

# Retrospective Vaccine Cohort of COVID - 19 Patients

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## ABSTRACT

### INTRODUCTION

In the control of the COVID - 19 pandemic, community immunity with vaccines is the main element.

### METHOD

A total of 360 cases who were hospitalized and followed up in the pandemic service with the diagnosis of COVID - 19 for 13 months were included in the study. In the first stage of data analysis; Those who were not vaccinated against COVID - 19, those who had 1 dose of Sinovac or BioNTech vaccine, and those who received 2 doses of vaccine and caught COVID - 19 within 2 weeks after the second dose were included in the undervaccinated group. Those who had 2 doses or more of Sinovac / BioNTech vaccine and who caught COVID - 19 two weeks after the 2<sup>nd</sup> dose were included in the full dose vaccinated group. In the second stage, those who had never been vaccinated and those who had 1 dose or more of the vaccine, and in the third stage, those who had 2 full doses of vaccine and those who had 3 full doses of vaccine were compared among themselves. In addition, the mutation type of all cases was recorded. In statistical analysis, p value < 0.05 was considered significant.

### RESULTS

44.5 % of the cases were male and 55.5 % were female. The mean age (Mean  $\pm$  SD, Min - Max) of 191 under - vaccinated cases was (58.29  $\pm$  15.61), while it was (72.12  $\pm$  12.65) of 169 full-dose vaccinated cases. The mean age (p = 0.000), comorbid disease (p = 0.000) was lower in the under vaccinated group. However, no significant difference was observed in ward length of stay (p = 0.562), mortality rate (p = 1.000), and ICU admission rate (p = 0.390). Of all cases, 44.17 % were unvaccinated, 6.94 % were single - dose vaccinated, 38.89 % were double - dose vaccinated, and 10 % were three - dose vaccinated. When the mutation status was examined, 36.11% of them were Delta mutation, 5.28 % of them were British mutations and 13.33 % of them were suspicious for variants. While the rate of mortality and admission to the ICU was 5.2 % in the English mutation, no mortality was observed in cases with delta mutations or suspected variants. The rate of going to the ICU was 3.8 % in delta mutation and 2 % in suspected variant cases.

### CONCLUSION

In our study, full dose vaccination was found to be more common in patients with advanced age and comorbid diseases. The fact that approximately half of the patients are unvaccinated shows the importance of the vaccine in the fight against the disease.

### KEYWORDS

COVID-19, Sinovac, BioNTech, Delta mutation, British mutation

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## INTRODUCTION

The COVID - 19 pandemic has compelled international scientists to find answers on antiviral treatments and vaccines to contain the epidemic.<sup>1</sup> Despite the use of masks, protection of social distance, practices for hand hygiene, isolation of contact and sick people, and restrictions affecting social life, the number of daily cases has decreased from time to time, but the pandemic has not been ended. Moreover, variant strains that are more contagious have emerged due to gene mutations of the virus. For all these reasons, it is of great importance to obtain effective vaccines for COVID - 19 infection.<sup>2</sup> Today, Oxford and Russian origin (Sputnik V) COVID - 19 vaccines, which are viral vector vaccines against the COVID - 19 epidemic, German (Biontech - Pfizer) and American (Moderna) vaccines from nucleic acid - based (RNA and DNA) vaccines, and Chinese origin vaccines in the inactivated vaccine group (Coronovac - Sinovac) vaccine are vaccines that are actively used.<sup>3,4</sup> When the effectiveness of five important COVID - 19 vaccines is examined; The effectiveness of CoronaVac / Sinovac was 90 %, Oxford / Astra Zeneca 70 %, Pfizer / BioNTech and Moderna / INH 95 %, and Sputnik V 92 %.<sup>5</sup> Numerous domestic vaccine studies continue in our country.<sup>6</sup> Thousands of mutations have been identified since the virus's appearance in its genome. As mutations are identified, new combinations of mutations are increasing. However, there is no significant evidence that these mutations will cause the virus to evade immunity generated by vaccines.<sup>7</sup>

The aim of this study is to determine the clinical reflection of vaccines and their effects on mutations by determining the retrospective vaccination rate, dose amount, type of vaccine, type of COVID - 19 mutation of patients who are followed up in our center with the diagnosis of COVID - 19.

