Investigation of association between ABO blood groups and COVID-19 clinical severity

Arzu İrvem, Abdurrahman Sarmış, Özlem Akgün Doğan, Jale Yıldız, Zafer Habip, Nihat Buğra Ağaoğlu, Betsi Köse, Gizem Alkurt, Lütфиye Nilsu Altunál, Ayşe Serra Özel, Mehtap Aydınlı, Sanem Dereli Bulut, Yasemin Kendir Demirkol, Esra Koçoğlu, Gizem Dinler Doğanay, Levent Doğanay, Yaşar Bükte, Sebahat Aksaray

1 Kanuni Training and Research Hospital Dept. of Microbiology, Istanbul, TR
2 Göztepe Süleyman Yalçın Training and Research Hospital İSLAB2, Istanbul, TR
3 GLAB genomics Lab, Istanbul, TR
4 Umraniye Training and Research Hospital, Dept. of Infection Diseases, Istanbul, TR
5 Umraniye Training and Research Hospital Dept. of Radiology, Istanbul, TR
6 Health Sciences University Hamidiye Faculty of Medicine, Dept. of Microbiology, Istanbul, TR

* Corresponding Author: Arzu İrvem E-mail: arzuirvem93@gmail.com

ABSTRACT

Objective: COVID-19 has been detected in Turkey since March 11, 2020. Istanbul has become an important center of the pandemic in Turkey. Various risk factors for COVID-19 infection, mortality, and morbidity are under investigation. Recent studies have suggested that certain blood groups are risk factors for the disease. The aim of this study is the evaluation the relationship between blood groups and the risk of contracting COVID-19 disease, clinical severity of the disease, and CT (computed tomography) imaging findings.

Material and Methods: Age, gender, blood group data, clinical severity and CT images of 300 patients who were positive with RT PCR (Reverse transcription-polymerase chain reaction) and were followed up in the clinic were retrospectively scanned and recorded. The clinical severity of the disease and CT imaging findings were scored, and the data were evaluated statistically.

Results: While the incidence of COVID-19 was high in the A blood group, it was low in the 0 blood group. Although there was no significant difference between blood types and clinical severity, the involvement in the B blood group was more severe on CT imaging.

Conclusion: People with A blood group should pay more attention to protection and isolation. Investigating this difference and underlying pathogenic mechanisms can guide science with advanced studies.

Keywords: COVID 19, Blood Group, Clinical Severity, CT imaging

INTRODUCTION

Introduction: COVID-19 emerged in 2019 in Wuhan, China (1). It is an enveloped RNA beta coronavirus. It has phylogenetic similarity to severe Middle East respiratory syndrome (MERS) and acute respiratory syndrome (SARS) coronavirus. While the disease can be asymptomatic, it can cause acute respiratory distress with symptoms such as myalgia, fatigue, dyspnea, cough, fever, and death. CT imaging findings are important in diagnosis and follow-up. In recent studies, it has been suggested that the ABO blood group is associated with virus infection, and people with different blood groups as genetic markers have different susceptibility to the virus and the risk of catching it (2). In our study, the data of the patients who were found to be positive for RT PCR in our hospital were scanned, and the blood group distribution was compared with the normal population. Turkish Red Crescent 5-year data was used (3). Clinical severity with the blood group of the patients: It is aimed to evaluate statistically by comparing blood group and CT imaging findings.
MATERIAL and METHODS

The files of the patients whose COVID-19 RT PCR test was positive and followed up in the COVID clinic were retrospectively scanned. Three hundred cases were selected. Blood type, age, gender, presence of comorbidity, clinical severity, and CT imaging findings were analysed.

The clinical severity of the patients was scored.
1 = Asymptomatic or outpatient group (Mild)
2 = Inpatient group (moderate)
3 = Group of patients requiring intensive care, intubated or deceased (severe)

The image (CT) was scored.
1 = Patient group that does not require CT or has mild pneumonia findings.
2 = Patient group with typical findings of ground glass appearance in the lung
3 = Group of patients with fibrosis and cobblestone appearance, pleural effusion or pericardial effusion in addition to the ground glass appearance of the lung

PCR method: Nasopharyngeal viral samples were collected and evaluated. ORF and N gene regions were studied using primers (Coyote Bioscience test kit, CHINE) and RT PCR method (CFx96 Biorad) device (4).

