Euras J Fam Med 2021;10(4):211-8. doi:10.33880/ejfm.2021100407 **Original Research**

Blood Types and Severity of COVID-19

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ABSTRACT

Aim: Since blood types first appeared, their association with diseases caused by microorganisms has been further investigated with several studies for many years. The bond of blood groups described as A, B, AB, and O with coronavirus has been the research subject in many countries.We aimed to elucidate whether there was a relationship between blood types and Rh factor and contracting COVID-19 disease and disease severity.

Methods: The study was designed as a retrospective case-control study. Between March 2020 - February 2021, 1110 patients were included (538 cases, 572 controls). Disease severity was classified according to where patients were treated: those who were outpatients considered as “mild disease”, hospitalized in a hospital ward considered as “moderate disease”, and treated in the intensive care unit were considered as “severe disease”.

Results: The number of people with blood type A was 447 (40.3%), blood type B was 197 (17.7%), blood type AB was 90 (%8), and blood type O was 376 (33.9%). There was no significant difference between the case and control groups according to the blood types. A 3.93 times increase of developing mild illness was detected compared to the control group in Rh-positive individuals. The rate of developing a severe disease was higher in females with blood type A than a mild disease, and A blood type caused the disease to be severe compared to other blood groups in females.

Conclusion: We concluded that blood type A caused more severe disease than other blood types in females, and females with B blood type survived the disease as outpatients. Our study can shed light on pathophysiological investigation of the relationship between COVID-19 disease causing a pandemic with high mortality and virulence and blood types.

Keywords: COVID-19 virus, blood group, disease

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Introduction

Coronavirus disease 2019 (COVID-19), also called new coronavirus pneumonia, was first reported in Wuhan in December 2019. The virus spread rapidly worldwide, and a global pandemic was declared in March 2020 by the World Health Organization (1). The contagious, sickening, and lethal effect of the virus is continuing seriously. The course of the disease is variable; it may present with a broad spectrum of clinical manifestations ranging from an asymptomatic carriage status presenting as a mild outpatient disease clinical picture to a progression into a severe disease that can cause Acute Respiratory Distress Syndrome (ARDS), septic shock, and even death. The underlying causes of the severe course or even mortal consequences of the disease and mild illness in some people have been the subject of research (2).

Since blood types first appeared, their association with diseases caused by microorganisms has been further investigated with several studies for many years. An increase in studies exploring the relationship between viral diseases and blood types, showing a significant link between norovirus, HBV, SARS-CoV, MERS-CoV, and blood types, has been observed in the 2000s (3-5).

This has been one of the questions that came to mind with COVID-19 since COVID-19 occurrence worldwide: Do blood types and Rh factors have a relationship with the course of the disease? The bond of blood groups described as A, B, AB, and O with coronavirus has been the research subject in many countries. Research conducted in China in the first months of the epidemic turned attention to the A blood type. It came to the scene that the disease might progress to a more severe disease in people with blood type A. As the epidemic progressed, so did the research. Moreover, research conducted in Spain and Italy has pointed out a more severe disease course for patients in blood group A and a lower risk of such clinical status for those in blood group O. Similarly, it has also been reported in research done in the United States of America that those with blood type O may have a milder disease (5).

To answer this question in this context, we aimed to elucidate whether there was a relationship between blood types and Rh factor and contracting COVID-19 disease and disease severity.

Methods

The study was designed as a retrospective case-control study. 1110 patients who applied to the X Hospital between March 2020-February 2021 were included (538 cases, 572 controls). The study participants were divided into case and control groups. The control group consisted of people admitted to our hospital between March 2020 - February 2021 and did not have COVID-19 disease, and those admitted to our hospital at the same period and had COVID-19 disease formed the case group. Patients in the case group who were COVID-19 PCR positive were then divided into 3 separate subgroups as those who survived the disease as outpatients, were hospitalized in a hospital ward, and were treated in the Intensive Care Unit (ICU). The demographic characteristics of the patients, including age and gender, were recorded. Patients' information in the case and control groups on blood types and Rh Factor was accessed via the web-based national healthcare system. Again, the RT-PCR test results obtained with combined throat and nasal swabs were reached via the web-based national healthcare system. Disease severity was classified according to where patients were treated: those who survived the disease as outpatients 'mild disease,' hospitalized in a hospital ward 'moderate disease,' and treated in the ICU were considered 'severe disease.' The identification number (ID) was created for each patient using the SPSS program. Patient information and data were recorded separately by two specialist physicians independently. A third specialist checked two data sets' accuracy.

