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Original Article

Vaccination Status and Outcome of Hospitalized Patients with Coronavirus Disease 2019 Before and After the Spread of Omicron Variant: An Observational Study from İzmir, Turkey

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Abstract

OBJECTIVE: Despite the efforts in vaccination against coronavirus disease 2019 (COVID-19), breakthrough infections occur and the need for hospitalization continues. We aimed to determine the relationship between severe acute respiratory syndrome coronavirus 2 vaccination and the severity of COVID-19 and mortality among hospitalized patients with COVID-19.

MATERIAL AND METHODS: This cross-sectional study was conducted between September 2021 and February 2022 in a university hospital in Turkey. Hospitalized patients with COVID-19 (both in clinics and in intensive care units), ≥18 years old, and who had no previous COVID-19 were included in the study. The demographic characteristics, clinical data, vaccination status, and outcome of the patients were analyzed retrospectively and the relationship between vaccination status and mortality was determined statistically.

RESULTS: Of the 674 patients, 180 (26.7%) had no vaccination, 282 (41.8%) had incomplete vaccination, and 212 (31.5%) were fully vaccinated according to the updated vaccination recommendations. While 44.0% of the patients were fully vaccinated before the occurrence of omicron variant, 15.9% of the patients were fully vaccinated during the wave of the omicron variant. The patients with no vaccination were younger and had fewer comorbidities. The overall mortality was 31.8%. Under 50 years old, all the patients with fully vaccination survived and the patients with no vaccination or incomplete vaccination had higher (10.1%) mortality. During the omicron period, mortality was lower in fully vaccinated pateints.

CONCLUSION: Immunization with and booster doses of BNT162b2 should be encouraged to protect both healthy and vulnerable populations.

KEYWORDS: COVID-19, omicron, vaccination, breakthrough infection, hospitalization
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INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been affecting the whole world since the beginning of 2020 and has been declared a pandemic by the World Health Organization (WHO).[1] The disease has a wide clinical course ranging from asymptomatic infection to pneumonia with severe respiratory failure and death, especially among the older and vulnerable population.[2,3]

Vaccine development studies have started rapidly to reduce the spread of the pandemic and to prevent morbidity and mortality. Various technologies have been used for vaccine development, but mainly inactivated, messenger RNA (mRNA) and viral vector (adenovirus) vaccines have been produced and used for mass vaccination. Currently, there are 183 vaccines in clinical and 199 vaccines in preclinical development.[4] Studies have shown that vaccines are highly effective in preventing symptomatic infection, reducing the need for hospitalization, and mortality.[5-7] Considering the increasing number of COVID-19 cases and deaths, emergency use authorization was granted for CoronaVac (Sinovac) by the Turkish Medicines and Medical Devices Agency on January 13, 2021.[8] As of January 14, 2021, health-care workers (HCWs) were vaccinated initially with 2 doses of CoronaVac 28 days apart. In April 2021, the mRNA vaccine BNT162b2 (Comirnaty, Pfizer–BioNTech) was introduced in Turkey, and the vaccination was expanded to cover the whole population over 12 years of age, starting from the groups at risk. In our country, homologous (only CoronaVac or only BNT162b2) or heterologous (2 doses of CoronaVac vaccination followed by BNT162b2) vaccination has been carried out for rappel doses.

Due to the fact that the current vaccines do not have 100% protection and newly emerged variants during the pandemic, breakthrough infections continue to be seen even in fully vaccinated people. Breakthrough infections can cause

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severe COVID-19 pneumonia, need for hospitalization and advanced respiratory support, and even mortality in vulnerable population.[9-11] Additionally, with the emergence and rapid spread of the omicron variant (B.1.1.529), current vaccination policies have changed, and the definition of fully vaccinated has been renewed.[12] In the course of the pandemic, because of the new emerging variants and changes in the immunity status of the population, the effectivity and safety of the current vaccination strategies should be monitored continuously.

In this study, we aimed to determine the relationship between SARS-CoV-2 vaccination status and the severity of COVID-19 and mortality among hospitalized patients with COVID-19.

