Research Article

COVID-19 Infection Risk Based on the Interactions between ABO and Rh Blood Groups in Northern Cyprus

Ozgur Neni[1], Ozgur Tosun[2], Eldem Albayrak[3], Yildiz Neni[3], Cenk Soydan[4], Selma Yılmaz[1], Rasime Kalkan[5,6*]

[1]Department of Medical Biology, Near East University, Near East Boulevard, Nicosia, Cyprus, [2]Department of Biostatistics, Near East University, Near East Boulevard, Nicosia, Cyprus, [3]Department of Biochemistry, DNA Laboratory, Dr. Burhan Nalbantoglu State Hospital, 99138 Nicosia, Cyprus, [4]Department of Medicine, Dr. Burhan Nalbantoglu State Hospital, Bi-Communal Health Committee, 99138 Nicosia, Cyprus, [5]Department of Medical Genetics, Near East University, Nicosia, Cyprus, [6]Department of Health Science, Cyprus Health and Social Sciences University, Guzelyurt, Cyprus

Corresponding author:
Rasime Kalkan, Department of Medical Genetics, Near East University, Nicosia, Cyprus, E-mail: kalkanr@yahoo.com
Received: 25-Nov-2022, Manuscript No. amhsr-22-78709;
Editor assigned: 28-Nov-2022, Pre QC No. amhsr-22-78709(PQ);
Reviewed: 13-Dec-2022, QC No. amhsr-22-78709;
Revised: 22-Dec-2022, Manuscript No: amhsr-22-78709(R);
Published: 30-Dec-2022, DOI: 10.54608.annalsmedical.2022.75

Abstract

Infected individuals suffer from a variety of symptoms due to Coronavirus infection and these can vary greatly from person to person. Understanding its nature and biological function is very important including the influence of variable patient genetic backgrounds and preexisting state of health on the underlying molecular mechanism of the disease. There has been an increase in research efforts aimed at understanding variable clinical manifestations of SARS-CoV-2 among infected populations as a result of the high infection rate. The ABO blood system polymorphism has been suggested to influence infection through any of several possible mechanisms. In this study, we aimed to determine whether there is a relationship between ABO blood type and the severity of COVID-19 disease in Northern Cyprus. People with blood group A, diabetes, COPD, and heart patients were found to be highly susceptible to COVID-19 infection (P<0.05).

Keywords: COVID-19; ABO; Rh; SARS-CoV-2

Keypoints

- The ABO blood system polymorphism has been suggested to influence infection.
- People with blood group A were found to be highly susceptible to COVID-19 infection.
- People suffered with diabetes, COPD, and heart patients were found to be highly susceptible to COVID-19 infection.

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), a positive-strand, enveloped RNA virus, infection causes Coronavirus disease (COVID-19). COVID-19 can cause disease ranging from pneumonia and even death, depending on the severity of the infection. Fever, cough, myalgia or fatigue, were the most common symptoms initially identified in an outbreak; atypical symptoms including sputum, headache, hemoptysis, and diarrhea have been reported [1]. Previous studies have tried to explain COVID-19 susceptibility by using information regarding demographics, culture, diet and genetic variations [2].

It has been reported that polymorphisms of the ABO blood group are associated with susceptibility and complications associated with a variety of diseases and infections. These conditions include tumors and coronary artery disease as well as infection with hepatitis B virus, SARS-CoV, and Helicobacter pylori [3,4]. The effect of the ABO blood group system on COVID-19 susceptibility was first reported by Zhao, et al. They concluded that infections with COVID-19 were more likely to occur in patients with the A blood type than in those with the O blood type [5]. This association between COVID-19 infection and ABO blood types have been explained by various mechanisms, including anti-A antibodies, gene expression, glycan antigen production, coagulation system changes, and genetic variations. Various cell types, including respiratory epithelial cells, are affected by glycosyltransferases of the A and B blood groups. Researchers have shown that, in combination with O and B blood group antibodies, the anti-A antibody inhibits SARS-CoV-2 S protein interaction with its membrane receptor ACE2 [6].

The Rh blood group has at least 45 independent antigens, making it the most polymorphic blood group among humans and the second most relevant blood group for transfusions after ABO [7]. COVID-19 was found to be less likely to occur among people with O and Rh (-) blood types according to a study and thrombotic risk is significantly reduced in O blood group individuals [8,9].

