

# Low seroprevalence of hepatitis B surface antibody among nursing students in Taiwan: An implication for boosting

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## Abstract

The national hepatitis B vaccination program in Taiwan began in July 1984. The purpose of this repeated survey was to investigate the levels of anti-HBs (hepatitis B surface antibody) in the first-year students of a 5-year nursing program in Taiwan. Each year during 2000–2006, the entering students of the 5-year nursing program at Fooyin University, a vocational university located in southern Taiwan, were examined for their HBsAg and anti-HBs status using commercially available microparticle enzyme immunoassay. The seroprevalence of HBsAg (+) showed a significant trend of decrease, dropping 57% from 4.9% in 2000 to 2.1% in 2006. The seroprevalence of anti-HBs (+) also showed a significant trend of decrease, dropping 49% from 77.1% in 2000 to only 39.7% in 2006. With the relatively low seroprevalence of anti-HBs (+) of the future healthcare workers and high HBV endemicity in Taiwan, recommendation of serology test before boosting to nursing students before they proceed their clinical practice is prudent.

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**Keywords:** Hepatitis B virus; Vaccination; Seroprevalence

## 1. Introduction

The national hepatitis B vaccination program in Taiwan has been considered as one of the most successful and effective public health programs to control hepatitis B virus (HBV) infection in the world. The national HBV vaccination program in Taiwan began in July 1984. During the first 2 years of the program, only the newborn infants of mothers who were HBsAg (hepatitis B surface antigen) carriers were vaccinated. After July 1986, the program was extended to include all newborn infants and in July 1987 to cover all children of preschool age. All vaccinated newborns received four doses

of plasma-derived hepatitis B vaccine at 0, 1, 2, and 12 months of age. In addition, newborns of mother who had positive HBV e antigen were also given 0.5 mL of hepatitis B immunoglobulin. Since November 1992, the vaccine used in this program was changed to recombinant vaccine with three doses at 0, 1, and 6 months of age. In the first 15 months after the vaccination program was implemented, hepatitis B vaccine coverage rates for the first, second, third, and fourth doses were 88%, 86%, 84%, and 71%, respectively, among infants born to 55,620 carrier mothers [1]. The overall vaccine coverage rates during mass vaccination period until December 2002 were 96.6%, 95.2%, and 92.8% for the first, second, and third doses, respectively, among 5,188,929 newborns, according to Center for Disease Control in Taiwan [2]. The vaccination program has significantly reduced mortality

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from fulminant hepatitis and the incidence of hepatocellular carcinoma in children [3].

The hepatitis B vaccine is very effective with more than 90% vaccinees reached 10 mIU/mL, the suggested protective levels of anti-HBs (hepatitis B surface antibody), after a primary course [4,5]. The proportion of vaccinees with protective anti-HBs levels decreased to approximately 80% after 5 years and 50–70% after 10–12 years of the primary vaccination [6–8]. It has been shown that approximately 30–62% Taiwanese children had anti-HBs levels lower than 10 mIU/mL 15 years after neonatal vaccination, suggesting waning immunity. Although immunologic memory was still present in all subjects 10 years after the primary vaccination regardless of their anti-HBs levels [9,10], anti-HB core antigen was detected in 4.4% of apparently healthy Taiwanese children whose anti-HBs levels were below 10 mIU/mL [11].

A single booster administered several years after the primary vaccination could increase anti-HBs levels to higher than 10 mIU/mL in majority of the subjects [11]. Several international agencies have recommended against the use of boosters in general population as no vaccinee has been identified as a carrier several years after the primary immunization [12–14]. On the other hand, advisory organizations in several countries stated that boosters should be administered in high-risk groups such as healthcare workers if their anti-HBs levels were below 10 mIU/mL [15–17].

The rates of exposure to HBV were estimated as 0.015–0.028 per healthcare worker per year in Taiwan in different categories of related jobs. There are estimated 308–924 healthcare workers at risk for seroconversion to HBV per year, based on 10–30% seroconversion rate after a needle stick injury [18]. However, most of the recommendations of using boosters in healthcare workers are based on serological data from general populations. There is no available information on the seroprevalence of anti-HBs in Taiwanese healthcare workers to provide solid evidence for policy on boosters. The purpose of this study was to investigate the levels of anti-HBs in the first-year students of a 5-year nursing program in Taiwan.

