Original Article

Immunologic Response to Hepatitis B Virus Vaccination among Human Immunodeficiency Virus Thai Adults without Hepatitis B Virus Infection

Varalee Terbsiri MD[1], Palakorn Panarat MD, MSc[2]

[1] Department of Medicine, Queen Savang Vadhana Memorial Hospital, Chonburi, Thailand

[2] Division of Infectious Diseases, Department of Medicine, Queen Savang Vadhana Memorial Hospital, Chonburi, Thailand

Background: It is currently recommended that hepatitis B virus (HBV) vaccine be provided for every HIV-infected patient with no HBV immunity. HBV immunization program for HIV-infected patients was suggested to be given in three doses of vaccine at zero, one and six months. HBV vaccine has been included in the Thai immunization program for newborns for three doses, at birth, M2, and M6. Hence, one dose of vaccination might respond in complete protective immunity in some of the HIV patients.

Objective: To evaluate HIV-infected patients' response to one dose of vaccine and their associated factors.

Materials and Methods: The present study was a Retrospective Cohort Study. It recruited patients who had come to Queen Savang Vadhana Memorial Hospital for their hepatitis B vaccination between January 1, 2018 and March 31, 2020. Eligible patients were infected with HIV, received ART, and had CD4 of more than 200 cells/mm^3. The authors collected data from the patients having anti-HBs of less than 10 mIU/mL with negative anti-HBc who received HBV vaccine. From the medical records, the authors evaluated their anti-HBs titer after the first dose of vaccination, and the titer after a third dose, in cases the result of the first dose was negative.

Results: Of the 88 HIV-infected patients who received HBV vaccination, 19 patients (21.6%) showed protective anti-HBs after the first dose of vaccination. Factors associated with the presence of anti-HBs after the first dose included age as the patients of 29 years or older had protective anti-HBs of 15% and the patients younger than 29 years old had protective anti-HBs of 43% (p=0.013), and anti-HBs titer before the vaccination as the patients with titer of less than 2 mIU/mL had protective anti-HBs of 17% and the patients with titer of 2 to less than 10 mIU/mL had protective anti-HBs of 44% (p=0.038).

Conclusion: Some HIV-infected patients have developed protective anti-HBs after the first dose of HBV vaccination especially the younger age of less than 29 years old and with an anti-HBs titer before vaccination of 2 mIU/mL or above. Almost half of them required only one HBV booster to achieve protective anti-HBs.

Keywords: Vaccine; Hepatitis B; HIV; Vaccination; Immunity

Received 29 June 2021 | Revised 6 September 2021 | Accepted 15 September 2021

J Med Assoc Thai 2021;104(11):1828-35

Website: http://www.jmatonline.com

Since human immunodeficiency virus (HIV) and hepatitis B virus (HBV) share the same routes of transmission, co-infection is common. The prevalence of chronic HBV infection in Thailand is 5.1% of the population, or about three million people in 2015[1], and the prevalence of HIV infection in Thai population is 1.1%, or about 480,000 people[2] in 2018. The prevalence of the HBV co-infection with HIV in Thai patients is 8.7% of HIV-infected patients in tertiary care[3]. HBV infection in people living with HIV is associated with the increasing rate of cirrhosis and the higher risk of hepatocarcinoma[4]. Thus, the current recommendation is to screen for HBV infection and HBV immunity among all HIV-infected patients right after the diagnosis of HIV infection.

The World Health Organization (WHO) recommended that patients without chronic HBV infection and without immunity to HBV or anti-HBs of less than 10 mIU/mL, should receive HBV vaccination[5]. The recommended regimen is HBV vaccine IM Engerix-B® 20 mcg/mL or Recombivax HB® 10 mcg/mL, at 0, 1, and 6 months, or HBV vaccine IM Engerix-B® 40 mcg/mL or Recombivax HB® 20 mcg/mL at 0, 1, 2, and 6 months. However,

Correspondence to:

Varalee T.

Department of Medicine, Queen Savang Vadhana Memorial Hospital, 290 Jermjomphon Road, Sriracha, Chonburi 20110, Thailand.