Yaylaci and colleagues found that patients with COVID-19 were most likely to have blood group A (+), and the Rh (+) blood group was found in all patients who died in the intensive care unit as a result of the disease. Although Rh (+) blood group had a significantly high rate among the patients admitted to the intensive care unit, there was no significant correlation between Rh blood group and mortality [10]. A recent study from the same group reported that ABO group and age were found to be significantly associated with COVID-19, and there was an increased COVID-19 incidence in the younger, O blood group individuals. They found no significant relationship between ABO-Rh group and mortality due to COVID-19, and indicated the importance of group heterogenicity [11]. Another study suggested that hospitalization due to COVID-19 may

How to Cite this Article: Neni O, et al. COVID-19 Infection Risk Based on the Interactions between ABO and Rh Blood Groups in Northern Cyprus. Ann Med Health Sci Res. 2022;12:

disproportionately affect different races and ethnic groups, and highlighted that there is no direct ABO group association for the severity of COVID-19, and the results favoring a certain group may be due to whether a proper comparison group was selected with care [12].

In this study, we investigated whether there is a relationship between the ABO blood type and COVID-19 severity in Northern Cyprus.

Methods

Study case

A retrospective case-control study was conducted that included 200 positive cases and 200 negative cases of COVID-19. An overview of demographics, comorbidities, and laboratory markers was provided as well as an analysis of inflammation. We also took history of hypertension, smoking, hyperlipidemia, Chronic Obstructive Pulmonary Disease (COPD), cardiovascular disease (history of coronary artery disease, stroke, diabetes mellitus, cancer, Chronic Kidney Disease (CKD), kidney failure, hemodialysis, cirrhosis, and Deep Vein Thrombosis (DVT). When a patient has taken medication within the past year, relevant information was obtained. Antiplatelet drugs such as aspirin, and p2y12 inhibitors, anticoagulants, antihypertensive drugs, and beta-blockers are among the drugs of interest. The informed consent form was approved among all participants. It was approved by Dr. Burhan Nalbantoglu State Hospital Ethics Committee (Number YTK. 1.01).

Statistical evaluation

Statistics were analyzed using Pearson's chi-square tests and Fisher's exact tests based on participant characteristics. Jamovi V2.0.0 software was applied for the calculations and the statistical significance level was accepted as $P<0.05$.

Results

A total of 400 patients (200 testing positive by PCR for SARS-CoV-2 RNA and 200 PCR negative) were included in this study. ABO and Rh blood groups distribution of control and patient groups; 0 blood group 160 (40%), A 146 (36.5%), B 66 (16.5%), AB 28 (7.0%), Rh (+) 381 (95.3%) and Rh (-) 19 (19%) individuals (Table 1).

Distribution of COVID-19 and ABO blood groups

A total of 160 people with blood type 0, 67 (41.9%) had COVID-19 infection, 86 (58.9%) of 146 people with blood type A had COVID-19 infection, 32 (48.5%) of 66 people with blood type B had COVID-19 infection. It was determined that 15 of 28 people with AB blood group (53.6%) had COVID-19 infection. Statistically significant associations were found between blood group A and COVID-19 and heart disease ($P=0.029$) (Table 2).

Distribution of COVID-19 and Rh groups

It was determined that 8 (42.1%) of 19 Rh-negative people had COVID-19 infection, an D-192 of 381 Rh-positive people had COVID-19 infection. No statistically significant relationship was found between the Rh group and COVID-19 ($P>0.05$) (Table 3).

Comparison of COVID-19 and diabetes status

It was determined that 43 (81.1%) of 53 diabetic people had COVID-19 infection, and 157 (45.2%) of 347 non-diabetic people had COVID-19 infection. There was a statistically significant association between COVID-19 and diabetes ($P<001$) (Table 4).

Comparison of COVID-19 and COPD patients

It was determined that all 12 people (100%) with COPD had COVID-19 infection and 188 (48.5%) of 388 people who did not have COPD had COVID-19 infection. A statistically significant relationship was found between COVID-19 and COPD ($P<001$) (Table 5).

Comparison of COVID-19 and heart disease

It was determined that 62 (77.5%) of 80 people with heart disease had COVID-19 infection, and 138 (43.1%) of 320 people without heart disease had COVID-19 infection. COVID-19 and heart disease have a statistically significant relationship ($P<001$) (Table 6).