Statistical analysis; NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. While evaluating the study data, Kruskal Wallis test was used to compare the descriptive statistical methods (median, mean, ratio, frequency, maximum, minimum, standard deviation) as well as the groups of three or more that did not show normal distribution in comparison with groups of three or more.

Fisher Freeman Halton test was used to compare quantitative data and qualitative data. Statistically significant results were evaluated at levels of $p < 0.05$.

RESULTS

The distribution of the blood groups of the cases according to the demographic data is given in Table 1. In the comparison of the blood groups of the cases and the distribution of the normal population blood groups, A RH (+) blood group ($p=0.003$) is more common in COVID-19 cases than in the normal population. 0 RH (+) blood group was seen less frequently ($p=0.001$) (Table 2, 3).

There was no significant difference in the blood groups of the cases in terms of age and gender (Table 4). The clinical severity of the cases and the presence of comorbidity were not associated with blood type. However, CT imaging findings showed a higher severity of lung involvement in B blood group (Table 5).

### Table 1: The distribution of descriptive characteristics of the cases

| Age (year) | Min-Max (Median) | Mean±SD |
|------------|-----------------|---------|
| 20-97 (61.5) | 59.45±17.52 |

| Sex | | |
|-----|---|---|
| Female | 139 (46.3%) |
| Male | 161 (53.7%) |

| ABO blood group | | |
|-----------------|---|---|
| A (Anti B) | 156 (52.0%) |
| B (Anti A) | 48 (16.0%) |
| AB (NA) | 24 (8.0%) |
| O (Anti A+Anti B) | 72 (24.0%) |

| Rh | | |
|-----|---|---|
| Rh (-) | 35 (11.7%) |
| Rh (+) | 265 (88.3%) |

| CT imaging Score | | |
|-----------------|---|---|
| Mild | 61 (20.3%) |
| Moderate | 209 (69.7%) |
| Severe | 30 (10.0%) |

| Clinical Score | | |
|-----------------|---|---|
| Mild | 42 (14.0%) |
| Moderate | 169 (56.3%) |
| Severe | 89 (29.7%) |

| Comorbidity | | |
|--------------|---|---|
| Negative | 105 (35.0%) |
| Positive | 195 (65.0%) |

Table 2. The ABO blood group distribution in patients with COVID-19 and normal population.
Table 3. The ABO blood group distribution in patients with COVID-19 and normal population.

| Blood Group | COVID-19 CASES (%) | General in Turkey (%) (5 million) | P value |
|-------------|-------------------|-----------------------------------|---------|
| A RH (-)    | 6,7               | 5,0                               | 0,185   |
| A RH (+)    | 45,3              | 37,0                              | 0,003** |
| B RH (-)    | 1,7               | 2,0                               | 0,680   |
| B RH (+)    | 14,3              | 14,0                              | 0,868   |
| AB RH (-)   | 0,3               | 1,0                               | 0,382   |
| AB RH (+)   | 7,7               | 7,0                               | 0,651   |
| O RH (-)    | 3,0               | 4,0                               | 0,377   |
| O RH (+)    | 21,0              | 30,0                              | 0,001** |

\( ^a \)Pearson Chi-Square Test  \(^b \)Fisher Freeman Halton Test  \( ^*p<0,01 \)

Table 4. Comparison of blood groups with age and gender

| Blood Group | Age (year) | Gender |
|-------------|------------|--------|
|             | Min-Maks (Median) | Ort±x  |
| A           | 21-96 (64)  | 59,27±19,11 |
| B           | 21-97 (63,5)| 61,67±16,22 |
| AB          | 28-90 (58,5)| 59,13±14,10 |
| O           | 20-97 (60)  | 58,49±15,90 |

Test value: \( F:0,390 \)  \( \gamma:0,761 \)

| Gender | A           | B           | AB          | O           |
|--------|-------------|-------------|-------------|-------------|
| Female | 72 (46,2)   | 23 (47,9)   | 12 (50,0)   | 32 (44,4)   |
| Male   | 84 (53,8)   | 25 (52,1)   | 12 (50,0)   | 40 (55,6)   |