## MATERIALS AND METHODS

The study was planned between October 1, 2020 and November 1, 2021 at Fatsa State Hospital (Ordu). Patients over the age of 18 who were hospitalized in the COVID - 19 services and diagnosed with COVID - 19 by Polymerase chain reaction (PCR) studied from a nasopharyngeal swab sample were included. The data were obtained by scanning our hospital's automation system "Fonet Web HBYS". A total of 360 cases were included in the study. Demographic data, vaccination status, mutation status, comorbid conditions, length of hospitalstay, admission to the intensive care unit, laboratory values, up take rate (CORADS score) in Computed Tomography (CT), and mortality were recorded for all cases. In the first stage of data analysis; those who were not vaccinated against COVID - 19, those who had 1 dose of Sinovac or BioNTech vaccine, and those who received 2 doses of vaccine and caught COVID - 19 within 2 weeks

after the second dose were included in the under vaccinated group. Those who were vaccinated with Sinovac / BioNTech for two or more doses and caught COVID - 19 2 weeks after the second dose were included in the full dose vaccinated group and evaluated. In the second stage; those who have never been vaccinated and those who have been vaccinated for 1 dose or more were examined. In the third stage, those who received 2 full doses of vaccine and those who received 3 full doses of vaccine were compared among themselves. Patients not hospitalized in pandemic services, patients aged < 18 years and > 95 years, patients whose vaccination information could not be reached, and patients who were withdrawn from the ICU or hospitalized in the ICU were excluded from the study.

## Statistical Analysis

The data in the study were obtained retrospectively from the hospital automation system and uploaded to the IBM SPSS v.26 package program. Mean ( $\pm$  standard deviation) and min - max values were given for quantitative variables, and numerical (percentage) values were given for qualitative variables. "Pearson *chi-square*" and "Fisher's exact" tests were used to compare independent categorical variables between groups. The "Mann Whitney U" test was used for the comparisons between groups of data that were not normally distributed. In statistical analysis, p value < 0.05 was considered significant.

## Ethics Committee Permission

An application was made to the Ordu University Clinical Research Ethics Committee for a study permit. Ethical permission was obtained with the decision numbered 2021 / 242 of the board meeting on 19 / 11 / 2021.

## RESULTS

All cases, 160 (44.4 %) were male and 200 (55.6 %) were female. When the vaccine cohort of the cases was analyzed, it was seen that 191 (53 %) cases were insufficiently vaccinated and 169 (47 %) cases were fully vaccinated. While the mean age (Mean  $\pm$  SD, Min - Max) was (58.29  $\pm$  15.61) in insufficiently vaccinated cases, it was (72.12  $\pm$  12.65) in full - dose vaccinated cases. It was observed that the mean age was statistically lower in the under - vaccinated group (p = 0.000). The history of comorbid disease was higher in the full - dose vaccine group (p = 0.000). However, there was no significant difference between the two groups in terms of length of service stay (p = 0.562), mortality rate (p = 1,000) and ICU admission rate (p = 0.390). The mean hospitalization times were (7.35  $\pm$  3.87) and (7.41  $\pm$  3.94), respectively. Cases that have never been vaccinated or that have not been vaccinated for 14 days after a single dose of vaccine are the first group (n = 163), and the cases that have received

1 dose or more of the vaccine are the second group (n = 197); again, no significant difference was observed between the two groups in terms of length of service stay (p = 0.381), mortality rate (p = 1,000) and ICU admission rate (p = 0.145). Full dose vaccinated cases; they were analyzed separately as 2 full - dose vaccines (N = 138) and 3 full-dose vaccines (N = 31). Again, no significant difference was observed between the two groups in terms of length of service stay (p = 0.769), mortality rate (p = 0.138), and rate of going to ICU (p = 0.228). A different grouping was made as one group (N = 31) with a single dose / two dose of COVID 19 vaccine but less than 14 days after the last dose, and cases with 2 doses or more of the vaccine and 2 weeks over the last dose in another group (N = 165). In this grouping, the aim was to compare the time to catch COVID - 19 after the last dose of vaccine. The mean duration was found to be 34.2 ± 55.3 in the first group (N = 31) (0 - 253) and 129.2 ± 64.2 (2 - 246) in the second group (N = 165). There was a significant difference between the two groups in terms of the duration of contracting COVID 19 after vaccination (p = 0.000). The CORADS score was reported similar in both groups (p = 0.172). The demographics of the cases and the clinical reflection of the vaccine are shown in Table 1.

