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Evaluation of COVID 19 Patients Who Developed after COVID 19 Vaccination

COVID 19 Aşısı Sonrası Gelişen COVID 19 Hastalarının Değerlendirilmesi

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Abstract

Aim | This study aims to evaluate the sociodemographic and clinical characteristics of patients with COVID-19 that developed after COVID-19 vaccination.

Material and Method | The study was conducted retrospectively in a public hospital between July 5 and August 5, 2021. Patients whose SARS-CoV-2 positivity was confirmed by molecular methods and who were hospitalized due to COVID-19 and who had a history of COVID-19 vaccination were included. Sociodemographic information and clinical observation results of the patients were recorded.

Results | 49.09% of the patients were female and the median age was 72.00 [62.00-79.00] years. 70.45% of patients had a chronic disease and 37.27% were constantly using medication. 82.73% of patients received the CoronaVac vaccine and 8.18% received COVID-19 mRNA vaccine; 9.09% had received both vaccines. 66.82% of patients received two doses of COVID-19 vaccine, 26.82% received three doses, 5.45% received one dose and 0.91% received four doses of COVID-19 vaccine. When the infection findings at the time of admission to the hospital are evaluated, the most common symptoms in patients are dyspnea (89.55%), cough (45.45%), weakness (37.73%), malaise (22.27%) and fatigue-exhaustion. (20.00%); 95% of them had COVID-19 findings in their lung imaging reports. 99.55% of patients receive oxygen therapy; 62.73% were connected to mechanical ventilation. 91.82% of patients were receiving steroid treatment, 89.09% were receiving favipiravir treatment, and 98.64% were receiving anticoagulant; 96.82% had received antibiotic treatment. 38.64% of patients were discharged; 61.36% died.

Conclusion | The average age of patients who contracted COVID-19 disease after the COVID-19 vaccine was high and the majority had chronic diseases. In addition, patients received the with a high rate of CoronaVac vaccine and received a maximum of two doses; It was observed that they did not receive the reminder dose of vaccination. Mortality and morbidity can be reduced by creating successful vaccination programs as well as protective measures in the fight against COVID-19.

Keywords | COVID-19 disease, COVID-19 vaccine, patient characteristics, vaccine

Özet

Amaç | Bu çalışmanın amacı, COVID-19 aşısı sonrası gelişen COVID-19 hastalarının sosyodemografik ve klinik özelliklerini değerlendirmektir.

Gereç ve Yöntem | Çalışma, 5 Temmuz-5 Ağustos 2021 tarihleri arasında bir devlet hastanesinde retrospektif olarak gerçekleştirildi. SARS-CoV-2 pozitifliği moleküler yöntemlerle doğrulanan ve COVID-19 nedeniyle hastaneye yatırılan, COVID-19 aşısı yapılma öyküsü olan hastalar dahil edildi. Hastaların sosyodemografik bilgileri ve klinik gözlem sonuçları kaydedildi.

Bulgular | Hastaların %49,09'u kadındı ve ortanca yaş 72,00 [62,00-79,00] yıldı. Hastaların %70,45'inin kronik hastalığı vardı ve %37,27'si sürekli ilaç kullanıyordu. Hastaların %82,73'üne CoronaVac aşısı, %8,18'ine ise COVID-19 mRNA aşısı yapılmıştı; %9,09'u her iki aşıyı da almıştı. Hastaların yüzde 66,82'sine iki doz, yüzde 26,82'sine üç doz, yüzde 5,45'ine tek doz ve yüzde 0,91'ine dört doz aşı yapılmıştı. Hastaneye başvuru anındaki enfeksiyon bulguları değerlendirildiğinde hastalarda en sık görülen semptomlar nefes darlığı (%89,55), öksürük (%45,45), halsizlik (%37,73), kırgınlık (%22,27) ve yorgunluk-bitkinlikti. (%20,00). Hastaların %95'inin akciğer görüntüleme raporlarında COVID-19 bulguları vardı. Hastaların %99,55'i oksijen tedavisi alırken; %62,73'ü mekanik ventilasyona bağlanmıştı. Hastaların %91,82'si steroid tedavisi, %89,09'u favipiravir tedavisi, %98,64'ü antikoagülan alırken; %96,82'si antibiyotik tedavisi almıştı. Hastaların %38,64'ü taburcu olurken; %61,36'sı ex oldu.

