Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1176884
J Health Sci Med 2023; 6(1): 7-12

Effect of vaccine on prognosis and mortality in COVID-19

Selda Tekin[1], Nilüfer Coşkun[1], Esra Adıyeke[1], Erman Şen[1], Özgün Topçuoğlu Sarı[1], Mücahit Uğur Aygün[1], Ayşe Şabablı Çetin[2], Fatma Yılmaz Karadağ[2], Nurten Bakan[1]

[1]Department of Anesthesiology and Reanimation, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital, University of Health Sciences, İstanbul, Turkey
[2]Department of Infectious Disease and Clinic Microbiology, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital, University of Health Sciences, İstanbul, Turkey

Cite this article as: Tekin S, Coşkun N, Adıyeke E, et al. Effect of vaccine on prognosis and mortality in COVID-19. J Health Sci Med 2023; 6(1): 7-12.

ABSTRACT

Aim: The aim of our study is to reveal the factors affecting the clinical course of COVID-19 infection and mortality in immune and non-immune patients aged 65 and over.

Material and Method: The study was carried out by scanning the files of a total of 1,642 COVID-19 cases aged 65 and over. The 1337 cases included in the study were divided into two groups as follows: patients who were vaccinated with the 2nd dose of CoronaVac but became infected with COVID-19 after the 14-day period in which immunization should develop (Group I) and the others who were unvaccinated, or infected with COVID-19 after a single dose of vaccination or infected after receiving a 2nd dose of vaccination in 14 days (Group II). The groups were compared with each other about mortality and the factors affecting mortality.

Results: The length of intensive care unit (ICU) stay, and the total length of hospital stay were significantly longer in Group II than Group I ($p<0.05$). The need for mechanical ventilation (MV) and the length of MV were also significantly higher in Group II than Group I ($p<0.05$). All patients enrolled in the study had lung involvement. The percentage of Computed tomography (CT) involvement over 50% was statistically significant in Group II ($p<0.05$). The percentage of severe and critically severe patients and mortality were significantly high in Group II vs. Group I ($p<0.05$).

Conclusion: When we compared the vaccinated and unvaccinated groups of 65 years of age, we found that hospitalization in the ICU and the need for MV increased mortality, and the vaccine reduced the need for intensive care and MV.

Keywords: Vaccine, COVID-19, elder age

Our research's data was presented in Antalya, TARK 55. National Congress as 'Oral Presentation' in October 2021.

INTRODUCTION

The COVID-19 infection is a fatal disease that has become a serious health problem for the whole world in the last 1.5 years, for which no definitive treatment has been found yet, and early diagnosis and early isolation are the most important subjects (1). Considering the fact that the persons who pulled through the disease with mild symptoms or no symptoms at all are the secret porters in the spread of the viral genome, it is obvious that the immunization plays a crucial role in protection from the disease (2).

Since the beginning of the pandemic, protein subunit vaccines, viral vector vaccines, m-RNA vaccines, and DNA vaccines have been, and continue to be, researched and developed in numerous centers to ensure immunity to the COVID-19 infection (3).

One of these vaccines, and the first one coming to our country, the CoronaVac vaccine is an inactivated vaccine, demonstrated in the research made to be inducing the neutralizing antibodies specific to SARS-COV-2 in mice, rats, non-human primates, and macaques. The Phase 1 and Phase 2 clinical studies conducted on healthy individuals between the ages of 18 and 59 and over 60 have demonstrated that the CoronaVac has been tolerated well and not caused dose-related safety concerns. The Phase 2 studies have demonstrated that the neutralizing antibodies have developed on day 14 and later following the 2nd dose of vaccination applied in divided doses. After 3 mcg doses administered on day 0 and 28, the seroconversion ratio of neutralizing antibodies detected in patients above 65 years was 94% (4).

Corresponding Author: Selda Tekin, selda-dikmen@hotmail.com
Received: 18.09.2022 **Accepted:** 25.10.2022

This work is licensed under a Creative Commons Attribution 4.0 International License.

Following the Emergency Use Authorization given in our country on January 13, 2021, the CoronaVac vaccine was administered first to the healthcare personnel designated as the high-priority group, then to the elderly patients group in which the infection could be the most severe and fatal and has been continued gradually. It has been administered in two divided doses (5).