Phone: +6638322157 ext. 3460

Email: varalee.terb@gmail.com

How to cite this article:

Terbsiri V, Panarat P. Immunologic Response to Hepatitis B Virus Vaccination among Human Immunodeficiency Virus Thai Adults without Hepatitis B Virus Infection. J Med Assoc Thai 2021;104:1828-35.

doi.org/10.35755/jmedassocthai.2021.11.13107

in a patient with low baseline CD4 cell count, vaccination should be deferred until CD4 reaches at least 350 cells/mm³. A low CD4 count of less than 200 cells/mm³ at time of vaccination has been associated with poor response to the vaccine. This recommendation is consistent with the Thailand National Guidelines on HIV/AIDS Treatment and Prevention 2017[6] to provide HBV vaccine to all HIV-infected patients without chronic HBV who have anti-HBs titer of less than 10 mIU/mL. The regimen is three doses of HBV vaccination, with the first dose at 0 month, the second dose at least one month after the first dose, and the last dose at least two months after the second dose and at least four months after the first dose but is commonly given at 0, 1, and 6 months. It is also recommended that anti-HBs titer should be checked one month after completing the vaccination regimen to ensure a good immune response.

Patients who have completed the HBV vaccine series might lose detectable anti-HBs when their immune systems are weakened. Thus, three doses of vaccination might not be necessary. Only one dose of the booster may be sufficient to promote development and achievement of protective anti-HBs[7,8] when the patients' immune systems is strong enough. HBV vaccine has been included in routine infant immunization programs in Thailand, starting with HBV vaccination to newborns in Chiang Mai and Chonburi in 1988. It extended to 12 provinces in 1990 and was later administered to all Thai newborns at birth, and then at 2 and 6 months of age in 1992. It is therefore expected that Thai adults who were born after the initiation of the HBV immunization program will have complete HBV vaccination. The authors' hypothesis is that HIV-infected patients whose CD4 count is more than 200 cells/mm³ do not require the three doses of HBV vaccine to gain protective immunity.

Queen Savang Vadhana Memorial Hospital is one of the hospitals that provides treatment and medication to numerous HIV-infected patients as well as performing blood test for HBsAg, anti-HBs, and anti-HBc to determine the co-infection status for all HIV patients. The authors also encouraged HBV vaccination to every patient who has never been infected with HBV and has anti-HBs titer below 10 mIU/mL. However, HBV vaccination for adults is not covered by the government health scheme, social security program, or by any insurance policy. All adult patients must pay for HBV vaccine themselves and most of them cannot afford it. If only one dose of HBV vaccine could be given to create protective immunity, the vaccine might become more accessible and affordable. The authors' objective was to determine the anti-HBs response after one dose of HBV vaccine among HIV-infected patients whose anti-HBs and anti-HBc were negative as well as determining factor associated with anti-HBs response.

Materials and Methods

Study population and study design

The present study was a retrospective cohort study that analyzed the data collected from Hepatitis B vaccination record at the General Practice and Internal Medicine Outpatient clinic at Queen Savang Vadhana Memorial Hospital, Chonburi. The retrospective data were extracted from medical records between January 1, 2018 and March 31, 2020. Eligible patients were over 18 years of age with HIV infection who received antiretroviral therapy (ART) regularly, had a CD4 count of more than 200 cells/mm³, and had anti-HBs of less than 10 mIU/mL with negative anti-HBc.

Inclusion criteria:

1. Patients older than 18 years
2. Eligible to receive vaccination and blood test collection
3. HIV-infected and CD4 of more than 200 cell/mm³ for at least six months
4. All negative results in serology test for HBsAg, anti-HBs, and anti-HBc

Exclusion criteria:

1. Failure to have their blood test collection for more than one appointment
2. Skin infection at the site of vaccination
3. Impossible vaccination due to personal problems

The present study used recombinant hepatitis B vaccine for vaccination from Engerix-B®, 20 mcg HBsAg/mL, GSK group, Belgium, at 294 Baht per dose, imported by GlaxoSmithKline (Thailand) Limited. These vaccines were stored in medical-grade refrigerators. All individual patients received a single dose of Engerix-B® 20 mcg intramuscular and were asked to revisit the hospital for their blood test of anti-HBs a month later, at the cost of 150 Baht. Patients who had anti-HBs of less than 10mIU/mL or negative, after the first dose should receive Engerix-B® at three months and then six months as well as a subsequent blood testing of anti-HBs a month after the last dose.