The association between different blood types and Rh Factor and COVID-19 was investigated in the selected population. According to gender, subgroups were stratified to assess whether there was a significant difference between blood types and the incidence of COVID- 19.

Approval for this study was obtained from Mustafa Kemal University Non-Interventional

Clinical Research Ethics Committee and TR Ministry of Health General Directorate of Health Services and Scientific Research Platform, numbered 2021-04-07T20_12_19.

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS) version 22.0. Kolmogorov-Smirnov test was performed for normality test. $p \geq 0.05$ was accepted as the normal distribution. Whether numeric categories have not a normal distribution, a non-parametric test (independent T-test) was performed. A chi-square test was performed for categorical variables. The ABO blood type and Rh Factor frequency in all populations and different gender subgroups were tested using chi-square tests and odds ratios (ORs) with 95% confidence interval (CI). A $p<0.05$ was considered significant.

Results

The mean age of the patients included in the study was 48.8±17.8 years (cases: 51.2±17.1 years; controls: 46.7±18.2 years). 589 (53.1%) were male, and 521 (46.9%) were female. There was no significant difference between the case and control groups in terms of the proportions of female or male (the number of male cases is 297 (55.2%); the number of male controls is 292 (51.0%); p=0.092). When the cases were classified by where the disease was treated evaluated according to gender, most of the patients who survived the disease as outpatients, who were hospitalized in a hospital ward, and were treated in the ICU were males (male patients, respectively, n=175 (53.0%); n=74 (62.7%); and n=48 (53.3%); p=0.178).

The number of people with blood type A was 447 (40.3%), blood type B was 197 (17.7%), blood type AB was 90 (%8.1%), and blood type O was 376 (33.9%). There was no significant difference in the frequency of blood types between the case and control groups (p=0.880). Comparing the severity of the disease and blood types, patients with blood type A (n=214; 39.8%) were more common in all three groups (mild, moderate, and severe); O blood type ranked the second (n=188; 34.9%). No statistically significant relationship between disease severity and blood types existed (p=0.202) (Table 1).

Table 1. Comparison of the effects of blood groups on contracting and severity of COVID-19 disease

Blood Types	Groups*		X^2	OR (95% CI)	p	Severity of Disease**			p
	Case n (%)	Control n (%)				Mild n (%)	Moderate n (%)	Severe n (%)	
A	214/402 (53.2)	233/421 (55.3)	0.543	0.918 (0.698-1.208)	0.295	124/235 (52.8)	47/96 (49.0)	43/71 (60.6)	0.321
B	92/280 (32.9)	105/293 (35.8)	0.453	0.876 (0.620-1.237)	0.254	64/175 (36.6)	14/63 (22.2)	14/42 (33.3)	0.115
AB	44/232 (19.0)	46/234 (19.7)	0.850	0.957 (0.604-1.515)	0.471	31/142 (21.8)	8/57 (14.0)	5/33 (15.2)	0.373
O	188/538 (34,9)	188/572 (32,9)	0.465	1.097 (0.856-1.407)	0.252	111/330 (33,6)	49/118 (41,5)	28/90 (31,1)	0.215

** A, B, AB blood groups were compared with O blood group using the chi-square test. The total number of patients with O blood group A, B, AB blood group was compared with the chi-square test. p<0.05; ** A, B, AB blood groups were compared with O blood group using the chi-square test. The total number of patients with O blood group A, B, AB blood group was compared with the chi-square test. OR could not be calculated in the comparison between disease severity and blood groups. p<0.05*

Rh Factor was positive in 960 (86.5%) out of 1110 people (Rh-positive cases: 460 (85.5%); Rh-positive controls: 500 (87.4%); p=0.200). When the relationship between disease severity and Rh factor was evaluated, Rh positivity was determined in 285 (%86.4%) cases in the mild disease group, in 94 (79.7%) cases in the moderate disease group, and 81 (90,0%) cases in the severe disease group. There was no statistically significant difference between disease severity and Rh factor (p=0.08) (Table 2).

