RESEARCH ARTICLE

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Relationship of ABO Blood Groups to SARS-COV-2 Infection Causing COVID-19 Disease

ABSTRACT

Objective: We aimed to investigate whether there is a predisposition to COVID-19 with ABO and Rh blood group systems.

Methods: The clinical data of 455 patients with COVID-19 seen between April 17, 2020 and June 30, 2020 at the Necip Fazıl City Hospital were retrospectively analyzed studied. The differences in the ABO blood group distribution between COVID-19 patients and the control group (7844 cases) were analyzed.

Results: The percentage of patients with type O blood in the COVID-19 group was significantly lower than that in the control group (29.7% vs. 35.6%, p = 0.009). The percentage of patients with type A and B blood in the COVID-19 set was higher than in the control group however, there were no significant difference, respectively (44.4% vs. 40.8%, 19.3% vs.16.6%, p = 0.134, p=0.123). Patients with blood group O had a lower risk of COVID-19 than A, B blood group patients (respectively; OR = 0.732, OR=0.594, p = 0.023, p=0.001). The risk of COVID-19 was higher for patients with blood groups A and B than with a blood group O (OR = 1.365, OR= 1.684, p = 0.023, p=0.001). The Rh blood group phenotype was not statistically significant in determining a patient's vulnerability.

Conclusions: The results of the present study suggest that while the blood group O had a low risk an decreased risk for infection with SARS-CoV-2, whereas blood group A and B was associated related with a increased risk, indicating that certain specific ABO blood groups were connected correlated with SARS-CoV-2 susceptibility.

Keywords: COVID-19, SARS-COV-2, Susceptibility, ABO Blood-Group System

ABO Kan Gruplarıyla SARS-COV-2 Enfeksiyonunun Neden Olduğu COVID-19 Hastalığı Arasındaki İlişki

ÖZET

Amaç: Çalışmamızda ABO ve Rh kan grubu sistemleri ile COVİD-19'a yatkınlık olup olmadığı araştırılması hedeflenmiştir.

Gereç ve Yöntem: 17 Nisan – 30 Haziran 2020 arasında Necip Fazıl Şehir Hastanesine başvuran 455 COVID-19 hastası retrospektif olarak çalışılmıştır. COVID-19 hastaları ile 7844 kontrol grubu arasındaki kan grubunun dağılım farklıkları araştırılmıştır.

Bulgular: O kan grubu taşyan COVİD 19 hastalarının oranı kontol grubu hastalarına göre anlamlı derecede düşük bulunmuştur (%29, %35, p = 0.009). A ve B kan grubu taşıyan Covid-19 hastalarının oranı kontrol grubuna göre daha yüksek bulunsa da istatistiksel olarak anlamlı bulunmadı (%44, %19.3, %16.6, p=0.123). COVİD 19 hastalarında O kan grubu taşıyan hastaların A kan grubu taşıyanlara göre daha düşük riskte bulundu (OR=0.732, OR=0.023, p=0.001). Covid -19 riski A ve B grubu taşıyan hastalarda O grubuna kıyasla daha fazla bulundu. (OR = 1.365, OR= 1.684, p = 0.023, p=0.001). Rh kan grup antigenleri hastalıkla istatistiksel olarak anlamlı bulunmadı.

Sonuç: Bu çalışmanın sonuçları; SARS-CoV 2 enfeksiyon riski O kan grubu taşıyan hastalarda daha düşük, A ve B kan grubu taşiyan hastalarda ise daha yüksek olup, ABO kan grubunun SARS-Cov-2 enfeksiyonu ile bağlantili olduğunu işaret etmektedir.

Anahtar Kelimeler: COVID-19, SARS-COV-2, Duyarlılık, ABO Kan Grubu Sistemi

INTRODUCTION

Corona viruses are enveloped viruses containing single stranded, positive–sens (+), non-segmented, ribonucleic acid (RNA) genome, the largest genome among RNA viruses. (1,2) Currently there are seven types of Corona viruse which known to be infected humans.(3) Among them; 229E, HKU1, OC43 and NL63 were not considered as profoundly pathogenic for humans and typically causes mild respiratory diseases. (3,4) Coronaviruses are known to cause outbreaks which occurred as the severe acute respiratory syndrome (SARS-CoV) in China and the Middle East (Middle East respiratory syndrome [MERS-CoV]). (5)

