ORIGINAL RESEARCH

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Overview of COVID-19 Vaccine and Investigation of Side Effects in Patients Over 65 Years of Age with Chronic Kidney Disease

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Abstract

Objective: The entire population should be vaccinated to prevent the spread of Coronavirus disease-2019 (COVID-19). In this study, we aimed to evaluate the acceptance of the COVID-19 vaccine and the frequency of side effects in patients over 65 years of age with chronic renal failure.

Materials and Methods: Patients with chronic renal failure over the age of 65 who applied to the nephrology outpatient clinic between 14.03.2021 and 15.04.2021 were included. Demographic characteristics, comorbidities, whether they were vaccinated, and post-vaccination symptoms were recorded.

Results: In our study, 112 patients with chronic renal failure were evaluated. 94% of the patients (105/12) reported a positive opinion about the vaccine. The most common cause of COVID-19 vaccine opposition was related to vaccine side effects (54%). Of the patients included in the study, 89 were vaccinated with CoronaVac. Side effects were seen in 23% of patients after at least one dose of CoronaVac. The most common side effects were uncontrolled blood pressure and pain at the injection site. In patients reporting adverse events after at least one dose of CoronaVac and 1st dose of vaccine; coronary vascular diseases (CVD) was significantly higher (p=0.012, p=0.001), patients receiving hemodialysis treatment had fewer adverse events (p=0.005, p=0.032), and injection site pain was more common in female patients (p=0.023, p=0.023). The most common adverse event after the 2nd dose was uncontrolled blood pressure and was significantly higher in female patients (p=0.023, p=0.001).

Conclusion: Although the rate of vaccination against COVID-19 is high in individuals over 65 years of age with chronic kidney disease, the most common reason for vaccine opposition was vaccine side effects. In addition, although the frequency of side effects was lower in our study population, uncontrolled blood pressure was observed differently and it was observed that the presence of cardiovascular disease increased the frequency of side effects.

Keywords: COVID-19 vaccine, vaccine side effects, chronic kidney disease, geriatrics

Introduction

Coronavirus disease-2019 (COVID-19) can cause a variety of illnesses, from mild respiratory infection to severe pneumonia. The COVID-19 pandemic is a life-threatening global pandemic, especially for patients and the elderly with concomitant diseases such as kidney disease (1). Controlling the COVID-19 pandemic is very important for public health. Because immunization is one of the most successful and cost-effective health interventions to prevent infectious diseases, vaccines against COVID-19 are considered of paramount importance to prevent and control COVID-19 (2). In many countries, COVID-19 vaccine hesitancy and misinformation about COVID-19 vaccines pose significant barriers to the provision of community immunity with the COVID-19 vaccine. The main reasons for COVID-19 vaccine hesitancy are the side effects that may develop due to vaccines and the lack of belief in the vaccine's protection against infections (3,4).

Uremia caused by chronic renal failure causes inflammation and immune suppression at the molecular level (5). Immunosuppression that occurs in chronic renal failure may change the immune response against viral vaccines (6). COVID-19 vaccines are newly developed vaccines. Although clinical data

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on the side effects of COVID-19 vaccines are available in general population studies, clinical data on the side effects of COVID-19 vaccines in patients with chronic kidney disease are limited (7,8). In our study, we aimed to reveal the acceptance of the COVID-19 vaccine in patients over 65 years of age with chronic renal failure and the side effects that developed in the early period.

Materials and Methods

The vaccination process in our country started on January 13, 2021. At the first stage, only CoronaVac was available in our country. Health workers and individuals over the age of 65 were determined as the groups to be overcome in the 1st stage. Individuals aged 65 and over; 1st group, individuals aged 90 and over, 2nd group individuals aged 85-89, 3rd group individuals aged 80-84, 4th group individuals aged 75-79, 5th group individuals aged 70-74, group 6 was classified to include individuals aged 65-69 years. Vaccination was done according to group order. As of February 12, 2021, the vaccination process started for individuals aged 65-69 years.

Patients with chronic renal failure over the age of 65 who applied to the nephrology outpatient clinic between 14.03.2020 and 15.04.2020 were included in this study. Demographic characteristics of patients (gender, age), chronic diseases [diabetes mellitus (DM), hypertension (HT), asthma, chronic obstructive pulmonary disease, congestive heart failure, coronary artery diseases (myocardial infarction, angina) pectoris, documented coronary heart disease)], vaccine requests/vaccination hesitations, post-vaccination symptoms (arm pain, cough, fever, shortness of breath, diarrhea, vomiting, nausea, abdominal pain, myalgia, conjunctivitis, loss of smell/taste, pruritus), blood pressure uncontrolled, dizziness, allergic reactions) were recorded.

