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Clinical comparison of omicron and delta variants in older COVID-19 patients and the effect of vaccination status

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ABSTRACT

Aim: It was aimed to investigate the clinical course of the Omicron vand Delta variant among the SARS-CoV-2 vaccinated and unvaccinated COVID-19 patients over 65 years old and to compare their effects on patients.

Material and Method: The study was conducted on 567 COVID-19 patients over 65 years old. All patients' gender, age, medical history, COVID-19 PCR test results, blood test results, thorax CT images, vaccination status, hospitalization status, and treatment results were recorded. When evaluating the chest CT images, a semiquantitative scoring system was used. The patients were divided into the Omicron and Delta variant subgroups, and vaccinated and unvaccinated groups. Comparisons were made between the Delta variant and Omicron variant groups, the vaccinated and unvaccinated patient groups,and SARS-CoV-2 mRNA vaccinated and inactivated SARS-CoV-2 vaccinated patient groups.

Results: A total of 519 patients were included in the study.337 patients were in the Omicron variant group, 182 were in the Delta variant group.The hospitalization rate, ICU admission rate, mortality rate, rate of symptomatic patients,and the median thorax CT severity score was significantly higher in the Delta variant group than the Omicron variant group.The hospitalization rate, ICU admission rate, mortality rate, median thorax CT score and the rate of asymptomatic patients was significantly higher in the unvaccinated patient group than in the vaccinated group.There was no significant difference in the mortality rates and in the ICU admission rates between the inactivated SARS-CoV-2 vaccinated group and the SARS-CoV-2 mRNA vaccinated group.

Conclusion: The SARS-CoV-2 Omicron variant compared to the Delta variant and the SARS-CoV-2 vaccinated patients compared to the unvaccinated patients had a milder clinical course and less mortality in COVID-19 patients over 65 years old.

Keywords: Chest CT, COVID-19, delta variant, older patients, omicron variant, SARS-CoV-2 vaccine

INTRODUCTION

Cases of corovirus disease 2019 (COVID-19) were first reported in December 2019 in Wuhan, China, and then it has been spread around the world. According to WHO statistics, COVID-19 has led to more than 580 million cases and more than 5.6 million deaths worldwide (1). Continuing as a global public health problem today, COVID-19 also causes significant social and economic global burdens.

COVID-19 can manifest itself in various clinical forms, ranging from asymptomatic to severe pneumonia (2). People of all ages are at risk of infection and severe illness. However, geriatric patients and patients with underlying medical comorbidities are at risk of developing severe illnesses (2,3).

Since COVID-19 was first reported, different variants of SARS-Cov-2 have been reported as a result of various mutations in the S protein (3). These variants have become the pre-dominant variants in the world from time to time. Features such as different clinical courses, vaccine responses, and contagiousness have been reported for each variant (4).

The term variant of concern (VOC) for the COVID-19 agent SARS-COV-2 refers to viral variants with mutations in the spike protein receptor binding site (RBD) that significantly increase binding affinity (5). According to WHO's latest epidemiological update as of 11 December 2021, five VOCs have been identified since the start of the pandemic (6). SARS-COV-2 Alpha variant is the first known VOC, reported in the UK in late December 2020.

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The Beta variant was first reported in South Africa in December 2020. The Gamma variant was first reported in Brazil in early January 2021. The Delta variant was first reported in India in December 2020. The Omicron variant was first reported in South Africa in November 2021 (5).

Currently, SARS-CoV-2 has spread worldwide as the Omicron variant. This variant carries 32 mutations on the spike (S) protein, which is the main antigenic target of antibodies produced by infections or vaccination (7). The Delta variant, which has spread globally and caused a severe clinical course, had 5 mutations in the S protein (8). Large changes in the RBD region of the Omicron variant may contribute to its high binding ability with ACE2, resulting in a higher spreading rate and a significant effect on pathogenesis compared to the Delta variant. There is limited information on the current status of the Omicron variant, such as its contagiousness, clinical course, treatment, management and efficacy of vaccines.

Since COVID-19 was first identified, several subunit proteins and inactivated virus vaccines have been offered for use in humans. Due to the mutations that lead to new variants, there is a debate about resistance to these vaccines or a decrease in the effectiveness of vaccines (8,9). Although we have various vaccines, the fight against this pandemic is getting harder worldwide due to mutations.

The Omicron variant has now become the pre-dominant variant in COVID-19 disease worldwide (12,13). It is thought to be more contagious than the previous pre-dominant variants, the Delta variant, but causes a milder clinical course. However, we have very little clinical data on this subject. We also have limited information on the effectiveness of vaccines in patients infected by these variants. Therefore, we need clinical studies on this subject. This study was aimed to examine the clinical course of the Omicron variant and the Delta variant in vaccinated and unvaccinated geriatric patients and compare their effects on this aged patient group.