Table 2. Comparison of the effect of Rh Factor on severity of COVID-19 disease

Rh Factor	Groups		OR (95% CI)	p	Severity of Disease			p
	Case n (%)	Control n (%)			Mild n (%)	Moderate n (%)	Severe n (%)	
Rh Positive	460 (85,5)	500 (87,4)	0.921 (0.720-1.089)	0.200	285 (86,4)	94 (79,7)	81 (90,0)	0.086
Rh Negative	78 (14,5)	72 (12,6)	1.085 (0.909-1.296)		45 (13,6)	24 (20,3)	9 (10,0)	

When classified by gender, the rate of developing a mild disease for females with B blood type was higher than a moderate disease; also, females with B blood type tended to have a mild disease compared to those with other blood types (a mild disease in females: n=33, 21.3%; a moderate disease in females: n=4 (9.1%); OR: 0.370; 95% CI: 0.123 to 1.108; p=0.047) (Table 3-4).

Table 3. Comparison of patients with COVID-19 and control groups according to gender

Blood Types	Male		X^2	OR (95% CI)	p	Female		X^2	OR (95% CI)	p
	Case n (%)	Control n (%)				Case n (%)	Control n (%)			
A	107/213 (50.2)	115/215 (53.5)	0.501	0.878 (0.601-1.283)	0.282	107/189 (56.6)	118/206 (57.3)	0.893	0.973 (0.653-1.450)	0.487
B	52/158 (32.9)	55/155 (35.5)	0.631	0.892 (0.559-1.423)	0.359	40/122 (32.8)	50/138 (36.2)	0.560	0.859 (0.514-1.434)	0.326
AB	32/138 (23.2)	22/122(18.0)	0.306	1.372 (0.747-2.520)	0.192	12/94 (12.8)	24/112 (21.4)	0.103	0.537 (0.252-1.142)	0.073
O	106/297 (35.7)	100/292 (34.2)	0.713	1.066 (0.759-1.495)	0.389	82/241 (34.0)	88/280 (31.4)	0.529	1.125 (0.780-1.624)	0.296

The rate of developing a severe disease was higher in females with blood type A than a mild disease, and A blood type caused the disease to be severe compared to other blood groups in females (a mild disease in females: n=62, 40.0%; a severe disease in females: n=25, 59.5%; OR: 0.453; 95% CI: 0.226 to 0.908; p=0.019) (Table 3-4).

Discussion

Individual factors that affect contracting COVID-19 disease or the disease severity are still under investigation. During the pandemic process, several studies, where different results emerged, have been done to examine whether blood types play a role in the severity of the disease. While Zhao et al. (6) study determined that COVID-19 disease was seen more in people with AB blood type, Zietz et al. (7) study demonstrated that people with the AB blood type had a lower frequency of COVID-19. Again, Zhao et al. (6) reported that mortality was higher in people with blood type A; in contrast, Zietz et al. (7) found no relationship between mortality and blood type. In our study, too, we found no relationship between contracting COVID-19 disease or disease severity and blood types or Rh factor. However, we concluded that blood type A caused more severe disease than other blood types in females, and females with B blood type survived the disease as outpatients.

In a study comparing the distribution of 2173 patients diagnosed with COVID-19 disease according to ABO blood types from 3 hospitals in the Wuhan and Shenzhen regions of China, while the risk of COVID-19 disease occurrence was found to be lower in people with O blood type (OR 0.67; p<0.001), it was higher in those with A blood type (OR 1.21; p=0.027) (6). Another trial studied 1559 people who had the SARS-CoV-2 PCR test in New York according to blood groups; a similar result was encountered. Besides, among those with positive PCR tests for COVID-19, the proportion of individuals with blood type A was higher, while those with blood type O were lower than other blood groups (7). In our study, 39.8% of patients with COVID-19 had A blood type, 17.1% had B blood type, 8.2% had AB blood type, and 34.9% had O blood

type. When evaluating the fatality rate in COVID-19 patients, it has been detected higher in people with blood type A than those with blood type O (OR 0.660; p=0.014) (8). Except for blood groups, a relationship between COVID-19 disease and Rh-positive blood type has also been observed (7). Contrary to these studies, there was no relationship between disease severity and both blood groups and Rh factor in our study.