MATERIAL AND METHODS

Study Design and Population

This retrospective, cross-sectional study was conducted between September 1, 2021, and February 28, 2022, in the Dokuz Eylül University Hospital located in İzmir, Turkey. Our hospital is a referral tertiary care hospital with 1100-bed capacity. At our center, a COVID-19 pandemic action plan was prepared to ensure that all patients could undergo the necessary intervention as soon as possible.[13] During the waves of the pandemic, as the number of COVID-19 patients who needed for hospitalization increased, the number of clinics for COVID-19 raised up to 7 separate clinics. Two separate intensive care units (ICUs) with 41 ICU beds were used for patients with severe/critical COVID-19.

Patients with COVID-19 [diagnosed with SARS-CoV-2 polymerase chain reaction (PCR) positivity] who needed hospitalization (both in clinics and in ICUs), were over the age of 18 years, and had no previous history of COVID-19 were included in the study. The patients who needed hospitalization for reasons other than COVID-19 but followed up in pandemic clinics or ICUs for isolation because of SARS-CoV-2 PCR positivity were also included in the study.

Data Collection

Hospitalization status of the patients (ICUs, clinics, and isolation); age; gender; comorbidities such as essential hypertension (HT), diabetes mellitus (DM), cardiovascular disease (CVD), chronic pulmonary disease, chronic kidney disease, autoimmune diseases, malignancies, solid-organ transplantation (SOT), and hematopoietic stem cell transplantation (HSCT); immunosuppressive drug use; corticosteroid use (>20 mg prednisone or equivalent >14 days); pregnancy; and the data of SARS-CoV-2 PCR positivity dates were retrospectively analyzed from hospital records. The vaccine tracking system of the Turkish Ministry of Health was used to determine the vaccination history of the patients. Vaccines administered within 14 days prior to PCR positivity were not included.

Participants and Definitions

We retrospectively evaluated 766 patients. A total of 92 patients were excluded from the study, as 34 patients were negative for SARS-CoV-2 PCR, 20 patients had a history of previous COVID-19, and 38 patients were under 18 years of age. The flowchart of the patient recruitment is given in Figure 1.

A total of 674 patients were included in the study. The patients were divided into 2 periods according to their PCR positivity time. Between September 1 and December 31, 2021 (4 months), the delta variant was predominant in Turkey, and this period was named the first period.[14] Between January 1 and February 28, 2022 (2 months), the omicron variant became predominant and caused the sixth wave in Turkey.[15] This period was named the second period.

The vaccination status of the patients was defined as ''no vaccination, incomplete vaccination, and fully vaccinated'' according to their vaccination status, for both periods separately according to their PCR positivity dates.[16]

The vaccination scheme for the first period

Fully vaccinated: ≥3 doses of CoronaVac, 2 doses of CoronaVac plus ≥1 dose(s) of BNT162b2, or ≥2 doses of BNT162b2.

Incomplete vaccination: All other vaccinations that do not match with fully vaccinated.

The vaccination scheme for the second period:

Fully vaccinated: 4 doses of CoronaVac, 3 doses of BNT162b2, or 2 doses of CoronaVac plus ≥2 doses of BNT162b2.

Incomplete vaccination: All other vaccinations that do not match with fully vaccinated.

Statistical Analysis

The statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 24.0 (IBM Corp., Armonk, NY, USA). The conformity of continuous variables to normal distribution was examined visually (using histograms and probability graphs) and statistically (using Kolmo gorov–Smirnov/Shapiro–Wilk tests). Descriptive statistics (the median and interquartile range or percentages, as appropriate) were used to summarize sociodemographic and clinical variables. A Mann–Whitney *U*-test was used to compare the continuous variables. The carriage was evaluated in terms of categorical variables using a chi-square test or a 2-sided Fisher's exact test when appropriate. A multivariate logistic

MAIN POINTS

- Despite efforts, less than one-third of hospitalized coronavirus disease 2019 (COVID-19) patients were fully vaccinated and the patients with no vaccination were younger and had less comorbidities.
- While mortality did not differ among older patients with and without vaccination, all of the younger patients with fully vaccination have survived.
- During the spread of Omicron, the patients who had boosters died less.
- The study emphasizes the necessity of targeted vaccination efforts for vulnerable populations, such as older individuals and those with underlying health conditions, to mitigate severe COVID-19 outcomes.

