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Original Article / Özgün Araştırma

Relationship between AB0 and Rh Blood Groups in COVID-19 Patients and In-Hospital Mortality

Hamza Gültekin[1]

1 Dicle University School of Medicine, Department of Neurology, Division of Intensive Care, Diyarbakır, Turkey

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Abstract

Aim: It is known that blood groups and susceptibility to thrombosis are related to each other. COVID-19 is a disease with a high mortality rate with thrombotic events. In this study, we aimed to investigate the relationship between blood types and the severity of COVID-19 disease and in-hospital mortality.

Methods: This study was carried out retrospectively using the data of PCR positive patients hospitalized for COVID-19 whose blood group was studied between 01.03.2020 and 01.06.2021. The patients were divided into four groups. Group 1 (control group) consisted of 37996 people whose blood group was studied within one year and 1437 outpatient PCR positive cases in Group 2, 1024 PCR positive hospitalized patients in Group 3, and 413 PCR positive patients hospitalized in the intensive care unit in Group 4 were presented. The groups were compared in terms of age, gender, AB0, and Rh blood groups. In addition, the data of the living and deceased patients in Group 4 were compared.

Results: The rate of PCR positive test was higher in the A and AB blood groups (p:0.037, p<0.001, respectively), and lower in the O blood group (p<0.001). There was no significant difference between AB0 and Rh blood groups in the hospitalization and mortality in the intensive care unit.

Conclusion: The present study found that blood group 0 may be protective against COVID-19, blood groups A and AB had a greater susceptibility to the disease, but blood group AB0 did not affect the course of the disease and was not associated with mortality.

Keywords: COVID-19, blood groups, in-hospital mortality

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Correspondence / Yazışma Adresi: *Hamza Gültekin,Dicle University School of Medicine, Department of Neurology, Division of Intensive Care, Diyarbakır, Turkey e_mail: hamzagultekin72@hotmail.com*

COVID-19 hastalarında ABO ve Rh kan gruplarının hastane içi mortalite ile ilişkisi

Öz

Amaç: Kan grupları ile tromboza yatkınlık arasında ilişkili olduğu bilinmektedir. COVID-19 trombotik olaylarla seyreden mortalitesi yüksek bir hastalıktır. Bu çalışmada kan grupları ile COVID-19' un şiddeti ve hastane içi mortalite ile ilişkisini araştırmayı amaçladık.

Yöntemler: Bu çalışma, retrospektif olarak 01.03.2020 ve 01.06.2021 tarihleri arasında COVID-19 nedeniyle yatan, kan grubu çalışılan, PCR+ hastaların verileri kullanılarak yapıldı. Grup-1'de (kontrol grup) bir yıl içerisinde kan grubu çalışılmış 37996 kişinin, grup-2'de PCR+ 1437 vakanın, grup-3'te serviste tedavi gören 1024 PCR+ hastanın ve grup-4'te yoğun bakımda yatan 413 PCR+ hastanın verileri karşılaştırıldı. Ayrıca grup-4'te yaşayan ve ölen hastalarının verileri karşılaştırıldı.

Sonuçlar: PCR+ olma oranı A ve AB kan gruplarında daha yüksek (sırasıyla p:0.037, p<0.001), O kan grubunda daha düşük (p<0.001) saptandı. Kan grupları ve Rh ile yoğun bakıma yatış ve mortalite açısından açısından anlamlı fark saptanmadı.

Tartışma: Sonuç olarak O kan grubunun COVID-19'a karşı koruyucu, A ve AB kan grubunun hastalığa yakalanma riskinin daha yüksek olabileceğini ama ABO kan grubunun hastalığın seyri ve mortalite açısından bir fark oluşturmadığını düşünmekteyiz.

Anahtar kelimeler: COVID-19, kan grupları, hastane içi mortalite.