The disease may either have an asymptomatic course or manifest itself with the mild upper respiratory tract infection symptoms like diminished taste and smell perception, back pain, joint pain, fatigue, fever, or with pneumonia, sepsis, septic shock, multiple organ dysfunction syndrome (6). It has been demonstrated that the old age, the presence of comorbid systemic diseases like chronic obstructive pulmonary disease (COPD), hypertension, cardiac disease, and the presence of lung involvement are closely related to poor prognosis and mortality (7).

The purpose of our study is to reveal the effect of the vaccine on prognosis and mortality by comparing vaccinated with CoronaVac and not vaccinated or vaccinated but deemed non-immune, ≥65 years COVID-19 patients which we have been followed in the services and ICU (intensive care units) of our hospital.

MATERIAL AND METHOD

The study was carried out with the permission of Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Scientific Researches Ethics Committee (Date: 23.06.2021, Decision No: 2021/178-23.06.2021). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The research planned as a retrospective clinical study and approved by the Ministry and the local ethics committee was conducted by screening the files of totally 1,642 65-year-old and older COVID- 19 cases monitored and treated in the relevant services and ICU of our hospital due to COVID-19 infection between the dates of 1 March 2021 and 15 May 2021. 305 patients excluded from the study for improvability by positive PCR result, treatment refusal of patient, referral to another center and hospitalization during data collection. 1,337 patients' vaccination details included in the study were recorded. The cases were examined in 2 groups: The COVID-19 patients vaccinated with the 2nd dose of CoronaVac but infected with after the 14-day period were defined as Group I (immunized), and unvaccinated, or vaccinated with a single dose, or 2 dose vaccinated but infected in 14 days after second dose vaccination as Group II (non-immunized) (**Figure 1**).

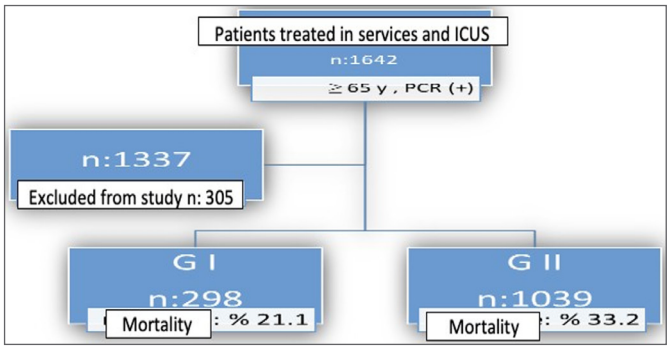

Figure 1. Study flow chart

In both groups' cases age, gender, comorbid diseases, lung involvement data according to pulmonary CT (Computed tomography) (its presence, being unilateral or bilateral, percentage) were recorded from patient's files. And also, for ICU patients, the number of transfers from the relevant service to ICU or direct ICU admissions, length of ICU stay, total length of hospital stay were noted. If ICU patients needed mechanical ventilation (MV), these patients' length of MV, and their exit methods were noted down. The mortality rate (the rate of the number of exitus cases to the number of inpatients for each group) was calculated for both groups.

All patients were categorized according to the disease severity scale against their clinical states and laboratory parameters. (Mild disease: symptomatic patients without radiographic findings; moderate disease: patients with fever, respiratory findings, and radiographically low lung involvement; severe disease: patients with dyspnea and respiratory distress, respiratory rate over 30, $PaO_2/FiO_2<300$, $SpO_2<90\%$ despite the oxygen therapy of 5 l/min; critical disease: respiratory failure, septic shock, and multiple organ dysfunction syndrome (8).

Our clinic has standard criteria for ICU admission: dyspnea and respiratory distress, respiratory rate over 30, $PaO_2/FiO_2<300$, $SpO_2<90\%$ or $PaO_2<70$ mmHg despite the oxygen therapy of 5 l/min, hypotension, development of acute organ failure, high lactate levels, arrhythmia, confusion, skin disorders such as capillary return disorder and cutis marmaratus, and immunosuppression.