Ethical approval

The protocol for the present study was approved by the Institutional Review Board of the Research Ethic Review Committee for Research Involving

Human Research Participants, Queen Savang Vadhana Memorial Hospital (No. 001/2563)

Data collection

Baseline demographics were extracted from the medical records and collected in case record forms, which gathered information on gender, age, nationality, comorbidities, and current medication (ART). Laboratory tests including CD4 cell count, CD4 percent, and HIV-viral load before vaccination, were extracted from the electronic medical records.

The blood test was obtained for anti-HBs, HBsAg, and anti-HBc, using the electrochemiluminescence immunoassay (ECLIA) method from Roche® company in a standard laboratory (ISO 15189/15190) conducted by experienced technician at Queen Savang Vadhana Memorial Hospital. The results were existence of anti-HBs before and one month after HBV vaccination as both first and last dose were collected. Protective anti-HBs' response was defined as anti-HBs of 10 mIU/mL or more or "positive". Also recorded were anti-HBs titer, which less than 2 mIU/mL and 2 to less than 10 mIU/mL for anti-HBs negative, 10 to 1,000 mIU/mL, and more than 1,000 mIU/mL for anti-HBs positive.

For substitution of the missing data, HIV-viral load before vaccination, viral load post-vaccination closest to the vaccination were applied. Moreover, for the patients who lost to follow up after the first dose, the result was substituted with anti-HBs after the next vaccination.

Outcome

The primary outcome was proportion of the presence of protective anti-HBs after one dose of vaccination in HIV-infected patients whose CD4 count was more than 200 cell/mm³ with anti-HBc negative. The secondary outcome was the identification of the factors associated with the presence of protective anti-HBs following the initial dose and anti-HBs titer in the various groups.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA) and p-value of less than 0.05 indicated statistical significance. Data used for analyses were anti-HBs positive or negative after one dose or three doses, and anti-HBs titer after one or three doses as patients who had anti-HBs of 10 mIU/mL or more after the first dose did not receive the third dose.

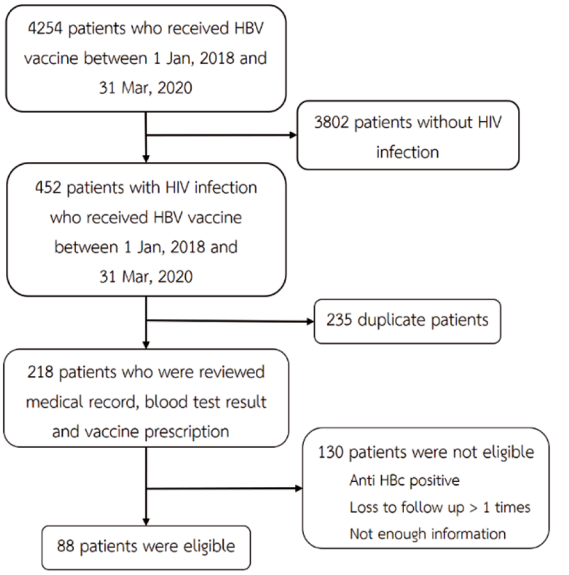

Figure 1. Flow chart of the study.

Baseline characteristics, including gender, age, nationality, CD4 cell count, CD4 percent, HIV-viral load, anti-HBs titer before vaccination, and comorbidities identified by diseases were presented in frequencies and percentages for qualitative data. Median (interquartile range [IQR]) represented non-normal distribution quantitative data and mean ± standard deviation (SD) in normal distribution for quantitative data.

