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Original Article

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Investigation of COVID-19 Vaccine Acceptance and Early Side Effects of COVID-19 Vaccine in Hemodialysis Patients

Kübra Aydın Bahat, Meral Meşe

Department of Nephrology, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Türkiye

ABSTRACT

Objective: We aimed to evaluate the acceptance of the COVID-19 vaccines and the frequency of side effects in hemodialysis patients.

Methods: Patients receiving regular hemodialysis treatment were included in the study. Patients were asked for their opinions about whether they should have the COVID-19 vaccine. It was recorded which side effects were seen in patients who had received the COVID-19 vaccine.

Results: Ninety-two patients who received hemodialysis treatment were evaluated, and 92.4% of them expressed a positive opinion about the COVID-19 vaccine. Patients who were not vaccinated for COVID-19 reported that they were not vaccinated because they thought the vaccine was ineffective. The mean age of patients who did not want to be vaccinated for COVID-19 was lower (P = .019). Among patients who experienced side effects after at least one of the vaccines, and patients who experienced side effects after the first dose of the COVID-19 vaccine, the frequency of side effects was significantly higher in those who received the Pfizer-BioNTech vaccine (P = .001 and P = .001). When the first dose, second dose, and 2 doses of the COVID-19 vaccine were evaluated together, the relationship between increasing age and the decrease in the frequency of side effects was significant (P = .00, P = .001, and P = .015).

Conclusion: The vaccination rate against COVID-19 was high in hemodialysis patients, and the most common reason for vaccine opposition was the thought that the vaccine was ineffective. In addition, the frequency of side effects was lower, it was observed that the side effects decreased with age, and the side effects were more frequent in mRNA.

Keywords: COVID-19 vaccine, vaccine side effects, hemodialysis

Corresponding author: Kübra Aydın Bahat ✉ asbkubra@gmail.com

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INTRODUCTION

Hemodialysis (HD) patients infected with COVID-19 have higher mortality than the general population due to the high burden of comorbidities such as hypertension, diabetes, cardiovascular disease, and malignancy.[1,2] Uremia caused by the chronic renal failure may also cause inflammation and immune suppression at the molecular level, leading to increased mortality.[3]

Hemodialysis patients usually receive HD treatments in dialysis centers. For this reason, they should spend an average of 10-15 hours a week with other patients and health personnel. Despite isolation methods and social distancing guidelines for COVID-19, HD patients are at higher risk of infection due to their frequent invasive procedures and crowded dialysis environments.[4] The reported prevalence of COVID-19 among HD patients is 5-16 times higher than the general population.[2,5] For this reason, vaccination programs gain importance in the prevention of COVID-19 in HD patients.

It is known that vaccination is a very effective method in the prevention of infectious diseases in HD patients as in the general population. In HD patients, the vaccine

Table 1. Reasons for Vaccine Hesitation

	Reasons for Vaccine Hesitation	Yes	No
1.	I have heard many negative news from the media about the vaccine.		
2.	Religious leaders/celebrities/social influencers I trust do not recommend the vaccine.		
3.	Getting the vaccine is against my religious beliefs.		
4.	I do not believe that the vaccine will prevent this disease.		
5.	My family/friends/colleagues do not want to be vaccinated.		
6.	I do not believe this vaccine will be safe for me (it has not been as rigorously tested as other vaccines).		
7.	I do not trust pharmaceutical companies to provide safe and effective vaccines.		
8.	Information on side effects is not openly shared by the authorities (I am afraid of side effects).		
9.	I've had side effects with vaccines other than the COVID-19 vaccine before.		
10.	Others		

has been shown to reduce the rates of some infectious diseases such as influenza, hepatitis B, and pneumococcal pneumonia.[6-8] COVID-19 vaccines are newly released vaccines, and immunosuppression secondary to uremia in chronic renal failure may alter the immune response to viral vaccines.[8] However, many nephrology societies around the world recommend the administration of COVID-19 vaccines.[9,10] Despite this, many HD patients avoid being vaccinated for COVID-19, especially because of side effects and a lack of belief in the vaccine's protection against infections.[11-13] Although clinical data on the adverse effects of COVID-19 vaccines are available in general population studies, clinical data on the adverse effects of COVID-19 vaccines in HD patients are limited.[15-17]

The vaccination process in our country started on January 13, 2021. At the first stage, only inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine (CoronaVac) was available in our country. The use of BNT162b2 (Pfizer-BioNTech) vaccine was started on April 12, 2021, and individuals were vaccinated by choosing the type of vaccine they preferred.

