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Effects of blood group types on risk of infection, disease severity, and mortality in COVID-19 patients

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ABSTRACT

Aim: COVID-19 is an epidemic communicable disease that has been declared as a pandemic caused by severe acute respiratory syndrome coronavirus 2. Clinical studies have demonstrated that advanced age and comorbid conditions enhance the severity of the infection. The objective of this study was to examine the of effects of blood group types on risk of infection, disease severity, and mortality in COVID-19 patients.

Material and Method: Included in this study were 1618 patients who had been diagnosed with PCR confirmed COVID-19 infection. The age, gender, blood type, disease severity, need for intensive care, and deaths of the patients were analyzed retrospectively. For the distribution of the blood types in a healthy population, statistics for the blood types of individuals in Ankara for 2020 were obtained from the Republic of Turkey Red Crescent Blood Services and used as a healthy control group for comparison with the data of the patients included in the study.

Results: Among the COVID-19 patients, blood type A was the most common type at a rate of 46.2%. This was followed by blood type O at a rate of 28.4%. The least common blood type was found to be type AB at a rate of 9%. When compared to the healthy population, blood type A was determined to be statistically significantly more common in COVID-19 infection ($p=0.07$,). In contrast, blood type O was determined to be less common when compared to the healthy population ($p<0.001$). No statistically significant differences were determined between the blood types and the risk of severe disease and mortality rate.

Conclusion: Based upon the results of the study, it can be hypothesized that blood group type O may be protective against the risk of contracting the disease and the development of severe infection, while blood group type A may be associated with an increased risk of contracting the disease. However, it was determined that there were no statistically significant associations of mortality and the development of severe disease with ABO blood types.

Keywords: Blood groups, COVID-19, SARS-CoV-2, disease severity, mortality

INTRODUCTION

Coronavirus disease 2019 (COVID-19) first emerged in Wuhan Province, China, as a severe infection involving respiratory system. After that, it was declared a pandemic by the World Health Organization due to the global spread of the disease (1).

Prognosis of the disease caused by COVID-19 infection varies with age, comorbidities, and gender, although a prognostic risk factor specific to this disease has not been determined. The association between blood types and prognosis of the disease is among the risk factors in the literature that have not yet been clarified.

As is known, susceptibility to some viral infections has been linked to antigenic determinants of ABO blood types. Several previous studies have revealed an association between Hepatitis B and Norwalk virus infections and blood types (2,3). Similarly, several studies have shown that ABO blood types also are important risk factors for cardiovascular diseases and venous thromboembolism (VTE) (4,5). Risk of thrombosis has been reported to be lower in individuals with type O blood when compared to those with other blood types and, according to the most recent data, ABO blood types have been shown to modulate the risk of thrombosis via biological mechanisms (6,7). In Turkey and worldwide,

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there have been a limited number of studies conducted that have examined the association between SARS-CoV-2 and ABO blood types (8-11). Therefore, in this study, it was aimed to conduct an examination of the effects of blood types on the risk of infection, disease severity, and mortality in COVID-19 patients.

MATERIAL AND METHOD

Ethics codes were followed, the patients were told about diagnostic and treatment protocols in detail, and informed consent forms regarding the use of their medical information were signed by the patients during their hospitalization. The study was carried out with the permission of Ankara City Hospital No:1 Clinical Research Ethics Committee (Date: 21.05.2020, Decision No: 626). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study was conducted at the department of Internal Diseases between March 2020 and January 2021. Patients with SARS-CoV-2 RNA polymerase chain reaction (PCR)-confirmed COVID-19 infection were included in the study. Patients with no data about their blood type on the system and those with no reachable data for their blood type were excluded from the study. For the PCR tests of the patients, nasopharyngeal swab samples were used. Patient medical data were examined retrospectively. The patient data, including age, gender, comorbidities, and need for intensive care, were obtained from medical records. According to the severity of the disease, we classified the patients into two groups as non-severe and severe patients (**Figure**) (12,13). For distribution of the blood types in a healthy population, statistics for blood types in Ankara for 2020 were obtained from the Republic of Turkey Red Crescent Blood Services and used as a healthy control group for comparison with patient data. A 10000-patient sample from data about blood types of the whole population in Ankara was obtained. These data were used as a healthy control group for comparison with the patient data.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics for Windows 25.0 (IBM Corp., Armonk, NY, USA). For evaluation of the study data, descriptive statistical methods [frequency, percentage, median, interquartile range (IQR)] were used, as well as the chi-square ($\chi 2$) test for comparison of the qualitative data. Conformity to normal distribution of the data was evaluated using the Kolmogorov-Smirnov and Shapiro-Wilk tests. For comparison of the data exhibiting normal distribution, the Mann-Whitney U test was used. Risk analysis was used to determine the risk rates. Statistical significance was considered as α=0,05.