Univariate and multivariate analyses were used to determine factors associated with the presence of anti-HBs after the first dose of vaccination. Fisher's exact test or Pearson's chi-square was used to analyze the qualitative data and unpaired' Student's t-test was used to compare quantitative data, presented in odds ratio (OR), 95% confidence interval (CI) and p-value. Multivariate logistic regression analysis was then performed to identify independent factors for the presence of anti-HBs.

Results

The data was collected as shown in the Figure 1 flowchart and the baseline characteristics are shown in Table 1. Of the 88 patients eligible, the mean (±SD) age was 36 (±9.16) years old and the median (IQR) CD4 level was 543 cells/mm³ at 24% with an IQR of 355 to 685 cells/mm³ for 17% to 28%. Eleven patients (13%) had a HIV-viral load of more than 20 copies/mL while all of them received regular ART, and 13.6% of the patients (12/88) had comorbidities, and included ten with dyslipidemia, one with diabetic

Table 1. Baseline characteristic of HIV-infected patients who received HBV vaccination (n=88)

Characteristic	n (%)
Sex: female	34 (38)
Age (year); mean±SD	36±9
Age group	
≥29 years	67 (76)
<29 years	21 (24)
CD4 cell count; median (IQR)	543 (355 to 685)
CD4 percent; median (IQR)	24 (17 to 28)
Viral load <20 copies/mL	77 (87)
Comorbidities*	12 (14)
ART	
Efravirenz based	59 (67)
Rilpivirine based	16 (18)
Nevirapine based	7 (8)
Protease inhibitor based	6 (7)
Anti-HBs titer before vaccination	
Titer <2 mIU/mL	72 (82)
Titer 2 to <10 mIU/mL	16 (18)

SD=standard deviation; IQR=interquartile range; ART=antiretroviral therapy; HBs=hepatitis B surface

* Any of dyslipidemia, HCV infection, diabetic mellitus, chronic kidney disease

mellitus, one with hepatitis C virus (HCV) infection, and one with chronic kidney disease. Regarding the ART, 59 had efavirenz based (67%), 16 had rilpivirine based (18%), seven had nevirapine based (8%), and six had protease inhibitor based (7%). In addition, the anti-HBs titer before vaccination was divided into less than 2 mIU/mL for 72 patients (82%) and 2 to less than 10 mIU/mL for 16 patients (18%).

Out of the 92 patients that received at least one dose of vaccination, 89% (82) returned for anti-HBs titer evaluation after the first dose. Four patients who failed to check anti-HBs after their first dose and then were found to be anti-HBs positive after their second dose were excluded from the study. Of the 88 patients eligible for the analysis, 19 (21.6%) patients have protective anti-HBs after one dose of vaccination. For univariate analysis, it was found that the factors associated with the presence of anti-HBs are age. The 29 years old and older group had less protective anti-HBs than the younger than 29 years old age group at 15% versus 43% [(p=0.013, OR 0.23 (95% CI 0.08 to 0.69)]. In addition, patients who had anti-HBs 2 to less than 10 mIU/mL before vaccination had more protective anti-HBs than those who had less than 2 mIU/mL at 44% versus 17% [(p=0.038, OR 3.89 (95% CI 1.21 to 12.5)] as shown in Table 2. On

Table 2. Univariate and Multivariate analyses of factors relating to presence of protective anti-HBs after 1 dose of HBV revaccination (n=88)

