

The Influence of SARS-CoV-2 Vaccination on 28-Day Mortality and Hospitalization Rate of COVID-19 Patients Age between 18-40 Years**

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ABSTRACT:

Purpose: The purpose of our research is to determine the protective impact of CoronaVac vaccine in individuals under the age of 40 and over the age of 18 who have had COVID-19 infection.

Material and Methods: Patients aged 18-40 years who applied to our hospital with COVID-19 + as a test were divided into two groups according to their CoronaVac vaccine status, and the morbidity and mortality of the patients were investigated.

Results: In the present research, the total mortality ratio in the unvaccinated patient group was 8.2%, while the overall mortality rate in the patient group vaccinated was 0% (p = .043).

Conclusion: The 0% mortality rate in persons who received two doses of CoronaVac vaccine clearly shows the effect of the vaccine on mortality.

Keywords: CoronaVac, Age, Vaccine

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INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was defined in China in December 2019 and announced as a pandemic by the World Health Organization on March 11, 2020. By April 11, 2022, there were 494 million infected patients and more than 6 million deaths caused by COVID-19 (World Health Organization, 2022a). COVID-19 disease can progress with different clinical symptoms, which are defined in several clinical studies; the most common findings are cough, fever, myalgia, dyspnea, anosmia, headache, and sore throat. In a study of critically ill people, it was found that more more than 50% for consistency of the cases had a high fever, and about 80% had cough and

shortness of breath during their stay in intensive care. On the other hand, symptoms such as fever, cough, sore throat appeared in 40% of subclinical cases. But it has been shown that none of them have dyspnea (Song et al., 2020). Depending on the clinic of the COVID-19 disease, normal or near-normal moderate changes may be observed in laboratory findings. In meta-analysis studies, laboratory findings revealed that C-reactive protein (CRP) was high in COVID-19 infection, low albumin, high erythrocyte sedimentation rate (ESR), decreased eosinophil count, lymphopenia, and rised interleukin-6 (IL-6) and lactate dehydrogenase (LDH) levels (Zhang et al., 2020). Many COVID-19 vaccines have been proven protective in the literature, and

many are widely used around the world. In April 2022, statistics showed that more than 11.25 billion doses of vaccine have been implemented against SARS-CoV-2 all over the World (Vasileiou et al., 2021). CoronaVac, was confirmed for emergency utilization in 22 countries by April 28, 2021 (Gao et al., 2020; McGill COVID19 Vaccine Tracker Team., 2021). CoronaVac has sufficient impact on both symptomatic SARS-CoV-2 infection and serious COVID-19 and has been safe among a group aged between 18 and 59 years (Gao et al., 2020). A research conducted in Tennessee, USA indicated a decrease of bigger than 95% in mortality in the vaccinated aged individuals between December 2020 and March 2021 (Roghani, 2021). It is known that morbidity and mortality in COVID-19 are less common in the younger age population. Based on this, our aim was to examine the influence of the vaccine on morbidity and mortality in individuals aged between 18-40 years who were vaccinated (two doses of CoronaVac) and the cases who were not.

MATERIAL and METHODS

Purpose and Type of the Study

The purpose of our research is to determine the protective impact of CoronaVac vaccine in individuals under the age of 40 and over the age of 18 who have had COVID-19 infection.

Sampling and Participant

Patients with the oropharyngeal/nasopharyngeal swab samples for A real-time reverse transcription–polymerase chain reaction (RT-PCR) COVID-19 + were examined. Our patients were separated into two groups as those who received 2 doses of CoronaVac and 14 days past the vaccine, and those who have never been vaccinated towards COVID-19. Patients who received a single dose of vaccine and were admitted to the hospital within 14 days after vaccination were excluded from the study. Gender, at least one comorbidity, Comorbid diseases, Vaccination status. Hospitalization status, radiologic lung involvement, at admission Hospitalization status, ICU admission, Invasive mechanical ventilation requirement, Mortality were evaluated. In addition, blood Urea, Creatinine, aspartate

transaminase (AST), alanine aminotransferase (ALT), LDH, Albumin, Ferritin, White blood cells, Neutrophils, Lymphocytes, C-reactive protein (CRP), procalcitonin (PCT), D-Dimer values were analysed through patient files and hospital data system.