In December 2019, atypical pneumonia of unknown cause emerged from the Huanan Seafood Market that is located in Wuhan, the capital city of Hubei Province in China. Unfortunately, livestock animals were also traded in the market. The virus, causing the pneumonia, was named COVID-19 (Coronavirus Disease-2019) by International Committee on Taxonomy of Viruses (ICTV). [(6)] COVID-19 disease was announced as a pandemic infection by World Health Organization in March 12, 2020. (7)

ABO blood group antigens are a complex of carbohydrate molecules which are existent on the membrane of erythrocytes. It was discovered in the early 19th- century. (8) The genome that regulates ABO blood group antigens, resides on chromosome 9 (9q34). The four major blood groups regulated by the existence or inexistence of the two antigens – A and B – on erythrocyte surface. (9) Previous studies showed the association between the major blood groups and virus infections caused by certain strains. (10)

In endemic areas, Type-O blood group was shown to be asossiated to a high risk of Hepatitis B virus (HBV) infection, while Type-B blood group was related to the lower risk for HBV infection. (11,12) In another study, Type-O blood group was linked to infection caused by Norwalk virus, while Type-B blood group demonstrated resistance to the infection. (13) The P/Gb3 blood group antigen was shown to be correlated to susceptibility to Human Immunodeficiency Virus (HIV) infection. (14) High frequency of Type-A and Type-B blood types among patients diagnosed with influenza (H1A1) in comparison to the individuals with Type-O and Type-AB blood types groups, (15) and the increased susceptibility to influenza A and B in Type-AB blood group were reported previously as well. (16,17) Type-O blood group, on the other hand, was suggested to inhibit the interaction between the spinous protein of SARS-COV and the angiotensin-converting enzyme 2 (ACE2) receptor of host cell, while the inhibitory effect was demonstrated to be dose-dependent. (18) These findings suggest the ABO blood group antigens to be significant factors in the cellular invasion of viruses.

The aim of this study is the investigation of relationship between the major blood group systems considering the ABO and Rh antigens and the rate of COVID-19 diagnosis in a single health center.

MATERIAL AND METHODS

Data Sources: All patients, who were diagnosed with COVID-19 in the period from April 17th, 2020 to June 30th 2020, were enrolled in this retrospective study.

Study Design: A total of 455 patients diagnosed with COVID-19 were included in this study. The patients were allocated to four study groups formed considering the major blood groups: Type-A group, Type-B group, Type-O group, and Type-AB group. The distribution of ABO blood groups among SARS-COV-2 nucleic acid positive patients was recorded and compared with the distribution of blood groups in the control group, which included 7844 patients with determined major blood type and admitted to the center before the onset of the COVID-19 outbreak (i.e. in the period from November 2019 to December 2019). The ABO blood types and demographic features were retrieved from the database of the center.

Laboratory Testing and Data Collection: The diagnosis of COVID-19 was reached by the positive result using the real time reverse transcription polymerase chain reaction (RT-PCR) (Bioeksen, Turkey) in COVID-19 nucleic acid test, applied to nasopharyngeal and oropharyngeal samples. The Rh and ABO blood types were determined using colon agglutination method (Ortho Clinical Diagnostic, USA).

E**thics Statement:** The approval for the study was obtained from the Ethical Committee of Clinical Trials in Kahramanmaras Sutcu Imam University Faculty of Medicine (26.08.2020/20).

Statistical Analysis: All statistical analyses were performed using SPSS 25.0 software. Continuous variables are stated as the mean ± standard deviation, median (minimum - maximum values), while the categorical variables are indicated by numbers and percentages. The difference between categorical variables was evaluated using Chi Square analysis. The association between the blood types and COVID-19 positivity was assessed using Logistic Regression models. A p value less than 0.05 was considered to be statistically significant.

RESULTS

Type-A was the most common whereas Type-AB was the least common blood groups both in the study and control groups. The blood group distribution in the control group was as follows: Type-A in 40.8%, Type-O in 35.6%, Type-B in 16.6%, and Type-AB in 7%. Rh positivity rate was 88.7% while Rh negativity rate was 11.3%. In the study group including PCR positive patients, 44.4% had Type-A blood group, 29.7% had Type-O blood group, 19.3% had Type-B blood group, and 6.6%

had Type-AB blood group in descending order of frequency (Table1).

