

Evaluation of Immunogenicity of Hepatitis B Vaccine in Hemodialysis Patients at Mazandaran Heart Center, Iran

AMIR SHAMSHIRIAN¹, SHAYAN ALIKHANI², REZA ALIPOOR³,
HAMED JAFARPOUR⁴, FATEMEH ESPAHBODI⁵ and SOHEIL AZIZI^{6*}

¹Department of Laboratory Sciences, Faculty of Paramedicine,
Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran.

²Department of Hematology, Tarbiat Modares University, Tehran, Iran

³Student Research Committee, Fasa University of Medical Sciences, Fasa, Iran.

⁴Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran.

⁵Endocrine research center, Imam Khomeini hospital,
Mazandaran University of Medical Sciences, Sari, Iran.

⁶Department of Laboratory Sciences, Faculty of Paramedicine,
Mazandaran University of Medical Sciences, Sari, Iran.

*Corresponding author E-mail: soheil_azizi@yahoo.com

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ABSTRACT

Hepatitis B Virus (HBV) infection is one of the most common issue worldwide. It is more common in hemodialysis (HD) patients which is sensitive to blood borne viral agents such as HBV more than other people and in terms of vaccine protection, immunogenicity of HBV vaccine in HD patients is still open for discussion. Therefore, aim of this study is to evaluating the immunogenicity of HBV vaccine in HD patients who admitted to the Mazandaran Heart Center hemodialysis unit in 2015. This cross-sectional study performed by using available data and Census method on all chronic HD patients in Mazandaran Heart Center in 2015. Patient's information was extracted from their records with ethical points including age, gender, HBS Ab level and the number of dialysis per week. Data was analyzed using chi-square test and SPSS 16 software. Of all patients with a mean age of 54.7 ± 13.76 years, Positive anti-HCV was observed in 7(7%) of them. For immune response to HBV vaccine, 35% with no response, 32% with poor response and 33% with complete response were obtained. Also did not observed significant relationship between sex, age and the number of dialysis per week with immunization of HBV vaccine. In conclusion based on the observed information, the immunogenicity of hepatitis B vaccine in hemodialysis patients of Mazandaran Heart Center was moderate to low that the rate of response to vaccine were reasonable according to the previous studies.

Keywords: hemodialysis patients, Hepatitis B virus, immune response.

INTRODUCTION

Hepatitis B (HB) is DNA virus of the Hepadnaviridae Family that is the greatest prevalent cause of viremia and one of the main causes of cirrhosis and liver disease. Its transmission occurs from different ways such as percutaneous or

mucosal exposition by contaminated blood products, multiple sexual contact, needle stick injury, unsafe drug injections and perinatal transmission. In total; Infected blood products and Contaminated equipment of hemodialysis (HD) unit are the most important factors in transmission of the virus in HD patients^{1, 2}. Acute and chronic hepatitis, cirrhosis,

hepatocellular carcinoma and decreasing the likelihood of transplantation are the problems that virus can cause³.

Studies have indicated that about 200 billion people worldwide have been infected with this virus and according to 2010 data is estimated that 350 million people are chronic carriers^{1,4,5}. In terms of prevalence, Iran is among the countries with moderate prevalence of the virus that 2-3% of the population are chronic carriers Hepatitis B Virus (HBV)(6). Universal vaccination against the virus from 1980 till now was accomplished and Serologic tests for safety assessment is The most important preventive measures against the virus, which greatly reduced the prevalence, but the prevalence of HB in HD patients on dialysis unit of less developed countries is still high and it is variable in different society^{5,7}. For example, previous studies show the prevalence of HBV through HD unit in western countries 0.6-6.6%, in Asia-Pacific region between 1.3% and 14.6% and in China the prevalence is 11.9% that shows the high range of prevalence in less developed countries and it depend on prevalence of HB in general population in each countries⁸.

