Evaluation of the efficacy of accelerated hepatitis B vaccine among students of Assiut Nursing School and College

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Introduction
Hepatitis B (HB) vaccine prevents infection with hepatitis B virus, thus reducing the incidence of chronic hepatitis, liver cirrhosis, hepatocellular carcinoma, and transmission of infection to susceptible individuals. Vaccine-induced immune response is defined as anti-HBs titer greater than 10 mIU/ml after complete vaccination schedule.

Aim
The aim was to evaluate the efficacy of accelerated HB vaccine among students of Assiut Nursing School and College.

Participants and methods
This study included 100 students of Assiut Nursing School and College, and 10% of them had received only a single dose of HB vaccine previously (in the period 6–12 months before the study) but had not completed the vaccination schedule, and their prestudy anti-HBs titer was less than 10 mIU/ml. Prevaccination testing of HBs Ag, Anti-HBs, Anti-HBc IgG, and HCV-Ab was negative. A vaccination schedule of 0, 1, and 2 months was used. Then, anti-HBs were measured one month after the last vaccine dose to detect antibody response by third-generation ELISA.

Results
Postvaccination anti-HBs titer was significantly higher in comparison with its prevaccination level (4.072.62 before vs 66.44±11.61 after vaccination; *P*=0.01). The authors found that students receiving a single dose of HB vaccine in the period 6–12 months before the study had high anti-HBs titer either before the study (9.78±2.01) and after the study (179.50±40.11) in comparison with those not receiving a vaccine dose recently.

Conclusion
Seroprotection rate was 100%, that is, all enrolled participants show postvaccination anti-HBs titer greater than 10 mIU/ml, and students with a higher prevaccination anti-HBs titer had a higher postvaccination anti-HBs antibody titer.

Keywords:
Hepatitis B virus, Hepatitis B vaccine, Accelerated hepatitis B vaccine immune response

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Introduction

Approximately an estimated 350–400 million persons are HBsAg carriers. So, hepatitis B virus (HBV) infection is one of the most important infectious diseases worldwide. Approximately one million persons die of HBV-related diseases yearly [1].

Clinical manifestations of HBV infection vary in acute and chronic disease. During the acute phase, manifestations range from subclinical or anicteric to icteric hepatitis and in some cases fulminant hepatitis. During the chronic phase, manifestations range from an asymptomatic carrier state to chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma. Extrahepatic manifestations occur in both acute infection and chronic infection [2].

Hepatitis B (HB) vaccination prevents infection with HBV, thus reducing the incidence of chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma in the vaccinated population, as well as reducing transmission by limiting the number of predisposed individuals [2].

A positive immune response to HB vaccine is the development of anti-HBs at a titer of greater than 10 mIU/ml, after a complete vaccination schedule, measured 1–3 months after the last vaccination dose [3].

The immune response rate is more than 95% in healthy infants, children, and adolescents, and the response decreases with increasing age, becoming 90% in adults

below the age of 40 years to reach 65–75% by the age of 60 years. Decreased vaccine response is associated with smoking, obesity, genetic factors, chronic diseases, and immune disorders [4].

Standard vaccination schedule consists of three doses, given according at 0, 1, and 6 months [5], and the following accelerated vaccination schedules are considered: either 0, 1, 2, and 12 months or 0, 7, 21, and 360 days. Both accelerated schedules require the administration of booster dose 1 year after the start of vaccination [6]; the need for accelerated schedules is to enhance the compliance or to reach protective levels of antibodies earlier without cutting on the immunogenicity of HB vaccination, as in high-risk situations, aiming to give protection against HBV as rapidly as possible [7].

Aim

The aim was to evaluate the efficacy of accelerated HB vaccine among students of Assiut Nursing School and College.

Participants and methods

The study was prospectively conducted in Assiut University Hospital at vaccination clinic which follow the guidelines of Tropical Medicine and Gastroenterology Department on Assiut Nursing School and College's students in the period between November 2016 to November 2017. Formal written consent for participation in the study was obtained from the participants. The study was approved by the Ethical Committee of Faculty of Medicine, Assiut University.

