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A POSSIBLE RELATIONSHIP BETWEEN COVID-19 AND ABO BLOOD GROUPS AND CLINICAL OUTCOMES

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ABSTRACT

Aim: Since March 11, 2020, when the World Health Organization accepted the COVID-19 disease (SARS-CoV 2) as a pandemic, it has become important to determine the risk factors for the disease. A relationship has been shownbetween blood groups and many diseases. We aimed to investigate whether blood groups and the Rh factor are risk factors for COVID-19 disease.

Methods: Patients who presented atour Hospital between 15 March 2020 and 30 November 2020 were evaluated retrospectively with an observational-sectional study. The demographic information of the patients, ABO blood groups, nasopharyngeal swab results, thorax CT results, number of days of hospitalization in COVID-19 inpatient clinics and/or intensive care units, theseverity of the disease, andtheclinical outcome results were recorded.

Results: A total of 21,144 patients with ICD codes of COVID-19 (U07.3) and observation for suspicious disease or condition, unspecified (Z03.9) were screened. A total of 4,515 patients, including 4,201 patients with positive PCR in nasopharyngeal and/or nasal swab samplesand 314 patients who were PCR negative but had appropriate radiological findingswere included in the study. The COVID-19 ABO Blood groups weredistributed asA in 50.8% (n=755), O in 25.5% (n= 379), B in14.4% (n=214), and AB in9.3% (n=138).TheABO blood groups were Rh [+] in 87.6% (n=1302). When the ABO and Rh distributions were compared with pre-pandemic ABO country data, the rate of blood group A was found to be significantly higher and the rate of blood group O to be lower in Covid-19 patients. No significant difference was detected between the Rh blood groups.

Conclusions: We think that determining the risk factors for COVID-19 disease is important for public health, and thattheABO blood groups can help in this regard. Individuals with the A blood group can be included in the priority group for the SARS CoV-2 vaccine.

Key words: COVID-19, ABO blood groups, SARS-CoV 2

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INTRODUCTION

Since the discovery of the ABO blood groups, it has been thought that these blood groups may be associated with various diseases, including infectious diseases [1-3]. A relationship between SARS-CoV and the ABO blood groups was considered after the Hong-Kong epidemic in 2003 [4]. The ABO blood group system includes the A and B antigens and corresponding antibodies. In humans, the ABO blood groupgeneis located on chromosome 9 (9q34) and consists of the A, B, AB, and O alleles with a total of 4 genetic phenotypes [5]. In a study on possible genetic factors fortheSARS predisposition, it was found that anti-A antibodies could specifically inhibit the interaction between S protein and Angiotensin Converting Enzyme-2 (ACE2), and it was shown that anti-A antibodies could block the SARS-CoV interaction in people with blood type O [6].

After 11 March 2020, when the World Health Organization recognized COVID-19 disease (SARS-CoV 2) as a pandemic, it has become important to investigate the possible factors affecting the morbidity and mortality of the disease [7]. Various variables such as economic factors, development and management of health systems, race, and geographical variations can affect the mortality and morbidity of COVID-19. The diversity of the symptom scale of the disease, the influence of different organ systems, and the wide range of severity of the disease in the affected systems suggestthat a genetic background of the disease could also be present. The frequency of the ABO blood groups can also vary geographically.

The current study investigated whether the patients' ABO blood groups and Rh statuswas related to the probability of getting COVID-19 and the clinical course of the disease. The study was conducted at a Thoracic Diseases and Thoracic Surgery branch training and research hospital serving as a Pandemic Hospital in Istanbul, which connects two continents.

Methods

Patients who presented at theUniversity of Health Sciences Istanbul Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital between March 15, 2020 and November 30, 2020 were retrospectively evaluated with an observational-cross-sectional study. The study protocol was approved by the institution's ethics committee (EC) (approval dateand number: April 2, 2021 / 116.2017.R-213) and was conducted in accordance with the ethical principles of the Helsinki Declaration. Patients with International Classification of Diseases - (ICD) 'U07.3COVID-19' and 'Z03.9- Observation for suspected disease or condition, unspecified',asrecommended by the Ministry of Health of the Republic of Turkey, were included in the study using the hospital electronic system (HES).

