The Effect of Vaccination with Pfizer-BioNTech or CoronaVac on Disease Prognosis Among Hospitalized COVID-19 Patients

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ABSTRACT

Objective: The Turkish Ministry of Health offered two types of vaccines by January 13, 2021, which are CoronaVac (Sinovac Biotech, China) and Pfizer-BioNTech. We aimed to describe the impact of the CoronaVac and Pfizer-BioNTech vaccines on clinical outcomes among hospitalized patients during a six-month period.

Methods: We included patients older than 18 years old and hospitalized because of COVID-19 when the vaccines were available. We conducted the study at Koç University Hospital and American Hospital between June 2021, six months after the vaccination started, and December 2021.

Results: In total, 444 RT-PCR confirmed hospitalized patients were included. The mean age of the patients was 59 (standard deviation [SD]=18), and 42.8% were female. The most common comorbidity was hypertension (39%), followed by diabetes mellitus (27%), cardiovascular diseases (18.4%), chronic lung diseases (14.6%), cancer (9.2%), and chronic renal diseases (8%). In multivariate analysis, no vaccination (OR=4.7, CI=2.25-10.06; $p<0.001$), age >65 (OR=5.2, CI=2.25-11.98; $p<0.001$), cancer (OR=7.6, CI=3.04-19.31; $p<0.001$), and chronic kidney disease (OR=3.1, CI=1.14-8.74; $p=0.026$) significantly increased mortality in COVID-19 patients. Eighteen percent of patients were in the intensive care unit (ICU). One hundred eighty-one patients (40.8%) were non-vaccinated before their admission, and their mortality (17.6%) was higher compared to the patients who were vaccinated with at least one type of vaccine ($p=0.002$). None of the patients who received two doses of Pfizer-BioNTech vaccines died.

Conclusion: Among the inpatients with COVID-19, the predictors for mortality were being unvaccinated, older age, cancer, chronic kidney disease, and cardiovascular diseases. Among the vaccinated inpatients, having two doses of the Pfizer-BioNTech vaccine was the only effective protective measure against mortality, and two doses of the CoronaVac vaccine had no significant effect in preventing fatality.

Keywords: CoronaVac, Pfizer-BioNTech, unvaccinated, mortality

INTRODUCTION

The coronavirus disease 2019 (COVID-19) caused more than 6 million deaths worldwide (1), and vaccination remains to be the most effective way to reduce the deaths in addition to infection control measures in the community. The Turkish Ministry of Health offered two types of vaccines by January 13, 2021, CoronaVac (Sinovac Biotech, China), and three months later, by April 12, 2021, Pfizer-BioNTech (Pfizer-BioNTech). Because of having two different types of vaccines, there was an opportunity to choose between Pfizer-BioNTech or CoronaVac vaccines. Meanwhile, for those who had already received two doses of CoronaVac, another booster dose of CoronaVac or two doses of Pfizer-BioNTech were offered. The decision to select one of two options sometimes caused confusion among the people and healthcare workers. Having two vaccines in Turkey allowed us to compare the outcomes of using different vaccines.

A recent meta-analysis, including the community-level studies, reported that the Pfizer-BioNTech vaccine had 91.2% effectiveness while CoronaVac had 65.7% (2). Our study aimed to describe the impact of the CoronaVac and Pfizer-BioNTech vaccines on outcomes among hospitalized patients during a six-month period.

MATERIALS AND METHODS
Study Design and Study Population
RT-PCR confirmed >18 years of age patients who were hospitalized between June 2021 and December 2021 were included. Having the 15% fatality rate among unvaccinated inpatients from previous data and considering a 10% reduction of fatality rate to 5%, with type I error of 5% and type II error of 20%, we calculated the sample size as 282 patients.

Age, gender, body mass index (BMI), admission and discharge dates, comorbidities, tocilizumab, anakinra, and dexamethasone use were retrieved from the medical records. The patients who had missing data were excluded. In addition, two patients having Janssen COVID-19 vaccines (Johnson&Johnson) were excluded from the data for the sake of comparison. The patients were categorized as mild, moderate, severe, and critical according to the World Health Organization (WHO) classification (3).

Full vaccination was defined as being vaccinated at least two weeks passed after the second dose of vaccines.

Koç University Committee on Human Research and Institutional Review Board approved the ethical considerations about study (reference number 2020.145.IRB1.034). Informed consent was obtained from the patients.

