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Vaccination status among patients with the need for emergency hospitalizations related to COVID-19

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ABSTRACT

Background: It is thought vaccines allowed for emergency use significantly reduce hospitalizations and emergency room visits. It is a matter of curiosity how many of the patients who come to the emergency department (ED) are vaccinated. We aimed to examine the characteristics of ED patients needing hospitalizations related to moderate and severe COVID-19 by vaccination status.

Methods: A retrospective study of 559 rRT-PCR-confirmed SARS-CoV-2 infection cases with moderate or severe COVID-19 needing hospitalization was performed in August 2021. Univariate and multivariate logistic regression analyses were performed for factors associated with mortality.

Results: The mean age of the patients was 60.8 ± 18.1 years old, and 54.2% ($n = 303$) of the patients were women. The most common comorbidities were hypertension (37.2%), diabetes mellitus (31.1%) and chronic obstructive pulmonary disease (13.8%), respectively. The number of patients with alpha variant was 399 (71.4%), and delta variant was 83 (14.8%). Fifty point 6% ($n = 283$) of the patients were fully vaccinated. The total number of patients who died in the study was 114 (20.4%), and the number of patients hospitalized in the intensive care unit was 168 (30.1%). The day between the last dose of vaccine and hospitalization was 117 ± 45.9 days. In multivariate logistic regression analysis: age (odds ratio (OR), 1.05; 95% confidence intervals (95% CI) 1.03–1.08-year increase), male gender (OR, 1.8; 95% CI, 1.1–2.9), presence of at least one comorbid disease (OR, 2; 95% CI, 1.1–3.7) and partial (OR, 0.24; 95% CI, 0.09–0.6) and fully vaccinated status (OR, 0.1; 95% CI, 0.05–0.18) were associated with mortality among COVID-19 patients.

Conclusions: In this study, age older than 65, unvaccinated, and comorbidities had significantly higher mortality. In multivariate regression analyses, age, vaccination status, comorbidities and the male gender were associated with mortality. Our study did not evaluate the vaccine efficacy but, a lower mortality rate was observed in those fully vaccinated with CoronaVac and Pfizer–BioNTech. Additionally, Alpha, Delta and other variants had the same mortality rates.

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1. Introduction

Since the pandemics started worldwide, as of Sept 14, 2021, there have been over 4 million deaths and over 200 million confirmed cases of coronavirus disease 2019 (COVID-19) reported to WHO. As of Sept 12, 2021, more than 5 billion vaccine doses have been administered worldwide [1]. Inactivated whole virion (CoronaVac) and BNT162b2 mRNA (Pfizer–BioNTech) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines have demonstrated high efficacy against symptomatic disease in phase 3 clinical trials [2,3]. A study of

nationwide national surveillance data in Israel reported that two doses of the Pfizer–BioNTech vaccine significantly reduced hospitalizations and emergency department (ED) visits for all age groups [4]. In the light of these studies, it is essential to examine the real-world effects of COVID-19 vaccines [5].

We aimed to examine the characteristics of ED patients needing hospitalization related to moderate and severe COVID-19 by vaccination status.

2. Method

2.1. Study design and patients

We conducted a retrospective analysis of hospitalized COVID-19 patients in the ED of an urban teaching hospital, with a bed capacity of

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1607 and 253 intensive care beds in Turkey between Aug 1 and Aug 31, 2021.

In August 2021, a total of 2371 patients were admitted to our ED with the suspicion of COVID-19. All those patients arrived by ambulance at the ED. Five hundred ninety-six of these patients were hospitalized with a preliminary diagnosis of COVID-19. Five hundred sixty-six patients were PCR confirmed, and there were seven patients whose vaccine information could not be reached. As a result, a total of 559 rRT-PCR-confirmed SARS-CoV-2 infections, moderate or severe COVID-19 cases, according to the NIH disease severity categories, were included in the study [6] (Fig. 1). The patients with mild illness may display various signs and symptoms (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell). The patients do not have dyspnea, shortness of breath with exertion, or abnormal imaging. Moderate illness is defined as evidence of lower respiratory disease during clinical assessment or imaging, with SpO₂ ≥ 94% on the room. The patients with COVID-19 are considered to have severe illness if they have SpO₂ < 94% on room air, PaO₂ /FiO₂ < 300 mmHg, a respiratory rate > 30 breaths/min, or lung infiltrates >50% [6]. A total of 1775 patients were considered mild because they did not have shortness of breath, exertional dyspnea, and abnormal imaging. A nasopharyngeal swab test was performed on these patients, and the first treatment of these patients is arranged in the ED, and they are referred to the pandemic outpatient clinics for follow-up.

