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Original article

A longitudinal study of hepatitis B surface antibody level after the accelerated vaccination protocol applied to health workers in a hospital of Thailand

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ABSTRACT

Background: Hepatitis B infection persists in Thailand, especially among health personnel. The current immunization protocol (3 doses in 6 months) is too slow to protect against infection; thus, an accelerated protocol has been in place as the accelerated protocol at a supra-tertiary hospital since 2014.
Aim: To measure the anti-HBs level 1, 2, and 5 years post-accelerated vaccination of health personnel who had received the hepatitis vaccine using.
Methods: A descriptive study was conducted. Electrochemiluminescence Immunoassay; ECLIA (Roche Diagnostic Cobas 6000, Indianapolis, IN) was used to measure the anti-HB level 1, 2, and 5 years after the third dose in 73, 58, and 20 participants, respectively.
Findings: The starting group number declined over time as workers resigned or transferred away, so the tested number in years 2 and 5 represents the remaining workers that started the study in year 1. The respective geometric mean titer after 1, 2, and 5 years was 1765.8, 164.7, and 107.9 mIU/mL. Fifty-four participants (93.1%) had lower antibody levels in the second year than in the first year. Nine participants (45.0%) had lower antibody levels in the fifth year than in the second year.
Conclusion: The anti-HBs level declined from the first to the second and fifth years; however, the anti-HBs level persisted at a protective level. The accelerated protocol benefited health personnel, protecting them from hepatitis B infection.

1. Introduction

Hepatitis B is a bloodborne infectious disease caused by the Hepatitis B virus (HBV), causing acute and chronic illness, with potential health effects including hepatic cirrhosis and risk of hepatocellular carcinoma.[1–3] Around two billion people had hepatitis B virus infection, and 240 to over 300 million suffered from chronic hepatitis B infection between 1990 to 2005.[1,4,5] HBV vaccines were developed to protect people from HBV infection, and these have a high efficacy (90%).[6] After the vaccine was made available, HBV infection worldwide appeared to decline; however, Southeast Asia had a persistent prevalence of 5–6%. Similarly, in the USA, there were 3322 new cases in 2018, while the trend of acute hepatitis B cases was also stable.[7] In Thailand, despite implementing a universal vaccine protocol in 1992 and the prevalence of HBV infection significantly declining to 0.6%, the prevalence of seroprotective (anti-HBs remained ≥10 mIU/mL) was 44.8%. Moreover, at the older age, the prevalence of seroprotective was lesser; 79.13% at the first five years, 43.89% at 5–10 years, and 16.95% at 11–20 years, respectively.[8] Therefore, assessing hepatitis B immunization in some specific occupations, especially health care personnel, is essential for containing HBV infection.

The current widely used vaccine protocol for adults is three doses of 20 mg recombinant vaccine: the first dose on day 1, the second dose 1–2 months later, and the third dose sixth months after the first dose.[9–11] A recommended accelerated protocol in Canada prescribes the second dose on day seven and the third on day 21.[10] The new vaccine Hepsilav-B is a 2-dose injection with 1-month of intervals, although not widely used.[11] Although the conventional protocol (0, 1, 6 months) is effective, the lengthy duration is unsuitable for persons working with the bloodborne pathogen with poor compliance to protective health

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measures.[12] The accelerated protocol may benefit such persons by encouraging quicker full-dosing. There have been some studies of the accelerated protocol that found a sufficient level of seroprotection and better vaccination compliance[13,14]

The Thai Guidelines for hepatitis B vaccination for healthcare personnel—launched by the Division of Vaccine Protection, Department of Disease Control—recommends only the conventional protocol despite the potential benefit of the accelerated protocol.[15] Srinagarind Hospital, Faculty of Medicine, Khon Kaen University has provided free HBV vaccine for all workers since 2007, and coverage of health care personnel is 100%.[16] The accelerated protocol was launched in 2014, and the proportion of the seroprotected was initially 95.9%[17]; however, there has been insufficient information regarding immunization levels in the years after vaccination. This study thus aimed to measure anti-HBs levels after 1, 2, and 5 years post-vaccination of health personnel who received the hepatitis vaccine at a supra-tertiary hospital using the accelerated protocol.

2. Methods

A descriptive study was conducted at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, between 2015 and 2020. The protocol was reviewed and approved by the Khon Kaen University Ethics Committee for Human Research (Ref No: RR59102).

