ORIGINAL ARTICLE

RISK PROFILES IN GERIATRIC COVID-19 PATIENTS: VACCINATION IMPACTS ON HOSPITALIZATION AND SURVIVAL DURING THE OMICRON WAVE

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Abstract

Introduction: The Omicron variant causes less severe disease than other variants. Although most patients experienced a mild course, an increase in hospitalizations and intensive care unit follow-ups was observed. The course of the disease was more severe, especially in the geriatric population. This study investigated the factors leading to hospitalization, intensive care needs, and mortality in older patients.

Materials and method: Between October 2022 and March 2023, COVID-19 patients aged > 60 years were included in the study. Patients' demographic features, underlying diseases, initial symptoms, vaccinations, treatment, secondary bacterial infections, and COVID-19 history were investigated. Mortality rates at the hospital and after discharge were investigated.

Results: Adding three or more mRNA vaccines to the vaccination schedule was associated with a reduced risk of hospitalization and intensive care unit admission. Patients with repeated vaccine doses had no mortality or intensive care unit follow-up, whereas unvaccinated patients had 13.3% mortality and 46.6% intensive care unit follow-up. 80-year-olds and older had higher mortality. The mortality rate of patients admitted to the hospital with a deteriorating general condition was considerably higher (28.8%) than that of other patients (5.4%). Patients with a COVID-19 history had fewer intensive care unit visits (10.25%). The mortality rate among hospitalized patients who did not receive molnupiravir was higher (40%) than that of those who received treatment (14%).

Conclusion: Repeated vaccine doses, heterologus, and full-dose mRNA vaccination reduced mortality and hospitalization rates. Patients aged ≥80 have a higher risk of mortality. Molnupravir treatment significantly decreased the mortality rate.

Keywords: COVID-19; SARS-CoV-2; Vaccination; Mortality.

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INTRODUCTION

The advent of novel variants has significantly altered the course of the COVID-19 pandemic. The Omicron variant, with its high infection transmission and increased hospitalization rates, has triggered a pandemic (1, 2). The Omicron variant was associated with a less severe disease course. The elevated hospitalization rates were attributed to high infectiousness and a considerable number of infected individuals (1). A significant proportion of patients exhibited mild disease manifestations. However, older patients, patients with underlying diseases, and patients with missing vaccine doses experienced more severe disease with the Omicron variant (3, 4).

While the efficacy of vaccines has generally declined over time, the efficacy of vaccines against the Omicron variant has fallen significantly (5). Booster vaccinations with updated vaccines should be administered to protect against the new variants (5).

During the period of the Omicron variant, older patients had to cope with a particularly severe disease compared to other patients. Hospitalizations and deaths also occurred mainly in the geriatric patient group (3,4). Despite this, many older patients were able to overcome the illness without being hospitalized (3).

In this study, we aimed to examine older COVID-19 patients' hospitalization, intensive care unit (ICU) admission, and short- and long-term mortality during the Omicron wave, despite all vaccinations and changes in the pathogenicity of the virus. In addition to examining the risk-posing conditions of the older patients, we aimed to evaluate older patients with different numbers and types of immunizations in terms of mortality and the risk of intensive care hospitalization. This study analyzes the geriatric population with COVID-19 and contributes to the management of older patients in terms of risk factors, immunization, and treatment approaches.

MATERIALS AND METHOD

All patients with a diagnosis of COVID-19 between October 2022 and March 2023, when the Omicron variant was dominant, were retrospectively analyzed. The patients who were followed up in the ICU and COVID-19 clinic, who were older than 60, were included in the study. In order to select the same age group, only outpatients aged 60 years and older were included in the study.

