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Relationships between vaccination, age, and mortality in the COVID-19 intensive care patients

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ABSTRACT

Objectives: To investigate the effects of vaccination on age, mortality, and healthcare workers among patients followed in the COVID-19 Intensive Care Unit.

Methods: We examined age, gender, occupation, demographic characteristics, comorbid diseases, hemogram, biochemistry parameters, coagulation tests, morbidity–mortality characteristics of 548 patients in Bozyaka Training and Research Hospital COVID-19 intensive care unit admitted between March and October 2021. In addition, the vaccination status of the patients and the type of vaccination were recorded via the Ministry of Health Vaccine Tracking System (VTS). Within the vaccine follow-up system, patients who received at least 2 doses of vaccine 4 weeks prior to study were considered vaccinated.

Results: The data of 548 patients in the COVID-19 intensive care unit between March 2021 and October 2021 were analyzed. The mortality rate was 50.7% (n = 278). It was determined that 428 (78.1%) of the patients followed in the COVID-19 intensive care unit were not vaccinated. In terms of age distribution, the number of patients under the age of 65 was 357 (65.1%), while the number of patients aged 65 and over was 191 (34.9%). When mortality rates were compared based on vaccination status, the mortality rate in the unvaccinated group was found to be statistically significantly higher than in the vaccinated group ($p < 0.05$). Mortality rate in the vaccinated group was 12.5% whereas it was 61.4% in the unvaccinated group.

Conclusions: Vaccination to protect against SARS-CoV-2 infection reduces intensive care unit admission and reduces mortality rates. Being unvaccinated increases hospitalization and mortality in intensive care units in addition to carrying risks for all age groups.

Keywords: COVID-19 intensive care, vaccination, mortality, age, healthcare workers

The new SARS-CoV-2 infection emerged in Wuhan, China in December 2019, and spread to countries in a short time, becoming a pandemic health problem that concerns the whole world on March 11, 2020. This pandemic infection has killed more than five million people by October 2021. It has caused many organ and function losses that cannot be detected on individuals in the society. In addition, it has been observed that this pandemic has very negative effects on the countries health system and economies [1].

SARS-CoV-2 virus affects every segment of society. Healthcare workers have been heavily affected due to exposure to infected cases, along with the most

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affected elderly group in the society. There have been more losses of lives in the elderly and healthcare workers than in any other period of time [2]. In Turkey, only 11% of COVID-19 cases were from group of patients over 65 years old while majority of deaths (71%) were from this group. While the elderly are 21% of the cases in the United States, 80% of the deaths are over the age of 65 years [3]. SARS-CoV-2 infection requires a need for intensive care and results in higher mortality rate with patients who have malignancy and immunosuppression or aging associated diseases such as hypertension, obesity, lung disease, cardiovascular disease, renal failure [4].

According to the data reported by the World Health Organization (WHO), while healthcare workers are 3% of the entire population, they constitute at least 14% of all COVID-19 infected cases. With these data, it has been observed that healthcare workers constitute one out of every seven COVID-19 patients in the world [5]. In Turkey, it was reported that 10.9% of the total COVID-19 cases were healthcare workers and 52 healthcare workers lost their lives until September 2, 2020 [6]. In England, 16.9% of the 235,685 participants who had COVID-19 infections were health workers and 1.4% of these were found to be severe disease cases. It has been stated that the possibility of a more severe course of COVID-19 disease in healthcare workers increases due to the excess viral load [7].

In SARS-CoV-2 infection, drug treatments such as antiviral drugs, nutritional supplements, intensive antibiotic, hydroxychloroquine, in addition to plasma, immunomodulators, anticoagulants are applied. All of these methods are individual treatment methods, and it has been seen that they cannot prevent a pandemic widespread infection. In the light of the scientific knowledge gained from previous experiences, it is thought that the most important and effective method in the fight against epidemic diseases is vaccination [8]. Therefore, there are 48 vaccine studies in which phase 2 and phase 3 studies are ongoing in various countries around the world. To protect against pandemic COVID-19 infection, inactive [Sinovac] and mRNA [BioNTech] vaccines have been started to be administered quickly, even though it is in the clinical research phase in Turkey. First, health workers were vaccinated due to high exposure and being a risky group, then it was widely used in the elderly population and in all age groups within a short time [9].

