0)	11 (3.5)	225 (71.2)	80 (25.3)	316 (100.0)
Vaccination surveillance group	1 (0.1)	33 (4.4)	575 (76.3)	145 (19.2)	754 (100.0)
Vaccinated	1 (0.2)	4 (0.9)	392 (84.3)	68 (14.6)	465 (100.0)
Non-vacinated	0 (0.0)	29 (10.0)	183 (63.3)	77 (26.6)	289 (100.0)

Table 2. Patient Distribution According to Anti-HBs Tters in Total Study Group

Anti-HBs titer (mIU/mL)	Male No.(%)	Female No.(%)	Total No.(%)
<10	281 (24.5)	91 (28.8)	372 (25.4)
≥10−100	280 (24.4)	69 (21.8)	349 (23.8)
>100−1000	446 (38.8)	103 (32.6)	549 (37.5)
>1000−10000	120 (10.4)	39 (12.3)	159 (10.9)
>10000	22 (1.9)	14 (4.4)	36 (2.4)
Total No. (%)	1149 (100.0)	316 (100.0)	1465 (100)

Patient distribution according to anti-HBs titers in the total study group (Table 2)

The positive rate of anti-HBs in the total study group was 74.6%. The rate of anti-HBs with lower titer (10−100 mIU/mL) was 23.8% (31.9% of anti-HBs positive cases). The rate of anti-HBs positive cases with titers from 100 to 1,000 mIU/mL was 37.5% (50.2% of anti-HBs positive cases). Anti-HBs positive cases with titers from 1,000 to 10,000 mIU/mL was 10.9% (14.5% of anti-HBs positive cases). Anti-HBs positive cases with titers greater than 10,000 mIU/mL were observed in 36 cases (3.3% of anti-HBs positive cases). Therefore, the overall rate of the higher titer group in anti-HBs positive cases was 68%. No statistical differences were noted between male and female ($p=0.731$).

Patient distribution and mean anti-HBs titers according to age and sex (Table 3)

We analyzed the patient distribution and mean anti-HBs titers according to age and sex. No statistical differences were seen between male and female according to age distribution ($p>0.05$). Apparently, the highest geographic mean titers in anti-HBs titrations were observed in the twenties in the male group and thirties in the female group. However, no statistical differences were observed among age groups in male ($p=0.127$) and female

Table 3. Distribution of Anti-HBs Titers according to Age and Sex

Ages	Male		Female		p value
	Cases (%)	Anti-HBs titer*	Cases (%)	Anti-HBs titer	
20−29	82 (7.1)	1799±3935	89 (28.2)	2978±11497	0.166
30−39	458 (39.9)	1226±5018	74 (23.4)	4413±20977	0.197
40−49	401 (34.9)	1064±2810	77 (24.4)	1301±3213	0.204
50−59	157 (13.7)	622±1598	55 (17.4)	407±730	0.711
≥60	51 (4.4)	532±1611	21 (6.6)	813±3178	0.407
Total	1,149 (100.0)	930±3797	316 (100.0)	2314±12013	

* Mean±SD.

Table 4. Patient Distribution According to Anti-HBs Titers and Number of Vaccinations

Anti-HBs titer (mIU/mL)	Number of vaccinations (%)					Total (%)
	0	1	2	3	4	
<10	106 (36.7)	22 (24.2)	20 (14.9)	26 (13.5)	4 (8.5)	178 (23.6)
≥10–100	54 (18.7)	25 (27.5)	46 (32.3)	63 (32.6)	12 (25.5)	200 (26.5)
>100–1000	104 (36.0)	35 (38.5)	50 (37.3)	74 (38.3)	20 (42.6)	283 (37.5)
>1000–10000	24 (8.3)	7 (7.7)	13 (9.7)	19 (9.8)	8 (17.0)	71 (9.4)
>10000	1 (0.3)	2 (2.2)	5 (3.7)	11 (5.7)	3 (6.4)	22 (2.9)
Total No (%)	289 (100)	91 (100.0)	134 (100)	193 (100)	47 (100)	754 (100)