Sonuç | COVID-19 aşısı sonrası COVID-19 hastalığına yakalanan hastaların yaş ortalamasının yüksek olduğu ve çoğunluğunun kronik hastalığı vardı. Ayrıca hastaların CoronaVac aşısı olduğu ve en fazla iki doz aşı olup; hatırlatma dozu aşı olmadıkları görüldü. COVID-19 ile mücadelede korunma önlemlerinin yanında başarılı aşı programlarının oluşturulmasıyla mortalite ve morbidite azaltılabilir.

Anahtar Kelimeler | COVID-19 hastalığı, COVID-19 aşısı, hasta özellikleri, aşı,

INTRODUCTION

Vaccines are important tools to improve health around the world, but the burden of death and disease caused by infectious diseases remains unacceptable. Even if there are vaccines that can prevent infectious diseases, limitations such as high costs, logistics difficulties, limited cold chain capacity, and chronic conditions that will cause the immune response of patients to decrease may reduce the effectiveness of the vaccine's effectiveness.[1] COVID-19 is an infectious disease that causes a pandemic, and the total cumulative global number of cases as of May 2024 is 776 million.[2] Many complications such as lung involvement, acute respiratory distress syndrome (ARDS), cytokine release syndrome, septic shock, gastrointestinal disorders, kidney diseases, hematological, neurogenic, and psychogenic disorders have been reported in association with this infectious disease, and multiple organ failure has been reported most frequently in patients with predisposing diseases.[3] Antiviral, anti-inflammatory, immunomodulatory agents and anticoagulants have been used to treat COVID-19, which manifests itself in different clinical severities.[4-7] Despite all the efforts made in the management of COVID-19 infection, the lack of a specific pharmacotherapy causes difficulties.[8] COVID-19 vaccines are important to reduce and prevent the severity and contagiousness of SARS-COV-2 infection.[9]

As of January 2021, vaccines such as BNT162b2, Moderna mRNA-1273, vector-based vaccines ChAdOx1 nCoV-19 Oxfort-AstraZeneca, Gam-COVID-Vac Sputnik-V, Covilo/BBIBP-CorV/Sinopharm by Pfizer-BioNTech are for emergency use in many countries. It started to be implemented within the scope of permission.[10,11] Turkovac (ERUCoV) is an inactivated SARS-CoV-2 vaccine developed and started to be implemented in Turkey in February 2022.[12] The role of these introductory COVID-19 vaccines in preventing SARS-CoV-2 infection and/or reducing hospitalization and mortality rates has been confirmed.[13,14] After the introduction of vaccines, the emergence of new variants has raised concerns about the decrease in vaccine effectiveness as a result of increased contagiousness. Post-vaccination infections may induce nonsterile immune response by promoting vaccine escape mutations and pose a serious risk.[11] It has been stated that post-vaccination infection is less severe than in unvaccinated individuals, but mortality remains high in case of hospitalization.[15] In the United Kingdom, the mortality rate for individuals hospitalized with COVID-19 within 21 days of vaccination has been reported to be 27%, which is similar to mortality rates observed during vaccination.[16]

Assessment of individuals who contract COVID-19 after vaccination is important for clinical utility in facilitating identification of risk groups for intervention, estimating medical resource requirements, and informing appropriate testing guidelines. There are limited studies in the literature evaluating COVID-19 cases after vaccination. This study aims to evaluate patients with COVID-19 that developed after COVID-19 vaccination.

MATERIALS and METHODS
Place and time of the study

The study was conducted at Sakarya Yenikent State Hospital (SYDH) between July 5 and August 5, 2021. SYDH is a secondary care hospital with a total of 255 beds, including 50 intensive care unit (ICU) beds.