2.1. Selection and description of participants

The study population included hospital personnel from the Faculty of Medicine vaccinated for hepatitis B virus, using the recombinant hepatitis B vaccine, following an accelerated vaccination program conducted between July 1, 2014, and July 22, 2015. The respective number of participants tested for hepatitis B virus markers after the first, second, and fifth year was 73, 58, and 20. The starting group number declined over time as workers resigned or transferred away, so the tested number in years 2 and 5 represents the remaining workers that started the study in year 1. If subjects could not be followed up within the first year, they were moved to the second-year follow-up group. Then, the year 1 and 2 short-term follow-up groups were analyzed.

2.2. Laboratory method

Electrochemiluminescence Immunoassay; ECLIA (Roche Diagnostic Cobas 6000, Indianapolis, IN) were used to measure anti-HBs. The respective level of anti-HBs according to the classification of no immune, low-responders, and good-responders was ≤10 mIU/mL, 10–99 mIU/mL, and ≥100 mIU/mL.

2.3. Statistical analysis

Data were analyzed using SPSS Version 26.0 (IBM, Armonk, NY). Descriptive statistics were implemented to analyze the sample characteristics such as age, sex, birth year, risk of hepatitis B infection level, and hepatitis B surface antibody (anti-HBs) levels.

3. Results

Almost all participants were female (78.1%–87.0%) born before 1992 (81.0%–87.0%). The primary age group was 20–29 years old (34.8–72.6%), with a respective average age of 28.1, 20.6, and 36.5 years in the first-, second-, and fifth-year group. The intermediate occupational risk is a majority of participants with patient assistants (21.7%–27.5%), nursing assistants (17.4%–20.7%), and registered nurses (16.4%–21.7%) (Table 1).

The geometric mean titer (GMT) of anti-HBs in the first-year group was 1765.8 mIU/mL, but the GMT was dramatically lower in the second-year and third-year groups (164.7 mIU/mL and 107.0 mIU/mL, respectively) (Fig. 1). The proportion of sero-protected in all groups was above 90% (97.3%, 93.1%, and 95.0% at 1, 2, and 5 years post-vaccination respectively). Anti-HBs levels dropped in the second-year group, but over half of them (55.0%) were higher in the fifth year than in the second year (Table 2). All 7 workers who had anti-HBs levels dropped to lower than 10 mIU/mL received another booster dose, only 1 worker at the 1-year post-vaccination remained in the study for follow-up at 2 years and the level raised to the protective level. The others did not remain. Furthermore, no participant was infected by the hepatitis B virus during the study.

Table 1
Characteristics of enrolled participants with measurable anti-HBs.

Characteristic	Year anti-HBs measured		
	first year	second year	fifth year
Number of participants	73	58	20
Sex, *n (%)*			
Females	57 (78.1%)	50 (86.2%)	20 (87.0%)
Males	16 (21.9%)	8 (13.8%)	3 (13.0%)
Year of birth, *n (%)*			
Before 1992	61 (83.6%)	47 (81.0%)	20 (87.0%)
After 1992	12 (16.4%)	11 (20.0%)	3 (13.0%)
Age group (years), *n (%)*			
20–29	53 (72.6%)	33 (56.9%)	8 (34.8%)
30–39	11 (15.1%)	16 (27.6%)	6 (26.1%)
40–49	9 (12.3%)	7 (12.1%)	6 (26.1%)
>49	–	2 (3.4%)	3 (13.0%)
Total, *mean ± SD*	28.05 ± 7.4	30.6 ± 8.0	36.5 ± 9.9
Job title, *n (%)*			
Patient assistants	20 (27.4%)	14 (24.1%)	5 (21.7%)
Nursing assistants	13 (17.8%)	12 (20.7%)	4 (17.4%)
Registered nurses	12 (16.4%)	11 (19.0%)	5 (21.7%)
Physicians	8 (11.0%)	4 (6.9%)	–
Janitors	5 (6.9%)	4 (6.9%)	1 (4.4%)
Public health officers	4 (5.5%)	3 (5.2%)	3 (13.0%)
Laundry staff	3 (4.1%)	3 (5.2%)	3 (13.0%)
Research assistants	2 (2.7%)	2 (3.5%)	1 (4.4%)
Other	6 (8.2%)	5 (8.8%)	1 (4.4%)
Occupational risk group, *n (%)*			
High-risk	21 (28.8%)	16 (27.6%)	6 (26.0%)
Intermediate-risk	37 (50.7%)	30 (51.7%)	12 (52.2%)
Low-risk	15 (20.5%)	12 (20.7%)	5 (21.7%)
Body Mass Index (BMI), *n (%)*			
<18.5	10 (13.7%)	9 (15.5%)	4 (17.4%)
18.5–22.9	36 (49.3%)	28 (48.3%)	10 (43.5%)
23.00–24.9	10 (13.7%)	9 (15.5%)	1 (4.4%)
≥25	17 (23.3%)	12 (20.7%)	8 (34.8%)
Total, *mean ± SD*	22.16 ± 3.4	22.0 ± 3.5	22.4 ± 3.9