Data Collection Tools

Since our study was planned retrospectively, patient consent was not required. Between July 2021 and January 2022, a total of 276 COVID-19 cases aged 18-40 years who were referred to Malatya Training and Research Hospital were included in the study.

Statistical Analysis

The data gained from the hospital database were edited and converted into Microsoft Excel tables, and the findings of the study were appraised. Statistical Package for Social Sciences (SPSS) version 23.0 for Windows was utilized for statistical analysis. The dispersion of variants was checked with Shapiro Wilk. Normally distributed data are given as mean \pm standard deviation; non-normally distributed data are given as median (min–max) values, as well as numbers and percentages. In the study, the t-test was utilized for the analysis of independent variables in the analysis of parametric data, the Mann-Whitney U test was utilized for the analysis of non-parametric data, and the Chi-Square test was utilized for the analysis of categorical data. Independent variables related to hospitalization in the univariate analysis were examined using multivariate logistic regression models. The odds ratio (OR) and 95% confidence interval (CI) were obtained using the “Enter” method. Outcomes were analysed at the 95% CI and significance level of $p < .05$.

Ethical Approval

This present study was planned retrospectively. Malatya Turgut Ozal University clinical research ethics committee approval numbered 2021/105 was obtained.

RESULTS

Between July 2021 and January 2022, a total of 276 COVID-19 patients age between 18- 40 years who were consulted to Malatya Training and Research Hospital were included in the study. The number of

male cases was 149 (54.0%) (female 127, 46.0 %), and the mean age was 31.31 ± 8.58 years in the all cases. Among the study patients, 38 (13.8%) had at least one comorbid disease; the most common comorbidities were diabetes mellitus (5.4%), chronic renal failure (2.5%), and asthma (1.8%). When the thorax computed tomography (CT) scans of the study population were evaluated in terms of lung involvement, it was determined that 170 (61.6%) of the cases had radiological involvement typical of COVID-19. Moreover, it was determined that 230 (83.3%) of the patients admitted to the hospital were unvaccinated, and 46 (16.7%) were vaccinated with two doses of CoronaVac (fully vaccinated) (Table 1). The number of male patients was 149 (54.0%) (female 127, 46.0 %), and the mean age was $31.31 \pm$

8.58 years in the all cases. Among the study patients, 38 (13.8%) had at least one comorbid disease; the most common comorbidities were diabetes mellitus (5.4%), chronic renal failure (2.5%), and asthma (1.8%). The study population was grouped as fully vaccinated (n=46) and unvaccinated (n=230). While no difference was obtained among the groups in terms of the frequency of comorbid disease and lung involvement, the mean age of the unvaccinated patients was lower than that of the patients who received two doses of CoronaVac ($p < .001$). The hospitalization rate was determined to be statistically significantly higher in the unvaccinated patient group than in the patient group vaccinated with two doses of CoronaVac ($p = .035$).

Table 1. Study population (n=276)

		%	n
Gender	Male	%54.0	149
	Female	%46.0	127
At least one comorbidity	Yes	%12.6	35
	No	%87.4	241
Comorbid diseases	Diabetes mellitus	%5.4	15
	Chronic kidney disease	%2.5	7
	Asthma	%1.8	5
	Hypertension	%1.4	4
	Rheumatic disorders	%0.7	2
	Chronic heart failure	%0.4	1
	Epilepsy	%0.4	1
Vaccination status	Fully vaccinated	%16.7	46
	Unvaccinated	%83.3	230
Hospitalization status	Yes	%53.3	147
	No	%46.7	129

Age; Mean \pm SD ; 31.31 ± 8.58

However, when the comparison of respiratory support, none of the patients in the patient group vaccinated with two doses of CoronaVac was provided with invasive mechanical ventilation and respiratory support; however, invasive mechanical ventilation support was applied to 8.2% of the patients in the unvaccinated patient group ($p = .043$). In addition, the overall mortality rate in the unvaccinated patient group was 8.2%, while the overall mortality rate in the patient group vaccinated with two doses of CoronaVac was 0% ($p = .043$) (Table 2).

