

Efficacy of BNT162b2 and CoronaVac in patients diagnosed with COVID-19

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ABSTRACT

This retrospective observational study is aimed to determine the efficacy of BNT162b2 (Pfizer-BioNTech) and CoronaVac (Sinovac) vaccines against symptomatic or severe disease in COVID-19-diagnosed patients. The secondary aim was to define the differences between vaccinated and un-vaccinated patients in terms of age, comorbidities and course of the disease, and to determine the survival rates. Of the 1463 PCR-positive patients, 55.3 % were vaccinated, and 44.7 % were unvaccinated. While 959 patients had mild-moderate symptoms, 504 patients had severe-critical symptoms and were treated in the intensive care unit. There was a statistically significant difference in the distribution of the type and doses of vaccines between the patient groups ($p = 0.021$). The rate of receiving 2 doses of Biontech was 18.9 % in the mild-moderate patient group but lower in the severe patient group (12.6 %). The rate of two doses of Sinovac and two doses of Biontech vaccine (four doses of vaccine) was 5 % in the mild-moderate patient group and 1.9 % in the severe patient group. The mortality rates were statistically significantly different ($p < 0.001$) between the patient groups: 65.3 % in the severe patient group and 1 % in the mild-moderate patient group. The multivariate model showed that the mortality risk of the unvaccinated patients was 1.5 times higher than the vaccinated ones ($p = 0.042$). In addition to being unvaccinated, advanced age, coronary artery disease (CAD), diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), and obesity were found to be associated with higher mortality risk. Besides, the reduction in mortality rate was more evident in individuals vaccinated with at least 2 doses of the BNT162b2 (Pfizer-BioNTech) vaccine than in CoronaVac group.

Keywords: COVID-19, anti-COVID-19 vaccine, BNT162b2 (Pfizer-BioNTech), CoronaVac (Sinovac) vaccine efficacy

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INTRODUCTION

Although COVID-19 infection is usually asymptomatic or mildly symptomatic, morbidity and mortality are high when it progresses to septic shock and organ failure. SARS-COV-2 is highly contagious and can also be transmitted from asymptomatic infected indi-

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viduals. Since the beginning of the pandemic, preventive measures have been taken in the fight against the disease, and specific treatment and effective vaccine development studies have accelerated. Despite the lack of a definitive treatment yet, numerous studies have documented the effectiveness of the developed vaccines in preventing the disease (1). Vaccine efficacy is evidenced by the percentage reduction in disease incidence in vaccinated compared to unvaccinated subjects. The antigenic target of vaccines developed against the virus is the outermost spike protein of the virion, which allows the SARS COV-2 virus to attach to the host cell. Two vaccines frequently used are the mRNA vaccine BNT162b2 (Pfizer-BioNTech) and the inactivated vaccine CoronaVac (Sinovac). The efficacy rate of the BNT162b2 vaccine, the first COVID-19 vaccine administered in Europe, was reported as 95 % (2). It is administered in two doses (21 days apart). In inactivated vaccines, antibodies were shown to develop not only against the spike protein but also against other parts of the virus. The CoronaVac vaccine, which is an inactivated vaccine, is administered in two doses, 28 days apart, and studies in different countries have found different efficacy rates due to voluntary participation. The efficacy and safety study of the CoronaVac vaccine determined the efficacy of the vaccine as 83.5 % in Turkey and 50.6 % in Brazil for preventing symptomatic disease and 100 % for preventing hospitalization in both countries (3–5).

Due to the mutations of the virus, the course of the disease and the level of contagiousness of the virus have changed. In the first months of 2021, the preventive efficacies of vaccines have been demonstrated against symptomatic disease and fatal consequences caused by the original virus and the alpha (B.1.1.7) variant, which was prevalent at that time (6). Despite its lower efficacy against the delta and beta (B.1.351) variants, the administration of two doses of the BNT162b2 vaccine has been shown to establish immunity that lasts for about 6 months and remains effective in protecting against severe disease (7). Compared to the delta variant, the neutralizing antibody response has been shown to decrease over time in the omicron variant (8). Numerous mutations have been identified in the omicron variant, including multiple mutations in the receptor binding site of the spike protein. These mutations are associated with increased contagiousness and immune evasion after natural infection and vaccination (9). Since antibodies decrease over time, the cellular immune response plays a critical role in protection from the SARS-CoV-2 virus and its variants (10). Emerging variants necessitated the periodic renewal of vaccines. The third dose of the BNT162b2 vaccine, namely, the reminder dose, was shown to increase the number of neutralizing antibodies and protection against reinfection and severe disease (2, 8, 11, 12).

Vaccine efficacy is determined by the reduced risk of infection or disease among vaccinated individuals and is influenced by many factors. Host-related factors include advanced age, previous infections, immunodeficiency, genetic polymorphism and comorbidities, while vaccine-related factors include the type of vaccine used, the number of doses administered, the time elapsed between doses, and the limitations of access to the vaccine (2). The high number of circulating viruses, the contact of the infected population with a large number of people, and the inability to reach the herd immunity level in a short time, reduce the effectiveness of the vaccine. On the other hand, high antibody levels and neutralization quality increase success.