Table 5. Association among HBsAg, Anti-HBs, Anti-HBc and HBV Vaccination History

Anti-HBc/ vaccination history		Group I HBsAg (+)/ anti-HBs(−) number	Group II HBsAg (−)/ anti-HBs (+) number	Group III HBsAg (−)/ anti-HBs (−) number	Total number (%)
Anti-HBc (+)	Vaccination (+)	4	91	8	103 (29.3)
	Vaccination (−)	15	73	10	98 (27.9)
Anti-HBc (−)	Vaccination (+)	0	88	21	109 (31.1)
	Vaccination (−)	0	10	31	41 (11.7)
Total number (%)		19 (5.4)	262 (74.6)	70 (19.9)	351 (100)

($p=0.310$).

Patient distribution according to anti-HBs titers and administration number (Table 4)

We analyzed 754 cases in the vaccination surveillance group according to the administration number and interval between the last dose and analysis time of anti-HBs titration. Among 289 subjects in the non-vaccinated group, 63.3% showed anti-HBs positivity. Among them, 54 cases (29.5% of positive cases) showed lower anti-HBs titers and 129 cases (70.5% of positive cases) showed higher anti-HBs titers. The total number in the incomplete vaccine group was 225 (29.8% of vaccination surveillance group and 48.4% of vaccinated group) and the positive rate of anti-HBs was 81.3% among them. The rate in the lower titer group was 38.8% and in the higher titer group it was 61.2% among them. The total number in the complete vaccine group was 240 cases (31.8% of the vaccination surveillance group and 51.6% of the vaccinated group) and 87.5% of them showed anti-HBs positivity. Among anti-HBs positive in the complete vaccinee group, 35.7% were included in the lower titer group and 64.3% in the higher titer group.

Association among HBsAg, anti-HBs, anti-HBc and HBV vaccination history

For the evaluation of HBV vaccination efficacy, anti-HBc test was performed in 351 cases among the vaccination surveillance group. According to the results of HBsAg and anti-HBs, they were divided into groups I, II and III (Table 5). The positive rates of anti-HBc were 100.0%, 62.6% and 25.7% in groups I, II and III, respectively. The positive rate of anti-HBc was 57.2% in the anti-HBc study group and 48.6% in vaccinated cases, respectively. In group II, group A, B and C were subdivided according to the presence of anti-HBc and vaccination history (Table 6). Group A represented the cases which received HBV vaccination regardless of its completion without HBV viral marker study, including anti-HBc.

Table 6. Comparison of Anti-HBs Titers, Number of Vaccinations and Intervals in HBsAg (−)/Anti-HBs (+) Groups

Parameter	Group A anti-HBc (+)/ vaccination (+)	Group B anti-HBc (+)/ vaccination (−)	Group C anti-HBc (−)/ vaccination (+)	p values
Number of cases	91	73	88	
Anti-HBs titer (mIU/mL)*	1024.2±3147.5	797.6±1722.3	3505.5±10219	0.022†
Number of vaccinations				0.024
1	16	not available	10	
2	36		24	
3	31		39	
4	2		11	
No record	6		4	
Interval (year)*	6.0±4.2	not available	5.6±4.0	0.601

* Mean±SD.
† p value between infection-induced anti-HBs groups (group A and B) and vaccination-induced anti-HBs group.