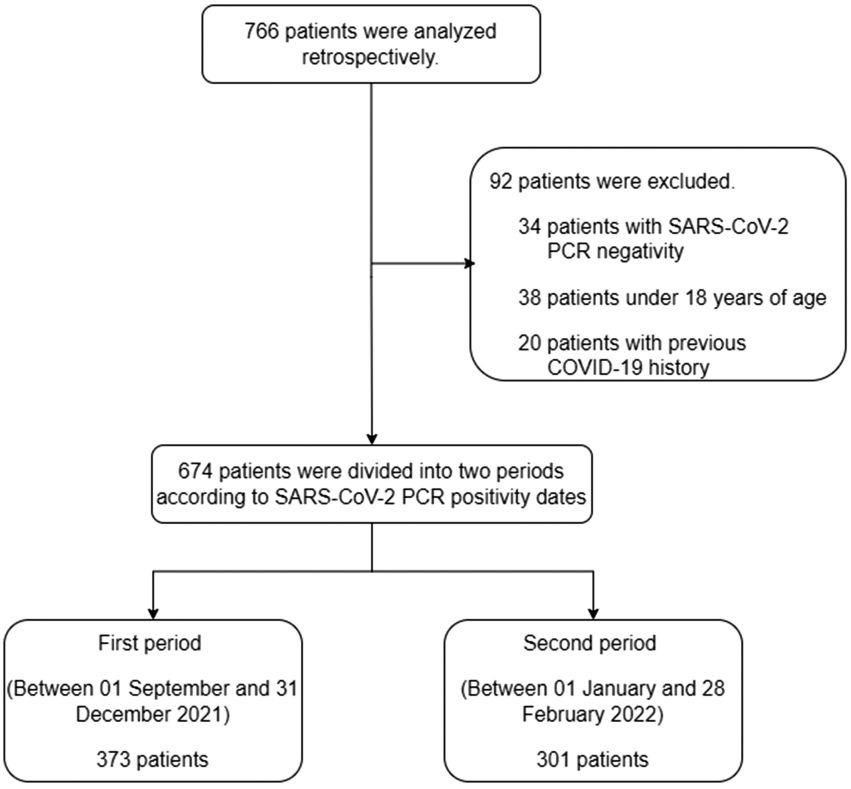

Figure 1. Flowchart of the patient recruitment.

model was applied to investigate demographic characteristics (age and sex) and clinical features (presence of comorbidities and other factors) associated with mortality. Statistical significance was set at $P < .05$.

Ethics Committee Approval

The study protocol was reviewed and approved by the Noninvasive Research Ethics Committee of Dokuz Eylül University as Decision No: 2022/10-08 on March 16, 2022. Permission was obtained from the Republic of Turkey Ministry of Health.

RESULTS

Demographic Data

The median age of the patients was 71 years (ranged between 18 and 98 years), 117 (17.4%) were younger than 50 years, 131 (19.4%) were between 50 and 64 years, and 426 (63.2%) were 65 years and over. Of the patients, 347 (51.5%) were men and 327 (48.5%) were women. Most of the patients (n = 546, 81.0%) had at least 1 comorbidity, and the median number of comorbidities was 2 (0-6). Of the patients, 166 (24.6%) had 1, 180 (26.7%) had 2, 145 (21.5%) had 3, and 55 (8.2%) had 4 or more comorbidities.

The most common comorbidities were HT (n = 343, 50.9%), CVD (n = 231, 34.3%), and DM (n = 211, 31.3%), followed by malignancy (n = 128, 19.0%), chronic pulmonary disease (n = 119, 17.7%), chronic kidney disease (n = 104, 15.4%), autoimmune disease (n = 32, 4.7%), SOT (n = 18, 2.7%), and HSCT (n = 8, 1.2%). Of the patients, 92 (13.6%) were using immunosuppressive drugs and 37 (5.5%) were using corticosteroids. The percentage of pregnancy was 3.1 among patients.

Hospitalization Status

In the first period 373 (55.3%) and the second period 301 (44.7%) patients with COVID-19 were hospitalized in pandemic clinics and ICUs. Of the patients, 398 (59.1%) patients with COVID-19, who met the criteria for hospitalization were admitted to the pandemic clinics, 134 (19.9%) patients who had severe/critical disease at presentation were admitted directly to ICU. One hundred forty-two (21.1%) patients, who were hospitalized for the indications other than COVID-19 in different clinics and had SARS-CoV-2 PCR positivity, were transferred to the pandemic clinics for isolation. In total, 284 (42.1%) patients had ICU attendance. The median hospitalization day was 8 (ranged between 1 and 116 days) and the median ICU hospitalization day was 8 (ranged between 1 and 68 days).