In the reporting ofthecases diagnosed with COVID-19 and Thorax CT findings of COVID-19 with PCR positivity at least once in nasopharyngeal and/or nasal swab samples, there

wasa typical radiological appearance according to the North American Association of Radiology (RSNA) Expert Consensus Statement [8]. Patients who had PCR negativity in nasopharyngeal and/or nasal swab samples and received COVID-19 treatment were included in the study. Typical radiological findings criteria were as follows:

a) Peripheral, bilateral, ground-glass opacities (GGO) with or without consolidation or visible intralobular lines (“crazy-paving”)

b) Multifocal GGO of rounded morphology with or without consolidation or visible intralobular lines (“crazy-paving”)

c) Reverse halo sign or other findings of organizing pneumonia [8].

The severity of the disease was divided into two groups as mild and severe. The severe case group was considered withevidence of diffuse bilateral pneumonia on chest X-ray or thorax CT and/or the presence of at least one of the following factors:

a) Respiratory rate ≥ 30 / min

b) PaO2 / FiO2<300 mmHg

c) Oxygen need, increasing in follow-up

d) SpO2<90% or PaO2<70 mmHg despite 5 L/min oxygen therapy

e) Hypotension (systolic blood pressure <90 mmHg and a decrease from usual SBP more than 40 mmHg and mean arterial pressure <65 mmHg, tachycardia> 100 / min

f) Patients with acute organ dysfunction such as acute kidney injury, acute liver injury, confusion, acute bleeding diathesis, and immunosuppression

g) Troponin elevation and arrhythmia

h) Lactate > 2 mmol / L

i) Presence of skin disorders such as capillary return disorder and cutis marmaratus [9]

Foreign nationals, patients under the age of 18, those who received COVID-19 treatment but were PCR negative, and those where the Thorax CT findings were unclear, atypical, ornegative were excluded from the study.

Demographic information of the patients (age, gender), blood type in the health records (Rh positive, Rh negative; A, B, AB, and O group), nasopharyngeal swab result (positive or negative), Thorax CT image (with COVID-19 infection compliance), the number of days of hospitalization in the COVID-19 inpatient clinics and/or intensive care unit, the severity of the disease,and the outcomes (discharge orexitus) were recorded.

Statistical analysis

The study analysis was performed with the SPSS software (IBM Corp. Release2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY). Study findings of dichotomous variables (gender, ABO) were summarizedwith frequency and relatedpercentage values. The chi-square test was used for dichotomous variables. The comparison of two group proportions was done with the Z test from MedCalc'scomparison of proportions calculator [10]. The type I error rate was set at 5%.

Results

During the study period, a total of 21.144 patients with a diagnosis of COVID-19 (U07.3) and observation for suspected disease or condition, unspecified (Z03.9) were screened. A total of 4.515 patients, including 4.201 patients who were found to be PCR positive in nasopharyngeal and/or nasal swab samples, and 314 patients with appropriate radiological findings although PCR results were negative were included in the study. Apart from demographic characteristics, the blood groups, nasopharyngeal swab results, PCR positivity time, hospitalization area (COVID inpatientclinic, ICU), lung involvement and disease severity were evaluated. The demographic characteristics of the patients are shown in Table 1.

