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Immune Response after Hepatitis B Vaccination among Egyptian Medical Students in Nile Delta

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Abstract

Background: Early promotion of hepatitis B (HB) vaccination among health care workers is an important component of the HBV infection control. No available data assess immune response of HB vaccination among Egyptian medical students. Objective: we conducted this study to evaluate the immune response among medical students after completion of their vaccination schedule. Methods: A total of 150 Egyptian medical students were included. Three doses of recombinant HB vaccine had been administered to all participating students at 0, 1 and 6 months. Antibody to hepatitis B surface antigen (Anti-HBs) titers, hepatitis B surface antigen (HBsAg), and total antibody to hepatitis B core antigen (anti-HBc) were measured by enzyme immunoassay, 1 to 2 months after completion of vaccination course. Results: Among 150 students included, the mean age was 22.4 ± 1.7 years (range 18 - 28 years). Fifty nine (39.4%) were males and 91 (60.6%) were females. All students have anti-HBs levels more than 100 IU/L. The mean anti-HBs of included students was 8994.2 ± 6373.1 IU/L. There was no significant difference of anti-HBs levels regarding age, sex, residence or body mass index distribution. Conclusion: Early HB vaccination of health care workers is associated with good immune response and should be encouraged.

Keywords

HBV, HB Vaccine, Medical Students, Anti-HBs, Egypt

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1. Introduction

Globally, hepatitis B is a major public health problem. It is estimated that more than 350 million suffer from chronic hepatitis B virus (HBV) infection worldwide [1]. Epidemiological studies proved that health care workers (HCWs) were among the highest risk groups for acquiring HBV infection [2]. Approximately 340,000 persons are employed in the health sector in Egypt [3].

Every health care worker (HCW) is at risk of infection with blood borne pathogens through occupational exposure to blood and infectious body fluids. HBV is the most contagious blood borne pathogen [4]. After needlestick exposure to hepatitis B surface antigen (HBsAg)-positive blood, unvaccinated HCWs are exposed to a risk of infection within a range of 6% to 30% [5] [6]. Five percent of Egyptian HCWs are infected each year with either hepatitis C virus (HCV) or HBV [7]. The highest occupational risk of HBV infection was reported during health professional training, where inadequate staff, lack of experience, insufficient training, duty overload and fatigue might have led to occupational sharp injuries [8] [9].

Promotion of hepatitis B (HB) vaccination in HCWs is an important component of HBV infection control strategy [10]. There is no clear policy for mandatory vaccination of Egyptian HCWs including medical students. Because of lack of resources, the Ministry of Health and Population (MOHP) offers vaccine only for HCWs who are employed in high-risk settings such as dialysis, surgery, and intensive care departments [3]. A survey of Egyptian health care workers revealed that HB vaccination was reported in only 14% of the surveyed individuals [7].

The immune response to HB vaccine is assessed by measuring antibody level after 6 - 8 weeks of completion of 3 vaccine doses. Antibody to hepatitis B surface antigen (anti-HBS) titer higher than 10 IU/l is generally taken to be protective. The recommended series of three intramuscular doses of HB vaccine has been reported to elicit a protective anti-HBs response in more than 90% of healthy adults and more than 95% of infants, children and adolescents [9]-[13]. Various studies that investigated HCWs response to HB vaccinations reported lower response rates (79% - 88%) to HBV vaccine [14]-[20]. Certain risk factors have been associated with decreased rates of responsiveness to HBV vaccine among HCWs. Old age as well as presence of antibody to HB core antigen (anti-HBc) was found to be associated with a decreased antibody response following vaccine administration in adult subjects [19] [21]-[23]. Data assessing immune response in Egyptian medical students are lacking. We conducted this study to evaluate the immune response among Egyptian medical students at the Nile delta region.

2. Method

This study was conducted at Al-Azhar University hospital, Cairo, Egypt from February 2013, to June 2014. All procedures were performed in accordance with the ethical standards of the Al-Azhar University committee on human experiments. Informed consent was obtained from all included persons.