Statistical Analysis

During evaluation of the results of the study, IBM SPSS Statistics 22 (IBM SPSS, Turkey) software was used for the statistical analyses. The Kolmogorov-Smirnov and Shapiro-Wilks tests were used to assess the compliance of the parameters with normal distribution; and it was found out that the distribution of the parameters was not normal. During evaluation of the study data, the Mann Whitney U test was used to compare quantitative data in addition to the descriptive statistical methods (Mean, Standard deviation, frequency). The Chi-Square test,

Fisher's Exact Chi-Square test, and the Continuity (Yates) correction were used to compare the qualitative data. The logistic analysis was used for the multivariate analysis. The significance level was p<0.05.

RESULTS

The study was conducted on 1337 cases in total; 631 males (47.2%) and 706 females (52.8%), between the ages of 65 and 99. The mean age was 75.0±7.99 years. Of the cases, 298 patients (22.3%) were immunized whereas 1,039 (77.7%) patients were non-immunized. The rate of male cases (p:0.001; p<0.05) and the mean age (p:0.001; p<0.05) were statistically significantly higher in Group I vs. Group II.

Table 1. The age- and gender-specific evaluation of groups

	Group I (n=298)	Group II (n=1039)	Total (n=1337)	p
Gender n (%)				
Male	168 (56.4%)	463 (44.6%)	631 (47.2%)	[1]0.001*
Female	130 (43.6%)	576 (55.4%)	706 (52.8%)	[2]0.001*
Age Mean±SD (median)	76.45±7.64 (76)	74.58±8.04 (73)	75.0±7.99 (74)	

[1]Chi-square test, [2]Mann Whitney U Test, *p<0.05 Group I: Immune Group II: Non-immunized

Transfer from service to ICU and direct ICU admission were significantly higher in Group II (p<0.05).

The length of ICU stays, and the total length of hospital stay were significantly longer in Group II vs. Group I (p<0.05).

The need for MV and the length of MV were also significantly higher in Group II (p<0.05) (**Table 2**). All patients enrolled in the study had lung involvement. It was lower than 50% in 61.7% of the cases in Group I, and higher than 50% in 62.4% of the cases in Group II. The percentage of CT involvement over 50% was statistically significant in Group II (p<0.05).

Table 2: Evaluations of groups

	Group I (n=298)	Group II (n=1039)	Total (n=1337)	p
Direct ICU admissionn (%)	81 (27.2%)	405 (39%)	486 (36.4%)	*[1]0.001
Transfer from Service to ICUn (%)	48 (16.1%)	298 (28.7%)	346 (25.9%)	*[1]0.001
Length of ICU stay Mean±SD (median)	2.29±4.96 (0)	3.94±8.11 (0)	3.58±7.56 (0)	*[2]0.001
Total length of hospital stay Mean±SD (median)	10.05±6.37 (9)	11.61±9.08 (9)	11.26±8.57 (9)	*[2]0.026
Need for MVn (%)	69 (23.2%)	335 (32.2%)	404 (30.2%)	*[1]0.003
Length of MV Mean±SD (median)	1.29±33.36 (0)	2.59±6.64 (0)	2.30±6.09 (0)	*[2]0.001

[1]Chi-square test, [2]Mann Whitney U Test, *p<0.05, ICU: Intensive care unit, MV: Mechanical ventilation

The rates of diabetes (DM), hypertension (HT), chronic renal failure (CRF), hyperlipidemia (HL), and cancer were higher in Group I (p<0.05). HT, DM, and coronary artery disease (CAD) were the top 3 comorbid diseases.

The rate (38.3%) of 3 and more comorbid systemic diseases in Group I was statistically significantly higher than Group II (30.9%) (p:0.017; p<0.05).

The rates of severe and critically severe patients and mortality were significantly higher in Group II vs. Group I (p<0.05) (**Table 3**).