A detailed analysis of the vaccination status of the patients was conducted during the study period. At the time of the vaccination initiation, only inactivated vaccines (CoronaVac (Sinovac, China)) were available in Turkey. Subsequently, mRNA vaccines (BNT162b; Pfizer/BioNTech, Germany) have been made available. However, an updated mRNA vaccine (bivalent BA.4/BA.5; Pfizer/BioNTech, Germany) is not available in Turkey. Most individuals received heterologous vaccinations. Those who received four doses of the vaccine were considered to have achieved full vaccination. The availability of booster doses in the last three months was examined. The study included an analysis of patients who died while hospitalized and those who died within one year of diagnosis. The presence of underlying diseases and a second diagnosis resulting in hospitalization were investigated. Additional secondary bacterial infections during the course of the patient's hospitalization and length of stay were examined. All patients were investigated for a history of COVID-19. Molnupiravir was the only antiviral treatment for COVID-19 during the Omicron wave, and only patients over 65 years of age or patients with underlying disease could receive molnupiravir treatment. Patients under 65 years of age, as well as patients with a long time since symptom onset at the time of hospitalization, were not able to receive molnupiravir treatment. Mortality rates were investigated in patients who received and did not receive the treatment.

Statistical Analysis

Statistical analysis was conducted using SPSS 29.00 software. We analyzed the differences in mean age between the groups using ANOVA. In addition to descriptive statistics for each group, we used the chi-square test and logistic regression to compare patients' immunization, hospitalization, and mortality. The Kruskal-Wallis test was employed to investigate the differences between the ICU and COVID-19 clinic lengths of stay for patients with different vaccinations.

RESULTS

A total of 249 patients who were followed up as outpatients or hospitalized were included in this study. Of these, 50.2% were female. The mean age was 72.38±5.9 years in 79 outpatients, 75.63±10 years in 92 patients in the COVID-19 clinic, and 78.77±9.5 years in 78 patients in the ICU. While the age difference between outpatients (p = 0.03, <0.001) and others was significant, the age distributions of the ICU and COVID-19 clinic (p = 0.1) patients were similar. No difference was observed in the sex distribution of the patients (p = *0.54).* The mean ICU hospitalization day of inpatients was 9.35±8.8, and the mean hospitalization day of patients in the COVID-19 clinic was 7.5±4.04.

A total of 55 (32.4%) patients were admitted to the hospital with upper respiratory symptoms; 70 (41.2%) patients were admitted with shortness of breath; and 45 (26.5%) patients were admitted with deterioration of their general condition. The most common underlying diseases among hospitalized patients were hypertension (55.7%), diabetes (33.7%), congestive heart failure (CHF) (29.3%), chronic obstructive pulmonary disease (COPD) (28.7%), and Alzheimer's disease (12%). A total of 35 patients had a secondary diagnosis, which was diagnosed at the time of hospital admission or while being followed up in the hospital with a diagnosis of COVID-19. Cerebrovascular events (CVE) were the most common second diagnosis.

The mortality rate was 18.87% among the patients with COVID-19. In the ICU, 29 (37.17%) patients died during follow-up, and 12 (15.38%) died within 1 year after discharge. In the COVID-19 clinic, 6 (6.52%) patients died within 1 year after discharge. Both in-hospital mortality and mortality in one year were significantly higher in patients aged 80 years and older (p=0.003, p <0.01). The patients 80 years of age and older were mostly hospitalized and fewer as outpatients (p <0.01). Mortality and total mortality did not differ between the sexes (p=*0.53*, p=0.4, respectively). Mortality was significantly higher in patients admitted to the hospital with a deteriorating general condition (28.8%) than lower respiratory distress (18.5%), and symptoms of upper respiratory tract infection (5.4%) (p=0.007). Among the hospitalized patients, only 20 did not receive molnupiravir treatment. The mortality rate was 40% for patients who were not treated with molnupiravir, whereas hospitalized patients treated with molnupiravir had a 14% mortality rate (p=0.008).

There were 168 (67.46%) full-dose vaccinated patients (Figure 1). The mortality rate within one year was statistically significantly lower in patients who were fully vaccinated (14.88%) compared to those who were not fully vaccinated (27.16%) (p=0.02).

Patients without a full dose of vaccination had an increased risk of hospitalization (OR 3.9 CI 0.6–6.1 p <0.01) and ICU admission (OR 4.9 CI 0.7–6.5 p<0.01) (Figure 2). The total mortality is higher in patients with only inactivated vaccines (34.78%) but lower in heterologous vaccinations (11.87%) and schedules with repeated mRNA vaccines (9.52%) (Table 1). Patients without three or more mRNA vaccines have an increased risk of hospitalization (OR 3.8 CI 1.4-9.7 p<0.01) and ICU admission (OR 4.6 CI 1.1-9.2 p<0.01) (Table 2). Patients who received a total of six doses of vaccine, mostly heterologous and booster mRNA doses, had no mortality (p <0.01) and no need for intensive care (p <0.01). The highest ICU needs

Table 1. Mortality rates and vaccine doses among the COVID-19 patients.

