Relationship Between ABO Blood Types and Coronavirus Disease 2019 Severity

Mufide Arzu Ozkarafakili, Nesrin Gareayaghi, Zeynep Mine Yalcinkaya Kara

Department of Chest Diseases, Sisli Hamidiye Etfal Training and Research Hospital, University of Health Sciences Turkey, Istanbul, Turkey
Department of Microbiology and Clinical Microbiology, Sisli Hamidiye Etfal Training and Research Hospital, University of Health Sciences Turkey, Istanbul, Turkey
Department of Biochemistry, Sisli Hamidiye Etfal Training and Research Hospital, University of Health Sciences Turkey, Istanbul, Turkey

Abstract

Objectives: Severe Acute Respiratory Syndrome Coronavirus-2 infection spreads rapidly around the world. The blood groups are recognized to influence susceptibility to certain viruses. The aim of this research was to determine any potential role of the patients' ABO and Rh blood groups in both the acquisition and severity of coronavirus disease 2019 (COVID-19). As a growing global health problem, to find any marker for COVID-19 may help to identify high-risk individuals and ease the strain on health system.

Methods: The patients who were hospitalized between March and August 2020 with a diagnosis of COVID-19 and had a documented ABO blood type in medical database were examined retrospectively. Patients were grouped as survivors (followed up in pandemic wards/ICU) and non-survivors. Their ABO blood types were correlated with general population's blood types. The laboratory findings of patients were evaluated according to the blood types.

Results: A total of 492 patients included, 233 (47.4%) were male. The mean age was 58.9±17.5. Data of ABO blood groups of 51,966 individuals in general population was used as a control group; the number of the patients in Rh (-) blood type 0, were significantly lower than the control group (p=0.008). Among the whole patient group (survivors and non-survivors), Blood type A 210 (42%) was the most common and type AB 52 (10%) was the least common. However, no statistically significant difference was noted between survivors (pandemic wards/ICU) and non-survivors unlike the previous studies (p=0.514). No correlation was found between laboratory findings (Hemoglobin, red cell distribution width, platelet, white blood cell, lymphocyte, D-Dimer, C-reactive protein, ferritin) and ABO blood groups of COVID-19 patients (p>0.05).

Conclusion: There was no association found between the ABO blood type and COVID-19 infection rate or disease severity. No evidence was noted to support the use of ABO blood type as a marker for COVID-19. Further efforts are warranted to better predict outcomes of hospitalized COVID-19 patients.

Keywords: ABO blood types, COVID-19, severity

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Since December 2019, the world has been dealing with Coronavirus disease 2019 (COVID-19), which was declared as a global health emergency by the World Health Organization with 169 million patients and 3.5 million deaths, caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). While massive vaccination campaign is going on, the whole world is trying to cope with the waves of epidemic and the burden it puts on the health system. COVID-19 can be seen in different forms; from asymptomatic patients to those with mild symptoms such as dry cough, fever, and weakness, to severe cases that result in acute respiratory distress syndrome and death. SARS-CoV-2 is transmitted by respiratory droplets. The fact that asymptomatic cases can transmit the virus and the excess of critical patients who overburden the intensive care units (ICUs) bring along the search for a biomarker that can predict the risk of being infected with SARS-CoV-2. Individuals have A, B, AB, and O blood types, depending on whether antigen is present on the erythrocyte surface or not. These antigens are also found in the epithelium, endothelium, platelets, and exocrine glands that secrete mucin and may have a role on the onset of various diseases. Blood groups are also called positive or negative according to the presence of Rhesus (Rh) factor protein. The Rh system is clinically the most important and complex protein-based system because Rh proteins are expressed only in the membranes of the red blood cells. Despite important geographical differences, the most common blood type in the world is the O blood group. In the (H1N1) epidemic caused by the influenza virus; it has been noted that people with A and B blood groups are more prone to infection than people with O and AB blood groups.

In 2003, the relationship between the SARS infection seen in Asia and blood groups was investigated; it has been found that those with blood type O are less affected by SARS-CoV than those with non-O blood group. There are numerous studies with contradictory results about the relationship between ABO blood groups and COVID-19 infection. We investigated the relationship with ABO blood group and the clinical characteristics, laboratory findings of 492 COVID-19 patients who were hospitalized and had a documented blood group in the medical database.