Table 3: Evaluations of lung involvement and clinical data by groups

	Group I (n=298) n (%)	Group II (n=1039) n (%)	Total (n=1337) n (%)	p
CT finding				
Below 50%	184 (61.7%)	391 (37.6%)	575 (43%)	
Over 50%	114 (38.3%)	648 (62.4%)	762 (57%)	[1]0.001*
Comorbid diseases				
DM	141 (47.3%)	376 (36.2%)	517 (38.7%)	[1]0.001*
HT	206 (69.1%)	627 (60.3%)	833 (62.3%)	[1]0.006*
CAD	79 (26.5%)	294 (28.3%)	373 (27.9%)	[1]0.544
CRF	53 (17.8%)	96 (9.2%)	149 (11.1%)	[1]0.001*
COPD	44 (14.8%)	195 (18.8%)	239 (17.9%)	[1]0.112
HL	23 (7.7%)	40 (3.8%)	63 (4.7%)	[1]0.005*
CVD	17 (5.7%)	57 (5.5%)	74 (5.5%)	[2]0.999
Alzheimer	23 (7.7%)	56 (5.4%)	79 (5.9%)	[1]0.133
HF	33 (11.1%)	101 (9.7%)	134 (10%)	[1]0.493
Cancer	24 (8.1%)	48 (4.6%)	72 (5.4%)	[1]0.021*
Number of comorbid diseases				
Below 3	184 (61.7%)	718 (69.1%)	902 (67.5%)	
≥3	114 (38.3%)	321 (30.9%)	435 (32.5%)	[1]0.017*
Outcomes				
Discharged	235 (78.9%)	694 (66.8%)	929 (69.5%)	
Exitus	63 (21.1%)	345 (33.2%)	408 (30.5%)	[1]0.001*
Severity of disease				
Mild	96 (32.2%)	301 (29%)	397 (29.7%)	
Moderate	110 (36.9%)	244 (23.5%)	354 (26.5%)	
Severe	27 (9.1%)	152 (14.6%)	179 (13.4%)	[1]0.001*
Critical	65 (21.8%)	342 (32.9%)	407 (30.4%)	[1]0.001*

[1]Chi-square test, [2]Continuity (Yates) correction, *p<0.05, CT: Computed tomography, DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, CRF: Chronic renal failure, COPD: Chronic obstructive pulmonary disease, HL: Hyperlipidemia, CVD: Cerebrovascular disease, HF: Hearth failure

In consequence of an examination of the prognostic factors (need for MV, CT involvement, ICU admission, Pulmonary Embolism (PE)) we considered to have potential impacts on mortality; in Group I, the mortality rate was significantly high among the patients who needed MV, had over 50% CT finding, were admitted to ICU, and developed PE (p<0.05) (**Figure 2**). There was no statistically significant difference between the number of comorbid diseases and the mortality rates (p>0.05).

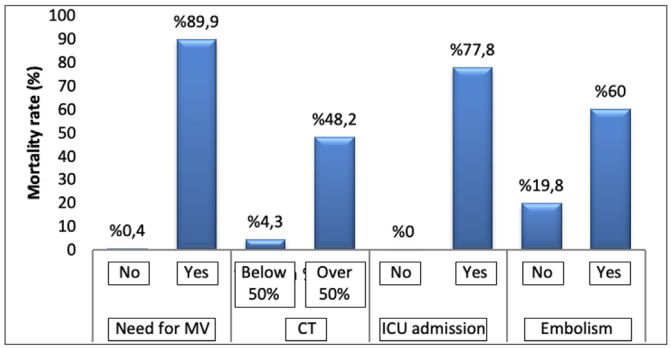

Figure 2. Evaluations of mortality in Group I

When we evaluated the effects of the parameters affecting mortality in the vaccinated cases significantly such as age, need for MV, CT finding, and ICU admission by Backward stepwise logistic regression analysis, we saw that the model was significant (p:0.001; p<0.05), the Nagelkerke R-square value was 0.897, and the exploratory factor of the model was good (97.3%). The effects of the parameters such as the need for MV and ICU admission on the model were found statistically important (p<0.05) (**Table 4**). It was seen that the need for MV increased the mortality rate by 93.25 times, and ICU admission by 30.274 times.