Statistics

Data were analyzed using the SPSS 21.0 statistical program. P-value below 0.05 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 in the analysis of continuous variables. This study was approved by the local institutional review board and waived the informed consent requirement.

Results

In our study, 112 patients with chronic renal failure were evaluated. Of the patients included in the study, 31 (28%) were hemodialysis patients and 81 (72%) patients were chronic renal failure patients who did not require dialysis treatment. Of all patients, 55 (49%) were female and 57 (51%) were male. The mean age was 72.4±6.6 years. Patients were asked for their opinions on getting the COVID-19 vaccine. While 94% (105/112) of the patients expressed a positive opinion about the vaccine, 6% (7/112) stated that they do not want to be vaccinated against COVID-19. The mean age of 7 patients who did not want to be vaccinated against COVID-19 was 72±7.6 years, and 4 (%57) were female and 3 (%43) were male. From patients who are not vaccinated against COVID-19; 57% (4/7) feared the side effects of the COVID-19 vaccine, and 29% (2/7) reported that they did not have the COVID-19 vaccine because they thought the COVID-19 vaccines were ineffective. Patients who thought they were very well protected against transmission of COVID-19 were 14% (1/7) of patients who were not vaccinated for COVID-19. There was no hemodialysis patient who did not want to have the COVID-19 vaccine. Of 105 patients who gave a positive opinion about getting the COVID-19 vaccine; 15% (16/105) were not yet vaccinated, 85% (89/105) were vaccinated against COVID-19.

Of the total 89 patients who received the COVID-19 vaccine, 27 (30%) were hemodialysis patients and 62 (%70) were chronic renal failure patients who were not on hemodialysis. Forty-six (52%) were male and 43 (48%) were female of the COVID-19 vaccinated patients. The mean age was 72.4±6.8 years. The most common comorbidities were HT (in 83 patients, 93%) and DM (in 49 patients, 54%).

Side effects were identified in 22% of patients (in 20 patients) after at least one of the vaccines. The most common adverse event was uncontrolled blood pressure (in 9 patients, 45%). All patients with uncontrollable blood pressure after the COVID-19 vaccine were previously diagnosed with hypertension. 45% (9 patients) of patients who reported adverse events after at least one of the COVID-19 vaccines, and 16% (11 patients) who did not report any COVID-19 vaccine-related adverse events had cardiovascular disease (p=0.012). Of the patients who reported side effects after at least one of the COVID-19 vaccines, 5% (in 1 patient) were hemodialysis patients, and 38% (in 26 patients) of 69 patients who did not report any side effects were hemodialysis patients (p=0.005). In addition, while there were 5 female patients with arm pain, there were no male patients with arm pain (p=0.023), among the side effects associated with the COVID-19 vaccine. There was no significant relationship between other questioned side effects related to COVID-19 vaccine and gender, age, and comorbidities.

Demographic characteristics of patients with COVID-19 vaccine and the main clinical features of the presence of adverse effects are detailed in Table 1.

After the 1st dose of COVID-19 vaccine, 17% of the patients (in 15 patients) described side effects. The most common side effects were pain at the injection site (in 5 patients, 33%) and uncontrolled HT (in 5 patients, 33%). CVD was present in

Table 1. Characteristics of patients classified according to the presence of adverse events after the COVID-19 vaccines

Parameters	Adverse effect (-) n=69	Adverse effect (+) n=20	Total n=89	p-value
Demographic features, n (%)				
Age, (mean + SD)	72.7±7.0	71.3±5.8	72.4±6.8	0.400
Sex	-	-	-	0.127
Male	30 (43)	13 (65)	46 (52)	-
Female	39 (57)	7 (35)	43 (48)	-
DM	39 (57)	10 (10)	49 (71)	0.620
Hypertension	65 (94)	18 (90)	83 (93)	0.613
CVD	11 (16)	9 (45)	20 (22)	0.012
CHF	8 (12)	4 (25)	12 (13)	0.456
COLD	4 (6)	1 (0.5)	5 (6)	1
Hemodialysis	26 (38)	1 (0.5)	27 (30)	0.005

COVID-19: Coronavirus disease-2019, SD: Standard deviation, DM: Diabetes mellitus, CVD: Coronary vascular diseases, CHF: Congestive heart failure, COLD: Chronic obstructive lung disease

60% (9/15) of patients who described adverse events after the first dose of the COVID-19 vaccine. CVD was present in 8% of patients who did not describe adverse events associated with the first dose of COVID-19 vaccine (p=0.001). Hemodialysis patients were 7% (1/15) of the patients describing adverse events related to the first dose of the COVID-19 vaccine. Of the patients who did not describe any side effects associated with the first dose of the COVID-19 vaccine, 35% (26/74) were hemodialysis patients (p=0.032). In addition, among the side effects associated with the COVID-19 vaccine, the complaint of arm pain was questioned in 33% (5/15) of the patients, and all of the patients were female. 45% (38/84) of the patients who did not describe arm pain were female (p=0.023). There was no significant relationship between other questioned side effects related to COVID-19 vaccine and gender, age, and comorbidities.