2.1. Studied Medical Students

A total of 150 medical students who had been vaccinated against HB were tested in the present study. Among them 148 were Egyptian and 2 were Malian. All students related to Tanta University, among them 144, 5 and 1 were related to Tanta schools of, Medicine, Dentistry and pharmacy respectively. Included Egyptian students were related to Gharbiah (n = 143), Munufia (n = 4) Behira (n = 2) and Kafr Elsheikh (n = 1) governorates.

2.2. Recruitment of the Medical Student

All students who had completed the three HB vaccine doses between February and September 2013, in the Scientific Society at Tanta school of Medicine were enrolled in this study. The researcher had collected the demographic and vaccination data from all study participants. Any patient with history of HBV infection, HCV infection, associated co-morbiditiy or who was receiving immunosuppressive drugs was excluded from the study. In addition students with incomplete three vaccination doses were also excluded.

2.3. Vaccination Schedule

Three doses of recombinant HB vaccine had been administered to all participating students at 0, 1 and 6 months

between February and September 2013, in the Scientific Society at Tanta school of Medicine. All students had completed the three vaccine doses 1 - 2 months before anti-HBs testing. A dose of 20 IU/L of HB vaccine was given through intramuscular route for all students. No HBV screening was done prior to HB vaccination. Body Mass Index (BMI), serum levels of anti-HBs, HBsAg and anti-HBc were measured in all students, 1 - 2 months after the last vaccination dose.

2.4. Blood Samples

Five milliliters of venous peripheral blood were obtained from all students 1 - 2 months after the last vaccination dose. Blood samples were centrifuged and then serum samples immediately stored at 21˚C.

2.5. Serology Tests

Viral markers of hepatitis B virus were measured by enzyme-linked immunosorbent assay (ELISA) including anti-HBs, HBsAg and anti-HBc. All sera were tested for anti-HBs (Biokit, Barcelona, Spain), where anti-HBs titers were classified as undetectable (0), <10 IU/L, 10 - 100 IU/L, 100 - 1000 IU/L, and >10000 IU/L. Those samples were also tested for HBsAg (Axiom GmbH, Germany). Total anti-HBc (Biokit SA, Barcelona, Spain) was tested for all students; anti-HBc reactive samples were retested and considered to be reactive if the repetition also gave a positive result.

2.6. Statistical Analysis of Data

The analysis was performed using statistical software package (SPSS 17.0 version for Windows; SPSS Inc., Chicago, IL, USA). Descriptive statistics were recorded as percentage (%) in relation to total number. Student t-test was used to compare the mean values of continuous variables. The Chi-square test was used for the analysis of categorical data in detecting statistically significant differences between different groups. P values below 0.05 were considered statistically significant. All values were presented as the mean ± standard deviation unless mentioned otherwise.

3. Results

3.1. Demographic Data

Among one hundred and fifty students included, the mean age was 22.4 ± 1.7 y (range 18 - 28 y). The majority of included students, 91 (60.6%) were females. Also, most of the sample were of urban residence as one hundred twenty six (84%) and 24 (16%) persons related to urban and rural residence respectively. The mean BMI of included students was; 25.6 ± 4 kg/m^2 (**Table 1**).

3.2. Anti-HBs Levels

All the included students showed a good response to HB vaccination “100%”. All included students showed an anti-HBs levels more than 100 IU/L, among them 8 (5.4%), 94 (62.6%), and 48 (32%) have anti-HBs titers from 100 - 1000, 1000 - 10000 and more than 10000 IU/L respectively. The mean anti-HBs titer of the included students was 8994 ± 6373 IU/L (range; 326 - 29648 IU/L) (**Table 1**). There was no significant difference of anti-HBs levels in relation to age, sex, residence or BMI ($P < 0.05$) (**Table 2**).

3.3. HBsAg and Anti-HBc Status Post Vaccination

None of the included students showed evidence of current HBV infection. Indeed HBsAg was not detected in any of included students. On the other hand the total anti-HBc was detected in 3 (2%), of the students, confirming previous HBV exposure. In an attempt to rule out the possibility of the presence of occult HBV infection among anti-HBc positive students, HBV DNA was tested by real time PCR and was not detected in any of them.

