ORIGINAL ARTICLE

The effect of abo and rh blood group antigens on admission to intensive care unit and mortality in patients with COVID-19 infection

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SUMMARY

AIM: *The aim of this study is to analyze the prognostic significance of ABO and Rh blood group antigens along with various parameters in patients followed-up with the diagnosis of COVID-19.*

METHODS: *We evaluated 397 patients who were follow-up and treated due to COVID-19 infections. The ages, genders, chronic diseases, ABO and Rh blood group antigens, admission rates to Intensive Care Units (ICU), and mortality rates of the patients were analyzed.*

FINDINGS: *The mean age of the 397 patients with COVID-19 was 47±17 years. In the blood group analysis of the patients, A Rh-positive (A +) was the most frequently seen blood type (176 patients, 44.3%) followed by O Rh-positive (0 +) (109 patients, 27,5%); 38 patients were Rh negative (Rh -) (9,6%). 53 of the patients (13,4%) were followed in ICU and 29 patients died (7,3%). Neither mortality nor admission to ICU was seen for Rh – group. The comparison of Rh groups concerning the need for ICU admission revealed a significantly high rate of ICU admission in the Rh + group (p=0,011), while no significant relationship was found between mortality and Rh antigen (p=0,069).*

CONCLUSION: *The most frequently seen blood type among COVID-19 patients was A +. The Rh + blood group was found in all cases who were admitted to ICU and had a death outcome. The Rh + blood group was found in a significantly high number of patients who were admitted to ICU, while no significant relationship was found between mortality and Rh blood group.*

KEYWORDS: *Coronavirus Infections. ABO Blood-Group System. Rh-Hr Blood-Group System. Intensive care units. Mortality.*

INTRODUCTION

Health care systems, diagnosis, and treatment processes have been struggling with difficulties concerning the pandemic caused by the novel coronavirus SARS-CoV-2 all over the world. This new

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coronavirus caused 309.827 deaths and 4.664569 confirmed cases as of 16 May 2020, spreading rapidly worldwide[1]. Thus, there is a need to identify who is at more risk and, according to this, provide protective measures as soon as possible.

Advanced age, chronic diseases, gender, and abnormalities in some laboratory parameters are known risk factors for morbidity and mortality in the course of COVID-19 infections[2-4]. The relationship between SARS-CoV-1 and ABO blood groups was defined firstly in 2005[5]. Although another study revealed a relationship between COVID-19 and ABO blood groups, there is not enough evidence in this respect[6]. Yet, the relationship between ABO and Rh blood types and mortality is not clear.

In our study, we aimed to analyze ABO and Rh blood group antigens and the effect of these blood group parameters on mortality and ICU admission in patients with COVID-19.

METHODS

A descriptive cross-sectional study was conducted among 397 COVID-19 patients between 19 March and 19 April 2020. Data such as age, gender, chronic diseases (diabetes mellitus, hypertension, chronic pulmonary diseases, malignant diseases, cardiovascular diseases, chronic renal failure, etc.), ABO and Rh blood type, ICU admission, and mortality of patients were recorded. The mean age, gender, and number of chronic diseases of the patients were analyzed. The distribution of COVID-19 patients according to blood groups was assessed. ICU admission and mortality rates according to ABO and Rh blood group of the patients were analyzed.

An ethics committee approval from Sakarya University Medical Faculty was provided for this study (approval number: 71522473/050.01.04/).180

Statistical analysis

Quantitative data were expressed as mean values ± SD, medians, and ranges. Qualitative data were expressed as numbers and percentages. After performing the Kolmogorov-Smirnov test to assess the normality of distribution, a nonparametric Mann-Whitney test was used to compare the ages of patients between Rh + and Rh - groups. The Chi-square or Fisher's exact test was used for categorical variables. P values < 0.05 were considered statistically significant. Analyses were performed using Statistical Package for the Social Sciences version 20.0 (IBM SPSS Statistics; Armonk, NY, USA).