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:12.01.2022, Decision No: 2022/259). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. For this study, written consent was obtained from the patients. However, written consent was not obtained because the patients in September 2021 were analyzed retrospectively.

Patients

The study was conducted on 567 patients over 65 years old who applied to Prof. Dr. Feriha Oz Emergency Hospital. Patients over 65 years old with positive COVID-19 PCR test, who had not been diagnosed with COVID-19 before, and who had thorax CT at admission to the hospital were included in the study. The diagnose of COVID-19 in patients had been confirmed by a positive result for SARS-Cov-2 RNA in nasopharyngeal swabs by using real-time fluorescence reverse transcription-polymerase chain reaction (RT-PCR) before the patients were applied to the inpatient clinic. Patients under the age of 65, previously diagnosed with COVID-19, and with negative COVID-19 PCR test results were excluded from the study. Patients who had received a single dose of SARS-CoV-2 vaccine and had received different types of vaccines were excluded from the study. The vaccination information of 11 patients could not be reached, 17 patients were diagnosed with COVID-19 for the second time, 13 patients were vaccinated with a single dose of SARS-CoV-2 vaccine, 7 patients were vaccinated with one dose of SARS-CoV-2 mRNA and one dose of inactive SARS-CoV-2 vaccine. Therefore, these 48 patients were excluded from the study. Two types of SARS-CoV-2 vaccines are administered in our country, namely the SARS-CoV-2 mRNA vaccine and inactivated SARS-CoV-2 vaccine. The vaccination dates of the patients and the type of vaccine they were vaccinated with were examined. According to the date of diagnosis of COVID-19, patients who had received two doses of vaccine with an interval of 4-6 weeks in the last 6 months were considered vaccinated. 337 COVID-19 patients admitted between 13-20 January 2022 during the Omicron variant pre-dominant period and 182 COVID-19 patients between 16-23 September 2021 during the Delta variant pre-dominant period were included in the study. All patients' gender, age, medical history, COVID-19 PCR test results, blood test results, chest CT images, vaccination status, hospitalization status, and treatment results were examined.

Chest CT Severity Score: When evaluating the COVID-19 related pneumonia on chest CT, a semiquantitative scoring system based on the extent of lobar involvement was used called Chest CT Severity Score. In this scoring system: Each of the five lung lobes was visually scored on a scale of 0–5, with 0 indicating no involvement, 1 indicating less than 5% involvement, 2 indicating 5–25% involvement, 3 indicating 26–49% involvement, 4 indicating 50–75% involvement, and 5 indicating more than 75% involvement (9,10).

The patients were divided into the Omicron and Delta variant groups, and vaccinated and unvaccinated groups. Comparisons were made between: i) the Delta

variant and Omicron variant groups, ii) the vaccinated and unvaccinated patient groups, and iii) SARS-CoV-2 mRNA vaccinated and inactivated SARS-CoV-2 vaccinated patient groups.

Statistical Analysis

The IBM SPSS (Statistical Package for Social Sciences; version 25.0 for windows, Chicago, USA) was used for statistical analyses. While evaluating the study data, the compatibility of the parameters with the normal distribution was evaluated with Kolmogorov-Smirnov and Shapiro Wilks tests, and the homogeneity of the group variables was evaluated with the Levene test. Percentage and mean±standard deviation (±SD) or median (interquartile range [IQR]) methods were used to indicate the baseline characteristics of the data according to the evaluation of the normality distribution. Differences in the values of the variables between the groups were evaluated by the Independent samples t-test or Mann–Whitney U test. Chi-square test was used to analyze qualitative data. p<0.05 was considered significant for all statistical analyses.

RESULTS

A total of 519 patients (312 females and 207 males) were included in the study. 337 patients were in the Omicron variant group, and 182 were in the Delta variant group. The median age was 72 (67-77) years in the Omicron group, and 73 (68-79.25) years in the Delta group. The hospitalization rate was statistically significantly higher in the Delta variant group than in the Omicron variant group (49.5% vs. 17.8%, respectively; p<0.001). ICU admission rate was significantly higher in the delta variant group (40% vs. 21.7% , respectively, p=0.019). There was no significant difference in length of stay in hospital and ICU between the Delta and Omicron variant groups. The median thorax CT score was significantly higher in the Delta variant group than in the Omicron variant group (p=0.001). The rate of asymptomatic patients was significantly higher in the Omicron variant group than in the Delta variant group (34,7% vs.13,7%, respectively, p<0,001). The mortality rate was significantly higher in the Delta variant group than in the Omicron variant group (15.9% vs. 3.9%, respectively, p<0.001) (**Table 1**).