Collection of patient information

The population of the study consisted of patients hospitalized in the SYDH COVID-19 clinic and intensive care unit (ICU). To work; Patients who were i) vaccinated against COVID-19, ii) - whose SARS-CoV-2 positivity was confirmed by molecular methods, and iii) - who received inpatient treatment in a clinic or ICU due to COVID-19 in the hospital and whose file records were complete were included. Sociodemographic information of the patients, COVID-19 vaccine information, COVID-19 infection findings at the time of admission to the hospital, laboratory examination and radiological imaging data, and clinical observation results were taken from the hospital informa-

tion management system and recorded in the standard form created by the researcher.

Evaluation of data

Data analysis was performed by using SPSS 22 for Windows (Statistical Package for Social Science, SPSS® Corp., Armonk, NY, USA). The variables were analyzed in terms of normality distribution using the Kolmogorov-Simirnov test. Depending on the normality of the distribution, continuous variables were reported as mean and standard deviation or median and interquartile range. Categorical variables were expressed using frequency tables.

Ethics committee approval for this study was received from Sakarya University Faculty of Medicine Ethics Committee with number E-71522473-050.01.04-39900-357.

RESULTS

Of the 220 patients included in the study, 49.09% were women and the median age was 72.00 [62.00-79.00] years. 92.73 of the patients were primary school graduates and 79.09% lived in the district. 70.45% of the patients had a chronic disease, and the three most common chronic diseases were hypertension (76.13%), diabetes mellitus (50.32%) and heart failure (18.71%). 37.27% of the patients were constantly using medication (Table 1).

Table 1. Sociodemographic information of the patients and clinical information about COVID-19 infection		
Features		n/mean (min-max)/median [Inter-quartile range]
The average age		7200 [62.00-79.00]
< 65		65 (29.54)
> 65		145 (70.46)
Age	18-34	2 (0.91)
	35-49	11 (5.00)
	50-64	52 (23.64)
	65-80	105 (47.73)
	> 80	50 (22.73)
Sex	Female	108 (49.09)
	Male	112 (50.91)

Educational background	Primary education	204 (92.73)
	High school	11 (5.00)
	University	5 (2.27)
Place of residence	Town center	43 (19.55)
	District	174 (79.09)
	Bay	3 (1.36)
Chronic Disease	Yes	155 (70.45)
	No	65 (29.55)
Distribution of chronic diseases	Hypertension	118 (76.13)
	Diabetes	78 (50.32)
	Heart failure	29 (18.71)
	Coronary artery disease	18 (1.61)
	COPD	10 (6.45)
	Malignancy	10 (6.45)
	Asthma	7 (4.52)
	Hypothyroidism	4 (2.58)
Continuous drug use	Yes	82 (37.27)
	No	138 (62.73)
Received COVID-19 vaccinations	Coronavac (Inactive vaccine)	182 (82.73)
	BNT162b2 (mRNA vaccine)	18 (8.18)
	Coronavac+ BNT162b2	20 (9.09)
COVID-19 vaccine doses	1 dose	12 (5.45)
		147 (66.82)
	3 doses	59 (26.82)
	4 doses	2 (0.91)
Vaccine doses in	1 doses	9 (4.09)
	COVID-19 cases	148 (67.27)
	3 doses	63 (28.63)
	4 doses	1 (0.45)

	Dyspnea	197 (89.55)
	Cough	100 (45.45)
	Weakness	83 (37.73)
	Disappoint-ment	49 (22.27)
	Fatigue-Ex-haustion	44 (20.00)
	Fire	28 (12.73)
	Unrest	11 (5.00)
	Confusion	11 (5.00)
	Muscle-Joint pain	8 (3.64)
	Pain in throat	5 (2.27)
	Chills-Trem-bling	5 (2.27)
	Sleep Disor-ders	4 (1.82)
	Stinging in chest	4 (1.82)
	Runny nose	4 (1.82)
COVID-19 Clinic	Insomnia	3 (1.36)
	Chest pain	2 (0.91)
	Fainting-Sei-zure	2 (0.91)
	Numbness	2 (0.91)
	Back-Waist pain	2 (0.91)
	Diarrhea	2 (0.91)
	Headache	1 (0.45)
	Blood pressure imbalance	1 (0.45)
	Sweating	1 (0.45)
	Nausea	1 (0.45)
	Visual impair-ment	1 (0.45)
	Loss of taste and smell	0
	Dry Mouth	0
	Stomach ache	0
	Heart palpita-tions	0
COVID-19 finding on CT	Yes	209 (95.00)
		11 (5.00)
SPO2 value		91.00 [86.00-95.00]