Methods

In this study, the electronic medical records of 492 patients who were diagnosed with COVID-19 and had a blood group record in the medical database and followed up in the hospital between March and August 2020 were retrospectively analyzed. Patients over 18 who were hospitalized and confirmed with real-time polymerase chain reaction test positive for SARS-CoV-2 in nasopharyngeal swab or who had epidemic history, symptoms, and Chest Computed Tomography findings compatible with COVID-19 and couldn’t be explained by other factors were included in the study. Those whose blood groups were not recorded in the medical database were excluded from the study. As the control group, the ABO blood group data of 51,966 people of general population, obtained from the Blood Bank for 3 years of screening in the same region were used. The patients were categorized as survivors (followed up in the pandemic wards/ICU) and non-survivors. Data include demographics, comorbidities, laboratory findings. The non-survivors’ data were collected 48 h before death. The survivors’ data were collected at time of admission to pandemic wards or at the time to transfer to the ICU. Our study was approved by the Ethics Committee of our hospital (No: 2738) and was conducted in accordance with the Helsinki Declaration.

Statistical Analysis

Descriptive values of the obtained data were calculated as mean, standard deviation (SD), number and % frequencies depending on the variable type. The distribution of blood groups in the general population and the distribution of blood groups in COVID-19 patients in the study group were compared with the t-test for two independent proportions. Categorical characteristics of surviving patients (pandemic wards/ICU) and those who died were compared with the Fisher-Freeman-Halton exact test. In addition, the Kruskal-Wallis and Mann Whitney U test was used to compare these groups in terms of numerical type characteristics. Groups that differed significantly were determined using the post-hoc Dunn test. Relationships between numerical characteristics and blood groups, and the patient’s current status (pandemic wards, ICU/death) were evaluated with analysis of variance and analysis of covariance (ANCOVA) models. In the ANCOVA model, these effects were eliminated by considering the effects of age and gender. Factors associated with patients’ clinical outcome were evaluated using the multivariate logistic regression model to determine the independent effect. Statistical significance level was accepted as p<0.05 and SPSS ver. 23 (IBM, Turkey) program was used for calculation.

Results

We enrolled 492 COVID-19 patients. 233 (47.4%) were male. The mean age was 58.9±17.5 (between 18 and 95 years); 58.71±15.81 for male, 59.15±19.43 for female. Data retrieved from Blood Bank, 51,966 individuals in the same region were used as a control group (Table 1). The patients in the blood group 0 Rh (-) was significantly lower than
the ones in the general population (p=0.008). The blood group distribution of COVID-19 patients were; type A 210 (42%), blood type 0 154 (31%), type B 76 (15%), type AB 52 (10%) respectively. Rh positivity was 444 (90%). Blood type A was found the most common and type AB was the least common. In terms of ABO blood type distribution, although there were percentile differences, this was not statistically significant when compared with the general population.

Patients were divided into two groups: Survivors (those followed in the pandemic wards or in the ICU) 458 93% and non-survivors 34 6.9%. The demographic characteristics, ABO blood groups, and comorbidities were examined in Table 2; the female patients followed up in the pandemic wards was found significantly higher (250.50%) and the male gender ratio was found to be significantly higher in patients who were transferred to the ICU (10.2%) and who died (26.5%) (p<0.01). Hypertension was the most common comorbidity 179.36%. No statistically significant difference was observed in terms of ABO blood types/Rh (Rh factor) between survivors and non-survivors.

The laboratory findings of the patients; (Red cell distribution width [RDW], D-Dimer, hemoglobin, red blood cell [RBC], lymphocyte, platelet, white blood cell [WBC]), ferritin, C-reactive protein [CRP]) were examined according to ABO blood groups and no statistically significant difference was found between the groups (p>0.05) (Table 3).

In Table 4, according to the clinical outcomes of the patients, the descriptive statistics of age and laboratory findings are shown. The mean age of the survivors and the deceased patients was found to be similar. RDW, D-Dimer, and hemoglobin were found to be significantly lower in the patients followed in the pandemic wards than in the other two groups (p<0.01). The average of RBC, lymphocyte and platelet were found significantly lower (p=0.014, p=0.018, p=0.02) and WBC, ferritin, CRP were found to be significantly higher in non-survivors than the survivors (p<0.01).

