Original Article

Serological Profiles of Hepatitis B Virus Infection among Pre-Clinical Dental Students at a University in Thailand

Piamkamon Vacharotayangul[1], Patrayu Taebunpakul[1] and Surapoom Klawsirirojana[1]

[1]Department of Oral Surgery and Oral Medicine, Faculty of Dentistry, Srinakharinwirot University, Bangkok, Thailand

Correspondence to:

Patrayu Taebunpakul, Department of Oral Surgery and Oral Medicine, Faculty of Dentistry, Srinakharinwirot University, 114 Sukhumvit 23, Wattana, Bangkok 10110 Thailand. Tel: 02-6495000 Ext. 15063 Fax: 02-6641882 Email: pathraya@g.swu.ac.th

Abstract

Thailand has implemented the HBV vaccination program for all newborns since 1992. The aim of this study was to investigate the serological profiles of HBV among pre-clinical dental students who were born before and in or after 1992 at a dental school, and to identify factors related to HBV serology in this population prior to their clinical practice. One hundred and eighty seven pre-clinical dental students participated in the study in 2011 - 2012. The information on seroprevalence of HBV infection, history of vaccination and immunization status, personal data, birthplace, work history, and risk factors related to HBV infection were assessed through a self-administered form. Blood collection was performed to investigate the level of HBsAg, anti-HBs antibody, and anti-HBc antibody. Descriptive statistics, prevalence ratio, with 95 % confidence interval, Chi-square test, and Fisher's exact test were used for statistical analysis. There was one subject (0.53 %) with positive anti-HBc antibody, and no subject with positive HBsAg. There was no significant difference in anti-HBs antibody protectivity between the group of dental students who were born before and after 1992 when omitting the history of recent vaccination. History of receiving recent vaccination increased anti-HBs antibody level significantly. The results from this study show that dental students who were born in or after the integration of HBV vaccine into the national immunization program still need HBV screening test for HBV serological profile. Those who are not immunized to HBV should receive vaccination, either a full 3-dose or 1 stimulation dose prior to exposure of clinical work.

Key words: Hepatitis B; Professional education; Serology; Vaccination

Received Date: Sep 18, 2015, Accepted Date: Mar 1, 2016

doi: 10.14456/jdat.2016.1

Introduction

Hepatitis B virus (HBV) infection is a significant public health concern worldwide. There were 240 million cases of chronic hepatitis B infection with approximate 600,000 deaths per year, and more than one-third of world population still live in the highly epidemic areas of the world.[1,2] People living with chronic HBV infection carry significant risk to develop liver cirrhosis and hepatocellular carcinoma when compared to uninfected controls.[1,3,4] Moreover, HBV may play an important role to promote cholangiocarcinoma, leading to more deaths from HBV infection.[5] Thailand is one of the countries with high prevalence of HBV infection, making one of the top twenty diseases in the country. Prevalence of HBV in Thailand was reported at 4 - 8 % of the population, with higher incidence in males.[6,7] The incidence of liver cancer due to HBV infection in Thailand was 65 %.[8]

Two major components are involved in prevention of HBV spreading, namely, the vaccination and the screening of HBV serology. For vaccination, the Center of Disease Control (CDC) recommended that all children should complete all three doses of intramuscular HBV vaccine by eighteen month-old. In Thailand, the national HBV vaccination program to all newborns started in 1992. This has led to a significant drop of the incidence of chronic HBV infection cases from 4.3 % to 0.7 % in 2004.[9] Hepatitis B serologic testing involves measurement of hepatitis B virus (HBV)-specific antigens and antibodies. Combination of positive anti-HBc antibody (for core antigen) and anti-HBs antibody (for surface antigen) with negative HBsAg suggest the person is immune to HBV due to natural infection. However, if anti-HBc antibody and HBsAg are negative with positive anti-HBs antibody, the person is immuned by a previous hepatitis B vaccination.[1] Approximately 90 % of subjects who have completed three doses of HBV vaccines develop immunity to HBV, monitored by the anti-HBs antibody in the sera at equal or more than 10 mIU/ml. The vaccine-induced anti-HBs antibody level may decline over time, however, the immune memory remains intact indefinitely, and therefore allows the 'boost' of anti-HBs antibody by revaccination at a later time in life. People who remain anti-HBs antibody negative even after six doses of HBV vaccine are considered non-responders implying that having been vaccination does not guarantee to have been immunized.[10] Consequently, it is important to recognize the importance of HBV serological profile study after a past history of HBV vaccination.