Oxygen therapy	Yes	219 (99.55)
	No	1 (0.45)
Intubation	Yes	138 (62.73)
	No	82 (37.27)
Taking ster-oids	Yes	202 (91.82)
	No	18 (8.18)
Faviripavir	Yes	196 (89.09)
	No	24 (10.91)
Antibiotic	Yes	213 (96.82)
	No	7 (3.18)
Anticoagulant	Yes	217 (98.64)
		3 (1.36)
Patient's outcome	Discharge	85 (38.64)
	Ex	135 (61.36)

82.73% of the patients received the CoronaVac (Sinovac Life Sciences, Beijing, China) vaccine, which is an inactive SARS-CoV-2 vaccine, and 8.18% received the COVID-19 mRNA vaccine (BNT162b2) developed in partnership with Pfizer-BioNTech; 9.09% had received both vaccines (Figure 1).
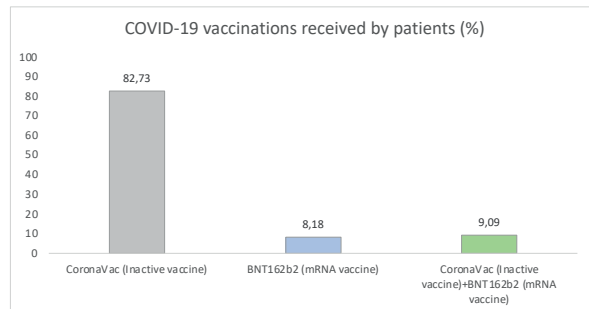

Figure 1. COVID-19 vaccinations received by patients

When the COVID-19 vaccine doses of the patients were evaluated, 66.82% received two doses, 26.82% received three doses, 5.45% received one dose and 0.91% received four doses of COVID-19 vaccine; 67.27% contracted COVID-19 infection after two doses of vaccine, 28.63% after three doses of vaccine, 4.9% after one dose of vaccine and 0.45% after four doses of COVID-19 vaccine. When the infection findings at the time of admission to

the hospital are evaluated, the most common symptoms in the patients are dyspnea (89.55%), cough (45.45%), weakness (37.73%), malaise (22.27%) and fatigue-exhaustion. (20.00%) (Table 1). 95% of the patients had COVID-19 findings in their lung imaging reports. 99.55% of patients receive oxygen therapy; 62.73% were connected to mechanical ventilation. 91.82% of the patients were receiving steroid treatment, 89.09% were receiving favipiravir treatment, and 98.64% were receiving anticoagulant; 96.82% had received antibiotic treatment. 38.64% of the patients were discharged; 61.36% died (Table 1). Information on the laboratory blood test parameters of the patients is shown in Table 2.

