Demographic Features and Laboratory Parameters Among Hospitalized Vaccinated Patients With COVID-19 in Istanbul, Turkey

Ayşegul Karahasan Yagci, MD, Gamze Alci, PhD,† Mehmet Mucahit Guncu, PhD,* Omer Bugrahan Yılmaz,‡ Eranalp Tekin,‡ Safa Emre Cakır,‡ Burak Cebe,‡ Cem Ozturk,‡ and Onder Sirikci, MD§*

Background: The number of COVID-19 cases has been decreasing recently, and the restrictions are waived in many countries. The data about vaccine efficacy are essential to be prepared for the future even if the pandemic ends and the disease becomes endemic.

Aims: The aim of this study was to define demographic and laboratory data for disease severity among vaccinated COVID-19 cases who were hospitalized.

Study Design: This is a retrospective cohort study.

Methods: SARS-CoV-2 polymerase chain reaction–positive patients who were fully vaccinated (2 doses of vaccines and 3 doses of vaccines) and had been hospitalized at least 15 days after the last vaccine dose were enrolled in this study. Patients' data including laboratory parameters were retrieved, and descriptive statistics and comparison of variables were calculated.

Results: Between September 1, 2021, and February 28, 2022, 685 patients (mean age, 67.84 years; 50.8% female) were hospitalized. Inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac) had been administered to 467 of the patients (68.4%), BNT162b2 mRNA vaccine (Pfizer-Pfizer-BioNTech) had been administered to 107 of the patients (15.6%), and to 111 of the patients (16%), a combination of 2 vaccines had been administered. At least 1 comorbidity was present in 160 participants (23%) and more than 4 comorbidities in 46 patients (6.6%). The most common comorbidity was hypertension (349, 50.2%). The presence of comorbidities was significantly higher in patients having 3 doses of vaccine. Increased ferritin levels were determined in 56.4% of the patients, increased D-dimer levels in 69.9% of the patients, increased C-reactive protein levels in 79.7% of the patients, and increased procalcitonin levels in 61.5% of the patients. A total of 36.4% of the patients had decreased lymphocyte counts, 20% had low lymphocyte/monocyte ratio, and 22% had decreased neutrophil/lymphocyte ratio. The only parameter that was significantly higher in patients having 3 vaccine doses was procalcitonin. Mean duration of hospitalization was 9.68 ± 7.29 days. In the CoronaVac and Pfizer-BioNTech groups, 68.5% and 21.4%, respectively, of the patients were older than 65 years. Seventeen (3.6%) patients in the CoronaVac group, 6 (5.4%) patients in the combination group, and 3 (2.8%) patients in Pfizer-BioNTech group had been admitted to the intensive care unit. Mortality rate was 0.3% (2 of 685 patients).

Conclusions: The incidence of severe COVID-19 disease among fully vaccinated patients is low even in the presence of comorbidities, older age, and presence of abnormal laboratory parameters, regardless of the vaccine type.

Key Words: COVID-19, vaccine, epidemiology

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From the *Medical Microbiology, Marmara University, School of Medicine, Pendik Education and Research Hospital, Istanbul; †Medical Microbiology, Kocaeli University, Kocaeli; ‡Student of Medicine, and §Medical Biochemistry, Marmara University, School of Medicine, Pendik Education and Research Hospital, Istanbul, Turkey.

Correspondence to: Aysegul Karahasan Yagci, MD, Medical Microbiology, Marmara University, School of Medicine, Pendik Education and Research Hospital, Muhsin Yazıcıoğlu Street, Kaynarca/Pendik, Istanbul, Turkey. E-mail: ayagci@marmara.edu.tr.