Although current studies provide new data on the long-term effects of the virus, prevention of asymptomatic infection, the severity of COVID-19, and the effectiveness of reminder doses administered with different vaccines, publications on the effects of vaccines

on survival are limited. Therefore, our study is aimed to contribute to the literature by determining the efficacy and survival rates of BNT162b2 (Pfizer-BioNTech) and CoronaVac (Sinovac) vaccines against symptomatic or severe disease in COVID-19 diagnosed patients. The secondary aim of the study was to define the differences between vaccinated and unvaccinated patients in terms of age, comorbidities and course of the disease, and to determine the survival rates.

EXPERIMENTAL

This retrospective observational study included 1463 SARS CoV-2 RT-PCR positive, symptomatic patients under 101 years of age, who were followed up in Çorlu State Hospital (Tekirdağ, Turkey) with a definite diagnosis of COVID-19, between May 2021 and June 2022. Patients over 101 years of age and negative for SARS CoV-2 RT-PCR were excluded from the study. Age, gender, comorbidities, discharge, transfer to the ward or intensive care unit, COVID-19 vaccination status, when and which vaccines were administered, the time between hospitalization and vaccination, and survival information of all cases were recorded. Comorbidities were classified as hypertension (HT), diabetes mellitus (DM), asthma, chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), cerebrovascular event (CVE), thyroid disease, obesity, chronic kidney disease (CKD), and other diseases.

The study started after the approval of the university ethics committee (the approval code: 2022.80.05.07 and date: 31.05.2022) and the approval of the Ministry of Health of the Republic of Turkey (the approval code: 2022-04-11T18-46-56).

The SARS-CoV-2 RT-PCR test was applied to all patients in our hospital who had symptoms specific to COVID-19 infection (fever, new-onset cough, loss of smell, taste, *etc.*) or had contact with people who tested positive. Nasopharyngeal and throat swab samples were placed in a viral nucleic acid buffer (Bio-Speedy vNAT, Bioeksen, Turkey) and examined under appropriate conditions in our microbiology laboratory with an RT-PCR test (Bio-speedy SARS CoV-2 double gene RT-qPCR kit, Biospeedy SARS CoV-2 + VOC202012/01 RT-qPCR kit, Biospeedy SARS CoV-2 emerging plus, Coronagen RT-qPCR COVID 19 mutation detection kit V2.0, Coronagen RT-qPCR SARS CoV-2 variants detection kit V1.0, Turkey). At the time of the study, the dominant variants in Turkey were delta and omicron.

The patients were divided into two groups according to the severity of their symptoms: mild-moderate and severe-critical. The mild-moderate disease was defined as the presence of symptoms such as fever, cough, sore throat, headache, weakness, *etc.*, but no shortness of breath, no respiratory distress, normal lung radiology, and oxygen saturation of 94 % or higher. The severe-critical disease was defined as the presence of respiratory rate above 30 breaths per minute, oxygen saturation less than 94 %, $\text{PaO}_2/\text{FiO}_2$ value below 300 mm Hg, or infiltration extending to more than 50 % of the lungs, septic shock and/or multiple organ failure (13).

Statistical analysis

Data were analyzed with IBM SPSS V23. Conformity to normal distribution was evaluated with the Kolmogorov-Smirnov test. Pearson chi-square test was used to compare

categorical data between groups, and multiple comparisons of ratios were analyzed with Bonferroni corrected Z test. The Mann-Whitney U test was used to compare the non-normally distributed data between the paired groups. Binary logistic regression analysis was used to examine the risk factors affecting mortality. Results were presented as mean ± SD and median (minimum-maximum) for quantitative data, and frequency (percentage) for categorical data. The significance level was accepted as $p < 0.050$.

RESULTS AND DISCUSSION

The safety and efficacy of BNT162b2 and CoronaVac vaccines have been reported previously and the performances of these two vaccines have been directly compared in some studies (5–17). Vaccines developed against the SARS-CoV-2 virus have slowed the pace of the COVID-19 pandemic and also enabled people to experience milder or no symptoms at all. Young-Eun Kim *et al.* (18) showed that the risk of developing thromboembolic events, ischemic attacks, and heart attacks, which are the most feared complications of infection, is reduced when the vaccine is administered in full dose.