Demographic characteristics of patients who received the first dose of COVID-19 vaccine and the main clinical features of the presence of adverse effects are detailed in Table 2.

After the 2nd dose of COVID-19 vaccine, 15% (in 13 patients) of the patients described side effects. Of the patients who described side effects after the second dose of the COVID-19 vaccine, 92% (12/13) were female and 8% (1/13) were male (p=0.001). The most common side effects were uncontrolled blood pressure (in 5 patients, 38%) and all patients with uncontrolled blood pressure were female. Of the patients who did not describe uncontrolled blood pressure, 45% (38/84) were female (p=0.023). There was no significant relationship between other questioned side effects related to COVID-19 vaccine and gender, age, and comorbidities.

While patients stated that they did not use drugs for side effects, they stated that these complaints of patients whose blood pressure was not under control lasted an average of 2 weeks.

Table 2. Characteristics of patients classified according to the presence of adverse events after the first dose of COVID-19 vaccine

Parameters	n=74	n=15	n=89	p-value
Demographic features, n (%)				
Age, (mean + SD)	72.9±7.0	70.7±5.0	72.4±6.8	0.141
Sex	-	-	-	0.239
Female	34 (46)	9 (60)	43 (48)	-
Male	40 (66)	6 (40)	46 (42)	-
DM	40 (54)	9 (60)	49 (71)	0.826
Hypertension	70 (95)	13 (87)	83 (93)	0.265
CVD	11 (15)	9 (60)	20 (22)	0.001
CHF	8 (11)	4 (27)	12 (13)	0.114
COLD	4 (5)	1 (1)	5 (6)	1
Hemodialysis	26 (35)	1 (1)	27 (30)	0.032

COVID-19: Coronavirus disease-2019, SD: Standard deviation, DM: Diabetes mellitus, CVD: Coronary vascular diseases, CHF: Congestive heart failure, COLD: Chronic obstructive lung disease

The demographic characteristics of patients who received the second dose of COVID-19 vaccine and the main clinical features of the presence of side effects are detailed in Table 3, and the distribution of side effects after COVID-19 vaccines are detailed in Table 4.

Discussion

Since COVID-19 vaccines are newly introduced vaccines; 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 presented data on COVID-19 vaccine acceptance and post-vaccine side effects in patients over 65 years of age with chronic kidney disease who were vaccinated in the first months of vaccination in our country. To date, several studies on the acceptance of COVID-19 vaccines have been reported in

Table 3. Characteristics of patients classified by presence of adverse events after the second dose of COVID-19 vaccine

Parameters	Adverse effect (-) n=76	Adverse effect (+) n=13	Total n=89	p-value
Demographic features, n (%)				
Age, (mean + SD)	72.5±6.9	71.7±6.2	72.4 ±6.8	0.609
Sex	-	-	-	0.001
Female	31 (41)	12 (92)	43 (48)	-
Male	45 (59)	1 (8)	46 (42)	-
DM	42 (55)	7 (54)	49 (71)	1
Hypertension	71 (93)	12 (92)	83 (93)	1
CVD	16 (21)	4 (30)	20 (22)	0.325
CHF	10 (13)	2 (15)	12 (13)	0.556
COLD	72 (95)	1 (1)	5 (6)	0.550
Hemodialysis	26 (34)	1 (1)	27 (30)	0.099

COVID-19: Coronavirus disease-2019, SD: Standard deviation, DM: Diabetes mellitus, CVD: Coronary vascular diseases, CHF: Congestive heart failure, COLD: Chronic obstructive lung disease

Table 4. Distribution of adverse effects after COVID-19 vaccines

Parameters	1. Post vaccination n=15	2. Post vaccination n=13	Total n=20
Adverse effects, n (%)			
Fever	2 (13)	0	2 (10)
Myalgia	1 (6)	3 (23)	3 (15)
Dizziness	1 (6)	1 (8)	1 (5)
Ageusia	1 (6)	0	1 (5)
Uncontrolled BP	5 (33)	5 (38)	8 (40)
Arm pain	5 (33)	4 (31)	5 (25)

COVID-19: Coronavirus disease-2019, BP: Blood pressure

the literature. In general population studies, COVID-19 vaccine acceptance rates are seen to be between 46-76% (3,4). Vaccine acceptance rates of patients over 65 years of age vary between 40% and 20% (3,9,10).