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Since January 11, 2020, when the World Health Organization declared the COVID-19 disease as a pandemic, all technological possibilities of our age have been mobilized to defeat the virus that has spread all over the world, and vaccines had been developed at an unprecedented speed in history and implemented in many countries. According to the "ourworldindata" Web site, where data on COVID-19 vaccine applications are compiled, 63.4% of the world population has received at least 1 dose of a COVID-19 vaccine, 10.9 billion doses have been administered globally, and 18.29 million are now administered each day as of March 2022.[1] The original virus that emerged in Wuhan has mutated many times. There is no country left in the world where the virus has not reached. In addition to experiencing major problems in accessing the vaccine, the mutation of the virus creates an obstacle for even the vaccinated people to be protected from this disease. The resulting Delta variant swept the world, increasing the number of patients hospitalized and unfortunately losing their lives. Unfortunately, globalization and the increase in human movements cause variants to spread all over the world in a short time. Even large states with financial power and technological resources cannot prevent deaths due to the pandemic. The great injustice in the income distribution in the world causes a great human tragedy because of the difficulties experienced by the poor countries and the poor people all over the world to access the vaccine. In our country, the ratio of those who have 2 doses of vaccines has reached to 85%, but, unfortunately, only 13.6% of the population in low-income countries could reach the vaccine.[2,3] It is the common expectation of the whole world that the pandemic will gradually fade and its devastating effects on our lives will be minimized by making vaccination widely accessible and free of charge.

Turkey has started mass vaccination with an inactivated whole-virion vaccine, CoronaVac (Corona Vac Life Science Co, Ltd, Beijing, China) in January 2021, and 2 doses were administered intramuscularly 28 days apart. BNT162b2 mRNA (Pfizer-Pfizer-BioNTech) vaccine was introduced in June 2021, and the government offered a third booster dose to health care workers (HCWs) and people older than 50 years who had received 2 doses of CoronaVac. Currently, people are free to choose the vaccine type, and as of April 2022, 85% of the total population (53,010,344) of Turkey had 2 doses of vaccine and 27,704,256 people had 3 vaccine doses. Because the information about the applied vaccine types has not been released by the authorities, we could not elaborate the percentages of inactivated and mRNA vaccines in Turkey.

Several studies revealed that age and comorbidities are important factors for poor prognosis of COVID-19, and some laboratory parameters like C-reactive protein (CRP), procalcitonin, ferritin, D-dimer, fibrinogen, and lactate dehydrogenase (LDH) are associated with the development of critical illness among nonvaccinated patients.[4–9] Vaccine breakthrough COVID-19 disease appearing in fully vaccinated patients is an emerging challenge.[10] The severity of the disease in vaccinated patients has

not often been described, and data regarding the groups most at risk and the prognosis and outcomes for hospitalized patients are scarce.[11–13]

Herein, we analyzed fully vaccinated patients with COVID-19 admitted to our hospital during a 6-month period and evaluated demographic and laboratory data for disease severity.

MATERIALS AND METHODS

Study Design

This retrospective study was conducted at the Marmara University Hospital, Istanbul, Turkey, and consists of data between September 1, 2021, and February 28, 2022. SARS-CoV-2 polymerase chain reaction (PCR)–positive patients who were fully vaccinated (2 doses of vaccine and 3 doses of vaccine) and had been hospitalized at least 15 days after the last vaccine dose were included. The study was approved by the ethics board of Marmara University, School of Medicine and Turkish Ministry of Health. All participants have provided written informed consent.

Biochemical Analyses

C-reactive protein was measured with an immunoturbidometric method, ferritin and procalcitonin were measured with an electrochemiluminescence immunoassay (ECLIA) method on Cobas 8000 series (Roche Diagnostics, Basel, Switzerland), D-dimer levels were determined with latex-based automated immunoturbidimetric assay (STA-R, Diagnostica Stago, USA), and blood cell counts were determined with Sysmex XN-3000 automated cell counter (Sysmex Corp, Kobe, Japan).

Quantitative reverse transcription polymerase chain reaction (RT-qPCR) for SARS-CoV-2

Viral RNA was extracted from respiratory samples by using Bio-Speedy viral nucleic acid buffer (Bioexen Ltd, Istanbul, Turkey), and reverse transcription PCR was performed with Bio-Speedy SARS-CoV-2 RT-qPCR detection kit, version 2 (Bioexen Ltd), using primers and probes targeting the nucleocapsid (N) and ORF-1ab gene regions found in all SARS-CoV-2 and human RNase P gene for the routine screening in a Bio-Rad CFX-96 System (Bio-Rad Laboratories Inc, California).