Statistical Analysis
Comparison of categorical variables was performed by chi-square test and continuous variables by t-test. Univariate and multivariate analysis for the fatality predictors was performed using logistic regression. The statistical significance was set as $p<0.05$.

RESULTS

In total, 444 RT-PCR confirmed >18 years of age inpatients were included (46.6% at American Hospital, 53.4% at Koç University Hospital). The mean age of the patients was 59.9, 44% were older than 65 years of age, and 42.8% were female (Table 1). The most common comorbidity was hypertension (39%), followed by diabetes mellitus (27%), cardiovascular diseases (18.4%), chronic lung diseases (14.6%), cancer (9.2%), and chronic renal diseases (8%). Univariate analysis showed that no vaccination (OR=2.4, CI=1.37-4.43; p=0.003), age >65 (OR=4.6, CI=2.39-8.90; p<0.001), hypertension (OR=1.9, CI=1.10-3.56; p=0.022), diabetes mellitus (OR=2.1, CI=1.20-3.98; p=0.010), cancer (OR=4.6, CI=2.18-9.74; p<0.001), cardiovascular diseases (OR=3.1, CI=1.65-5.83; p<0.001), and chronic kidney disease (OR=4.1, CI=1.84-8.92; p<0.001) significantly

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HIGHLIGHTS

- Non-vaccinated patients' mortality rate was higher than those vaccinated with at least one type of vaccine.
- None of the patients who received two doses of Pfizer-BioNTech vaccines died.
- Two doses of the CoronaVac vaccine had no significant effect in preventing fatality.

Table 1. Characteristics of the patients and univariate analysis for fatality.

	Total n=444 (%)	Survived n=391 (%)	Fatal n=53 (%)	p
Mean Age (SD)	59.9 (18)	57.3 (18)	71.4 (15)	<0.001
Age >65	196 (44)	156 (40)	40 (75)	<0.001
Gender (female)	190 (43)	166 (42)	24 (45)	0.696
Mean BMI (SD)	27.9 (5.7)	27.7 (5.5)	29.7 (6)	0.022
Comorbidities				
Hypertension	165 (37)	137 (35)	28 (53)	0.019
Diabetes mellitus	115 (26)	93 (21)	22 (42)	0.009
Cancer (solid and hematologic)	39 (9)	26 (6)	13 (25)	<0.001
Cardiovascular diseases	78 (18)	59 (15)	19 (36)	<0.001
Chronic lung diseases	62 (14)	52 (13)	10 (19)	0.315
Chronic renal diseases	34 (8)	23 (6)	11 (21)	<0.001
Intensive care unit	80 (18)	31 (8)	49 (92)	<0.001
Vaccination status				
No vaccination	181 (41)	149 (38)	32 (60)	0.002
CoronaVac (2 doses)	89 (20)	79 (20)	10 (19)	0.813
Pfizer-BioNTech (2 doses)	52 (12)	52 (13)	0 (0)	0.005
CoronaVac (3 doses)	41 (9)	36 (9)	5 (9)	0.962
CoronaVac (2 doses) + Pfizer-BioNTech (1 dose)	32 (7)	29 (7)	3 (6)	0.639

BMI: Body mass index, **SD:** Standard deviation.

Table 2. Univariate and multivariate analysis for the predictors of fatality.

	Univariate analysis			Multivariate analysis		
	OR	CI	p	OR	CI	p
No vaccination	2.4	1.37-4.43	0.003	4.7	2.25-10.06	<0.001
Age >65	4.6	2.39-8.9	<0.001	5.2	2.25-11.98	<0.001
Gender (female)	0.9	0.50-1.59	0.708	1.3	0.64-2.68	0.447
Hypertension	1.9	1.10-3.56	0.022	0.8	0.34-1.73	0.529
Diabetes mellitus	2.1	1.20-3.98	0.01	1.6	0.70-3.45	0.268
Cancer	4.6	2.18-9.74	<0.001	7.6	3.04-19.31	<0.001
Cardiovascular disease	3.1	1.65-5.83	<0.001	1.2	0.53-2.73	0.655
Chronic kidney disease	4	1.84-8.92	<0.001	3.1	1.14-8.74	0.026
BMI	1.05	1.01-1.1	0.024	1.04	0.99-1.1	0.106