	Mortality at the hospital N (p) %	Total mortality in one year N (p) %	Total patient number N
Three mRNA vaccine doses	5 (0.28) 7.93%	6 (0.02) 9.52%	63
Three inactivated vaccine doses	11 (0.75) 12.5%	21 (0.13) 23.86%	88
Fully vaccinated	17 (0.27) 10.11%	24 (0.02) 14.28%	168
Heterologous Vaccination	14 (0.11) 8.75%	19 (0.00) 11.87%	160
Only inactivated vaccines	12 (0.11) 17.39%	24 (0.00) 34.78%	69
A total of six doses of vaccines	0 (0.00) 0%	0 (0.00) 0%	22
Booster in the last 3 months	2 (0.39) 6.89%	2 (0.07) 6.89%	29
No vaccine	2 (0.014) 13.33%	2 (0.01) 13.33%	15

Table 2. Vaccine doses and ICU and hospitalization needs of the patients.

	ICU N (%)	COVID-19 Clinic N (%)	Not hospitalized N (%)	Total patient N(*p*)
Three mRNA vaccine doses	10 (15.87%)	16 (25.39%)	37(58.73%)	63 (0.00)
Three inactivated vaccine doses	31(35.22%)	32(36.36%)	25(28.4%)	88 (0.56)
Fully vaccinated	42(25%)	57(33.92%)	69(41.07%)	168 (0.00)
Heterologous Vaccination	38(23.75%)	56(35%)	66(41.25%)	160 (0.03)
Only inactivated vaccines	32(46.37%)	27(39.13%)	10(28.98%)	69 (0.03)
A total of six doses of vaccines	0(0%)	7(31.81%)	15(68.18%)	22 (0.00)
Booster in the last 3 months	4(13.79%)	9(31.03%)	16(55.17%)	29 (0.01)
No vaccine	7(46.66%)	6(40%)	2(13.33%)	15 (0.00)

were in unvaccinated patients (46.66%) and patients vaccinated with inactivated vaccines (46.37%).

Of the patients, 38 (15.26%) had a history of COVID-19. There was no significant difference in mortality between patients with and without a COVID-19 history. While mortality during hospitalization was not different in patients with a second diagnosis (p=0.12), mortality within one year was statistically significant (p=0.007). Among the underlying diseases, CVE history and diabetes were associated with post-discharge mortality (p=0.04,