Of the 1463 patients included in the study, 46.1 % were female, 53.9 % were male, 55.3 % were vaccinated, and 44.7 % were unvaccinated. While 959 patients had mild-moderate symptoms, 504 patients had severe-critical symptoms and were treated in the intensive care unit. 53.0 % of those who had the disease with severe symptoms were male patients. Xie *et al.* (19) reported the male gender to be at higher risk for COVID-19 disease. A comparison of gender, comorbidities, vaccination status, survival rates, and administered vaccines by the patient group are given in Table I. The median age values were significantly

Table I. Gender, comorbidities, hospitalization service, vaccination status, intensive care and service survival rates, and administered vaccines

Patient No. (%)	Critical-severe patients	Mild-moderate patients	Total	Test statistic ^a	p-value ^b
Gender					
Female	237 (47)	437 (45.6)	674 (46.1)	0.282	0.596
Male	267 (53)	522 (54.4)	789 (53.9)		
Comorbidity					
HT	175 (40) ^c	146 (34.3) ^c	321 (37.2)	134.045	< 0.001
DM	142 (32.4) ^c	145 (34) ^c	287 (33.2)		
Asthma	25 (5.7) ^c	17 (4) ^c	42 (4.9)		
COPD	47 (10.7) ^c	49 (11.5) ^c	96 (11.1)		
CAD	52 (11.9) ^c	58 (13.6) ^c	110 (12.7)		
CVE	38 (8.7) ^c	24 (5.6) ^c	62 (7.2)		
Thyroid	8 (1.8) ^c	6 (1.4) ^c	14 (1.6)		
Obesity	9 (2.1) ^c	4 (0.9) ^c	13 (1.5)		
CKD	67 (15.3) ^c	62 (14.6) ^c	129 (14.9)		
Other	361 (82.4) ^c	197 (46.2) ^d	558 (64.6)		

Hospitalization service					
1	– ^e	842 (87.8)	842 (87.8)		
2	–	105 (10.9)	105 (10.9)		
3	–	10 (1)	10 (1)	–	–
4	–	2 (0.2)	2 (0.2)		
Vaccination status					
Vaccinated	270 (53.6)	539 (56.2)	809 (55.3)	0.927	0.336
Unvaccinated	234 (46.4)	420 (43.8)	654 (44.7)		
Intensive care survival rates					
Alive	166 (32.9)	–	166 (32.9)		
Exitus	329 (65.3)	–	329 (65.3)	–	–
Transferred	9 (1.8)	–	9 (1.8)		
Service survival rates					
Discharged	–	791 (82.5)	791 (82.5)		
Transferred to ICU	–	93 (9.7)	93 (9.7)		
Exitus	–	10 (1)	10 (1)	–	–
Another hospital	–	13 (1.4)	13 (1.4)		
Service	–	52 (5.4)	52 (5.4)		
Mortality					
No	175 (34.7)	949 (99)	1124 (76.8)	765.722	< 0.001
Yes	329 (65.3)	10 (1)	339 (23.2)		
Vaccines and doses					
BioNTech1	20 (7.4) ^c	32 (5.9) ^c	52 (6.4)		
BioNTech2	34 (12.6) ^c	102 (18.9) ^d	136 (16.8)		
BioNTech3	9 (3.3) ^c	23 (4.3) ^c	32 (4)		
BioNTech4	1 (0.4) ^c	1 (0.2) ^c	2 (0.2)		
Sinovac1	6 (2.2) ^c	14 (2.6) ^c	20 (2.5)		
Sinovac2	87 (32.3) ^c	142 (26.3) ^c	229 (28.3)		
Sinovac3	54 (20.1) ^c	124 (23) ^c	178 (22)	26.705	0.021
Sinovac4	8 (3) ^c	15 (2.8) ^c	23 (2.8)		
1BioNTech2Sinovac	41 (15.2) ^c	66 (12.2) ^c	107 (13.2)		
1BioNTech3Sinovac	1 (0.4)	0 (0)	1 (0.1)		
2BioNTech2Sinovac	5 (1.9) ^c	27 (5) ^d	32 (4)		
2BioNTech1Sinovac	2 (0.7)	0 (0)	2 (0.2)		
3BioNTech2Sinovac	1 (0.4)	0 (0)	1 (0.1)		
3BioNTech1Sinovac	1 (0.4)	0 (0)	1 (0.1)		

CAD – coronary artery disease, CKD – chronic kidney disease, COPD – chronic obstructive pulmonary disease, CVE – cerebrovascular event, DM – diabetes mellitus, HT – hypertension, ICU – intensive care unit

^a Test statistic is calculated using sample data and compared to a critical value or *p*-value to determine if the hypothesis is correct; ^b Pearson chi-square test; ^{c,d} No significant difference between groups with the same letter in the line; ^e Could not be calculated due to the lack of observations.

Table II. Mean (minimum, maximum) levels and standard deviations of the age and time between hospitalization and vaccination by patient group

	Critical-severe		Mild-moderate		Total		Test statistic ^a	p-value ^b
	Mean ± SD	Mean (min-max)	Mean ± SD	Mean (min-max)	Mean ± SD	Mean (min-max)		
Age (year)	71.04 ± 14.77	73 (2–101)	60.4 ± 22.39	65 (0–96)	64.07 ± 20.71	68 (0–101)	175333.5	< 0.001
Time (day)	– ^c	–	125.13 ± 78.43	120 (20–450)	125.13 ± 78.43	120 (20–450)	–	–

^aTest statistic is calculated using sample data and compared to a critical value or p-value to determine if the hypothesis is correct; ^bMann-Whitney U test; ^cCould not be calculated due to the lack of observations.

different between the patient groups ($p < 0.001$): 73 in the severe patient group and 65 in the mild-moderate patient group. The median time that elapsed between the administration of vaccines and hospitalization of service patients was 120 days (Table II).