Table 4: Evaluation of parameters affecting mortality in vaccinated group significantly by logistic regression analysis

Vaccinated	OR	95% C.I.for OR		p
		Lower	Upper	
Step 3a				
Need for MV	93.25	14.253	610.09	0.000*
ICU admission	30.274	2.564	357.389	0.007*

aVariable(s) entered on step 1: Need for MV, CT finding, ICU admission, PE., MV: Mechanical ventilation, ICU: Intensive care unit CT: Computed tomography PE:Pulmonary emboli

In consequence of an examination of the prognostic factors (need for MV, CT involvement, ICU admission, PE) we considered to have potential impacts on mortality; in Group II, the mortality rate was high among the patients who needed MV, were admitted to ICU, and had over 50% CT involvement (p<0.05).

The mortality rate among the patients who needed MV (97%) was statistically significantly higher than the patients who did not MV (2.8%) (p:0.001; p<0.05). The mortality rate among the patients who were admitted to ICU (82%) was statistically significantly higher than the patients who were not admitted to ICU (2.1%) (p:0.001; p<0.05). There was no statistically significant difference between the mortality rates and the presence of PE (p>0.05).

The mortality rate among the patients who had minimum three comorbid diseases (38.6%) was statistically significantly higher than the patients who had less than three comorbid diseases (30.8%) (p:0.013; p<0.05).

Table 5: Evaluations of mortality in Group II

Without vaccination	Outcomes		p
	Discharged n (%)	Exitus n (%)	
Need for MV			[1]0.001*
No	684 (97.2%)	20 (2.8%)	
Yes	10 (3%)	325 (97%)	
ICU admission			[1]0.001*
No	621 (97.9%)	13 (2.1%)	
Yes	73 (18%)	332 (82%)	
PE			[1]0.844
No	671 (66.9%)	332 (33.1%)	
Yes	23 (63.9%)	13 (36.1%)	
CT			[2]0.001*
Below 50%	338 (86.4%)	53 (13.6%)	
Over 50%	356 (54.9%)	292 (45.1%)	
Number of comorbid diseases			[2]0.013*
Below 3	497 (69.2%)	221 (30.8%)	
≥3	197 (61.4%)	124 (38.6%)	

[1]Continuity (Yates) correction, [2]Chi-square test, *p<0.05, MV: Mechanical ventilation, ICU: Intensive care unit CT: Computed tomography PE:Pulmonary emboli

DISCUSSION

Many studies have demonstrated that the old-age is a strong risk factor for the poor prognosis cases such as severe disease, hospitalization, ICU admission, and death in the course of COVID-19 infection (9, 10). The purpose of our study is to reveal the factors affecting the clinical course of the COVID-19 infection and mortality in the immunized and non-immunized 65-year-old and older patients. In consequence, we have found out that the need for intensive care and MV increases the mortality, that the vaccination reduces the need for intensive care and MV, and that the persons not vaccinated have more lung involvement and a more severe course of the disease.

Regardless of the factor (viral & bacterial & fungal…), bronchopneumonia is generally severe for elder patients. The changes in the lung parenchyma, decreasing compliance, chest wall deformities developing in old age increases the patient's respiratory workload during bronchopneumonia. In case of accompanying comorbidity especially, the functionality may decrease more and cause respiratory failure, and ICU monitoring may become necessary (11). A study conducted by Richardson et al. (12) had examined 5,700 inpatients monitored due to the COVID-19 infection; of these patients, 14.2% with a mean age of 68 had needed ICU treatment. The most frequently seen comorbidities in the hospitals were DM, HT, and obesity. In our study, the ICU admission rates, and ICU stay lengths of the immunized 65-year-old and older cases were statistically significantly lower than the non-immunized cases. Although HT, DM, CAD, CRF, and COPD were the most frequently observed comorbidities in all cases, the rate of presence of 3 and more systemic diseases in the immunized cases was

statistically significantly higher vs. the non-immunized cases; however, there was no significant difference between the number of comorbid diseases and the rate of mortality in the immunized group. We consider that good management of the comorbidities during infection, good evaluation of the interactions between the treatment applied and the medicines taken for a long time, and close monitoring of the clinical stability will mitigate the relevant risks.