In Tables 5 and 6, the demographic characteristics and the clinical outcomes of the patients are analyzed with multivariate logistic regression model. In the multivariable analysis, blood type was not determined to be independently associated with COVID-19 disease severity. No significant difference was found in terms of blood group distribution between the patients followed up in the pandemic wards and the ICU (95% CI. for OR, P=0.946) (Table 5).

Similarly, no significant difference was found in terms of blood groups distribution of patients who were hospitalized in the pandemic wards and who died with the multivariable analysis (95% CI. for OR, p=0.685) (Table 6).

**Discussion**

Several studies have been conducted to date on relationship between blood groups and COVID-19. Literature revealed that ABO blood group was associated not only with COVID-19 susceptibility but also with severe outcomes and death. In our retrospective analysis, no correlation between the blood groups and the acquisition of COVID-19 was found, also there was no association noted between ABO blood type and COVID-19 disease severity. Blood type AB had the lowest and blood type A had the highest frequency of the disease in our study. But no statistical significance was found. The prevalence between genders was equal, but the mortality rate was higher in men than women in our data. The study results
of Zhao et al. corresponded a significantly increased risk of blood type A and decreased risk of blood type 0 for COVID-19 and similar distribution pattern for mortality also. Ellinghaus et al. study on genetics data suggested blood type A is associated with higher risk of acquiring COVID-19 than non-A blood groups. Latz et al. and Zietz et al. showed Rh (-) patients had lower risk of infection by SARS-CoV-2. After multivariable analysis, blood type was not independently associated with risk of surviving or death (95% CI. for OR). No association between ABO subtype (Rh factor) and severe disease was found in our study. Our data are different from the experiences of Zhao et al., Ellinghaus et al., Latz et al., and Zietz and Tatonetti. Despite these prior studies, Jeffrey et al. had shown no association between ABO blood type and COVID-19 predisposition or severity. Some hypothesis raised for the vari-

|                         | Survivors | Non-survivors | P*  |
|-------------------------|-----------|---------------|-----|
|                         | Pandemic wards | Intensive care unit |     |
|                         | n   | %      | n   | %      | n  | %     |
| Gender                  |     |        |     |        |     |       |
| Male                    | 197 | 84.5a  | 10  | 4.3a   | 26 | 11.2a <0.001 |
| Female                  | 250 | 96.5b  | 1   | 0.4b   | 8  | 3.1b  |
| ABO Rh                  |     |        |     |        |     |       |
| 0 Rh (+)                | 133 | 93.7   | 2   | 1.4    | 7  | 4.9   0.514 |
| 0 Rh (-)                | 11  | 91.7   | 1   | 8.3    | 0  | 0     |
| A Rh (+)                | 170 | 90.9   | 4   | 2.1    | 13 | 7     |
| A Rh (-)                | 19  | 82.6   | 1   | 8.3    | 3  | 13    |
| B Rh (+)                | 61  | 85.9   | 3   | 4.2    | 7  | 9.9   |
| B Rh (-)                | 5   | 100    | 0   | 0      | 0  | 0     |
| AB Rh (+)               | 41  | 93.2   | 0   | 0      | 3  | 6.8   |
| AB Rh (-)               | 7   | 87.5   | 0   | 0      | 1  | 12.5  |
| ABO                     |     |        |     |        |     |       |
| Group 0                 | 144 | 93.5   | 3   | 1.9    | 7  | 4.5   0.596 |
| Group A                 | 189 | 90     | 5   | 2.4    | 16 | 7.6   |
| Group B                 | 66  | 86.8   | 3   | 3.9    | 7  | 9.2   |
| Group AB                | 48  | 92.3   | 0   | 0      | 4  | 7.7   |
| Hypertension            |     |        |     |        |     |       |
| No                      | 285 | 91.1   | 7   | 2.2    | 21 | 6.7   0.966 |
| Yes                     | 162 | 90.5   | 4   | 2.2    | 13 | 7.3   |
| Diabetes                |     |        |     |        |     |       |
| No                      | 339 | 91.4   | 10  | 2.7    | 22 | 5.9   0.200 |
| Yes                     | 108 | 89.3   | 1   | 0.8    | 12 | 9.9   |
| COPD/Asthma             |     |        |     |        |     |       |
| No                      | 398 | 91.3   | 9   | 2.1    | 29 | 6.7   0.459 |
| Yes                     | 49  | 87.5   | 2   | 3.6    | 5  | 8.9   |
| Congestive heart failure|     |        |     |        |     |       |
| No                      | 426 | 90.8   | 11  | 2.3    | 32 | 6.8   0.802 |
| Yes                     | 21  | 91.3   | 0   | 0      | 2  | 8.7   |
| Chronic renal disease   |     |        |     |        |     |       |
| No                      | 406 | 90.8   | 11  | 2.5    | 30 | 6.7   0.596 |
| Yes                     | 41  | 91.1   | 0   | 0      | 4  | 8.9   |
| Coronary artery disease |     |        |     |        |     |       |
| No                      | 392 | 90.7   | 10  | 2.3    | 30 | 6.9   0.947 |
| Yes                     | 55  | 91.7   | 1   | 1.7    | 4  | 6.7   |
| Malignity               |     |        |     |        |     |       |
| No                      | 430 | 90.9   | 11  | 2.3    | 32 | 6.8   0.762 |
| Yes                     | 17  | 89.5   | 0   | 0      | 2  | 10.5  |