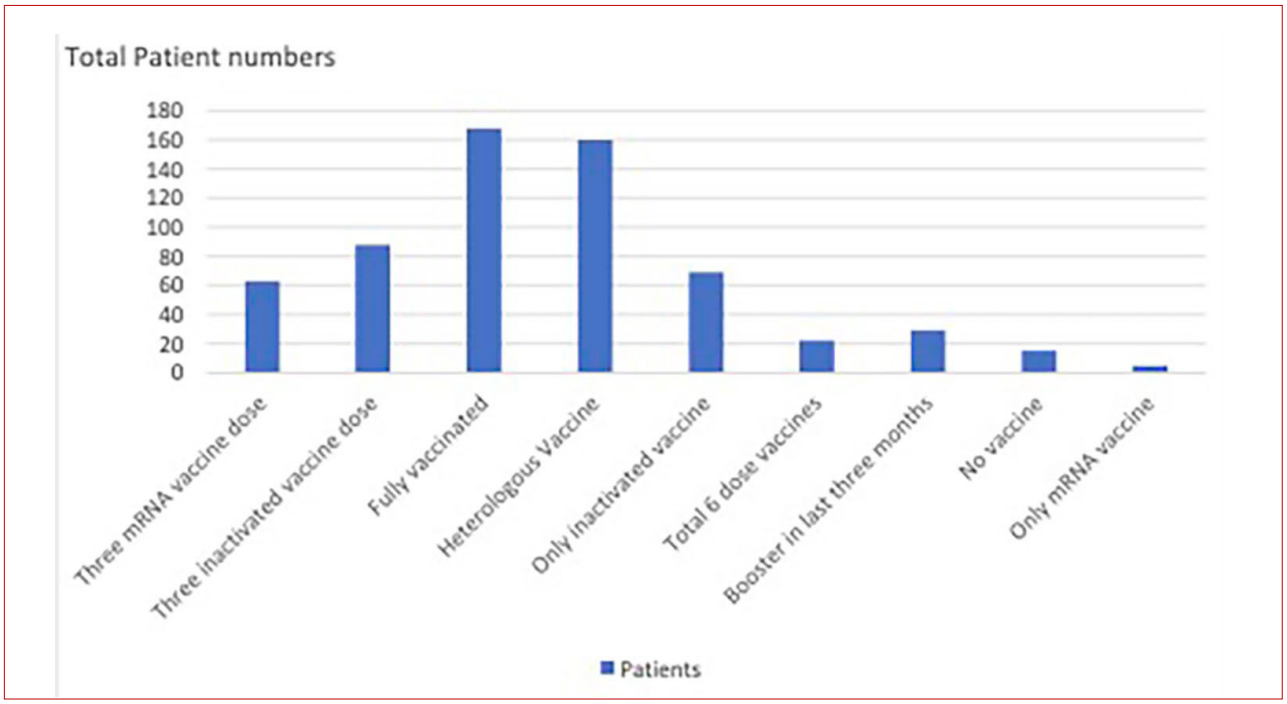

Figure 1. Vaccination types and administered total patients.

Table 3. Mortality among the patients with COVID-19 history, second diagnosis, and underlying diseases.

	Mortality at the hospital N(p)	**Total Mortality N(p)**
COVID-19 history	4 (*p* 0.8)	8 (*p* 0.7)
Second diagnosis	20 (*p* 0.12)	31 (*p* 0.007)
The Most Common Underlying disaeases among the hospitalized patients		
Hipertension	14 (*p* 0.66)	21 (*p* 0.15)
Diabetes	6 (*p* 0.21)	9 (*p* 0.03)
Chronical obstructive pulmonary disease	6 (*p* 0.41)	10 (*p* 0.25)
Alzeimer	5 (*p* 0.25)	8 (*p* 0.16)
Concestive heart failure	8 (*p* 0.97)	12 (*p* 0.64)
Cerebrovascular event	3 (*p* 0.57)	7 (*p* 0.04)
Chonic renal failure	2 (*p* 0.73)	4 (*p* 0.21)

0.03, respectively) (Table 3). The mortality rate of 28 patients who developed secondary bacterial infection while being followed up in the ICU (71.4%) was statistically significantly higher compared to patients who did not develop secondary bacterial infection ($p<0.01$).