The distribution of comorbidities was significantly different between the patient groups ($p < 0.001$). The rate of those with comorbidities was 82.4 % in the severe patient group and 46.2 % in the mild-moderate patient group. Mortality rates also differed significantly between the patient groups ($p < 0.001$). The survival rate was 34.7 % in the severe patient group and 99.0 % in the mild-moderate patient group.

The most common comorbidities were hypertension (37.2 %), diabetes mellitus (33.2 %), chronic kidney damage (14.9 %) and coronary artery disease (12.7 %). Sandalçı *et al.* (20) stated that the presence of diabetes mellitus, hypertension, cardiovascular diseases and chronic lung diseases caused an increase in the need for intensive care. Likewise, our study revealed a significantly higher comorbidity rate in the severe-critical patient group compared to the mild-moderate symptomatic patient group ($p < 0.001$). The most common comorbidity was hypertension (40.0 %) in the severe-critical patient group and diabetes mellitus (37.2 %) in the mild-moderate patient group.

Mortality rates were 65.3 % in the severe-critical patient group and 1.0 % in the mild-moderate patient group. Of mild-moderate symptomatic patients, 82.5 % were discharged, 9.7 % were transferred to the intensive care unit, 5.4 % were transferred to a different service due to comorbidities, and 1.4 % were transferred to another hospital. Mortality risk was 125.6 times higher in severe-critical patients compared to mild-moderate patients ($p < 0.001$). The risk of mortality increased by 1.041 times with increasing age in the univariate model ($p < 0.001$) but in the multivariate model, this ratio was 1.039 fold ($p < 0.001$). Again, the risk of mortality was 1.7 times higher in the presence of other comorbidities ($p = 0.001$). The higher risk of mortality in patients with HT, DM, COPD, CAD, CVE, obesity and CKD was found in the univariate analysis but was found statistically insignificant in the multivariate analysis.

Risk factors affecting mortality were analyzed with binary logistic regression analysis as univariate and multivariate models (Table III). In the univariate model, the risk of mortality in patients with severe disease was 178.4 times higher than in those with mild-moderate disease ($p < 0.001$). In the multivariate model, this ratio was 125.6 ($p < 0.001$). The risk of mortality increased by 1.039 times with increasing age in the multivariate model ($p < 0.001$). The patients with HT had a 2.2₅-fold greater risk of mortality in the univariate model than those without HT ($p < 0.001$), but the difference was not significant in the multivariate model. Mortality risk was found 1.7 times higher in individuals with DM compared to those without DM in the univariate model ($p < 0.001$), though not significant in the multivariate model. Those with COPD had 1.8 times greater risk of mortality than those without ($p = 0.008$) in the univariate model, but the difference was again not significant in the multivariate model. Similarly, those with CAD had a 1.5 times greater risk of mortality than those without CAD ($p = 0.047$) in the univariate model, though not significant in the multivariate model. Mortality risk was also 3.1 times higher in those with CVE compared to those without CVE in the univariate model ($p < 0.001$), but this difference was not significant in the multivariate model. Obese individuals had a 3.9-fold higher mortality risk in the univariate model than those

Table III. Binary logistic regression analysis of risk factors for mortality

	Univariate		Multivariate	
	OR (95 % CI)	<i>p</i>	OR (95 % CI)	<i>p</i>
Group (reference: mild-moderate patient)	178.41 (93.18–341.57)	< 0.001	125.55 (63.99–246.35)	< 0.001
Age (year)	1.04 (1.03–1.05)	< 0.001	1.03 (1.02–1.05)	< 0.001
Gender (reference: female)	0.95 (0.75–1.22)	0.726	1.08 (0.74–1.58)	0.673
Time (hour)	0.99 (0.97–1.02)	0.948	– ^a	–
HT (reference: none)	2.24 (1.71–2.94)	< 0.001	0.82 (0.53–1.27)	0.384
DM (reference: none)	1.70 (1.27–2.26)	< 0.001	0.93 (0.60–1.45)	0.764
Asthma (reference: none)	1.88 (0.98–3.57)	0.054	0.85 (0.35–2.04)	0.722
COPD (reference: none)	1.81 (1.17–2.82)	0.008	1.26 (0.65–2.44)	0.490
CAD (reference: none)	1.53 (1.00–2.34)	0.047	0.88 (0.48–1.64)	0.710
CVE (reference: none)	3.09 (1.84–5.17)	< 0.001	1.66 (0.77–3.58)	0.189
Thyroid (reference: none)	2.51 (0.86–7.29)	0.090	1.90 (0.37–9.56)	0.434
Obesity (reference: none)	3.92 (1.31–11.77)	0.015	2.68 (0.52–13.77)	0.237
CKD (reference: none)	2.20 (1.51–3.22)	< 0.001	1.58 (0.87–2.86)	0.129
Other (reference: none)	7.15 (5.44–9.40)	< 0.001	1.71 (1.13–2.59)	0.010
Vaccination status (reference: vaccinated)	1.19 (0.93–1.52)	0.154	1.53 (1.04–2.24)	0.029

CAD – coronary artery disease, CKD – chronic kidney disease, COPD – chronic obstructive pulmonary disease, CVE – cerebrovascular event, DM – diabetes mellitus, HT – hypertension, OR – odds ratio, CI – confidence interval.

