The clinical characteristics of 541 fully vaccinated hospitalized COVID-19 patients in a Tertiary Care Hospital in Turkey

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Abstract

Purpose

We aimed to examine the characteristics of Turkish patients hospitalized with COVID-19 despite being fully vaccinated.

Method

A retrospective, single-center study was conducted in fully vaccinated patients with inactivated whole virion (CoronaVac) and or BNT162b2 mRNA (Pfizer-BioNTech) vaccines and admitted to the hospital. We evaluated the hospitalized patients regarding the intensive care unit admission and death.

Results

We conducted the study with 541 patients. The mean age was 70.2, and 52.1% of the patients were women. 73.6% of the patients were 65 years or older. The most common comorbidities were hypertension, diabetes mellitus, and COPD. The rate of the alpha variant was 54.3%, and the delta variant was 29.4%. The mortality rate was 45.8%, and the ICU admission rate was 55.3%. In our study, the delta variant had higher ICU admission, and the alpha variant had a higher mortality rate. Patients vaccinated with two-dose Sinovac-CoronaVac had a higher mortality rate. There was no difference between the time between the last vaccination dose to hospitalization, ICU admission, and mortality. LOS in the hospital was longer in ICU and mortality patients.

Conclusion

Our results suggest administering a third and fourth dose of mRNA vaccine to subjects vaccinated primarily with two doses of CoronaVac.

Introduction

Intercalarily to high death rates, the COVID-19 pandemic has created one of the biggest health crises in recent history, demonstrating the importance of the number of vaccinated people within countries [1]. The mRNA and inactivated whole virion SARS-CoV-2 vaccines have demonstrated high efficacy in preventing symptomatic COVID-19, hospitalization, severe illness, and death [2, 3]. However, a small proportion of fully vaccinated people may become infected and experience significant morbidity or mortality. Therefore, it is essential to examine the real-world effects of COVID-19 vaccines [4].

The Turkish Ministry of Health agreed with two pharmaceutical companies. Individuals received Sinovac-CoronaVac on January 14, 2021, and the Pfizer-BioNTech vaccine on April 12, 2021. We aimed to

examine the characteristics of Turkish patients hospitalized with COVID-19 despite being fully vaccinated by CoronaVac and BioNTech.

Method

Study Design and Patients

We conducted a retrospective analysis of hospitalized COVID-19 patients in an urban teaching hospital with a bed capacity of 1607 and 253 intensive care (ICU) beds in Turkey between August 1 and October 31, 2021. According to the NIH disease severity categories, the rRT-PCR-confirmed moderate or severe COVID-19 patients admitted to the infectious disease wards and ICU were included in the study [5]. We had only fully vaccinated patients in this study. The fully vaccinated patients (two doses given) were given the second dose of CoronaVac or Pfizer-BioNTech ≥14 days before hospital admission. Two chart abstractors recorded age, gender, comorbid conditions, and vaccination status data. Total hospital stays until hospital outcome (death or discharge) was calculated.

Hospitalization criteria

Bio-Speedy® SARS-CoV-2 Emerging Plus kit (Bioeksen, Istanbul, Turkey) test was used in the SARS-CoV-2 PCR test on nasopharyngeal swabs to determine the presence of SARS-CoV-2 infection. Bio-Speedy® SARS-CoV-2 Emerging Plus kit can determine Delta (B.1.617.2 and all AY lineages), Alpha (B.1.1.7 and all Q. lineages), Gamma (P.1), Mu (B. 1.621) variants.

Sample size estimation

We used the Stat Calc (Epi Info 7.2.5.0) program to perform sample size calculation, based on the assumptions of a 95% confidence level, 5% margin of error, and an estimated 60% of fully vaccinated individuals in the population, and found 369.

Statistical Analysis

The study's statistical analysis assessed frequency and percentage by categorical data. Also, the continuous data were evaluated as a mean, standard deviation, or median (minimum-maximum) value based on the data distribution. The Shapiro-Wilk test was used to control the normality of continuous measurements. Descriptive statistics for categorical variables was performed using the Chi-square test, while an independent sample t-test was used for continuous data. The level of significance was considered to be 0.05.

Ethical Approval

The ethics committee approved this study of Kayseri City Hospital (Approval No. 59/11022022). The signed informed consent was exempted due to the retrospective character of the research.

Results

The study included 541 patients. The mean age of the patients was 70.2± 14.9 (min:21, max:98), and 52.1% (n=282) of the patients were women. 73.6% (n=398) of the patients were 65 years or older. One hundred thirty-one patients (24.2%) had no comorbidity. The most common comorbidities were hypertension 47.7% (n=258), diabetes mellitus 36% (n=195) and chronic obstructive pulmonary disease (COPD) 19.6% (n=106), respectively.

The number of patients with alpha variant was 294 (54.3%), and the number of patients with delta variant was 159 (29.4%). The total number of patients who died in the study was 248 (45.8%), and the number of patients hospitalized in the intensive care unit was 299 (55.3%). The day between the last dose of vaccine and hospitalization was 120.7± 56.2 days.

