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Comparison of the Prognosis and Mortality of Sars-Cov-2 Variants in Critically İll Patients

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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ABSTRACT

Backround: Since the beginning of the pandemic,the globally circulation of SARS-CoV-2 has caused the virus to constantly mutate,resulting in the emergence of new variants.Some of these variants have been designated as variants of concern(VOC),defined by the WHO as variants associated with increased infectivity,increased disease severity,or change in clinical disease presentation.
Aim and Objective: We aimed to evaluate and compare the prognosis and mortality of the critically ill patients infected with SARS-CoV-2 and SARS-CoV-2 variants.
Materials and Methods: A total of 335 critically ill patient who were positive for SARS-CoV-2 by polymerase chain reaction enrolled in the study.
Results: Hypertension was significantly higher in the patients in delta group(p=0,02).The presence of comorbidity was statistically significantly associated with mortality in all groups(p <0,05). Unvaccinated patients were significantly higher in all groups and being unvaccinated was associated with mortality in all groups(p <0,05).Mortality was statistically significantly associated with all groups(p=0,01).The delta variant poses a higher risk of mortality compared to other variants(p=0,0001).

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Conclusion: The study indicates that severe disease requiring intensive care admission were common in the elderly.Hypertension was higher in the patients in delta group and the presence of comorbidity was associated with mortality in all variant types of COVID-19.Severe disease requiring intensive care admission was more common in the unvaccinated population, regardless of variant type, and being unvaccinated was associated with mortality.All variant types were associated with mortality, but the mortality risk was higher in patients infected with delta variant compared to other variants.

Keywords: COVID-19; variants of concern; mortality; prognosis; unvaccinated.

1. INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was first detected in Wuhan, China, in December 2019 and rapidly spread all over the world. The World Health Organization (WHO) declared Coronavirus disease of 2019 (COVID19) a global pandemic in March 2020 [1].

All viruses, including SARS-CoV-2 that cause COVID-19, evolve continuously as changes in the genetic code (genetic mutations) occur during the replication of the genome. Most genetic variations occur as a result of drift and have little or no effect on the traits of the virus. Since the beginning of the pandemic, the globally circulation of SARS-CoV-2 has caused the virus to constantly mutate, resulting in the emergence of new variants. Some of these variants have been designated as variants of concern (VOC), defined by the WHO as variants associated with increased infectivity, increased disease severity, or change in clinical disease presentation [2].

The first identified SARS-CoV-2 VOC was the Alpha variant (B.1.1.7), that was first documented in the United Kingdom in September 2020 [3] and had increased transmissibility compared with the previous wildtype lineage [4]. The other VOCs were the Beta variant (B.1.351) which was first documented in South Africa in October 2020 and the Gamma variant (P.1), that was first documented in Brazil in November 2020 [5]. The delta variant (B.1.617.2) was first documented in India in December 2020 and was designated as a VOC on May 6, 2021 [6]. The viral load of the delta variant was higher than the other VOCs [7] and the delta variant has been associated with a higher risk of hospitalization, more severe outcomes, admission of ICU, and mortality than other variants [8-10].

Various studies have been conducted examining the high contagiousness, the need for hospitalization, disease severity and mortality rates of these variants [8-11].

We aimed to evaluate and compare the prognosis and mortality of the critically ill patients infected with SARS-CoV-2 and SARS-CoV-2 variants in our study.

2. MATERIALS AND METHODS

2.1 Study Design

This retrospective single center observational study was performed between May 1st, 2021 and September 30th,2021 in Ersin Arslan Training and Research Hospital Mücahitler Covid Intensive Care Units. Republic of Turkey Ministry of Health 2021-09-18T22_38_39 numbered and Gaziantep University Medical Ethics Committee 2021/322 numbered approval have been received.

2.2 Patients

All patients who were admitted to Ersin Arslan Training and Research Hospital Mücahitler Covid Intensive Care Units due to COVID-19 infection from May 1st,2021 and September 30th,2021 were included (n=375). The exclusion criteria was negative PCR(polymerase chain reaction) (n=40). At last, 335 patients were enrolled the study.

2.3 Clinical Data Collection

Data was collected a five month period (May 2021 –September 2021) using the intensive care units(ICUs) database; all patients who tested positively for COVID-19 were evaluated. Data collection included demographic data, comorbidities, vaccination status, PCR test results, severity of disease. Prognosis was evaluated in terms of mortality, need of renal replacement therapy, need of mechanical ventilation and the length of ICU stay. According to the PCR test results, the patients were grouped as follows; SARS-CoV-2 (Orf1ab+N), delta (B.1.617.2), alpha (B.1.1.7), other mutant (beta, gamma, eta, zeta, theta, lota; one of the variants containing E484K mutation).