Characteristic	Presence of protective anti-HBs after 1 dose (n=19); n (%)	Absence of protective anti-HBs after 1 dose (n=69); n (%)	OR (95% CI)	p-value§	Adjusted OR (95% CI)	p-value§
Sex: female¤	7 (37)	27 (39)	0.97 (0.32 to 2.59)	1.00	2.84 (0.69 to 11.63)	0.15
Age groupϕ			0.23 (0.08 to 0.69)	0.01	0.19 (0.05 to 0.83)	0.03
≥29 years	10 (53)	57 (82)				
<29 years	9 (47)	12 (17)				
CD4 cell count; median (IQR)	425 (324 to 787)	563 (370 to 680)		0.70	1.00 (0.99 to 1.00)	0.96
CD4 percent; median (IQR)	23 (17 to 31)	24 (18 to 28)		0.87	1.02 (0.92 to 1.13)	0.73
Viral load <20 copies/mL	15 (79)	62 (90)	2.36 (0.61 to 9.13)	0.24	2.60 (0.47 to 14.47)	0.28
Comorbidities*	1 (5)	11 (16)	0.29 (0.03 to 2.42)	0.45	0.83 (0.08 to 8.76)	0.88
ART						
Efravirenz based	16 (84)	43 (62)	Reference		Reference	
Rilpivirine based	2 (11)	14 (20)	0.38 (0.08 to 1.88)	0.23	0.21 (0.03 to 1.43)	0.11
Nevirapine based	1 (5)	6 (9)	0.45 (0.05 to 4.02)	0.47	0.45 (0.04 to 5.52)	0.53
Protease inhibitor based	0 (0)	6 (9)	-		-	
Anti HBs titer before vaccination°			3.89 (1.21 to 12.50)	0.04	7.47(1.70 to 32.69)	<0.01
Titer <2 mIU/mL	12 (63)	60 (87)				
Titer 2 to <10 mIU/mL	7 (37)	9 (13)				

OR=odds ratio; CI=confidence interval; IQR=interquartile range; ART=antiretroviral therapy; HBs=hepatitis B surface

* Any of dyslipidemia, HCV infection, diabetic mellitus, chronic kidney disease; ¤ Male was the reference group; ϕ <29 years old group was the reference group; ° Titer <2 mIU/mL group was the reference group; § p<0.05, statistical significance

Table 3. Univariate subgroup analyses of factors relating to presence of protective anti-HBs after 1 dose of HBV revaccination in those who completed the blood test strictly with the protocol (n=75)

Characteristic	Presence of protective anti-HBs after 1 dose (n=19); n (%)	Absence of protective anti-HBs after 1 dose (n=56); n (%)	p-value	OR (95% CI)
Age ≥29 year	10, (53)	45, (80)	0.03	0.27 (0.09 to 0.83)
Anti HBs titer before vaccination			0.05	3.50 (1.06 to 11.50)
Titer <2 mIU/mL	12 (63)	48 (86)		
Titer 2 to <10 mIU/mL	7 (37)	8 (14)		

OR=odds ratio; CI=confidence interval; HBs=hepatitis B surface

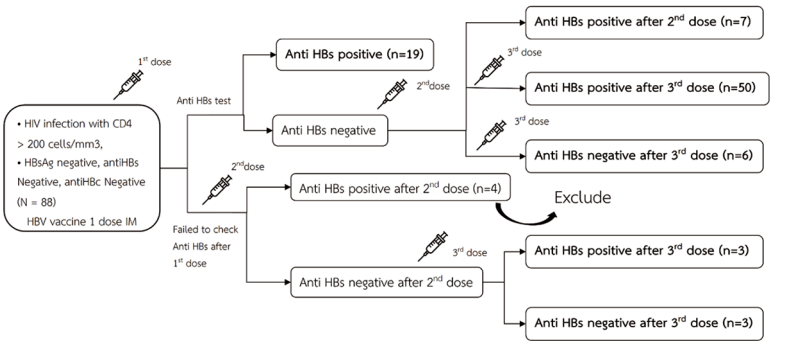

Figure 2. Timeline of the study.

multivariate analysis, the factor that was predictive of the presence of anti-HBs are age group [adjusted OR 0.19 (95% CI 0.05 to 0.83), p=0.03] and anti-HBs titer before vaccination [adjusted OR 7.47 (95% CI 1.7 to 32.7), p≤0.01].