4. Discussion

Occupational exposure to blood and/or other body fluids within healthcare sector facilities is a major risk of

Table 1. Basic characteristics of studied students.

	Mean ± SD (range)	N (%)
Age	22.4 ± 1.7 y (18 - 28 y)	
Males		59 (39.4%)
Females		91 (60.6%)
BMI	25.6 ± 4.0	
Underweight		3 (2%)
Normal (healthy weight)		79 (52.7%)
Overweight		54 (36%)
Obese		14 (9.3%)
Anti-HBs	8994.2 ± 6373.1	
Anti-HBs titer 100 - 1000 IU/L		8 (5.4%)
Anti-HBs titer 1000 - 10000 IU/L		94 (62.6%)
Anti-HBs titer Over 10000 IU/L		48 (32%)
HBsAg positive		0 (0%)
HBsAg negative		150 (100%)
Anti-HBc positive		3 (2%)
Anti-HBc negative		147 (98%)

SD: standard deviation, BMI; body mass index, Anti-HBs; antibody to hepatitis B surface antigen, HBsAg: hepatitis B surface antigen, Anti-HBc: antibody to hepatitis B core. Underweight (16 - 18.5 Kg); Normal (18.5 - 25 Kg); Overweight (25 - 30 Kg); Obese (>30 Kg).

Table 2. Predictors of anti-HBs immune response after HB vaccination in medical students.

	Anti-HBs titer (Mean ± SD)	**t**	**P value**
Age ≤ 22 (n = 84)	9012 ± 705.7	0.04	0.97
Age > 22 (n = 66)	8971 ± 775.4		
Male (n = 59)	8884 ± 860.0	0.17	0.87
Female (n = 91)	9066 ± 655.5		
Urban residence (n = 105)	9071 ± 623.0	0.22	0.82
Rural residence (n = 45)	8816 ± 956.6		
Underweight (n = 3)	5815 ± 2923	−0.83	0.41
Overweight (n = 54)	9628 ± 980.9	0.74	0.46
Obese (n = 14)	8478 ± 1338	−0.17	0.86

Anti-HBs: antibody to hepatitis B surface antigen, SD: standard deviation; Underweight (16 - 18.5 Kg); Normal (18.5 - 25 Kg); Overweight (25 - 30 Kg); Obese (>30 Kg).

HBV transmission to HCWs [2]. This risk is highest during medical training [8] [11]. Egyptian HCWs are at high risk of needle stick injuries and HBV infection [7]. The needle stick injuries in Egyptian health care staff showed a high frequency that was comparable with reports from Pakistan [24]. Among 1485 Egyptian HCWs the estimated annual number of needle sticks was 4.9 per worker [7]. Using Kane's model to predict infections after needle stick exposures, 8617 HBV infections occur each year in Egypt as a result of occupational exposure in the health care environment [7]. This problem is aggravated by the lack of national HB vaccination strategy. Conversely, 55% - 86% of Egyptian HCWs were not vaccinated to HBV [5] [25]. It is recommended that all health care workers and interns should be vaccinated against HBV [26].

Evidence of anti-HBs titer > 100 IU/L is required before medical students are allowed to access patients in United Kingdome (UK). Furthermore, medical students with anti-HBs < 10 IU/L have to repeat the full vaccination course and those with anti-HBs 10 - 99 IU/L have to receive a single booster vaccination [26] [27]. The anti-HBs response rate in our medical students was 100%. This was similar to the results reported from Sudanese

medical students [28]. While 95% of Sudanese medical students had anti-HBs levels more than 100 IU/L [28], all students in our study had anti-HBs levels > 100 IU/L. The higher immune response detected in our young adults after HB vaccination favors previous data [19] [21]-[23], and infers that early HB immunization offers a greater proportion of anti-HBs response in younger HCWs. Zeeshan *et al*., reported that the highest rate of immune response (91%) was observed in younger HCWs (<25 y) [29]. Earlier reports observed the inadequate levels of anti-HBs in relation to increasing age [14]. These results suggested that early HB vaccination of HCWs during training is not only protective but it also optimizes the effectiveness of vaccination. In addition pre-exposure vaccination of health care workers has proven to be coast effective compared to post exposure prophylaxis with hyperimmunoglobulins [29]. Taken together these data suggested the importance of HB vaccination as early as possible during health care training period.