COVID-19 vaccination in Turkey has started on January 2021 with CoronaVac (Sinovac). Sinovac is an inactivated vaccine containing attenuated virus that does not cause disease but produces an immune response. The second vaccine application is an mRNA vaccine, which is a state-of-the-art technology using genetically engineered RNA particles to produce the viral antigenic protein that induces an immune response [10]. Active mRNA and inactivated vaccine are available to public use while the domestic vaccine TurcoVac is only administered to volunteers. It is recommended that a two-dose application regimen at least 4-6 weeks apart is required for developing protection against COVID-19. The protection of the vaccine was found to be between 90.7-100.0% with the phase II studies of Sinovac in Turkey, and it was between 50-84.0% in Phase III studies [11]. The efficacy of the Pfizer/BioNTech vaccine, which is the second type of vaccine used in Turkey, was evaluated in 43538 volunteers aged 16 years and older in a phase III randomized and controlled trial conducted in most countries, including Turkey. Two doses of vaccines administered 4-6 weeks apart and placebo groups were compared. When all age groups were evaluated, the effectiveness of the vaccine in protection against COVID-19 infection was found to be 95%. It was observed that only local adverse events occurred in 84% of the vaccinated patients, who were found to have similar adverse effects as side effects in both vaccine administrations, and most of them were mild to moderate. Fatigue, headache, and fever arthralgia were to be the most common reported as systemic vaccine adverse events [12, 13]. There are many epidemiological studies in the community that support the effectiveness of both vaccines, but there are not many comprehensive studies on intensive care. In our study, we aimed to investigate the relationship between age profiles, occupations, vaccination status, and mortality of the patients followed in the COVID-19 intensive care unit of our hospital in the post-vaccination period.

METHODS

We obtained ethical approval for the study from the Ethics Committee of Bozyaka Training and Research Hospital on October 27, 2021.

We investigated the age, gender, occupation, demographic characteristics, comorbid diseases, hemogram, biochemistry parameters, coagulation tests, morbidity-mortality of 548 patients diagnosed with COVID-19 in the COVID-19 intensive care unit of Bozyaka Training and Research Hospital between March 2021 and October 2021. In addition, the vaccination status of the patients and the type of vaccination were recorded through the Ministry of Health Vaccine Tracking System (VTS). Patients who received at least 2 doses of vaccine 4 weeks prior to study were considered vaccinated.

Statistical Analysis

Statistical analyzes on clinical data collected were performed with SPSS version 25.0. The conformity of the variables to the normal distribution was examined using the Kolmogorov-Smirnov /Shapiro Wilk tests. In the analysis of continuous data, t-test was used for independent groups in normal distribution, and Mann-Whitney U test was used in case of non-normal distribution. Fisher's Exact and Pearson's Chi Square tests were used to compare categorical variables. A p value below 0.05 was considered statistically significant.

RESULTS

The data of 548 patients in our hospital's COVID-19 intensive care unit between March 2021 and October 2021 were examined. Of the patients, 301 (55%) were males and 247 (45%) were females (Table 1, Fig. 1). The mortality rate was found to be 50.7% (n = 278). The mortality rate was found to be 64.9% (n = 180) for males and 35.1% (n = 98) for females. It was determined that 428 (78.1%) of the patients followed in the COVID-19 intensive care unit were not vaccinated. In terms of age distribution, the number of patients under the age of 65 was 357 (65.1%), while the number of patients aged 65 and over was 191 (34.9%).

When mortality rates were compared according to vaccination and non-vaccination status in Table 2. The mortality rate in the unvaccinated group was found to be statistically significantly higher than in the vaccinated group ($p < 0.05$). While mortality was 12.5% in the vaccinated group, it was 61.4% in the unvaccinated group.

It was found that mortality rates decreased in patients followed up in the COVID-19 intensive care unit with vaccination, and very significant mortality rates were detected in the unvaccinated patient group. Being unvaccinated carries a risk for all age groups (Table 3).