Population study

A total of 100 students of Assiut Nursing School and College who wanted to be vaccinated against HBV were included in the present study.

All participants were subjected to the following:

(1) Through history, as regarding name, age, sex, smoking, concurrent medical diseases (diabetes mellitus, hypertension, autoimmune diseases, etc.), and history of previous vaccination (number of doses and time elapsed after the last dose till the study).
(2) Laboratory testing for HBs Ag, anti-HBc, anti-HBs, and HCV-Ab by third-generation ELISA before the first dose of HB vaccination.

Vaccination schedule

Three doses of recombinant HB vaccine (EUVAX-B 20 μg/ml) had been administered to all participating students by injecting 1 ml (20 μg/ml) of that vaccine intramuscularly at deltoid region according to the schedule of 0, 1, and 2 months, and postvaccination testing of anti-HBs was done 1 month after the last vaccination dose.

Blood samples

Five milliliters of peripheral venous blood was obtained from all students before the start of vaccination schedule and 1 month after the last vaccination dose.

Serological tests and its principle

Viral markers of HBV (HBs Ag, anti-HBc) and HCV (HCV-Ab) were measured by third generation enzyme-linked immunosorbent assay (ELISA).

All sera were tested for anti-HBs antibody titer before the start and 1 month after the last vaccine dose by quantitative anti-HBs kits (WKEA Med Supplies Crop., Changchun 130012, China), which use the antigen 'Sandwich' ELISA methods where polystyrene microwell strips were precoated with recombinant HBsAg. Patient's serum or plasma sample was added to the microwells together with a second HBsAg conjugated to horseradish peroxidase (HRP-conjugate).

Statistical analysis of data

Data were collected and analyzed those using SPSS (statistical package for the social sciences, version 20; IBM, Armonk, New York, USA). Continuous data were expressed in the form of mean ± SD or median (range), whereas nominal data were expressed in the form of frequency (percentage).

Student's *t*-test was used to compare between those who previously received a single dose of HB vaccination 6–12 months before the study and those without as regarding level of anti-HBs Ab, whereas paired *t*-test was used to compare the level before and after vaccination in all participants. The level of confidence was kept at 95%, hence a *P* value less than 0.05 indicated a significant association.

Results

Baseline data of the enrolled candidates

Mean age of participants was 21.65 ± 1.31 years, with range between 18 and 24 years. The majority (70%) of them was males and 60% of them came from rural areas. All participating students had no history of smoking or concurrent medical diseases (diabetes mellitus, hypertension, autoimmune diseases, etc.);

were negative for HBs Ag, Anti-HBc, and HCV-Ab; and had pre-vaccination anti-HBs titer of less than 10 mIU/ml. We noticed that 10 (10%) students previously had received a single dose of HB vaccine in the period 6–12 months before the start of the study but had not completed the vaccination course, and their pre-study anti-HBs antibody titer was less than 10 mIU/ml, as shown in Table 1.

Table 1 Baseline data of enrolled candidates

Data	*n*=100
Age (years)	21.65±1.31
Range	18-24
Sex	
Male	70 (70)
Female	30 (30)
Residence	
Rural	60 (60)
Urban	40 (40)
Receiving previous HB vaccination dose	10 (10)

Data were expressed in form of mean (SD) and frequency (percentage). HB, hepatitis B.

Level of anti-HBs titer before and after vaccination

Postvaccination anti-HBs titer was significantly higher in comparison with its prevaccination level (66.44 ± 11.61 vs 4.07 ± 2.62; $P = 0.01$), as shown in Table 2.

Table 2 Level of antihepatitis Bs titer before and after vaccination

	Mean±SD
Before vaccination	4.07±2.62
After vaccination	66.44±11.61
P	0.01

P<0.05.