INTRODUCTION

The coronavirus disease-2019 (COVID-19) epidemic, which emerged in Wuhan, China's Hubei province in December 2019, spread rapidly around the world[1]. COVID-19 was declared a global pandemic by the World Health Organization (WHO) in March 2020[2].

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) primarily targets the respiratory tract[1]. The most common symptoms of COVID-19 are fatigue, fever, and dry cough. These symptoms are usually accompanied by myalgia, anorexia, and dyspnea[3]. Gender, age, clinical condition, and laboratory findings are important factors determining the prognosis of COVID-19[4,5]. Also, comorbidities such as hypertension, diabetes mellitus, and asthma are strong prognostic and predictive factors.

In recent studies, it has been determined that individuals with different blood groups have different susceptibility to diseases. In a study, it was observed that individuals with non-O blood groups were prone to thrombotic events of venous or arterial origin[6]. Another study found an association between AB0 blood groups and viral infections such as rotavirus, norovirus, dengue virus, Norwalk virus, and Hepatitis B virus[7]. Recent studies have shown that AB0 blood groups might be effective in the course and outcomes of COVID-19[4,8,9]. In this study, we aimed to investigate the relationship between AB0-Rh blood groups and the rate of contracting COVID-19, the severity of the disease, and in-hospital mortality.

METHODS

This study was carried out retrospectively using data from patients hospitalized in a State Hospital (determined to be a pandemic hospital) due to COVID-19 between March 2020 and June 2021, whose blood group was studied and nasopharyngeal and oropharyngeal swab results were positive for SARS-CoV-2.

The patients were divided into four groups. Group 1 (control group) consisted of 37996 people whose blood group was studied in 2019 and 1437 outpatient PCR positive cases in

Group 2, 1024 PCR positive hospitalized patients in Group 3, and 413 PCR positive patients hospitalized in the intensive care unit in Group 4 were presented. The groups were compared in terms of age, gender, AB0, and Rh blood groups. In addition, the data of the living and deceased patients in Group 4 were compared.

According to the Berlin classification[10], Group 3 consisted of patients who had PaO2/FiO2 between 200-300 mild ARDS (Acute respiratory distress syndrome) or more than 300 non-ARDS and whose clinical condition is not severe, nasal oxygen support was sufficient.

Group 4 consisted of patients with moderate ARDS PaO2/FiO2 between 100-200 or severe ARDS PaO2/FiO2 <100, who were hospitalized in the intensive care unit, had a severe clinical condition and were under invasive mechanical ventilator or high-flow oxygen therapy. The control group consisted of using the data of patients whose blood group was studied in Şırnak province between January 2019 and December 2019.

Patients older than 18 years of age, whose blood group information was registered in the hospital database system, and who had positive PCR (Polymerase Chain Reaction) test results were included in the study. Patients whose blood group information was not registered in the hospital database system and PCR test results were negative, and who were younger than 18 years of age were excluded from the study.

Statistical Analysis

Statistical evaluation was performed using Statistical Package for the Social Sciences (SPSS) 28.0.1.0, macOS, (IBM, Chicago, Illinois, United States). Categorical variables were represented by nominal numbers (percentages). Non-normal distribution continuous variables were summarized as median with interquartile ranges. The Chi-square test was used for the comparison of categorical variables. The Mann-Whitney U test was used to compare non-normal distribution continuous variable data. P < 0 .05 was considered statistically significant. Ethical approval was obtained from the local Ethics Committee of Dicle University Faculty of Medicine (2022-124).

RESULTS

In the comparison of Group 1 (control group) and Group 2 (PCR positive outpatients), PCR positive test was found higher in A and AB blood groups (p:0.037, p<0.001 , respectively) and lower inblood group O (p<0.001). In addition, a statistically significant difference was found between PCR positive test results and age (p<0.001), gender (p<0.001) (Table 1).