Statistics

The data were collected in Excel 2013 (Microsoft Office Professional Plus). Statistical Product and Service Solutions (Statistical Package for Social Sciences) for Windows 24.0 was used for statistical analysis. Descriptive statistics were prepared to include frequency (n), percentages, mean, and SD. Frequency and percentages were provided for categorical variables. Categorical variables were compared using the χ^2 test. The Kruskal-Wallis test was used to compare continuous variables for independent groups. The results were evaluated at the 95% confidence interval, and the significance level was $P < 0.05$.

TABLE 1. Characterization of Patient Groups in Terms of Age and Gender Distribution, Comorbidities, Hospitalization Parameters and Outcome

	All Patients	2 Doses	3 Doses	*P*
No. patients: N	685	391	294	
Age of patients, mean	67.84	64.68	72.03	<0.0001
Age groups				
18–49 years, n (%)	77 (11.2)	66 (19.8)	11 (3.7)	
Mean ± SD	39.78 ± 7.39	40.15 ± 7.60	37.55 ± 5.77	0.139
50–64 years, n (%)	169 (24.2)	127 (32.3)	42 (14.3)	
Mean ± SD	58.68 ± 4.08	58.04 ± 4.05	60.62 ± 3.57	0.035
≥65 years, n (%)	439 (64.1)	198 (50.1)	241 (81.9)	
Mean ± SD	76.28 ± 7.83	77.12 ± 8.33	75.59 ± 7.33	0.121
Sex (female), n (%)	348 (50.8)	177 (45.3)	160 (54.4)	0.018
Duration of hospitalization, mean ± SD, d	9.68 ± 7.29	9.28 ± 6.87	10.21 ± 7.81	0.196
Admission to ICU (yes), n (%)	26 (3.8)	17 (2.5)	9 (1.3)	0.383
Duration of stay in ICU, mean ± SD, d	11.88 ± 16.56	16 ± 11.42	18 ± 15.29	0.047
Death, n (%)	2 (0.3)	1 (0.3)	1 (0.3)	0.839
Comorbidity				
Hypertension (yes), n (%)	349 (50.2)	190 (48.6)	159 (54.1)	0.155
Diabetes mellitus (yes), n (%)	240 (34.5)	129 (33)	111 (37.8)	0.196
Chronic lung disease (yes), n (%)	146 (21)	80 (20.5)	66 (22.4)	0.529
Chronic heart disease (yes), n (%)	162 (23.3)	76 (19.4)	86 (29.3)	0.003
Chronic kidney disease (yes), n (%)	68 (9.8)	39 (10)	29 (9.9)	0.962
Malignancy (yes), n (%)	82 (11.8)	44 (11.3)	38 (12.9)	0.505
No. comorbidity				
0	189 (27.2)	121 (30.9)	68 (23.1)	0.023
1	160 (23)	91 (23.3)	69 (23.5)	0.952
2	176 (25.3)	97 (24.8)	79 (26.9)	0.541
3	114 (16.4)	59 (15.1)	55 (18.7)	0.208
4+	46 (6.6)	23 (5.9)	23 (7.8)	0.315

RESULTS

A total of 685 patients were included in the study. The characteristics of the study groups are presented in Table 1. The mean age of the patients was 67.84 years, and 50.8% were female. In total, 439 of 685 patients (64.1%) and 241 of 294 patients (81.9%) having 3 vaccine doses were older than 65 years ($P < 0.05$). Mean duration of hospitalization was 9.68 ± 7.29 days. Twenty-six (3.8%) patients were admitted to the intensive care unit (ICU), and mean duration of ICU stay was 11.88 ± 16.56 days. Mortality rate was 0.3% (2 of 685 patients).

At least 1 comorbidity was present in 160 participants (23%) and more than 4 comorbidities in 46 (6.6%) patients. The most common comorbidity was hypertension (349, 50.2%). The presence of comorbidities was significantly higher in patients having 3 vaccine doses.

The distribution of the vaccine types according to the age groups is given in Table 2. Inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac) was administered in 467 of the patients (68.4%), BNT162b2 mRNA (Pfizer-Pfizer-BioNTech) in 107 of the patients (15.6%), and combination of 2 vaccines in 111 of the patients (16%). In the CoronaVac group and in the Pfizer-BioNTech group, 68.5% and 21.4%, respectively, of the patients were older than 65 years. Seventeen (3.6%) patients in CoronaVac group, 6 (5.4%) patients in the combination group, and 3 (2.8%) patients in the Pfizer-BioNTech group were admitted to the ICU.