2.2. Hospitalization criteria

Bio-Speedy® SARS-CoV-2 Emerging Plus kit (Bioeksan, 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 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 can be determined.

According to the National Institutes of Health (NIH) severity of illness categories, rRT-PCR-confirmed SARS-CoV-2 infection cases with moderate or severe COVID-19 patients were included in the study [6].

Data on age, gender, comorbid conditions, and vaccination status were recorded. Patients had three groups by vaccination 1) not vaccinated (never vaccinated, and patients who received only one dose of

any COVID-19 vaccine 14 days before hospitalization) 2) partially vaccinated (1 dose of CoronaVac or Pfizer-BioNTech ≥14 days before hospital admission or two doses, second dose <14 days before hospital admission) 3) fully vaccinated (both doses given); the second dose of CoronaVac or Pfizer-BioNTech ≥14 days before hospital admission. Total hospital stays until hospital outcome (death or discharge) was calculated.

2.3. Sample size estimation

To perform sample size calculation, we viewed data from preliminary results from our study. The sample size was calculated using Medcalc software with a power of $\alpha = 0.05$ and 80%, based on the assumption that 25% of hospitalized patients would be fully vaccinated. And the mortality rate would be 25% in unvaccinated patients and 12.5% (50% reduction) in vaccinated patients. The required sample size was 500, and 559 patients were included in our study.

2.4. Statistical analysis

In the study's statistical analysis, categorical data were assessed frequency and percentage. 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 /Mann Whitney U was used for continuous data. Univariate and multivariate logistic regression analyses were applied for factors associated with in-hospital mortality. In-hospital mortality was assessed at any time, with a minimum of 1 and a maximum of 59 days. The crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were estimated. The level of significance (*p*-value) was considered to be 0.05.

2.5. Ethical approval

This study was approved by the ethics committee of XXX City Hospital (Approval No. 18112021/ 518). The signed informed consent was exempted due to the retrospective character of the research.

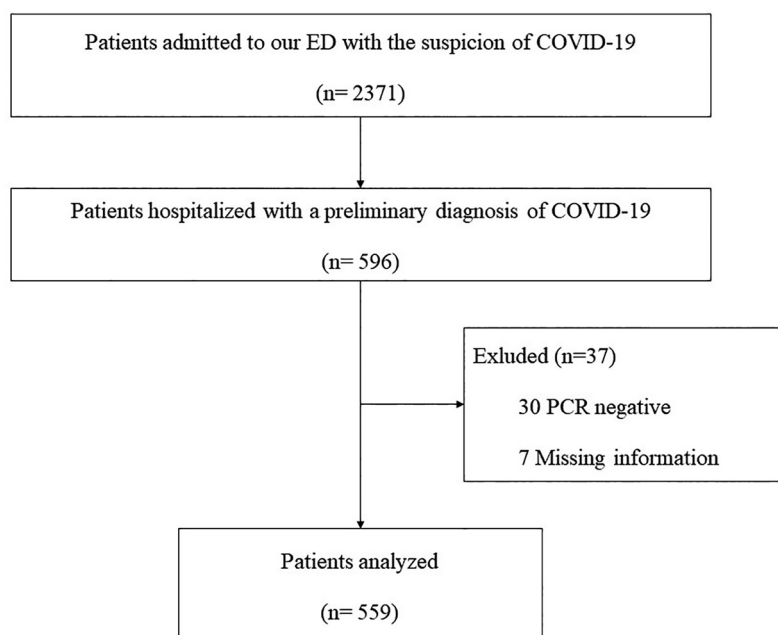


Fig. 1. Flowchart for patient selection.