Comparison of COVID-19 and COVID vaccine

It was observed that 156 (46.4%) of 336 vaccinated patients were found to be COVID positive, and 44 (68.8%) of 64 unvaccinated patients were found to have COVID infection. A statistically significant relationship was found between COVID-19 and vaccine status ($P<001$) (Table 7).

Table 1: ABO and Rh blood groups distribution.

Levels	Counts	% of Total	Cumulative%
O	160	40.00%	40.00%
A	146	36.50%	76.50%
B	66	16.50%	93.00%
AB	28	7.00%	100.00%
Frequencies of Rh			
Levels	**Counts**	**% of Total**	**Cumulative%**
Negative	19	4.80%	4.80%
Positive	381	95.30%	100.00%

Table 2: COVID 19 and ABO blood groups distribution.

Blood Group	%	COVİD Positive	COVİD Negative	Total
O	Observed	67	93	160
	% within row	41.90%	58.10%	100.00%
A	Observed	86	60	146
	% within row	58.90%	41.10%	100.00%
B	Observed	32	34	66
	% within row	48.50%	51.50%	100.00%
AB	Observed	15	13	28
	% within row	53.60%	46.40%	100.00%
Total	Observed	200	200	400
	% within row	50.00%	50.00%	100.00%
		X^2 Tests		
	Value	**df**	**P**	
X^2	9.06	3	0.029	
N	400	-	-	

Table 3: COVID 19 and Rh blood groups distribution.

Rh	%	COVİD Positive	COVİD Negative	Total
Negative	Observed	8	11	19
	% within row	42.10%	57.90%	100.00%
Positive	Observed	192	189	381
	% within row	50.40%	49.60%	100.00%
Total	Observed	200	200	400
	% within row	50.00%	50.00%	100.00%
		X^2 Tests		
	Value	**df**	**P**	
X^2	0.497	1	0.481	
N	400	-	-	

Table 4: Differentiation of COVID 19 and diabetes patients.

Diabetes	%	COVİD Positive	COVİD Negative	Total
There are	Observed	43	10	53
	% within row	81.10%	18.90%	100.00%
None	Observed	157	190	347
	% within row	45.20%	54.80%	100.00%
Total	Observed	200	200	400
	% within row	50.00%	50.00%	100.00%
		X^2 Tests		
	Value	**df**	**P**	
X^2	23.7	1	<.001	
N	400	--	-	

Table 5: Differentiation of COVID 19 and COPD patients.

COPD	%	COVİD Positive	COVİD Negative	Total
There are	Observed	12	0	12
	% within row	100.00%	0.00%	100.00%
None	Observed	188	200	388
	% within row	48.50%	51.50%	100.00%
Total	Observed	200	200	400
	% within row	50.00%	50.00%	100.00%
		X^2 Tests		
	Value	**df**	**P**	
X^2	12.4	1	<.001	
N	400	-	-	

Table 6: Differentiation of COVID 19 and Heart disease.

Heart Disease	%	COVİD Positive	COVİD Negative	Total
There are	Observed	62	18	80
	% within row	77.50%	22.50%	100.00%
None	Observed	138	182	320
	% within row	43.10%	56.90%	100.00%
Total	Observed	200	200	400
	% within row	50.00%	50.00%	100.00%
		X^2 Tests		
	Value	**df**	**P**	
X^2	30.3	1	< .001	
N	400	-	-	

Table 7: Differentiation of COVID19 and COVID vaccine.

COVID Vaccine	%	COVİD Positive	COVİD Negative	Total
There is a vaccine	Observed	156	180	336
	% within row	46.40%	53.60%	100.00%
No Vaccine	Observed	44	20	64
	% within row	68.80%	31.30%	100.00%
Total	Observed	200	200	400
	% within row	50.00%	50.00%	100.00%
		X^2 Tests		
	Value	**df**	**P**	
X^2	10.7	1	0.001	
N	400	-	-	