RESULTS

The mean age of the 397 patients with COVID-19 was 47±17.5 years (min-max: 17-92). Out of these, 176 of the patients were male (44.3 %) and 221 were female (55.7 %). In the blood group analysis of the patients, A Rh-positive (A +) was the most common blood type (176 patients, 44.3%), followed by O Rh-positive (O +) (109 patients, 27.5%); 53 patients were B + (13.4%), 25 patients were A – (6.3%), 21 patients were AB + (5.3%), 11 patients were 0 – (2.8%), 2 patients were B – (0.5%) and no patients were AB -. A total of 38 patients were Rh - (9.6%), while 359 patients were Rh + (90.4%). Of all patients, 53 (13.4%) were followed in ICU. In the blood group analysis of the 53 ICU patients, we found that 17 were 0 + (15.6%), 8 were B + (15.1%), 26 were A + (14.8%), 2 were AB + (9.5%). The lowest ratio of ICU admission among Rh + blood group patients was found for the AB + group (9.5%). In the analysis of mortality ratios according to blood types (29 dead patients, 7.3%), it was found that 5 of B + patients (9.4%), 15 of A + patients (8.5%), 8 of O + patients (7.3%), 1 of AB + patients (4.8%) died in ICU. Neither mortality nor admission to ICU was seen for the Rh – group (Table 1). The variables of age, gender, and having at least one chronic disease were statistically similar for Rh + and Rh - patients (Table 2). In the comparative analysis of Rh groups regarding ICU admission, a statistically significant relationship was found between having Rh + blood group and the ICU admission rate (p=0.011). Nevertheless, in the comparison analysis of Rh groups regarding mortality rates, no significant relationship was found between Rh factor and mortality rates (p=0.069). The lowest mortality

TABLE 1. DISTRIBUTION OF ABO AND RH BLOOD GROUPS, MORTALITY AND ICU ADMISSION RATES OF COVID-19 PATIENTS

BLOOD GROUP	n	%	ICU (n-%)		Mortality	
O Rh -	11	2,8	0	0	0	0
O Rh +	109	27,5	17	15,6	8	7,3
A Rh -	25	6,3	0	0	0	0
A Rh +	176	44,3	26	14,8	15	8,5
AB Rh +	21	5,3	2	9.5	1	4,8
AB Rh -	0	0	0	0	0	0
B Rh -	2	,5	0	0	0	0
B Rh +	53	13,4	8	15,1	5	5,9
Total	397	100	53	13,4	29	7,3

ratio was found in AB + patients among the Rh + blood group (4.8%, Table 3). None of the comparative analyses of O, A, B, and AB groups with other blood groups revealed a significant relationship with ICU admission and mortality (Table 4).

DISCUSSION

Advanced age, comorbid diseases, male gender, and high levels of lactate dehydrogenase (LDH), neutrophil/lymphocyte ratio, and D-dimer are known as poor prognostic factors for COVID-19 infection[3,4,7]. The pathogenesis and prognostic indicators of COVID-19 disease are still not fully known. İn this study, we investigated whether there is an association between COVID-19 disease progression and blood groups. The surface of red blood cells is covered with antigens (sugars and proteins) which are integrated with membrane proteins and lipids. ABO and Rh blood type systems are crucial for safe blood and organ transplantation processes. Blood group antigens exist on the surface of each erythrocyte. If there is only antigen A on the erythrocyte, it becomes group A, and if there is only antigen B on the erythrocyte, it becomes group B. If antigen A and B exist at the same time on the surface of the erythrocyte, it becomes group AB; while if there is no antigen on the surface of that erythrocyte, it becomes group O. On the other hand, reciprocal antibodies exist in the plasma of human body. Group B antibody is present in the plasma of the A blood group while A antibody is present in the plasma of the B blood group. A and B antibody exist at the same time in the plasma of the O blood group. Rh antigens are also located on the membrane of erythrocytes and consist of three pairs, i.e., Dd, Cc, and Ee. Besides these, there are many other antigens such as Duffy,

TABLE 2. COMPARISON OF AGES, GENDERS, AND HAVING AT LEAST ONE CHRONIC DISEASE, ACCORDING TO THE PATIENT'S RH FACTORS (N=397)

Patient Characteristics	Rh+. n: 359 (90.4 %)	Rh-. n: 38 (9.6 %)	p
Mean age±SD (min.-med.-max)	49.6±17.5 (17.0-47.0-92.0)	44.4±15.9 (19.0-43.0-85.0)	0.099*
Sex (M/F)	176/221 (45.7 %/54.3 %)	12/26 (31.6 %/68.4 %)	0.136**
At least one chronic disease (yes/no)	132/226 (36.9 %/63.1 %)	13/25 (34.2 %/65.8 %)	**0.883

* Mann-Whitney test was used.** Chi Square test was used.

