



## An Investigation of the Immune Response to Hepatitis B Vaccination in Hemodialysis Patients at Dialysis Centers of Tehran (2016)

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### Abstract

**Background:** Hemodialysis (HD) patients are at an increased risk of acquiring the hepatitis B (HB) virus and having lower protective antibody levels as well as shorter durations of seroprotection. This study aims to determine the immune response of HB vaccination in HD patients referring to dialysis centers of the Tehran North Health Network.

**Materials and Methods:** This descriptive study was conducted among all HD patients who referred to dialysis centers of the Tehran North Health Network in 2016. A total of 304 HD patients were included in this study using the census sampling method. Data were collected using a checklist, and the HBsAb level was evaluated by the ELISA test. The collected data were analyzed using analytical tests, including a chi-square test and the independent t-test.

**Results:** The mean±sd values of the serum level of HBsAb were 90.44±97.51 and 105.73±100 IU/L in men and women, respectively. There was no association between the rate of the response to the HB vaccine and gender (P=0.82), age (P=0.13), weight (P=0.09), vaccine injection frequency (P=0.45), number of dialysis sessions/week (P=0.36), and blood type (P=0.97). In addition, there was no association between the response to the HB vaccine and the history of T2DM, HTN, renal transplantation, and cigarette smoking among the participants (P>0.05).

**Conclusion:** One could conclude that the dialysis duration and the last injection of the HB vaccine would have a negative effect on the immune response rate among HD patients.

**Keywords:** Hepatitis B Virus, Vaccination, Hemodialysis, Seroconversion

### Introduction

The hepatitis B (HB) virus is a global public health problem that is considered a major cause of cirrhosis and liver cancer [1]. A total of 240 million people have a chronic HB infection worldwide, which results in approximately 780,000 deaths per year from the HB infection, 650,000 deaths from cirrhosis and liver cancer due to the chronic HB infection, and another 130,000 deaths from an

acute HB infection. The prevalence of HB varies across the world. In East Asia and in the Middle East, the estimated 5-10% and 2-5% of the general population are chronically infected with HB, respectively [2]. The prevalence of the hepatitis B virus (HBV) is moderate in Iran [3], which has been 3% (95% CI:0.87-8.86) among the general population in the past 25 years [4]. Research shows that the prevalence of HB has

decreased due to the routine vaccination of newborns against HBV since 1992 [5].

Hemodialysis (HD) patients are at an increased risk of acquiring HBV. Despite the completion of their vaccination schedule, they have lower seroconversion rates, lower protective antibody levels, and shorter seroprotection durations [6-8]. While the rate of the response to the HB vaccine is 90% among healthy people, it is 50-70% among HD patients [1, 9]. The reasons for high susceptibility to HBV among HD patients include invasive medical HD procedures, increased exposure to blood product transfusions, shared machines and equipment, and high prevalence of HBV among HD patients [7, 10]. Prominent fibrosis, silent clinical presentations, and atypical serologic evolution are prevalent among dialysis-treated HB patients [11]. A comprehensive systematic review of the HBV infection in Iranian HD patients showed that the HBV rate varied from 0 to 9.75% among these patients across different provinces [12].

Various strategies have been employed to improve the rates of the response to the HB vaccine in HD patients, including doubling the vaccine dose (40 µg/dose), doing annual serological control tests, and administering a new booster dose in patients with antibody titers less than 10 mIU/mL [3, 7, 13]. In such cases, the rate of the response to HBV could improve by up to 80% in HD patients [14]. Identifying the factors affecting the effectiveness of vaccination against HBV is crucial in reducing the prevalence of this disease among HD patients. Therefore, this study aims to determine the immune response of HB vaccination in hemodialysis patients referring to dialysis centers in the Tehran North Health Network in 2016.

## Materials and Methods

This descriptive study was conducted on all HD patients who referred to dialysis centers in the Tehran North Health Network in 2016. These centers included Imam Hossein Hospital, Shahid Labbafinejad Medical Center, Hashemi Nejad Kidney Hospital, as well as Partian and Daroshafa Clinics.

In this study, due to the availability of all HD patient profiles and their limited number, the census sampling method was used, with a total of 304 HD patients included. The inclusion criteria of the study were being negative HBsAg and HBcAb, being given three dose series at a 0-, 1-, and 6-month interval at least one month after the last injection. Patients who underwent renal transplantation during the study and no longer

referred to the center for dialysis were excluded from the study.

