

IMMUNIZATION STATUS AGAINST HEPATITIS B VIRUS AND DETERMINATION OF ANTI-HBS ANTIBODY TITER IN MEDICAL AND DENTAL STUDENTS

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ABSTRACT

Objective: This study was aimed to determine anti-HBs antibodies titer in medical and dental students to monitor success of hepatitis B vaccination.

Material and Methods: This study was conducted on students of Khyber Medical College and Khyber College of Dentistry, Peshawar. Serum samples from students who were vaccinated were tested for the determination of anti-HBs antibody titer using microparticle enzyme immunoassay (MEIA).

Results: Out of 520 students surveyed, only 176 (33.84%) had either one injection or complete course of vaccine. None of them had checked their anti-HBs antibodies titer; 119 students (67.61%) had used Engerix-B, 41 (23.30%) students did not remember the brand of the vaccine while only 16 (9.09%) had used Heber-biovac HB. Twelve (6.8%) students tested were non-reactive for antibodies (titer <10.0 mIU/ml) while in 36 (20.5%) students antibodies titer was 10 and 100 mIU/ml respectively and 128 (72.7%) had antibodies titer more than 100 mIU/ml. Time lapsed between vaccination and detection of antibody titer was 0 - 6 years, 76 (43.1%) students had been tested after one year and 5 (2.8%) after 6 years and 41 (23.5%) students after 2 years.

Conclusion: Only one third had their partial or complete course of their vaccination. Antibody titers were reactive in majority of students who had completed the course. Students entering medical and dental schools need to be better educated about hepatitis B and its vaccination.

Key Words: anti-HBs antibodies titer, vaccination, HBs Ag.

INTRODUCTION

Hepatitis B virus (HBV) infection and its consequences are major health problems worldwide. Immunization with hepatitis B vaccine is the most effective means of preventing HBV infection and its consequences. In the past, the recommended strategy of prevention from hepatitis B was selective vaccination of persons with identified risk factors. However this strategy has not lowered the incidence of hepatitis B in the United States. In addition many infected persons had no identifiable source for their infection and thus could not be targeted for vaccination¹.

HBV infection is responsible for an estimated 1-2 million deaths worldwide every year. There are at least 300 millions carriers of HBV; at least 80% of these carriers reside in Asia². The prevalence of hepatitis B is about 10% in southern parts of Saudi Arabia³. Hepatitis delta virus (HDV)

infection occurs as co-infection with HBV or super-infection of HBV carriers. Co-infection usually resolves but super-infection, however, frequently causes chronic HDV infection and chronic active hepatitis or acute fulminant hepatitis⁴. In the United States, the incidence of acute hepatitis B has increased by 37% from 1979 to 1989 and estimated 200,000 to 300,000 new infections occurred annually during the period 1980-1991⁵.

Acute hepatitis B infection has a fatality rate of 1% while 10% of individuals infected with HBV progress to chronic liver disease leading to cirrhosis and might end up with hepatocellular carcinoma (HCC)⁶. In a study from Karachi, 67% of patients infected with HBV developed HCC⁷. In Pakistan, the rate of HBV and hepatitis C virus (HCV) infection ranges from 8-15% in general population with variations in the frequency and

**DISTRIBUTION OF AGE OF MEDICAL AND DENTAL STUDENTS
SCREENED FOR ANTI-HBS ANTIBODIES (N=176)**

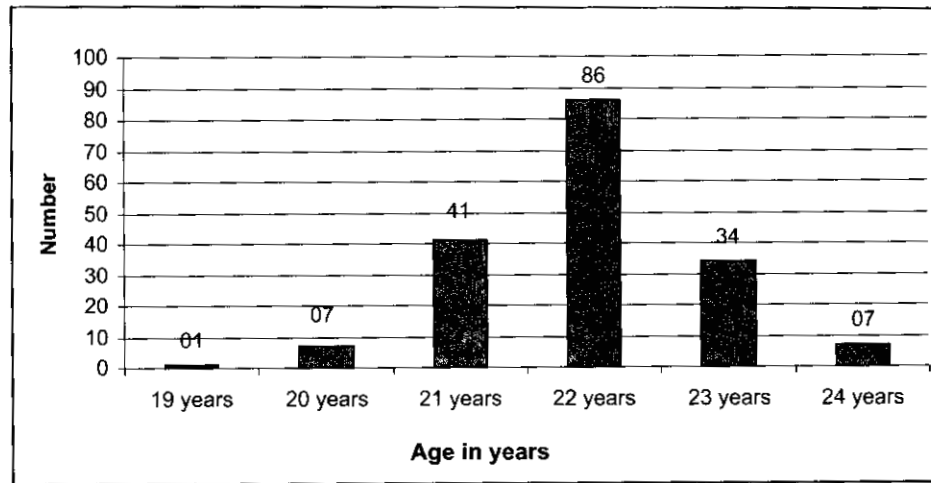


Figure 1

characteristics in various parts of the country^{7,8}.