CT is important in diagnosis, treatment, and prognosis establishment of the bronchopneumonia. According to the result of the literature review carried out by Ojha et al. (13) (with 45 studies) covering 4,410 patients, the most prevalent CT findings in the COVID-19 infection were the ground glass pattern and the mixed pattern that includes ground glass and consolidation simultaneously. The studies that have compared the CT imaging findings by age report that the rates of widespread multilobar involvement and pleural thickening are higher at the old age group. Xu et al. (14) examined the relation between the disease severity and the CT involvement in their study and found out that the rates of widespread multilobar involvement, widespread consolidation, atelectasis, and effusion were higher in the critically severe patients. When we compared the immunized and non-immunized groups in our study, we found out that the rate of over 50% involvement according to the CT examination was statistically significantly high in the non-immune group vs. the immune group even though the lung involvement was present in both groups. Consequently, we consider that the vaccine is effective in reducing the lung involvement.

In the patients with advanced pulmonary involvement caused by bronchopneumonia, the increasing need for oxygen can be met supplied by nasal cannula, high flow nasal oxygen (HFNO), non-invasive mechanical ventilation (NIMV), or mechanical ventilation. The studies conducted reveal that, the patients receiving MV are under higher risk in terms of mortality (15, 16). The study conducted by Grasselli et al. (15) on 1,591 intensive care patients (mean age: 63) has informed that 99% of the patients needed respiration support, 88% of whom needed MV support, and that the rate of mortality among the elder patients (age >64) monitored in the ICU was higher than the young patients. In a meta-analysis study conducted by Zheng Jie Lim et al. (16), the COVID-19 patients receiving invasive MV treatment were categorized in terms of case mortality rates by age group, and it was seen that the mortality increased in patients' group > 80 years old. In our study too, the need for and length of MV was statistically significantly higher among the non-immunized cases than the immunized cases; and the need for MV was increasing the mortality by 93%.

Mine Durusu et al. (17) conducted CoronaVac vaccine Phase III study on healthy adults ranging between 18 and 59 years of age, and it was shown at the end of that study that the rate of effectiveness of the vaccine was 83.5%, and that the vaccine prevented hospitalization by 100%. The study conducted by Jara et al. (18) on the other hand has reported the effectiveness of the vaccine as 65.9%. The subgroups were also examined in this study, and it was reported that the vaccine prevented the COVID-19 infection by 66%, hospitalization by 85.3%, ICU admission by 89.2%, and death by COVID-19 by 86.5% in patients' group > 60 years old. In our study, we found 21% mortality rate among the >65-year-old patients immunized with 2 doses of vaccination. This rate was significantly lower than the non-immunized Group II.

Emire Seyahi et al. (19) evaluated the Anti-spike IgG antibody levels in > 65-year-old healthy subjects and immunodeficient patients (who had negative COVID-19 anamnesis) 21 days after the 2nd dose of vaccination and found out that the antibody titers were lower in the > 60-year-old patients and immunodeficient patients' group. The Anti-spike IgG antibody study conducted on the hospital personnel immunized with CoronaVac by Aysen Bayram et al. (20) has demonstrated that the antibody levels were low in the subjects over 60 years of age and suffering from chronic diseases as well. Another vaccination study that compared the elder and young individuals for immunization is the study conducted about the Biontech vaccine, and this study found out too, that the number of neutralizing antibodies was lower in the elder individuals (21).

The immune system aging, which occurs with aging, the antibody deficiency arising from the decrease in the response, may explain the higher mortality despite vaccination among the elder people. In our study, we evaluated the factors affecting the mortality in the immune group by using the logistic regression analysis; we found out that need for MV and ICU admission increased the mortality. Therefore, we consider that the vaccination can not prevent mortality at the old age group by one hundred percent, and thus this patient group must be supported with additional measures and applications.

Limitations

During our study, only the coronavac vaccine was approved for use over the age of 65. Therefore, we could not evaluate the clinical efficacy of other vaccines in this age group. We think that comparative clinical studies showing the efficacy of different vaccines for 65 years and older will be useful.

CONCLUSION

In our study in which we examined retrospectively 1,337 patients (298 of which were immunized) above 65 years Covid-19 PCR (+) patients, we found out that the ICU admission and the need for MV raised the mortality rate. In addition, the vaccination reduced the need for intensive care and MV. Besides, the disease was more severe, and the mortality rate was higher among the patients who were not vaccinated, or who have not developed immunity despite vaccination.