TABLE 3. ANALYSIS OF ICU ADMISSION AND MORTALITY RATES ACCORDING TO PATIENTS' RH FACTORS

Rh	ICU admission		p	Mortality		p
	No n (%)	Yes n (%)		No n (%)	Yes n (%)	
Rh -	38 (100.0 %)	0 (0.0 %)	0.011	38 (100.0 %)	0 (0.0 %)	0.069
Rh +	306 (85.2 %)	53 (14.8 %)		330 (91.9 %)	29 (8.1 %)	
Total	344 (86.6 %)	53 (13.4 %)		368 (92.7 %)	29 (7.3 %)	

* Chi-Square test was used.

TABLE 4. COMPARISON OF EACH BLOOD GROUP WITH OTHER BLOOD GROUPS RELATING TO ICU ADMISSION AND MORTALITY RATES

Blood groups	ICU Admission		p	Mortality		p
	No n (%)	Yes n (%)		No n (%)	Yes n (%)	
Group O	103 (85,8 %)	17 (14.2 %)	0.877*	112 (93.3 %)	8 (6.7 %)	0.911*
Other	241 (87.0 %)	36 (13.0 %)		256 (92.4 %)	21 (7.6 %)	
Group A	175 (87.1 %)	26 (12.9 %)	0.922*	186 (92.5 %)	15 (7.5 %)	0.903*
Other	169 (86.2 %)	27 (13.8 %)		182 (92.9 %)	14 (7.1 %)	
Group B	47 (85,5 %)	8 (14.5 %)	0.946*	50 (90.9 %)	5 (9.1 %)	0.577**
Other	297 (86.8%)	45 (13.2 %)		318 (93.0 %)	24 (7.0 %)	
Group AB	19 (90.5 %)	2 (9.5 %)	1.000**	20 (95.2 %)	1 (4.8 %)	1.000**
Other	325 (86.4 %)	51 (13.6 %)		348 (92.6 %)	28 (7.4 %)	
Total	344 (86.6 %)	53 (13.4 %)		368 (92.7 %)	29 (7.3 %)	

* Chi-Square test was used.** Fisher's Exact Test was used.

Lewis, Kidd, MNS, and Kell[8]. Additionally, some red blood cell surface antigens have clinically important cellular functions, while some others are targets for immune system attacks in the course of infections[8].

For blood donors, the O blood group was evaluated as a higher risk in terms of HIV and Hepatitis B infection[9]. In another study, blood group O and Rh + were associated with a higher risk of Hepatitis B infection[10].

In our study, we tried to analyze the frequencies of ABO and Rh blood types in COVID-19 patients and the relationships of these frequencies with ICU admissions and mortality rates. To our knowledge, no study published in peer-reviewed journals related to this subject could be found in the literature. A few preprint or non-refereed studies have been published so far. Blood group A was reported to be associated with a higher risk of COVID-19, and blood group O was reported to be associated with a lower risk of COVID-19 in these studies[6,11,12]. People with O blood group were reported to be at lower risk for SARS coronavirus infection in a study published in 2005[5]. It is stated that the A-type antibody may provide protection by inhibiting the interaction between the virus and ACE2 receptor[13]. In a series of blood group analyses performed in our country, the frequencies of blood groups A, B, AB, and O were 40-45%, 15-19%, 5-14%, and 28-36%, respectively. The frequency of Rh positivity was reported as 84-92%, while the frequency of Rh negativity was reported as 8-16%[14]. In a study including 13116 cases from our local region, frequencies of blood groups were analyzed and frequencies of blood types A +, O +, and Rh – were found as 38.1%, 30.2%, and 15.2%, respectively[15]. A comparison of the data from these studies with our data reveals a quite similar distribution of blood groups, as well as a higher frequency of blood group A in COVID-19 patients. The detection of a high frequency of COVID-19 patients with blood group A may be caused by the deficiency of the A-type antibody protection, but it is not clear yet. The mechanism behind the susceptibility of blood group A to COVID-19 infection needs advanced analysis to be well understood.

