



Post Vaccination Hepatitis B Antibody Titer among Medical Students and Interns Vaccinated during a Vaccination Campaign, 2021-2022

Sahar Mohamed Sabbour, MD; Maha Mohamed Elgaafary, MD

Department of Community, Environmental and Occupational Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt.

ABSTRACT

Background: Healthcare workers (HCWs) are vulnerable to occupational exposures to hepatitis B (HB) infection. The Centers for Disease Control and Prevention (CDC) stipulate a post-vaccination anti-HBs titers ≥ 10 mIU/mL is protective. **Objective:** To determine the response rate of medical students and interns to a HB vaccination campaign and describe their post-vaccination immune status. **Methods:** A three-dose HB vaccination campaign was organized in the Faculty of Medicine of Ain Shams University between November 2021 and July 2022. Participants were asked to test for anti-HBs titer 1–2 months after receiving at least one dose of HB vaccination to verify their immune status. **Results:** A total of 950 medical students and interns received the first dose while 29% completed three doses. Interns and fifth year students were the highest group completing the full regimen; 60.5% and 47% respectively as well as female gender (35.6%). Out of 950, only 92 participants performed the post-vaccination testing for anti-HBs titer at variable intervals. Overall, 67.4% demonstrated a positive immune status for anti-HBs, 14.1% were low responders, and 18.5% were nonimmune/non-responders. Among participants who performed anti-HBs titer before vaccination, 70% were nonimmune. Non-responders among participants completing the three doses were 3.3%. There was a significant association between the number of doses received and positive immune status ($p < 0.01$). **Conclusions:** Most participants who checked their immune status developed protective anti-HBs levels. This campaign was an initiative that raised the awareness of participants to the importance of being immune for HB. HB immune response should be monitored in HCWs.

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INTRODUCTION

Hepatitis B vaccine has contributed to the reduction in hepatitis B virus infections and chronic disease globally. In Egypt, the national compulsory infantile immunization of hepatitis B virus (HBV) through the expanded program of immunization was applied in 1992 and have resulted in decline in the prevalence rate of HBV to 1.3%-1.5%.¹ Other studies have demonstrated decline in the prevalence of chronic HBV among children to $< 2\%$ after routine infant vaccination in areas with high HBV endemicity.²

After vaccination, seroconversion rates are important. Specific anti-hepatitis B surface antigen (anti-HBsAg) titers are a major index associated with protection. Screening to establish the extent of vaccine induced immune response and provision of booster dose are limited in most low-and-middle income countries.³ Moreover, Hepatitis B virus status is not routinely checked among Egyptian healthcare workers.

According to the Centers for Disease Control and Prevention (CDC) a post-vaccination anti-HBs titers ≥ 10 milli-international units per milliliter (mIU/mL) is associated with hepatitis B immunity protective level. Inadequate immune response to HBV vaccination is considered if quantitative anti-HBs level was < 10.0 mIU/mL, based on the CDC guidelines.⁴ Immunocompetent adults and children who have vaccine-induced anti-HBs levels of ≥ 10 mIU/mL 1–2 months after having received a complete, ≥ 3 -dose HepB vaccine series are considered seroprotected and deemed vaccine responders according to CDC guidance.⁴

A previous study in Tanta hospitals, Egypt showed that the frequency of HBsAg active infection among Egyptian health care workers in governmental and non-governmental hospitals was 1.4%.⁵

Persistence of hepatitis B antibodies (anti-HBs) and ability of the immune system to mount a response to exposure of HBV later in life is necessary for long term protection against hepatitis B virus infection. Some studies have confirmed persistence of antibodies and immune memory following hepatitis B vaccination,⁶ while others confirm waning of antibody concentrations 13–15 years after primary vaccination among those vaccinated at birth.⁷ The current vaccination of adult individuals against hepatitis B virus is premised on the fact that sufficient anti-HBs concentrations and immune memory is formed against HBV. However, unless routine post-vaccination serological testing is performed, it remains unclear what proportion of individuals who complete all 3 doses schedule of hepatitis B vaccine get protected.⁸

A prior study conducted in Egypt, which screened 400 university students aged 17 to 25 to assess anti-HBs antibody titers following mandatory childhood vaccinations, found that 54.5% of these students exhibited non-protective titers of less than 10 IU/l.⁹

Health care workers are vulnerable to occupational exposures of needle stick and sharps injuries and that makes them at a higher risk for acquiring HBV infection. In Egypt, among health care workers, 35.6% are exposed to at least 1 needlestick injury during their work.¹⁰ A protective adequate antibody titer of at least 100 IU/mL; termed as high responders; among this high-risk group is aimed (*personal communication with hepatology physicians, Ain Shams University*).