Table 1: Demographic characteristics of the patients

	n	%	Mean age
Female	2.125	47.1	46
Male	2.390	52.9	46
Total	4.515	100	46

The data of a total of 1.486 patients whose blood groups were previously determined (ABO, Rh) were evaluated through the hospital's electronic system. Of these, the A blood group was most common at50.8%. The percentage for blood type Owas 25.5%, B 14.4%, AB 9.3%, Rh positive 87.6%, and Rh negative 12.4%, respectively. Our data were compared with the normal blood group distribution results of Istanbul province, which were obtained from a total of 123,900 volunteer blood donors between 2012 and 2018 in the pre-pandemic period [11]. AmongCOVID-19 patients, those with blood type A were significantly more common thanin thenormal blood group distribution ($p < 0.001$) and the rate of those with the O blood group were found to be significantly lower ($p < 0.001$). A Rh (+) was significantly more common among those with blood type A while O Rh (+) was similarly significantly more common among those with blood type O. Although no statistically significant difference was observed, those with the AB blood type weremore commonthan the normal distribution, and those with blood type B were lower in comparision. In terms of Rh factor, no significant difference was found for any blood group. The statistical data of the blood groups are presented in Table 2.

According to the blood group distribution, there was no significant difference between the duration of nasopharyngeal swab positivity, presence of radiological findings in the lungs, the severity of the disease, intensive care admission, and mortality.

Table 2: Statistical data of the blood groups

	2020 Sureyyapasa COVID Cohort		**2012-2018 Istanbul Pre-COVID**		
	n	%	n	%	p value
A	**755**	**50.8**	**54289**	**43.8**	**<0.001**
O	**379**	**25.5**	**41878**	**33.8**	**<0.001**
B	214	14.4	18854	15.2	0.393
AB	**138**	**9.3**	**8879**	**7.2**	**0.002**
A Rh +	**662**	**44.5**	**47496**	**38.3**	**<0.001**
A Rh -	93	6.3	6793	5.5	0.197
O Rh +	**330**	**22.2**	**36427**	**29.4**	**<0.001**
O Rh -	**49**	**3.3**	**5451**	**4.4**	**0.019**
B Rh -	29	2	2560	2.1	0.789
B Rh +	185	12.4	16294	13.2	0.365
AB Rh -	12	0.8	908	0.7	0.646
AB Rh +	**126**	**8.5**	**7971**	**6.4**	**0.001**
Rh +	1302	87.6	108188	87.3	0.730
Rh -	184	12.4	15712	12.7	0.730
Total	1486	100	123900	100	

Discussion

The distribution of the ABO blood groups in theCOVID-19 patients in our hospital and the normal distribution of ABO blood groups in Istanbul were compared in the current study. The possibility of being infected with SARS-CoV-2 was higher in those with the A blood group and lower with the O blood group. However, the severity and clinical course of the disease were found to be similar in these groups. The results of large series of studies conducted on blood groups and the course of COVID-19 in the first year of the pandemicare are controversial (Table 3) [12-24].

Although we found a positive correlation of COVID-19 infectivity with blood group A and a negative correlation with blood group O, there is heterogeneity among the studies listed in the table 3. The reason for heterogeneity may be the different characteristics such as sociological, racial, and ethnic identity in different countries in the studies. In one study, a similar distribution

was observed among blood groups regardless of ethnic identity, while it was found that those with blood type A were affected more than expected and group O was affected less as a subgroup [20]. Dzik S. et al. reported all groups to be similar in their study, and no comment was made on ethnic identity [14].