According to vaccination status, 85.7% of all patients were vaccinated. The hospitalization rate was significantly higher in the unvaccinated patient group than in the vaccinated patient group (21.8% vs. 71.6%, respectively, p<0.001). The ICU admission rate was significantly higher in the unvaccinated patient group than in the vaccinated patient group (52.8% vs. 21.6%, respectively, p<0.001). The median thorax CT score was significantly higher in the unvaccinated patient group than in the vaccinated patient group (p<0,001). The rate of asymptomatic patients was significantly higher in the vaccinated patient group than in the unvaccinated patient group (30,6% vs. 8,1%, respectively, p<0,001). The mortality rate was significantly higher in the unvaccinated patient group than in the vaccinated patient group (37.8% vs. 3.1%, respectively, p<0.001). (**Table 2**)

Table 1. Demographic characteristics of all participants, Delta and Omicron variant subgroups and comparative analyses of these subgroups.

	All Patients (n=519)	Delta Variant Group (n=182, 35.1%)	Omicron Variant Group (n=337, 64.9%)	p value
Median (IQR) or n (%)				
Gender				0.651[a]
Females	312 (60.1%)	107 (58.8%)	205 (60.8%)	
Males	207 (39.9%)	75 (41.2%)	132 (39. 2%)	
Age (year)	72 (67-78)*	73 (68-79.25)*	72 (67-77)*	0.213[b]
Hospitalization				<0.001[a]
No	369 (71.1%)	92 (50.5%)	277 (82.2%)	
Yes	150 (28.9%)	90 (49.5%)	60 (17.8%)	
Hospitalized in				0.019[a]
Ward	101 (67.3%)	54 (60%)	47 (78.3%)	
ICU	49 (32.7%)	36 (40%)	13 (21.7%)	
Length of Hospital Stay (day)	8 (6-14.50)*	9 (6-16)*	8 (5-12.75)*	0.142[b]
Length of ICU Stay (day)	7.50 (5-11)*	8 (5-11)*	7 (5.50-10.50)*	0.722[b]
Thorax CT score	6 (2-10)*	0 (0-7)*	0 (0-3)*	0.001[b]
Symptomatic				<0.001[a]
Yes	377 (72.6%)	157 (86.3%)	220 (65.3%)	
No	142 (27.4%)	25 (13.7%)	117 (34.7%)	
Result				<0.001[a]
Healed	477 (91.9%)	153 (84.1%)	324 (96.1%)	
Exitus	42 (8.1%)	29 (15.9%)	13 (3.9%)	

*Median (IQR), aChi-Square Testi, bMann-Whitney U Test, ICU:Intensive care unit,CT:Computerized tomography

Table 2. Demographic characteristics of all participants, the vaccinated and unvaccinated subgroups and comparative analyses of these subgroups.

	All Patients (n=519)	Vaccinated Group (n=445, 85.7%)	Unvaccinated Group (n=74, 14.3%)	p value
Median (IQR) or n (%)				
Gender				0.895[a]
Females	312 (60.1%)	267 (60%)	45 (60.8%)	
Males	207 (39.9%)	178 (40%)	29 (39.2%)	
Age (year)	72 (67-78)*	71 (67-77)*	76 (69.75-85)*	<0.001[b]
Hospitalization				<0.001[a]
No	369 (71.1%)	348 (78.2%)	21 (28.4%)	
Yes	150 (28.9%)	97 (21.8%)	53 (71.6%)	
Hospitalized in			.	<0.001[a]
Ward	101 (67.3%)	76 (78.4%)	25 (47.2%)	
ICU	49 (32.7%)	21 (21.6%)	28 (52.8%)	
Length of Hospital Stay (day)	8 (6-14.50)*	9 (6-14)*	8 (6-16)*	0.994[b]
Length of ICU Stay (day)	7.50 (5-11)*	9 (7-11)*	7 (5-10)*	0.147[b]
Thorax CT score	6 (2-10)*	0 (0-3)*	2.50 (0-10)*	<0.001[b]
Symptomatic				<0.001[a]
Yes	377 (72.6%)	309 (69.4%)	68 (91.9%)	
No	142 (27.4%)	136 (30.6%)	6 (8.1%)	
Result				<0.001[a]
Healed	477 (91.9%)	431 (96.9%)	46 (62.2%)	
Exitus	42 (8.1%)	14 (3.1%)	28 (37.8%)	