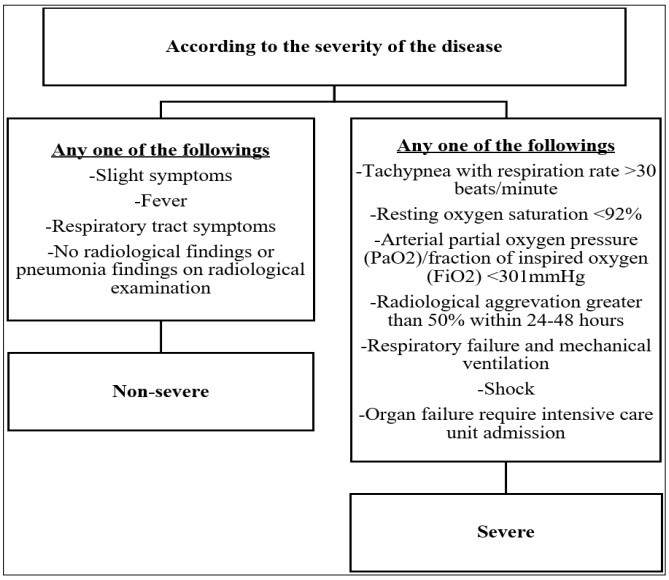

Figure. Flowchart of COVID-19 disease stage as non-severe and severe

RESULTS

A total of 1618 patients with a positive COVID-19 PCR test were included in the study population. The clinical and demographic findings of the patients, as well as their distribution by blood type and disease severity are represented in **Table 1** and **Table 2**. The median age of the patients was determined to be 63 years. For the distribution by gender, 57.8% of the patients were male. Among the COVID-19 patients, type A was the most common blood type, at a rate of 46.2%. This was followed by type O at a rate of 28.4%. The least common was type AB, at a rate of 9%.

When compared to the healthy population, type A was determined to be statistically significantly more common in COVID-19 infection (46.2% versus 42.6%; p=0.007, OR: 1.157). In contrast, type O was determined to be less common when compared to the healthy population (28.4% versus 33.1%; p < 0.001, OR: 0.802).

The distribution of COVID-19 patients by disease severity and mortality rates are given in **Table 3** and **Table 4**. No statistically significant difference was determined between the blood types with regards to the risk of severe disease (p=0.990) and, among the COVID-19 patients, no statistically significant difference was determined between the blood types with regards to the mortality rates (p=0.907).

Table 1. Demographic evaluation of groups with mild and severe diseases

	All Patients	ICU Admission (Severe Disease)		p value
	(n=1618)	Severe (n=814)	Non-severe (n=804)	
Gender Male	936 (57.8%)	478 (58.7%)	458 (57.0%)	0.474[a]
Age (year)	63.00 (27.00)	72.00 (20.00)	52.00 (27.00)	0.000[b]

a: Chi-square test (n/%), b: Mann-Whitney U test (median/IQR)

Table 2. Comparison of the Blood Groups of the Healthy Controls and COVID-19 Patients

Blood Type	Group		P-value*		
	COVID-19 (n=1618)	Healthy Controls (n=10000)			
O	459 (28.4%)	3305 (33.1%)			
A	748 (46.2%)	4264 (42.6%)	0.002		
B	265 (16.4%)	1629 (16.3%)			
AB	146 (9.0%)	802 (8.0%)			
Blood Type	**COVID-19 (n=1618)**	**Healthy Controls (n=10000)**	**P-value***	**OR**	**95% CI**
O	459 (28.4%)	3305 (33.1%)	0.000	0.802	0.714–0.901
A	748 (46.2%)	4264 (42.6%)	0.007	1.157	1.041–1.285
B	265 (16.4%)	1629 (16.3%)	0.929	1.006	0.873–1.160
AB	146 (9.0%)	802 (8.0%)	0.171	1.138	0.946–1.368