While this cohort of medical students has received the compulsory childhood immunizations, it remains uncertain how many are adequately protected or have waning immunity. There is evidence suggesting that the hepatitis B vaccine may not offer the long-term protection that is commonly believed.¹¹ Furthermore, they face a risk of occupational exposure to infection. According to CDC guidelines¹², there is no harm in administering additional booster doses or even repeating the entire vaccination schedule to at-risk groups. The rationale for implementing a three-dose vaccination campaign targeting medical students and young physicians was to enhance their protection against hepatitis B as previous studies demonstrated reduced immune response among similar population despite receiving childhood vaccination.

The objective of this study was to determine the frequency of hepatitis B vaccination among medical students and interns during a vaccination campaign held in the faculty of medicine, Ain Shams University. Additionally, to assess the immune status of vaccinated students by measuring their anti-HBs titer levels.

METHODS

A Hepatitis B Vaccination campaign was organized by the administration of the faculty of medicine Ain Shams University in conjunction with the community medicine department and VACSERA (The Egyptian Company for Production of Vaccines, Sera and Drugs) in the period between November 2021 and July 2022. The vaccination campaign was organized according to a three-dose schedule, administered at 0, 1, and 6 months.

The study was conducted into phases. *Phase 1*: A cross-sectional study conducted at the start of the campaign in November 2021 to determine the rate of vaccination during the campaign. *Phase 2*: A follow-up study of participants who joined phase 1 to measure those who completed the three doses of the hepatitis B vaccine and describe the antibody response to vaccination. Prior testing of antibody titers of participants before the initiation of the vaccination campaign was not feasible, as individuals presented directly for vaccination, perceiving themselves to be at risk and in need of immediate protection. They were informed that receiving an additional vaccine dose would be

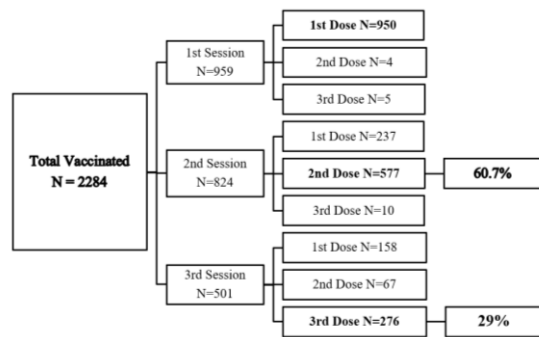


Figure 1: Flow Diagram of students and interns participating in the vaccination campaign sessions at Faculty of Medicine, Ain Shams University

beneficial rather than harmful as booster doses significantly trigger memory immune response.

Data collection: A registration form was available on all scheduled days of vaccination for participants to fill the required data before receiving the vaccine. The form included their demographic data, academic year and the number of the booster dose received.

Vaccination campaign: Medical students and interns were informed about the campaign through announcements displayed on screens in the Faculty Media Center, as well as via student platforms across all academic levels. They were invited to attend and receive the vaccination on the scheduled days at the Medical Clinic Center, conveniently located within the Faculty of Medicine for easy access. Participants enrolled in the vaccination campaign were instructed to test their levels of Hepatitis B surface antibody titer (HBsAb or Anti-HBs) at the accredited Central laboratory of Ain Shams faculty hospitals. They were asked to return their lab results to document their immune status. Participants were advised to conduct the post-vaccination anti-HBs test at least 1–2 months after receiving one dose to confirm their immune response. Additionally, campaign staff informed them that receiving extra doses or repeating the entire vaccination series poses no harm, in accordance with CDC guidelines regarding hepatitis B vaccination.¹² The administration of the third dose was postponed by two months to accommodate the examination period for students in May and June. It is important to note that the interval of 0,1, and 6 months specified for the vaccination series represents the minimum duration required to achieve protection. While maintaining a minimum interval between doses is crucial, the CDC guidance, 2024 indicates that vaccine doses

administered at longer intervals provide equally satisfactory protection.¹³ To improve the response rate of the antibody titer result, a reminder message was posted on the Moodle platform two months after the campaign ended. This led to an increase in students' response.