The major transmission of HBV infection is via blood and secretions. Healthcare personnel who contact blood and secretions more often therefore are considered having high risks to contract HBV infection through daily routine work. There are several protocols promoting the importance of prevention of HBV infection in hospitals, clinics, medical-related institutions, and schools. It is recommended to perform the HBV serological profile study in health personnels if vaccination was undocumented or history was unclear, and give vaccination to appropriate cases prior to the beginning of their work.[11-14] However, pre-exposure testing may be preferred

for trainees, certain occupations, and healthcare practitioners working in certain populations. Dental healthcare workers and dental students in dental schools are considered high-risk groups as well. Together with the high prevalence of HBV infection in Thailand, it should be included in the mission of all dental schools in Thailand to perform the HBV serological profile study and vaccinate students prior to students' clinical years. However, this protocol has not been widely implemented in dental schools in Thailand, and there has been no published report on the HBV serological profiles in Thai dental students in the past twenty years. In addition, with the introduction of the national HBV vaccination program in Thailand since 1992, all newborns should receive HBV vaccination since neonatal and infantile period. Assuming that all newborns in and after 1992 were given HBV vaccination at neonatal/infantile period, the HBV serological profiles of dental students born before and in or after 1992 should be different. This might lead to an adaptation on the suggested protocol regarding the HBV serological study for pre-clinical dental students prior to their clinical years. For example, if all students who were born in or after 1992 have completed the vaccination since childhood, most of them should all still have protective level (more than 10 mIU/ml of anti-HBs antibody) and need no serological profile screening or revaccination prior to their clinical years. This assumption has not been challenged and published. Our current study aimed to investigate the serological profiles of HBV among pre-clinical dental students at a university in Bangkok, Thailand, and to identify factors related to HBV infection in this population.

Materials and Methods

The study has been approved by the Ethics Committee of the Faculty of Dentistry, Srinakharinwirot University. Two hundred pre-clinical dental students were invited to participate and only those who gave consent were included in the study. One hundred and eighty seven pre-clinical dental students participated and completed the self-administered form confidentially, with questions on their HBV serology (if known), history of HBV vaccination, personal data, birthplace, work history, and risk factors related to HBV infection. Blood sample collection was done and sent to profile for the levels of HBsAg (HBV surface antigen), anti-HBs antibody (HBV surface antigen antibody), and anti-HBc antibody (HBV core antigen antibody). The HBV serological screening profiles were investigated by Electrochemiluminescence Immunoassay (ECLIA) technique using automated Modular analytics E170 machine (Roche Diagnostics Thailand) at a private laboratory in Bangkok, Thailand. Descriptive statistics, prevalence ratio, with 95 % confidence interval, Chi-square test, and Fisher's exact test were used for statistical analysis.

Results

Table 1 shows the characteristics of the study population. Of 187 subjects, approximately 20 % were those who were born before 1992. The serological profile of participants showed 102 (54.54 %) subjects had positive anti-HBs antibody but there was only one participant (0.53 %) with a possible HBV exposure from the past (positive anti-HBc and anti-HBs antibodies, data not shown). Interestingly, none of the participants had chronic hepatitis B infection (none with positive HBsAg result, data not shown).

Table 1 *Characteristics of the study population*

Description	Number (%)		*p*
	Born before 1992 (N = 39)	Born in or after 1992 (N = 148)	
Gender			
Male	14 (35.90)	36 (24.32)	0.146
Female	25 (64.10)	112 (75.68)	
Birthplace			
Northern region	0 (0)	3 (2.03)	1.000*
Northeastern region	11 (28.20)	40 (27.03)	
Central region	22 (56.42)	80 (54.05)	
Eastern region	1 (2.56)	5 (3.38)	
Southern region	5 (12.82)	20 (13.51)	

Significant level at the 0.05 level (2-tailed)