Vaccination Status

During the 6-month study period, 180 (26.7%) patients with COVID-19 had no vaccination, 282 (41.8%) had incomplete vaccination, and 212 (31.5%) were fully vaccinated according to the updated vaccination recommendations. In the first period, 125 (33.5%) patients had no vaccination, 84 (22.5%) had incomplete vaccination, and 164 (44.0%) were fully vaccinated. In the second period, 55 (18.3%) patients had no vaccination, 198 (65.8%) had incomplete vaccination, and 48 (15.9%) were fully vaccinated. The percentage of the patients vaccinated with only CoronaVac was 45.0% in the first and 46.8% in the second period. The percentage of the patients with BNT162b2 (homologous or heterologous) vaccination was higher in the second period (21.4% vs. 34.8%). The vaccination status of the patients according to the periods is given in Table 1.

The median age of the patients who were vaccinated was higher than the patients with no vaccination ($P < .001$).

Table 1. Vaccination Status of the Hospitalized Patients with COVID-19 According to the Periods

Vaccine Type	First Period, n (%)	Second Period, n (%)
No vaccination	125 (33.5)	55 (18.3)
1 dose of CoronaVac	3 (0.8)	0 (0)
2 doses of CoronaVac	77 (20.6)	50 (16.6)
3 doses of CoronaVac	88 (23.6)	73 (24.3)
4 doses of CoronaVac	0 (0)	18 (6.0)
2 doses of CoronaVac + 1 dose of BNT162b2	44 (11.8)	48 (15.9)
2 doses of CoronaVac + 2 doses of BNT162b2	5 (1.3)	17 (5.6)
1 dose of BNT162b2	4 (1.1)	2 (0.7)
2 doses of BNT162b2	25 (6.7)	21 (7.0)
3 doses of BNT162b2	2 (0.5)	11 (3.7)
2 doses of CoronaVac + 3 doses of BNT162b2	0 (0)	2 (0.7)
3 doses of CoronaVac + 1 dose of BNT162b2	0 (0)	4 (1.3)
Total	373 (100.0)	301 (100.0)

COVID-19, coronavirus disease 2019.

The percentage of the patients with no vaccination was higher under 50 years of age, same in the age group of 50-64 years. The number of patients with vaccination history was higher in 65 years and older. The percentage of men (P = .002) and those having comorbidities (P < .001) were higher in the vaccinated group (Table 2).

There was no difference in ICU attendance (P = .53), duration of hospitalization (P = .78), duration of ICU stay (P = .21), and mortality (P = .84) between unvaccinated, incomplete, and fully vaccinated patients (Table 2).

Outcome

In-hospital mortality was 31.8% (32.7% in the first and 30.6% in the second period, P = .552). The median age of the patients with mortality was higher (P < .001). In the deceased group, the percentage of being under 50 years of age was lower, being between 50 and 64 years of age was similar, and being 65 years and older were significantly higher than the survivors (Table 3).

The mortality was significantly higher in men (P = .034) and in the patients with comorbidities (P = .002) such as DM (P = 0.007) and malignancy (P = .05). None of the patients with pregnancy had died. The patients who died had a significantly higher need for ICU stay (P < .001) and had longer hospitalization (P < .001). There was no relationship between vaccination status and mortality (Table 3).

While overall mortality was 8.5% under 50 years of age, all the patients with full vaccination have survived and the patients with no vaccination or incomplete vaccination had higher (10.1%) mortality. Between 50 and 64 years, the overall mortality was 28.2%, 36.6% in fully vaccinated patients, and 24.4% in unvaccinated or incomplete vaccinated patients. Of the patients 65 years and older, 39.2% of patients have died.