Table 2. Distribution of laboratory parameters of the COVID-19 patients

WBC K/uL	9.13 [6.14-12.06]	Glucose mg/dL	167.00 [120.25-224.00]
RBC M/uL	4.25 [3.81-4.60]	Urea mg/dL	55.50 [36.00-84.75]
HGB g/dL	12.05 [10.92-13.47]	Uric acid mg/dL	6.10 [4.70-8.00]
HCT %	37.00 [33.17-40.70]	Creatinine mg/dl	1.00 [0.74-1.52]
PLT K/uL	200.90 [155.00-257.00]	AST U/L	32.50 [24.00-49.75]
MCH pg	29.10 [27.70-30.40]	ALT U/L	22.00 [15.00-35.00]
MCHC g/dL	32.70 [32.00-33.20]	CK	88.50 [51.00-205.50]
RDW %	14.30 [13.70-15.80]	CK-MB	19.00 [13.00-25.00]
MCV fl	89.10 [85.20-92.10]	LDH U/L	342.00 [271.50-451.50]
MPV fl	10.70 [9.50-11.60]	D-Dimer ugFEU/L	1.41 [0.44-602.00]
PCT %	0.21 [0.16-0.27]	Ferritin	427.77 [194.11-836.67]
PDW	16.40 [16.10-16.70]	CRP mg/L	115.85 [67.25-183.54]
NEU%	86.10 [78.32-90.50]	Sedim 30 min	44.00 [23.00-67.50]
NEU K/uL	7.34 [4.94-10.52]	Sedim 1 hour	62.76±30.75 (9.00-149.00)
LYM %	9.35 [5.82-15.27]	Procalcitonin	0.32 [0.14-0.66]
LYM	0.79 [0.50-1.32]	INR	1.22 [1.14-1.35]
MONO %	3.75 [2.22-5.30]	Prothrombin Time (Coagulometer) sec	12.60 [11.80-13.80]
MONO	0.34 [0.18-0.52]	Fibrinogen g/L	4.76 [4.14-6.34]
EOS %	0.10 [0.00-0.30]	Albumin g/L	31.41±4.32 (14.90-43.50)
EOS K/uL	0.01 [0.00-0.02]	Lactate	1.80 [1.30-2.67]
BASO %	0.10 [0.00-0.20]	Blood gas oxygen	51.00 [36.55-69.20]
BASO K/uL	0.00 [0.00-0.01]	Interleukin 6	49.68 [18.80-143.27]

DISCUSSION

One of the situations encountered at every stage of life is infectious diseases. Vaccines are the most important element in reducing or eradicating the effects of infectious diseases that began with the existence of humans and are tried to be cured by various methods. The COVID-19 pandemic, which emerged towards the end of 2019 and affected the whole world in a short time, is an infectious disease with high contagion and mortality, so society needs to be immunized by vaccination. Vaccination studies have started with COVID-19 vaccines that were approved after COVID-19 vaccine studies. Even though some people are fully vaccinated, they can still be infected with the COVID-19 virus and transmit the virus to people around them. The aim of our study is to evaluate patients with COVID-19 that developed after COVID-19 vaccination.

The median age of patients who developed post-vaccination infection was found to be 72 years, and the majority of patients were 65 years and above. Elderly individuals are a group prone to be infected with the SARS-CoV-2 virus. Due to aging-related comorbidities and reduced immunological competence, older individuals are at very high risk of adverse outcomes due to infectious diseases.[17] Decreased immune system functions in elderly individuals increase susceptibility to SARS-CoV-2 infection and also limit the effectiveness of COVID-19 vaccines. This may cause differences in vaccine effectiveness between young individuals (<55 years of age) and the elderly. Vaccines that

are effective in young individuals may not produce immunity in older individuals.[18] In a study conducted at Yale New Haven Hospital in the USA to measure the course of the disease as a result of COVID-19 cases despite vaccination, it was found that the majority of individuals who developed COVID-19 infection despite vaccination survived the infection asymptomatic or mild, but older individuals had a more severe infection and some even died.[19] However, the study reported that the mean age among those with severe or critical illness was 80.5 (IQR 76.5–85.0) years. The result of our study supports the literature.

In addition to elderly individuals, young people and people with various chronic diseases have a high risk of being infected with the virus again after receiving the COVID-19 vaccine.[20] Individuals with chronic diseases may experience a more severe disease and even death may occur.[21] People with pre-existing medical conditions such as kidney diseases, obesity, cardiovascular diseases, cancer, type 2 diabetes, and chronic obstructive pulmonary disease (COPD) may face more serious health problems with COVID-19 infection.[22] When the literature was examined, Hung et al. first stated that 13 of 41 confirmed patients (32%) had underlying diseases, and these diseases were diabetes (20%), hypertension (15%), and cardiovascular diseases (15%).[23] In the study conducted by Wang et al., 64 of 138 patients (46.4%) had one or more concomitant chronic diseases, and these diseases were respectively hypertension (31.2%), diabetes (10.1%) and cardiovascular disease (14.5%) and malignancy (7.2%).[24] In the study where the characteristics and clinical course of 1000 COVID-19 patients in the USA were examined, the common comorbidities were as follows; hypertension (60.1%), obesity (48.3%), diabetes mellitus (37.2%), lung disease (22.3%), kidney disease (13.7%), coronary artery disease (13%), asthma (11.3%), and congestive heart failure (10.2%).[25] In a study conducted in Italy, 709 (68%) of 1043 patients had at least one comorbidity, and the most common comorbid diseases were; hypertension, cardiovascular disease, hypercholesterolemia, and diabetes mellitus have been reported.[26] In a meta-analysis