*Fisher's exact test

The introduction of HBV vaccination program since childbirth in Thailand started in 1992. We hypothesized that the anti-HBS antibody titers of students who were born before and in or after 1992 should be different. The vaccine-induced anti-HBs antibody level may decline over time, but with the 'boost' of anti-HBs antibody by revaccination, this antibody level could be increased again. To test our hypothesis, we excluded students who reported having a clear history of HBV vaccination other than neonatal/infantile period and performed statistical analysis. Data in Table 2 shows that the immunity to HBV did not significantly relate to the year of birth of study participants. This result may be interpreted as 1) the immunity to HBV in participants who received vaccines in 1992 and after could be worn out and needs boosting, or 2) not all of the participants who were born in or after 1992 received HBV vaccination at neonatal and infantile period. There were nine participants who were born in or after year 1992 with a clear history or record of vaccination at neonatal/infantile period, and only five of them (55.6 %) still had a protective level of anti-HBs antibody without revaccination at the time of the study (data not shown). This suggested that the immunity to HBV indeed decreased in level over time. Taken together, our data suggested that the HBV serological profiles of students who were born before and in or after year 1992, and did not receive recent vaccination (or boosting), are not significantly different. The anti-HBS antibody titer may not be at the protective level for all students who might already have received neonatal vaccination after 20 years. This warrants the need for the HBV serological profile study in all dental students prior to their clinical practice, despite their birth year.

Table 2 *Comparison of anti-HBs antibody positivity in study participants who were born before and in or after 1992*

Anti-HBs antibody positivity	Number (%)			**PR**	**95 % CI**
	Protective	Non-protective	Total		
Born in or after 1992 (now younger than 21 years old)	32 (23.5)	104 (76.5)	136	0.53	0.33 - 0.85
Born before 1992 (now older than 21 years old)	16 (44.4)	20 (55.6)	36		

We next wanted to identify factors that are related to the HBV infection in the study participants. Since there were no HBsAg positivity and only one person with positive anti-HBc antibody, we focused on the factors that are related to the anti-HBs antibody levels only. We did not find the difference in anti-HBs antibody levels when we assumed that all students who were born in or after 1992 were vaccinated since neonatal/infantile period, and only some who were born before the national HBV vaccination program began in 1992 might be vaccinated since neonatal time (Table 2). We used the questionnaire to survey for any clear and recent histories of HBV vaccination among students. Of 187 participants, only 30 (16%) of them could positively report a history of HBV vaccination in the past, from birth to recent years. We hypothesized that a history of recent HBV vaccination increased the chance of a student having protective level (> 10mUI/ml) of anti-HBs antibody. Indeed, those with a clear history of recent vaccination within the past 6 years had 2.39 times (CI 1.55-3.68) higher chance to have a protective level of anti-HBs antibody at the time of study, when compared to those who reported unclear or no history of recent HBV vaccination (Table 3). In addition, those who had a recent history of vaccination with completion of three dosages had a slightly higher chance of developing protective levels of anti-HBs antibody (Table 4).

Table 3 *Comparison of anti-HBs antibody levels among participants with the history of receiving recent vaccination*

Anti-HBs antibody positivity	Number (%)			**PR**	**95 % CI**
	Protective	Non-protective	Total		
History of receiving recent vaccination*	10 (66.7)	5 (33.3)	15	02.39	1.55 - 3.68
Not received recent vaccination**	48 (27.9)	124 (72.1)	172		

* Recent vaccination: vaccination received other than birth years

**Includes those with a clear history of vaccination at neonatal/infantile period, or unsure date of vaccination, and no history or unsure of any vaccination

Table 4 *Anti-HBs antibody positivity in participants who received revaccination with regards to the dosage completion*

Anti-HBs antibody positivity	Number (%)			PR	95 % CI
	Protective	Non-protective	Total		
Complete 3 doses	3 (75)	1 (25)	4	1.18	0.57 - 2.42
Incomplete 3 doses	7 (63.6)	4 (36.4)	11		