Table 4. Comparison of the severity of the disease according to blood types and men and women infected with COVID-19

Blood Group	Male		OR	p	OR (95% Cl)	Female		OR	p	OR (95% Cl)
	Outpatient n (%)	Non-ICU Hospitalized n (%)				Outpatient n (%)	Non-ICU Hospitalized n (%)			
A	62(35.4)	27(36.5)	1.047	0.492	0.595-1.843	20(45.5)	62(40.0)	1.250	0.316	0.637-2.455
Non-A	113(64.6)	47(63.5)				24(54.5)	93(60.0)			
B	31(17.7)	10(13.5)	0.726	0.268	0.336-1.569	33(21.3)	4(9.1)	0.370	0.047	0.123-1.108
Non-B	144(82.3)	64(86.5)				122(78.7)	40(90.9)			
AB	23(13.1)	5(6.8)	0.479	0.105	0.175-1.312	8(5.2)	3(6.8)	1.345	0.454	0.341-5.298
Non-AB	152(86.9)	69(93.2)				147(94.8)	41(93.2)			
O	59	32	1.498	0.100	0.859-2.613	52	17	1.247	0.325	0.624-2.492
Non-O	116	42				103	27			
	Outpatient n (%)	ICU n (%)				Outpatient n (%)	ICU n (%)			
A	62(35.4)	18(37.5)	0.914	0.548	0.472	62(40.0)	25(59.5)	0.453	0.019	0.226-0.908
Non-A	113(64.6)	30(62.5)				93(60.0)	13(40.5)			
B	31(17.7)	11(22.9)	0.724	0.267	0.333-1.575	33(21.3)	3(7.1)	3.516	0.024	1.022-12.099
Non-B	144(82.3)	34(77.1)				122(78.7)	39(92.9)			
AB										
Non-AB										
O	59	15	1.119	0.446	0.563-2.222	52	13	1.126	0.452	0.540-2.347
Non-O	116	33				103	29			
	Outpatient n (%)	Hospitalized n (%)				Outpatient n (%)	Hospitalized n (%)			
A	62(35.4)	45(36.9)	0.939	0.446	0.580-1.519	62(40.0)	45(52.3)	0.607	0.044	0.357-1.033
Non-A	113(64.6)	77(63.1)				93(60.0)	41(47.7)			
B	31(17.7)	21(17.2)	1.035	0.520	0.563-1.905	33(21.3)	7(8.1)	3.053	0.006	1.288-7.238
Non-B	144(82.3)	101(82.8)				122(78.7)	79(91.9)			
AB	23(13.1)	9(7.4)	1.900	0.810	0.847-4.263	8(5.2)	4(4.7)	1.116	0.564	0.326-3.818
Non-AB	152(86.9)	113(92.6)				147(94.8)	82(95.3)			
O	59	47	0.812	0.233	0.502-1.313	52	30	0.942	0.471	0.541-1.641
Non-O	116	75				103	56			
	Non-ICU Hospitalized n (%)	ICU n (%)				Non-ICU Hospitalized n (%)	ICU n (%)			
A	27(36.5)	18(37.5)	0.957	0.530	0.451-2.031	20(45.5)	25(59.5)	0.567	0.138	0.241-1.333
Non-A	47(63.5)	30(62.5)				24(54.5)	17(40.5)			
B	10(13.5)	11(22.9)	0.526	0.136	0.204-1.355	4(9.1)	3(7.1)	1.300	0.526	0.273-6.190
Non-B	64(86.5)	37(77.1)				40(90.9)	39(92.9)			
AB	5(6.8)	4(8.3)	0.797	0.502	0.203-3.131	3(6.8)	1(2.4)	3.000	0.326	0.300-30.048
Non-AB	69(93.2)	44(91.7)				41(93.2)	41(97.6)			
O	32	15	1.676	0.127	0.781-3.599	17	13	1.405	0.302	0.575-3.428
Non-O	42	33				27	29			

It was revealed with a gender-stratified analysis in a case-control study involving 208 people that the risk of contracting the COVID-19 disease in women with blood type A was greater (OR 1.56; p=0.02) (8). Similarly, Xiong et al. (9) reported that women and men were different in getting this disease. In a study

evaluating 233,709 cases in Italy, the proportion of women contracting the COVID-19 disease was established to be 1.18 times higher than that of men, but disease severity and deaths in men were shown to be at a higher rate compared to women (10). Likewise, Jin et al. (11) disclosed that males died 2.4 times more than females from COVID-19 disease. It has been hypothesized that these differences between men and women may be caused by the circulating level of Angiotensin-Converting Enzyme (ACE) being at a higher level in men than women, and sex hormones' effect on ACE2 and transmembrane serine protease-2 (TMPRSS2) (10,12). Although the purpose of our study was not directed towards the relationship of COVID-19 disease to gender, we detected no relationship between contracting the disease or disease severity and ABO blood types in males, and that the disease was more severe in females with blood type A and that females with B blood type survived the disease as being outpatients. These results suggest that there may be many different phenotypic and genotypic factors, which affect immune response mechanisms triggered by inflammation.