Level of anti-HBs before and after the study based on receiving a single previous vaccination dose in the period 6–12 months before the study but not completed the vaccination schedule

The level of anti-HBs titer was significantly higher in those who previously received a dose of HB vaccine in the period 6–12 months before the start of the study vsvs in comparison with those participants who did not receive a vaccine dose before the study (before the study: 9.78 ± 2.01 vs 3.43 ± 1.89, respectively; $P = 0.01$ and after the study: 179.50 ± 40.11 vs 53.87 ± 19.08, respectively; $P = 0.01$), as shown in Table 3.

Table 3 Level of antihepatitis B before and after the study based on single previous vaccination dose (in the period 6-12 months before the study but not complete the vaccination schedule)

	Previously receiving a vaccination dose (6-12 months before)	No previous vaccination recently	*P*
Before the study	9.78±2.01	3.43±1.89	0.01
After the study	179.50±40.11	53.87±19.08	0.01

Data were expressed in form of mean±SD. *P*<0.05.

Level of postvaccination anti-HBs titer according to sex

It was noticed that level of anti-HBs was insignificantly higher in female participants in comparison with male participants (69.53 ± 6.89 vs 65.11 ± 12.09; $P = 0.69$), as in Table 4.

Table 4 Level of postvaccination antihepatitis B according to sex

	Mean±SD
Male (*n*=70)	65.11±12.09
Female (*n*=30)	69.53±6.89
P	0.69

P<0.05.

Factors associated with higher postvaccination anti-HBs titer greater than or equal to 100 mIU/ml and lower titer less than 100 mIU/ml

There were insignificant differences between those participants with high level of post-vaccination anti-HBs titer greater than or equal to 100 mIU/ml ($N = 17$) and those with low level of postvaccination titer less than 100 mIU/ml ($N = 83$) regarding age, sex, and residence, but majority 58.8% ($N = 10$) of those with high level had a history of receiving a single dose of HB vaccination 6–12 months before enrolment in the study and also had higher prevaccination titer (8.57 ± 1.59) (Table 5).

Discussion

HB vaccine is the most effective protective way against HBV infection. Recombinant-HBsAg vaccines are a viral subunit produced by yeast after being transfected with a plasmid that contains the S gene. It is either present as a single agent preparation or in a combined form with other vaccines [8].

In Egypt, HB vaccination program was applied in 1992 with a schedule of 2, 4, and 6 months of age by using monovalent HB vaccine or combined vaccine doses and provide adequate protection 1–16 years after vaccination [9].

The need for booster vaccination against HBV for immunocompetent children and adults after complete primary vaccination series is not recommended for long-term protection [10]. However, immunocompromised patients should be monitored and receive a booster vaccination if anti-HBs titer decrease below 10 mIU/ml [11].

Table 5 Factors associated with higher postvaccination antihepatitis B titer greate than or equal to 100 IU/l

	High level (≥100 mIU/ml)	Low level (<100 mIU/ml)	*P*
Number	17	83	
Age			
(≥20 and <20 years)	22.01±0.86	21.57±1.16	0.16
Sex			
Male	4 (23.5)	26 (31.3)	0.37
Female	13 (76.5)	57 (68.7)	
Residence			
Rural	12 (70.6)	48 (57.8)	0.24
Urban	5 (29.4)	35 (42.2)	
Receiving a vaccine dose 6-12 months previously	10 (58.8)	0	0.01
Prevaccination anti HBs-Ab titer	8.57±1.59	3.14±1.16	0.01

Data were expressed in the form of frequency (percentage) and mean (SD). *P*<0.05.

Egyptian health care workers (HCWs) are at high risk of needle stick injuries and HBV infection [12]. The needle stick injuries in Egyptian HCWs showed a high incidence in comparison with reports from Pakistan [13]. The estimated annual number of needle sticks injury was 4.9 per worker among 1485 Egyptian HCWs [12].

Evidence of anti-HBs titer greater than 100 mIU/ml is necessary before medical students are allowed to deal with patients in United Kingdome. Additionally, medical students with anti-HBs less than 10 mIU/ml have to repeat a complete vaccination course and those with anti-HBs 10–99 mIU/ml have to receive a single booster dose [14].