Table 2. Demographic Characteristics and Outcomes of Patients Hospitalized with Coronavirus Disease 2019 by Vaccination Status

	No Vaccination, 180 (26.7%)	Incomplete Vaccination, 282 (41.8%)	Fully Vaccinated, 212 (31.5%)	*P*
Age, years (median)	58 (18-96)	73 (19-98)	73 (18-95)	**<.001***
Age group				
<50 years	74 (41.1)	25 (8.9)	18 (8.5)	**<.001****
50-64 years	38 (21.1)	52 (18.4)	41 (19.3)	
≥65 years	68 (37.8)	205 (72.7)	153 (72.2)	
Sex (male)	76 (42.2)	143 (50.7)	128 (60.4)	**.002****
Comorbidity	105 (58.3)	250 (88.7)	191 (90.1)	**<.001****
ICU attendance	73 (40.6)	115 (40.8)	96 (45.3)	.533**
Duration of hospitalization, days (median)	9 (1-39)	8 (1-116)	8 (1-86)	.780*
Duration of ICU stay, days (median)	8 (1-30)	8 (1-68)	7 (1-57)	.207*
Mortality	54 (30.0)	91 (32.3)	69 (32.5)	.839**

*Mann-Whitney U test.**Chi-square test.ICU, intensive care unit.

Table 3. Characteristics of Patients Hospitalized with Coronavirus Disease 2019 by Mortality

	First Period (n = 373, %)			Second Period (n = 301, %)			Total (n = 674, %)		
	Survived 251 (67.3%)	**Died 122 (32.7%)**	***P***	**Survived 209 (69.4%)**	**Died 92 (30.6%)**	***P***	**Survived 460 (68.2%)**	**Died 214 (31.8%)**	***P***
Age, years (median)	66 (18-94)	75 (38-97)	**<.001***	71 (18-98)	78 (34-94)	**<.001***	67 (18-98)	77 (34-97)	**<.001***
Age group									
<50 years	70 (27.9)	8 (6.6)	**<.001****	37 (17.7)	2 (2.2)	**<.001****	107 (23.3)	10 (4.7)	**<.001****
50-64 years	50 (19.9)	24 (19.7)		44 (21.1)	13 (14.1)		94 (20.4)	37 (17.3)	
≥65 years	131 (52.2)	90 (73.8)		128 (61.2)	77 (83.7)		259 (56.3)	167 (78.0)	
Sex (male)	114 (45.4)	70 (57.4)	**.030****	110 (52.6)	53 (57.6)	.425**	224 (48.7)	123 (57.5)	**.034****
Comorbidity	187 (74.5)	103 (84.4)	**.031****	171 (81.8)	85 (92.4)	**.018****	358 (77.8)	188 (87.9)	**.002****
Essential hypertension	120 (47.8)	61 (50.0)	.691**	111 (53.1)	51 (55.4)	.709**	231 (50.2)	112 (52.3)	.608**
Diabetes mellitus	67 (26.7)	40 (32.8)	.222**	62 (29.7)	42 (45.7)	**.007****	129 (28.0)	82 (38.3)	**.007****
Cardiovascular disease	65 (25.9)	42 (34.4)	.087**	88 (42.1)	36 (39.1)	.629**	153 (33.3)	78 (36.4)	.417**
Pulmonary disease	43 (17.1)	27 (22.1)	.246**	30 (14.4)	19 (20.7)	.173**	73 (15.9)	46 (21.5)	.075**
Renal disease	38 (15.1)	22 (18.0)	.476**	27 (12.9)	17 (18.5)	.208**	65 (14.1)	39** (18.2)	.171**
Autoimmune disease	11 (4.4)	3 (2.5)	.562**	11 (5.3)	7 (7.6)	.429**	22 (4.8)	10 (4.7)	.950**
Malignancy	42 (16.7)	29 (23.8)	.104**	36 (17.2)	21 (22.8)	.253**	78 (17.0)	50 (23.4)	**.048****
Solid-organ transplantation	8 (3.2)	2 (1.6)	.509***	6 (2.9)	2 (2.2)	1.000***	14 (3.0)	4 (1.9)	.379***
Hematopoietic stem cell transplantation	4 (1.6)	1 (0.8)	1.000***	2 (1.0)	1 (1.1)	1.000***	6 (1.3)	2 (0.9)	1.000***
Immunosuppressive drug use	36 (14.3)	17 (13.9)	.916**	28 (13.4)	11 (12.0)	.713**	64 (13.9)	28 (13.1)	.770**
Corticosteroid use	13 (5.2)	6 (4.9)	.914**	10 (4.8)	8 (8.7)	.187**	23 (5.0)	14 (6.5)	.413**
Pregnancy	16 (6.4)	0 (0.0)	**.004*****	5 (2.4)	0 (0.0)	.328***	21 (4.6)	0 (0.0)	**<.001*****
ICU attendance	60 (23.9)	116 (95.1)	**<.001****	27 (12.9)	81 (88.0)	**<.001****	87 (18.9)	197 (92.1)	**<.001****
Duration of hospitalization, days (median)	8 (1-86)	10 (1-63)	**.008***	6 (1-63)	13 (1-116)	**<.001***	7 (1-86)	11 (1-116)	**<.001***
Duration of ICU stay, days (median)	7 (2-48)	8 (1-68)	.764*	7 (1-59)	8 (1-68)	.384*	7 (1-59)	8 (1-68)	.416*
Vaccination status									
No vaccination	89 (35.5)	36 (29.5)	.521**	37 (17.7)	18 (19.6)	.646**	126 (27.4)	54 (25.2)	.839**
Incomplete vaccination	55 (21.9)	29 (23.8)		136 (65.1)	62 (67.4)		191 (41.5)	91 (42.5)	
Fully vaccinated	107 (42.6)	57 (46.7)		36 (17.2)	12 (13.0)		143 (31.1)	69 (32.2)	