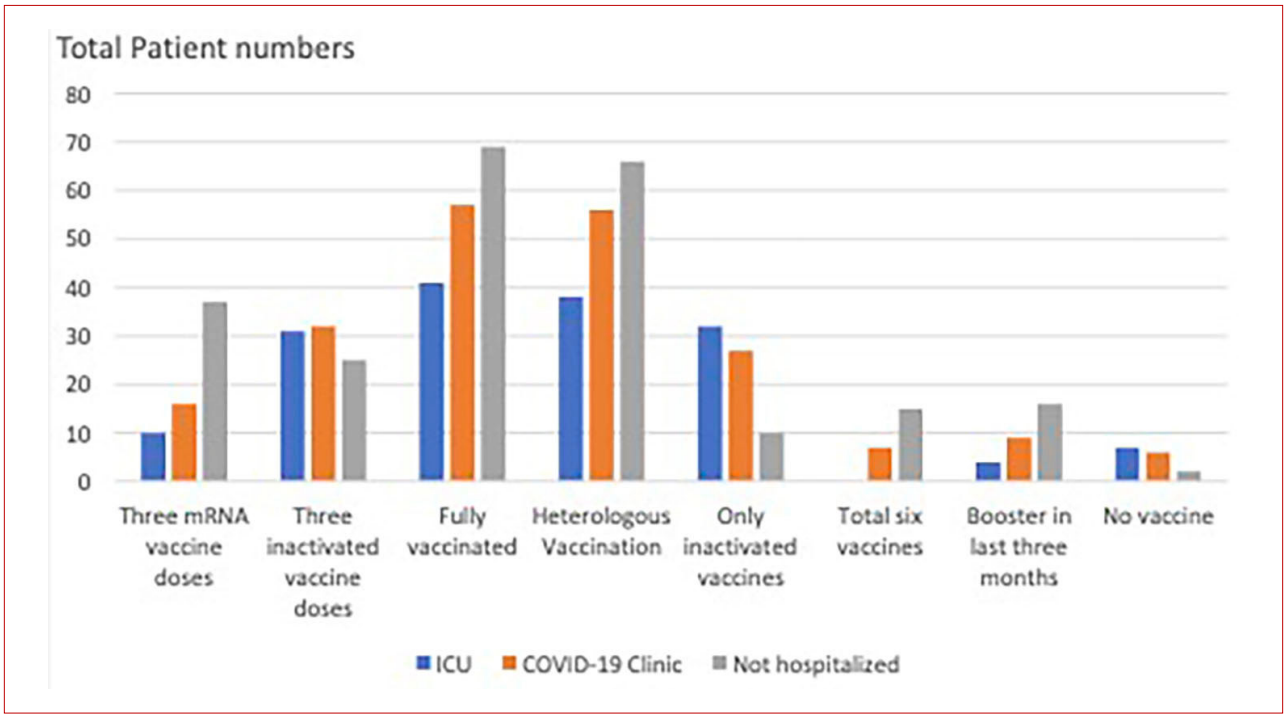

Figure 2. Vaccinations and hospitalizations among COVID-19 patients.

DISCUSSION

Although we included only patients aged over 60 years in our study design, hospitalized patients' mean age was higher than outpatients. Mortality increased with age > 80 years. Most patients received heterologous vaccinations, whereas 69 patients received homologous vaccinations using inactivated vaccines.

Mortality is known to increase in older patients and those with underlying medical conditions (6). Increased mortality has been associated with congestive heart failure, chronic kidney failure, and cirrhosis (3, 6). During the early stages of the pandemic, underlying diseases and age were associated with a poor prognosis (7, 8). Researchers have linked age, particularly 80 years and older, and dementia to a poor prognosis in patients infected with the Omicron variant (4). On the other hand, some studies reported no relationship between the underlying disease and a poor prognosis (9). In our study, patients aged 80 years and older had a higher mortality rate, but no underlying disease or second diagnosis increased in-hospital mortality. In one year, diabetes and CVE increased total mortality. However, some studies have reported no association between long-term mortality and underlying diseases (10). Secondary bacterial infections increase mortality in COVID-19 patients (11). Our study demonstrates that secondary bacterial infections are one of the primary causes of ICU mortality in patients with COVID-19.

Studies have shown that patients initially admitted to the hospital with respiratory distress symptoms have a poor prognosis (8). Respiratory distress was the most common symptom reported during the early stages of the pandemic (74%) (7). In our study, 41.2% of the older patients presented to the hospital with respiratory distress. Patients

admitted to the hospital with deterioration in their general condition had the highest mortality rates.

It is well known that SARS-CoV-2 can cause long-term negative effects on patients, particularly those who are elderly and have several underlying diseases (12). The all-cause mortality rate following hospital discharge ranges from 0% to 37%. A systematic review and meta-analysis reported a mortality rate of 7.5% within one year. The results of our study are comparable to those of the aforementioned study, with a mortality rate of 7.2%. Our study also identified a correlation between age and post-discharge mortality. A higher post-discharge mortality rate was observed in patients aged 80 and older (12). Patients with moderate or severe disease have a higher risk of post-discharge mortality (10, 13). In our study, while patients in the ICU exhibited the highest post-discharge mortality, those who were not hospitalized demonstrated no mortality for over one year.