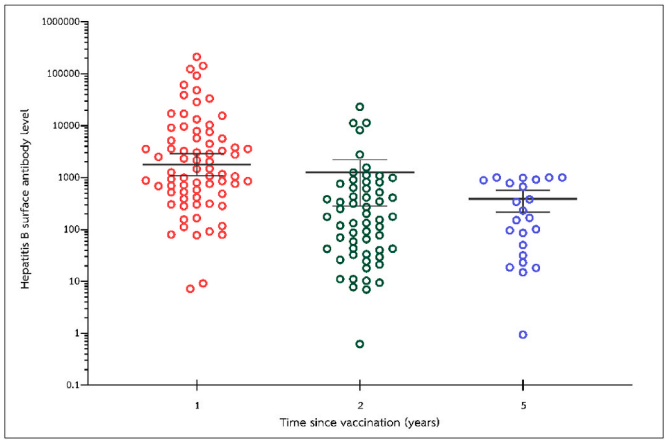

Fig. 1. Levels of hepatitis B surface antibody by year.

Table 2
Level of Anti-HBs of participants who had their accelerated Hepatitis B vaccination program.

	Level of Anti-HBs of participants		
	first year	second year	fifth year
Number of participants	73	58	20
Seroprotected (%)	97.3	93.1	95.0
GMT ± GSD (mIU/mL)	1765.8 ± 3.3	164.7 ± 7.8	107.9 ± 6.1
Mean ± SD	13,306.8 ± 34887.7	1258.3 ± 3708.3	291.1 ± 338.5
Median (min-max)	1473.0 (7.2–212,299.0)	164.6 (0.6–23,064.0)	126.0 (0.9–986.0)
Range of Percent change from the previous test, *n (%)*			
Increase	–	4 (6.9%)	11 (55.0%)
Decrease	–	54 (93.1%)	9 (45.0%)
Average duration to next test (years) ±SD	2.27 ± 0.4	2.61 ± 0.2	4.76 ± 0.5

4. Discussion

After receiving a completed dose of recombinant hepatitis B vaccine, inoculated HBsAg presented $CD4^+$ memory T cells. The cytokines from $CD4^+$ cells constitute the primary mechanism for enhancing plasma cell proliferation and producing antibodies, resulting in protective anti-HBs.[6] The recombinant hepatitis B vaccine has been widely used for over 30 years since its original approval.[18]

The total number of participants declined from 73 in the first year to 58 and 20 in the second and fifth years due to resignations or transfers. Thus, the results may not be generalizable. The small number of participants available in the fifth year may be a weakness of this study. However, they strongly suggest the benefit of the accelerated protocol of hepatitis B vaccination among HCWs.

Due to delayed specimen collection, the duration between the last dose of vaccination and the first and second year was not exactly one and two years. The fifth year after the last dose was consistently five years.

The one-year and two-year response of the accelerated protocol trended to be superior to the conventional protocol with a high GMT and a high proportion of seroprotected workers. The respective anti-HBs antibody GMT measured one and two years after the last dose of the accelerated protocol was higher at 1765.8 mIU/mL and 164.7 mIU/mL than in a previous study using the conventional protocol in Japan. In addition, the proportion of seroprotected workers at one and two years (97.3% and 93.1%, respectively) was also slightly higher than the conventional protocol (92.7% and 81.3%, respectively).[19]

The anti-HBs antibody titer was significantly lower when comparing one and five years after the last dose administered, which agrees with the previous study of the conventional protocol in India (mean = 128.4 mIU/mL)[20] but is superior to the result reported in a study from China (GMT = 35.1 mIU/mL).[21] Furthermore, the proportion of seroprotected personnel was high at 95% in the five years after the last dose administered that not different from the study in India (94.1%)[20] but also superior to the study in China (73.3%).[21] Accordingly, the accelerated protocol results were not inferior to the conventional protocol regarding the humoral antibody effect. Moreover, 95% of seroprotected health personnel showed that a booster dose might not require in the first five years after the last dose of the accelerated protocol.