^a Could not be calculated due to the lack of observations.

non-obese ($p = 0.015$), though also not significant in the multivariate model. Those with CKD had a 2.2 times higher risk of mortality compared to those without CKD ($p < 0.001$) in the univariate model, but there was no significant difference in the multivariate model. The mortality risk of patients with other diseases was 7.2 times higher than of those without ($p < 0.001$) in the univariate model and it was 1.7 in the multivariate model ($p = 0.010$). In the multivariate model, the mortality risk was 1.5 times higher in the unvaccinated than in the vaccinated persons ($p = 0.029$), although not significant in the univariate model. Other variables showed no statistically significant effects.

Risk factors affecting mortality in the severely ill group were analyzed using binary logistic regression analysis as univariate and multivariate models (Table IV). As the age increased, the risk of mortality increased 1.031 times ($p < 0.001$) in the univariate model and 1.035 times in the multivariate model ($p < 0.001$). The risk of mortality in patients with other diseases was 1.634 times higher than in those without ($p = 0.027$) in the multivariate model, though not significant in the univariate model. The multivariate model showed that the mortality risk of the unvaccinated was 1.511 times higher compared to the vaccinated ($p = 0.042$). However, this difference was not significant in the univariate model. Other variables had no statistically significant effects.

The comparison of vaccinated and unvaccinated patient groups supported the importance of vaccines, as being unvaccinated was found to increase mortality 1.51 times ($p = 0.042$). Of the patients, 55.3 % were vaccinated and 44.7 % were unvaccinated. While the number of vaccinated patients in the severely ill group was 270, the number of unvac-

Table IV. Binary logistic regression analysis of risk factors affecting mortality in the severe patient group

	Univariate		Multivariate	
	OR (95 % CI)	<i>p</i>	OR (95 % CI)	<i>p</i>
Age (year)	1.03 (1.01–1.04)	< 0.001	1.03 (1.02–1.04)	< 0.001
Gender (reference: female)	1.02 (0.71–1.48)	0.894	1.10 (0.74–1.63)	0.637
HT (reference: none)	0.95 (0.64–1.40)	0.808	0.85 (0.54–1.33)	0.498
DM (reference: none)	0.85 (0.57–1.27)	0.442	0.93 (0.59–1.47)	0.780
Asthma (reference: none)	0.78 (0.34–1.79)	0.570	0.86 (0.35–2.08)	0.743
COPD (reference: none)	1.14 (0.60–2.18)	0.671	1.22 (0.61–2.44)	0.557
CAD (reference: none)	1.00 (0.55–1.83)	0.986	0.94 (0.49–1.77)	0.855
CVE (reference: none)	1.78 (0.82–3.85)	0.142	1.81 (0.81–4.05)	0.144
Thyroid (reference: none)	1.60 (0.32–8.04)	0.564	2.06 (0.37–11.30)	0.403
Obesity (reference: none)	1.88 (0.38–9.15)	0.434	2.67 (0.50–14.13)	0.247
CKD (reference: none)	1.29 (0.73–2.25)	0.369	1.42 (0.77–2.62)	0.258
Other (reference: none)	1.42 (0.95–2.12)	0.084	1.63 (1.05–2.52)	0.027
Vaccination status (reference: vaccinated)	1.24 (0.86–1.80)	0.241	1.51 (1.01–2.24)	0.042

CAD – coronary artery disease, CKD – chronic kidney disease, COPD – chronic obstructive pulmonary disease, CVE – cerebrovascular event, DM – diabetes mellitus, HT – hypertension, OR – odds ratio, CI – confidence interval

nated patients was 234. The vaccination rate in patients with mild-moderate symptoms was 56.2 %. There was a statistically significant difference in the distribution of vaccines between the patient groups ($p = 0.021$). The rate of receiving 2 doses of Biontech was 18.9 % in the mild-moderate patient group but lower in the severe patient group (12.6 %). The rate of 2 doses of Sinovac and 2 doses of Biontech vaccine (four doses of vaccine) was 5 % in the mild-moderate patient group and 1.9 % in the severe patient group. Our findings show that being vaccinated is effective in preventing severe disease and mortality in COVID-19 infection. F. Rammauro *et al.* (16) showed that the administration of a reminder dose with BNT162b2 increased humoral immunity 22 times compared to 2 doses of the CoronaVac vaccine. Again, a large-scale meta-analysis showed that being fully vaccinated against the omicron variant reduces the risk of infection and that the administration of a reminder dose provides additional benefits (21). Although the decrease in the level of neutralizing antibodies below the level of protection over time increases the spread of variants, studies have shown that vaccines increase viral clearance through memory B responses. Administration of the 3rd dose of vaccine increased the level of neutralizing antibodies against the omicron (BA.1, BA.1.1, and BA.2) variant 10 times more than the 2nd dose and 80 times more than the 1st dose (22). A cohort study on healthcare workers in Israel reported the infection rates as 6.9 % in those who received the 4th dose of the COVID-19 vaccine and 19.8 % in those who were vaccinated with 3 doses (23). In a study by Yan *et al.* (24) vaccine effectiveness against omicron BA.2 variant-related mortality after two doses of Biontech and CoronaVac were 90.7 and 74.8 %, resp. Both vaccinations were found to be effective against COVID-19-related mortality and severe complications. In our study, the higher rate of protection from severe infection in patients with 2 doses of Biontech vaccine and 2 doses of Biontech plus 2 doses of Sinovac vaccine supports the efficacy of the Biontech vaccine.