*Fisher-Freeman-Halton exact test, n: Data set, COPD: Chronic obstructive pulmonary disease.
ability of contagiousness of SARS-CoV-2, infection rates and the severity of the disease. Angiotensin-converting enzyme 2 (ACE2) is the primary receptor and major way for SARS-CoV-2 entering into host cells. During the SARS outbreak in 2003, the scientists reported higher risk for SARS-CoV-1 infection for blood type A and explained it by, spike protein/ACE2 dependent adhesion to ACE2 cell lines was inhibited by monoclonal or natural human anti-A antibodies. In the individuals with blood type 0 and B, these anti-A antibodies may protect from SARS-CoV-2 infection by blocking the interaction between coronavirus and ACE2.

Cheng et al. had shown that blood type 0 was found to be less common in SARS-CoV-1 infection. As the geographical dependence of the blood type distribution could affect the regional infection rates, Mattio et al.'s present paper help us understand the importance of some other population-dependent antigens' role in COVID-19. Some reports reveal that the ABO blood group antigen alters the inflammatory response. Non-0 blood types have been previously shown to effect hemostasis by increasing Von Willebrand Factor and Factor VIII, that can lead to thrombotic events, which is the cornerstone for COVID-19. Inflammation is a condition known as related to COVID-19 disease state and severe outcomes. The cytokine storm leads to T cell dysfunction and peripheral lymphopenia in most hospitalized patients and building up to severe forms of the disease. No difference was demonstrated for inflammatory markers (WBC, CRP) according to ABO blood type in our study. Furthermore, WBC, CRP, ferritin were found to be significantly higher in non-survivors than the survivors (p<0.01), and RBC, lymphocyte and platelet were found significantly lower in non-survivors than the survivors in our study (p=0.014, p=0.018, p=0.02).

We had some limitations; the sample size was small, and the number of blood type O Rh (-) patients were significantly lower than the general population which might lead to bias in the results. Only the patients who had the