Health workers and individuals over the age of 65 were determined as the groups who should be vaccinated at the first stage. Those who should be vaccinated in the second stage were determined as 50-64 years old, and those who should be vaccinated in the third stage were determined as those under 50 years of age and those with chronic diseases. As of June 10, 2021, the vaccination process has started for individuals under the age of 50 and with chronic diseases. Vaccination was done according to group order.

In our study, we aimed to reveal the acceptance and early side effects of the COVID-19 vaccine in HD patients.

MAIN POINTS

- Vaccination is of great importance in controlling infectious diseases such as COVID-19.
- The fear of side effects and the ineffectiveness of vaccines, which cause vaccine opposition in society, can be overcome by providing the right information sources about vaccines.
- COVID-19 vaccines, especially inactivated vaccines, have less potential for side effects in hemodialysis patients. However, the incidence of side effects increases at younger ages.

METHODS

Between February 1, 2021, and September 1, 2021, 92 adult patients who received regular HD treatment in our hospital's dialysis center were included in the study. Demographic characteristics of patients (gender, age), chronic diseases (diabetes mellitus [DM], hypertension [HT], asthma, chronic obstructive pulmonary disease, congestive heart failure [CHF], coronary artery diseases [myocardial infarction, angina pectoris]), their education level, whether they were actively working or not, and whether they had COVID-19 or not were recorded. All patients diagnosed with COVID-19 were diagnosed by performing real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) test for SARS-CoV-2.

All our patients were informed about COVID-19 vaccines by the responsible dialysis nurses working in our center. Patients were asked whether they would regularly receive the COVID-19 vaccine during their dialysis sessions. Patients who stated that they would not be vaccinated against COVID-19 were asked questions about the reasons for vaccine hesitancy. Details of questions regarding COVID-19 vaccine hesitations are available in Table 1.

Patients who gave a positive opinion about the COVID-19 vaccine were asked whether they experienced any side effects within 24-48 hours after the COVID-19 vaccine in order to determine the early side effects. Details of early stage vaccine side effects related to COVID-19 are available in Table 2.

Statistical Analysis

All statistical analyses were performed with the software program Statistical Package for Social Sciences for Windows,

Table 2. Side Effects of COVID-19 Vaccines

	Adverse Effects	Yes	No		Adverse Effects	Yes	No
1	Pain at the injection site			10	Weakness		
2	Shortness of breath			11	Cough		
3	Nausea			12	Anaphylaxis		
4	Vomiting			13	Diarrhea		
5	Fever			14	Abdominal pain		
6	Headache			15	Dizziness		
7	Itching			16	Conjunctivitis		
8	Muscle pain			17	Loss of smell/taste		
9	Uncontrolled tension			18	Other		

version 21 software (IBM Corporation, Armonk, NY, USA). A *P* value below .05 was accepted as the statistical significance limit. Numerical variables were given as mean ± standard deviation for normally distributed variables and median (minimum–maximum) for skewed continuous variables. Categorical variables are shown as frequencies. Chi-square test was used to evaluate categorical data. Independent sample *t* test was used in the analysis of continuous variables, and Mann–Whitney *U*-test was used for skewed continuous variables.

This study was approved by the Ethics Committee. Ethics committee decision number: 2021/514/200/36. All participants gave their informed consent.

RESULTS

In our study, 92 patients who received regular HD treatment were evaluated. Thirty-four (37%) of the patients were female and 58 (63%) were male. The mean age was 53.7 ± 15 years (med: 53). The most common comorbidities were HT (72.8% in 67 patients).

Table 3. Characteristics of Patients Classified According to Their Views of Being Vaccinated for COVID-19