The laboratory parameters are given in Table 3. A total of 56.4% of the patients had increased ferritin levels, 69.9% had increased D-dimer levels, 79.7% had increased CRP, and 61.5% had increased procalcitonin levels. Decreased lymphocyte count was observed in 36.4% of the patients, low lymphocyte/monocyte ratio (LMR) in 20% of the patients, and low neutrophil/lymphocyte ratio (NLR) in 22% of the patients. The only parameter that is significantly higher in patients having 3 vaccine doses was procalcitonin.

Characteristics of the patients admitted to the ICU and the laboratory parameters are given in Table 4; however, because the number of patients are low (n = 26), statistical comparison cannot be made.

DISCUSSION

Immunity against SARS-CoV-2 can be reached by either previous infection or vaccination. The number of vaccine booster doses required to reduce severe disease and keep people out of the hospital must be clarified. Several mutations of the virus limit the protective immune response, and a person might be infected more than once. Vaccines must offer wider protection against future variants, and the World Health Organization has warned that "a vaccination strategy based on repeated booster doses of the original vaccine composition is unlikely to be appropriate or sustainable." SARS-CoV-2 Omicron variant (BA.1/B.1.1.529) harboring up to 36 mutations in spike protein, which is the target of neutralizing antibodies, might escape vaccine-induced humoral immunity. When the neutralization potency of sera from vaccinated people was determined, individuals boosted with mRNA vaccines exhibited potent neutralization of Omicron, suggesting enhanced cross-reactivity of neutralizing antibody responses.[14]

TABLE 2. Characterization of Vaccine Groups According to the Vaccine Used, Age Distribution, Hospitalization Parameters, and Outcome

Vaccine Groups	2 Doses	3 Doses	Total n (%)
CoronaVac only, n (%)	288 (100)	179 (100)	467 (100)
18–49 years, n (%)	34 (8.3)	6 (3.4)	40 (8.6)
50–64 years, n (%)	79 (27.4)	28 (15.6)	107 (22.9)
≥65 years, n (%)	175 (60.8)	145 (81.1)	320 (68.5)
Days of hospitalization, mean	9.65	10.10	9.82
Admission to ICU (yes), n (%)	14 (4.8)	3 (1.6)	17 (3.6)
Duration of stay in ICU, mean, d	8.01	11.6	8.64
Death, n (%)	1 (0.3)	—	1 (0.2)
CoronaVac + Pfizer-BioNTech, n (%)	1 (100)	110 (100)	111 (100)
18–49 years, n (%)	—	3 (2.7)	3 (2.7)
50–64 years, n (%)	—	12 (10.1)	12 (10.8)
≥65 years, n (%)	1	95 (86.3)	96 (86.4)
Days of hospitalization, mean	7	10.60	10.57
Admission to ICU (yes), n (%)	—	6 (5.5)	6 (5.4)
Duration of stay in ICU, mean, d	—	25.3	25.3
Death, n (%)	—	1 (0.9)	1 (0.9)
Pfizer-BioNTech only, n (%)	102 (100)	5 (100)	107 (100)
18–49 years, n (%)	32 (31.4)	2 (40)	34 (31.7)
50–64 years, n (%)	48 (47.1)	2 (40)	50 (46.7)
≥65 years, n (%)	22 (21.5)	1 (20)	23 (21.4)
Days of hospitalization, mean	8.36	5.80	8.16
Admission to ICU (yes), n (%)	3 (2.9)	—	3 (2.8)
Duration of stay in ICU, mean, d	2.33	—	
Death n (%)	—	—	