The biochemical parameters of the patients hospitalized in the COVID-19 intensive care unit such as hemoglobin, leukocyte, thrombocyte, D-dimer, fibrinogen, lactate dehydrogenase (LDH), urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), prothrombin time (PT), activated partial thromboplastin time (aPTT), international normalized ratio (INR), creatine kinase (CK), total-bilirubin, C-reactive protein (CRP), procalcitonin (PCT), and intubation parameters were examined de-

Table 1. Demographic features (n = 548)

Variables	Frequency (n)	Percentage (%)
Gender		
Male	301	55.0
Female	247	45.0
Mortality		
Death	278	50.7
Live	270	49.3
Gender/Mortality Rate		
Male	180	64.9
Female	98	35.1
Vaccination		
Not Vaccinated	428	78.1
Vaccinated	120	21.9
Intubation		
Not Vaccinated	280	88.0
Vaccinated	38	12.0
Age Groups		
> = 65	191	34.9
< 65	357	65.1
Mortality/Age Groups		
> = 65	132	47.3
< 65	146	52.7
Profession		
Healthworkers	0	0
Non-healthworkers	548	100

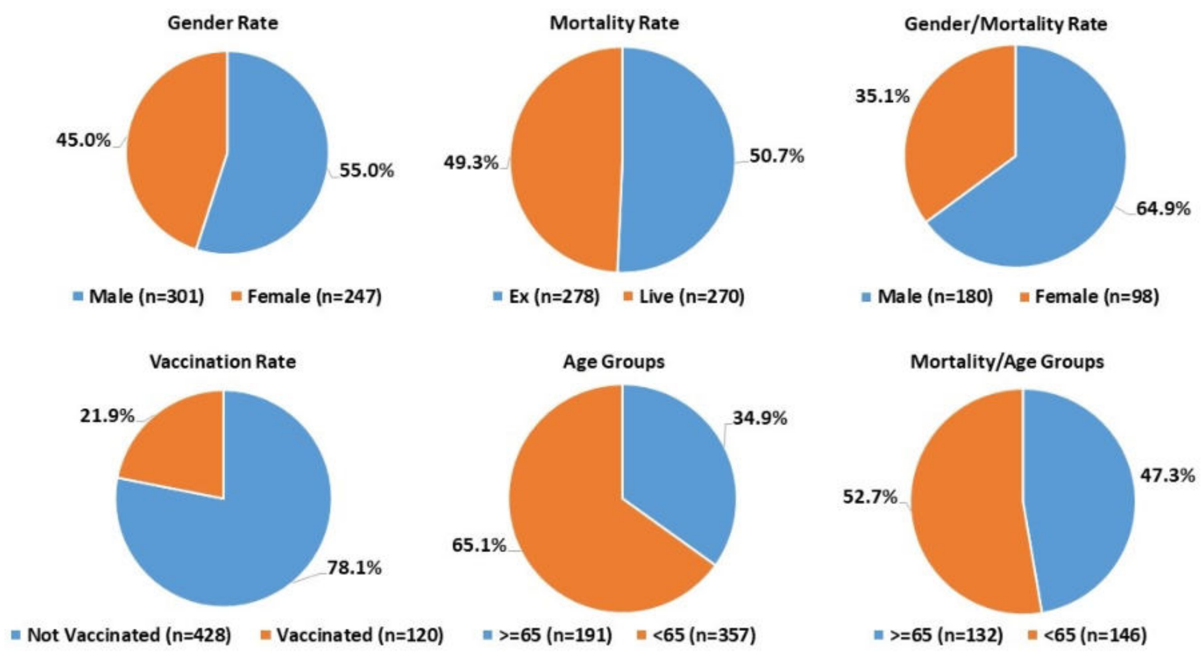

Fig. 1. Distrubition of demographic features.

pending on their status of mortality and found to carry statistically significant differences between the comparison groups (Table 4). However, glucose parameter alone was found to have no statistically significant difference between live and death groups.

DISCUSSION

In our study, one of the most prominent findings from the 548 patients we followed in the COVID-19 intensive care unit was that 78.1% (n = 428) of the patients followed-up were unvaccinated. On the other hand, only 21.9% (n = 120) of the patients were vaccinated. In Turkey, 85% of the population over the age of 18 are vaccinated for two doses [14]. If the vaccinations had no effect, we would have expected that 85% ICU patients to be vaccinated. However, we encountered the opposite results in our findings. In other words, 78.1% of the patients followed in the intensive care units were unvaccinated as opposed to 21.9% vaccinated. Therefore, this observation shows that the vaccine is protective in the community and the need for intensive care in the vaccinated group is low.