*Mann-Whitney U test.**Chi-square test.***Fisher's Exact test.ICU, intensive care unit.

The mortality was lower in the fully vaccinated group compared to the other group (35.3% vs. 41.4%).

Mortality was not statistically different in patients with no, incomplete or full vaccination (30.0%, 32.3%, 32.5%, $P = .839$). In the first period, mortality was 28.8% in patients with no vaccination, 34.5% with incomplete vaccination, and 34.8% with full vaccination ($P = .521$). In the second period, mortality was lower in patients with full vaccination (25.0%) than in patients with no (32.7%) or incomplete vaccination (31.3%), but the rate was not statistically significant ($P = .646$).

In multivariate analysis of all patients, age [odds ratio (OR): 1.088; 95% CI: 1.053-1.123; $P < .001$], being 65 years and older (OR: 2.794; 95% CI: 1.137-6.867; $P = .02$), having comorbidities (OR: 2.343; 95% CI: 1.056-5.196; $P = .036$), malignancy (OR: 0.334; 95% CI: 0.174-0.641; $P = .001$), and need for ICU (OR: 0.015; 95% CI: 0.008-0.029; $P < .001$) were significantly associated with mortality. In multivariate analysis stratified by periods, vaccine effectiveness against death in fully vaccinated group was 82.8% (95% CI: 34.1%-95.5%; $P = .01$) in the second period, when adjusted for age, gender, comorbidity, and need for intensive care.

DISCUSSION

In this study, we took a picture of the vaccination status of the hospitalized patients with COVID-19 before and after the emergence of the omicron variant. Less than one-third of the patients were fully vaccinated according to the updated SARS-CoV-2 vaccine recommendations. After the rapid spread of the omicron variant, the percentage of fully vaccinated patients decreased from 44.0% to 15.9%. The overall mortality was 31%. Although the mortality rate did not differ among the groups with different vaccination status, the patients with no vaccination were younger and had less comorbidities. Under 50 years of age, while all of the patients with fully vaccination survived, 10.1% patients with an incomplete or no vaccination have died. In multivariate analysis, vaccine effectiveness against death in fully vaccinated group was 82.8% in the second period.

As expected, the median age of the patients was high and most of the patients had at least 1 comorbidity in this study, in accordance with other studies evaluating the hospitalized patients with breakthrough infections.[17-19] In their study, Suleyman et al[20] evaluated 982 fully vaccinated patients with COVID-19 breakthrough infections and 16% patients required hospitalization. Age, cardiovascular disease, and immunosuppressive drug status were independent risk factors for hospitalization.