study, comorbid chronic diseases in COVID-19 patients included hypertension (21%), diabetes (9.7%), respiratory system disease (1.5%), and cardiovascular diseases (8.4%) has been reported.[27] In our study, it was found that 79.45% of the patients had at least one chronic disease, and these chronic diseases were hypertension, diabetes mellitus, heart failure, coronary artery disease, COPD, malignancy, asthma, and hypothyroidism, respectively. The results of our study were found to be similar to the literature.

For individuals who are considered immune-compromised or impaired, the CDC recommends receiving a third COVID-19 vaccine 28 days after receiving two doses of the COVID-19 vaccine. The CDC explains that reminder vaccines try to create an updated defense mechanism of the body against COVID-19 disease. In a long-term cohort study conducted in England, it was determined that the protection against infection decreased after six months in patients infected with COVID-19 and vaccinated in the research group. However, it has been reported that it is also important which COVID-19 vaccine the second and third doses of COVID-19 vaccines are given. Because if two doses of the same type of vaccine are administered and the third dose of a different type of COVID-19 vaccine is administered; it is estimated that vaccination will not have a positive effect and, as a result, vaccination will reduce the level of protection from the disease.[28,29] In another cohort study conducted in Sweden, a similar result was reached; It was determined that the effectiveness of the vaccine was gradually decreasing in all study groups and the necessity of the third dose of vaccination was highlighted. Also in the study; it has been reported that the effect of the vaccine decreases more quickly in older individuals than in younger individuals. It is stated that the most important reason for the decrease in the effectiveness of vaccines is the deterioration of antibody-producing cells and immune system functions in the elderly with advanced age.[30] In our study, it was found that the majority of patients received 2 doses of COVID-19 vaccine (CoronaVac (Inactive vaccine)) and infection developed after 2 doses of vaccine. Although the

results of our study support the literature, it is thought that this result is due to the high number of older age patients in the patient population and the lack of booster dose vaccinations.

Previous reports have described different mortality rates in COVID-19 patients, ranging from 16% to 38%, 62% to 67%, and 78%.[23,24,31-33] In our study, 38.64% of COVID-19 patients were discharged; it was determined that 61.36% of them died. Our study has shown that COVID-19 patients have higher mortality rates than cases in the epicenters of other countries so far. It is thought that these high rates may be due to the high average age of the patients, the high rate of comorbid diseases, and the lack of booster dose vaccinations.

The limitations of the present study include the fact that it was conducted on a small group of respondents. The data came from a single clinical research center, as opposed to multiple clinical research centers. The findings of this study may vary from those of other domestic and international researchers, and they should be tested in clinical settings.

CONCLUSION

In conclusion; In our study, the average age of post-vaccine COVID-19 patients, comorbidity, and mortality rates were high, the majority of the patients were vaccinated with CoronaVac, an inactive SARS-CoV-2 vaccine, they received two doses of vaccine at the highest rate and did not receive a reminder dose of vaccine, and COVID-19 after 2 doses of vaccine. It was determined that they had the infection. Our results demonstrated vaccine efficacy and ineffective immune response to vaccines in the oldest age group and those with comorbid chronic diseases. Mortality and morbidity can be reduced by creating successful vaccination programs as well as protective measures in the fight against COVID-19. Overall, although vaccines have undoubtedly provided widespread protection against COVID-19 infection worldwide, future studies are needed to identify and mitigate factors associated with suboptimal vaccine response in individuals with hyperreactive infections.

Ethics Committee Approval
Ethics committee approval for this study was received from Sakarya University Faculty of Medicine Ethics Committee with number E-71522473-050.01.04-39900-357.

Peer-review
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Author contributions
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Conflicts of interest
The authors declared no conflict of interest.

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