Another finding of our study in the patients we followed up in the intensive care unit was that the mortality rates were lower in the vaccinated group than in the unvaccinated group. In our study, we found a mortality rate of 12.5% (n = 15) in the vaccinated group, while it was 61.4% (n = 263) in the unvaccinated group. Vaccination has reduced the need for intubation, intensive care unit stay, and follow-up in patients. While the intubation rate was 12% (n = 38) in the vaccinated patient group, it was 88% (n = 280) in the unvaccinated group. Vaccination results in a decrease in

Table 2. The effect of vaccination status on mortality

Mortality n (%)	Vaccination status n (%)		Total n (%)	*p* value	χ^2
	Yes	**No**			
Yes	15 (12.5)	263 (61.4)	278 (50.7)	**< 0.0001**	***89.8***
No	105 (87.5)	165 (38.6)	270 (49.3)		
Total	120 (21.9)	428 (78.1)	548		

Pearson's Chi-Square analysis was used and $p < 0.05$ was considered significant.

Table 3. The effect of vaccination status on mortality in patients under 65 years of age and over

Age Groups	Mortality n (%)	Vaccination Status n (%)		Total n (%)	*p* value	χ^2
		Yes	No			
< 65	Yes	9 (5.1)	162 (92.1)	171 (48.1)	< 0.0001	271.1
	No	172 (94.9)	14 (7.9)	186 (51.9)		
	Total	181 (50.7)	176 (49.4)	357		
> = 65	Yes	8 (12.0)	108 (88.6)	116 (60.9)	< 0.0001	109.4
	No	61 (88.0)	14 (11.4)	75 (39.1)		
	Total	69 (36.2)	122 (63.8)	191		

Pearson's Chi-Square analysis was used and $p < 0.05$ was considered significant.

mortality in patients, shorter hospital stays, and less intensive care needs.

Another finding in our study is the change in the age profile of the patients we followed up in the intensive care unit in the post-vaccination period. When the age data of the patients followed in the intensive care unit are compared with the pre-vaccine periods, we observed that the age profile was reversed. Among our findings, 66.9% (n = 357) of the 548 patients we followed up in the intensive care unit were under the age of 65, and 23.1% (n = 191) of the patients were over the age of 65. Based on the results we previously reported as a subgroup analysis of d-dimer-fibrinogen mortality relationship before vaccination [15], 69% of the patient group in our intensive care unit serving in the same region was over the age of 65. In the post-vaccination period, we find that this rate is 23.1% of the patients over 65 years of age. This significant change in the post-vaccination period clearly demonstrates the effectiveness of vaccination.

Another finding in our study is the changing age profile in intensive care units as well as the change in total mortality rates over 65 years of age. In our study, we found a mortality rate over 65 years of age 47.3% (n = 146), while a mortality rate under 65 years old was 52.7% (n = 171). Previously, we reported a mortality rate of 64.7% over the age of 65 during pre-vaccination period. With these findings, we see that it also changes the mortality risk that occurs with aging due to vaccination in the geriatric age group. In the study of Guilon *et al*. [16], the demographic characteristics of the patients they followed in the intensive care unit were 72% in the geriatric age group, and they found mortality over 65 years old as 62.5% in the intensive care unit and 72.1% for the age group over 80 years old. They found a significantly higher mortality in the elderly group compared to the younger patient group [16]. Similar findings were reported from Italy. They found that 74% of all deaths in COVID-19 cases were in the geriatric age group [17]. In the United States, 67% of the cases were found to be ≥ 45 years old, with the same characteristics as in China, with 80% of the deaths being over the age of 65 [18]. These observations show that, with vaccination, COVID-19 infection is no longer an important risk in the elderly, and that the vaccine is effective.