Discussion

A significant issue in controlling the epidemic of HBV, especially in countries with high prevalence such as Thailand, and in countries with high volume of immigrants such as the USA, is the healthcare access of these vulnerable populations to HBV screening test and vaccination.[9,15] It is well documented that healthcare personnel, including dental-related, are at high risk of exposure to HBV-contaminated blood and secretions.[11-16] Thailand has introduced the HBV vaccination at birth to all newborns since 1992 but the screening program for HBV serological profiles in health-related institutions is not yet mandatory. HBV immunity could decrease over time and revaccination helps boosting the necessary immunity. Most dental schools in Thailand do not have the policy to screen HBV profiles for their students and personnel; therefore, a number of dental students would start working and contacting patients without knowledge of their HBV immunity status. In this study, we reported the HBV serological profile study of pre-clinical dental students in one dental school in Thailand. Approximately, 54.5 % of the dental students had anti-HBs antibody (data not shown), corresponding to other studies in Thai healthcare personnel, which reported at 48.3 - 69.5 %.[16,17] There was no case with positivity of HBsAg, in contrary to the national report of 4 - 8 % prevalence.[7,9] This might be due to the early-life vaccination among most of the participants. Assuming that those participants who received vaccination at neonatal/infantile period completed all the three doses, they should have long-term immunogenicity up to 20 - 30 years.[18,19] The anti-HBs antibody titer might decrease to very low or undetectable in some cases, but previous studies showed that a boosting revaccination of one dosage could induce an anamnestic response and increase the titer to several folds in a short period of time.[19, 20] As evident in our study, not all of the participants who were born in or after year 1992 remained to have immunization against HBV at the time when they were in pre-clinical years of the

dental school (approximate age of twenty-one years old). Omitting the year of birth and relying on the history of HBV vaccination by each individual, our data suggested that having a clear, recent history of HBV vaccination in the past significantly increased the chance of developing immunity against HBV. Completion of three dosages of vaccination also slightly increased this chance (Table 4, PR = 1.18). As a number of participants in this analysis were those who were born in or after 1992 with probable neonatal/ infantile immunization, their 'incomplete' vaccination in recent time successfully increased the anti-HBs antibody titer to the protective level already, in accordance to aforementioned studies,[19,20] making the prevalence ratio of complete/incomplete revaccination not significant statistically ($\chi 2$ = 0.71, p = 0.6797, data not shown). Based on our investigation, if the individual recalls having a recent vaccination within the last six years, it is likely that he/she has had the protective level of anti-HBs antibody.

CDC recommends healthcare personnel, who perform tasks that may involve exposure to blood or body fluids, to receive a three-dose series of HBV at 0-, 1-, and 6- month intervals. However, it is not guaranteed that the person will respond to the three doses of HBV vaccination, as only 90 % of vaccine receivers would develop adequate level of anti-HBs antibody after three doses.[13,14] CDC further recommends testing for anti-HBs antibody to document immunity at 1 - 2 months after 3rd dose. If anti-HBs antibody is less than 10 mIU/ ml, the person is not protected from HBV infection, and revaccination with a three-dose series is recommended.[20] Non-responders should be considered susceptible to HBV and counseled prior to starting clinical work. It is also possible that non-responders are people who have been HBsAg positive and they should be counseled and medically evaluated. On the other hand, a person who has contracted HBV and bear both HBsAg and anti-HBs antibody already does not need to receive vaccination again. Taken with the national HBV vaccination program, we suggested that all dental schools in Thailand should perform the HBV serological profiles for all students in their pre-clinical years in order to determine whether one needs a revaccination, counseling, medically evaluated prior to patient contacts, or do nothing. Basic knowledge of the risks of transmission of HBV infection should be given to all trainees to prevent HBV transmission to other healthcare personnel, patients, friends and families.

Acknowledgement

The authors would like to thank Dr. Supawadee Naorungroj, Faculty of Dentistry, Prince of Songkla University, for her assistance and advice in statistical analysis of this manuscript. We would like to thank the staff at Department of Oral Surgery and Oral Medicine, Srinakharinwirot University for their assistance in management of study procedure.