Table I: Comparison of PCR+ COVID-19 patients and reference population

		PCR+	Control group	X	p value
A blood group		605(42.1%)	14956(%39.4%)	4.343	**0.037***
Bblood group		257(17.9%)	6929(%18.2%)	0.116	0.734
ABblood group		109(7.6%)	1282(%3.4%)	72.147	**<0.001**
0 blood group		466(32.4%)	14827(%39%)	25.33	**<0.001**
Rh+		1304(90.7%)	34000(%89.5%)	2.351	0.125
Rh-		133(9.3%)	3996(%10.5%)	2.351	0.125
Age		60(IQR, 40.5-72)	29(IQR,23-37)		**.000****
Gender	Male	800(55.7%)	11185(29.4%)	450.446	**<0.001**
	Female	637(44.3%)	26811(70.6%)		

*PCR (Polymerase Chain Reaction). Categorical data were presented as numbers (percentage). Continuous variables that did not have a normal distribution (interquartile range (IQR)) were shown as the median. P < 0.05: statistically significant; *P < 0.05 (chi-square test; **P < 0.05 (Mann-Whitney test).*

In the comparison of Group 3 (inpatient) and Group 4 (intensive care patients), no significant difference was found in admission to the intensive care unit of AB0 and Rh blood groups.

There was a significant difference between the patients' age and gender (p<0.001, p:0.001, respectively) (Table 2). Intensive care patients were divided into two groups as deceased and surviving patients. There was no significant difference between the groups in AB0, Rh blood groups and gender. A significant difference was found between the ages of the patients in the two groups (p<0.001) (Table 3).

Table II: Comparison of COVID-19 inpatients and intensive care unit

		Inpatient	Intensive care patients	X	p value
A blood group		427(41.7%)	178(43.1%)	0.237	0.627*
B blood group		188(18.4%)	69(16.7%)	0.547	0.459
AB blood group		76(7.4%)	33(8%)	0.136	0.713
0 blood group		333(32.5%)	133(32.2%)	0.013	0.908
Rh+		931(90.9%)	373(90.3%)	0.127	0.721
Rh-		93(9.1%)	40(9.7%)	0.127	0.721
Age		53.5(IQR, 36-67)	71(IQR,61-81)		**<0.001****
Gender	**Male**	543(53%)	257(62.2%)	10.094	**0.001**
	Female	481(47%)	156(37.8%)		

*Categorical data were presented as numbers (percentage). Continuous variables that did not have a normal distribution (interquartile range (IQR)) were shown as the median. P < 0.05: statistically significant; *P <0.05 (chi-square test; **P < 0.05 (Mann-Whitney test).*

Table III: Comparison of COVID-19 patients who died and lived in intensive care

		Deceased	Survivor	X	p value
A blood group		47(44.3%)	131(42.7%)	0.089	0.765*
B blood group		13(12.3%)	56(18.2%)	2.023	0.155
AB blood group		10(9.4%)	23(7.5%)	0.404	0.525
0 blood group		36(34%)	97(31.6%)	0.202	0.653
Rh+		100(94.3%)	273(88.9%)	2.641	0.104
Rh-		6(5.7%)	34(11.1%)	2.641	0.104
Age		76(IQR,68-84)	70(IQR,59-81)		**<0.001****
Gender	**Male**	73(68.9%)	184(59.9%)	2.675	0.102
	Female	33(%31.1)	123(%40.1)		

*Categorical data were presented as numbers (percentage). Continuous variables that did not have a normal distribution (interquartile range (IQR)) were shown as the median. P < 0.05: statistically significant; *P < 0.05 (chi-square test; **P < 0.05 (Mann-Whitney test).*

DISCUSSION

The AB0 gene, which determines the AB0 blood group, is located on the short arm of the 9th chromosome. AB0 blood groups mainly include A and B antigens and anti-A and anti-B antibodies[11,12]. Blood group antigens are specific antigens on the erythrocyte membrane, but are also found on bronchial epithelial cells,

alveolar epithelial cells, and in even body fluids[13]. These antigens act as receptors for some microorganisms. In addition, blood group antigens can modify the innate immune response to infection[14].