*Median (IQR), aChi-Square Testi, bMann-Whitney U Test, ICU:Intensive care unit, CT:Computerized tomography

Of the vaccinated patients, 51.5% were vaccinated with the inactivated SARS-CoV-2 vaccine and 48.5% with the SARS-CoV-2 mRNA vaccine. The hospitalization rate was significantly higher in the inactivated SARS-CoV-2 vaccinated group than in the SARS-CoV-2 mRNA vaccinated group (p<0.001). There was no significant difference in the ICU admission rates between the inactivated SARS-CoV-2 vaccinated group and the SARS-CoV-2 mRNA vaccinated group. The median thorax CT score was significantly higher in the inactivated SARS-CoV-2 vaccinated group than in the SARS-CoV-2 mRNA vaccinated group (p=0,001). The rate of asymptomatic patients was significantly higher in the SARS-CoV-2 vaccinated group than in the SARS-CoV-2 mRNA vaccinated group (p=0,001). There was no significant difference in the mortality rates between the inactivated SARS-CoV-2 vaccinated group and the SARS-CoV-2 mRNA vaccinated group (**Table 3**).

Table 3. Demographic characteristics of all participants and the inactivated SARS-CoV-2 vaccinated and SARS-CoV-2 mRNA vaccinated subgroups and comparative analyses of these subgroups.

	Vaccinated Group (n=445)	Inactivated SARS-CoV-2 vaccinated group (n=229, 51.5%)	SARS-CoV-2 mRNA vaccinated group (n=216, 48.5%)	p value
Median (IQR) or n (%)				
Gender				0.615[a]
Females	267 (60%)	140 (61.1%)	127 (58.8%)	
Males	178 (40%)	89 (38.9%)	89 (41.2%)	
Age (year)	71 (67-77)*	72 (67-78)*	71 (67-77)*	0.412[b]
Hospitalization				<0.001[a]
No	348 (78.2%)	159 (69.4%)	189 (87.5%)	
Yes	97 (21.8%)	70 (30.6%)	27 (12.5%)	
Hospitalized in				0.083[a]
Ward	81 (83.5%)	58 (82.9%)	18 (66.7%)	
ICU	16 (16.5%)	12 (17.1%)	9 (33.3%)	
Length of Hospital Stay (day)	9 (6-14)*	8 (6-14)*	10.50 (5.75-15)*	0.664[b]
Length of ICU Stay (day)	9 (7-11)*	11 (6-15)*	9 (5.75-11)*	0.370[b]
Thorax CT score	0 (0-3)*	0 (0-4.50)*	0 (0-0.75)*	0.001[b]
Symptomatic				0.001[a]
Yes	309 (69.4%)	174 (76.4%)	134 (62%)	
No	136 (30.6%)	54 (23.6%)	82 (38%)	
Result				1.000[c]
Healed	431 (96.9%)	222 (96.9%)	209 (96.8%)	
Exitus	14 (3.1%)	7 (3.1%)	7 (3.2%)	

*Median (IQR), a Chi-Square Testi, b Mann-Whitney U Test, c Fisher's Exact Test, ICU:Intensive care unit, CT:Computerized tomography

DISCUSSION

COVID-19 continues to be a widespread public health problem all over the world and causes serious social and economic consequences. The Omicron variant is currently the pre-dominant variant circulating globally (11,12). Although it is stated that the Omicron variant has a milder clinical course than other variants, there are very few clinical studies on this subject. In the current study, we examined the clinical courses of Omicron and Delta variant COVID-19 patients over 65 years old and compared them. We also accomplished comparisons according to the vaccination status and vaccine types of the patients.

We found that the hospitalization rate, the ICU admission rate, and the mortality rate were significantly higher in the Delta variant group than the Omicron variant group. In the Omicron variant group, the hospitalization rate was 31.7%, the ICU admission rate was 18.3%, the rate of symptomatic patients was 21% and the mortality rate was 12% lower than the delta variant group. These indicators suggest that the Delta variant causes a more severe clinical course than the Omicron variant. Although there are not enough studies on this subject, the results of some studies are similar to ours. After the Omicron variant was reported, in the early studies conducted on the general population in England, Scotland, and South Africa, it has been reported that patients infected with the Omicron variant of SARS-CoV-2 are 50-70% less likely to be admitted to the hospital, 31%-45% less likely to be admitted to the ICU and 76% less likely to be death than patients infected with the delta variant (13-15). A Swedish study comparing the Omicron and Delta variant periods found that the risk of severe disease was 40% lower in unvaccinated patients and 71% lower in vaccinated patients in the Omicron variant period (16).