Laboratory testing: All students underwent the hepatitis B antibody testing at the Central Laboratories of Ain Shams University Hospitals, as requested. The entire process, including blood sample collection, analysis and laboratory report was done on-site. Prior arrangements were made with the head of the Clinical Pathology Department at Ain Shams University, faculty of medicine to refer all participants from the vaccination campaign for antibody testing with a reduced cost.

Outcome variables: Number of participants vaccinated during the three vaccination sessions, coverage rate of the vaccination campaign, classification of participants' immune status based on hepatitis B antibody testing.

Data analysis: Analysis was done using statistical software statistical package for social sciences (SPSS 22.0). Descriptive statistics were recorded as frequency and percentage (%). The Chi-square test (χ^2 test) was used test association between categorical data. P values ≤ 0.05 was considered statistically significant.

RESULTS

Three sessions of Hepatitis B vaccination were done starting in November 2021 in the current study. A total of 2,284 medical students and interns received at least one dose of the hepatitis B vaccine during all sessions of the campaign as shown in Figure 1. Given that there are approximately 1,250 registered students in each of the six medical grades, along with an additional 1,250 interns, the served individuals represents 26% of the total population (2,284 out of 8,750).

Participants in this study included individuals who received their first dose of the hepatitis B vaccine in November 2021, their second dose in December 2021, and their third dose in July 2022. Of the 950 participants who received their first dose in November, 577 (60.73%) completed their second dose in December. As a result, 276 participants (29.05%) completed all three doses during the campaign, leading to an overall coverage rate of 29%. Participants who received hepatitis B vaccine doses at

Table 1: Distribution of vaccinated participants receiving partial or full hepatitis B vaccination by gender and academic year

Variable	Participants who started the first dose of HB vaccine* n= 950	Participants who completed the three doses of HB vaccine** n= 276
Gender		
Male	414 (43.58%)	85 (20.53%)
Female	536 (56.42%)	191 (35.6%)
$\chi^2 = 25.85$ P <0.001		
Academic year		
Year 1	62 (6.55%)	12 (19.35%)
Year 2	34 (3.53%)	11 (32.3%)
Year 3	84 (8.84%)	24 (28.6%)
Year 4	114 (11.96%)	45 (39.5%)
Year 5	213 (22.4%)	100 (46.9%)
Year 6	400 (42.14%)	58 (14.5%)
Interns	43 (4.57%)	26 (60.5%)

*Percentages were calculated as column percentages ** Percentages were calculated as row percentages.

the Medical Clinic Center outside the scheduled timeline were vaccinated but were excluded from the analysis of the study, as shown in Figure1.

Table 1 shows that among 950 participants who received the first dose of the vaccine, more than half were females (56.4%). This cohort serves as the baseline for assessing the completion rates of the full three-dose vaccination series. Most students receiving the vaccine through the campaign were from sixth year (42%) and fifth year (22.4%) respectively. Female students completed the vaccination schedule at a significantly higher rate (35.6%) than male students (20.5%) ($p < 0.05$). Among interns, nearly 60% completed all three doses, whereas only 19% of first-year students did so. First-year and sixth-year students had the lowest completion rates for the three doses (Table 1). Of the initial 950 participants receiving dose 1 in November 2021, 92 (9.68%) underwent anti-HBs testing and submitted their laboratory results to the campaign staff. Among these participants, a low antibody titer (<100 IU/ml), indicative of a negative or low immune status for healthcare workers, was observed in 32.6% (30 out of 92). Conversely, 67.4% (62 out of 92) demonstrated a positive immune status for anti-HBs. When applying a cutoff value of ≥ 10 IU/ml to define positive immune status, it was found that 75 participants (81.5%) tested positive (immune) for anti-HBs. Table 2 categorizes immune status into three groups: non-responders, low responders and high responders. Among 92 participants who underwent antibody testing, 18.5%

were classified as non-responders (nonimmune) with an antibody titer level of less than 10 IU/ml. Additionally, 14.1% were low responders (with titers ranging from 10 to less than 100 IU/ml), while 67.4% were high responders (with titers of 100 IU/ml or higher).

Table 3 demonstrates a significant association between participants' immune status and the timing of antibody titer testing ($P < 0.001$). A greater positive immune response was observed in participants who received additional doses of the vaccine. Among those who underwent anti-HBs titer testing prior to vaccination, 70% were found to be nonimmune. In contrast, only 3.3% of participants who completed all three doses were classified as nonimmune (non-responders).