The GMT was slightly lower in the second compared to the fifth year, but interestingly 55.0% of health personnel had increased anti-HBs antibody levels. Natural boosters—due to accumulative exposure to a bloodborne pathogen—could explain this phenomenon. In addition, accidental occupational exposure from healthcare procedures could boost the antibody level thereby extending the protection.[22]

Several studies demonstrated the decline of antibody levels over time.[20,23,24] Despite the trend in benefits of the accelerated protocol demonstrated by our study, the persistence of long-term antibody levels after five years is debated. However, there was no new infection during the period of the study although some of them lost their protective antibody to an unprotective level. Moreover, a number of studies have shown the proportion of seroprotected persons ranges between 44.8% and 50.0%,[9,25,26] and some of them demonstrate that albeit the antibody is dropped over time or lost, the protectivity still lasts long at least 30 years after conventional protocol.[26] However, the information about the accelerated protocol is still limited. There is only 1 study that showed a similar rate of anti-HBs antibody loss, so further study on the longer duration after the accelerated protocol is needed to confirm protectivity.[27]

Lastly, the evidence supports the recommendation for an accelerated protocol for high-risk groups such as prisoners,[13] health workers,[14] and drug users [28]. As such, our study confirms the benefit of the accelerated protocol for health workers as a protection against bloodborne pathogens and recommends such a policy be endorsed as soon as possible.

5. Conclusion

Anti-HBs levels appear to decline from the first to the second and fifth years post-vaccination. Nevertheless, anti-HBs levels persisted above a protective level. The accelerated protocol has benefited health personnel, protecting them from hepatitis B infection.

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Ethical considerations

This study is ethical reviewed and approved by the Khon Kaen University Ethics Committee for Human Research based on the Declaration of Helsinki and ICH Good Clinical Practice Guidelines. Institutional review board number; IRB00001189, project No. HE591222. The date of approval is September 6th, 2016.

Conflicts of interest

There is no conflict of interests to conduct this manuscript.

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References

1 *World Health Organization [online]*. Geneva: The Organization; 2021. Hepatitis B [updated 2021 Jul 21; cited 2022 Feb 20]. Available from: https://www.who.int/news-room/fact-sheets/detail/hepatitis-b.
2 *Centers for Disease Control and Prevention [online]*. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2021. Hepatitis B [updated 2021 Oct 12; cited 2022 Feb 20]. Available from: https://www.cdc.gov/hepatitis/hbv/index.htm#:~:text=Related%20Pages,someone%20who%20is%20not%20infected.
3 *National Library of Medicine [online]*. Bethesda: US Department of Health and Human Services, National Institutes of Health, National Library of Medicine; 2016. Hepatitis [updated 2021 Nov 15; cited 2022 Feb 20]. Available from: https://medlineplus.gov/hepatitis.html.
4 Ott JJ, Stevens GA, Groeger J, Wiersma ST. Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity. *Vaccine*. 2012 Mar 9;30(12):2212–2219.
5 Maynard JE. Hepatitis B: global importance and need for control. *Vaccine*. 1990 Mar 1;8:S18–S20.
6 Koff RS. Immunogenicity of hepatitis B vaccines: implications of immune memory. *Vaccine*. 2002 Nov 1;20(31-32):3695–3701.
7 *Centers for Disease Control and Prevention [online]*. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2017. Viral hepatitis surveillance-the United States, 2017 [updated 2019 Sep 10; cited 2022 Feb