In a study conducted in the hemodialysis patient population, the acceptance rate of COVID-19 vaccines was found to be 80%, and it was observed that there was a decrease in COVID-19 vaccine hesitancy with increasing age (11). 6% of our patients hesitated to have the COVID-19 vaccine. The relatively less hesitancy about vaccination in our patients may be due to the high number of deaths due to COVID-19 in our country during the study, the older patient population, and the presence of comorbidities.

Immunization is one of the most successful and cost-effective health interventions to prevent infectious diseases. Side effects of vaccines are among the most important reasons for hesitation against vaccines. In some studies, it has been found that the presence of side effects on COVID-19 vaccine hesitations is associated with COVID-19 vaccine opposition (8,10). In our study, more than half of the patients who did not want to be vaccinated against COVID-19 reported that they were afraid of the side effects of the COVID-19 vaccine in accordance with the literature.

In our study, we analyzed the early side effects of the CoronaVac vaccine and the factors that may be associated with side effects. The side effects associated with CoronaVac was present in 32-62% of individuals in the general population in studies (8,12). In our study, side effects were seen in 22% of patients after at least one dose of CoronaVac vaccine (17% of patients after 1 dose and 15% after 2nd dose). In general population-based studies, it has been shown that the frequency of side effects decreases with increasing age. The lower incidence of side effects in our study may be due to the fact that our study population included patients over the age of 65 (8). In addition, it may cause less reactions to vaccines in immunosuppression due to uremia in patients with chronic kidney disease, especially in the patient group receiving hemodialysis treatment (5,13).

Consistent with the literature, one of the most common side effects after CoronaVac vaccine was pain at the injection site and side effects were more pronounced in females (8,12,14). Unlike other studies on the side effects of COVID-19 vaccines, the frequent uncontrolled blood pressure in our patients may be due to the inadequacy of information about the vaccine and stress disorders caused by the side effects of the vaccine. In many studies in the literature, it is known that psychological and physical stress contribute to both acute and long-term blood pressure variability. *In vitro* studies have shown that acute blood pressure reactivity to emotional stress differs between individuals (15-17). The fact that blood pressure uncontrolled is more common especially in female patients may be associated with factors such as activation of the sympathetic nervous system, activation of the renin-angiotensin-aldosterone system,

and endothelial dysfunction, which cause an increased incidence of hypertension in postmenopausal women (18).

In addition, the existence of a significant relationship between the presence of cardiovascular disease and the frequency of side effects in our study may be a result of vascular endothelial cell aging and vascular dysfunction, which are involved in the pathogenesis of cardiovascular diseases. Dysregulation of the cell cycle, oxidative stress, altered calcium signaling, hyperuricemia, and vascular inflammation, which contribute to aging, play a role in the development and progression of vascular endothelial cell vascular disease. Vascular endothelial cell aging induces vascular structural and functional changes, increases thrombosis, inflammation and atherosclerosis with deterioration in vascular tone, angiogenesis and vascular integrity (19). Various studies have shown that cardiovascular side effects of COVID-19 vaccines are due to the presence of endothelial dysfunction, especially in the elderly population (20,21). The presence of cardiovascular diseases secondary to endothelial dysfunction, which became evident due to the fact that our study population consisted of elderly patients, may increase the frequency of side effects related to the COVID-19 vaccine by the same mechanisms.

Study Limitations

Our study has some limitations. The small number of patients studied should be noted as a limitation. In addition, the fact that the social characteristics of the study population, such as educational status, were not recorded, should also be noted as a limitation. However, since the number of studies on the side effects of the CoronaVac vaccine in individuals over 65 years of age with chronic kidney disease is low, clinicians interested in managing this patient group should be informed.

Conclusion

The vaccination rate against COVID-19 in individuals with chronic kidney disease over 65 years of age was higher than in general population studies, and the most common reason for COVID-19 vaccine opposition was fear of the side effects of vaccines. In addition, the side effects of those who had CoronaVac were similar to those in the general population, and the frequency of side effects was found to be lower. Unlike other general population studies, it was observed that blood pressure uncontrollability was observed and the presence of cardiovascular disease increased the frequency of side effects.

Ethics

Ethics Committee Approval: This study was approved by the Local Institutional Review Board (Kartal Dr. Lütfi Kırdar City Hospital, no: 2021/514/200/36, date: 28.04.2021).

Informed Consent: Waived the requirement for informed consent.

Peer-review: Externally peer-reviewed.

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