## 2. Methods

### 2.1. Subjects

Each year during 2000–2006, the entering students of the 5-year nursing program at Fooyin University, a vocational university located in southern Taiwan, were examined for their HBsAg and anti-HBs status. The 5-year nursing program is designed for students graduated from regular junior high schools. The majority of the students entered the program at the age of 15. According to the statistics of Ministry of Education, the study population represented 14.5% and 34.6% of all students entering the similar program nationwide and in southern Taiwan in 2003, respectively. These proportions became 11.8% and 24.6% in 2006 because the

total number of students entering the similar program in Taiwan has increased. The subjects in this study represented a cohort of individuals who participated in the first 7 years of the national HBV vaccination program in Taiwan. Students entering in 2000 and 2001 experienced the vaccination program covered newborns of HBsAg carrier mothers, while students entering from 2002 to 2006 experienced the universal newborn vaccination. The study was approved by the Institution Review Board of Fooyin University Hospital (No. FYH-IRB-96003).

### 2.2. Serology and statistical tests

All studied individuals received tests for the presence of HBsAg and anti-HBs using commercially available microparticle enzyme immunoassay (AxSYM, Abbott, North Chicago, IL, USA). Samples with HBsAg greater than 2.0 S/N were considered positive. Samples with anti-HBs above 10 mIU/mL were considered positive. The differences in the prevalence of HBsAg and anti-HBs among students entering in different years were examined by  $\chi^2$ -test for linear trend using SPSS for Windows 10.0 (SPSS Inc., Chicago, IL, USA). A *p*-value less than 0.05 was considered statistically significant. The sample size of over 850 each year allowed us to estimate the seroprevalence with 95% confidence interval less than 3.4%, assuming the seroprevalence was 50% and the sampling fraction was 25%.

## 3. Results

There were 6184 nursing students (97.2% female, 2.8% male) in this study. The seroprevalence of HBsAg (+) showed a significant trend of decrease, dropping 57% from 4.9% in 2000 to 2.1% in 2006. The HBsAg (+) seroprevalence of subjects who were born in the first 2 years of the vaccination program when only newborns of HBsAg (+) mothers were vaccinated was 4.2%, comparing to only 2.2% in subjects who were universally vaccinated during infancy. The difference was statistically significant. The seroprevalence of anti-HBs (+) also showed a significant trend of decrease, dropping 49% from 77.1% in 2000 to only 39.7% in 2006. The anti-HBs (+) seroprevalence of those who were born in the first 2 years of vaccination was 74.0%, while it was only 43.4% for students who had been vaccinated universally during infancy (Table 1; Fig. 1).

## 4. Discussion

This study showed that in this group of future healthcare workers, 26% of selected vaccination cohort and 56.6% of mass vaccination cohort had undetectable level of anti-HBs. In a nationwide study in Taiwan, 38% of the selected vaccination cohort and 34.6% of mass vaccination cohort had undetectable level of anti-HBs when entering elementary

Table 1  
HBsAg and anti-HBs status for the first-year nursing students surveyed during 2000–2006 in southern Taiwan

| Year of survey                     | 2000                         | 2001                       | 2002                       | 2003                       | 2004                       | 2005                       | 2006                       |
|------------------------------------|------------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|
| Birth cohort of entering students  | September 1984–August 1985   | September 1985–August 1986 | September 1986–August 1987 | September 1987–August 1988 | September 1988–August 1989 | September 1989–August 1990 | September 1990–August 1991 |
| Vaccination program for the cohort | Selected vaccination program |                            | Mass vaccination program   |                            |                            |                            |                            |
| Number of students                 | 974                          | 957                        | 840                        | 824                        | 848                        | 870                        | 871                        |
| HBsAg (–) and anti-HBs (–)         | 175 (18.0%)                  | 246 (25.7%)                | 421 (50.1%)                | 454 (55.1%)                | 463 (54.6%)                | 471 (54.1%)                | 507 (58.2%)                |
| HBsAg (–) and anti-HBs (+)         | 751 (77.1%) <sup>a</sup>     | 678 (70.8%)                | 398 (47.4%)                | 351 (42.6%)                | 365 (43.0%)                | 386 (44.4%)                | 346 (39.7%)                |
| HBsAg (+) and anti-HBs (–)         | 48 (4.9%)                    | 33 (3.4%)                  | 21 (2.5%)                  | 19 (2.3%)                  | 20 (2.4%)                  | 13 (1.5%)                  | 18 (2.1%)                  |
|                                    | (3.5–6.3%)                   | (2.3–4.5%)                 | (1.5–3.5%)                 | (1.3–3.3%)                 | (1.4–3.4%)                 | (0.7–2.3%)                 | (1.1–3.1%)                 |

<sup>a</sup> 95% confidence interval.

school [19]. This proportion increased to 60.1% in adolescents who were born in mass vaccination era [20].