3. Results

3.1. Patient characteristics

A total of 559 patients were included in the study. The mean age of the patients was $60.8 \pm (18.1)$ (min:16, max:102), and 54.2% ($n = 303$) of the patients were women. 49.6% ($n = 277$) of the patients were 65 years or older. There was at least one comorbid disease in 65.1% ($n = 364$) of the patients. The most common comorbidities were hypertension (37.2%), diabetes mellitus (31.1%) and chronic obstructive pulmonary disease (13.8%), respectively. The number of patients with alpha variant was 399 (71.4%), and the number of patients with delta variant was 83 (14.8%). 50.6% ($n = 283$) of the patients were fully vaccinated. The total number of patients who died in the study was 114 (20.4%), and the number of patients hospitalized in the intensive care unit was 168 (30.1%). The day between the last dose of vaccine and hospitalization was 117 ± 45.9 days.

There was no significant difference between genders regarding mortality ($p = 0.101$). While the mean age of non-survivors was 67.4 ± 14.4 years, that of survivors was 59.2 ± 18.6 years, which was statistically significant ($p < 0.001$). The age group with 65 years and older showed a significant difference of 62.3% than fewer 65 years old ($p < 0.001$). There was no significant difference between variants in mortality ($p = 0.208$). There was a statistically significant difference in mortality

between the fully vaccinated and unvaccinated groups (36.8% vs. 57%, $p < 0.001$). Fully vaccinated patients were divided into groups regarding the time between the last dose of vaccination and hospitalization. There was no statistically significant difference between the group over 120 days and 14–120 days ($p = 0.118$). Other clinical features of the patients are shown in Table 1.

There was a statistically significant difference between the groups 65 years and older versus 65 years fewer in vaccination status ($p < 0.001$). In particular, the rate of unvaccinated patients under 65 years was significantly higher than that of patients aged 65 and over (63.1% vs. 17%). The vaccination status by two age groups is shown in Table 2.

3.2. Univariate and multivariate logistic regression analysis for mortality

In univariate analysis, age, over 65 years of age, comorbid diseases, partial and full vaccination status were associated with mortality. In multivariate logistic regression analysis: age (odds ratio (OR), 1.05; 95% confidence intervals (95% CI) 1.03–1.08- year increase), male gender (OR, 1.8; 95% CI, 1.1–2.9), presence of comorbid diseases (OR, 2; 95% CI, 1.1–3.7) and partial (OR, 0.24; 95% CI, 0.09–0.6) and fully vaccination status (OR, 0.1; 95% CI, 0.05–0.18) were associated with mortality among COVID-19 patients. The results of multivariable regression analysis are presented in Table 3.

Table 1
Baseline characteristics of patients.