Accordingly, we can say that the vaccination has positive effects on the course of the disease and reduces mortality among the 65-year-old and older Covid-19 patients. However, mortality can be seen despite vaccination due to cellular aging and immune system aging as well as organ dysfunctions caused by comorbidities. We consider that this age group requires more precautions and more studies on vaccination and medication.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Scientific Researches Ethics Committee (Date: 23.06.2021, Decision No: 2021/178-23.06.2021).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Wang FS, Zhang C. What to do next to control the 2019-nCoV epidemic? Lancet 2020; 395: 391-3.
2. Shang W, Yang Y, Rao Y. The outbreak of SARS-CoV-2 pneumonia calls for viral vaccines. NPJ Vaccines 2020; 5: 1-3
3. Kaur SP, Gupta V. COVID-19 Vaccine: A comprehensive status report. Virus Res 2020; 288: 198114.
4. Zhang, Y, Zeng G, Pan H, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18-59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. The Lancet 2021; 21: 181-92.
5. COVID-19 Aşı Uygulanacak Grup Sıralaması. Access address: https://covid19asi.saglik.gov.tr/TR-77707/asi-uygulanacak-grupsiralamasi.html. Access date: 23.03.2021.
6. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020; 395: 1054-62.
7. Lian J, Jin C, Hao S, et al. High neutrophil-to- lymphocyte ratio associated with progression to critical illness in older patients with COVID-19: A multicenter retrospective study. Aging (Albany NY) 2020; 12: 13849-59.
8. National Health Commission of China. The guidelines for diagnosis and treatment of novel coronavirus (2019-nCoV) infected pneumonia (the sixth edition draft) issued by the National Health Commission of China. http: //www.gov.cn/zhengce/zhengceku/2020-02/19/content_5480948.htm2020. Accessed February, 2020.
9. Chen Y, Klein SL, Garibaldi BT, et al. Aging in COVID-19: Vulnerability, immunity and intervention. Ageing Res Rev 2021; 65: 101205.
10. Carbone M, Lednicky J, Xiao SY, Venditti M, Bucci E. Coronavirus 2019 infectious disease epidemic: where we are, what can be done and hope for. J Thorac Oncol 202; 16: 546-71.
11. Henig O, Kaye KS. Bacterial pneumonia in older adults. Infect Dis Clin North Am 2017; 31: 689-13.
12. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City Area. JAMA 2020; 323: 2052-9.
13. Ojha V, Mani A, Pandey N, Sharma S, Kumar, S. CT in coronavirus disease 2019 (COVID-19): a systematic review of chest CT findings in 4410 adult patients. European radiology2020; 30,6129-38.
14. Xu Y-H, Dong J-H, An W-M, et al. Clinical and computed tomographic imaging features of novel coronavirus pneumonia caused by SARS-CoV-2. J Infect 2020; 80: 394-00.
15. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. JAMA 2020; 323: 1574-81.
16. Lim ZJ, Subramaniam A, Ponnapa Reddy M, et al. Case fatality rates for patients with COVID-19 requiring invasive mechanical ventilation. a meta-analysis. Am J Respir Crit Care Med 2021; 203: 54-66.
17. Tanriover MD, Doğanay HL, Akova M, et al. CoronaVac Study Group. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. Lancet 2021 Jul 17; 398: 213-22.
18. Jara A, Undurraga EA, González C, et al. Effectiveness of an Inactivated SARS-CoV-2 Vaccine in Chile. N Engl J Med 2021; 385: 875-84.
19. Seyahi E, Bakhdiyarli G, Oztas M, et al. Antibody response to inactivated COVID-19 vaccine (CoronaVac) in immune-mediated diseases: a controlled study among hospital workers and elderly. Rheumatol Int 2021; 41: 1429-40.
20. Bayram A, Demirbakan H, Günel Karadeniz P, Erdoğan M, Koçer I. Quantitation of antibodies against SARS-CoV-2 spike protein after two doses of CoronaVac in healthcare workers. J Med Virol 2021; 93: 5560-67.
21. Müller L, Andrée M, Moskorz W, et al. Age-dependent immune response to the Biontech/Pfizer BNT162b2 COVID-19 vaccination. Clin Infect Dis 2021; 73: 2065-72.