Angiotensin-Converting Enzyme, synthesized in lung tissue, gastrointestinal and vascular systems, is an enzyme that activates pro-inflammatory and oxidative stress. In studies investigating the relationship between COVID-19 disease and ACE, it has been stated that ACE plays an essential role in disease severity due to its pro-inflammatory effect (13). It has also been noted that there is a relationship between cough that develops in ACE inhibitor users and ABO blood types and that this is associated with ACE level (14,15). A positive relationship was emphasized between ACE activity and people with O blood type in a previous study (16). In another study, Interleukin-6 (IL-6) levels were higher in people with O blood type than those with other blood types (17). IL-6, the molecule that plays a vital role in the inflammatory process, is also responsible for disease severity.

The basic chemical structure that determines blood group antigens is glucose. Since A blood type has an extra N-acetyl galactosamine on the cell surface, A blood type cells are thought to have more contact with the pathogen (18). Another hypothesis trying to explain the higher prevalence of the disease in people with blood type A is that Coronavirus surface proteins that bind to glucose may have a high affinity for people with A blood type (19).

Researchers have agreed that the SARS-CoV-2 virus binding to ACE2 receptors via spike proteins is blocked in the presence of antibodies against surface antigens containing A or B glycan. Another reason why the disease is less common in those with O blood type has been mentioned as the virus blocking from adhering to the epithelium since both anti-A and anti-B antibodies are present in O blood type (20). Demonstrating an association of COVID-19 disease with blood types only in women in our study suggests that other mechanisms and factors other than blood groups also affect contracting the disease and disease severity.

P-selectin and hemostasis, responsible for the adhesion of leukocytes to the endothelium, and intercellular adhesion molecule-1 (ICAM1) involved in T-lymphocyte and neutrophil migration are reported to be higher in people with blood type A (21,22). A more severe course of COVID-19 disease in people with blood type A may be due to the effect of these two molecules increasing hemostasis and inflammation. ICAM-1, which has also been found to act as a receptor in Plasmodium malaria and Rhinovirus infections, is also an important biomarker in the early diagnosis of sepsis (22). The severe course of COVID-19 disease in people with certain blood types suggests that it is due to individual differences in the pro-inflammatory and especially T-cell and humoral response. Since the difference in blood groups is also associated with antigen-antibody associated responses, the different course of disease severity in COVID-19 in individuals may not be caused only by the difference in blood groups. However, it may also be associated with the varying responses of molecules from individual to individual, which especially play a role in the cellular and humoral responses involved in the inflammation process and perhaps oxidative stress stiffness.

Conclusion

It is not yet clear whether all these hypotheses for the relationship between COVID-19 disease and blood types are true. These studies, including our study, can shed light on pathophysiological investigation of the relationship between COVID-19 disease causing a pandemic with high mortality and virulence and blood types.

At the same time, these studies will also guide the planning of further research for elucidating whether the blood type of donor and recipient shows benefit in plasma and IL-6 inhibitor therapy widely used in COVID-19 disease.