When the laboratory data of the two groups were compared, it was found that the serum LDH, ferritin,

CRP and PCT levels at the time of admission to the hospital were statistically significantly higher in the unvaccinated patient group ($p = .009$, $p = .003$, $p < .001$, $p = .001$) (Table 3).

Hospitalized and non-hospitalized patients were evaluated in the study. In the hospitalized group, the vaccination rate was lower (39.1% vs. 56.0%, $p = .035$), the frequency of comorbid diseases was higher (23.1% vs. 3.1%, $p < .001$), and the frequency of cases with lung involvement on thorax CT was higher (85.0% vs. 34.8%, $p < .001$).

Table 2. Comparison of study population demographic and clinical data by vaccination status

	Unvaccinated (n=230)		Fully vaccinated (n=46)		p	
Mean age (Me±SD)	30.45±8.79		35.63±5.77		<0.001*	
	%	n	%	n		
Gender	Male	% 57.3	132	%36.9	17	0.011
	Female	%42.7	98	%63.1	29	
At least one comorbidity	Yes	%12.6	29	%13.0	6	0.876
	No	%87.4	201	%87	40	
Radiologic lung involvement at admission	Yes	%63.9	147	%50.0	23	0.077
	No	%36.1	83	%50.0	23	
Hospitalization status	Yes	%56.0	129	%39.1	18	0.035
	No	%44.0	101	%60.9	28	
ICU admission	Yes	%11.3	26	%2.1	1	0.057
	No	% 88.7	204	%97.9	45	
Invasive mechanical ventilation requirement	Yes	%8.2	19	%0	0	0.043**
	No	%91.8	211	%100	46	
Mortality	Yes	%8.2	19	%0	0	0.043**
	No	%91.8	211	%100	46	

Me: mean, SD: standard deviation, ICU: intensive care unit, * Independent sample t test, Chi-squared test

Table 3. Laboratory outcomes of the patients

	Unvaccinated (n=230)	Fully vaccinated (n=46)	p
Urea, mg/dL Median (min-max)	24 (15-239)	21 (10-105)	0.037*
Creatinin, mg/dL Median (min-max)	0.80 (0.50-2.30)	0.75 (0.55-1.67)	0.168*
AST, U/L Median (min-max)	28 (1-301)	21 (11-154)	0.008*
ALT, U/L Median (min-max)	28 (2-770)	27 (7-288)	0.578*
LDH, IU/L Median (min-max)	301 (30-1425)	234 (130-662)	0.009*
Albumin, g/dL (Me±SD)	3.58±0.71	3.53±0.86	0.714
Ferritin, ng/dL (Me±SD)	467±110	228±337	0.003
White blood cells, mm ³ Median (min-max)	7000 (3100-27500)	7200 (3300-18900)	0.960*
Neutrophils, mm ³ Median (min-max)	4540 (370-29160)	4650 (1540-16360)	0.626*
Lymphocytes, mm ³ Median (min-max)	1450 (200-8660)	1630 (350-3590)	0.526*
CRP, mg/dL (Me±SD)	5.17±7.31	1.38±2.29	<0.001
PCT, ng/mL Median (min-max)	0.08 (0.01-36.90)	0.04 (0.01-0.25)	0.001*
D-Dimer, µg/mL Median (min-max)	0.33 (0.05-21.00)	0.28 (0.04-12.90)	0.410*

AST: aspartate aminotransferase, LDH: lactate dehydrogenase, PCT: procalcitonin, ALT: alanine transaminase, Min: minimum, Max: maximum, Me: mean, SD: standard deviation, CRP: C-reactive protein, * Mann-Whitney U test, Independent sample t test

In addition, the mean age and serum LDH, ferritin, and CRP levels of the patients who were hospitalized were detected to be statistically significantly higher at the time of admission ($p < 0.001$, $p < 0.001$, $p = .020$, $p < .001$). However, it was determined that the most important risk factor for hospitalization was the presence of pneumonic infiltration on thorax CT (OR: 6.06, 95% CI: 2.609–14.075, $p < .001$).