Table 4 indicates that 48 participants (52.2%) who underwent antibody titer testing were females. Approximately 54% of males were classified as nonimmune at the <10 IU/ml cutoff, whereas 56.7% of females were nonimmune at the <100 IU/ml cutoff. No significant association was found between participants' gender and immune status at either cutoff points ($P > 0.05$).

DISCUSSION

In the present study, a hepatitis B vaccination campaign was organized targeting medical students and interns to enhance their protection against hepatitis B. Participants engaged in the vaccination campaign at the medical faculty; however, the overall coverage for full doses was low at 29%.

Table 2: Immune Status of participants according to anti-HBs antibody titer levels (n=92)

Immune status	n (%)
Non-responders/Nonimmune (< 10 IU/ml)	17 (18.5)
Low responders (10 - < 100 IU/ml)	13 (14.1)
High responders (≥ 100 IU/ml)	62 (67.4)
Total number	92 (100)

A similar coverage rate of 29.1% was previously reported among medical personnel at the Faculty of Medicine, Ain Shams University.¹⁴ In contrast, higher coverage rates of up to 81.7% have been documented among Egyptian healthcare workers at the Gastrointestinal Surgical Center, Mansoura University.¹⁵ It appears that students may be less inclined to complete their vaccination doses compared to healthcare workers, who are more exposed and motivated to protect themselves.

To improve vaccination coverage rates among students, it is essential to utilize targeted communication methods, such as sending reminders and announcements through student platforms. This approach ensures that students are consistently informed about vaccination days. Furthermore, enhancing access to vaccination services is crucial, especially considering that medical students often have demanding teaching schedules. Extending clinic hours and offering vaccinations on additional days can accommodate their availability, thereby facilitating higher participation rates.

Among the participants, interns had the highest completion rate for all three booster doses at 60.5%, while first-year students had the lowest at 19.4%. Interns may be more motivated to complete the vaccination series due to their daily exposure to potential needle-stick injuries. However, for those who did not finish the course during the campaign and considered dropouts for missing the second or third doses, it is unclear whether they completed their vaccinations elsewhere. Participants were informed that if they missed the scheduled vaccination days during the faculty campaign, they could receive their doses at any other branch of VACSERA.

Higher compliance with HB vaccination being 60% was shown in 2020 among interns at Zakazik University Hospitals, Egypt.¹⁶ Completed vaccination

schedule rate in the current study showed a significant higher rate among females, however other studies showed no gender difference in vaccine uptake among healthcare workers.¹⁷

Nearly 10% of students performed their hepatitis B surface antibody (anti-HBs) tests as requested by the campaign organizers. The low percentage of students undergoing antibody testing may be attributed to the fact that they participated individually and voluntarily, rather than being part of a structured follow-up system for vaccine uptake and subsequent immune testing. Additional research is necessary to explore this further.

In the current study participants performed their lab test for hepatitis B antibody at different timings. Some before receiving the first dose in the campaign, others did it after receiving the first, or the second or the third dose. The variation in timing occurred in practice, and so the analysis was conducted based on the timing of vaccination and the number of doses received by the participants. However, this variability in the time of testing led to a significant finding, thereby contributing valuable insights to the study results. An association was revealed between the number of vaccine doses received in relation to the immune status against HB among different categories of participants.

Only 10 participants from 92 underwent the anti-HBs titer testing before receiving any booster doses during the campaign, and 70% of these participants had antibody levels below the immune threshold, indicating that immunity from childhood vaccination can diminish over time. Additionally, several prior studies have shown nonprotective titer levels (non-immune) among medical students who had received the childhood HBV vaccine, with rates of 54.5% and 64.9% reported in Egypt,^{9,18} 51% in Madinah,¹⁹ 56% in South Africa,²⁰ 24.3% among adults in Saudi Arabia,²¹ in comparison to the current findings.

The present study found that 94% of participants who received 2 or 3 doses (47 out of 50) had protective anti-HBs levels greater than 10 mIU/mL, consistent with previous research conducted in Mexico.²² Among healthcare workers in Suez Canal University Hospital, immunity after HB vaccination was found in 75%.¹⁷

A significant association was observed between the number of booster doses received by participants and their positive immune status $P < 0.001$.