### Table 3. Distribution of laboratory findings according to blood types

| Blood Type | AGE | RDW | RBC | LYM | WBC | FERRITIN | CRP | DDIMER | HGB | PLT |
|------------|-----|-----|-----|-----|-----|----------|-----|--------|-----|-----|
| 0 RH (-)   | Mean 50 | 13.87 | 4.15 | 1.34 | 9.23 | 237.70 | 95.08 | 1083.08 | 124.92 | 231.25 |
|            | SD 18 | 1.61 | 0.59 | 0.64 | 5.32 | 253.39 | 104.36 | 1115.05 | 22.84 | 111.01 |
| 0 RH (+)   | Mean 59 | 14.54 | 4.32 | 1.47 | 7.97 | 223.35 | 59.94 | 1296.85 | 122.87 | 218.99 |
|            | SD 18 | 2.26 | 0.83 | 1.07 | 4.01 | 222.97 | 78.59 | 1598.24 | 27.72 | 92.02 |
| A RH (-)   | Mean 61 | 14.58 | 4.41 | 7.11 | 15.23 | 233.37 | 75.53 | 1061.74 | 126.17 | 207.09 |
|            | SD 16 | 2.11 | 0.70 | 28.47 | 30.11 | 233.12 | 98.79 | 1050.06 | 24.77 | 92.06 |
| A RH (+)   | Mean 59 | 14.39 | 4.25 | 1.48 | 7.60 | 228.95 | 60.56 | 1983.81 | 121.18 | 215.15 |
|            | SD 17 | 2.13 | 0.88 | 0.97 | 4.93 | 242.75 | 73.08 | 7940.34 | 25.50 | 89.86 |
| AB RH (-)  | Mean 58 | 15.39 | 4.43 | 2.66 | 14.39 | 256.90 | 10.88 | 850.00 | 118.75 | 240.63 |
|            | SD 19 | 2.16 | 1.33 | 1.37 | 15.61 | 200.02 | 12.38 | 1198.77 | 29.42 | 77.04 |
| AB RH (+)  | Mean 61 | 14.23 | 4.57 | 1.55 | 8.47 | 190.84 | 60.54 | 1046.64 | 127.73 | 220.59 |
|            | SD 16 | 1.46 | 1.60 | 0.87 | 3.90 | 197.03 | 71.46 | 855.28 | 20.64 | 98.94 |
| B RH (-)   | Mean 49 | 13.58 | 4.78 | 2.23 | 13.94 | 220.38 | 56.66 | 366.00 | 141.60 | 235.60 |
|            | SD 9 | 0.75 | 0.34 | 0.96 | 10.61 | 203.37 | 78.06 | 205.64 | 12.34 | 16.21 |
| B RH (+)   | Mean 59 | 14.32 | 4.47 | 2.77 | 11.93 | 182.94 | 64.95 | 2332.59 | 124.11 | 237.87 |
|            | SD 18 | 1.88 | 0.80 | 11.49 | 23.63 | 172.50 | 77.30 | 9642.40 | 24.52 | 88.59 |

P-value* 0.742 0.742 0.191 0.070 0.019 0.882 0.335 0.896 0.330 0.727

*Corrected differences between blood groups by eliminating the impact of gender and age differences, RDW: Red cell distribution width, RBC: Red blood cell, LYM: Lymphocyte, WBC: White blood cell, CRP: C-reactive protein, HGB: Hemoglobin, PLT: Platelet.
The documented ABO blood type were included in the study, so these results might not truly reflect the correct number of COVID-19 cases.

**Conclusion**

Despite the early reports suggesting that blood type A might be more susceptible while blood type O might be less susceptible to infect COVID-19; we found no evidence for association between ABO blood groups and COVID-19, also there was no correlation noted for disease severity and mortality throughout our analysis. The conflicting data in the literature necessitates further higher-quality studies to identify the role of ABO blood groups in SARS-CoV-2 infection.
Disclosures

Ethics Committee Approval: Our study was approved by the Ethics Committee of our hospital (No: 2738) and was conducted in accordance with the Helsinki Declaration.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – M.A.O.; Design – M.A.O.; Supervision – M.A.O.; Data collection &/or processing – N.G.; Analysis and/or interpretation Z.M.Y.K.; Literature search – M.A.O.; Writing – M.A.O.; Critical review – M.A.O., Z.M.Y.K., N.G.