Parameters	Total n = 92	Positive Opinion (–) n = 85	Negative opinion (+) n = 7	*P*
Demographic features				
Age (years)	53.7 ± 15.0 (53.0)	54.7 ± 14.8 (55.0)	41.9 ± 12.0 (40.0)	.019
Sex				
Male, n (%)	58 (63.0)	52 (61.2)	6 (85.7)	.196
Female, n (%)	34 (37.0)	33 (38.8)	1 (14.3)	
Dialysis age (month)	56.7 ± 73.6 (21.3)	55.4 ± 70.6 (21.8)	71.9 ± 109.7 (27.0)	.269
DM, n (%)	36 (39.1)	34 (40.0)	2 (28.6)	.551
Hypertension	67 (72.8)	63 (74.1)	4 (57.1)	.232
CVD, n (%)	12 (13.0)	12 (14.1)	0	1
CHF, n (%)	7 (7.6)	7 (8.2)	0	.286
Story COVID-19 PCR+, n (%)	17 (18.5)	17 (20.0)	0	.617
Literacy, *n* (%)	81 (88.0)	76 (89.4)	5 (71.4)	.196
Education status				
Uneducated, n (%)	20 (21.7)	17 (20.0)	3 (42.9)	.683
Elementary school, n (%)	31 (33.7)	29 (34.1)	2 (28.6)	
Middle school, n (%)	17 (18.5)	16 (18.8)	1 (14.3)	
High school, n (%)	18 (19.6)	17 (20.0)	1 (14.3)	
University, n (%)	6 (6.5)	6 (7.1)	1 (14.3)	
Working status				
Active worker, n (%)	12 (13.0)	12 (14.1)	0	.363
Retired, n (%)	27 (29.3)	25 (29.5)	2 (28.6)	
Not retired, n (%)	53 (57.6)	48 (56.4)	5 (71.4)	
Working status				
Active worker, n (%)	12 (13.0)	12 (14.1)	0	.538
Non-working, n (%)	80 (87.0)	73 (85.8)	7 (100)	

Data are given as (mean ± standard deviation) or (median).
CHF, congestive heart failure; CVH, coronary vascular diseases; DM, diabetes mellitus, PCR, polymerase chain reaction.

Patients were asked for their opinions on getting the COVID-19 vaccine. While 92.4% (85/92) of the patients expressed a positive opinion about the vaccine, 7.6% (7/92) stated that they did not want to be vaccinated against COVID-19. Of the 85 patients who gave a positive opinion about getting the COVID-19 vaccine, 4.7% (4/85) were infected with COVID-19 and therefore not yet vaccinated (because it was not time to vaccinate after infection), and 85.3% (81/85) were vaccinated against COVID-19.

All of the patients who did not have the COVID-19 vaccine reported that they did not receive it because they thought it was ineffective. The mean age of patients who do not want to be vaccinated against COVID-19 is 41.0 ± 12.2 years (med: 40). The mean age of patients with a positive opinion about the COVID-19 vaccine was 54.7 ± 14.8 years (med: 55) (P = .019).

All but one of the patients who received the COVID-19 vaccine had received a double dose of vaccine. The patient who did not receive the second dose of vaccine developed anaphylaxis after the first dose of Pfizer-BioNTech. There were no patients with cross-vaccination.

No significant relationship was found between their views on getting the COVID-19 vaccine and gender, history of having COVID-19, dialysis age, literacy, educational status, active work, retirement, and comorbidities.

Characteristics of patients classified according to their views of being vaccinated for COVID-19 are detailed in Table 3.

Of the 81 patients who had received the COVID-19 vaccines, 51 (63%) were male and 30 (37%) were female. The mean age was 54.6 ± 14.9 (med: 55) years. The most common comorbidities were HT (72.8% in 59 patients). Considering all vaccinated patients, 19.8% (16/81) preferred Pfizer-BioNTech and 80.2% (65/81) chose CoronaVac.

Side effects were detected in 27.2% (22 patients) of the patients after at least one of the vaccines. The most common adverse event was pain at the injection site (16.8% in 13 patients). Of the patients who reported an adverse event after at least one of the COVID-19 vaccines, 50% (11/22) received the Pfizer-BioNTech vaccine, and 8.4% (5/59) of the patients who did not report any adverse events related to the COVID-19 vaccine received the CoronaVac vaccine (P = .001).

In addition, the mean age of the patients who reported an adverse event after at least one of the COVID-19 vaccines was 45.7 ± 13.1 years, and the mean age of the patients who did not describe any adverse events was 58.0 ± 14.3 years (P = .001). There was no significant relationship between the side effects questioned regarding the COVID-19 vaccine and gender, history of having COVID-19, dialysis age, and comorbidities.

The demographic characteristics of patients with the COVID-19 vaccine and the main clinical features of the presence of side effects are detailed in Table 4.

Side effects were described in 24.6% (in 20 patients) of the patients after the first dose of the COVID-19 vaccine. The most

Table 4. Characteristics of Patients Classified According to the Presence of Adverse Events After the COVID-19 Vaccines

