

Case report:

High unprotective anti-HBs antibodies level among vaccinated students in a tertiary teaching hospital in north-eastern Malaysia

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Abstract

Introduction: Universal hepatitis B vaccination to all newborns have been implemented in Malaysia, since 1989, with nationwide coverage of 96.26%. In this study, we aimed to assess the prevalence of anti-HBs and HBsAg among selected undergraduate students who presumably had completed hepatitis B vaccination during their early childhoods.

Methods: Results of hepatitis B screening were obtained retrospectively from 239 newly enrolled undergraduate students at Health Campus, UniversitiSains Malaysia, in 2018. Serum samples were previously tested for the presence of anti-HBs and HBsAg using chemiluminescence immunoassay. Epidemiological data, anti-HBs and HBsAg were analysed using a descriptive statistical method. **Results:** Anti-HBs was undetected in 82.2% ($n = 194/236$) of the tested students. None of these students had detectable HBsAg.

Conclusion: This study showed anti-HBs level weaned after almost two decades of vaccination. Therefore, an alternative new testing algorithm such as the administration booster dose of hepatitis B vaccination can be considered in order to ensure that the new students are protected against potential exposure to hepatitis B during their clinical practices.

Keywords: seroprevalence, student, anti-HBs, HBsAg, memory persistence.

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Introduction

Hepatitis B virus (HBV) is an oncogenic virus that causes acute hepatitis and chronic complications, such as chronic hepatitis and hepatocellular carcinoma. In 2015 alone, it was estimated that 887 000 people succumbed to the long-term complications of HBV infection. In most circumstances, HBV infection is effectively preventable by vaccination with highly immunogenic HBV surface antigen (HBsAg).

This vaccine is typically administered via intramuscular injection, usually at the anterolateral thigh muscle, in three doses (10 µg intramuscular (IM) dose), during birth, followed by at 1 month and 6 months of age¹. In Malaysia, HBV vaccination is compulsory and included

in the Expanded Programme on Immunisation (EPI) since 1989². Subsequently, the coverage of HBV vaccination rate in this country improved, and was reported as high as 96.29%, with the effectiveness rate of up to 98% of the immune-competent population^{3,4}. Despite the effectiveness of the HBV vaccination program, hepatitis B infection remains as a major occupational health hazard among the healthcare personnel⁵. As such, majority academic and healthcare institutions employ mandatory screening of HBV infection and anti-HBs antibody level among the prospective students upon admission. This preventative measure is undertaken to reduce the risk of students with undetectable protective anti-HBs of contracting hepatitis B infection from the

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reactive patients and *vice versa*⁶. Therefore, in this study, we aimed to assess the level of anti-HBs antibody among newly enrolled-undergraduate students in the year 2018 at Health Campus, Universiti Sains Malaysia. These students are presumed to have completed all three doses of hepatitis B vaccination, during their early childhood. In addition, the prevalence of HBsAg among those students and the effectiveness of screening for anti-HBs were also evaluated.

Methodology

This is a retrospective study involving analysis of serum results of 236 undergraduate students who were enrolled at Health Campus, Universiti Sains Malaysia for the year 2018. All students were presumed to have received complete hepatitis B vaccination during infancy. Their samples were screened for the presence of anti-HBs antibody and HBsAg using Elecsys HBs antigen II and Elecsys Anti-HBs II chemiluminescence assays on Roche Cobas e 601 analyser. The limit of detection and limit of quantification of HBsAg were 2.0 IU/L and 1.5 million IU/L respectively.

Adequate serological protection is defined as an anti-HBs antibody level of ≥ 10 IU/L. All serum with reactive HBsAg and anti-HBs were retested using the same analyser. Only samples repeatedly reactive HBsAg were reported as HBsAg reactive. Epidemiological data and serology results were analysed for descriptive statistics using SPSS Statistical software.

Result

As shown in Table 1, the age distributions of the 239 students were between 18 and 25 years old (Median: 19 years old). Of all, 78% were female and most were of the Malay ethnicity. In terms of HBsAg reactivity, none of the tested samples was positive. Noticeably, the vast majority of the students did not have a protective level of anti-HBs antibodies (82.2%, $n = 194/236$). Of those with a protective level of anti-HBs antibodies, the mean antibody titre was 99.1 IU/L (Range: (11.1 – 1000.0)). All serum with reactive anti-HBs yield consistent results when retested.