*: Chi-square test (n / %)

Table 3. Disease Severity in COVID-19 Patients by Blood Group

Blood Type	ICU admission (Severe Disease)		P-value*		
	Severe (n=814)	Non-severe (n=804)			
O	233 (28.6%)	226 (28.1%)			
A	373 (45.8%)	375 (46.6%)	0.990		
B	134 (16.5%)	131 (16.3%)			
AB	74 (9.1%)	72 (9.0%)			
Blood Type	**ICU Admission (Severe Disease)**		**P-value***	**OR**	**95% CI**
	Severe (n=814)	**Non-severe (n=804)**			
O	233 (28.6%)	226 (28.1%)	0.818	0.975	0.785–1.210
A	373 (45.8%)	375 (46.6%)	0.957	1.005	0.827–1.222
B	134 (16.5%)	131 (16.3%)	0.927	0.988	0.759–1.285
AB	74 (9.1%)	72 (9.0%)	0.924	0.984	0.700–1.382

*: Chi-square test (n/%)

Table 4. Status of the Life of COVID-19 Patients by Blood Group

Blood Type	Survivor/Non-survivor		P-value*		
	Survivor (n=1211)	Non-survivor (n=407)			
O	338 (27.9%)	121 (29.7%)			
A	562 (46.4%)	186 (45.7%)	0.907		
B	200 (16.5%)	65 (16.0%)			
AB	111 (9.2%)	35 (8.6%)			
Blood Type	**Survivor/Non-survivor**		**P-value***	**OR**	**95% CI**
	Survivor (n=1211)	**Non-survivor (n=407)**			
O	338 (27.9%)	121 (29.7%)	0.481	1.093	0.854–1.399
A	562 (46.4%)	186 (45.7%)	0.804	0.972	0.776–1.218
B	200 (16.5%)	65 (16.0%)	0.797	0.961	0.708–1.304
AB	111 (9.2%)	35 (8.6%)	0.730	0.932	0.626–1.388

*: Chi-square test (n/%)

DISCUSSION

In this study, it was determined that, among the COVID-19 patients, the most common blood type was A, while the least common was type AB. Type A was determined to be statistically significantly more common in the COVID-19 group when compared to the healthy control, whereas type O was determined to be less common. While the types differed between the COVID-19 and healthy control groups, no association with disease severity or mortality was found.

The relationship between ABO blood groups and COVID-19 has been evaluated in previous studies and meta-analyses (14-18). In a meta-analysis published by Pendu et al., a general consensus emerged that O blood type appears to be associated with a lower risk of COVID-19 and non-O blood types appear to be harmful in 34 current studies. They supported this with two opinion. Natural anti-A and anti-B antibodies may be partially protective against SARS-CoV-2, which carries blood group antigens originating from non-O patients. In addition, O patients are less prone to thrombosis and vascular dysfunction than non-O patients and may be less at risk in the case of severe lung dysfunction (15). Parallel to this, in our study, it was also thought that type A blood may be associated with an increased risk for COVID-19, and the same pathophysiological hypothesis may play a role in this effect.

A meta-analysis of 21 studies published by Franchini et al was found low/very low evidence that patients with O blood were less susceptible to SARS-CoV-2 infection compared to the non-O blood type. No evidence was found to indicate the effect of type O blood on disease severity in SARS-CoV-2 infection (14). In a study from Turkey conducted by Goker et al. (9), in which the effects of blood types on COVID-19 were examined, it was reported that the risk of disease may be increased in individuals with type A. In the current study, it was determined that the risk of disease was significantly increased in individuals with type A, but it was not significant with regards to mortality or the need for intensive care. In the current study, type O, however, was determined to be protective against contracting the disease. Nevertheless, the number of patients with type O was higher in the non-severe and survivor groups, although this was not statistically significant. The results of these studies support our study. In another study conducted in Turkey, Aktimur et al. found that A blood type was associated with a higher risk for COVID-19 than other blood types. Again, in the same study, it was stated that patients with A blood type had a longer intensive care unit stay, and they might have a higher risk in terms of disease severity (10). Unlike our study, a relationship was found between disease severity, intensive care hospitalization and blood group type. This difference may be due to the fact that comorbid conditions were not evaluated together with blood group. In parallel with this study, in a study conducted by Ray et al. in which 225 COVID-19 patients were included, type O was reported to be associated with less severe disease and lower mortality risk (19). COVID-19 infection is known to be associated with hipercoagulability subsequently the microtrombi that spread through pulmonary vascular structure leads to acute respiratory distress syndrome (ARDS), which is one of the most severe complications of the disease (20-22). The lower risk of severe disease in individuals who have type O blood may be explained by the lower risk of thrombosis in patients with type O blood. Blood type antigens may act as a receptor or trap for communicable organisms and may influence susceptibility to the disease in various ways, including regulating the immune response as ABO antibodies (23). In in vitro trials, it was shown that the interaction between the SARS-CoV-1 spike protein and the ACE-2 receptor may be alleviated via anti-A antibodies (24). In a population-based prospective cohort study reported from Spain, a higher incidence of complications was found in other blood groups and especially in type B blood compared to type O blood when patients were followed up for complications of COVID-19 (18). In a study conducted by Guillon et al., in which 265 COVID-19 patients were included, it was determined that the incidence of type O blood was lower among the patients who required longer hospitalization and the incidence of type A blood was higher in patients with severe COVID-19 infection when compared to the normal population (24). In our study and current literature data, it is seen that type O blood may be protective for COVID-19, but no clear data on disease severity and mortality can be obtained.