Table 3: Large series studies on ABO Blood groups and COVID-19

Author (Reference)	Geographic Region/Year	N	A n (%)	AB n (%)	B n (%)	O n (%)	Study main results (Likelihood of Infection)
Zhao J,et al. [12]	China/2020	1888	715 (37.9)	193 (10.2)	494 (26.1)	486 (25.7)	High in the A blood group, low in the O blood group
LatzCA, et al. [13]	USA/2020	1289	440 (34.2)	61 (4.7)	201 (15.6)	587 (45.5)	High in the B and AB blood groups, low in the O blood group
Dzik S, et al. [14]	USA/2020	957	311 (32.5)	41 (4.3)	140 (14.6)	465 (48.6)	Similar in all blood groups
Bamkob MB, et al. [15]	Denmark /2020	7422	3296 (44.4)	378 (5.1)	897 (12.1)	2851 (38.4)	Low in the O blood group
Abdollahi A, et al. [16]	Iranian /2020	397	160 (40.3)	37 (9.3)	89 (22.4)	111 (28)	High in the AB blood group, low in the O blood group
Joel G, et al. [17]	Canada/2020	7071	2420	390	1378	2883	Low in the O and Rh (-) blood groups
Qian F, et al. [18]	China/2020	105	45 (42.8)	9 (8.6)	28 (26.7)	23 (21.9)	High in the A blood group in women
Aljanobi GA, et al. [19]	Saudi Arabia /2020	72	17 (23.6)	7 (9.7)	24 (33.3)	24 (33.3)	High in the AB blood group,low in the O blood group
Leaf RK, et al. [20]	USA/2020	561	253 (38)	32 (36)	64 (19.5)	212 (22.3)	In whites; high in the A blood group, low in the O blood group
Göker H, et al.[21]	Turkey/2020	186	106 (57)	14 (7.5)	20 (10.8)	46 (24.8)	High in the A blood group, low in the O blood group
Muñiz-Diaz E, et al.[22]	Spain/2020	854	403 (47.2)	32 (3.8)	65 (7.6)	354 (41.4)	High in the A blood group, low in the O blood group
Solmaz I, et al. [23]	Turkey/2020	1167	753 (45.2)	156 (9.4)	311 (18.2)	447 (26.8)	High in the A blood group, low in the O blood group
Boudin L, et al. [24]	France/2020	1279	521 (40.7)	54 (4.2)	135 (10.6)	553 (43.2)	Similar in all blood groups
Gündoğuş B, et al. (current study)	Turkey/2020	1486	755 (50.8)	138 (9.3)	214 (14.4)	379 (25.5)	High in the Ablood group, low in the O blood group

Another study included cases of COVID-19 outbreaks on a nuclear aircraft carrier. We thought that the fact that all crew members were kept on board during the pandemic, and created a local and closed group, together with the increased possibility of living differently compared to a routine life and the lack of close contact, may have resulted in a similar outcome and the distribution of disease among the different blood groups, in addition to other possible factors [24]. In the study of Qian F. et al., the infectivity among blood group A was found to be high only in women. The small number of the case group was striking in this study [18]. The common result of all the other studies has been reported as those with blood type O have been less affected by COVID-19.

The dominant isotype of anti-B or anti-A antibodiesis IgM in blood groups A and B, and IgG in group O [25]. Zhao et al. [12] and Gerard C. et al. [26] have emphasized that IgG anti-A antibodies should be considered as an important factor in the relationship between COVID-19 susceptibility and ABO blood groups.

A different hypothesis has been proposed stating that there may be a relationship between the blood group and COVID-19. Blood groups are determined by sugars. Coronaviruses in cattle have surface proteins that bind to sugars. Those with blood group O, but not those with blood group A, have N-acetylglucosamine, an extra sugar, on their cell surface. It has been stated that this could possibly result in more exposure to pathogen [27].

The limitations of our study were that our blood group detection rate in the total COVID-19 cohort in our hospital was 32.9%, the sample size was small, and the data were from a single center. Excluding foreign patients from the study due to the geographical difference of their blood groups and ensuring homogeneity is the strength of our study.

Conclusions

We found that the likelihood of being infected with SARS-CoV-2 was higher in those with blood type A and lower in those with blood type O. Due to the existence of subtypes of the ABO blood groups, the homogeneity of the population is important. We believe that SARS-Cov-2 infectivity may be variable according to the ABO blood group subtypes. Priority groups for vaccination can be determined by blood group studies. There is a need for better planned, prospective, comprehensive multi-center studies involving more patients.

Conflicts of interest: The authors have nothing to disclose.

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