These samples were also categorized by the study timeline (see Figure 2). Of the 66 patients whose anti-HBs was less than 10 mIU/mL after the first dose, nine (13.6%) patients still had anti-HBs of less than 10 mIU/mL after receiving the three doses (see Figure 2). On subgroup analysis, of the 75 patients who strictly adhered to the blood test protocol, 19 (25%) patients had protective anti-HBs after the first dose. Nevertheless, the factors associated with the response of anti-HBs were age group (p=0.033) and anti-HBs titer before vaccination (p=0.048) (see Table 3).

By examining the relationship between the anti-HBs titer before and after vaccination, there were 72 patients with pre-vaccination anti-HBs of less than 2 mIU/mL, 45 of whom (62.5%) showed anti-HBs titer 10 to 1,000 mIU/mL after vaccination, while only 18 patients (25%) showed anti-HBs titer of more than 1,000 mIU/mL after vaccination. Among 16 patients with pre-vaccination anti-HBs titer of 2 to less than 10 mIU/mL, 15 (93.7%) showed anti-HBs titer 10 to

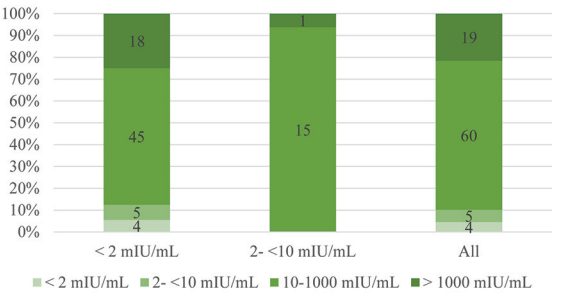

Figure 3. Anti-HBs levels after vaccination among individuals with varying anti-HBs titer before vaccination.

1,000 mIU/mL after vaccination and 6.25% showed anti-HBs titer of more than 1,000 mIU/mL. None of the patients with pre-vaccination anti-HBs titer of 2 to less than 10 mIU/mL was unresponsive to the HBV vaccine (see Figure 3).

Discussion

The vaccine response relied on T cell, B cell, and antigen presenting cell activity to express a peptide-based vaccine. Some HIV-infected patients had no immunity to HBV because of the low-level immunity[9-11]. In the early stages of HIV infection, the response to the vaccine was poor in relation to

lower CD4 values[12]. In case of having had previous immunity, anti-HBs can diminish by aging. In national survey of the HBV seroprevalence throughout Thailand[13], only 16.9% of population between 11 and 20 years of age had protective immunity, although HBV vaccine coverage in Thailand was at 94% during that period. Thus, the purpose of the present study was to determine the response rate to one dose of HBV immunization and associated factors. The authors selected HIV-infected patients who regularly take ART and CD4 of more than 200 cell/mm^3 due to the high chance of response to vaccines. To reduce the confusion among HBV-infected people, the authors also selected only those HIV-infected patients without HBV immunity who had anti-HBc-negative. The patients were divided into 29 years or older, and less than 29 years age groups because HBV vaccination had been a part of the immunization program for Thai's newborns since 1988. As a result, this could imply that patients who were born after 1988 were completely vaccinated with HBV vaccine but had weakened immunity with older age resulting in the loss of anti-HBs.

For those who did not have a blood test at one month after one dose of vaccination, if the anti-HBs after the second vaccination was negative, consequential data from the second vaccination would be used instead, and the data were collected separately by groups. However, if the results were positive, they would be excluded from the study because of unpredictability of anti-HBs after the first dose.

The present study results showed the response rate after one dose of HBV vaccination of 21.6% of HIV-infected patients with protective immunity, which was lower than the previous study. The previous study[7] found that among HIV-infected children in Thailand who regularly took ART and had all negative HBsAg, anti-HBs, and anti-HBc, 58% (94/162) had developed protective immunity after one dose of HBV vaccination. Compared to the present study in adults, there were no data obtained on HBV vaccination at birth. This may be the reason for the lower response rate than that in pediatric patients who had previously been vaccinated with HBV vaccine. These reasons were consistent with the results of the present study, showing that age had a statistically significant effect on response to vaccination. In other words, the 29 years or older group had protective anti-HBs less than the younger than 29 years group after one dose of vaccination ($p=0.013$ on univariate analysis and $p=0.03$ on multivariate analysis).