Proper level of Hepatitis B surface antibody (HBs Ab) after vaccination against HB shows the individual Immune that the higher level of antibody will follow the higher immunogenicity. Individuals who carry HBs antibodies above 10 mIU/mL are considered to be protected^{1,3,9}. The effect of hepatitis

B vaccine in healthy individuals is above 90%, While in chronic hemodialysis patients for different reasons, such as immunosuppression because of uremia, malnutrition, loss of CD4 T cells, hepatitis C virus infection and the patient's age, Have a lower response rate about 50 to 80 percent^{4,10,11}. Thus, the first function for protection of patients on dialysis is a programmed vaccination strategy against HBV. And annually serological control test it is necessary to performed on patients who respond to vaccine and Antibody titers less than 10 mIU/mL require booster doses and re-vaccination¹. However, the prevalence of the problem in different areas due to various factors is different and high.

As regards such a study has not been conducted at Mazandaran Heart Center recently, and the specific conditions of patients referred to the center, we decided to perform this study with the aim of determining the immunogenicity of hepatitis B vaccine in chronic HD patients in Mazandaran Heart Center in Iran, to be aware of the results of this study and take the necessary actions to prevent the disease and increase the safety in these patients with the cooperation of staff working in this center.

METHODS

This cross-sectional study performed by using available data and Census method on all chronic HD patients in Mazandaran Heart Center in 2015 and at the end of the study the number of patients reached to one hundred. Inclusion criteria

Table 1: Frequency distribution of the hepatitis B vaccine immunization by sex, age and anti-HCV

Variables		Number & Percentage (%) of Vaccination			P-value
		Non-Responder	Poor Response	Strong Response	
Sex	Male	19(54.3)	21(65.6)	19(57.6)	0.793
	Female	16(45.7)	11(34.4)	14(42.4)	
Anti-HCV	Positive	2(5.7)	2(6.3)	3(9.1)	0.251
	Negative	33(94.3)	30(93.8)	30(90.9)	
Age	< 45	7(20)	4(12.5)	6(18.2)	0.399
	45-65	20(57.1)	21(65.6)	22(66.7)	
	< 65	8(22.9)	7(21.9)	5(15.2)	
Total		35(35%)	32(32%)	33(33%)	

included medical records of patients who received all 3 doses of hepatitis B Vaccine and exclusion criteria of the study was the lack of vaccination and HIV patients. For ethics and confidentiality, all information contained in the records which studied will be kept confidential and after reviewing were delivered to hospital's archive.

A checklist used to collect the data in this study, Including age, sex, Hepatitis B Surface Antibody (HBs Ab) and the number of dialysis per week. The results of the HBs Ab titers extracted 6 months after the last dose of the vaccination for HB that the test mentioned was measured by STAT Fax Machine Made in the United States of America and HBs Ab Kits of Total Quick Company Made in France by ELISA method. According to instructions of the used kit, Patients were separated into three groups based on antibody titer: More than 100 mIU/mL as strong response, 20-100 mIU/mL as poor response and less than 20 mIU/mL as Non-Responder.

After collecting the information, the data examined by use of descriptive statistics such as mean and standard deviation. To analyze the data, the normal distribution of data was evaluated by Kolmogorov-Smirnov test and due to the significance of the above test, chi-square test was used to assess the relationship between independent variables. The P-value less than 0.05 was considered as a minimum value for statistical significance. All data

were analyzed using the Statistical Package for the Social Sciences 16.0 (SPSS Inc., Chicago, IL, USA) software.

RESULTS

Of 100 hemodialysis patient's follow-up, 59 (59%) were males and (41%) were female (Fig 1). Their age ranged were 13 to 89 years and it's the mean and SD were about 54.7 ± 13.76 years (Fig 2). In terms of hemodialysis duration, 72% of patients had Hemodialysis 3 times a week, 18% of them 2 times a week, 7% of patients once a week and 3% of them 4 times a week. Just 7 (7%) patients were positive for anti-HCV and the rest of the 93 (93%) patients were anti-HCV negative. range of patient's anti-HBS were from 0 to 1046 mIU/ml with a mean (SD) 124.67 ± 204.74 (Fig 3). In terms of immunogenicity response, 35 (35%) patients had no response, 32 (32%) patients had poorly response and 33 (33%) patients had a complete response (Table1).