Table 7. Comparisons of Liver Function Test and HBV DNA PCR Tests in Anti-HBs (−)/Anti-HBc (+) Groups

HBsAg/vaccination	Group D	Group E	Group F	Group G
LFT/HBV PCR	HBsAg (+)/ vaccination (+)	HBsAg(+)/ vaccination (−)	HBsAg (−)/ vaccination (+)	HBsAg (−)/ vaccination (−)
Cases (number)	4	15	8	10
Cases (%) of abnormal LFT	1 (25%)	3 (20%)	0 (0%)	3 (30%)
Cases (%) of HBV DNA PCR (+)	4 (100%)	15 (100%)	0 (0%)	2 (20%)

These patients happened to be already HBsAg positive or anti-HBc positive in the latent or window period before our surveillance study. Group B seemed to be the cases which had naturally-acquired anti-HBs through transient infection. Group C seemed to be the cases which acquired anti-HBs purely from vaccination. So, the rates of naturally-acquired anti-HBs and vaccine-induced anti-HBs were estimated as 46.7% (164/351) and 25.1% (88/351), respectively in the general Korean adult population. Anti-HBs titers were statistically higher in group C (vaccine-induced anti-HBs group) compared to those of group A and B (infection-induced anti-HBs group) ($p=0.022$). No statistical difference was observed between group A and B in anti-HBs titers ($p=0.582$). Statistical difference was seen in administration number ($p=0.024$), but not in intervals ($p=0.601$) between group A and group C.

The 10 cases showing HBsAg (−)/anti-HBs (+) /anti-HBc (−)/HBV vaccination (−) results could not be exactly explained. Their anti-HBs titer ranges were from 12.8 to 614.2 mIU/mL (mean±SD; 249.4±219.7). The titers were too high to be estimated as non-specific reactions, except for two cases (12.8 and 15.4 mIU/mL). Incorrect or untruthful answers to surveillance questions about vaccination were presumed to be one of the reasons. There were no problems about the reliability of test results because control materials and calibrators were used daily.

Evaluation of HBV infectivity in anti-HBc (+)/anti-HBs (−) cases (Table 7)

For the evaluation of HBV infectivity in anti-HBc positive cases among anti-HBs negative groups, we tested transaminase (ALT and AST) and HBV DNA PCR in 37 cases belonging groups I and III and classified them into groups D, E, F and G. Rates of abnormal LFT were 25%, 20%, 0% and 30% in groups D, E, F and G respectively. Abnormal LFT results were observed in 21.1% of HBsAg positive groups (groups D and E) and 16.7% of HBsAg negative groups (groups F and G) ($p=0.427$) and in 8.3% of vaccinated groups and 24% of non-vaccinated groups ($p=0.003$) As expected, all of the cases in groups D and E showed HBV DNA. There were no cases representing abnormal LFT and HBV DNA in group F. Two of the three cases with abnormal LFT in group G represented HBV DNA.

DISCUSSION

Many studies about the prevalence of HBV have been performed and the positive rates of HBsAg and anti-HBs have been determined. These studies were widely performed in the population of children, adolescents, adults, health care center visitors and special job groups in Korea.[1-10] Now, the prevalence rates of HBsAg are known to be about 3−6%.[1-10] The rates have decreased in the past 20 years since HBV vaccination was introduced. The positive rate of HBsAg did not show much variation according to several authors. Positive rates of HBsAg in our study was also 4.5% in the total study group. As expected, it was higher in the non-vaccinated group than in the vaccinated group ($p<0.001$). However, many variations were noted in the positive rates of anti-HBs. There were two reasons. One was the variation in the study population and time and the other was the test method of anti-HBs. More than 10−20% variations could be observed in the different study populations using the same passive-hemagglutination (PHA) test method.[2-7] A tendency toward increasing positive rates of anti-HBs was observed in the early 1990s.[7-10] Though variations according to the study time and populations were observed, the most prominent factor regarding the variations of positive rates in anti-HBs was the difference in test methods. Very contradictive data could be seen in several studies according to the different methods. Most of the mass screen studies had been done by the PHA method. They only represented 16−28% positivity in the early 1980s and 30−47.2% positivity in early 1990s. Conversely, most studies except one[11] using the radioimmunoassay (RIA) method or enzymeimmunoassay (EIA) method showed 61.8−84.8% positivity in anti-HBs regardless of the study population and time.[1,8-10] Even the study done by the RIA in the 1980s[1] showed 62.4% positivity compared to the 30−40% positive rates done by the PHA method in the early 1990s. As is well known, the PHA method only detects levels of ug/mL molecules, compared to the RIA or EIA method which detect the pg/mL level of molecules.[12] About 33% of anti-HBs negative cases by the PHA method showed anti-HBs positive by the EIA method.[13] So it should be necessary to replace the PHA method with the EIA or RIA method regardless of the test cost for precise evaluation of the prevalence of anti-HBs. This would be the most cost-efficient method in real terms. In our study, the positive rate of anti-HBs in the total study group was 74.5%, which was similar or somewhat higher than those of other studies using the EIA or RIA methods in Korea. The higher anti-HBs positive rate in the vaccinated group than in the non-vaccinated group (84.5% vs 63.3%) obviously reflected the HBV vaccination effects against HBV infection. Another study done in 1994 showed similar rates between vaccinated and non-vaccinated groups.[8] So the positive rates of anti-HBs in Korean adults seemed to have been little changed in the 1990s.