Case	Insufficient vaccination N = 191 (%)	Full dose vaccinated N = 169 (%)	p value
Gender			
Male	80 (41,89)	80 (47,34)	0,299
Female	111 (58,11)	89 (52,66)	
Age, (Mean ± SD)	58,29 ± 15,61	72,12 ± 12,65	0,000
Service length of stay, (Mean ± SD)	7,35 ± 3,87	7,41 ± 3,94	0,562
Going to ICU	9 (4,71)	5 (2,96)	0,390
Mortality	1 (0,52)	1 (0,59)	1,000
Presence of comorbidity	158 (82,72)	161 (95,27)	0,000
CORADS score			
Normal / low involvement	22 (11,51)	18 (10,65)	
Moderate involvement	4 (2,09)	10 (5,92)	0,172
High involvement	165 (86,39)	141 (83,43)	

**Table 1. Demographics of Cases and Vaccination.**

When insufficiently vaccinated cases and full-dose vaccinated cases are examined in terms of laboratory values, in full-dose vaccinated cases; Blood White Blood Cell (WBC) (p = 0.000), Neutrophil (NE) (p = 0.001), Urea (p = 0.000), Creatinine (p = 0.000), Alkalinephosphatase (ALP) (p = 0.024), C-reactive Protein (CRP) (p = 0.015) and Creatine kinase-MB (CK-MB) (p = 0.004) were higher, while Hemoglobin (HB) (p = 0.003), Alanine aminotransferase (ALT) (p = 0.005), Aspartate

Aminotransferase (AST) (p = 0.038) and Gamma Glutamyl Transferase (GGT) (p = 0.018) were found to be statistically significantly higher in the undervaccinated group. No significant difference was observed between the two groups in terms of Platelet (PLT) (p = 0.455), Lymphocyte (LE) (p = 0.702), D- dimer (p = 0.200), Ferritin (p = 0.911) and Troponin (p = 0.078) values. The laboratory values of the cases are given in Table 2.

Laboratory values	Insufficient vaccination (n = 191) Mean ± SD (Min-Max)	Full dose vaccinated (n = 169) Mean ± SD (Min-Max)	p degeri
WBC (10 <sup>3</sup> / μL)	7,5 ± 4,0 (1,1 - 26,8)	9,1 ± 5,0 (1,7-35,4)	0,000
HB (g / dL)	12,8 ± 1,7 (6,7 - 16,1)	12,3 ± 1,7 (7,2-16,6)	0,003
PLT (10 <sup>3</sup> / μL)	219,1 ± 99,0 (19-658)	208,6 ± 87,4 (7-516)	0,455
NE (10 <sup>3</sup> / μL)	5,8 ± 3,6 (0,8 - 22,7)	7,2 ± 4,7 (0,8-32,8)	0,001
LE (10 <sup>3</sup> / μL)	1,3 ± 1,6 (0,1 - 22,4)	1,2 ± 0,7 (0-3,6)	0,702
Urea (mg / dl)	38,6 ± 25,8 (3,1 -154)	51,7 ± 31,3 (14-228)	0,000
Creatinine (mg / dl)	0,9 ± 0,7 (0,3 - 7,9)	1,1±0,7 (0,2-6,3)	0,000
ALT (U / L)	30,3 ± 35,3 (4-325)	24,9 ± 25,8 (3-201)	0,005
AST(U / L)	36,5±32,9 (7-383)	32,8 ± 26 (4-187)	0,038
GGT (U / L)	54,1 ± 77,4 (3-534)	42,4 ± 64,7 (6-570)	0,018
ALP (U / L)	77,6 ± 40,9 (22 - 298)	103,3 ± 233,2 (28 - 2933)	0,024
CRP (mg / dl)	88,9 ± 72,6 (0,2-362)	105,7 ± 74,6 (0,6 - 315)	0,015
D-dimer (ng / ml)	815,2 ± 1107 (90 - 7920)	975,9 ± 1304,5(98 - 8797)	0,200
Ferritin (μg / L)	451,2 ± 436 (9 -2755)	452,8 ± 563,2 (9-5010)	0,911
CK-MB (ng / ml)	1,5 ± 1,4 (0,3 - 10,1)	4,7 ± 25,6 (0,3 -253)	0,004
Troponin (ng / ml)	0,1 ± 0,1 (0-1,2)	0,2 ± 0,3 (0 - 3,38)	0,078

**Table 2. Laboratory Values of the Cases.**

When the vaccination status of all cases was examined, it was determined that 44.17 % of them were unvaccinated, 6.94 % of them were single-dose vaccinated, 38.89 % of them were double-dose vaccinated and 10 % of them were three-dose vaccinated. Vaccination status of the cases is listed in Table 3.