In a study conducted during the SARS epidemic in Hong Kong, the incidence of SARS-CoV-1 was found to be lower in patients with type O when compared to those with the other blood types (25). In addition, individuals with type O blood have been known to have a a lower risk of thrombosis and cardiovascular diseases due to varying glycosyltransferase activity, and increased clearance of von Willebrand Factor (vWF) and reduced circulating FVIII levels due to vWF. The lower rates of thrombosis and endothelial dysfunction may be based upon this argument (26). Further studies are needed in order to shed light on the importance of vWF-FVIII levels and endothelial cells in coagulopathy and pulmonary microvascular occlusion, which are induced by COVID-19 infection. Coagulopathy and endothelial injury in COVID-19 patients leads to a predisposition to cardiovascular events, especially in the case of underlying diabetes mellitus and hypertension. Previous studies have reported that individuals with type A blood have an increased risk of developing hypertension as a result of impaired blood flow in the vascular bed, through increasing adhesion and inflammation in the epithelial cells, which is caused when P-selectin and intracellular cell adhesion molecule 1 (ICAM1) are prevented from enzymatic clearance in the vascular wall by antigen A. Therefore, hypertensive patients with type A blood are at higher risk for severe COVID-19 infection (27,28). Due to hypercoagulability, anticoagulation is of vital importance, particularly in the treatment and follow-up of patients with lung involvement and potential microthrombi, and subsequent manifestations of ARDS may be prevented with appropriate medical treatment. The current study was important with regards to the possibility of an evaluation of the effects of ABO blood types on infectivity, severe infection, and mortality in a Turkish population and the fact that it was conducted with a large sample.

The retrospective design of this study was, however, its major limitation. Moreover, the most important limitations included the failure to determine the comorbid conditions that were effective in the disease severity and mortality, and the inability to examine the severity–mortality association. This limitation may have been related to the failure to determine an association between the blood types and the severity–mortality.