In our study, 26.7% of the hospitalized patients were not vaccinated, 41.8% had incomplete vaccination, and 31.5% were fully vaccinated. The patients with no vaccination were younger and had fewer comorbidities than the vaccinated patients. In a multicenter study from Turkey, 1401 patients were evaluated, who were hospitalized during the first 10 days of August 2021. Almost half (47.8%) of the patients had no vaccination and the patients with no vaccination were younger and had less comorbidities.[19] In a study conducted in 21 centers from 18 states of the USA, among 1197 patients with COVID-19 hospitalized between March and July 2021, 14.9% were vaccinated and 88.1% were unvaccinated. The patients with vaccination were older and had more chronic medical conditions.[9] As time passed during the pandemic, the vaccination coverage has expanded in different risk groups, and in some of the vulnerable groups, such as elderly or immunosuppressed individuals, the acquired immunity from various SARS-CoV-2 vaccines has decreased and new variants of concern (VOCs), such as the omicron variant, have emerged. Because of this, while the percentage of hospitalized patients with vaccination was low at the beginning, this percentage has increased as the pandemic continued to affect more people around the world.

CoronaVac was the first SARS-CoV-2 vaccine in Turkey and HCWs were vaccinated with CoronaVac. Studies have shown that the elicited immunity of inactivated vaccines decreases with time, especially after the fourth month of the last dose. After primary immunization, booster doses with CoronaVac or BNT162b2 have been recommended. In a study conducted at our center among HCWs with primary immunization with 2 doses of CoronaVac, the antibody level increased after BNT162b2 booster 10 times higher than that of the CoronaVac booster.[21] With the emergence of heavily mutated variant omicron, concerns of breakthrough infections among fully vaccinated patients have increased.[22] Both BNT162b2 and CoronaVac provided limited protection against the omicron variant, and a booster dose with BNT162b2 increased protection but the immunity waned over time.[23,24] In Turkey, while 93.2% of the population (18 years and older) have received a single dose of vaccine, 85.5% received a second dose, and less than half (44.8%) of the population received 3 or more doses. There are no data about the type of the vaccine and percentage of the population vaccinated with CoronaVac (homologous) or BNT162b2 (homologous or heterologous).[25] According to the results of our study, while the percentage of the patients with incomplete vaccination increased 3-fold, the percentage of the patients with complete vaccination 2.7-fold decreased in the omicron period. This significant change may be attributed to either the new definition of fully vaccinated for the omicron variant and low percentage of the fully vaccinated persons in the population of Turkey.

In this study, one-third of the patients died during their hospitalization. In multivariate analysis, advanced age, having comorbidity and malignancy, and a need for ICU attendance were associated with mortality. The percentage of mortality did not differ between groups of no vaccination, incomplete vaccination, or fully vaccinated during both study periods, but in multivariate analysis for the periods separately, mortality was 82.8% lower in the patients with full vaccination significantly. On the other hand, the group with no vaccination was younger and had fewer comorbidities. Under 50 years of age, while all fully vaccinated patients have survived, 10% patients with no vaccination or incomplete vaccination have died. In their study, Moreno-Perez et al[17] compared the mortality between the patients with fully and incomplete vaccination (a total of 145 patients). Although the main outcomes did not differ significantly between 2 groups, the patients with incomplete vaccination were younger and had fewer

comorbidities.[17] In contrast, Myers et al[26] showed that fewer fully vaccinated patients died compared to matched unvaccinated (9.0% vs. 16.3%, $P < .001$) and fully vaccinated patients were significantly older and had more comorbidities.These results show the importance of immunization and booster doses with BNT162b2 to protect both the healthy younger population and older people with multiple comorbidities.

Several limitations should be considered. The study was conducted in a single center and had a retrospective design. We evaluated only the patients with hospitalization. A population-based multicenter study evaluating both asymptomatic and symptomatic patients followed in outpatient or inpatient clinics can reflect the vaccine effectiveness accurately. We could not perform variant analysis within the scope of the study due to diagnostic limitations, but the distribution of cases was consistent with the pandemic waves caused by VOCs in Turkey. Our results are important to demonstrate the situation of countries like Turkey, where both inactivated and mRNA vaccines have been used.

CONCLUSION

Only one-third of the hospitalized patients were fully vaccinated and the patients with no vaccination were younger and had less comorbidities. While mortality did not differ among older patients with and without vaccination, all of the younger patients with fully vaccination have survived. During the spread of the omicron variant, the patients who had boosters died less. Immunization and booster doses with BNT162b2 to protect both the healthy younger population and older people with multiple comorbidities should be encouraged. Vaccination recommendations should be updated with the emergence of new variants for public health.

Ethics Committee Approval: This study was approved by Ethics Committee of Dokuz Eylül University (Approval No: 2022/10-08, Date: March 16, 2022).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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