The mean age was 44.21±19.72 years (Med:41) and 33.88±21.92 (Med:29) in the study group and control group, respectively. The patients in the former group was significantly older than the latter group. The mean age of patients was about ten years higher than uninfected individuals. The age was found as a risk factor in cases of SARS-CoV-2 infection (p=0.0001, OR=1.021) (Table 2). The rate of male patients (8.5%) were significtly high compared to the rate of female patients (3,6%) in the study group. Men were infected more than women by coronavirus among patients. The male gender was found as a risk factor in cases of SARS-CoV-2 infection, which demonstrated a statistically significant difference. (OR= 2.091) (p=0.0001) (Table 2). When the blood groups of the patients with PCR positive of COVID-19 and the normal individuals taken as a control group were compared, the major blood groups were compared between the study and control groups. The rate of Type-O blood group was low in the COVID-19 patients compared to the control group (29.7% vs. 35.6%, p = 0.009). Type-A and Type-B blood groups were more frequent in the COVID-19 patients than the control group. However, the differences were insignificant (p = 0.134 for Type-A blood group, p=0.123 for Type-B blood group). The difference between the study group and control group was minor considering the Rh antigen as well (p= 0.532) (Table 1).

Table 1. Covid-19 with diagnosis PCR (+) blood group distribution and analysis of patients and healthy individuals

		Patients (+) n=455 (%)	**Controls n=7844 (%)**	**X^2**	**P**
Age mean, med, range		44.21±19.72 (Med:41) (0-95)	33.88±21.92 (Med:29) (0-95)	Z= -9.57	0.0001*
Sex	**Male**	271 8.5%	2905 91,5%	92.37	0.0001*
	Female	184 3,6%	4939 96,4%		
A blood Type		202 44.4%	3204 40.8%	2.239	0.134
O blood type		135 29.7%	2793 35.6%	2.369	0.009*
B blood Type		88 19.3%	1300 16.6%	6.644	0.123
AB blood type		30 6.6%	547 7%	0.096	0.756
Rh positive		408 89.7%	6959 88.7%	0.389	0.532
Rh negative		47 10.3%	885 11.3%	0.389	0.532

Based on multiple logistic regression model, the patients with Type-O blood group demonstrated to have a lower risk of acquiring COVID-19 than the patients with Type-A group (OR=0.732, p=0.023) and Type-B blood group (OR=0.594, p=0.001).

The likelihood of COVID-19 positivity was high in patients with Type-A group (OR=1.365, p=0.023) and Type-B blood group (OR=1.684, p=0.001) compared to those patients with Type-0 blood group (Table 2).

DISCUSSION

COVID-19 disease, the latest worldwide viral infection, caused social and economic impacts which appear to continue for several years from the onset of the disease. Male gender, elderliness, and the presence of comorbidities such as hypertension and diabetes mellitus have been reported as the risk factors of the disease so far [19]. The results of the present study were consistent with the established knowledge since the study group was old with significant difference as compared to the uninfected control group and the male patients considerably prevailed in the study group that involved the COVID-19 cases.

Numerous researches have reported the association between the blood groups and various diseases. (10-18,20-27) In other words, each of those researches suggested relative resistance or vulnerability of certain blood groups to several viral infections. Researchers have recently reported a significant relation between the ABO blood types and the rate of SARS-CoV-2 infection as well as the duration of the disease. (26) Regular antibodies of the ABO framework were suggested to hinder the interaction between SARS CoV spike protein and angiotensin converting enzyme 2. (18)

Table 2. Multiple logistic regression models of Covid-19 patients

Reference Category		**Multiple**			
		p	O.R.	95% C.I.for O.R.	
				Lower	Upper
-	age	0.0001*	1.021	1.016	1.025
Female	sex(male)	0.0001*	2.091	1.671	2.617
0	A	0.023*	1.365	1.044	1.786
	B	0.001*	1.684	1.227	2.311
	AB	0.082	1.489	0.951	2.331
Reference Category		Multiple			
		p	O.R.	95% C.I.for O.R.	
				Lower	Upper
-	age	0.0001*	1.021	1.016	1.025
Female	Sex(male)	0.0001*	2.091	1.671	2.617
A	0	0.023*	0.732	0.560	0.958
	B	0.161	1.233	0.920	1.653
	AB	0.695	1.090	0.708	1.679
Reference Category		Multiple			
		p	O.R.	95% C.I.for O.R.	
				Lower	Upper
-	age	0.0001*	1.021	1.016	1.025
Female	Sex(male)	0.0001*	2.091	1.671	2.617
B	0	0.001*	0.594	0.433	0.815
	A	0.161	0.811	0.605	1.087
	AB	0.602	0.884	0.556	1.405
Reference Category		Multiple			
		p	O.R.	95% C.I.for O.R.	
				Lower	Upper
-	age	0.0001*	1.021	1.016	1.025
Female	Sex(male)	0.0001*	2.091	1.671	2.617
AB	0	0.082	0.672	0.429	1.052
	A	0.695	0.917	0.596	1.413
	B	0.602	1.131	0.712	1.798

Although the association between the ABO/RH blood types and vulnerability to various viral infections has previously been studied, the relation between the blood types and SARS-CoV-2 infection has not been established yet.