In addition, other factors associated with vaccine response rates. Besides age, the authors found that the pre-vaccination aniHBs titer had an effect on vaccine response, which was consistent with a previous study[8]. Out of 291 medical students after one booster vaccination showed that 85% (184/216) had protective immunity, which anti-HBs titer before vaccination had found influenced. Similarly, the present study also suggested that patients with pre-vaccination anti-HBs titer of less than 2 mIU/mL had less response rate than those whose pre-vaccination anti-HBs titer of 2 to less than 10 mIU/mL. Although differences existed in the sample population, both studies pointed out that the anti-HBs titer before vaccination has an impact on response rate of vaccination. It is possible that the anti-HBs titer before vaccination is an indicator that the patient had previously been vaccinated or did not have a much-weakened immunity. However, the level of anti-HBs titer before vaccination was not related to level of anti-HBs titer after vaccination. With that, having anti-HBs of 10 mIU/mL or more was sufficient to prevent HBV infection.

In addition, the present study found that out of the 66 patients who completed three vaccinations, nine (13.6%) had no protective immunity, which is lower than from other studies as 35.8% of 310 HIV-infected patients in Kenya[14] and 34.1% of HIV-infected patients with good virus control[15]. It is possible that the present study recruited only those patients highly susceptible to the vaccine and some patients may have been previously vaccinated resulting in higher response to the vaccine. It is also possible to point out some limitations in the present study. Firstly, this was a retrospective study, in which all variables that could affect the outcome were not controlled. Secondly, the number of participants in the present study was too small compared to the previous studies, thereby affecting the interpretation and analysis of the subgroups. Finally, to interpret results after HBV vaccination, the vaccination history of each patient should be known. Unfortunately, such information was not initially obtained because of the retrospective design and some of the patients suspected to be vaccinated at birth had no record of their vaccination.

Currently, Thailand's National Guidelines on HIV/AIDS Treatment and Prevention[6] recommend vaccination against hepatitis B infection in all HIV-infected patients who have never been infected by HBV and have no immunity when CD4 count is greater than 200 cells/mm^3. Three doses of vaccine are recommended. Although the present study has some limitations, it has shown that some groups of HIV-infected patients do not need three HBV vaccination

to have protective immunity, especially in patients younger than 29 years old and whose pre-vaccination anti-HBs titer is 2 mlU/mL or more. Almost half of these patients requires only one dose of HBV vaccine to have protective anti-HBs. In the future, data from a randomized controlled trial of each group may be required to control the variables. A larger number of patients is also needed to be recruited to magnify an outcome to the general population. Further research is still needed to analyze the long-term immunity of these patients.

Conclusion

The present study concluded that among the patients with HIV who take ART regularly, with a CD4 count of more than 200 cells/mm³, never been infected with HBV, and had anti-HBs titer below 10 mIU/mL, 21.6% of them have protective immunity to HBV after one dose of vaccination. The associated factors are age group of less than 29 years old and anti-HBs titer 2 to less than 10 mlU/mL prior to their vaccination.

What is already known on this topic?

Thailand's National Guidelines on HIV Treatment recommend HBV vaccination to all HIV-infected patients for three doses and HBV vaccine has been included in infant immunization programs in Thailand. Some HIV-infected patients have weakened immunity resulting in the loss of anti-HBs after vaccination. However, the evidence of the proportion of protective anti-HBs presence after one dose of HBV vaccination in this population has not yet been reported.

What this study adds?

This study revealed that 21.6% of HIV-infected patients has developed protective anti-HBs after the first dose of vaccination, especially younger patients of less than 29 years old and anti-HBs titer before vaccination of 2 mlU/mL or more. The findings support that only one dose HBV vaccine given is enough to achieve protective immunity in this group of HIV infected patients.