TABLE 3. Laboratory Parameters of the Patients

	All Patients	2 Doses	3 Doses	*P*
Laboratory findings (mean ± SD)	685	391	294	
Ferritin >300 mL/ng, n (%)	386 (56.4)	243 (62.1)	168 (57.1)	
Mean ± SD	786.24 ± 653.9	751.2 ± 646.8	837.35 ± 662.8	0.081
Neutrophil >6.5 mm^3, n (%)	261 (38.1)	132 (33.8)	130 (44.2)	
Mean ± SD	11.38 ± 24.58	12.62 ± 34.54	1.15 ± 3.49	0.277
Lymphocyte <0.8 mm^3, n (%)	249 (36.4)	125 (32.0)	124 (42.2)	
Mean ± SD	0.52 ± 0.16	0.52 ± 0.17	0.53 ± 0.15	0.936
Monocytes <0.4 mm^3, n (%)	288 (42.0)	161 (41.2)	127 (43.2)	
Mean ± SD	0.21 ± 0.07	0.21 ± 0.08	0.22 ± 0.06	0.706
LMR <1.5, n (%)	137 (20.0)	73 (18.7)	64 (21.8)	
Mean ± SD	1.01 ± 0.32	1.01 ± 0.33	1.00 ± 0.32	0.769
NLR <3.13, n (%)	151 (22.0)	99 (25.3)	52 (17.7)	
Mean ± SD	2.04 ± 0.71	2.05 ± 0.7	2.02 ± 0.71	0.678
D-dimer <1. mg/L, n (%)	477 (69.9)	283 (72.4)	194 (66.0)	
Mean ± SD	0.42 ± 0.24	0.42 ± 0.24	0.430.24	0.521
CRP >30 mg/dL, n (%)	546 (79.7)	304 (77.7)	248 (84.4)	
Mean ± SD	124.3 ± 73.3	121.15 ± 72.36	128.24 ± 74.41	0.271
Procalcitonin >0.25 ng/mL, n (%)	421 (61.5)	228 (58.3)	214 (72.8)	
Mean ± SD	21.18 ± 54.6	16.61 ± 37.45	25.87 ± 67.64	0.020[2]

Because variant analysis is not done routinely in Turkey, we had no data about the real incidence of variants, but drawing conclusion from world data, we may assume that the Delta variant was predominant in summer months and that it was replaced by the Omicron variant by December 2021. Although the rank of Turkey with regard to total COVID-19 cases among 227 countries is 7th, its rank in the total cases per 1 million population is 66th and deaths per 1 million population is 83th, as of March 2022.[3]

Current data from the United States, the United Kingdom, and Israel show that a third (booster) shot of an mRNA vaccine protects most people against hospitalization for up to 5 months against Delta—and for 3 months or more against Omicron.[11–13] Effectiveness of a third dose of the BNT162b2 mRNA vaccine for preventing severe COVID-19 outcomes was evaluated in matched groups of 728,321 individuals per group in an Israeli study. Participants had a median age of 52 years (interquartile range, 37–68), and 51% were female; the median follow-up time was 13 days (interquartile range, 6–21) in both groups. The authors suggest that a third dose of the BNT162b2 mRNA vaccine is effective in protecting individuals against severe COVID-19–related outcomes, compared with receiving only 2 doses at least 5 months ago.[12] Kojima et al[13] compared the relative effectiveness of a booster dose of BNT162b2 to only a 2-dose primary course and a significantly increased protection was detected from the booster vaccine dose against mild and severe disease irrespective of the primary course. Garcia- Beltran et al[14] state that although studies have shown a strong protection from reinfection which persists for more than 10 months of follow-up, it is unknown how long protective immunity will truly last. Individuals boosted with mRNA vaccines were exhibited potent neutralization of Omicron, only 4-6-fold lower than wild type, suggesting enhanced cross-reactivity of neutralizing antibody responses.[15]

The data about inactivated vaccination are scarce. A Brazilian study searched the vaccine efficacy among elderly people and stated that after a single dose, there was already a significant reduction in COVID-19–related deaths, and higher protection ratios were observed after the application of 2 doses of the vaccine, with an attributable protection ratio of 99.2%.[16] Moreno-Perez et al showed that fully vaccinated patients hospitalized due to breakthrough COVID-19 who received different commercial vaccines tend to be elderly with comorbidities and have higher mortality.[17]