Vaccination status	n	%
Unvaccinated	159	44,17
Single dose vaccine	25	6,94
Sinovac	20	
BioNTech	5	
Double dose vaccine	140	38,89
Sinovac	128	
BioNTech	12	
Three doses of vaccine	36	10

Sinovac	20	
2 Sinovac + 1 BioNTech	16	
Total, n (%)	360	100

**Table 3. Vaccination Status.**

While no comorbid condition was observed in 11.4 % of the cases, one or more comorbid conditions were detected in 88.6 % of the cases. While there were no mortal COVID 19 patients in cases without comorbid conditions, it was observed that only 1 (2.4 %) case needed ICU. It was observed that 2 (0.6%) of the cases with at least one or more non-COVID - 19 comorbid conditions were mortal and 13 (4 %) needed ICU. The comorbidities and prognoses of the cases are given in Table 4.

	Comorbidity (-)	Comorbidity (+)	
	N = 41 (%)	N = 319 (%)	p value
Case			
Mortality	0 (0)	2 (0,62)	1,000
Going to ICU	1 (2,43)	13 (4,07)	1,000

**Table 4. Relationship of Cases with Comorbidity and Prognosis.**

When the mutation status of the cases was examined, Delta mutation was observed in 130 (36.1 %) cases, British mutation was observed in 19 (5.2 %) cases, and 48 (13.3 %) cases were suspicious for variants. The mutation status of 163 (45.2 %) cases was not specified. No significant numerical difference was observed in mutations in terms of gender. While the mortality rate and the rate of admission to the ICU were 5.2 % in the English mutation, no mortality was observed in cases with delta mutations and suspected variants. The rate of going to the ICU was 3.8 % in Delta mutation and 2 % in suspected variant cases. The rate of full - dose vaccination was 68.4 % in British mutations, 64.7 % in Delta mutations, and 60.4 % in variant suspects. The presence of comorbid conditions was found in all groups at rates close to each other. Mutation status, prognosis, vaccine and comorbidity relationships of the cases are given in Table 5.

Case	Mutation status				Total N = 360 (%)
	British N = 19 (%)	Delta N = 130 (%)	Suspected variant N = 48 (%)	Unspecified N = 163 (%)	
Gender					
Male	8 (5)	52 (32,5)	23 (14,4)	77 (48,1)	160 (100)
Female	11 (5,5)	78 (39)	25 (12,5)	86 (43)	200 (100)

Going to ICU	1 (5,2)	5 (3,8)	1 (2)	7 (4,3)	14 (3,8)
Mortality	1 (5,2)	0 (0)	0 (0)	1 (0,6)	2 (0,5)
Vaccination status insufficient	6 (31,5)	46 (35,3)	19 (3,9)	120 (73,6)	191 (53)
Full dose	13 (68,4)	84 (64,7)	29 (60,4)	43 (26,3)	169 (47)
Comorbidity (+)	18 (94,7)	116 (89,2)	42 (87,5)	143 (87,7)	319 (88,6)

**Table 5. Mutation Status of Cases, Prognosis, Vaccine and Comorbidity.**

## DISCUSSION

Age is one of the important factors affecting mortality in cases of COVID - 19. In cases requiring hospitalization, the average age ranges from 47 to 73 years. 74 - 86 % of inpatients are at least 50 years of age or older. Male gender is more common than females. While the rate for 5 - 17 year olds in the USA is 0.3 per 1000, it increases to 304.9 per 1000 for 85 years and older (8 - 12). While no significant difference was observed in terms of gender in our study, the mean age was  $58.29 \pm 15.61$  in the inadequately vaccinated group and  $72.12 \pm 12.65$  in the full dose vaccinated group, which is similar to the studies. There is a significant difference between the inadequately vaccinated group and the fully vaccinated group in terms of mean age ( $p = 0.000$ ). In the under-vaccinated group, the mean age at admission to the hospital after vaccination due to COVID - 19 was lower. The reason for this may be that the protection of the vaccine in younger patients is more effective. Another reason may be the high rate of vaccination in the elderly population due to pandemic concerns.

Since the onset of the COVID - 19 pandemic in many countries, a total of 326 vaccine studies of different types, 132 of which are in clinical development and 194 are in preclinical development stage, are ongoing.<sup>13</sup> In one study, the results of the first 100 days of the mRNA - based BNT162b<sub>2</sub> (Pfizer-BioNTech) and mRNA - 1273 (Moderna) vaccine were examined. At least 100 days after vaccination, the specific antibody titers and the amount of neutralizing antibodies were found to be higher than the antibody formed during the recovery period in cases with COVID - 19. Preliminary results of another multicenter placebo-controlled study were shared, in which the safety and efficacy of the mRNA - based BNT162b<sub>2</sub> (Pfizer-BioNTech) vaccine were examined. In the study, 2 doses were administered to randomly selected individuals aged 16 years and over, 21 days apart. The results were found to be 95 % effective in preventing COVID - 19. It was observed that variables such as age, gender, race, ethnicity, and body mass index did not affect the results. There are other trials examining the efficacy of COVID vaccines and found to be effective.<sup>15-18</sup> Sinovac vaccine was administered intramuscularly in two doses in a total of 742 volunteers in Phase I and Phase II studies. It was

shown that SARS – CoV - 2 developed antibodies against the RBD region of the S protein in 92.4 % of the subjects when administered with 14-day intervals, and in 97.4 % when administered with 28 - day intervals.<sup>19</sup>