CONCLUSION

It can be hypothesized that the type O blood may be protective against contracting COVID-19 and the development of severe infection, while type A blood, however, may be associated with an increased risk of contracting the disease. However, no statistically significant association of mortality and the development of severe disease with ABO blood types was determined. Further studies are needed in order to shed light on the association between the blood types and COVID-19 infection.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara City Hospital No:1 Clinical Research Ethics Committee (Date: 21.05.2020, Decision No: 626).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. World Health Organization. Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. http: //www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020 (Accessed on February 12, 2020).
2. Lindesmith L, Moe C, Marionneau S, et al. Human susceptibility and resistance to Norwalk virus infection. Nat Med 2003; 9: 548-53.
3. Jing W, Zhao S, Liu J, Liu M. ABO blood groups and hepatitis B virus infection: a systematic review and meta-analysis. BMJ Open 2020; 10: e034114.
4. Franchini M, Favaloro EJ, Targher G, Lippi G. ABO blood group, hypercoagulability, and cardiovascular and cancer risk. Crit Rev Clin Lab Sci 2012; 49: 137-49.
5. Ibrahim-Kosta M, Bailly P, Silvy M, et al. ABO blood group, glycosyltransferase activity and risk of venous thromboembolism. Thromb Res 2020; 193: 31-5.
6. Bowen DJ. An influence of ABO blood group on the rate of proteolysis of von Willebrand factor by ADAMTS13. J Thromb Haemost 2003; 1: 33-40.
7. Dunne E, Qi QM, Shaqfeh ES, et al. Blood group alters platelet binding kinetics to von Willebrand factor and consequently platelet function. Blood 2019; 133: 1371-7.
8. Latz CA, DeCarlo C, Boitano L, et al. Blood type and outcomes in patients with COVID-19. Ann Hematol 2020; 99: 2113-8.
9. Göker H, Aladağ Karakulak E, Demiroğlu H, et al. The effects of blood group types on the risk of COVID-19 infection and its clinical outcome. Turk J Med Sci 2020; 50: 679-83.
10. Aktimur SH, Sen A, Yazicioglu B, Gunes AK, Genc S. The assessment of the relationship between ABO blood groups and Covid-19 infection. UHOD - Int J Hematol Oncol 2020; 30: 121-5.
11. Zietz M, Zucker J, Tatonetti NP. Associations between blood type and COVID-19 infection, intubation, and death. Nat Commun 2020; 11: 5761.
12. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected: interim guidance, https: //apps.who.int/iris/handle/10665/330854 (Accessed on January 25, 2020).
13. Ding X, Yu Y, Lu B, et al. Dynamic profile and clinical implications of hematological parameters in hospitalized patients with coronavirus disease 2019. Clin Chem Lab Med 2020; 58: 1365-71
14. Franchini M, Cruciani M, Mengoli C, et al. ABO blood group and COVID-19: an updated systematic literature review and meta-analysis. Blood Transfus 2021; 19: 317-26.
15. Pendu JL, Breiman A, Rocher J, Dion M, Ruvoën-Clouet N. ABO blood types and COVID-19: spurious, anecdotal, or truly important relationships? a reasoned review of available data. Viruses 2021; 13: 160.
16. Wu BB, Gu DZ, Yu JN, Yang J, Shen WQ. Association between ABO blood groups and COVID-19 infection, severity and demise: A systematic review and meta-analysis. Infect Genet Evol 2020; 84: 104485.
17. Liu N, Zhang T, Ma L, et al. The impact of ABO blood group on COVID-19 infection risk and mortality: A systematic review and meta-analysis. Blood Rev 2021; 48: 100785.
18. Domènech-Montoliu S, Puig-Barberà J, Pac-Sa MR, et al. ABO Blood Groups and the Incidence of Complications in COVID-19 Patients: A Population-Based Prospective Cohort Study. Int J Environ Res Public Health 2021; 18: 10039.
19. Ray JG, Schull MJ, Vermeulen MJ, Park AL. Association between ABO and Rh blood groups and SARS-CoV-2 infection or severe COVID-19 illness: a population-based cohort study. Ann Intern Med 2021; 174: 308-15.
20. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost 2020; 18: 844-7.
21. Fogarty H, Townsend L, Ni Cheallaigh C, et al. More on COVID-19 coagulopathy in Caucasian patients. Br J Haematol 2020; 189: 1060-1.
22. McGonagle D, O'Donnell JS, Sharif K, Emery P, Bridgewood C. Immune mechanisms of pulmonary intravascular coagulopathy in COVID-19 pneumonia. Lancet Rheumatol 2020; 2: e437-e45.
23. Cooling L. Blood groups in infection and host susceptibility. Clin Microbiol Rev 2015; 28: 801-70.
24. Guillon P, Clément M, Sébille V, 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: 1085-93.
25. Cheng Y, Cheng G, Chui CH, et al. ABO blood group and susceptibility to severe acute respiratory syndrome. JAMA 2005; 293: 1450-1.
26. O'Sullivan JM, Ward S, Fogarty H, O'Donnell JS. More on 'Association between ABO blood groups and risk of SARS-CoV-2 pneumonia'. Br J Haematol 2020; 190: 27-8.
27. Dai X. ABO blood group predisposes to COVID-19 severity and cardiovascular disease. Eur J Prev Cardiol 2020; 27: 1436-7.
28. Wu O, Bayoumi N, Vickers MA, Clark P. ABO(H) blood groups and vascular disease: a systematic review and meta-analysis. J Thromb Haemost 2008; 6: 62-9.