\( ^a \)One-way ANOVA  \(^b \)Pearson Chi-Square Test

Table 5. CT imaging score, clinical score and comorbidity comparison according to blood groups

| CT imaging Score | A (%) | B (%) | AB (%) | O (%) | Test value |
|------------------|-------|-------|--------|-------|------------|
| Mild             | 43 (27,6) | 5 (10,4) | 4 (16,7) | 9 (12,5) | \( \chi^2:14,179 \) |
| Moderate         | 103 (66,0) | 35 (72,9) | 17 (70,8) | 54 (75,0) | \( \chi^2:0,023^* \) |
| Severe           | 10 (6,4)   | 8 (16,7)  | 3 (12,5)  | 9 (12,5)  | \( \chi^2:14,179 \) |

| Clinical Score  | A (%) | B (%) | AB (%) | O (%) | Test value |
|-----------------|-------|-------|--------|-------|------------|
| Mild            | 26 (16,7) | 1 (2,1)  | 4 (16,7) | 11 (15,3) | \( \chi^2:8,470^* \) |
| Moderate        | 83 (53,2) | 30 (62,5) | 15 (50,0) | 44 (61,1) | \( \chi^2:0,206 \) |
| Severe          | 47 (30,1) | 17 (35,4) | 8 (33,3)  | 17 (23,6) | \( \chi^2:2,280 \) |

| Comorbidity     | A (%) | B (%) | AB (%) | O (%) | Test value |
|-----------------|-------|-------|--------|-------|------------|
| Negative        | 54 (34,6) | 13 (27,1) | 10 (41,7) | 28 (38,9) | \( \chi^2:2,280 \) |
| Positive        | 102 (65,4) | 35 (72,9) | 14 (58,3) | 44 (61,1) | \( \chi^2:0,516 \) |

\( ^a \)Fisher Freeman Halton Test

DISCUSSION

In our study, in accordance with other studies, high rate of blood group A and low rate of blood group 0 were detected in cases followed up with COVID-19 (2,5,6). According to a meta-analysis study covering the years 2019 and 2020; The relationship between blood types and COVID 19 varies according to different regions and races. However, it has been found that people with 0 blood group are less susceptible to COVID-19, and people with A blood group are more susceptible. It has been emphasized that people with blood group A should provide better personal protection (2). Zhao et al. reported that case fatality rates are high in the A blood group (5). However, in our study, no relationship was observed between clinical severity and blood group, while those with B blood group in CT imaging scoring had more severe lung involvement. Zietz M. et al. found that Rh positivity was seen at a high rate in blood groups, but it was not associated with comorbidity (6). In our study, Rh positivity is already high in the normal population and no significant relationship was found with the disease.

There are many possible reasons why the risk is higher in blood group A. In cases with type A blood, extra sugar N-acetyl galactosamine is found on the cell surface. This excess sugar is not in group 0. The presence of extra galactosamine is thought to be effective in catching the virus(7). In addition, the relationship of the COVID-19 spike protein with the ACE 2 receptor has been shown (8,9). There is no anti-A in blood group A. Anti A and spike protein are thought to compete in binding to the cell ACE 2 receptor, so those who are Anti A positive have a lower risk of disease. Cross duplication was detected in the 3p21.31 chromosome region. SLC6A20 encodes a known interaction partner with ACE2 at 3p21.31. The coupling signal at 9q34 is located at the ABO blood group locus, and this blood group specific analysis demonstrated a high risk of developing the disease in A-positive individuals (10). Recent studies with flow cytometry have determined that the predominant isotype of anti-A and anti-B immunoglobulin is IgM in the serum of people with blood group A and B, and IgG is the predominant isotype of anti-A immunoglobulin in people with blood group 0 (11).
In conclusion, the presence of anti-A antibodies and more specifically IgG anti-A in the serum explains why blood group 0 is less risky. In a different study, people with blood type 0 were found to have genetically higher levels of IL 6. IL 6 level has been associated with low ACE 2 receptor and blood pressure (12).

CONCLUSIONS

While blood group and clinical severity were not found to be associated with COVID19-infected patients, it was determined those individuals with A blood group were more likely to develop the disease and individuals with 0 blood group had a low risk of contracting the disease. People with A blood group should pay more attention to protection and isolation. In terms of more severe tomography findings in B blood group and better understanding of these differences, investigation of the underlying pathogenic mechanisms may guide science with further studies.

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