BMI: Body mass index, **OR:** Odds ratio, **CI:** Confidence interval.
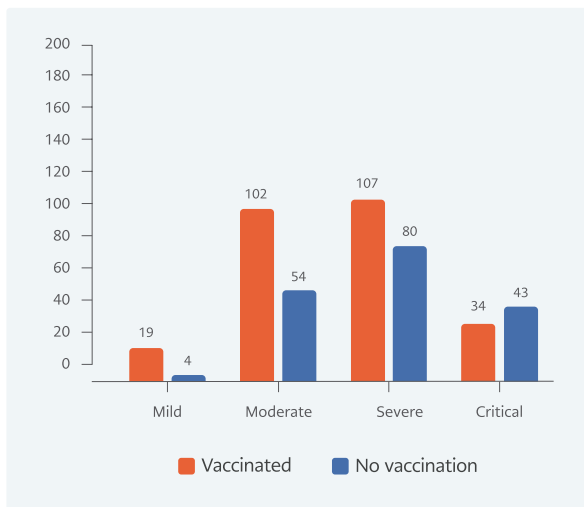
Figure 1. Disease severity among vaccinated and unvaccinated patients.

increase mortality in COVID 19 patients. The fatality rate among the patients who stayed in ICU was 92.4%, and it was 95% among the patients intubated at Koç University Hospital ($p<0.001$) (Table 2).

In total, 181 patients (40.8%) were unvaccinated before admission, constituting 60% of the fatal cases (p=0.002). None of the patients who were vaccinated with two doses of Pfizer-BioNTech vaccines died ($p=0.005$). However, the booster dose of Pfizer-BioNTech after two doses of CoronaVac has no clinical significance for preventing mortality ($p=0.639$).

The proportion of critically ill patients in the unvaccinated group was 23.8%, whereas it was 12.9% among the patients who received at least one type of vaccine ($p=0.002$, Figure 1).

In multivariate analysis for the fatality prediction, unvaccinated patients were 4.7 times more likely to die than vaccinated patients (OR=4.7, CI=2.25-10.06; $p<0.001$). Besides being unvaccinated, other significant predictors of fatality were age >65, cancer, and chronic kidney disease (Table 2).

DISCUSSION

The clinical observations reflecting real-life experiences are important to provide more convincing information about the COVID-19 vaccines. In this study, we described the clinical impact of having Pfizer-BioNTech or CoronaVac vaccines. We approved the findings of in vitro studies which showed that the Pfizer-BioNTech vaccine had higher effectiveness than CoronaVac. In previous in vitro studies, the neutralizing antibody levels after three months of the Pfizer-BioNTech booster were higher than the antibody levels after CoronaVac in fully, at least two doses of the vaccine according to WHO recommendations, vaccinated individuals (4, 5, 6). In our study, two doses of the Pfizer-BioNTech vaccine were 100% protective against mortality among hospitalized patients because of COVID-19. Since the Pfizer-BioNTech vaccine was 100% protective and predicted the outcome, we did not include it in the multivariate model for mortality.

After the introduction of the Pfizer-BioNTech vaccine on April 12, 2021, there were two options for booster doses after two doses of the CoronaVac vaccine. Studies performed in diverse populations suggested that both Pfizer-BioNTech and CoronaVac booster doses were effective against mortality, and heterologous boosters were found to be superior to homologous boosters in terms of IgG production (7, 8). In our study, a booster dose of Pfizer-BioNTech after two doses of CoronaVac was not found to be preventive against mortality ($p=0.639$); however, this result might be related to the small sample size in our study.

A study among hospitalized patients with COVID-19 from Turkey reported that full vaccination with CoronaVac or Pfizer-BioNTech was protective against mortality (9), and another study among 1401 hospitalized patients reported Pfizer-BioNTech was more effective than CoronoVac in terms of protection from mortality (10). Vaccines are not only protective against mortality but also decrease disease severity as well as hospital admission. Unvaccinated patients have higher ICU admission, which means critical disease and mechanical ventilation use, compared with vaccinated inpatients in our study.

A Turkish study shows that 53% of unvaccinated patients were admitted to the ICU due to disease severity, which decreased while vaccine doses increased (10). A case-control study of 1197 inpatients

showed that the Pfizer-BioNTech vaccine decreased disease severity significantly, and the vaccinated group had lower ICU admission than unvaccinated patients, 24.6% and 40.1%, respectively (*p*<0.001) (11). Regardless of the type of the vaccine, mechanical ventilation needs, or death was shown significantly lower (*p*<0.001) among vaccinated patients in a multicenter study. It was 24.9% among vaccinated groups and 40.5% among unvaccinated controls (12). In our study, we do not have the data of non-hospitalized patients, but a comprehensive study from England with more than 150,000 patients included showed that one dose of the Pfizer-BioNTech vaccine had protection against symptomatic disease and reduced the risk of emergency hospital admission by 43% (33% to 52%) (13). In addition, another large study from the UK showed that vaccinated patients were hospitalized less and experienced symptoms of the disease less than others (14). More than 80% percent of the hospitalized patients in our study were either unvaccinated or vaccinated with two doses of CoronaVac.