The current study had revealed seroprotection rate of 100% in all participating candidates (anti-HBs titer before vaccination 4.07 ± 2.62 vs 66.44 ± 11.61 after vaccination; $P = 0.01$), and this goes along with a study by Chowdhury *et al.* [15], where 100% of vaccinated adolescents reached an anti-HBs level more than 10 mIU/ml, 1 month after the primary part of an accelerated vaccination schedule 0, 1, and 2 months.

In Egypt, Elmaghlob *et al.* [14], had founded that all studied medical students had an anti-HBs levels more than 100 mIU/ml, and among them, 5.4, 62.6, and 32% had anti-HBs titers from 100–1000, 1000–10000, and more than 10 000 mIU/ml, respectively. The mean anti-HBs titer of the included students was 8994 ± 6373 mIU/ml (range: 326–29 648 mIU/ml). There was no significant difference of anti-HBs levels in relation to age, sex, and residence, and this goes along with the results of our study, where there is no statistically significant difference regarding sex.

Additionally, Zeeshan *et al.* [16], had observed that the response rate (anti-HBs Ab titer >10 mIU/ml) was seen only in 86% of participating HCWs 6–8 weeks after recommended routine HB vaccination. Additionally, Nashibi *et al.*[17] had reported that 5.9% were nonresponders, 15.5% poor responders, and 78.6% good responders. Moreover, Ibrahim *et al.* [18], on hemodialysis patients at Kasr Al-Eini Nephrology and Dialysis Center reported the response rate to primary course (0, 1, 2, and 6 months) of HB vaccine was 93.1%.

In our study, we found that students with a higher prevaccination anti-HBs titer (8.57 ± 1.59) had a higher postvaccination level greater than or equal to 100 mIU/ml, and this is agreed with a study by Lu *et al.* [19]. These results also go along with a previous study done by Chiara *et al.* [20], who found that 2 mIU/ml prebooster anti-HBs titer might be predictive of an anamnestic response to booster vaccination, and 0.1 mIU/ml prebooster levels were prone to be predictive of failing to achieve the protective antibody level after HB vaccine booster. Additionally, Spradling *et al.* [21], observed that a prebooster anti-HBs titer of 1 mIU/ml or more could potentially respond to a booster dose of HB vaccination.

Certain risk factors have been associated with decreased response rate of HB vaccine in HCWs. Increasing age and presence of anti-HBc have been associated with decreased antibody response to HB vaccine in adult participants [16]. Moreover, Yang *et al.* [22], reported lower response rate in older adults (especially ≥40 years and might be a result from the waning immunity with age), male adults, overweight adults (BMI ≥ 25), smoker, and adults with underlying disease after complete vaccination schedule against HBV.

Notably, we could not find any statistically significant difference in anti-HBs response as regarding sex, that is, in female participants in comparison with male participants (69.53 ± 6.89 vs 65.11 ± 12.09; $P = 0.69$), in the studied group, and this goes along with a previously discussed study [14]. The younger mean age of included students, the possibility of early HB vaccination during infancy, and small sample size may partially explain the disagreement between our results and the reported studies as regarding sex and age.

Mast *et al.* [4], had reported that the immune response rate after the use of standard vaccination schedule (2, 4, and 6 months) is more than 95% in healthy infants, children, and adolescents, and the response decreases with increasing age, becoming 90% in adults below the age of 40 years to reach 65–75% by the age of 60 years. In comparison of these results with our results, the use of accelerated vaccination schedule appear to be more

immunogenic, and owing to its short interval, it may appear to be more compliant.

Conclusion and recommendations

It was found that the seroprotection rate after HB vaccine in the studied students was 100% (All of them reached the protective level of anti-HBs titer >10 mIU/ml).

The higher the prevaccination anti-HBs titer, the higher its postvaccination level, conveying that more protection against HBV infection and HB vaccination at young age results in excellent seroprotection rate.

The use of accelerated HB vaccination schedule at 0, 1, and 2 months had an excellent seroprotection rate, and owing to its short interval and compliance, we recommend its use in vaccination clinic of Assiut university hospital.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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