In our study, we found that individuals with A and AB blood groups had a higher risk of contracting COVID-19 (p:0.037 and p<0.001, respectively), and individuals with O blood group were less likely to catch COVID-19 (p<0.001). In addition, we did not find a significant difference between AB0 and Rh blood groups and disease severity in patients with mild clinical findings and intensive care patients with moderate-severe clinical findings. There was no statistically significant relationship between in-hospital mortality of intensive care patients and AB0- Rh blood groups.

In accordance with our study, some studies reported that blood group O was protective against COVID-19, while blood group A made the individual more vulnerable to the disease[15,16]. One study reported that individuals with O blood group were less prone to thrombosis and vascular dysfunction than non-O blood groups and might be at less risk for severe lung dysfunction[17].

Gérard et al. stated that people with B and/or O blood types were less likely to catch COVID-19 and anti-A antibodies might be protective against the disease[18]. Studies have found that anti-A antibodies inhibit the adhesion of SARS-CoV S-protein to cells expressing ACE-2 (Angiotensin Converting Enzyme-2)[19]. Considering the genomic similarity between SARS-CoV-2 and SARS-CoV, it was suggested that anti-A antibodies might also be protective against COVID-19[20].

Hoiland et al reported that critically ill COVID-19 patients with blood group A and AB (without anti-A antibodies) were more likely to be mechanically ventilated and long-term intensive care admissions compared to patients with blood group B and 0 (anti-A antibodies)[8].

In a meta-analysis, COVID-19 disease severity was higher in AB blood group individuals, lower in O blood group individuals, and mortality rate was higher in AB blood group individuals[21]. However, Bhattacharjee et al., similar to our study, did not find a relationship between AB0 blood group and disease severity or mortality[20]. The relationship between COVID-19 severity and anti-A antibodies is important. There are many other possible factors, such as the immunoglobulin subtype of antibodies, the presence of ACE1/C3 polymorphisms, and variable levels of factor VIII/VWF (Von Willebrand factor)[22]. In addition, the effect of genetic risk factors on COVID-19 is known[23]. We also thought that the severity of the disease and mortality could not be explained only by AB0 blood group and anti-A, and we should consider other influencing factors, especially genetic factors.

In our study, the rate of catching Covid-19, the severity of the disease and the in-hospital mortality rate were observed to be higher in men and in older ages. Contrary to our findings, Dursun et al, in their retrospective study with 50 PCR-positive patients hospitalized in the intensive care unit found that mortality was higher in women[24]. It is also supported by previous studies that COVID-19 was more common in males[25-27]. This could be explained by multiple factors, including sex chromosomes and hormones that increase women's immunity. Women had higher resistance and stronger immune responses to infectious agents[28].

We did not find a significant difference between Rh- and Rh+ blood groups and the rate of getting the disease, the severity of the disease, and the mortality rate. The results of the retrospective study of Solmaz et al., which included 1667 PCR-positive patients, were similar to our study[15]. In a retrospective study of 7071 PCR-positive

patients in Canada, patients with Rh - blood group had lower disease severity and mortality rates[29]. We believed that AB0 blood groups, environmental and genetic factors were more determinant than Rh blood group on the course of the disease.

CONCLUSION

As a result, we thought that O blood group was protective against COVID-19, individuals with A and AB blood groups might have a higher risk of developing the disease, but AB0 blood group did not show any difference on the course of the disease and mortality. We believed that patients with risky blood group (especially elderly men) should be more careful about avoiding the disease and should be followed closely for prognosis in case of disease. Larger, multicenter and prospective studies should be conducted to determine the relationship between blood groups and COVID-19.

Ethics Committee Approval: Ethical approval was obtained from the local Ethics Committee of Dicle University Faculty of Medicine (2022-124).

Conflict of Interest: The authors declared no conflicts of interest.

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