2.4 Statistical Analysis

The sample size was determined 95% confidence interval and 90% power of test in this study. Chi-Square Test was used for statistical analyzed.

3. RESULTS

3.1 Characteristics of Patients With COVID-19

A total of 335 critically ill patients with positive PCR test enrolled our study. Of these patients 154 (45,97%) were in SARS-CoV-2 group, 121 (36,11%) were in delta group, 51 (15,22%) were in the other mutant group and 9 (2,68%) were in the alpha group. The patients of SARS-CoV-2 group involved 89 male, 65 female, delta group 68 male,53 female, other mutant group 30 male, 21 female and alpha group 6 male, 3 female . Although male gender was more common in all groups, there was no statistically significant relationship.

The mean age of patients with SARS-CoV-2 group was 64,48±2,18, delta group was 64,74±2,81, the other mutant group was 64,8±4,3 and the alpha group was 66,9±7,28. Compared to the other groups,the proportion of the patients aged between 41-60 was significantly higher in SARS-CoV-2 group(p=0,05). In SARS-CoV-2 group 57 (30,64%), in delta group 85 (45,69%), in other mutant group 37 (19,89%) and in alpha group 7 (3,76%) patients had comorbidty. Hypertension was significantly higher in the patients in delta group(p=0,02). The presence of comorbidity was statistically significantly associated with mortality in all groups(p <0,05).

44 (48,8%) patients in SARS-CoV-2 group, 29 (32,2%) patients in delta group, 13 (14,4%) patients in other mutant group, 4 (4,4%) patients in alpha group were fully vaccinated. Unvaccinated patients were significantly higher in all groups and being unvaccinated was associated with mortality in all groups (p<0,05) (Table 1, Table 2).

3.2 Outcomes

The patients who needed tracheal intubation were significantly higher in SARS-CoV-2 group (p=0,04). There was no significantly difference for needing renal replacement theraphy among the groups. The length of icu stay were in SARS-CoV-2 group; 10,31±1,37 days, in delta group 9,73±1,2 days, in other mutant group 9,76±1,52days and in the alpha group 7,9±4,7 days respectively. Mortality rate was from high to low as SARS-CoV-2, delta, other mutant and alpha groups, and mortality was statistically significantly associated with all groups (p=0,01). The delta variant poses a higher risk of mortality compared to other variants(p=0,0001) (Table 1, Table 2).

4. DISCUSSION

The severe SARS-CoV-2 virus has evolved continuously since the onset of the COVID-19 pandemic in December 2019, with many variants emerging around the world. To date, many studies have been conducted comparing the genomic, clinical and laboratory features of these variants [12-14]. In this study, we grouped patients hospitalized in ICU with the diagnosis of COVID-19 according to variant types and analyzed their demographic characteristics and clinics.

Peckham et al. reported that males and females are at equal risk of infection from a large-scale meta-analysis of 3,111,714 global cases of COVID-19. These large-scale data show that although there is no gender difference in the proportion of people infected with SARS-CoV-2, males are at a significantly higher risk of serious illness and death than females [15]. In our study, which supports the literature, there was no significant difference in terms of gender between the groups and in the whole population, although male gender was more common in all groups.

Venkatraja et al. found in their study that the age of the deceased was high in all variants, indicating that elderly individuals infected with any variant of COVID-19 are at high risk of death. However, the median age of recovery was lowest for delta (40 years) for recovered patients infected with different VOCs, and it was alarming that the delta variant lowered the mean age of recovery [16]. In our study, our population was severe covid 19 patients hospitalized in the intensive care unit. Similar to previous studies, the mean age in all groups was >60 years. In addition, the number of patients aged 40-60 years was higher in the SARS-CoV-2 group.

Osibagun et al., in their study in which they examined 2184 COVID-19 patients with comorbidities, they discovered that the most common comorbidities were hypertension and diabetes, and that patients with 2 or more comorbidities were more likely to die from COVID-19.They also found that the comorbidities

predicting death were hypertension, diabetes, kidney disease, cancer, and HIV [17]. Wern hang et al., in a meta-analysis, defined that hypertension as a comorbidity has the highest prevalence in COVID-19 patients. While patients with chronic kidney disease are at higher risk of death, hypertension, diabetes and cancer have been found to significantly exacerbate the severity of COVID-19 in patients resulting in mortality [18]. Gunadi et al., in their study examining the association of SARS-CoV-2 delta variant with the outcomes of COVID-19 patients, determined that; comorbidities,including obesity, diabetes, and hypertension, were independent prognostic factors for the mortality of patients with COVID-19 [19]. In our study we found that hypertension was higher in the patients in delta group and the presence of comorbidity was associated with mortality in all variant types of COVID-19.

