Protection status against hepatitis B infection assessed fromanti-HBs level, history of vaccination andhistory of infection based on anti-HBc in medical students

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Abstract. Hepatitis B virus (HBV) is one of the most contagious pathogens where the risk of exposure is very high among health care workers, especially students in the clerkship. This study describes the protection status by measuring anti-HBs level, history of vaccination, and history of HBV infection in medical students.Forty-four (44) students over 18 years old were randomly selected, interviewed for their vaccination history and then had their blood serum taken for anti-HBs and anti-HBc examinations to determine the protectivity and history of infection.There were 81.8% students without a protective anti-HBs level. Before starting their clerkship, 18.2% students received thevaccination, and only one-fourth formed protective antibody level above 10mIU/mL. Seventeen (38.6%) students had been exposed to HBV(positive anti-HBc), and only six of them showed protective anti-HBs level. None of the students that received vaccine underwent a post-vaccination serological test (PVST) to determine their immune response. These results indicated the vulnerability of medical students to the risk of HBV transmission while performing medical care. With the high incidence of HBV transmission, educational institutions are encouraged to make provisions for vulnerable students to receive a booster and an adequate PVST before their clerkship.

1. Introduction

Hepatitis B virus (HBV) infection was one of the most common chronic viral infections in the world, with a chronic carrier global prevalence varying between 0.1 and 20%. The most common hepatitis infection in Indonesia was Hepatitis B infection. The natural course of Hepatitis B might present from asymptomatic to identifiable liver damage, where chronic HBV infection may progress to cirrhosis and hepatocellular carcinoma (HCC).[1-5] HBV was a DNA virus from the hepatotropic Hepadnaviridae family with a nondirect cytopathic effect in its mechanism of liver damage, and instead, the damage resulted from interactions between HBV and the host's immune system.[6-9]

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HBV was transmitted percutaneously through mucosal exposure to infected blood or other body fluids from hepatitis B patients. One of the riskiest occupations were healthcare workers, especially medical students due to their lack of experience in procedures made them susceptible to accidental exposure.[10-14] Needle injuries were often experienced by healthcare workers in endemic areas, but such cases had notreported in Indonesia.[15-19]

In addition to universal standard precautions against infections, another preventive measure against HBV is vaccination, which has been a mandatory program in Indonesia. Vaccine response might vary, characterized by the formation of anti-HBs above 10mIU/mL. Some individuals might not form adequate immune response.[20-24] Levels of anti-HBs might decline over time, and although immunity to hepatitis B has a strong anamnestic response, some studies still recommend boosters especially in individuals with the low initial response, living in theendemic area, and often in contact with hepatitis B.[23-27]

2. Material and Methods

2.1. Location, time and population

This study was in March 2017 at the Faculty of Medicine, University of Muhammadiyah Sumatera Utara, Medan. This faculty of medicine, like many other medical faculties in Indonesia, did not have clear rules about the medical profession's prerequisites, especially in disease screening or vaccination programs.The population of this study was medical students who enrolled in clerkship at the institution. The inclusion criteria werehealthy subjects aged over 18 years. Subjects were at random as representatives of all students enrolled in clerkship from 2016 to 2017.

2.2. Collecting data

Subjects were given a questionnaire containing the history of vaccinations, type of vaccine, and the number of doses administered. Theywere asked about previous diseases, especially hepatitis, and also a history of hepatitis-related examinations such as Hepatitis B Surface Antigen (HBsAg) and Hepatitis B Surface Antibody (Anti-HBs) tests. Then the subjects had their blood samples taken for quantitative examination of anti-HBs and Total Hepatitis B Core Antibody (total anti-HBc).

2.3. Serological testing

Serology test was performed using ELISA method for quantitative anti-HBs and total anti-HBc using Rayto (RT 2100-C) and Cortez Diagnostics reagent. Anti-HBs had a cut-off value of 10 mIU/mL.

2.4. Ethics

Ethical Committee of Medical Faculty had approved theEthical clearance, University of Sumatera Utara. all participated subjects agreed with informed consents.

2.5. Data analysis

The data obtained were processed with computer software and then calculated as a descriptive statistical analysis of the demographic data, history of vaccinations, anti-HBs levels, and history of infections.

3. Results

3.1. Characteristic of subjects

Researchers identified 44 students consisting of 29 (65.9%) females and 15 (34.1%) men, and all of them aged over 20 years (Table 1). All subjects were medical students enrolled in the clerkship.

Table 1. Characteristic of subjects.

Demography	N	%
Gender		
Male	15	34.1
Female	29	65.9
Age		
<20 years old	0	0
>20 years old	44	100%

3.2. Questionnaire and interview

Subjects were given a questionnaire and interviewed with questions about the history of the disease, especially liver disease. One (2.7%) subjects previously had hepatitis A. None (0%) had ever been diagnosed with Hepatitis B. Subjects were asked for a history of vaccinations, either before education or at infant age, involving communication with parents and family to provide adequate information. The majority of subjects [31 (70.4%)] had ever been vaccinated for mandatory Hepatitis B at infancy. Eight (18.2%) subjects received vaccination recently in adulthood (Table 2). All of them (100%) usedtherecombinant vaccine. None were screened to determine the status of hepatitis B infection and immunity before and after vaccination.