HBV infection is highly prevalent in the age group of 30-55 years, the real productive lifetime. If we calculate estimated total number in Pakistan, using recent local data (1.9% HBV infection rate) then at least 2.622 million healthy young individuals are infected⁹.

The most common route of transmission of hepatitis B is blood transfusion but it is not the only route transmission, as at maximum only 1% of general population receives blood transfusion in one year time¹⁰. Other hepatitis viruses such as HGV have also been isolated from 4% blood donors¹¹.

Accidental needle stick injuries in healthcare workers and organs transplantation from infected donors have also been implicated as routes of transmission for HBV and HCV^{12,13}.

Two types of products are available for prophylaxis against HBV infection, vaccine and hepatitis B immunoglobulin (HBIG). Vaccine provides long term protection against hepatitis B and is recommended for both pre-exposure and post-exposure prophylaxis. HBIG provides temporary protection (3-6 months) and is indicated only in certain post-exposure setting. The currently available vaccines are produced by recombinant DNA technology.

Hepatitis B vaccine prevents hepatitis B disease and its serious consequences like hepatocellular carcinoma hence it may be called the first effective anti-cancer vaccine. Different brands of vaccine are marketed in Pakistan. A full course of three injections (I/M) is recommended at time zero, one month after the first injection and 3 months after the first injection¹⁴. Due to poor

socioeconomic conditions in Pakistan and lack of education and awareness regarding hepatitis B vaccine schedules, some people do not complete their full courses while expecting protection from this virus.

Healthcare workers such as medical and dental students are at higher risk and are required to be protected from at least hepatitis B. This study was designed to investigate how many medical students had completed their vaccination course for hepatitis B and to assess the level of antibodies against HBV. Another objective of the study was to compare the effectiveness of different brands of vaccines marketed in Pakistan in terms of development of protective level of antibodies in the vaccinated subjects.

MATERIAL AND METHODS

This study was conducted on students of Khyber medical college and Khyber college of Dentistry, Peshawar. Students from 2nd year BDS, 3rd and 4th year MBBS were screened for anti hepatitis B antibody titer using AxSYM, MEIA technology (Abbott, USA).

Selection of subjects: Healthy male and female medical and dental students between the age of 19-24 years who had completed or partially completed their vaccination course.

Specimen collection and preparation: Fresh blood specimens (5 ml) were collected from the subjects for processing. Specimens were handled gently to avoid haemolysis of blood. After clotting of blood, serum was separated by centrifugation for 20 minutes, initially at 3500 rpm (Labofuge, Heraeus, Germany). Serum was transferred into an Eppendorf tube (1.5 ml) and centrifuged again at 10,000 rpm (Heraeus Germany) for 20 minutes to

**ANTI-HBS ANTIBODY TITER (MIU/ML) DETERMINED IN
MEDICAL AND DENTAL STUDENTS (N = 176) AFTER USING
DIFFERENT BRANDS OF VACCINE**

| Antibody titer (mIU/ml) range | Total (n= 176) | Brand of vaccine used (%) | | |
|----------------------------------|-------------------|---------------------------|-------------------------|---------------------|
| | | Engerix-B (n= 119) | Heber-biovac (n= 16) | Unknown? (n= 41) |
| 00 | 06 (3.4%) | 3 (50%) | 0 (0%) | 3 (50%) |
| > 0 - < 10 | 06 (3.4%) | 2 (33.3%) | 1 (16.7%) | 3 (50%) |
| ≥ 10 - < 100 | 36 (20.5%) | 26 (72.2%) | 7 (19.4%) | 3 (8.4%) |
| ≥ 100 - < 1000 | 77 (43.7%) | 52 (67.6%) | 4 (5.1%) | 21 (27.3%) |
| ≥ 1000 | 51 (29.0%) | 36 (70.6%) | 4 (7.8%) | 11 (21.6%) |

?: Did not remember the brand of vaccine

Table 1

remove most of the medium weight interfering substances.

Proper quality control procedures were followed in the laboratory as recommended by manufacturer (Abbott laboratories, USA). Calibration of each kit was carried out according to manufacturer's instructions.

Interpretation of the results: Samples with concentration less than 10mIU/ml are non-reactive by AxSYM AUSAB (anti hepatitis B surface antibodies) assay. Samples whose concentrations are = 10.00 mIU/ml are considered reactive. The German permanent vaccination commission (STIKO) recommends regular evaluation for those with antibodies titer 10-100mIU/ml¹⁵.