According to Table 1 for complete immunization response, in men with 19 (6.57%) patients were more than women with 14 (4.42%) that it shows the poor coverage of vaccination for HB in hemodialysis patients of this study. Based on the results of Table 1, did not exist A significant relationship between sex and immunization of HBV vaccine ($P=0.793$) and also there was no

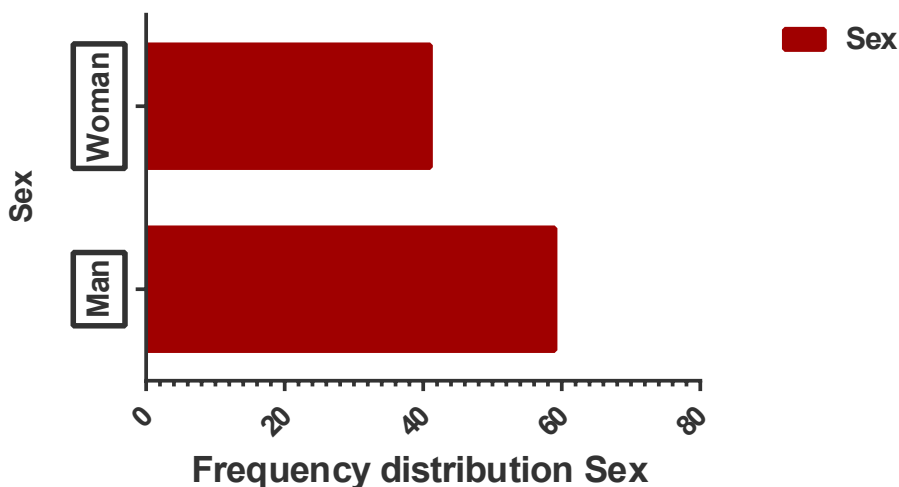


Fig.1: Histogram of frequency distribution sex

significant relationship between anti-HCV and HBV vaccine immunization ($P=0.251$) Based on the results, in terms of anti-HCV, 6 (6%) males and 1 (1%) female were positive for anti-HCV, which is a significant relationship between sex and anti-HCV antibodies was not observed. In terms of age distribution, a significant relationship between age and immunization of HBV vaccine ($P=0.399$) and also between age and anti-HCV ($P=0.703$) was not observed. Likewise, the number of dialysis per week had no significant difference with the hepatitis vaccine Immunization ($P=0.887$).

DISCUSSION

Hepatitis B is one of the remarkable world problems and Individuals undergoing dialysis because of exposure to blood products, Hemodialysis equipment that is shared between different people, defects in the skin and immune deficiency, are at risk of developing the disease more than other people and with all prevention and vaccination and reducing the incidence, prevalence of HBV in HD patients unacceptably remains high⁵.