The HBsAg (+) seroprevalence rate in selected vaccination cohort in our study was similar to that reported by Lin et al., which showed that the HBsAg carrier rates for teenagers who were born in 1985 and 1986 were 4.7% and 3.4% in eastern Taiwan [21]. The mass vaccination program has resulted in a significant decline in HBsAg (+) seroprevalence rate due to reduced incidence of vertical and horizontal transmission.

Shiao et al. reported that 87.3% of the healthcare workers in Taiwan had experienced recent sharps injuries [18]. The risk of transmission of HBV to nonimmunized healthcare workers after a needle stick depends on the titer of virions in the contaminant and correlates with the presence or absence of hepatitis B e antigen in the source patient, ranging from 2% (HBeAg negative) to 40% (HBeAg positive)

[22,23]. Other tissues and body fluid may also be infectious [24]. The virus can be transferred through undetected cuts, pre-existing breaches in the epithelium, or bites [17]. With the estimated HBV seroprevalence rate of 15–21% in Taiwan [25], the risk for infection of HBV among healthcare workers could be considerable.

It has been shown that a booster administered several years after the primary vaccination can induce a protective level of anti-HBs in almost all subjects [9]. The guidelines recently provided by The Steering Committee for the Prevention and Control of Infectious Diseases in Asia include boosting approximately 10–15 years after the primary vaccination and boosting healthcare workers based on the endemicity of the particular country [26]. On the other hand, European Consensus Group on Hepatitis B Immunity recommended against providing boosters to healthcare workers because no known instance of any patient being infected by healthcare workers who had lost their immunity and developed a breakthrough infection [12]. However, they did not consider the incidence of healthcare workers being infected by patients. The Immunization Practices Advisory Committee in US [13] and National Advisory Committee on Immunization in Canada [27] also recommended against providing boosters to healthcare workers. In Taiwan and other Asian countries where HBV endemicity was higher than that in Europe and North America, the likelihood of non-protected healthcare workers being exposed to HBV may be higher compared to that in Europe and North America.

The necessity of booster vaccination to prevent hepatitis B has been under debate in the last decade and more studies are needed to elucidate this issue. A recent study has suggested that universal HBV vaccination provides long-term protection up to 20 years, and a universal booster is not necessary before adulthood in Taiwan [28]. The healthcare workers whose antibody titer waned below the protective level are probably protected from the HBV infection due

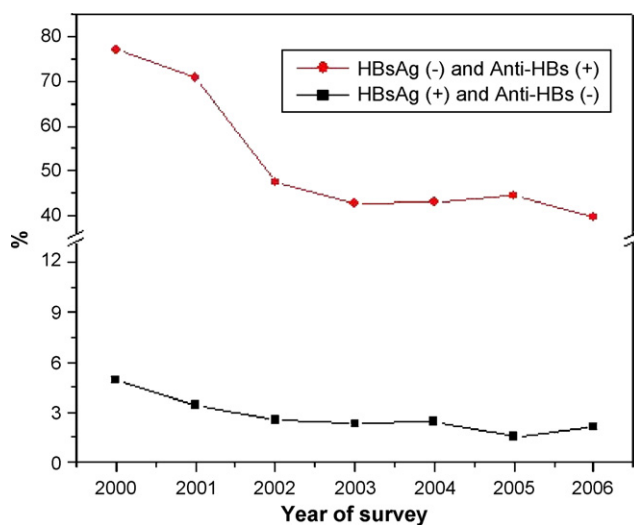


Fig. 1. Seroprevalence of HBsAg (+) and anti-HBs (+) among nursing students in Taiwan, 2000–2006.

to immunologic memory [9,10]. However, those who were non-responders to the vaccination are susceptible to the infection. Unfortunately, it is often difficult to identify the non-responders because post-vaccination antibody testing has not been a common practice [29]. With the relatively low seroprevalence of anti-HBs (+) in these future healthcare workers and high HBV endemicity in Taiwan, recommendation of serology test before boosting to nursing students before they proceed their clinical practice is prudent.

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