RESULTS

Out of a total of 520 students (2nd year BDS, 3rd and 4th year MBBS) only 176 (33.85%) had either completed or had their single dose of vaccine. These 176 students were screened for the anti-HBs antibodies titer.

Out of 176 students, 102 (58%) were females and 74 (42%) were males. Age range was between 19 and 24 years. Distribution of age of these students is shown in Fig. 1. A total of 86 (48.85%) students tested were 22 years old, 41 (23.30%) were 21 years old, 34 (19.32%) were 23 years old, 07 (3.98%) were 20 and 21 years old each (Fig 1). Only 01 (0.57%) student was 19 years old in this study group.

The schedule of three doses of vaccination followed in this study was such that all the students (100%) received their 1st dose at first contact. The 2nd dose was received after one month by 173 (98.3%) students. Three (1.70%) students dropped out at this stage and they did not receive second and third doses. The 3rd and the last dose was received by 159 (91%) students. Thirteen students (8.3%) did not receive the 3rd dose of the

vaccine. The time period between the first and the third dose was not uniform, 79 (44%) students received the 3rd dose 03 months after the first injection while 72 (41%) received the third dose 06 months after the first injection.

The most common brands of the vaccine used in this study was, Engerix-B (119 subjects, 67.61%) Heberbiovac IIB (C.I.B.G. La Habana, Cuba) (16 subjects, 9.09%) and the rest of students did not remember the brand of the vaccine (41 subjects, 23.30%).

A total of 12 (6.8%) of the students tested were non-reactive for antibody titer (<10 mIU/ml) and 36 (20.5%) of the vaccinated students had antibodies titer > 10.0 and <100 mIU/ml while 128 (72.7%) had their antibody titer >100 mIU/ml (Table 1). Six of the students (3.4%) tested did not develop antibodies (titer = 00 mIU/ml).

Out of 119 students who used Engerix B, 52 (43.7%) students had their antibody titer of > 100 and <1000 mIU/ml and 36 (30.3%) had antibody titer of >1000 mIU/ml, while 3 (2.5%) students did not develop antibodies (titer = 00 mIU/ml).

Out of 16 students who used Heberbiovac HB, 7 students (43.7%) had antibodies level of > 10.0 and <100 mIU/ml, 4 (25%) students had their antibody titer of > 100 and <1000 mIU/ml, 4 (25%) had antibody titer of >1000 mIU/ml while none of the students had antibodies titer = 00 mIU/ml.

Figure 2 indicates that 76 (43.1%) of the students had completed their vaccine course one year ago, 41 (23.5%) had completed their course 2 years ago and 5 (2.8%) had completed their vaccine course 6 years ago.

DISCUSSION

Healthcare workers such as medical and dental students are at high risk and expected to be

DURATION OF TIME (YEARS) LAPSED AFTER COMPLETION OF VACCINATION FOR HEPATITIS B VIRUS IN MEDICAL AND DENTAL STUDENTS (N=176)

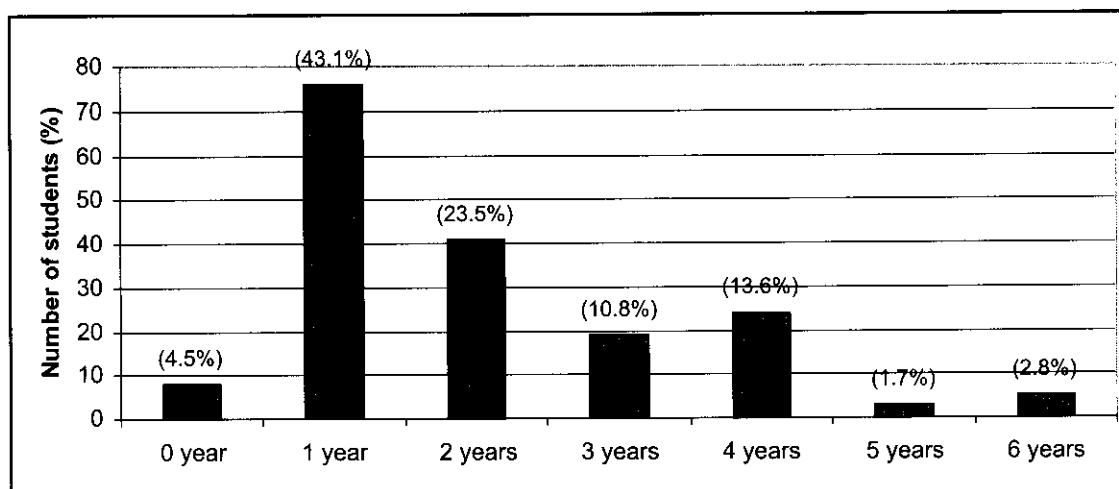


Figure 2

protected from at least hepatitis B virus. Complete protection of health care workers not only requires completion of the HBV vaccination course according to the schedule recommended but also needs to determine the antibody titers for the confirmation of the development of immunity against this deadly infectious condition.