In our study, no relationship was found between blood groups and mortality or ICU admission. The variables of age, gender, and having at least one chronic were similar in Rh + and Rh - patients. Regarding ICU admission, a statistically significant relationship was found between having Rh + factor and the ICU admission rate (p=0,011), and no significant relationship was found between Rh factor and mortality rates (p=0,069). Neither comparison analysis of O, A, B, and AB groups with other blood groups revealed a significant relationship with ICU admission and mortality.

According to these results, we can state that patients with A blood group might be at higher risk for COVID-19 infection and Rh + patients might show poor outcomes as they are at higher risk for ICU admission. More multicenter researches with a higher number of cases are needed to clarify the effects of ABO and Rh blood types on the prognosis.

CONCLUSION

A specific blood group might face more risk of COVID-19 infection. More need for ICU admission is seen in Rh + COVID-19 patients. Although statistically insignificant, all cases in which the outcome was death were found in the Rh + group.

Limitations

Our study has some limitations. It was conducted in a single center and has a relatively small number of patients.

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Conflict of interest

The authors declare that they have no competing interests. Ethical standard: This study was conducted in accordance with the Declaration of Helsinki.

The study was approved by the Ethics Committee of Sakarya University Medical Faculty.

Author's Contribution

SY, HD: Data analysis and interpretation, drafting the article, critical revision of the article, final approval of the version; KI, ABG, DS, HK: Data collection, conception or design of the work, data analysis and interpretation, critical revision of the article, final approval of the version; EG, KS, HE, MK: Data analysis and interpretation, final approval of the version to be published.

RESUMO

OBJETIVO: *O objetivo deste estudo é analisar o significado prognóstico dos antígenos do grupo sanguíneo ABO e Rh, juntamente com vários parâmetros em pacientes acompanhados com o diagnóstico de COVID-19.*

MÉTODOS: *Foram avaliados 397 pacientes que foram acompanhados e tratados devido à infecção por COVID-19. Foram analisadas as idades, gêneros, doenças crônicas, antígenos do grupo sanguíneo ABO e Rh, taxas de internação em unidades de terapia intensiva (UTI) e taxas de mortalidade dos pacientes.*

A idade média de 397 pacientes com COVID foi de 47 ± 17 anos. Na análise do grupo sanguíneo dos pacientes, A Rh positivo (A +) foi o tipo sanguíneo mais frequentemente observado (176 dos pacientes, 44,3%), seguido pelo O Rh positivo (0 +) (109 dos pacientes, 27,5%) 38 dos pacientes eram Rh negativos (Rh -) (9,6%). 53 dos pacientes (13,4%) foram acompanhados em UTI e 29 faleceram (7,3%). Não houve mortalidade nem admissão na UTI para o grupo Rh. A comparação dos grupos Rh quanto à necessidade de admissão na UTI revelou uma taxa significativamente alta de admissão na UTI no grupo Rh + (p = 0,011), enquanto não foi encontrada relação significativa entre mortalidade e antígeno Rh (p = 0,069).

CONCLUSÃO: *O tipo sanguíneo mais frequentemente observado foi o A + entre os pacientes com COVID-19. O grupo sanguíneo Rh + foi encontrado em todos os casos admitidos na UTI e com evolução mortal. O grupo sanguíneo Rh + foi encontrado em um número significativamente alto de pacientes internados na UTI, enquanto nenhuma relação significativa foi encontrada entre a mortalidade e o grupo sanguíneo Rh.*

PALAVRAS-CHAVE: *Infecções por Coronavirus. Sistema ABO de Grupos Sanguíneos. Sistema do Grupo Sanguíneo Rh-Hr. Unidades de terapia intensive. Mortalidade.*

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