Our final determination in our study is that active healthcare workers do not need intensive care as patients. Before the vaccination period, 2% of our intensive care patients were health workers. There are many studies report that health workers are affected all over the world. It was determined that 16.9% of COVID-19 cases in England were healthcare workers and 1.4% of these cases were severe disease cases. They stated that due to the excess viral load, the likelihood of a more severe course of COVID-19 disease in healthcare workers increased [19]. It was determined that 6.4% of the actively working hospital personnel from the Netherlands were positive for COVID-19 and the deaths of active and retired healthcare workers were 14% of all deaths [20]. In a study from Russia, %5 of those Who died in the pandemic were found to be healthcare workers [21]. In Turkey, the need for follow-up in intensive care units has decreased with regular widespread vaccination (as almost all of our healthcare workers are vaccinated). There was no vac-

Table 4. Comparison of biochemistry parameters according to mortality status in COVID-19 patients (n = 548)

Parameters	Death (n = 278)	Live (n = 270)	*p* value
Hemoglobin (g/dL)	10.1 ± 2.1	11.6 ± 1.8	**< 0.0001**
Leukocyte	9600 ± 6700	8800 ± 3700	**< 0.0001**
Thrombocyte	236000 ± 192000	212000 ± 160000	**< 0.0001**
D-dimer (mg/dL)*	1525.5 ± 658.2	618.4 ± 651.2	**< 0.0001**
Fibrinogen (mg/dL)	893.0 ± 307.3	605.4 ± 213.7	**< 0.0001**
LDH (U/L)	132.3 ± 239.2	109.2 ± 63.1	**< 0.0001**
Glucose (mg/dL)	107.2 ± 79.2	82.2 ± 33.6	0.339
Urea (mg/dL)*	82.4 ± 53.9	33.3 ± 14.1	**< 0.0001**
Kreatinin (mg/dL)*	3.8 ± 0.8	1.5 ± 0.9	**< 0.0001**
ALT (U/ml)	165.6 ± 436.4	42.2 ± 25.5	**< 0.0001**
AST (U/mL)*	213.4 ± 560.5	67.7 ± 11.0	**< 0.0001**
PT (seconds)	15.6 ± 21.4	10.1 ± 12.1	**0.0002**
aPTT (seconds)	38.6 ± 15.2	29.7 ± 4.3	**< 0.0001**
INR	2.4 ± 2.7	1.6 ± 3.2	**0.048**
CK (mg/dL)	641.0 ± 766.1	185.5 ± 32.1	**< 0.0001**
Bilirubin-total (mg/dL)	4.0 ± 3.9	1.6 ± 1.2	**< 0.0001**
CRP (mg/dL)**	410.2 ± 111.3	291.1 ± 12.3	**< 0.0001**
Ferritin (mg/dL)*	446.5 ± 389.7	212.4 ± 297.7	**< 0.0001**
PCT (mg/dL)*	40.5 ± 10.2	33.3 ± 5.8	**< 0.0001**
SOFA Score	12.5 ± 2.5	9.0 ± 1.8	**< 0.0001**
APACHE II Score	22.7 ± 4.3	18.1 ± 3.3	**< 0.0001**
Time of stay (day)*	9.4 ± 8.0	6.7 ± 5.9	**< 0.0001**
Intubation, n (%) **	250 (90)	68 (25)	**< 0.0001**

Data are shown as mean ± standard deviation or n (%). LDH = lactate dehydrogenase, ALT = alanine aminotransferase, AST = aspartate aminotransferase, PT = prothrombin time, aPTT = activated partial thromboplastin time, INR = international normalized ratio, CK = creatine kinase, CRP = C-reactive protein, PCT = procalcitonin, SOFA = sequential organ failure assessment, APACEHE-II = acute physiology and chronic health evaluation II

Independent t-test was used and $p < 0.05$ was considered significant.

*Mann-Whitney U test was used. ** Pearson Chi-Square test was used.

cinated health worker that we followed in the intensive care units of our hospital where we conducted our study. The fact that there is no healthcare worker with vaccination who needs intensive care is clearly the result of the vaccine protection.

CONCLUSION

Vaccination to protect against SARS-CoV-2 infection reduces the COVID-19 intensive care unit stay and reduces mortality rates. Being unvaccinated increases the intensive care unit admission and mortality. Being unvaccinated carries risks for all age groups. As a result, COVID-19 vaccine studies continue rapidly in many countries around the world. However, more studies are needed on the efficacy and safety of these vaccines. We believe that one of the COVID-19 vaccines, which has high efficacy and safety, will positively affect the course of the pandemic and end it.

Authors' Contribution

Study Conception: İD; Study Design: İD; Supervision: ŞÇ; Funding: ŞÇ; Materials: BK; Data Collection and/or Processing: RSY; Statistical Analysis and/or Data Interpretation: RSY, HÖ; Literature Review: İD; Manuscript Preparation: İD and Critical Review: İD.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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