While the mean age of non-survivors was 75.8 ± 10.3 years, that of survivors was 65.5 ± 16.5 years, which was statistically significant (p <0.001). The age group 65 years and older showed a significantly higher than fewer 65 years old by ICU admission and mortality (all p values were <0.001). There was no significant difference between genders regarding mortality (p= 0.109). But, female patients were less admitted to the ICU (p= 0.04).

Except for diabetes, there was a statistically significant difference in ICU admission and mortality in the comorbidities; hypertension, COPD, cardiovascular disease, chronic kidney disease, and malignancy (Table 1). When the number of comorbidities exceeded one, ICU admission and mortality rates were higher (p <0.001).

There was a significant difference between variants in ICU admission and mortality (p values= <0.001). Delta (B.1.617.2) variant had higher ICU admission and mortality rate.

There was no statistically significant difference in ICU admission between the vaccine product groups (p= 0.107). But two-dose Sinovac-CoronaVac group had a higher mortality rate (p= <0.001).

We divided patients into two groups regarding the time between the last vaccination dose and hospitalization. There was no statistically significant difference between the group over 120 days and 14-120 days in ICU admission and mortality (p= 0.973 and 0.928, respectively).

There was a significant difference between the length of stay in the hospital and ICU admission and mortality (p values= <0.001). ICU and mortality groups had long days in the hospital than the others.

We showed the Demographic and clinical characteristics of patients in Table 1.

Discussion

We conducted the study with 541 patients. The mean age was 70.2, and 52.1% of the patients were women. 73.6% of the patients were 65 years or older. The most common comorbidities were

hypertension, diabetes mellitus, and COPD. The rate of the alpha variant was 54.3%, and the delta variant was 29.4%. The mortality rate was 45.8%, and the ICU admission rate was 55.3%. The day between the last dose of vaccine and hospitalization was 120± 56 days. Sixty-five years and older was higher ICU admission and mortality, and female patients were less admitted to the ICU. Except for diabetes, ICU admission and mortality were higher in the comorbidities. While the delta (B.1.617.2) variant had higher ICU admission, the alpha (B.1.1.7) variant had a higher mortality rate. There was no difference between the time between the last vaccination dose to hospitalization, ICU admission, and mortality. Patients vaccinated with two-dose Sinovac-CoronaVac had a higher mortality rate.

Consistent with the literature, advanced age, male gender, and comorbidities are associated with poor outcomes such as mortality and ICU admission in our study [6]. Diabetes mellitus prepare the ground for the severe course of COVID-19 and is known to increase the risk of death [7]. But we did not find this result in our study.

In our study, the in-hospital mortality rate was relatively high compared to the literature [8,9]. We think the mortality rate is high, as our research mainly included elderly patients with moderate and severe COVID-19.

There is a higher risk of hospital admission and death for COVID-19 patients infected with the delta variant than the alpha variant. The delta variant causes a more significant health burden than the alpha variant, especially in unvaccinated populations [10,11]. Our study included only vaccinated individuals, and individuals infected with the delta variant had higher ICU admission, but the alpha variant had a higher mortality rate. We think this difference maybe because most of the patients had the alpha variant in our study.

For approximately six months after two vaccine doses, protective antibodies decrease about five times in the BNT162b2 vaccine and six times in the CoronaVac vaccine [12,13]. In our study, the average time between hospitalization after the second dose was four months and was not associated with death or ICU admission. Our research results conclude that both vaccines effectively prevent death and ICU admission.

CoronaVac, produced by the Sinovac company, is the world's most widely used COVID-19 vaccine. The CoronaVac vaccine is an inactivated vaccine that uses the killed SARS-CoV-2 virus and is less effective because it triggers an immune response against many viral proteins. In contrast, mRNA vaccines start reacting to the spike protein the virus uses to enter human cells [14]. The Chilean government has reported that, based on data from nearly two million people who received two doses of CoronaVac and the third dose of CoronaVac, Pfizer-BioNTech or Oxford-AstraZeneca vaccine, protection against COVID-19 increased from fifty percent to eighty percent after two vaccinations [15]. In our study, patients were given a third or fourth dose of the Pfizer-BioNTech vaccine after two doses of the CoronaVac vaccine. In the light of this information, we suggest administering a third and fourth dose of mRNA vaccine to subjects vaccinated primarily with two doses of CoronaVac.

Our study has several limitations. The main limitations of our study include its retrospective design, short follow-up period, and assessment of hospitalized patients only. Another limitation of the study; we only examined moderate and severe patients.

In conclusion, our study found that patients vaccinated with only two-dose CoronaVac had a higher mortality rate. However, there was no difference in ICU hospitalization between the CoronoVac, BioNTech, and CoronaVac plus BioNTech groups. Although the patients were hospitalized four months after the vaccination, there was no significant difference between the post-vaccination time and ICU/ mortality. In our study, the delta variant had higher ICU admission, and the alpha variant had a higher mortality rate. Our study suggests a third and fourth dose of mRNA vaccine to subjects vaccinated primarily with two doses of CoronaVac.