Acknowledgement

The authors gratefully acknowledge Chuenruthai Yeekian PhD, Center for Supporting and Developing Research, at Queen Savang Vadhana Memorial Hospital, for assistance with data analyses, and Nopavut Geratikornsupuk MD, Teerarat Shanthachol MD, Department of Medicine, Queen Savang Vadhana Memorial Hospital, for the review & editing of this research.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Leroi C, Adam P, Khamduang W, Kawilapat S, Ngo-Giang-Huong N, Ongwandee S, et al. Prevalence of chronic hepatitis B virus infection in Thailand: a systematic review and meta-analysis. Int J Infect Dis 2016;51:36-43.
2. UNAIDS Data 2018. HIV prevalence [Internet]. 2019 [cited 2019 Nov]. Available from: https://www.unaids.org/sites/default/files/media_asset/unaids-data-2018_en.pdf.
3. Sungkanuparph S, Vibhagool A, Manosuthi W, Kiertiburanakul S, Atamasirikul K, Aumkhyan A, et al. Prevalence of hepatitis B virus and hepatitis C virus co-infection with human immunodeficiency virus in Thai patients: a tertiary-care-based study. J Med Assoc Thai 2004;87:1349-54.
4. Colin JF, Cazals-Hatem D, Loriot MA, Martinot-Peignoux M, Pham BN, Auperin A, et al. Influence of human immunodeficiency virus infection on chronic hepatitis B in homosexual men. Hepatology 1999;29:1306-10.
5. Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the CDC [Internet]. The NIH, and the HIV Medicine Association of the IDSA. 2019 [cited 2019 Nov 15]. Available from: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf.
6. Thailand national guidelines on HIV/AIDS treatment and prevention 2017. HIV Thai guideline [Internet]. 2019 [cited 2019 Nov 15]. Available from: http://aidssti.ddc.moph.go.th/contents/view/1767.
7. Lapphra K, Angkhananukit P, Saihongthong S, Phongsamart W, Wittawatmongkol O, Rungmaitree S, et al. Persistence of hepatitis B immunity following 3-dose infant primary series in HIV-infected Thai adolescents and immunologic response to revaccination. Pediatr Infect Dis J 2017;36:863-8.
8. Posuwan N, Vorayingyong A, Jaroonvanichkul V, Wasitthankasem R, Wanlapakorn N, Vongpunsawad S, et al. Implementation of hepatitis B vaccine in high-risk young adults with waning immunity. PLoS One 2018;13:e0202637.
9. Yao ZQ, Moorman JP. Immune exhaustion and immune senescence: two distinct pathways for HBV vaccine failure during HCV and/or HIV infection. Arch Immunol Ther Exp (Warsz) 2013;61:193-201.
10. Kim HN, Harrington RD, Crane HM, Dhanireddy S, Dellit TH, Spach DH. Hepatitis B vaccination in HIV-infected adults: current evidence, recommendations

and practical considerations. Int J STD AIDS 2009;20:595-600.
11. van den Berg R, van Hoogstraten I, van Agtmael M. Non-responsiveness to hepatitis B vaccination in HIV seropositive patients; possible causes and solutions. AIDS Rev 2009;11:157-64.
12. Ungulkraiwit P, Jongjirawisan Y, Atamasirikul K, Sungkanuparph S. Factors for predicting successful immune response to hepatitis B vaccination in HIV-1 infected patients. Southeast Asian J Trop Med Public Health 2007;38:680-5.
13. Posuwan N, Wanlapakorn N, Sa-Nguanmoo P, Wasitthankasem R, Vichaiwattana P, Klinfueng S, et al. The success of a universal hepatitis B immunization program as part of Thailand's EPI after 22 years' implementation. PLoS One 2016;11:e0150499.
14. Irungu E, Mugo N, Ngure K, Njuguna R, Celum C, Farquhar C, et al. Immune response to hepatitis B virus vaccination among HIV-1 infected and uninfected adults in Kenya. J Infect Dis 2013;207:402-10.
15. Okulicz JF, Mesner O, Ganesan A, O'Bryan TA, Deiss RG, Agan BK. Hepatitis B vaccine responsiveness and clinical outcomes in HIV controllers. PLoS One 2014;9:e105591.