As a result of extensive research, the effectiveness of the vaccine against B.1.1.7, B.1.351 and B.1.617.2 has been demonstrated. A study of B.1.617.2 showed a reduction in clinical severity with a faster reduction in viral loads in vaccinated individuals [20-23]. Bayrakçı et al. found in their study that unvaccinated patients required more lung involvement, hospital stay, higher CT scores, and more intensive care needs [24]. We determined that unvaccinated patients were higher in all groups and according to our study being unvaccinated was associated with mortality.

Table 1. Characteristics and outcomes of patients with Covid-19

Parameters	**n**	**Mean**	**SD**	**95% CI**
Ages	335	64.6 (20-95)	14.98	± 1.52
20-40	17	5.1%	0.23	± 0.02
41-60	106	31.7%	0.46	± 0.04
>60	212	63.2%	0.48	± 0.04
Gender				
Male	193	57.6%	0.49	± 0.05
Female	142	42.4%		
Comorbidity				
Yes	186	55.5%	0.48	± 0.05
No	149	44.5%		
Hospital Stay (days)	335	9.95 (1-45)	Tem.47	± 0.79
	Sars-CoV-2	**Delta**	**Other Mutant**	**Alpha**
	n(%)	**n(%)**	**n(%)**	**n(%)**
Gender	154 (45,97%)	121 (36,11%)	51 (15,22%)	9 (2,68%)
Male	89 (46.1%)	68 (35,2%)	30 (15,5%)	6 (3,1%)
Female	65 (45,7%)	53 (37,3%)	21 (14,7%)	3 (2,1%)
Ages	64,48±2,18	64,74±2,81	64,8±4,3	66,9±7,28
20-40	5(29,4%)	9(52,9%)	3(17,6%)	0
41-60	57(53,7%)	31(29,2%)	16(15%)	2(1,8%)
>60	92(43,4%)	81(38,2%)	32(15%)	7(3,3%)
Comorbidity				
	57(30,64%)	85(45,69%)	37(19,89%)	7(3,76%)
Diabetes mellitus	47(40,8%)	40(34,7%)	23(20%)	5(4,3%)
Hypertension	58(49,5%)	33(28,2%)	21(17,6%)	5(4,2%)
Cardiovascular disease	42(47,7%)	29(32,9%)	14(15,9%)	3(3,4%)
Chronic kidney failure	11(40,7%)	11(40,7%)	4(14,8%)	1(3,7%)
Other comorbid disease	50(45,8%)	41(37,6%)	11(10,0%)	7(6,4%)
No comorbidity	97(65,1%)	36(24,1%)	14(9,4%)	2(1,3%)
Vaccination				
Completed	44(48,8%)	29(32,2%)	13(14,4%)	4(4,4%)
Uncompleted	16(43,2%)	14(37,8%)	6(16,2%)	1(2,7%)
Unvaccinated	93(44,9%)	78(37,6%)	32(15,4%)	4(1,9%)
Intubation	106(50,2%)	72(34,1%)	28(13,2%)	5(2,3%)
Dialysis	21(44,6%)	15(31,9%)	8(17,0%)	3(6,3%)
Length of icu stay	10,31±1,37	9,73±1,2	9,76±1,52	7,9±4,7
Mortality	88(47,0%)	68(36,3%)	26(13,9%)	5(2,6%)