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Declarations

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Author Contributions:

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Ayşin Kılınç Toker, Ayşe Turunç Özdemir, Recep Civan Yüksel and Esma Eryilmaz Eren. The first draft of the manuscript was written by İlhami Çelik and İbrahim Toker and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability

The datasets generated during and/or analyzed during the current study are not publicly available due to the vaccination detail of patients but are available from the corresponding author upon reasonable request.

Ethics approval: The ethics committee approved this study of Kayseri City Hospital (Approval No. 59/11022022).

Consent to participate: The signed informed consent was exempted due to the retrospective character of the research.

Tables

Table 1. Demographic and clinical characteristics of hospitalized and fully vaccinated patients with COVID-19

n (%)							
	non-ICU	ICU	p-value	Survive	Death	Total	p-value
Age. mean (± SD), y	64.3± 16.8	75.1± 11	<0.001*	65.5± 16.5	75.8± 10.3	70.2± 14.9	<0.001*
n (%)	242 (44.7)	299 (55.3)		293 (54.2)	248 (45.8)	541 (100)	
Age, range,y							
< 50	48 (19.8)	8 (3)	<0.001	51 (17.4)	6 (2.4)	57 (10.5)	< 0.001
50-59	23 (9.5)	18 (6)		29 (9.9)	12 (4.8)	41 (7.6)	
60-69	65 (26.9)	54 (18.1)		80 (27.3)	39 (15.7)	119 (22)	
70-79	69 (28.5)	112 (37.5)		81 (27.6)	100 (40.3)	181 (33.5)	
≥ 80	37 (15.3)	106 (35.5)		52 (17.7)	91 (36.7)	143 (26.4)	
Age groups							
< 65y	100 (41.3)	43 (14.4)	<0.001	112 (38.2)	31 (12.5)	143 (26.4)	<0.001
≥ 65 y	142 (58.7)	256 (85.6)		181 (61.8)	217 (87.5)	398 (73.6)	
Gender							
Female	138 (57)	144 (48.2)	0.04	162 (55.3)	120 (48.4)	282 (52.1)	0.109
Male	104 (43)	155 (51.8)		131 (44.7)	128 (51.6)	259 (47.9)	
Comorbidities							
Hypertension	99 (40.9)	159 (53.2)	0.005	127 (43.3)	131 (52.8)	258 (47.7)	0.028
Diabetes	78 (32.2)	117 (39.1)	0.097	99 (33.8)	96 (38.7)	195 (36)	0.235
COPD	37 (15.3)	69 (23.1)	0.023	45 (15.4)	61 (24.6)	106 (19.6)	0.007
Cardiovascular disease	10 (4.1)	30 (10)	0.009	15 (5.1)	25 (10.1)	40 (7.4)	0.028
Chronic kidney disease	16 (6.6)	50 (16.7)	<0.001	19 (6.5)	47 (19)	66 (12.2)	<0.001
Malignancy	9 (3.7)	25 (4.6)	0.027	13 (4.4)	21 (8.5)	34 (6.3)	0.050
Number of comorbidities							
0	85 (35.1)	46 (15.4)	<0.001	92 (31.4)	39 (15.7)	131 (24.2)	<0.001
1	78 (32.2)	97 (32.4)		98 (33.4)	77 (31)	175 (32.3)	
2 or more	79 (32.6)	156 (52.2)		103 (35.2)	132 (53.2)	235 (43.4)	
Variants							
Alpha (B.1.1.7)	180 (74.4)	114 (38.1)	<0.001	209 (71.3)	85 (34.3)	294 (54.3)	<0.001
Delta (B.1.617.2)	31 (12.8)	128 (42.8)		42 (14.3)	117 (47.2)	159 (29.4)	
Others	31 (12.8)	57 (19.1)		42 (14.3)	46 (18.5)	88 (16.3)	
Vaccinated patients. by vaccine product							
2 Sinovac- CoronaVac	167 (69)	198 (66.2)	0.107	205 (70)	160 (64.5)	365 (67.5)	<0.001
2 Pfizer-BioNTech	13 (5.4)	13 (4.3)		19 (6.5)	7 (2.8)	26 (4.8)	
2 Sinovac + 1 BioNTech	31 (12.8)	28 (9.4)		38 (13)	21 (8.5)	59 (10.9)	
2 Sinovac + 2 BioNTech	31 (12.8)	60 (11.1)		31 (10.6)	60 (24.2)	91 (16.8)	
LOS in hospital. mean (± SD), day	8.8± 4.2	16± 9.6	<0.001*	10.5± 6.5	15.4± 9.7	12.7± 8.5	<0.001*
n (%)	242 (44.7)	299 (55.3)		293 (54.2)	248 (45.8)	541 (100)	
By the time between fully vaccinated and illness onset							
14-120 Days	108 (44.6)	133 (44.5)	0.973	130 (44.4)	111 (44.8)	241 (44.5)	0.928
>120 Days	134 (55.4)	166 (55.5)		163 (55.6)	137 (55.2)	300 (55.5)	

Other variants: Variants except for Delta, Alpha, Gamma, and Mu variants

LOS: Length of stay

*p= Student's t-test, other p values calculated by chi-square test.