What is the purpose of the titration of anti-HBs? Some authors classified the vaccine groups according to the anti-HBs titers after the basic course of HBV vaccination.[14-18] An individual with a peak anti-HBs titer of less than 10 mIU/mL after the basic course of HBV vaccination was regarded as a non-responder or inadequate responder. Individuals with anti-HBs levels of 10−100 mIU/mL were considered as low responders, whereas anti-HBs levels above 100 mIU/mL were regarded as good responders and were usually followed by long-term immunity. However, recent published papers reported that once a level above 10 mIU/mL of anti-HBs is acquired, it is unnecessary to give a booster dose even when the level of anti-HBs falls below 10 mIU/mL.[19-21] By contrast, in immune compromised patients infected with human immuno-deficiency virus (HIV), only 40−53% of the vaccined cases developed antibody.[22] Moreover, diminished responses to HBV vaccine have also been noted in patients with chronic renal failure, alcoholics, and others with advanced liver disease, persons with type I diabetes, and cancer patients.[20,21] The advisory committee of immunization practices (ACIP) has endorsed that for hemodialysis patients, vaccine-induced protection may be less complete and may persist only as long as antibody levels are ≥ 10 mIU/mL. For these patients, the need for booster doses should be assessed by annual antibody testing, and a booster dose should be administered when antibody levels decline to <10 mIU/mL.[19]

Though our study was a cross-sectional study and the anti-HBs titers were not at the peak level after a basic course of vaccination, the rate of higher anti-HBs titer cases in our study seemed to be meaningful. Even the rates of cases with more than 1,000 mIU/mL level of anti-HBs was 17.8% among anti-HBs positive cases. There have been some reports about the decline of anti-HBs titer. The level of anti-HBs does wane after vaccination, quite rapidly within the first year and more slowly thereafter.[14] The actual anti-HBs titers are shown to be proportional to the peak titer one month post-booster, but inversely proportional to the number of months between the time of booster and of retesting. Anti- HBs titers over 10,000 mIU/mL which are sometimes accomplished by hepatitis B vaccination may last much longer than the period of 7-10 years.[22] Persistence of anti-HBs is known to be related to the maximum antibody response.[14,16] As vaccinated cases developing a higher titer will naturally retain antibody for a longer period than those with lower levels of antibody, our study suggested that about 70% of anti-HBs positive Korean adults (about 53% of the general adult population) seemed to have long-lasting immunity against HBV infection as good responders.