The target of this study was a high risk population and like other high risk population they need protection on priority basis. Though a study conducted in the United States shows no significant decrease in the incidence of hepatitis B¹ after vaccinating high risk group.

In this study a young age group (19-24 years) of population has been surveyed because hepatitis B is more prevalent in younger age group as has been shown in other studies conducted in Peshawar⁹.

The presence of anti-HBs antibodies has been shown to be important in the protection against hepatitis B virus infection¹⁶. Numerous studies have demonstrated the effectiveness of hepatitis B vaccine in preventing HBV infection¹⁷. Post vaccination testing (1-6 months after completion of vaccine series) is required for persons with occupational risk such as health care workers but not recommended for healthy individuals with intact immune system and without known risk factors.

Results of the present study indicate that even the high risk population i.e. the medical and dental students are not aware of the importance of hepatitis B vaccine or screening antibody titers. This finding is identical to a study that was conducted in Thailand¹⁸. Only 33.84% of our students had completed their vaccination schedule

or had only one injection of vaccine. None of them had screened antibodies titer. Therefore none of them could claim protection from hepatitis B. Out of those who were screened for antibody titer, only 128 (72.7%) had their antibody titer >100.0mIU/ml. A total of 12 (6.8%) were non-reactive for antibody titer (<10.0mIU/ml) and 36 (20.5%) of the vaccinated students had antibodies titer > 10.0 and <100 mIU/ml (Table 1).

The most commonly used brand of vaccine was Engerix-B 119 students (67.61%) followed by Heber-biovac 16 students (9.09%) while 41 (23.30%) of the students did not remember the brand of the vaccine they used. Engerix-B is available in the vaccination camps organized by Social Welfare Society (SWS) of Khyber Medical College, Peshawar every year. Most of the students were vaccinated in these camps from time to time.

A logarithmic decline of antibodies level occurs over time (13-60% after 9 years) of the primary vaccination series¹⁹. Five of the students (2.8%) had their vaccine course completed six years ago but even then they had not screened their antibody titer (Fig 2). According to manufacturer's recommendations healthcare workers and special patients group should maintain their antibody level >100mIU/ml or follow their country policy in this regard¹⁴. Following these recommendations, 128 (72.7%) of the students screened in this study are protected, having an antibody titer of =100mIU/ml, the rest of the 48 students (27.3%) require a booster dose for their antibody titer to be in the protective levels i.e. =100mIU/ml. In a study conducted in Thailand, more than 40% of the pre-clinical students in Thai medical schools did not know their HBV status and fewer than 50% had been vaccinated against

the virus¹⁸.

Medical, dental students and surgeons continue to be at risk for occupationally acquired HBV infection. Immunization against HBV is safe and effectively prevents transmission of HBV from patients to surgeons and surgeons to patients²⁰. Such immunization is also the most effective way to reduce the risk of transmission of HBV. Until all healthcare workers are successfully immunized, HBV is likely to remain a threat. This study will also provide rationale for a comprehensive strategy to eliminate transmission of HBV and ultimately reduce the incidence of hepatitis B associated chronic liver disease in Pakistan.

CONCLUSION AND RECOMMENDATIONS

Only one third of the medical students had their partial or complete course of their vaccination. Antibody titers were reactive in majority of students who completed the course and the available vaccines are reasonably effective in providing protection against HBV.

For persons in health-care fields, vaccination should be completed during training in schools of medicine, dentistry, nursing, laboratory technology, and other allied health professions, before trainees have their first contact with blood. This can be made compulsory after proper legislation in the admission policy of all health-related institutions of Pakistan.

At the time of recruitment, all the healthcare workers must be tested for the presence of protective levels of antibodies. Those who lack protective levels of antibodies may be advised a booster dose or a full course of vaccine as required.

As there is no national policy regarding maintenance of protective antibody level in Pakistan, therefore we should follow the manufacturer's recommendation for defining protective levels. If protective antibodies titer has not been developed after vaccination, either a booster dose of vaccine or full course of re-vaccination is recommended for those at risk.

The Government of Pakistan has recently included vaccine for hepatitis B in the national immunization programme for children less than one year. There is no such programme for the mass vaccination for adults. The Government should also consider such a mass vaccination programme for adult population of this country.

The importance of screening anti hepatitis B antibodies titer must be explained to every individual undergoing vaccination for hepatitis B. Volunteers from non-governmental organizations

(NGOs) should be provided proper training and involved in this mass campaign in villages. Print media must also be involved in this campaign in educating public regarding the importance of vaccine and the screening of antibodies titer.

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