CoronaVac was shown to have high efficacy against PCR-confirmed symptomatic COVID-19 with a good safety and tolerability profile, yielding a vaccine efficacy of 83.5% and 100% protection against severe disease in Turkey.[18] The rate of breakthrough cases after CoronaVac vaccine was found to be 7% among HCWs [age (mean ± SD), 34.8 ± 9.4; 536 vaccinated and 92 nonvaccinated]. The hospitalization rate was similar in the breakthrough cases and those who had COVID19 before CoronaVac vaccination. In 234 (37.2%) subjects, there was a history of COVID-19 infection, and 188 (35%) had been vaccinated and 46 (50%) not vaccinated. The rate of experiencing COVID-19 disease was significantly lower in the vaccinated than in the unvaccinated HCWs.[19] Uzun et al[19] collected data from 25 hospitals in 16 cities from patients hospitalized between August 1 and 10, 2021, in Turkey.[20] They identified 1401 patients, of which 529 (37.7%) were admitted to ICUs. Nearly half (47.8%) of the patients were not vaccinated, and those with 2 doses of CoronaVac formed the second largest group (32.9%). There were 285 cases with 2 doses CoronaVac (mean age, 69.3 years); the number of comorbidities was 1.6, ICU admission was 33.2%, and mortality rate was not stated. Hospitalizations were lower in the group that received 2 doses of CoronaVac and a booster dose of Pfizer-BioNTech (0.9%) than in the group that received 3 doses of CoronaVac (3.2%).

Several laboratory parameters were found to be related with poor prognosis and death among patients who had no vaccine. However, there are limited studies analyzing laboratory data that could be associated with poor prognosis of COVID-19 in vaccinated patients who needed hospitalization. Previous studies revealed a direct relationship between COVID-19 severity with high levels of ferritin, CRP, D-dimers, and LDH.[5–7,9,21–23] In a prospective cohort study including 477 PCR-positive patients with COVID-19 admitted to our hospital from March 12 to May 12, 2020, the age, comorbidity number, World Health Organization scale, LDH, and procalcitonin were independently associated with

TABLE 4. Characteristics and the Laboratory Parameters of the Patients Admitted to Intensive Care Unit

	All Patients	2 Doses	3 Doses
No. patients	26	17	9
Vaccine groups, n (%)			
CoronaVac	17 (65)	14 (82)	3 (33)
CoronaVac + Pfizer-BioNTech	6 (23)	—	6 (67)
Mean patient age			
Age groups			
18–49 years, n (%)	4 (15)	4 (23)	—
Mean ± SD	46 ± 2.94	46 ± 2.94	
50–64 years, n (%)	5 (19)	3 (18)	2 (22)
Mean ± SD	59.4 ± 3.57	59.6 ± 5.65	59.0 ± 5.65
≥65 years, n (%)	17 (65)	10 (59)	7 (78)
Mean ± SD	76.05 ± 8.16	77.6 ± 9.52	73 ± 5.66
Sex (female), n (%)	13 (50)	9 (53)	4 (44)
Duration of hospitalization, mean ± SD, d	16.4 ± 12.06	15.8 ± 11.4	17.5 ± 15.28
Death, n (%)	1 (3.8)	1 (5.9)	—
Comorbidity			
Hypertension (yes), n (%)	20 (76.9)	12 (70.6)	8 (88.9)
Diabetes mellitus (yes), n (%)	12 (46.2)	7 (41.2)	5 (55.6)
Chronic lung disease (yes), n (%)	9 (34.6)	8 (47.1)	1 (11.1)
Chronic heart disease (yes), n (%)	13 (50)	10 (58.8)	3 (33.3)
Chronic kidney disease (yes), n (%)	1 (3.8)	1 (5.9)	—
Malignancy (yes), n (%)	5 (19.2)	3 (17.6)	2 (22.2)
No. comorbidities			
0	5 (19)	4 (24)	1 (11)
1	1 (4)	—	1 (11)
2	6 (23)	3 (18)	3 (33)
3	10 (38)	6 (35)	4 (44)
4+	4 (15)	4 (24)	—
Laboratory findings, mean ± SD			
Ferritin >300 mL/ng, n (%)	13 (50)	10 (59)	3 (33)
Mean ± SD	684.39 ± 377.9	680.29 ± 422.43	698.07 ± 223.15
Neutrophil >6.5 mm^3, n (%)	14 (54)	9 (53)	5 (56)
Mean ± SD	11.6 ± 7.84	12.07 ± 9.71	10.8 ± 3.13
Lymphocyte <0.8 mm^3, n (%)	15 (58)	9 (53)	6 (67)
Mean ± SD	1.49 ± 0.48	1.36 ± 0.44	1.68 ± 0.53
Monocytes <0.4 mm^3, n (%)	12 (46)	9 (53)	3 (33)
Mean ± SD	0.79 ± 0.57	0.87 ± 0.65	0.57 ± 0.12
LMR <1.5, n (%)	18 (69)	9 (53)	9 (100)
Mean ± SD	4.68 ± 3.48	5.11 ± 4.57	4.25 ± 2.10
NLR <3.13, n (%)	20 (77)	14 (82)	6 (67)
Mean ± SD	12.23 ± 8.88	12.34 ± 8.89	11.97 ± 9.69
D-dimer <1 mg/L, n (%)	12 (46)	8 (47)	4 (44)
Mean ± SD	2.78 ± 1.83	2.44 ± 1.96	3.45 ± 1.54
CRP >30 mg/dL, n (%)	19 (73)	11 (65)	8 (89)
Mean ± SD	152.57 ± 97.9	138.68 ± 80.7	171.39 ± 119.7
Procalcitonin >0.25 ng/mL, n (%)	19 (73)	12 (71)	7 (78)
Mean ± SD	14.2 ± 28.4	10.7 ± 16.2	20.13 ± 43.2