Guillon et al. reported that the individuals with Type-O group were relatively resistant to infection. The study included a cell model of adhesion to investigate the effect of common antibodies of the ABO framework on the interaction between the S protein and angiotensin converting enzyme 2. The authors mentioned that anti-A antibodies might inhibit the engagement of SARS-CoV antigen and its receptor, which was based on the relative vulnerability of individuals with Type-A blood group to SARS-CoV infection and the relative resistance of individuals with Type-O blood group in the study. (18)

Arac et al. reported the preponderance of Type-A blood group among the COVID-19 patients as compared to the other blood groups, particularly the Type-O group. However, the statistical analysis was mentined to demonstrate no significant difference between the infected patients and healthy individuals in terms of ABO blood groups. Furthermore, the authors suggested a relationship between Rh (D) positivity and the susceptibility to SARS-CoV infection. (25)

Zhao et al. analyzed the rates of ABO blood groups among COVID-19 patients diagnosed by using SARS-CoV-2 test in a multicenter study. The authors mentioned the patients with O histo-blood group are less likely to suffer from a COVID-19 infection. On the other hand, according to the study, individuals with A histo-blood group were identified as high-risk. (27)

The investigation on the prevalance of SARS among healthcare workers, who were exposed to infected patients without protection, reported diminished susceptibility to SARS disease in individuals with Type-O group. It has been reported that severe acute respiratory syndrome coronavirus (SARS-CoV) is less likely to infect people with blood group O compared with other blood groups. (21)

Another research, including the rates of blood groups among SARS-CoV-2 infected patients from 105 countries, suggested increased vulnerability to the infection and severity of COVID-19 disease among individuals with Type-A blood group. Type-B and Type-O blood groups, on the other hand, were found to be more resistant to the SARS-CoV-2 infection and developing less severe COVID-19 diease. (24)

Abdollahi et al. suggested a relationship between the ABO histo-blood phenotypes and vulnerability to the COVID-19 disease as well. A higher rate of infection was mentioned for the patients with the Type-AB blood group, in contrast to the lower rate of infection for the patients with the Type-O blood group. However, the Rh blood phenotypes were reported to display no significant effect on the susceptibility to the disease. (23)

It can be speculated that the decreased susceptibility of individuals with Type-O blood group and the increased susceptibility of individuals with Type-A and Type-B blood groups to COVID-19 could be linked to the presence of natural anti-blood group antibodies, particularly anti-A antibody, in the serum. However, other possible mechanisms, which obviously necessitate further researches to unveil the mystery, may cause those correlations between the blood types and rate of COVID-19 infection.

In the present study, it was determined that the proportion of patients that had COVID-19 with Type-O blood group was significantly less than the proportion of other blood groups among the infected individuals. An insignificant difference was found between the Type-A and Type-B blood groups when compared among the individuals infected with SARS-CoV-2. In all COVID-19 patients diagnosed by PCR positivity, no significant difference could be demonstrated between the Rh groups in terms of frequencies observed in this study. Also, it was found that the COVID-19 affects older individuals to a greater extent so that the mean age of patients was about ten years higher than uninfected individuals. Furthermore, according to our survey, the male gender demonstrated as a risk factor in cases of SARS-CoV-2 infection, too, which demonstrated a statistically significant difference. Our study demonstrated that men were infected more than women by coronavirus so that among patients, (OR= 2.091) (p=0.0001).

This study had some limitations. First, we couldn't reach how many patients followed-up in the intensive care unit and how many patients die due to COVID-19 in our study population. Second, we couldn't add the relationship between the severity of the disease and ABO groups in our study.

CONCLUSION

This study supports the previous observations indicating that individuals with O histo-blood group are less susceptible to SARS-CoV-2 virus infection, unlike the Type-A and Type-B blood groups contribute to the risk of COVID-19 disease. Additionally, our study suggested that age and male sex are a risk factor for the development of COVID-19. The inuence of blood group antigens on the body's immunity still needs further research to better understand the pathophysiology of SARS-COV-2 infection, which could be helpful in patient management and disease control.

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