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Table 5. Multivariate logistic regression model of patients in intensive care unit and the pandemic wards.

|                                      | P   | OR  | 95% CI for OR | Lower | Upper |
|--------------------------------------|-----|-----|---------------|-------|-------|
| Blood Types                          | 0.946 |     |               |       |       |
| Type (A/0)                           | 0.543 | 1.754 | 0.288 | 10.688 |
| Type (AB/0)                          | 0.997 | 0.000 | 0.000 | --     |
| Type (B/0)                           | 0.749 | 1.416 | 0.168 | 11.959 |
| Age                                  | 0.354 | 0.974 | 0.920 | 1.030  |
| Gender (Female/Male)                 | 0.012 | 0.031 | 0.002 | 0.460  |
| RDW                                  | 0.578 | 0.889 | 0.587 | 1.347  |
| RBC                                  | 0.019 | 5.338 | 1.321 | 21.569 |
| LYM                                  | 0.282 | 0.499 | 0.141 | 1.770  |
| WBC                                  | 0.840 | 1.020 | 0.838 | 1.243  |
| Ferritin                             | 0.536 | 0.999 | 0.995 | 1.003  |
| CRP                                  | 0.039 | 1.013 | 1.001 | 1.026  |
| D-Dimer                              | 0.536 | 1.000 | 1.000 | 1.001  |
| HGB                                  | 0.003 | 0.917 | 0.865 | 0.971  |
| PLT                                  | 0.194 | 1.005 | 0.997 | 1.013  |
| CVD (Yes/No)                         | 0.998 | 0.000 | 0.000 | --     |
| COPD (Yes/No)                        | 0.220 | 3.832 | 0.447 | 32.841 |
| CHF (Yes/No)                         | 0.997 | 0.000 | 0.000 | --     |
| CAD (Yes/No)                         | 0.280 | 0.238 | 0.018 | 3.213  |
| HT (Yes/No)                          | 0.764 | 1.308 | 0.227 | 7.526  |
| DM (Yes/No)                          | 0.224 | 0.209 | 0.017 | 2.609  |
| Constant                             | 0.741 | 6.558 |       |       |

Table 6. Multivariate logistic regression model of patients in the pandemic wards and the non-survivors

|                                      | P   | OR  | 95% CI for OR | Lower | Upper |
|--------------------------------------|-----|-----|---------------|-------|-------|
| Blood Types                          | 0.685 |     |               |       |       |
| Type (A/0)                           | 0.352 | 2.380 | 0.383 | 14.771 |
| Type (AB/0)                          | 0.288 | 3.701 | 0.331 | 41.372 |
| Type (B/0)                           | 0.320 | 3.112 | 0.331 | 29.232 |
| Age                                  | 0.727 | 0.991 | 0.939 | 1.045  |
| Gender (Female/Male)                 | 0.162 | 0.319 | 0.064 | 1.585  |
| RDW                                  | 0.229 | 1.205 | 0.889 | 1.634  |
| RBC                                  | 0.763 | 0.898 | 0.447 | 1.805  |
| LYM                                  | 0.234 | 0.566 | 0.222 | 1.444  |
| WBC                                  | 0.003 | 1.175 | 1.057 | 1.305  |
| Ferritin                             | 0.460 | 1.001 | 0.998 | 1.004  |
| CRP                                  | 0.015 | 1.009 | 1.002 | 1.016  |
| D-Dimer                              | 0.576 | 1.000 | 0.999 | 1.000  |
| HGB                                  | 0.546 | 0.987 | 0.948 | 1.029  |
| PLT                                  | 0.102 | 0.994 | 0.986 | 1.001  |
| CVD (Yes/No)                         | 0.999 | 0.000 | 0.000 | --     |
| COPD (Yes/No)                        | 0.998 | 0.000 | 0.000 | --     |
| CHF (Yes/No)                         | 0.328 | 3.467 | 0.288 | 41.800 |
| CAD (Yes/No)                         | 0.416 | 0.356 | 0.030 | 4.284  |
| HT (Yes/No)                          | 0.282 | 2.319 | 0.501 | 10.731 |
| DM (Yes/No)                          | 0.725 | 1.320 | 0.280 | 6.222  |
| Constant                             | 0.285 | 0.007 |       |       |

OR: Odd ratio, CI: Confident interval, CVD: Cerebrovascular disease, COPD: Chronic obstructive pulmonary disease, CHF: Congestive heart failure, CAD: Coronary artery disease, HT: Hypertension, DM: Diabetes mellitus, RDW: Red cell distribution width, RBC: Red blood cell, LYM: Lymphocyte, WBC: White blood cell, CRP: C-reactive protein, HGB: Hemoglobin, PLT: Platelet.
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