CONCLUSIONS

In conclusion, our study investigating the effects and survival rates of BNT162b2 and CoronaVac vaccine administration in the prevention of severe disease revealed significantly higher mortality in the case of advanced age, comorbidity and severe clinical symptoms. COVID-19 vaccines are still the most effective weapon in the fight against the pandemic, not only to prevent the disease but also to prevent severe illness and consequent intensive care hospitalizations and to reduce mortality.

REFERENCES

1. V. J. Hall, S. Foulkes, A. Saei, N. Andrews, B. Oguni, A. Charlett, E. Wellington, J. Stowe, N. Gillson, A. Atti, J. Islam, I. Karagiannis, K. Munro, J. Khawam, M. A. Chand, C. S. Brown, M. Ramsay, J. Lopez-Bernal, S. Hopkins, and SIREN study group, COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study, *Lancet* (London) **397**(10286) (2021) 1725–1735; [https://doi.org/10.1016/S0140-6736\(21\)00790-X](https://doi.org/10.1016/S0140-6736(21)00790-X)
2. J. S. Tregoning, K. E. Flight, S. L. Higham, Z. Wang and B. F. Pierce, Progress of the COVID-19 vaccine effort: viruses, vaccines and variants versus efficacy, effectiveness and escape, *Nat. Rev. Immunol.* **21**(10) (2021) 626–636; <https://doi.org/10.1038/s41577-021-00592-1>