Table 2. Statistical analysis data of the study according to the variables

	SARS-CoV-2	Delta	Other Mutant	Alpha	Intubation	Mortality
	p< / ODDS	**p< / ODDS**	**p< / ODDS**	**p< / ODDS**	**p< / ODDS**	**p< / ODDS**
Ages						
20-40	0.1	0.1	0.7	0.4	**0.003 / 0.227**	**0.0002 / 0.096**
41-60	**0.05 / 1.583**	0.07 / 0.638	0.9	0.5	**0.05 / 0.636**	**0.01 / 0.567**
>60	0.2	0.2	0.9	0.3	**0.001 / 2.085**	**0.0001 / 2.526**
Gender						
Male	0.9	0.6	0.8	0.5	0.3	0.2
Female	0.9	0.5	0.9	0.8	0.3	0.2
Comorbidity						
Hypertension	0.3	**0.02 / 0.580**	0.3	0.1	0.7	**0.0001 / 1.037**
Diabetes mellitus	0.1	0.7	0.07 / 1.714	0.1	0.8	**0.0001 / 0.843**
Coronary artery disease	0.7	0.4	0.8	0.6	0.8	**0.0001 / 1.198**
Chronic renal failure	0.5	0.6	0.9	0.7	0.9	**0.0001 / 0.988**
No comorbidity	**0.0001 / 4.222**	**0.0001 / 0.379**	0.07	0.1	0.9	0.1
Dialysis	0.8	0.5	0.7	0.09 / 3.205	**0.0001 / 7.679**	**0.0001 / 6.646**
Intübation times (days)						
1-4						**0.0001 / 14.186**
5-8	0.2	0.2	0.7	0.6		**0.0001 / 10.438**
>8	0.4	0.8	0.2	0.7		**0.0001 / 5.806**
Hospital Stay (days)						
1-5	**0.0001 / 1.302**	0.7	**0.0001 / 0.632**	**0.0001 / 2.825**	**0.0001 / 0.212**	**0.0001 / 0.347**
6-10	**0.0001 / 0.714**	0.1	**0.0001 / 1.589**	**0.0001 / 0.278**	**0.0001 / 0.874**	**0.0001 / 1.014**
11-15	**0.0001 / 0.968**	**0.0001 / 0.910**	0.1	**0.0001 / 1.217**	**0.0001 / 3.052**	**0.0001 / 2.152**
>15	**0.0001 / 1.130**	**0.0001 / 1.076**	0.1	**0.0001 / 0.512**	**0.0001 / 6.186**	**0.0001 / 2.156**
Intübation	**0.04 / 1.598**	0.3	0.1	0.6		**0.0001 / 91.142**
Mortality	**0.01 / 1.004**	**0.0001 / 1.024**	**0.0001 / 0.795**	**0.0001 / 0.989**		
Vaccine						
Completed	0.5	0.3	0.8	0.2	0.2	0.1
Uncompleted	**0.0001 / 0.883**	**0.0001 / 1.087**	0.1	**0.0001 / 1.007**	**0.0001 / 0.746**	**0.0001 / 0.817**
Unvaccinated	**0.0001 / 0.896**	**0.0001 / 1.195**	**0.0001 / 1.049**	**0.0001 / 1.485**	0.1	**0.05 / 1.464**

Endotracheal intubation rates vary between 3.2% and 88% in recent studies. This rate difference may be due to variability in study populations, study environments, or intubation criteria [25-27]. Endotracheal intubation rate was 62,98% in our study and was higher in SARS-CoV-2 group.

Gupta et al., in their multicenter cohort study, found that 20.6% of the patients admitted to the intensive care unit developed acute kidney injury requiring renal replacement therapy after admission to the intensive care unit, and 54.9% of these patients died within 28 days of admission [28]. According to our study there was no difference among the groups for needing renal replacement theraphy but needing renal replacement theraphy was associated with mortality.

Venkatraja et al also found that patients infected with the Delta variant and/or its descendants were associated with a significant increased probability of death from COVID-19 compared to other variants [16].

Patone et al. determined that patients with lineage B.1.1.7 were at increased risk of 28-day mortality compared with patients with non-B.1.1.7 SARS-CoV-2 [29].

In their study, Challen et al. found that the risk of death due to infection with alpha is likely to be increased and if this finding can be generalized to other populations, infection with alpha has the potential to cause significantly additional deaths compared to previously circulating variants [30].

In our study, we found that all variant types were associated with mortality, but the mortality risk was higher in patients infected with delta variant compared to other variants.

5. CONCLUSION

This study analyzed the characteristics, prognosis and mortality of the critically ill patients infected with SARS-CoV-2 and SARS-CoV-2 variants. We showed that severe disease requiring intensive care admission were common in the elderly. And also we showed that hypertension was higher in the patients in delta group and the presence of comorbidity was associated with mortality in all variant types of COVID-19. Severe disease requiring intensive care admission was more common in the unvaccinated population, regardless of variant type, and being unvaccinated was associated with mortality. All variant types were associated with mortality, but the mortality risk was higher in patients infected with delta variant compared to other variants.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHİCAL APPROVAL

Gaziantep University Medical Ethics Committee 2021/322 numbered approval have been received.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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