Apparently, no statistical differences were seen in the distribution of lower and higher anti-HBs titers between the non-vaccinated group and vaccinated (incomplete and complete) group (Table 4). However, we must consider the distribution of anti-HBs in relation to anti-HBc and HBV vaccination doses and intervals. Anti-HBc is a remarkable marker to differentiate vaccine-induced anti-HBs from infection-acquired anti-HBs. The positive rate of anti-HBc was 57.2% in the total anti-HBc study group and 48.6% in vaccinated cases, respectively (Table 5). Although the high rate of anti-HBc was unusual in the vaccinated group, we suggest that many Korean adults might take HBV vaccination during a window period or latent period or had an irregular booster dose after acquisition of infection-induced anti-HBs without full HBV marker study, including anti-HBc. Incomplete HBV vaccination seemed to be one of the reasons. The positive rates of anti-HBc in Korea were reported as 55.8% in 1985[11] and 24.9% in 1997[9] respectively. The rates of anti-HBc-alone positive cases were 5.1% in our study, but 19%[11] and 1.9%[9] in other studies. Moreover, anti-HBs-alone positive rates and co-positive rates with anti-HBs and anti-HBc were different. The rate of co-positive cases was higher in our study (46.7%) than those in two other studies (25%[11] and 21%[9]). The rates of anti-HBs-alone positive cases were 27.9% in our study and 1.2%[11] and 40.7%[9] in other studies. The inoculation rate of HBV vaccination was reported as only 36% in 1994 in Korean adults,[8] and if based on the basic 3-dose course, it was similar to the rate in our study (31.8%). So the inoculation rate was still low in Korean adults to prevent HBV infection and much anti-HBs in Korean adults was acquired from HBV infection rather than HBV vaccination (46.7% vs. 25.1% in our study). Though the reasons why the rates of anti-HBs positive cases were so different among the studies could not be determined, we could differentiate the anti-HBs titers according to the presence of Anti-HBc. Anti-HBs titers were significantly higher in the vaccine-induced anti-HBs group (group C) compared to those in groups A and B (infection-induced anti-HBs) ($p=0.022$). Although the reason why anti-HBs titers in vaccine-induced anti-HBs groups were higher than those of infection-acquired antibody could not be exactly resolved, and although we could also not exclude the natural booster effect, this suggested that individuals with vaccine-induced anti-HBs had more effective long-term protective levels of anti-HBs against HBV infection than individuals with infection-induced anti-HBs. Kim et al also reported higher anti-HBs titers in the anti-HBc negative group than in the anti-HBc positive group after HBV vaccination.[23] In the aspect of the number of vaccinations and intervals, anti-HBs titer was correlated with the number of vaccinations ($p=0.024$) and not with the intervals in our study. We thought these represented that the complete three-dose basic vaccination schedules should be followed for successful HBV vaccination and an additional 4th or more dose could be given to low responders or non-responders to increase the seroconversion rate of anti-HBs.[16-19,23-25] Once we acquired the desirable level of anti-HBs, the booster interval did not seem to be so serious. From another aspect, a few persons who adequately responded to HBV vaccine developed HBV infection following exposure years after vaccination. Thus, the issue of waning anti-HBs and regular booster doses is still recommended by some authors.[20,26,27] We think one of the reasons for recommending regular booster doses was because there were discrepancies between the test methods or kits for detecting anti-HBs. West et al noted a few circumstances under which a titer of 10 mIU/mL might not completely exclude significant HBV infection.[20]

In 70 cases with HBsAg (−)/anti-HBs (−), 18 cases (25.7%) showed only anti-HBc and 2 of these cases (2.9% of the HBsAg (−)/anti-HBs (−) group and 11.1% of HBsAg (−)/anti-HBs (−)/anti-HBc (+)) finally had HBV DNA. Jilg et al reported that HBV was found using PCR in 32.9% of individuals with anti-HBc alone.[28] In spite of the difference in positive rates of anti-HBc and some controversies about anti-HBc,[9,11,28-30] the anti-HBc test is recommended for the evaluation of HBV vaccination efficacy and the detection of risk donor because Korea is such an endemic areas of HBV.

We concluded that about 70% of anti-HBs positive Korean adults (about 53% of the general adult population) had a level of more than 100 mIU/mL of anti-HBs, suggesting they will not need a booster dose for a long time. Further study about post-vaccination anti-HBs titer decay in Koreans should be performed to help cut vaccination costs. Booster vaccinations could be performed on a more individual basis, taking into consideration the actual antibody concentration of the prospective subject.

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