We found that the median chest CT severity score was significantly higher in the Delta variant group than in the Omicron variant group. Accordingly, pulmonary involvement due to COVID-19 was milder in the Omicron variant group. In a study of mice infected with the Delta and Omicron variant of SARS-CoV-2, it was found that mice infected with the Omicron variant resulted in less severe clinical signs, lower levels of inflammation, and less injury to the lungs than mice infected with Delta variant viruses (17). In our study, the rate of asymptomatic patients was significantly higher in the Omicron variant group than in the Delta variant group. Although there are not many studies on this subject, the rate of asymptomatic Omicron infections is estimated to be between 25-54%. In a study conducted on healthcare workers, the rate of asymptomatic patients was found to be 50% in patients infected with the Omicron variant (18).

The reason why the Omicron variant causes a milder clinical course may be the high number of mutations in the virus compared to other variants. Immune response induced by vaccination or reinfections may also be causes of mild clinical course. However, since our study is in the group of patients over 65 years of age, different results are likely to occur compared to the general population. Patients over 65 years of age are expected to have a more severe clinical course than the general population.

When we compared the vaccination status of the patients, we found that the hospitalization rate, the ICU admission rate, the mortality rate, and the asymptomatic patient rate were significantly higher in the unvaccinated patient group. The hospitalization rate was 49.8%, the ICU admission rate was 37.2%, the symptomatic patient rate was 22.5%, and the mortality rate was (34.7%) higher in the unvaccinated patient group than in the vaccinated patient group. In unvaccinated patients, these findings were expected results. Many studies have shown that vaccines improve prognosis in COVID-19 patients (19,20). The median thorax CT score was significantly higher in the unvaccinated patient group than in the vaccinated patient group. Thorax CT involvement was more severe in the unvaccinated patient group. Similarly, other studies have shown that the CT severity score is lower in vaccinated patients (20).

When we compare vaccinated patients according to inactivated SARS-CoV-2 and SARS-CoV-2 mRNA vaccine types, we found that the hospitalization rate, the asymptomatic patient rate, and the median thorax CT score were significantly higher in the inactivated SARS-CoV-2 vaccinated group than in mRNA vaccine group. There was no significant difference in the mortality rates and the ICU admission rates between the inactivated SARS-CoV-2 vaccinated group and the SARS-CoV-2 mRNA vaccinated group. As is well known, two vaccines reduce the severe course of the disease and the risk of death in COVID-19. Similar to our results, various studies have shown that these two types of vaccines are effective in COVID-19 (19-21). Although two vaccines similarly prevented a very severe course, we found that the mRNA vaccine provided better clinical outcomes in terms of hospitalization rate, asymptomatic patient rate, and CT involvement, which are some indicators of severe disease. Different types of vaccines can induce different immune responses in the same individual. In addition, different individuals may produce different levels of antibodies from the same vaccine due to different characteristics such as race, gender, age, and medical conditions. Like another RNA viruses, Coronaviruses and as well as COVID-19 evolving some mutations and this fact also affects the vaccine success (22). Comprehensive clinical studies are needed on this subject. There are some studies

on the ability of vaccines to produce antibodies. Recently, Lim et al. (23) found that two doses of mRNA vaccine produced more antibodies against SARS-CoV-2 than the inactivated vaccine.

In our study, we compared the clinical course of Omicron variant and Delta variant, vaccinated and unvaccinated patients in COVID-19 patients over 65 years old. We found that the Omicron variant compared to the Delta variant and the vaccinated patients compared to the unvaccinated patients had a milder clinical course and less mortality.

Study Limitations

There are some limitations of our study. An important limitation is that the SARS-Cov-2 variants of the patients were not confirmed by PCR testing, the patients were grouped according to the period in which the dominant variants were present. Another limitation is that vaccinated and unvaccinated patient groups cannot be compared according to SARS-Cov-2 variants.

CONCLUSION

Our study showed that the SARS-CoV-2 Omicron variant compared to the Delta variant and the SARS-CoV-2 vaccinated patients compared to the unvaccinated patients had a milder clinical course and less mortality in COVID-19 patients over 65 years old. Although we found that the Omicron variant which is the pre-dominant variant of COVID-19 today, causes a milder clinical course, especially in the elderly, COVID-19 is still a very serious health problem. In other words, vaccination is very important on the prognosis in geriatric patients.

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:12.01.2022, Decision No: 2022/259).

Informed Consent: Written informed consent was obtained from the patients. However, written consent was not obtained because the patients in September 2021 were analyzed retrospectively.

Referee Evaluation Process: Externally peer-reviewed.

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

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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.

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