3. A. Kazak, S. Hintistan and Ö. Betül, Dünyada ve Türkiye’de COVID-19 aşısı geliştirme çalışmaları (COVID-19 vaccine development studies in the world and in Turkey), *Celal Bayar Üniversitesi Sağlık Bilimleri Enstitüsü Dergisi (J. Celal Bayar Uni. Health Sci. Inst.)* 7(4) (2020) 571–575; <https://doi.org/10.348087/cbusbed.749009>
4. M. D. Tanrıöver, H. L. Doğanay, M. Akova, H. R. Güner, A. Azap, S. Akhan, Ş. Köse, F. Ş. Erdinç, E. H. Akalın, Ö. F. Tabak, H. Pullukçu, Ö. Batum, S. Ş. Yavuz, Ö. Turhan, M. T. Yıldırım, İ. Köksal, Y. Taşova, V. Korten, G. Yılmaz, M. K. Çelen, S. Altın, İ. Çelik, Y. Bayındır, İ. Karaoğlu, A. Yılmaz, A. Özkul, H. Gür, S. Unal, and the 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* (London) 398(10296) (2021) 213–222; [https://doi.org/10.1016/S0140-6736\(21\)01429-X](https://doi.org/10.1016/S0140-6736(21)01429-X)
5. T. Fiolet, Y. Kherabi, C. J. MacDonald, J. Ghosn and N. Peiffer-Smadja, Comparing COVID-19 vaccines for their characteristics, efficacy and effectiveness against SARS-CoV-2 and variants of concern: a narrative review, *Clin. Microb. Infect.* 28(2) (2022) 202–221; <https://doi.org/10.1016/j.cmi.2021.10.005>
6. M. G. Thompson, J. L. Burgess, A. L. Naleway, H. L. Tyner, S. K. Yoon, J. Meece, L. E. W. Olsho, A. J. Caban-Martinez, A. Fowlkes, K. Lutrick, J. L. Kuntz, K. Dunnigan, M. J. Odean, K. T. Hegmann, E. Stefanski, L. J. Edwards, N. Schaefer-Solle, L. Grant, K. Ellingson, H. C. Groom, T. Zunie, M. S. Thiese, L. Ivacic, M. G. Wesley, J. M. Lamberte, X. Sun, M. E. Smith, A. L. Phillips, K. D. Groover, Y. M. Yoo, J. Gerald, R. T. Brown, M. K. Herring, G. Joseph, S. Beitel, T. C. Morrill, J. Mak, P. Rivers, K. M. Harris, D. R. Hunt, M. L. Arvay, P. Kutty, A. M. Fry, M. Gaglani, Interim estimates of vaccine effectiveness of BNT162b2 and mRNA-1273 COVID-19 vaccines in preventing SARS-CoV-2 infection among health care personnel, first responders, and other essential and frontline workers – Eight U.S. locations, December 2020–March 2021, *Morb. Mortal. Weekly Rep.* 70(13) (2021) 495–500; <https://doi.org/10.15585/mmwr.mm7013e3>
7. V. Hall, S. Foulkes, F. Insalata, P. Kirwan, A. Saei, A. Atti, E. Wellington, J. Khawam, K. Munro, M. Cole, C. Tranquillini, A. Taylor-Kerr, N. Hettiarachchi, D. Calbraith, N. Sajedi, I. Milligan, Y. Themistocleous, D. Corrigan, L. Cromey, L. Price, S. Stewart, E. de Lacy, C. Norman, E. Linley, A. D. Otter, A. Semper, J. Hewson, S. D’Arcangelo, M. Chand, C. S. Brown, T. Brooks, J. Islam, A. Charlett and S. Hopkins (for the SIREN Study Group), Protection against SARS-CoV-2 after Covid-19 vaccination and previous infection, *N. Engl. J. Med.* 386 (2022) 1207–1220; <https://doi.org/10.1056/NEJMoa2118691>
8. N. Andrews, J. Stowe, F. Kirsebom, S. Toffa, T. Rieckard, E. Gallagher, C. Gower, M. Kall, N. Groves, A.-M. O’Connell, D. Simons, P. B. Blomquist, A. Zaidi, S. Nash, N. I. B. A. Aziz, S. Thelwall, G. Dabrera, R. Myers, G. Amirthalingam, S. Gharbia, J. C. Barrett, R. Elson, S. N. Ladhani, N. Ferguson, M. Zambon, C. N. J. Campbell, K. Brown, S. Hopkins, M. Chand, M. Ramsay and J. Lopez Bernal, Covid-19 vaccine effectiveness against the Omicron (B.1.1.529) variant, *New Engl. J. Med.* 386(16) (2022) 1532–1546; <https://doi.org/10.1056/NEJMoa2119451>
9. European Centre for Disease Prevention and Control, *Implications of the Further Emergence and Spread of the SARS CoV-2 B.1.1.529 Variant of Concern (Omicron) for the EU/EEA – first update*, December 2, 2021; <https://www.ecdc.europa.eu/sites/default/files/documents/threat-assessment-covid-19-emergence-sars-cov-2-variant-omicron-december-2021.pdf>; last access data March 3, 2023.
10. R. R. Goel, M. M. Painter, S. A. Apostolidis, D. Mathew, W. Meng, A. M. Rosenfeld, K. A. Lundgreen, A. Reynaldi, D. S. Khoury, A. Pattekar, S. Gouma, L. Kuri-Cervantes, P. Hicks, S. Dysinger, A. Hicks, H. Sharma, S. Herring, S. Korte, A. E. Baxter, D. A. Oldridge, J. R. Giles, M. E. Weirick, C. M. McAllister, M. Awofolaju, N. Tanenbaum, E. M. Drapeau, J. Dougherty, S. Long, K. D’Andrea, J. T. Hamilton, M. McLaughlin, J. C. Williams, S. Adamski, O. Kuthuru, U. Penn COVID Processing Unit; I. Frank, M. R. Betts, L. A. Vella, A. Grifoni, D. Weiskopf, A. Sette, S. E. Hensley, M. P. Davenport, P. Bates, E. T. Luning Prak, A. R. Greenplate and E. J. Wherry, mRNA vaccines induce durable immune memory to SARS-CoV-2 and variants of concern, *Science* (New York) 374(6572) (2021) Article ID 1214 (17 pages); <https://doi.org/10.1126/science.abm0829>