Discussion

In this study, a low number of new students had a protective anti-HBs antibody level. This scenario of weaning of anti-HBs level occurs after ~two decades of HBV vaccination and is consistent with findings from a similar Taiwanese group which evaluated their college students who received HBV vaccine during infancy⁷. Theoretically, the production of anti-HBs peaks after 1 – 2 month

of the primary vaccination, and can last for approximately 10 – 31 years⁸. Therefore, a distant anti-HBs result cannot readily distinguish between a responder and a non-responder. According to the Centre for Disease Control and Prevention (CDC), a non-responder is defined as an individual with an anti-HBs level of 10 IU/L, after completion of two HBV vaccination doses⁶. Meanwhile, lifetime persistence of anti-HBs level at a concentration of ≥ 10 IU/L may be not necessary for protection because of the memory persistence that confers effective protection against infection as well as against disease (i.e. acute hepatitis, prolonged viremia, carriership, and chronic infection). Such immune response can be re-activated even though the vaccinated individuals have weaning or undetectable anti-HBs titres⁸.

CDC does not recommend routine serological anti-HBs test-

Table 1. Epidemiological distribution and serological prevalence among newly enrolled students ($n = 236$)

Parameters	Number (% or range)
<u>Age average</u>	Median 19 (18 – 25)
< 18 years	0 (0.0)
18-20 years	224 (94.9)
21-23 years	7 (3.0)
>23 years	5 (2.1)
<u>Gender</u>	
Male	52 (22.0)
Female	184 (78.0)
<u>Race</u>	
Malay	201 (85.2)
Chinese	15 (6.3)
Indian	14 (5.9)
Others	6 (2.5)
<u>HBsAg level</u>	
Negative	236 (100.0)
Positive	0 (0.0)
<u>Anti-HBs antibody titres</u>	
Nonprotective level (< 10 IU/L)	194 (82.2)
Protective level (≥ 10 IU/L)	42 (17.8)
Range of detectable level of anti-HBs	Mean 99.1 (11.1 – 1000.0)

ing for newly recruited healthcare practitioners (HCP)¹. Nevertheless, upon enrolment, the new recruits should provide written and dated records of HBV vaccination with documented post vaccination anti-HBs antibody titre of ≥ 10 IU/L¹. For a fully vaccinated group with nonprotective anti-HBs titres, a challenge dose of HBV vaccine may be administered to determine the presence of vaccine-induced immunologic memory through the generation of an anamnestic response¹. An immunologic response (anti-HBs) of ≥ 10 IU/L following a challenge dose is considered protected, regardless of the subsequent titre (i.e. declines of anti-HBs)⁶. Meanwhile, the unvaccinated and incompletely vaccinated group should receive complete doses of HBV retested for a serological response after 1 – 2 months of vaccination¹.

Post-vaccination testing is useful as Lu et al. (2008) found that 28.7% of subjects who had received a complete series of HBV vaccine failed to mount an adequate anamnestic response. Moreover, the team also reported that a proportion of these subjects (27.2%) lost the hepatitis B vaccine conferred protective memory response, as evident by the lack of HBsAg-specific IFN-gamma or IL-5-secreting PBMCs⁷. Similarly, a local study in Malaysia by Othman et al. (2018) involving 352 completely HBV-vaccinated individuals reported that only 27.6% had a protective level of anti-HBs titre⁹. Meanwhile, the remaining subjects had a nonprotective level of anti-HBs and been given a booster dose of hepatitis B vaccine. Of the latter group, 208 students (59.1%) mounted an adequate anamnestic response, while the rest of the subjects were given a complete series of hepatitis B vaccine. Two students (0.6%) were determined as non-responder⁹. These reports reflect the necessity of booster dose in order to mount adequate memory response in a high-risk group such as the HCP, medical students and volunteers. Moreover, this strategy is more valuable than conducting a generalized distant anti-HBs testing in fully vaccinated group⁶⁻⁷.

To date, CDC reaffirmed that booster dose is not necessary for the immunocompetent individuals with a protective level of anti-HBs antibodies¹.

However, a booster dose of hepatitis B vaccine remains as an important strategy that is employed as a screening tool for evaluating memory persistence due to the lack of documentation of post-vaccination baseline of anti-HBs titre among the subjects^{2,9,10}. Furthermore, a booster dose after almost twenty years of vaccination can benefit certain occupation groups of fully vaccinated individuals that had lost vaccine-conferred memory persistence. Thus, this study allows the institution to identify this special group which is indicated to complete the second series of hepatitis B vaccination before deemed as non-responders¹.

Conclusion

Weaning of anti-HBs level in fully vaccinated individuals is evident after two decades of HBV vaccination. Academic institutions or healthcare providers should employ a more comprehensive strategy to determine the level of immunity against HBV infections among the fully vaccinated students/healthcare worker. Furthermore, such institutions should consider a booster vaccination strategy to demonstrate vaccine-conferred memory persistence, instead of continuing the traditional routine screening policy of anti-HBs titres for all students.

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Conflict of interests : None declared.

Ethics Statement

The institutional Human Research Ethics Committee indicated this report is exempted from ethical review.

Authors' Contributions:

Conception and Design: MHH, NI, ZZD

Analysis and interpretation of the data: MHH, ZM

Drafting of the article: MHH

Critical Revision of the article for important intellectual content: ZM, ZZD, HH

Final approval of the article: All authors

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