DISCUSSION

Vaccination is the most effectual way of defence against COVID-19. Persons under the age of 40, who have a lower risk of mortality than the general population, may die from COVID-19. In our study, the CoronaVac vaccine was found to be effective in reducing mortality and morbidity in this patient population. SARS-CoV-2 vaccines may be able to decrease the disease incidence and as well as transmission in a population. Vaccination is thus a critical step in controlling the transmission chain of SARS-CoV-2 infections. It is also necessary to decrease both morbidity and mortality due to SARS-CoV-2 (Hodgson et al., 2021). Our study revealed that the clinical course of vaccinated individuals under the age of 40 was mostly mild, pulmonary involvement was rare or absent, and mortality was not observed. Although the clinic of the patient who develops due to COVID-19 varies from patient to patient, the most frequent clinical findings are fever, weakness, sputum, nausea, and shortness of breath, and vary according to the stages of the disease. The disease is most commonly associated with respiratory tract infections, such as pneumonia, colds, and flu (Hussin et al., 2020). Associated with the disease are thromboembolic processes as a result of mucosal damage and/or vasculitis due to virus inoculation, cardiovascular (Myocardial infarction (MI), myocarditis, pericarditis), digestive (anosmia, diarrhea, ischemic colitis, hepatitis, thyroiditis), central nervous system (encephalitis, stroke, Cerebrovascular disease SVD), urinary (various findings and complications may develop in different systems such as acute renal failure), urogenital (estrogen, testosterone hormone level imbalances). Susceptibility to venous hypercoagulability is increase (Chaimayo et al., 2020).

SARS-CoV-2 is believed to mainly infect the respiratory system, inducing inflammation, interstitial injury, alterations in the parenchyma, and cell death (Ye et al., 2020). The most frequent CT finding of COVID-19 pneumonia is ground glass opacities, and its typical model has been reported as bilateral, peripheral, multilobar, and posterior localization (Hani et al., 2020). Ground glass opacity can be seen alone or in conjunction with different findings, such as consolidation, interlobular septal thickening, and vascular dilatation (Cömert and Kırıl, 2020). Consolidations are typically multifocal, segmental, patchy, mostly located in the lower lobe and peripheral and may include air bronchograms (Eastin and Eastin, 2020). Pan et al. found that consolidation was rare in the early stages and that the consolidations widened and diffused in the later stages (Pan et al., 2020). While consolidations are more common, severe, and fatal among those with chronic diseases (diabetes, chronic heart and lung disease, chronic kidney and liver disease, immunosuppressive disease, or treatment), obese, pregnant, and postpartum women, it progresses less and much milder in the pediatric age group (Liu et al., 2020). When CT scans were analyzed for lung involvement, it was determined that 170 (61.6%) of our cases had radiological involvement typical of COVID-19. While pulmonary involvement was 50.0% in the vaccinated group, it was 63.9% in the unvaccinated group. However, it should be noted that many people survive the disease asymptotically (Diken, 2021). Responses to vaccines may differ in younger adults from older adults due to the aging of their immune systems (Chen, 2021). Phase 1/2 CoronaVac trials in volunteers aged 18-59 years and over 60 years indicated that the vaccine doses and schedules studied (3 µg or 6 µg, administered 14 days or 28 days apart) all had analogous safety and immunogenicity (Zhang et al., 2021). Different efficacy rates were discovered in studies evaluating CoronaVac vaccine efficacy based on age groups. The CoronaVac vaccine provided 83.5% protection towards symptomatic infection compared to a placebo in a study conducted in Turkey among volunteers aged 18-59 (Tanrıover et al., 2021). WHO data shows that as of 08.05.2022,