In our country, Sinovac and Pfizer-BioNTech vaccines are the most frequently applied COVID - 19 vaccines.<sup>20</sup> When the cases hospitalized in the pandemic wards of our center were randomly selected and their vaccination histories were examined, it was seen that 191 (53 %) cases were insufficiently vaccinated and 169 (47 %) cases were fully vaccinated. It was determined that 44.17 % of the cases were unvaccinated, 6.94 % were single - dose vaccinated, 38.89 % were double-dose vaccinated and 10 % were three-dose vaccinated. Since Sinovac came to our country earlier, it was seen that it was used more frequently.

When insufficiently vaccinated cases and full-dose vaccinated cases are examined in terms of laboratory values, in full-dose vaccinated cases; WBC ( $p = 0.000$ ), NE ( $p = 0.001$ ), CRP ( $p = 0.015$ ) and CK - MB ( $p = 0.004$ ) were found to be higher. When the clinical reflection of the vaccines was evaluated, no significant difference was observed between the full-dose vaccinated group and the insufficient vaccinated group in terms of length of hospital stay ( $p = 0.562$ ), mortality rate ( $p = 1,000$ ), and rate of going to ICU ( $p = 0.390$ ). When the cases were divided as unvaccinated ( $N = 163$ ) and vaccinated for 1 dose or more ( $N = 197$ ), the service length of stay ( $p = 0.381$ ), mortality rate ( $p = 1,000$ ) and ICU admission rate ( $p = 0.145$ ) were also divided between the two groups, no significant difference was observed. Full dose vaccinated cases; They were analyzed separately as 2 full-dose vaccines ( $N = 138$ ) and 3 full-dose vaccines ( $N = 31$ ). Similarly, no significant difference was observed between the two groups in terms of length of service stay ( $p = 0.769$ ), mortality rate ( $p = 0.138$ ), and ICU admission rate ( $p = 0.228$ ). In observing similar prognosis between the groups; a) higher mean age in full-dose vaccines, b) The mean values of laboratory values such as CRP, CKMB, NE, which are considered to be among the poor prognostic factors of COVID-19<sup>21,22</sup> in full-dose vaccinated patients, are higher at the time of admission, c) The majority of the patients who were followed up in the ward who were mortal were excluded from the study because their vaccination information could not be accessed, d) higher rate of comorbid conditions which are also considered as poor prognostic factors in full - dose vaccinated patients, e) exclusion of patients with ICU admission, we think that factors such as.<sup>23</sup> Although the effect of the vaccine on the prognosis could not be demonstrated due to existing reasons, it was observed that the average time to catch COVID - 19 after vaccination was higher in the full dose vaccinated group ( $p = 0.000$ ).

SARS – CoV - 2 is a frequently mutating RNA virus. In November 2020, transmission of the VUI - SARS -

CoV - 2 variant reported from the UK and other variants reported from South Africa and Brazil was also reported. At the same time, regional epidemiological data were shared that these mutations can evade immunity acquired by vaccine or disease and cause more severe disease.<sup>24</sup> However, studies have reported that vaccines are also effective in mutations. When the nasopharyngeal swab PCR results reports of SARS - CoV - 2 were examined in our study, Delta mutation was the most common mutation, the second most common variant was suspected, and the third most frequent was British mutation. The rates of full-dose vaccination of the cases with the mutation type were found to be similar. There is no obvious difference between mutations in terms of prognosis.

As a result, it was seen that 44 % of the patients who were hospitalized and followed up in the ward in our hospital were unvaccinated. It was observed that full dose vaccination showed a positive correlation with advanced age and comorbid status. In this study, no significant difference in prognosis was observed between individuals who were vaccinated with an insufficient dose and those who were vaccinated with a full dose. The reasons for this are age, poor prognostic factors, differences in comorbid status between groups, inaccessibility of vaccination information for some mortal cases, and exclusion of cases hospitalized in the ICU. In addition, no significant difference was observed between mutations in terms of mortality and admission to the ICU. The longer the time passes after the last dose of vaccine, the greater the risk of contracting OVID-19. For this reason, booster doses are needed.

#### CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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