11. Y. M. Bar-On, Y. Goldberg, M. Mandel, O. Bodenheimer, L. Freedman, N. Kalkstein, B. Mizrahi, S. Alroy-Preis, N. Ash, R. Milo and A. Huppert, Protection of BNT162b2 vaccine booster against Covid-19 in Israel, *New Engl. J. Med.* **385**(15) (2021) 1393–1400; <https://doi.org/10.1056/NEJMoa2114255>
12. D. S. Khoury, D. Cromer, A. Reynaldi, T. E. Schlub, A. K. Wheatley, J. A. Juno, K. Subbarao, S. J. Kent, J. A. Triccas and M. P. Davenport, Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection, *Nat. Med.* **27**(7) (2021) 1205–1211; <https://doi.org/10.1038/s41591-021-01377-8>
13. World Health Organization, *WHO COVID-19 Case Definition* – Updated in Public health surveillance for COVID-19, WHO, 22 July 2022; https://www.who.int/publications/i/item/WHO-2019-nCoV-Surveillance_Case_Definition-2020; last access date March 3, 2023.
14. Republic of Turkey – Ministry of Health, Covid-19 Vaccine Information Platform, *Covid-19 Aşısı Ulusal Uygulama Stratejisi (Covid-19 Vaccine National Implementation Strategy)*; <https://covid19asi.saglik.gov.tr/TR-77706/covid-19-asi-si-ulusal-uygulama-stratejisi.html>
15. C. K. P. Mok, C. A. Cohen, S. M. S. Cheng, C. Chen, K. O. Kwok, K. Yiu, T. O. Chan, M. Bull, K. C. Ling, Z. Dai, S. S. Ng, G. C. Lui, C. Wu, G. K. Amarasinghe, D. W. Leung, S. Y. S. Wong, S. A. Valkenburg, M. Peiris and D. S. Hui, Comparison of the immunogenicity of BNT162b2 and CoronaVac COVID-19 vaccines in Hong Kong, *Respirology* (Carlton, Vic.) **27**(4) (2022) 301–310; <https://doi.org/10.1111/resp.14191>
16. F. Rammauro, F. Carrión, N. Olivero-Deibe, M. Fló, A. Ferreira, O. Pritsch and S. Bianchi, Humoral immune response characterization of heterologous prime-boost vaccination with CoronaVac and BNT162b2, *Vaccine* **40**(35) (2022) 5189–5196; <https://doi.org/10.1016/j.vaccine.2022.07.023>
17. W. W. Lim, L. Mak, G. M. Leung, B. J. Cowling and M. Peiris, Comparative immunogenicity of mRNA and inactivated vaccines against COVID-19, *Lancet Microbe* **2**(9) (2021) e423; [https://doi.org/10.1016/S2666-5247\(21\)00177-4](https://doi.org/10.1016/S2666-5247(21)00177-4)
18. Y. E. Kim, K. Huh, Y. J. Park, K. R. Peck and J. Jung, Association between vaccination and acute myocardial infarction and ischemic stroke after COVID-19 infection, *JAMA* **328**(9) (2022) 887–889; <https://doi.org/10.1001/jama.2022.12992>
19. J. Xie, Z. Tong, X. Guan, B. Du, H. Qiu and A. S. Slutsky, Critical care crisis and some recommendations during the COVID-19 epidemic in China, *Int. Care Med.* **46**(5) (2020) 837–840; <https://doi.org/10.1007/s00134-020-05979-7>
20. B. Sandalc, O. A. Uyaroglu and G. S. Guven, COVID-19'da kronik hastaliklarnin roli, onemi ve oneriler (The role and importance of chronic diseases in COVID-19 and related recommendations), *Flora* **25**(2) (2020) 132–138; <https://doi.org/10.5578/flora.69700>
21. Y. Zou, D. Huang, Q. Jiang, Y. Guo and C. Chen, The vaccine efficacy against the SARS-CoV-2 Omicron: A systemic review and meta-analysis, *Front. Public Health* **10** (2022) Article ID 940956 (9 pages); <https://doi.org/10.3389/fpubh.2022.940956>
22. L. Wang, M. H. Kainulainen, N. Jiang, H. Di, G. Bonenfant, L. Mills, M. Currier, P. Shrivastava-Ranjan, B. M. Calderon, M. Sheth, B. R. Mann, J. Hossain, X. Lin, S. Lester, E. A. Pusch, J. Jones, D. Cui, P. Chatterjee, M. H. Jenks, E. K. Morantz, G. P. Larson, M. Hatta, J. L. Harcourt, A. Tamin, Y. Li, Y. Tao, K. Zhao, K. Lacek, A. Burroughs, W. Wang, M. Wilson, T. Wong, S. H. Park, S. Tong, J. R. Barnes, M. W. Tenforde, W. H. Self, N. I. Shapiro, M. C. Exline, D. C. Files, K. W. Gibbs, D. N. Hager, M. Patel, A. L. Halpin, L. K. McMullan, J. S. Lee, H. Xia, X. Xie, P.-Y. Shi, C. T. Davis, C. F. Spiropoulou, N. J. Thornburg, M. S. Oberste, V. G. Dugan, SSE Bioinformatics Working Group, D. E. Wentworth and B. Zhou, Differential neutralization and inhibition of SARS-CoV-2 variants by antibodies elicited by COVID-19 mRNA vaccines, *Nature Commun.* **13**(1) (2022) Article ID 4350 (10 pages); <https://doi.org/10.1038/s41467-022-31929-6>
23. M. J. Cohen, Y. Oster, A. E. Moses, A. Spitzer, S. Benenson and Israeli-Hospitals 4th Vaccine Working Group, Association of receiving a fourth dose of the BNT162b vaccine with SARS-CoV-2

- infection among health care workers in Israel, *JAMA Network Open* 5(8) (2022) e2224657 (7 pages); <https://doi.org/10.1001/jamanetworkopen.2022.24657>
24. V. K. C. Yan, E. Y. F. Wan, X. Ye, A. H. Y. Mok, F. T. T. Lai, C. S. L. Chui, X. Li, C. K. H. Wong, P. H. Li, T. Ma, S. Qin, V. K. C. Wong, T. C. Tsang, S. H. Tsui, W. C. M. Chui, B. J. Cowling, G. M. Leung, C. S. Lau, I. C. K. Wong and E. W. Y. Chan, Effectiveness of BNT162b2 and CoronaVac vaccinations against mortality and severe complications after SARS-CoV-2 Omicron BA.2 infection: a case-control study, *Emerg. Microbes Infect.* 11(1) (2022) 2304–2314; <https://doi.org/10.1080/22221751.2022.2114854>