20]. Available from: https://www.cdc.gov/hepatitis/statistics/2017surveillance/index.htm.
8 Posuwan N, Wanlapakorn N, Sa-Nguanmoo P, et al. The success of a universal hepatitis B immunization program as part of Thailand's EPI after 22 years' implementation. *PLoS One*. 2016 Mar 3;11(3), e0150499.
9 *Vaccine Preventable Disease Section [online]*. Saint Paul: Minnesota Department of Health, Vaccine Preventable Disease Section; 2020. Recommended Doses of Hepatitis B Vaccine [updated 2020 Apr 3; cited 2022 Feb 20]. Available from: https://www.health.state.mn.us/diseases/hepatitis/b/hcp/hbvrec.html#:~:text=*The%20schedule%20for%20hepatitis%20B,4%20months%20(16%20weeks).
10 *Public Health Agency of Canada [online]*. Ottawa: The Organization; 2021. Hepatitis B vaccine: Canadian immunization guide [updated 2020 Sep 23 ; cited 2022 Feb 20]. Available from: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-7-hepatitis-b-vaccine.html#tab2.
11 *Centers for Disease Control and Prevention [online]*. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2022. Adult immunization schedule [updated 2022 Feb 17; cited 2022 Feb 20]. Available from: https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fschedules%2Fhcp%2Fadult.html#note-hepb.
12 Akande TM, Aderibigbe SA. A study of compliance to hepatitis B vaccination among health workers in a Nigerian tertiary health institution. *Niger Hosp Pract*. 2010;5:13–16.
13 Asli AAZ, Moghadami M, Zamiri N, et al. Vaccination against hepatitis B among prisoners in Iran: accelerated vs. classic vaccination. *Health Pol*. 2011;100:297–304.
14 Shefer A, Atkinson W, Friedman C, et al. Immunization of health-care personnel recommendations of the advisory committee on immunization practices. *MMWR (Morb Mortal Wkly Rep)*. 2011;60:3–8.
15 Division of Disease Prevention with Vaccine. *Guidelines of Hepatitis B Vaccination in Health Workers*. Nonthaburi: Department of Disease Control, Division of Disease Prevention with Vaccine; 2021.
16 Jongkumchok W, Chaiear N, Soonthornvinit W, et al. Immunity to hepatitis B virus as a fitness for duty program for health workers at the University Hospital in Thailand. *J Med Assoc Thai*. 2019 Jan 1;102(1):S21–S26.
17 Simarugumpai U, Chaiear N, Mairiang P, et al. Hospital personnel sero-protected against hepatitis B virus following an accelerated vaccination program. *Southeast Asian J Trop Med Publ Health*. 2017 Jul 1;48:819–827.
18 Tulchinsky TH. Chapter 19 - maurice hilleman: creator of vaccines that changed the world. *Case Studies in Public Health*. 2018:443–470 [n.d.
19 Kakisaka K, Sakai A, Yoshida Y, et al. Hepatitis B surface antibody titers at one and two years after hepatitis B virus vaccination in healthy young Japanese adults. *Intern Med*. 2019;58(16), 2231-18.
20 Sahana HV, Sarala N, Prasad SR. Decrease in anti-HBs antibodies over time in medical students and healthcare workers after hepatitis B vaccination. *BioMed Res Int*. 2017 Sep 26:2017.
21 Wu WL, Yan BY, Lyu JJ, et al. Antibody persistence following primary vaccination with hepatitis B vaccine among normal and high-responder adults: a 5-year follow-up study. *Zhonghua yu Fang yi xue za zhi [Chinese Journal of Preventive Medicine]*. 2016 Jun 1;50(6):484–490.
22 Pokorska-Lis M, Marczyńska M. Influence of natural boosters on long-term immunity against hepatitis B. *Med Wieku Rozwoj*. 2011 Jan;15(1):62–68.
23 Lee KH, Shim KS, Lim IS, et al. Changes in hepatitis B virus antibody titers over time among children: a single-center study from 2012 to 2015 in an urban of South Korea. *BMC Pediatr*. 2017 Dec;17(1):1–8.
24 Li SQ. A study on the relationship between maximal titers of anti-HBs antibodies and persistence of protective level after vaccination. *Zhonghua liu Xing Bing xue za zhi= Zhonghua Liuxingbingxue Zazhi*. 1992 Jun 1;13(3):134–137.
25 Phattraprayoon N, Kakheaw J, Soonklang K, et al. Duration of hepatitis B vaccine-induced protection among medical students and healthcare workers following primary vaccination in infancy and rate of immunity decline. *Vaccines*. 2022 Feb;10(2):267.
26 Bruce MG, Bruden D, Hurlburt D, et al. Antibody levels and protection after hepatitis B vaccine: results of a 30-year follow-up study and response to a booster dose. *JID (J Infect Dis)*. 2016 Jul 1;214(1):16–22.
27 Shah DP, Grimes CZ, Nguyen AT, Lai D, Hwang LY. Long-term effectiveness of accelerated hepatitis B vaccination schedule in drug users. *Am J Publ Health*. 2015;105(6):36–43.