Parameters	Adverse Effect (–) n = 81	Adverse Effect (+) n = 59	Total n = 22	*P*
Demographic Features				
Age (year)	54.6 ± 14.9 (55.0)	58.0 ± 14.3 (60.0)	45.7 ± 13.1 (49.0)	,001
Sex				
Male, n (%)	51 (62.9)	38 (64.5)	13 (59.0)	.797
Female, n (%)	30 (37.1)	21 (35.5)	7 (41.0)	
Dialysis age (month)	55.0 ± 69.2 (22.4)	58.9 ± 74.6 (26.6)	44.3 ± 52.3 (21.0)	.500
DM, n (%)	32 (39.5)	24 (61.5)	8 (36.3)	.802
Hypertension, n (%)	59 (72.8)	45 (76.2)	14 (66.6)	.273
CVD, n (%)	11 (13.6)	8 (13.5)	3 (13.6)	1
CHF, n (%)	7 (8.6)	4 (6.7)	3 (13.6)	.382
Vaccine type, n (%)				
Biontec, n (%)	16 (19.8)	5 (8.5)	11 (50.0)	.001
Sinovac, n (%)	65 (80.2)	54 (91.5)	11 (50.0)	
Story COVID-19 PCR+, n (%)	13 (16.0)	12 (20.3)	1 (4.5)	.726

Data are given as (mean ± standard deviation) (median).
CHF, congestive heart failure; CVH, coronary vascular diseases; DM, diabetes mellitus; PCR, polymerase chain reaction.

Table 5. Distribution of Adverse Effects After COVID-19 Vaccines

Parameters	First Dose of Vaccine n = 20	Second Dose of Vaccine n = 11	Total n = 22
Adverse effects, n (%)			
Weakness	1 (5.0)	1 (9.0)	1 (4.5)
Pain at the injection site	12 (60.0)	8 (72.7)	13 (59)
Nausea	3 (15.0)	0	3 (13.6)
Anaphylaxis	1 (5.0)	0	1 (4.5)
Fever	0	1 (9.0)	1 (4.5)
Headache	1 (5.0)	0	1 (4.5)
Itching	1 (5.0)	1 (9.0)	1 (4.5)
Muscle pain	1 (5.0)	0	1 (4.5)

common side effect was pain at the injection site (14.8% in 12 patients). Of the patients who described adverse events after the first dose of the COVID-19 vaccine, 55% (11/20) had received Pfizer-BioNTech vaccine. Of the patients who did not describe adverse events associated with the first dose of the COVID-19 vaccine, 8.1% (5/61) received the Pfizer-BioNTech vaccine (P = .001). In addition, the mean age of the patients who reported an adverse event after at first dose of the COVID-19 vaccines was 45.3 ± 13.7 years, and the mean age of the patients who did not describe any adverse events was 57.7 ± 14.1 years (P = .001). There was no significant relationship between the side effects questioned regarding the COVID-19 vaccine and gender, history of having COVID-19, dialysis age, and comorbidities.

After the second dose of the COVID-19 vaccine, 11.7% of the patients (in 11 patients) described side effects. The most common side effect was pain at the injection site (12.5% in 8 patients). In addition, the mean age of the patients who reported an adverse event after the second dose of the COVID-19 vaccine was 44.5 ± 13.3 years, and the mean age of the patients who did not describe any adverse events was 56.3 ± 13.3 years (P = .015). There was no significant relationship between the side effects questioned regarding the COVID-19 vaccine and gender, history of having COVID-19, dialysis age, vaccine type, and comorbidities.

The distribution of side effects after COVID-19 vaccines is detailed in Table 5.

DISCUSSION

COVID-19 vaccines are newly introduced vaccines. Therefore, data on COVID-19 vaccine acceptance and COVID-19 vaccine-related adverse events are much needed to assist and guide clinicians. In this study, we present data on COVID-19 vaccine acceptance and early post-vaccine side effects in patients undergoing regular HD.

To date, several studies on the acceptance of COVID-19 vaccines have been reported in the literature. In general population studies, COVID-19 vaccine acceptance rates are seen to be between 46% and 76%.[11,18,19] In studies conducted in HD patients, the COVID-19 vaccine acceptance rates range from 80% to 93%, and there is an inverse relationship between decreasing age and COVID-19 vaccine hesitations.[13,20]

In our study, in accordance with the literature, 92% of the patients reported positive opinions about the COVID-19 vaccine, and the mean age of the vaccinated patients in our patient group was found to be significantly higher than the unvaccinated patients. There was no statistically significant difference between the education levels of the patients who were hesitant about the COVID-19 vaccine and could not be vaccinated and the patients who gave a positive opinion about the COVID-19 vaccine. However, the rate of uneducated was 42.9% in the group with vaccine hesitancy, and the rate of uneducated was 20% in the group without vaccine hesitation. The young age and low education level of the vaccine-hesitant group may have caused them to prefer social media to get information about the COVID-19 vaccine. This situation may have led to hesitations about the vaccine as a result of the opposition to the vaccine on social media and the propaganda that the disease is mild at a young age.