Researchers explained the goals of the study to the participants and obtained verbal informed consent from eligible ones. Data were collected using a pre-designed checklist that included data about age, gender, weight, blood type, frequency of vaccine injections, duration of vaccination completion, cigarette smoking status, history of hypertension (HTN), type 2 diabetes mellitus (T2DM), renal transplantation, number of dialysis per week, and dialysis duration. Next, the HbsAb level was measured using an ELISA test. In this study, patients with an anti-HBs titer above 10 mIU/mL were considered protected, and an inadequate response was defined as anti-HBs < 10 IU/mL.

Statistical analysis was performed using descriptive methods and analytical tests, including the independent samples t-test using SPSS Statistics V21.0. The significance level was set at  $p < 0.05$ , and the confidence interval was 95%.

The study protocol conformed with the ethical guidelines of the Declaration of Helsinki 1975.

In this study, we considered the HD patients' consent, personal data confidentiality, and free measurements as the principles of medical ethics.

## Results

A total of 304 HD patients, including 211 (69.41%) men and 93 (30.59%) women were included in this study. The mean±sd of the age of the participants was 57.14±17.21 and 52.23±16.58 in men and women, respectively. In addition, the mean±sd of the weight of the patients was 70.74±14.93 and 67.17±18.30 kg in men and women, respectively. The mean±sd of the number of vaccine injection was 3.57±1.33 and 3.43±0.92 in men and women, respectively. Besides, the mean±sd of the vaccination completion duration was 28.53±21.44 months in the study population.

In terms of the dialysis procedure, the mean±sd of the dialysis frequency in a week was 3.67±0.31 and 3.59±0.26 in men and women, respectively. In addition, the mean±sd of the dialysis duration was 40.67±58.45 months, i.e. 37.46±53.89 months in men and 48.15±67.37 months for women. In this study, 56 (18.42%) men and 17 (5.59%) women had a history of renal transplantation. A total of 85 (27.96%) men and 52 (17.11%) women had a history of T2DM. Similarly, the history of HTN was observed in 128 (42.10%) men and 49 (16.12%) women, respectively. In addition, 50 (16.45%) men and 4 (1.32%) women were cigarette smokers.

In this study, serological HB status was negative in all participants before the first dialysis. The mean±sd of the serum level of HBsAb was 95.2±98.3 (IU: 90.44±97.51) and 105.73±100 IU in men and women, respectively. In addition, the mean±sd of the anti-HBs titer was far higher than the antibody titers considered protective.

According to the data analysis results, there was no relationship between the rate of the response to the HB vaccine and gender in the HD patients (P=0.82). The results of the independent t-test showed no relationship between the rate of the

response to the HB vaccine and age (P=0.13), weight (P=0.09), vaccine injection frequency (P=0.45), as well as the dialysis number per week (P=0.36). In addition, no relationship was found between the rate of the response to the HB vaccine and blood type (P=0.97).

However, there was a significant association between the rate of the response to the HB vaccine and the last injection duration of the HB vaccine (P<0.001) as well as between the rate of the response to the HB vaccine and the dialysis duration (P=0.03) (Table 1).

**Table 1.** The status of the response to the hepatitis B virus by hemodialysis patients (n=304) at the Tehran North Health Network in 2016

	Response to HBV	Mean±SD	P-value
Age (Year)	Negative	59.67±18.52	0.15
	Positive	51.38±17.85	
Weight (Kg)	Negative	70.87±13.61	0.09
	Positive	68.51±16.60	
Frequency of vaccine injections (Number)	Negative	3.67±1.34	0.44
	Positive	3.55±0.76	
Duration of vaccination completion (Month)	Negative	44.11±22.84	<0.001
	Positive	21.57±19.33	
Dialysis number (Per Week)	Negative	3.04±0.27	0.32
	Positive	3.63±0.31	
Dialysis duration (Month)	Negative	25.60±6.53	0.03
	Positive	51.27±11.65	

Independent samples t-test; at a 5% level;

As Table 2 shows, there was no association between the response to the HB vaccine and T2DM, HTN, renal transplantation, as well as

cigarette smoking status among participants (P=0.8, P=0.2, P=0.8, and P=0.2, respectively).