References

1. World Health Organization: Department of communicable diseases surveillance and response. 2002 [homepage on the internet] Hepatitis B [updated 2015 September; cited 2014]. Available from: http://www.who.int/csr/disease/hepatitis/whocdscsrlyo20022/en/.
2. World Health Organization. 2012 [homepage on the internet] Hepatitis B [updated 2015 July; cited 2014 August, 15]. Available from: http://www.who.int/mediacentre/factsheets/fs204/en/#.
3. Hepatitis B vaccines. ***Wkly Epidemiol Rec*** 2009;84:405-19.
4. Lertpipopmetha K, Auewarakul CU. High incidence of hepatitis B infection-associated cirrhosis and hepatocellular carcinoma in the Southeast Asian patients with portal vein thrombosis. ***BMC Gastroenterol*** 2011;11:66.
5. Srivatanakul P, Honjo S, Kittiwatanachot P, Jedpiyawongse A, Khuhaprema T, Miwa M. Hepatitis viruses and risk of cholangiocarcinoma in northeast Thailand. ***Asian Pac J Cancer Prev*** 2010;11:985-8.
6. Averhoff F. Centers for Disease Control and Prevention. 2015 [homepage on the internet] Hepatitis B [updated 2015 July, 10; cited 2014 August, 15]. Available from: http://www.nc.cdc.gov/travel/yellowbook/2016/chapter-3-infectious-diseases-related-to-travel/hepatitis-b.
7. Sangrajrang S, Chokvanitphong V, Sumetchotimaytha W, Khuhaprema T Evaluation of health status of a population underwent routine medical check up at the high risk screening clinic in National Cancer Institute. ***Asian Pac J Cancer Prev*** 2012;13:5759-62.
8. Tangkijvanich P, Hirsch P, Theamboonlers A, Nuchprayoon I, Poovorawan Y. Association of hepatitis viruses with hepatocellular carcinoma in Thailand. ***J Gastroenterol*** 1999;34:227-33.
9. Chongsrisawat V, Yoocharoen P, Theamboonlers A, Tharmaphornpilas P, Warinsathien P, Sinlaparatsamee S, *et al*. Hepatitis B seroprevalence in Thailand: 12 years after hepatitis B vaccine integration into the national expanded programme on immunization. ***Trop Med Int Health*** 2006;11:1496-502.
10. Immunization Action Coalition 2014 [homepage on the internet] Healthcare Personnel Vaccination Recommendations [updated 2014 May, 23; cited 2014 Aug, 15]. Available from: http://www.immunize.org/catg.d/p2017.pdf.
11. Anonymous. Protecting health care workers and patients from hepatitis B. ***Commun Dis Rep CDR Wkly*** 1994;4:217.
12. Kohn WG, Collins AS, Cleveland JL, Harte JA, Eklund KJ, Malvitz DM, *et al*. Guidelines for infection control in dental health-care settings--2003. ***MMWR Recomm Rep*** 2003;52:1-61.
13. Advisory Committee on Immunization Practices; Centers for Disease Control and Prevention (CDC). Immunization of health-care personnel: recommendations of the Advisory Committee on Immunization Practices (ACIP). ***MMWR Recomm Rep*** 2011;60:1-45.
14. Updated CDC recommendations for the management of hepatitis B virus-infected

health-care providers and students. ***MMWR Recomm Rep*** 2012;61:1-12.

15. Nguyen TT, McPhee SJ, Stewart S, Gildengorin G, Zhang L, Wong C, *et al*. Factors associated with hepatitis B testing among Vietnamese Americans. ***J Gen Intern Med*** 2010;25:694-700.
16. Chanmekha J. Seroprevalence and Risk Factor of Hepatitis B Immunities Among Thai Health Care Workers. ***Srinagarind Med J*** 2011;26:113-9.
17. Chaiwarith R, Ngamsrikam T, Fupinwong S, Sirisanthana T. Occupational exposure to blood and body fluids among healthcare workers in a teaching hospital: an experience from northern Thailand. ***Jpn J Infect Dis*** 2013;66:121-5.
18. Grosso G, Mistretta A, Marventano S, Ferranti R, Mauro L, Cunsolo R, *et al*. Long-term persistence of seroprotection by hepatitis B vaccination in healthcare workers of southern Italy. ***Hepat Mon*** 2012;12:e6025. doi: 10.5812/hepatmon.6025.
19. Poovorawan Y, Chongsrisawat V, Theamboonlers A, Crasta PD, Messier M, Hardt K Long-term anti-HBs antibody persistence following infant vaccination against hepatitis B and evaluation of anamnestic response: a 20-year follow-up study in Thailand. ***Hum Vaccin Immunother*** 2013;9:1679-84.
20. Lopes MH, Sartori AM, Souza TV, Mascheretti M, Chaves Tdo S. Hepatitis B revaccination for healthcare workers who are anti-HBs-negative after receiving a primary vaccination series. ***Rev Soc Bras Med Trop*** 2012;45:639-42.