critical illness development.[4] In our study, the only parameter that is significantly higher in patients having 3 vaccine doses was procalcitonin. Increased PCT levels are shown to be associated with disease severity and mortality in patients with COVID-19 in previous studies.[24]

We detected decreased lymphocyte level in 36.4% of the patients, low LMR in 20% of the patients, and low NLR in 22% of the patients. However, no significant difference was found among groups. A decrease in lymphocyte count is shown to be correlated with multiorgan injury in patients with COVID-19.[25] Neutrophil/lymphocyte ratio is also suggested to be important in the course of the disease. Numerous studies have demonstrated the effectiveness of NLR in predicting patient outcomes, including but not limited to severe disease, hospitalization, ICU admission, intubation, and death. In a Turkish study, significantly more patients in the high-NLR (>3.13) group were symptomatic compared with the

low-NLR group, and CRP and procalcitonin levels were found to be significantly higher in symptomatic children.[26] Similarly, the patients' group with NLR ≥10 and D-dimer ≥2 μg/mL had a higher death risk than the group with NLR <10 and D-dimer <2 μg/mL, and the authors suggested that high NLR and D-dimer, especially when combined, are predictors of death risk for patients with severe COVID-19.[27] Mousavi-Nasab et al[27] stated that NLR and CRP may lead to improved predictions and is recommended as a valuable early marker to assess prognosis and evaluate the severity of clinical symptoms in patients with COVID-19. Karimi et al[28] stated that NLR seems to be the most robust marker, and patients with higher NLR seem to have more comorbidities and are more prone to severe COVID-19. A temporal analysis showed that on admission, NLR correlates well with the need for ICU and poor outcomes and can be a potential risk-stratification tool. However, the clinical utility of NLR was lost in week 3 postadmission.[29] Lymphocyte/monocyte ratio might have limited benefits in prognosticating COVID-19, but its abilities seem to be lower than NLR and PLR, especially in predicting disease severity, ICU admission, and mortality.[30]

Our study revealed that among vaccinated patients, even in the presence of comorbidities and abnormal laboratory parameters, 26 (3.8%) patients were admitted to the ICU and the mortality rate was 0.3%. In a study that we performed in 2020 in our hospital, when the original Wuhan virus was the source, in 284 hospitalized patients with COVID-19, the mean age was 58, 45 (15.8%) were admitted to the ICU, and 27 (9.5%) of them had died (32%).[31] In the current study, we may conclude that the incidence of severe COVID-19 is low among fully vaccinated patients, regardless the vaccine type, even in the presence of comorbidities, in older age, and in the presence of abnormal laboratory parameters, and mortality rate is low. As of April 2022, the number of cases is at its lowest level in Turkey, and all the restrictions regarding COVID-19 were waived. We believe that the data about vaccinated communities are vital to be prepared for the future even if the pandemic ends and the disease becomes endemic.

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