Immunization is a cost-effective and highly successful healthcare practice to prevent infectious diseases.[2,8] Side effects of vaccines, false information about vaccines, and the thought that they are ineffective are the most important reasons for hesitations against vaccines.[21]

In some studies, it has been determined that the most common causes of COVID-19 vaccine hesitations are the presence of side effects and the idea of vaccine ineffectiveness.[11-13] In our study, all of the patients who did not want to be vaccinated for COVID-19 thought that the vaccine was ineffective. Unlike other studies, the lack of hesitation about the side effects of the COVID-19 vaccine may be due to the small number of patients in our center describing serious side effects.

In studies on vaccines, side effects occurring within 24-48 hours after vaccination were defined as early side effects.[14] In our study, we examined the early side effects of COVID-19 vaccines (Pfizer-BioNTech and CoronaVac) and the factors that can be associated with side effects.

In general population studies, side effects related to COVID-19 vaccines are seen in 78%-96% of individuals.[22,23] In addition, although the reason is not fully explained, it has been observed that side effects are seen more frequently after m-RNA vaccines such as Pfizer-BioNTech, and less side effects are observed in inactivated vaccines such as CoronaVac.[15,24]

In studies conducted with dialysis patients, the side effects associated with COVID-19 vaccines were similar to those of the

general population, but the frequency of side effects was found to be lower than in the general population. Similar to general population studies, side effects after m-RNA-based COVID-19 vaccines are more common in dialysis patients than the side effects of inactivated COVID-19 vaccines.[16,25]

In addition to these findings, in studies based on both the general population and HD patients, it has been shown that the frequency of side effects decreases with increasing age, the most frequently described side effect is injection site pain, and the frequency of side effects decreases in second-dose vaccines.[16,22,26]

The majority of the patients included in our study were vaccinated with CoronaVac, as it is the first vaccine provided in our country during the COVID-19 vaccination process. Consistent with the literature, side effects related to COVID-19 vaccines in our study were relatively few in our patient group compared to studies performed on the general population. In addition, it was observed that side effects decreased with age in vaccinated patients, the most common side effect was injection site pain, the frequency of side effects was higher in patients with the m-RNA vaccine, and the frequency of side effects decreased after the first vaccine.

The lower incidence of side effects in our patient group compared to the general population may be due to the fact that uremia-related immunosuppression in HD patients may reduce immune reactions to vaccines.[3,27] In addition, the fact that antibody titers were found to be lower in HD patients after COVID-19 vaccines compared to the normal population may have contributed to the low frequency of side effects.[28,29] Similarly, the higher frequency of Pfizer-BioNTech vaccine-related adverse events may be due to the higher antibody titers of m-RNA-based vaccines.[30]

In addition, in the immune system, whose function decreases with aging, changes such as the gradual disappearance of naive cells, an increase in the number of memory cells, and a decrease in the diversity of T cell and B cell repertoire occur. As a result of these changes, both inflammatory reactions and protective immune responses become slower than in young healthy adults. These changes in the immune system may have caused the decreasing frequency of side effects with increasing age.[31-34]

The most common side effect seen in our study was pain at the injection site, similar to other studies with COVID-19 vaccines and other injectable vaccines such as the whole cell pertussis vaccine or human papillomavirus vaccine.[23,35] It may be caused by the injury caused by the injection procedure or by the local inflammatory response to the active substance of the vaccine.

Our study has some limitations. The small number of patients studied should be noted as a limitation. In addition, the large difference between the number of patients according to the types of vaccine should be noted as a limitation. The fact that antibody titers were not measured after the COVID-19 vaccine is an important limitation, but in some studies investigating post-vaccine side effects in the literature, post-vaccine antibody titers were not measured due to limitations in accessing antibody tests or high cost.[15,22] However, since the number of studies on COVID-19 vaccine acceptance and side effects in HD patients is low, clinicians interested in managing this patient group should be informed.

CONCLUSION

In conclusion, in this study, the rate of vaccination against COVID-19 in HD patients was found to be higher compared to general population studies. It has been found that the most common reason for opposing the COVID-19 vaccine is the thought that COVID-19 vaccines are ineffective. In addition, the side effects of HD patients who received the COVID-19 vaccine were similar to those in the general population, the frequency of side effects was less, the side effects decreased with age, and they were more pronounced in m-RNA vaccines.

Ethics Committee Approval: Ethics committee approval for this study was received by Kartal Dr. It was obtained from the Lütfi Kırdar City Hospital Clinical Research Ethics Committee (Date: April 28, 2021, Decision No: 2021/514/200/36).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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