**Table 2.** The relationship between the rate of the response to the hepatitis B virus and the history of renal transplantation, type 2 diabetes mellitus, smoking, as well as history of hypertension among hemodialysis patients (n=304) at Tehran North Health Network in 2016

		Response to hepatitis B virus		P-value
		Negative n (%)	Positive n (%)	
Renal transplantation	Yes	21 (6.91)	66 (21.71)	0.83
	No	43 (14.14)	174 (57.24)	
Type 2 diabetes mellitus	Yes	26 (8.55)	90 (29.60)	0.87
	No	40 (13.16)	148 (48.69)	
Cigarette smoking	Yes	25 (8.22)	47 (15.46)	0.21
	No	46 (15.13)	186 (61.18)	
History of hypertension	Yes	40 (13.16)	131 (43.09)	0.25
	No	31 (10.20)	102 (33.55)	

Independent t-test; at a 5% level;

**Discussion**

There was no association between gender and the rate of the response to the HB vaccine. Different results have been reported for the relationship between these two variables in various studies, with positive correlations reported in some studies [9, 15-17] and negative correlations in some others [1, 3]. These differences could be explained by intrinsic differences between men and women in their ability to respond to superficial hepatitis

antigens. In this study, there were no differences in the rate of the response to the HB vaccine in terms of the participants' age, while most studies report an association between older ages and an impaired immune response to the HB vaccine [13, 15, 18-20]. In some other reviews, similar to the present one, no relationship of this type has been reported [1, 3]. The reduction in the response to vaccination in older ages could stem from a change in the immune system in older ages due to

thymus problems and decreased T cell functionality [21].

The results of this study showed no association between the rate of the response to the HB vaccine and T2DM, HTN, as well as renal transplantation among participants. There are controversial findings in similar studies about the relationship between these variables, especially between T2DM and the response to the HB vaccine [1, 13, 16, 17]. There are some hypotheses about the impaired response to the HB vaccine in diabetic persons, which include a reduction in the number of circulating helper T cells, the CD4-to-CD8 lymphocyte ratio, lymphocyte blastogenesis, and the presence of DR3, DR7, and DQ2 human leukocyte antigen alleles in diabetic people [22].

In this study, cigarette smoking was not shown to be associated with HBV immunization. This finding was consistent with the results of similar past studies that reported no relationship between tobacco smoking and the response to the HB vaccine in HD patients [13, 23, 24]. However, another research showed contradictory results [25]. Regarding the high percentage of non-response cases in hemodialysis patients, especially in the elderly, the obese, and smokers, more attention should be paid to screening these groups of people for the anti-HBs antibody after vaccination.

Another finding of this study was that the duration of dialysis was associated with the seroconversion rate because the level of the immune response to the HB vaccine was lower in patients with prolonged HD. Some studies show a negative association between the duration of dialysis and the seroconversion rate [5, 13, 16]. According to another finding of the present study, a reduction in the rate of the immune response to HBV was associated with an increase in the duration of the last injection of the HB vaccine in HD patients. In general, the immune response to the HB vaccine decreased over time. Nevertheless, there has been a higher decrease in the mean of the serum level of HBsAb in HD patients than in the general population, and this reduction has increased more in HD patients [8, 13, 19]. In this study, like similar ones, the number of dialysis per week was not associated with the rate of the response to HBV [3]. Although some studies have reported that body mass is a determinant of the response to the HB vaccine [15], the results of the present study showed no relationship between these variables. In addition, there was no relationship between the response to the hepatitis B vaccine in hemodialysis patients and the length of time during which the patient was dialyzed. In hemodialysis patients,

humoral and cellular immunity is altered due to impaired phagocytosis as well as T and B lymphocyte functions. The number of memory B cells in patients with renal failure is remarkably low, which results in lower immunoglobulin levels. As a result, the response to the hepatitis B vaccine is lower in these patients [26].

It is worth noting that the major limitations of the present study were the lack of collaboration among health centers in terms of obtaining information as well as the large number of incomplete patient records.

According to the findings of this study, given that some participants were not suitable for antibody titers, booster dose injections were administered to these subjects. In addition, the time elapsed from vaccination was effective in antibody titers, and antibody titers could be periodically controlled to inject booster doses before reducing them.

## Conclusion

The results from the present study showed that the durations of vaccination completion and dialysis were associated with the rate of the response to the HB vaccine in HD patients. It seems that annual serological control tests should be performed in HD patients. In addition, a booster dose of HBV vaccination is recommended for patients with antibody titers less than 10 mIU/mL, who are considered non-immune patients.

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**Conflict of interest:** None declared.

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