15.038.495 cases were seen in our country, and 98.819 people died. The total vaccine dose is 147, 426, 248 (World Health Organization, 2022b). The Chile study found 65.9% efficacy for symptomatic infection, 87.5% for hospitalization, 90.3% for intensive care unit admission, and 86.3% for death (Jara et al., 202). In the Brazilian study, the efficacy of CoronaVac towards symptomatic COVID-19 was 50.7%, moderate and severe cases (score ≥ 4) 83.7% (95% CI 58.0-93.7), and 100% (95% CI 563.4-1000.0), respectively (Palacios et al., 2021). The CoronaVac vaccine has been proven to be 51% effective in symptomatic infections. It has also been detected to be 100% protective against hospitalization and serious diseases (World Health Organization, 2022c). When our patients were compared based on their vaccination status, the rate of hospitalization was observed to be statistically significantly higher in the unvaccinated patient group than in the patient group vaccinated with two doses of CoronaVac ($p = 0.035$). While vaccination continues in the areas of the world where the COVID-19 pandemic persists, studies have focused on the decrease in immunity with two doses of vaccination over time and the necessity of a third-dose vaccination (Wilder-Smith and Mulholland, 2021). It is emphasized that the third vaccination dose produces more neutralizing antibodies (Yorsaeng et al., 2022). Recent data have raised several concerns that the immunity developed by two doses of vaccination towards COVID-19 diminishes over time, concluding in decreased protection towards SARS-CoV-2, raising the question of whether a third dose would be necessary for an extended period (Wilder-Smith and Mulholland, 2021).

We concluded that the vaccine's effect persisted because the period between our patients in the vaccinated group and the time of infection was less than four months. Advanced age, male gender, and the existence of at least one comorbidity have been declared to be independently related to mortality among COVID-19 cases (Fang et al., 2020). DM (5.4%), chronic renal failure (2.5%) and asthma (1.8%) were the most frequent comorbidities in our patient group. The COVID-19 mortality rate is estimated to be 2.34%. When only hospitalized cases are considered, the COVID-19 mortality rate rises to

an estimated 14%, approaching the overall SARS case mortality rate of around 15% (18). While 20% of infected patients require hospitalization, 5% need intensive care and mechanical ventilation (Amato et al., 2021). When our patients were compared in terms of respiratory support; While none of the patients in the patient group who received two doses of CoronaVac were provided with invasive mechanical ventilation and respiratory support; Invasive mechanical ventilation support was applied to 8.2% of the cases in the unvaccinated patient group ($p = 0.043$). In a study carried out with COVID-19 cases in the intensive care unit, the mortality ratio was found to be 40.8% (Ganesan et al., 2021). In the present analysis, the total mortality ratio in the unvaccinated patient group was 8.2%, while the overall mortality rate in the patient group vaccinated with two doses of CoronaVac was 0%. Studies indicate that the lymphopenia observed in patients may be related to disease seriousness and mortality in critical COVID-19 cases (Yang et al., 2020). Furthermore, when the laboratory data of the groups at the time of hospitalization were compared, it was discovered that the serum LDH, ferritin, CRP, and PCT levels were statistically significantly higher in the unvaccinated patient group at the time of hospitalization.

Limitation of the Research

This present study has some limitations. First, our study was conducted in a single center. The antibody titers of subsequently vaccinated cases were unknown.

CONCLUSION

Persons who received two doses of the CoronaVac vaccine had a lower disease effect in terms of both laboratory results and lung involvement. As a result, there is less need for intensive care. In terms of mortality, no patient died in the vaccinated group, while 19 patients died in the unvaccinated group, demonstrating that the two doses of the CoronaVac vaccine are quite effectual towards the disease.

Conflict of Interest

The authors declare that there is no conflict of interests.

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