Vaccination, particularly booster doses, reduces mortality (3, 6). Full-dose vaccination regimens reduce mortality, the need for ICU admission, and intubation requirements (14). Some studies have reported a mortality reduction of up to 10-fold among patients receiving the full vaccination dose (14). In contrast, in other studies, in-hospital mortality was not reduced in critically ill patients (15). The observed mortality rates were similar among fully vaccinated, unvaccinated, and partially vaccinated patients. In our study, only patients who received six doses of the vaccine and those who did not receive any vaccine exhibited statistically significant differences in in-hospital mortality. Our results are comparable with those of several studies in terms of post-discharge mortality up to one year and vaccination. These studies reported that vaccination reduced post-discharge mortality rates (13). Repeated doses, especially with mRNA, have been shown to reduce post-discharge mortality, and patients administered six vaccine doses showed no mortality in our study.

Vaccination with three doses of the mRNA vaccine reduced mortality and hospitalization risks in elderly patients infected with the Omicron variant (4). A study from Japan reported 74% vaccine efficacy against the Omicron variant after the 3rd dose of the vaccine (16). Another study reported no significant waning immunity for more than 120 days with three doses of the vaccine against emergency room visits and hospitalization (17). Patients receiving three or more doses of the mRNA vaccine had lower mortality and hospitalization rates in our study; however, almost all were part of the heterologous vaccination.

A study comparing vaccines found that mRNA vaccines were more effective than inactivated vaccines, especially among older people (18). Two or even three doses of the inactivated vaccine did not affect mortality in the later stages of the pandemic; however, the addition of the mRNA vaccine had a positive effect (19, 20). Some studies have reported improved immunity after repeated doses of heterologous vaccinations (20). We observed higher mortality rates among patients with only inactivated vaccines (23.86%) than among heterologously vaccinated patients, who had lower mortality rates (11.87%).

Even after receiving a full vaccination, elderly and immunocompromised patients may experience poor prognosis and hospitalization, particularly when infected with new variants. Therefore, studies have emphasized the importance of booster doses (18, 21). In our study, patients receiving the six-dose, mostly heterologous vaccination showed no mortality and no ICU requirement. Previous studies have found that a fourth dose of mRNA vaccines reduces mortality, particularly in the elderly, immunosuppressed, and high-risk individuals (22). One study revealed that individuals who received a booster dose of the vaccine experienced fewer symptoms and disease severity than those who did not receive the vaccine or booster dose (23).

Some studies have suggested that prior COVID-19 infection, especially in vaccinated individuals, protects against disease, particularly severe disease (22). According to them, the Omicron wave was less severe in nations with widespread prior infections than in nations with widespread vaccination but fewer infections (22). Our mortality rates were similar in patients with a history of COVID-19; however, these patients required less ICU care.

During the pandemic, antiviral treatments significantly reduced COVID-19 mortality rates, (24). In our study, the mortality rate was lower in patients who received molnupiravir treatment. A study of patients aged > 65 years showed that molnupiravir treatment significantly reduced mortality and hospitalization rates, regardless of other factors such as age, vaccination, previous infection, and underlying diseases, during the Omicron wave (25).

The study was able to examine many of the existing risk factors, especially in elderly patients who continue to be a risk group. In particular, it was able to compare heterologous vaccination with booster doses of mRNA and vaccination with inactivated vaccine. One of the limitations of this study is that the majority of our study group consisted of patients who received heterologous vaccinations. The number of patients who received only the mRNA vaccine was too low. Therefore, we could not compare patients who received only full-dose mRNA vaccines with other patients. To fully analyze some risk factors, such as underlying comorbidities, it would have been more efficient to compare with younger patients, but since all inpatients were elderly patients with many comorbidities, younger patients could not be included in the study.

CONCLUSION

The advent of the SARS-CoV-2 variants led to an increase in hospitalizations and mortality rates, particularly among individuals aged 80 and above. Underlying diseases did not influence the mortality rate of hospitalized patients. Administration of molnupiravir has been shown to result in a significant reduction in mortality rates. The acquisition of resistant bacterial infections during hospitalization has been found to increase mortality. The administration of heterologous vaccinations, adding mRNA vaccinations, and repeated doses was shown to reduce mortality and lessen disease severity.

Conflict of Interest: The authors declare no conflict of interest.

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Ethics approval: The study was approved by the Ethics Committee of the YBU Yenimahalle Training and Research Hospital on 13.10.2023 with an E-2023-53 registration number.

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