Table 3: Non/low responders to hepatitis B vaccination by number of doses (n=92)

Timing of titer measurement	Total number	Non/low responders (< 100 IU/ml) n (%)	Non responders at (< 10 IU/ml) n (%)
Before receiving any dose	10	9 (90.0)	7 (70.0)
After receiving 1 st dose of vaccine	32	12 (37.5)	7(21.9)
After receiving 2 nd dose of vaccine	20	2 (10.0)	2 (10.0)
After receiving 3 rd dose of vaccine	30	7 (23.3)	1 (3.3)
Total	92	30 (32.6)	17 (18.5)
Chi squared test		$\chi^2 = 21.16$ p <0.001	$\chi^2 = 23.38$ p <0.001

Table 4: Anti-HBs antibody titer levels by gender and different cutoff points (n= 92)

	≥10 IU/ml n (%)	<10 IU/ml n (%)	χ^2 test P value
Gender (n)			
Males (44)	35 (46.7)	9 (53.85)	0.219 P >0.05
Females (48)	40 (53.3)	8 (46.15)	
Total	75	17	
	≥100 IU/ml n (%)	<100 IU/ml n (%)	χ^2 test P value
Gender (n)			
Males (44)	31 (50.0)	13 (43.3)	0.360 P >0.05
Females (48)	31 (50.0)	17(56.7)	
Total	62	30	

A similar finding was reported in one of the teaching hospitals in Egypt upon 228 healthcare workers, which reported a higher HBs-Ab titer among fully vaccinated healthcare workers as compared to those not fully vaccinated.²³ No significant difference was found regarding gender and anti-HBs levels in the current study, a similar finding was also reported among Egyptian medical students in Nile Delta²⁴. However, a previous study revealed that female gender and young age were associated with a higher response rate for HBV vaccination antibody.²⁵

In the current study, the negative immune status of participants following uptake of three doses of hepatitis B vaccine was 3.3% at a titer of <10 IU/ml, while 23.3% of participants were classified as low responders at a titer of <100 IU/ml. A similar finding was reported in a study involving Indian healthcare workers; where 3.5% were non-responders at a titer < 10 IU/ml.²⁶

The non-responder rate observed in the present study is lower than the approximately expected 8% non-responder rate reported by the CDC in 2013 Morbidity and Mortality Weekly Report for healthcare personnel

under 40 years.²⁷ In contrast, at Zakazik University Hospitals in Egypt, 9.7% of interns who received the third dose of the HB vaccine were non-responders at a titer of <10 IU/ml, a higher rate than that observed in the current study¹⁶. Conversely, a study in the Nile Delta, Egypt, found that all students (100%) were immune after vaccination, with anti-HBs levels exceeding 100 IU/L.²⁴

Although the majority of persons who are vaccinated against hepatitis B successfully responded to vaccination, an estimated 5-15% of persons may not respond. Of the possible causes of non-responders is older age, obesity, smoking, and other chronic illness.²⁸ Other studies have reported higher rates of non-responders following full vaccination with the HBV vaccine compared to the current research. In a study involving healthcare workers at Suez Canal University Hospital in East Egypt, only 75% achieved adequate immune levels, with non-responder rates reaching approximately 7%,¹⁷ which is higher than that observed in this study. Additionally, research on medical students in Japan found that 6.9% were antibody-negative after receiving three doses of the

HBV vaccine.²⁵ Similar rates were reported in South Africa (7%)²⁰ and among healthcare workers in Uganda (6.4%).³ These findings indicate a variable range of non-responders, which is an expected outcome.

CONCLUSIONS

HBV immunization coverage in the current campaign was low, with only 29% of students completing all three doses. Interns and fifth-year medical students had the highest completion rates for the vaccination campaign. Overall, the HBV vaccination campaign successfully raised awareness of the importance of immunity against HBV infection and the necessity for monitoring immune status. Additionally, those who underwent testing after completing all three vaccine doses demonstrated a higher immune status compared to others.

Promoting HBV vaccination and implementing strategies to enhance vaccination coverage rates is essential, particularly given the risk of occupational exposure faced by healthcare workers. Ongoing monitoring of immune responses in healthcare workers is recommended, along with further studies involving larger samples.

Ethical Consideration

Initially, approval was obtained from the faculty administration to announce and conduct the Hepatitis B vaccination campaign, scheduled at 0, 1 and 6 months. During the campaign, each participant provided informed consent, registered their demographic data and voluntarily received the vaccine. They also consented to share their antibody titer level results with the campaign staff, who ensured that these data would be processed anonymously.

The study obtained all required approvals from the Institutional Review Board of Ain Shams university, (FMASU Ro1/2025)

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