	Total n (%)	Survived n (%)	Died n (%)	p-Value
Age in years, Mean (\pm SD)	60.8 \pm 18.1	59.2 \pm 18.6	67.4 \pm 14.4	<0.001*
Age groups				
< 65y	282 (50.4%)	239 (53.7%)	43 (37.7%)	0.002
\geq 65 y	277 (49.6%)	206 (46.3%)	71 (62.3%)	
Sex distribution				
Female	303 (54.2%)	249 (56%)	54 (47.4%)	0.101
Male	256 (45.8%)	196 (44%)	60 (52.6%)	
Variants				
Alpha (B.1.1.7)	399 (71.4%)	310 (69.7%)	89 (78.1%)	0.208
Delta (B.1.617.2)	83 (14.8%)	70 (15.7%)	13 (11.4%)	
Others*	77 (13.8%)	65 (14.6%)	12 (10.5%)	
Vaccination status				
Not vaccinated	225 (40.3%)	160 (36%)	65 (57%)	< 0.001
Partially vaccinated	51 (9.1%)	44 (9.9%)	7 (6.1%)	
Fully vaccinated	283 (50.6%)	241 (54.2%)	42 (36.8%)	
Sinovac- CoronaVac				
Partially vaccinated	21 (3.8%)	18 (85.7%)	3 (14.3%)	0.003
Fully vaccinated	243 (43.5%)	205 (84.4%)	38 (15.6%)	
Pfizer-BioNTech				
Partially vaccinated	30 (5.4%)	26 (86.7%)	4 (13.3%)	
Fully vaccinated	20 (3.6%)	19 (95%)	1 (5%)	
Sinovac plus BioNTech	20 (3.6%)	17 (85%)	3 (15%)	
By the time between fully vaccinated and illness onset				
14–120 Days	103 (47.6%)	83 (34.4%)	20 (47.6%)	0.118
> 120 Days	180 (52.4%)	158 (65.6%)	22 (52.4%)	
Comorbidities				
Absent	195 (34.9%)	171 (38.4%)	24 (21.1%)	0.001
Present	364 (65.1%)	274 (61.6%)	90 (78.9%)	
Comorbidities				
Hypertension	208 (37.2%)	152 (34.2%)	56 (49.1%)	0.003
Diabetes	174 (31.1%)	131 (29.4%)	43 (37.7%)	
COPD	77 (13.8%)	55 (12.4%)	22 (19.3%)	0.055
Cardiovascular disease	29 (5.2%)	18 (4%)	11 (9.6%)	0.016
Chronic kidney disease	41 (7.3%)	23 (5.2%)	18 (15.8%)	< 0.001
Malignancy	24 (4.3%)	17 (3.8%)	7 (6.1%)	
Hospitalization				
ICU	168 (30.1%)	54 (12.1%)	114 (100%)	< 0.001
Non-ICU	391 (69.9%)	391 (87.9%)	0 (0%)	
Length of stay in hospital wards, median IQRs, day	8 (6–11)	8 (6–11)	7 (4–12)	0.113**
Length of stay in ICU, median IQRs, day	7 (3–13)	7 (5–12)	7 (3–14)	0.583**

Other p values calculated by chi-square test.

* p = Independent sample t-test.

** p = Mann-Whitney U test.

Table 2
The vaccination status by age groups.

	No. of cases, by age group (yrs)		Total	p-Value
	< 65	≥65		
Vaccination status				
Not vaccinated	178 (63.1%)	47 (17%)	225 (40.3%)	p < 0.001
Partially vaccinated	37 (13.1%)	14 (5.1%)	51 (9.1%)	
Fully vaccinated	67 (23.8%)	216 (78%)	283 (50.6%)	
Vaccinated patients, by vaccine product				
Sinovac- CoronaVac	61 (21.6%)	203 (73.3%)	264 (47.2%)	p < 0.001
Partially vaccinated	12 (4.3%)	9 (3.2%)	21 (3.8%)	
Fully vaccinated	49 (17.4%)	194 (70%)	243 (43.5%)	
Pfizer-BioNTech	39 (13.8%)	11 (4%)	50 (8.9%)	
Partially vaccinated	25 (8.9%)	5 (1.8%)	30 (5.4%)	
Fully vaccinated	14 (2.5%)	6 (1.1%)	20 (3.6%)	
Sinovac plus BioNTech	4 (1.4%)	16 (5.8%)	20 (3.6%)	

4. Discussion

In our study, moderate to severe COVID-19 cases hospitalized from the emergency department were included. In this study, with 559 patients, the mortality rate was 20.4%. And, only 50.6% of the patients with moderate and severe COVID-19 hospitalized from the ED during August were fully vaccinated. Our study showed that those younger than 65, fully vaccinated, and those without comorbid conditions had significantly lower mortality. Also, in multivariate regression analysis, in addition to age, vaccination status, and additional disease status, the male gender was associated with mortality.

Increasing age and comorbidities are among independent predictors of mortality in COVID-19 patients. It is thought that immune cell defects that increase with age may cause an above-normal inflammatory response, leading to higher mortality in the elderly [7–9]. In our study, the mortality rate was significantly higher in patients over 65 years of age and with comorbidities. The higher mortality rate in comorbidities may be explained by lower vaccine efficacy and the risk of exacerbating comorbidity after infection or both.

A global meta-analysis of 3 million people reported that while there was no difference in the proportions of men and women with confirmed COVID-19, higher admission rates to the intensive care unit (OR = 2.84; 95% CI = 2.06, 3.92) and death (OR = 1.39; 95% CI = 1.31, 1.47) in men than women [10]. In our study, male patients had almost two times the odds of mortality (OR, 1.8; 95% CI, 1.1–2.9).