Table 2. History of vaccination.

Vaccination history	N	%
Infant Vaccination		
Yes	31	70.4
No	13	29.5
Recent (adult) Vaccination		
Yes	8	18.2
No	36	81.8

3.3 Laboratory test result

Of the 44 healthy subjects examined for ELISA total anti-HBc, 17 (38.6%) subjects had been exposed to hepatitis B virus. The majority [36 (81.8%)] of subjects examined for anti-HBs level did not form protective antibodies against hepatitis B (Table 3).

Table 3. Test results for total anti-HBc and anti-HBs.

Serology test	n	%
Total Anti-HBc		
Positive	17	38.6
Negative	27	61.4
Anti-HBs		
<10mIU/mL	36	81.8
≥10mIU/mL	8	18.8

Both male and female subjects were generallyunprotected against Hepatitis B. Nearly half [12 (41.3%)] of females, and one-third [5 (33%)] of males had been exposed to HBV. Based on infant vaccination history, 25 (80.6%) subjects who had been vaccinated had ananti-HBs level below10mIU/mL, and 12 (38.7%) infected subjects were positive against anti-HBc. Six (75%) subjects who received the recentvaccination before clerkship had an anti-HBs level below 10mmIU/mL. (Table 4) of the eight people who had recent vaccinations, five of them received itin infancy, but only twoformed protective antibody level while the remaining three did not form protective level at all.

Table 4. Serology results of anti-HBc and anti-HBs based on demography and vaccination history.

		Anti – HBs		Anti – HBc	
		≥10mIU/mL	<10mIU/mL	Positive	Negative
Gender	Male	5 (33%)	10 (67%)	5 (33%)	10 (67%)
	Female	3 (10.3%)	26 (89.7%)	12 (41.3%)	17 (58.7%)
Infant Vaccination	Yes	6 (19.4%)	25 (80.6%)	12 (38.7%)	19 (61.3%)
	No	2 (22.2%)	11 (77.8%)	5 (38.5%)	8 (61.5%)
Recent (adult) vaccination	Yes	2 (25%)	6 (75%)	4 (50%)	4 (50%)
	No	6 (16.7%)	30 (83.3%)	13 (36.1%)	23 (63.9%)

Serologic examination showed that from 17 subjects who were positive for total anti-HBc, only six (35.3%) of them formed anti-HBs above10mIU/mL. Four of them had a level above 100 mIU/mL, and two people had a level of 1071mIU/mL and 969mIU/mL respectively.Eleven (64.7%) showed an unprotected anti-HBs level despite the evidence of the previous infection.

Table 5. Anti-HBs and anti-HBc.

Anti - HBc	Anti – HBs level	
	≥10mIU/mL	<10mIU/mL
Positive	6 (35.3%)	11 (64.7%)
Negative	2 (7.4%)	25 (92.6%)

4. Discussion

We enrolled 44 medical students as subjects and most of them were females. This number coincides with the fact that the majority of medical students are females in the study site and the sampling does not discriminate the sexes involved because there was no hepatitis B prevalence data that distinguish between genders.[27-29]

We identifiedonly 70.5% participants who received hepatitis B vaccination in childhood, even though this program was mandatory in Indonesia. From the entire vaccination procedure, none had done a post-vaccination test as recommended by CDC to see the individual response to form adequate antibody after completing vaccination dose.Studies regarding vaccination response after immunization in infancyshowed responses varied between 60 to above 90 percent. History taking found the majority of HBsAg-positive or anti-HBc-positive mothers had an impact on the baby's serologic status, but no study had sought to elucidate the relationship between the two, which was difficult to explain properly due to many influencing variables.[30-33]

Only eight (18.1%) subjects showed a protective antibody level above 10mIU/mL, even though the actual subjects that received vaccination was 34 (77.3%). Antibodies against HBsAg might decrease over time, and this statement had already been in many studies. The level of antibody declined gradually from the first year, and by the age of 10, half the recipient of the vaccine will lose its protective titer.But immunity against hepatitis B had a durable memory. The problem was the absence of adequate serological testing before and after vaccination, i.e. PVST (post-vaccination serological testing) as recommended by many global guidelines.[31,34,35]

Twelve (38.7%) of the 31 subjects who had received a mandatory vaccination at infancy had a positive anti-HBc which showed a previous history of hepatitis B infection. Five of these subjects had even undergone another course of vaccination before clinical rotation, so the absence of adequate antibodies to these students indicates the non-responsiveness of the subjects to the administration of hepatitis B vaccine. Vaccine administration, especially boosters in individuals whose previous response were adequate, should be able to provide a very significant increase in antibody level (anamnestic response). These students were vulnerable to hepatitis B infection and also had the risk of transmitting the disease to the patients in their care.[35-37]

5. Conclusion

We found 81.9% of participants had no protective antibody level against hepatitis B. Hepatitis B vaccine was one of the mandatory vaccines in Indonesia, but not all students received the vaccine as they should. Although immunity against hepatitis B had a memory, without an adequate PVST examination the medical students were considered vulnerable while performing their duties as healthcare workers. All healthcare personnel including medical student should take anti-HBs and HBsAg screening test before making any risky contact and also received a booster dose if necessary.

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