Certain risk factors have been associated with decreased rates of responsiveness for recombinant vaccines in HCWs. Increasing age and presence of anti-HBc antibody have been associated with decreased antibody response to HB vaccine in adult subjects [19] [25]-[30]. Notably we could not find any difference in anti-HBs levels among included students with respect to age. 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. There is no available data about the prevalence of anti-HBc among Egyptian general population. The prevalence of anti-HBc among Egyptian [31] and Taiwanese [19] HCWs was 2% and 31.2% respectively. Three (2%) of our students were reactive to anti-HBc. In fact this rate is significantly lower than that reported among Egyptian blood donors (13.3%) [32] born before national HB vaccination program. This may be attributed to the effect of national HB vaccination. While anti-HBc positive students tested negative for HBV DNA, one had tested positive for anti-HBe excluding occult HBV status, and false positive results respectively. The immune response rate of isolated anti-HBc to HB vaccination is largely dependent on the etiology of anti-HBc positivity. The response rate among isolated anti-HBc in our students was 100%; all of them had anti-HBs titer more than 1000 IU/L. This was similar to the poster response reported among patients with remote HBV infection. Indeed the response rate of anti-HBc was 48.6% [19] and 89.6% [33] among HCWs derived from hyperendemic and moderately endemic areas respectively. The lower response rate to HB vaccine among anti-HBc HCWs from hyperendemic area may be due to higher rates of occult HBV infection compared with HCWs from moderately endemic areas like Egypt.

Periodic monitoring of anti-HBs levels in all vaccinated HCWs was recently recommended due to progressive waning of anti-HBs levels one year after the primary response. Whether HB vaccinated HCWs are on need for booster doses or not is a controversial issue. Scientists engaged in HB vaccination research are clearly in two schools of thoughts. One group strongly believes that immunological memory is sufficient to prevent HBV infection and booster doses are not needed. While others trust that booster doses will cause not only a boosting effect in previously responder but also may induce an immune response among majority of non responders [34]. Jilg *et al*., proposed that subjects with anti-HBs < 100 IU/L after the last vaccine dose should be revaccinated within 6 months. Those with anti-HBs between 101 - 1000 IU/L should be checked up 1 - 2 years after the first vaccination; people with 1001 - 10000 IU/L should be checked up after 2 - 4 years and those with levels > 10000 IU/L should be checked after 4 - 6 years [34]. Given the high anti-HBs levels after HB vaccination in our medical students, this lent us support to suggest that early HB vaccination of HCWs may prolong the intervals of anti-HBs post-vaccination checkup and delay the need for booster doses. More prolonged follow up studies are needed to determine the rate of HBV breakthrough and durability of HB vaccine as well as the cost effectiveness of boosting vaccination in medical students.

We are aware of the limitations of this study. The sample number in addition to the limited age group cannot provide a strong evidence of the conclusion. However the design of the study had targeted this specific group to prove the hypothesis, in only one school of medicine. The other limitation was the lack of serological evidence about anti-HBc and HBsAg prior to vaccination. We believe that other studies recruiting larger numbers of different age groups and involving HBV serological back ground are needed to reach a solid conclusion about the actual response rate of HB vaccination in HCWs.

5. Conclusion

Early vaccination of HCWs during training periods optimizes the effectiveness of vaccination and may reduce the risk of HBV infection. In addition, it may prolong the intervals of anti-HBs post-vaccination check up and

the need for booster doses. Vaccination during training periods and before exposure to patients should be encouraged.

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