A study conducted in Israel showed that two doses of Pfizer-BioNTech vaccine significantly reduced hospitalizations, severe illness and death for all age groups, including the alpha variant. These findings suggest that the COVID-19 vaccine may help control the pandemic and

reduce ED visits [4]. In our study, only 50.6% of the patients were fully vaccinated; this finding emphasizes the importance of the vaccine.

As of March 2021, three variants are considered variants of concern (VOCs); Alpha (B.1.1.7), Beta (B.1.351) and Gamma (P.1) SARS-CoV-2 variant. A matched cohort study examining 813 viral genomes showed that Pfizer–BioNTech vaccine efficacy against B.1.1.7 and B.1.351 variants decreased in a certain time window [11]. The B.1.617.2 variant, which causes an increase in Covid-19 cases, especially in India and England, has been detected worldwide. The effectiveness of the CoronaVac and Pfizer–BioNTech vaccines against the B.1.617.2 variant is uncertain [12]. VOCs are spread throughout Turkey, also. The B.1.1.7 variant continues to cause more than half of new COVID-19 cases in Turkey [13]. Vaccine efficacy was not evaluated in our study. However, a statistically significantly lower mortality rate was observed in those fully vaccinated with CoronaVac and Pfizer–BioNTech. In addition, there was no significant difference in mortality rates in terms of variants in the vast majority of patients with the B.1.1.7 variants.

Mortality rates in cohort studies of vaccinated and unvaccinated hospitalized COVID-19 patients were similar [9,14,15]. Parallel to these studies, the mortality rate in all patients was around 20% in our study. However, the mortality rate in unvaccinated patients was statistically higher in our study.

A recent comprehensive study in Qatar showed that the protection of the Pfizer–BioNTech vaccine increases rapidly after the first dose, peaks in the first month after the second dose, and gradually declines over the following months. However, the Pfizer–BioNTech vaccine was effective for up to six months in protection against hospitalization and death. [16]. There is no evidence suggesting that vaccines' effectiveness in preventing hospitalization and death decreases over time. It has also been shown that recurrent infections in vaccinated persons are less contagious than primary infections in unvaccinated persons [16,17]. Our study grouped the time elapsed after the second dose of vaccine as 120 days (four months) and 14–120 days. However, there was no difference in mortality between these two groups ($p = 0.118$).

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, and mild patients were not included because we could not access their information. Other limitations include the chart abstractors were not trained before data collection, abstractors were not blinded to the study objectives, abstractors' performance was not monitored, and abstractor interrater-reliability was not assessed.

5. Conclusion

In our study, age older than 65, unvaccinated, and comorbidities had significantly higher mortality. In multivariate regression analyses, age, vaccination status, comorbidities and the male gender was associated with mortality. Male patients and comorbidities had almost two times

Table 3
Univariate and multivariate logistic regression analysis for mortality.

Factors	Unadjusted OR (95% CI)	p-Value	Multivariate logistic regression analysis	
			Adjusted OR (95% CI)	p-Value
Age in years	1.02 (1.01–1.04)	<0.001	1.05 (1.03–1.08)	<0.001
Age groups				
< 65 y	Reference	0.003	Reference	0.901
≥ 65 y	1.9 (1.25–2.9)		0.9 (0.4–2.1)	
Gender				
Female	Reference	0.101	Reference	0.008
Male	1.41 (0.9–2.1)		1.8 (1.1–2.9)	
Comorbidities				
Absent	Reference	0.001	Reference	0.018
Present	2.3 (1.4–3.8)		2 (1.1–3.7)	
Vaccination				
Not vaccinated	Reference		Reference	
Partially vaccinated	0.39 (0.16–0.91)	0.030	0.24 (0.09–0.60)	0.003
Fully vaccinated	0.42 (0.27–0.66)	<0.001	0.1 (0.05–0.18)	<0.001

the odds of mortality. Vaccine efficacy was not evaluated in our study. But lower mortality rate was observed in those fully vaccinated with CoronaVac and Pfizer–BioNTech. Alpha, Delta and other variants had the same mortality rates.

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Declaration of Competing Interest

None.

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