References

1. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020;323(11):1061-9. doi: 10.1001/jama.2020.1585.
2. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020;323(13):1239-42. doi: 10.1001/jama.2020.2648.
3. Barua D, Paguio AS. ABO blood groups and cholera. Ann Hum Biol 1977;4(5):489-92. doi 10.1080/03014467700002481.
4. Borén T, Falk P, Roth KA, Larson G, Normark S. Attachment of Helicobacter pylori to human gastric epithelium mediated by blood group antigens. Science 1993;262(5141):1892-5. doi 10.1126/science.8018146.
5. Beyazcicek Ö, Beyazcicek E, Demir S. Are blood groups protective against COVID-19?. Konuralp Medical Journal 2021;13(1):160-7. doi: 10.18521/ktd.840276.
6. Zhao J, Yang Y, Huang H, Li D, Gu D, Lu X, et al. (2020). Relationship between the ABO blood group and the COVID-19 susceptibility. MedRxiv 2020:1-18. (Epub ahead of print). doi: 10.1101/2020.03.11.20031096.
7. Zietz M, Zucker J, Tatonetti NP. Testing the association between blood type and COVID-19 infection, intubation, and death. medRxiv 2020:1-27. doi: 10.1101/2020.04.08.20058073.
8. Fan Q, Zhang W, Li B, Li DJ, Zhang J, Zhao F. Association between ABO blood group system and COVID-19 susceptibility in Wuhan. Front Cell Infect Microbiol 2020;10:404. doi: 10.3389/fcimb.2020.00404.
9. Zhao J, Yang Y, Huang H, Li D, Gu D, Lu X, et al. Relationship between the ABO blood group and the coronavirus disease 2019 (COVID-19) susceptibility. Clin Infect Dis 2021;73(2):328-31. doi: 10.1093/cid/ciaa1150.
10. Foresta C, Rocca MS, Di Nisio A. Gender susceptibility to COVID-19 : a review of the putative role of sex hormones and X chromosome. J Endocrinol Invest 2021;44(5):951-6. doi: 10.1007/s40618-020-01383-6.
11. Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, et al. Gender differences in patients with COVID-19: focus on severity and mortality. Front. Public Health 2020;8:152. doi: 10.3389/fpubh.2020.00152.
12. Patel SK, Velkoska E, Burrell LM. Emerging markers in cardiovascular disease: where does angiotensin-converting enzyme 2 fit in? Clin Exp Pharmacol Physiol 2013;40(8):551-9. doi: 10.1111/1440-1681.12069.
13. Wentao N, Yang X, Yang D, Bao J, Li R, Xiao Y, et al. Role of angiotensin-converting enzyme 2 (ACE2) in COVID-19. Crit Care 2020;24(1):422. doi:10.1186/s13054-020-03120-0.
14. Dai X. ABO blood group predisposes to COVID-19 severity and cardiovascular diseases. Eur J Prev Cardiol 2020;27(13):1436–7. doi:10.1177/2047487320922370.

15. Fang Y, Gao F, Liu Z. Angiotensin-converting enzyme 2 attenuates inflammatory response and oxidative stress in hyperoxic lung injury by regulating NFkappaB and Nrf2 pathways. QJM 2019;112(12):914–24. doi: 10.1093/qjmed/hcz206.
16. Luo JQ, He FZ, Luo ZY, Wen JG, Wang LY, Sun NL, et al. Rs495828 polymorphism of the ABO gene is a predictor of enalapril-induced cough in Chinese patients with essential hypertension. Pharmacogenet Genomics 2014;24(6):306-13. doi: 10.1097/FPC.0000000000000050.
17. Naitza S, Porcu E, Steri M, Taub DD, Mulas A, Xiao X, et al. A genome-wide association scan on the levels of markers of inflammation in Sardinians reveals associations that underpin its complex regulation. PLoS Genet 2012;8(1):e1002480. doi:10.1371/journal.pgen.100248.
18. Ewald DR, Sumner SC. Blood type biochemistry and human disease. Wiley Interdiscip Rev Syst Biol Med 2016;8(6):517-35. doi: 10.1002/wsbm.1355.
19. Wu SC, Arthur CM, Wang J, Verkerke H, Josephson CD, Kalman D, et al. The SARS-CoV-2 receptor-binding domain preferentially recognizes blood group A. Blood ADV 2021;5(5):1305–9. doi: 10.1182/bloodadvances.2020003259.
20. Guillon P, Clément M, Sébille V, Rivain JG, Chou CF, Ruvoën-Clouet N, et al. Inhibition of the interaction between the SARS-CoV spike protein and its cellular receptor by anti-histo-blood group antibodies. Glycobiology 2008;18(12):1085-93. doi: 10.1093/glycob/cwn093.
21. Şensoy E, Öznurlu Y. Hücre adezyon molekülleri. Atatürk Üniversitesi Veteriner Bilimleri Dergisi 2009;4(1):57-68.
22. Hamad MNM. Blood group type, Intercellular Adhesion Molecule-1 (ICAM-1) and Angiotensin-2 impact on COVID.19 outcomes. EC Endocrinology and Metabolic Research 2020;5(11):48-55.