Discussion

COVID-19 is being investigated as a risk factor for blood type in recent studies [13,14]. ABO polymorphisms were associated with susceptibility to SARS-CoV-1 infection in one study1. Research has demonstrated that anti-A antibodies are protective against SARS-CoV-1 uptake in cells [15,16]. It has been reported that human anti-A antibodies inhibit angiotensin-converting enzyme-2-dependent cellular adhesion and angiotensin-converting enzyme-2-dependent cellular adhesion in cells [15,16]. Goker, et al. demonstrated that; blood type A is associated with higher infection rates but not with disease severity in Turkey [17]. Kibler, et al. showed that the patients with aortic stenosis and blood group A were more likely to contract COVID-19 [18]. Similarly, in our study, we found a high susceptibility to COVID-19 infection in patients with blood group A and heart disease in the literature. Ray, et al.,showed that individuals with O and Rh-negative blood are protected from a viral infection, severe illness, and mortality[8]. According to Zietz, et al. infection, mechanical ventilation, and death are also associated with ABO and Rh types[19]. The study by Holland and colleagues in 2020 focused primarily on critically ill patients and found that blood groups A and AB were associated with an increased risk of intubation, chronic renal replacement therapy, and long-term ICU stays [20]. In our study, 67 (41.9%) of 160 people with blood type O had COVID-19 infection, 86 (58.9%) of 146 people with blood type A had COVID-19 infection and 32 (48.5%) of 66 people with blood type B. We found that 15 (53.6%) of 28 AB blood group patients had COVID-19 infection and had COVID-19 infection. Li, et al. also found an association between type A and viral infection, although not mortality [21]. In our study, we found that blood group A has a high susceptibility to COVID-19 infection, in accordance with the literature. In the largest study to date, Barnkob, et al. found that blood group O has a protective effect on viral susceptibility [22,23]. In a similar study, Leaf, et al. found that patients with blood type O and Rh-negative blood did not have an increased risk of infection but had no association with mortality [14].

Several studies have found that Rh-negative patients are less likely to contract viral infections, suffer severe illness, and die from post-infection complications [8,19]. An additional study by Leaf, et al. found that Rh-negative subjects had a lower infection rate, but that there was no effect on deaths observed due to COVID-19 [14]. In our study, we determined that 8 (42.1%) of 19 Rh-negative people had COVID-19 infection, anD-192 of 381 Rh-positive people had COVID-19 infection. However, no statistically significant relationship was found between the Rh group and COVID-19 ($p>0.05$).

In SARS-CoV-2 infection, the outcome of the disease seems to be strongly related to pre-existing health conditions, host thromboinflammatory response, and acquired factors such as age, history of smoking, diabetes and hyperlipidemia. Genetic factors may also influence the underlying molecular mechanisms of the disease and contribute to the clinical outcome. One possible mechanism relates ABO(H) expression on the platelets and as a part of glycoproteins such as Von Willebrand Factor's (VWF) and Factor VIII (FVIII) which are found in reduced

amount in O group individuals to a lower risk of thrombotic effects compared to non-O group individuals [23].

Even though, ABO groups may have an important influence on COVID-19 related hospitalization, more research is needed on the potential mechanisms involved. At present, there is no basis for suggesting differential precautions based on blood type.

Furthermore, there is evidence suggests that severity of SARS-CoV-2 infection may disproportionately affect racial and ethnic minorities. Since the proportion of blood types can vary between ethnic groups, proper controls will be necessary to avoid confounding effects of other factors [12].

The information provided from previous studies contributes to a better understanding of the causes of disease. To develop countermeasures against viral infection and disease, further studies with properly selected comparison groups and analysis of additional data sets from all around the world including both acquired and genetic factors will be required to understand the molecular mechanisms of SARS-CoV-2 infection.

Conclusion

The results of this study show that Mg concentration in the sampled athletes' blood was within the normal range. However, exercise intensity and competition time during the season may affect Mg concentration in the long term. Frequent measurements could detect differences and deficiencies of electrolytes in athletes. In addition, dietary and fluid intake and loss assessments should be carefully considered before planning nutritional strategies for athletes. Mg supplements can help athletes to enhance performance, especially if not enough Mg is being consumed in meals.

Conflict of Interest

The authors have no conflicts of interest to declare that relevant to the content of this article.

Contributions

RK conceived and designed research. EA, YN, CS and ON conducted experiments. OT analyzed data. RK and SY wrote the manuscript. All authors read and approved the manuscript.