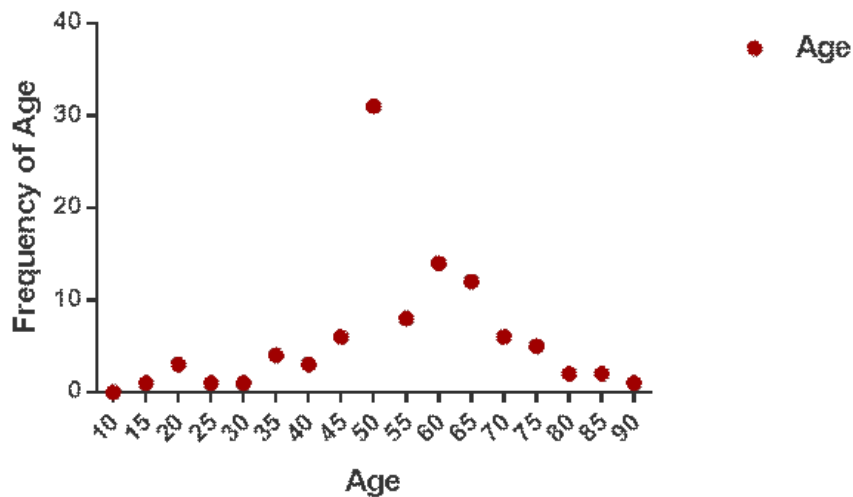


Fig.2: Histogram of frequency distribution age

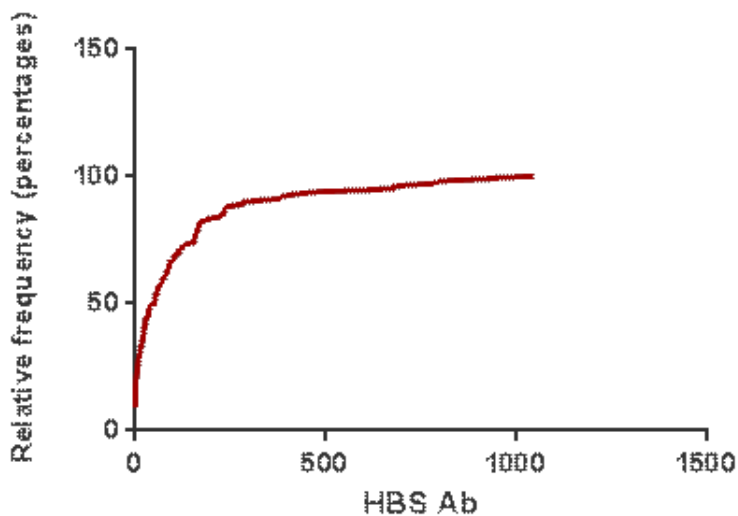


Fig.3: Histogram of frequency distribution HBS-Ag

According to the study conducted on 100 cases, in this study, there was not a significant relationship between gender and immunization of Hepatitis Vaccine, also significant relationship between anti-HCV and HBV vaccine immunization and between gender and anti-HCV was not observed. Of all 100 cases of hemodialysis patients studied, 33% had an adequate response to the vaccine, 32% had poor response and 35% of patients did not respond to vaccine, so 65 percent did not adequate response to vaccine. In a study that performed by Andrew I. Chin, aimed at Hepatitis B virus vaccine response in hemodialysis: baseline patient characteristics, has shown that 50 to 80% of patients have shown poor response to vaccine¹², So The results of our study which states that 65% of patients had not a good response to the vaccine is consistent with the current study. Although, several studies in the world showing the relationship between age and vaccine response and states that by age increasing the response will be reduced⁷, In this study there was no significant relationship between age and vaccine response. There are different results about the relationship between these two variables in different studies around the world. In a study performed by Parmar, Z and *et al*⁶, in the year 2011, As well as study was done by Al Saran, K. and colleagues¹³, in the year 2014, Was not a significant relationship between the age and immune response. But in the study that conducted by Bahri, F *et al*¹⁴. That was in the year 2016 a significant relationship between the age and immune response to hepatitis C vaccine was observed. Some other studies in the world showing the relationship between age and vaccine response and suggests the response is reduced with age^{7, 14}. These differences can be explained due to the small sample size or the age distribution in this study or some local factors that may effect on. The meta-analysis study conducted by Khedmat, H. *et al*¹⁵, showed in most studies, it was found that Male had a significantly lower response to hepatitis B vaccine than the Female. The present study shows; our results are inconsistent with results of other studies and this may also be due to the small sample size or could point to poor vaccination coverage of hepatitis in hemodialysis patients in this study.

In our study, the duration of dialysis had no significant difference with hepatitis vaccine

immunization that is in agreement with results reported by Khalid Al Saran *et al* and Hasanjani Roushan MR *et al*^{3, 16}. One of the interesting factors were investigated in previous studies that we did not study on, showed that; the intradermal injection of hepatitis vaccine, as well as increasing the dose used for patients on dialysis can be significantly keep reduce the prevalence of hepatitis in these patients^{4, 8, 13, 17}.

This study includes some limitations. For example, small sample size could be responsible for significant fail in relationship between variables which was completely significant in most previous studies. Also entering patients with HIV which considered as exclusion criteria into study, could be a significant increase in population and variable changes. Another limitation that could be effected the results, was age distribution that ranged from 13 years to 89 years. Therefore, it is recommended that conducting a study on larger population and entering the patients with HIV, will be able to coverage the gaps that became apparent in this study.

In conclusion based on the observed information, the immunogenicity of hepatitis B vaccine in Mazandaran Heart Center HD patients is moderate to low that the rate of response to vaccine were reasonable according to the previous studies. So given that hepatitis B is a major problem for dialysis patients and by all measures which is done to reduce the prevalence of it, the risk of the disease, still extremely limiting the patients on dialysis. It is recommended to comply with quality control issues in the hemodialysis unit to reduce transmission of the HBV and reduce the incidence of that in Hemodialysis Patients, moreover by conducting comprehensive researches, take a step to find more effective methods of prevention and treatment.

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