In our multivariate analysis, being older than 65 years of age, having cancer, and having chronic kidney disease were found to be significant predictors of COVID-19-related fatality. Above-normal inflammatory responses causing higher mortality in older adults may stem from impaired immune system defects increasing with age (9, 15-17). The higher mortality rates in patients with comorbidities may stem from lower vaccine efficacy and risk of morbidity exacerbation (9).

Cancer was a significant contributor in both univariate and multivariate analyses. Patients with cancer are considered highly vulnerable and prone to developing severe COVID-19 symptoms, possibly due to an immunosuppressive state caused directly by the growing tumor itself or indirectly by antineoplastic agents (18). Besides, antineoplastic agents that our patients were using could cause impaired vaccine response, which explains higher mortality. Chronic kidney disease is found to be an important contributor to COVID-19 mortality, the mechanism of which, however, is yet to be found (19). However, it was reported that the patients requiring hemodialysis have lower antibody levels than controls (19). Therefore, it may explain lower vaccine response among patients with chronic kidney disease.

In our univariate analysis, hypertension and diabetes were found to be significantly associated with higher mortality rates; however, in multivariate analysis, these were not significantly associated with mortality. Recent findings showed that hypertension is one of the most common comorbidities in patients with COVID-19, whose prevalence ranges between 10% to 34% (20). However, there is still no consensus about the impact of hypertension on COVID-related mortality (20). Similar to hypertension, the effect of diabetes mellitus on mortality still lacks evidence (21). Although its effect on mortality was reported (22), we did not detect a significant impact in the multivariate analysis.

The major limitation of this study is its retrospective observational design. Our sample size was limited to the number of patients hospitalized in our two hospitals, but we reached statistical significance. We did not include the variants of the SARS-CoV data; however, during the study period, the circulating variants were Delta and Omicron. It is reported that patients who received inactive vaccines are protected from severe disease, and an additional third booster dose is effective (23, 24). In contrast, third doses of CoronaVac were found to be ineffective against severe and fatal diseases in our study. However, the low number of patients with three doses may have an impact on our results.

Among the inpatients with COVID-19, the predictors for mortality were being unvaccinated, older age, cancer, chronic kidney disease, and cardiovascular diseases. Among the vaccinated inpatients, having two doses of the Pfizer-BioNTech vaccine was the only effective protective measure against mortality; however, two doses of the CoronaVac vaccine had no significant effect in preventing fatality.

REFERENCES

1. WHO coronavirus (COVID-19) dashboard [Internet]. Geneva: World Health Organization (WHO). [cited September 02, 2022]. Available from: https://covid19.who.int/

2. Zheng C, Shao W, Chen X, Zhang B, Wang G, Zhang W. Real-world effectiveness of COVID-19 vaccines: a literature review and meta-analysis. Int J Infect Dis. 2022;114:252-60. [CrossRef]

3. Living guidance for clinical management of COVID-19 [Internet]. Geneva: World Health Organization (WHO). [cited September 02, 2022]. Available from: https://apps.who.int/iris/bitstream/handle/10665/349321/WHO-2019-nCoV-clinical-2021.2-eng.pdf

4. Kuloğlu ZE, El R, Guney-Esken G, Tok Y, Talay ZG, Barlas T, et al. Effect of BTN162b2 and CoronaVac boosters on humoral and cellular immunity of individuals previously fully vaccinated with CoronaVac against SARS-CoV-2: A longitudinal study. Allergy. 2022;77(8):2459-67. [CrossRef]

5. Mok CKP, Cohen CA, Cheng SMS, Chen C, Kwok KO, Yiu K, et al. Comparison of the immunogenicity of BNT162b2 and CoronaVac COVID-19 vaccines in Hong Kong. Respirology. 2022;27(4):301-10. [CrossRef]

6. Lim WW, Mak L, Leung GM, Cowling BJ, Peiris M. Comparative immunogenicity of mRNA and inactivated vaccines against COVID-19. Lancet Microbe. 2021;2(9):e423. [CrossRef]