Acknowledgments

We would like to thank all of the participants involved in this study and the Dr. Burhan Nalbantoglu State Hospital DNA laboratory.

Consent of Participate

The study protocol was approved by the Dr. Burhan Nalbantoglu State Hospital Ethics Committee (Number YTK. 1.01). Written informed consent form was obtained from all the subjects.

Data Availability Statement

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

References

1. Huang C, Wang Y, Li X, Ren L, Zhao J, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497-506.
2. Fricke-Galindo I, Falfán-Valencia R. Genetics insight for COVID-19 susceptibility and severity: A Review. Front Immunol. 202;12:622176.
3. Liu N, Zhang T, Ma L, Zhang H, Wang H, 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.
4. 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.
5. Zhao J, Yang Y, Huang H, Li D, Gu D, et al. Relationship between the abo blood group and the coronavirus disease 2019 (COVID-19) susceptibility. Clin Infect Dis. 2021;73:328-331.
6. Miotto M, Di Rienzo L, Gosti G, Milanetti E, Ruocco G. Does blood type affect the COVID-19 infection pattern? PLoS One. 2021;16:e0251535.
7. Simsek S, Faas BH, Bleeker PM, Overbeeke MA, Cuijpers HT, van der Schoot CE. Rapid Rh D genotyping by polymerase chain reaction-based amplification of DNA. Blood. 1995;85:2975-80.
8. 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;174:308-315.
9. 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;190:27-28.
10. Yaylacı S, Dheir H, İşsever K, Genc AB, Şenocak D, et al. The effect of abo and rh blood group antigens on admission to intensive care unit and mortality in patients with COVID-19 infection. Rev Assoc Med Bras (1992). 2020;66:86-90.
11. Nalbant A, Aydın A, Yaylacı S, Kaya T, Wermeulen CL, et al. Association of ABO blood group and age with COVID-19 positive test. Rev Assoc Med Bras. 1992:202;67:46-50.
12. Dzik S, Eliason K, Morris EB, Kaufman RM, North CM. COVID-19 and ABO blood groups. Transfusion. 2020;60:1883-1884.
13. Latz CA, Carlo DC, Boitano L, Png CYM, Patell R, et al. Blood type and outcomes in patients with COVID-19. Ann Hematol. 2020;99:2113-2118.
14. Leaf RK, Al-Samkari H, Brenner SK, Gupta S, Leaf DE. ABO phenotype and death in critically ill patients with COVID-19. Br J Haematol. 2020;190:e204-e208.
15. Guillon P, Clément M, Sébille V, Rivain JG, Chou CF, 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.
16. Ritchie G, Harvey DJ, Feldmann F, Stroeher U, Feldmann H, et al. Identification of N-linked carbohydrates from Severe Acute Respiratory Syndrome (SARS) spike glycoprotein. Virology. 2010;399:257-69.

17. Göker H, Aladağ Karakulak E, Demiroğlu H, Ayaz Ceylan ÇM, Büyükaşik Y, Inkaya AÇ, et al. The effects of blood group types on the risk of COVID-19 infection and its clinical outcome. Turk J Med Sci. 2020;50:679-683.

18. Kibler M, Dietrich L, Kanso M, Carmona A, Marchandot B, et al. Risk and severity of COVID-19 and ABO blood group in transcatheter aortic valve patients. J Clin Med. 2020;9:3769.

19. Zietz M, Zucker J, Tatonetti N. Testing the association between blood type and COVID-19 infection, intubation and death. medRxiv Preprint.2020.

20. Hoiland RL, Fergusson NA, Mitra AR, Griesdale DEG, Devine DV, et al. The association of ABO blood group with indices of disease severity and multiorgan dysfunction in COVID-19. Blood Adv. 2020;4:4981-4989.

21. Li J, Wang X, Chen J, Cai Y, Deng A, et al. Association between ABO blood groups and risk of SARS-CoV-2 pneumonia. Br J Haematol. 2020;190:24-27. ,

22. Barnkob MB, Pottegård A, Støvring H, Haunstrup TM, Homburg K, et al. Reduced prevalence of SARS-CoV-2 infection in ABO blood group O. Blood Adv. 2020;4:4990-4993.

23. Jenkins PV, O'Donnell JS. ABO blood group determines plasma von Willebrand factor levels: A biologic function after all? Transfusion. 2006;46:1836-44.