7. Costa Clemens SA, Weckx L, Clemens R, Almeida Mendes AV, Ramos Souza A, Silveira MBV, et al; RHH-001 study team. Heterologous versus homologous COVID-19 booster vaccination in previous recipients of two doses of CoronaVac COVID-19 vaccine in Brazil (RHH-001): a phase 4, non-inferiority, single blind, randomised study. Lancet. 2022;399(10324):521-9. [CrossRef]

8. Marra AR, Miraglia JL, Malheiros DT, Guozhang Y, Teich VD, da Silva Victor E, et al. Effectiveness of heterologous coronavirus disease 2019 (COVID-19) vaccine booster dosing in Brazilian healthcare workers, 2021. Clin Infect Dis. 2023;76(3):e360-6. [CrossRef]

9. Toker İ, Kılınç Toker A, Turunç Özdemir A, Çelik İ, Bol O, Bülbül E. Vaccination status among patients with the need for emergency hospitalizations related to COVID-19. Am J Emerg Med. 2022;54:102-6. [CrossRef]

10. Uzun O, Akpolat T, Varol A, Turan S, Bektas SG, Cetinkaya PD, et al. COVID-19: vaccination vs. hospitalization. Infection. 2022;50(3):747-52. [CrossRef]

11. Tenforde MW, Self WH, Adams K, Gaglani M, Ginde AA, McNeal T, et al; Influenza and Other Viruses in the Acutely Ill (IVY) Network. Association between mRNA vaccination and COVID-19 hospitalization and disease severity. JAMA. 2021;326(20):2043-54. [CrossRef]

12. Aslam J, Rauf Ul Hassan M, Fatima Q, Bashir Hashmi H, Alshahrani MY, et al. Association of disease severity and death outcome with vaccination status of admitted COVID-19 patients in delta period of SARS-COV-2 in mixed variety of vaccine background. Saudi J Biol Sci. 2022;29(7):103329. [CrossRef]

13. Lopez Bernal J, Andrews N, Gower C, Robertson C, Stowe J, Tessier E, et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. BMJ. 2021;373:n1088. [CrossRef]

14. Antonelli M, Penfold RS, Merino J, Sudre CH, Molteni E, Berry S, et al. Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study. Lancet Infect Dis. 2022;22(1):43-55. [CrossRef]

15. Imam Z, Odish F, Gill I, O'Connor D, Armstrong J, Vanood A, et al. Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States. J Intern Med. 2020;288(4):469-76. [CrossRef]

16. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City Area. JAMA. 2020;323(20):2052-9. Erratum in: JAMA. 2020;323(20):2098. [CrossRef]

17. Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. BMJ. 2020;369:m1966. [CrossRef]

18. Liu C, Zhao Y, Okwan-Duodu D, Basho R, Cui X. COVID-19 in cancer patients: risk, clinical features, and management. Cancer Biol Med. 2020;17(3):519-27. [CrossRef]

19 Jdiaa SS, Mansour R, El Alayli A, Gautam A, Thomas P, Mustafa RA. COVID-19 and chronic kidney disease: an updated overview of reviews. J Nephrol. 2022;35(1):69-85. [CrossRef]

20 Tadic M, Cuspidi C, Grassi G, Mancia G. COVID-19 and arterial hypertension: Hypothesis or evidence? J Clin Hypertens (Greenwich). 2020;22(7):1120-6. [CrossRef]

21 Zhou Y, Chi J, Lv W, Wang Y. Obesity and diabetes as high-risk factors for severe coronavirus disease 2019 (Covid-19). Diabetes Metab Res Rev. 2021;37(2):e3377. [CrossRef]

22 Mahamat-Saleh Y, Fiolet T, Rebeaud ME, Mulot M, Guihur A, El Fatouhi D, et al. Diabetes, hypertension, body mass index, smoking and COVID-19-related mortality: a systematic review and meta-analysis of observational studies. BMJ Open. 2021;11(10):e052777. [CrossRef]

23 Yu X, Qi X, Cao Y, Li P, Lu L, Wang P, et al. Three doses of an inactivation-based COVID-19 vaccine induces cross-neutralizing immunity against the SARS CoV-2 Omicron variant. Emerg Microbes Infect. 2022;11(1):749-52. [CrossRef]

24 Xu H, Li H, You H, Zhang P, Li N, Jiang N, et al. Effectiveness of inactivated COVID-19 vaccines against mild disease, pneumonia, and severe disease among persons infected with SARS-CoV-2 Omicron variant: real-world study in Jilin Province, China. Emerg Microbes Infect. 2023;12(1):2149935. [CrossRef]