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# Investigation of the clinical course of Covid-19 patients according to blood groups

**Alper ÖMEROĞLU[1], Süleyman ERSOY[2], Emin PALA[2*], Velittin Selçuk ENGİN[3]**

[1]Department of Family Medicine, Hasan Paşa Family Health Center, Istanbul, Turkey
[2]Department of Family Medicine, University of Health Sciences, Umraniye Training and Research Hospital, İstanbul, Turkey
[3]Department of Family Medicine, Melekhatun Family Health Center, Istanbul, Turkey

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**Abstract**

The aim of this study is to evaluate the effect of blood groups (BGs) on Covid-19 contraction and prognosis and to reveal the coefficients. Patients who referred to Covid-19 outpatient clinics and had an established diagnosis of Covid-19 were included in the study. Their BGs, previous diagnoses and blood examination findings were retrospectively analyzed. Duration of hospitalization, clinical course and survival were recorded. The mean age of 365 subjects, 210 female and 155 male, was 45,5 years. Subjects with BG A developed Covid-19 at significantly higher rates ($p = 0.001$), while BG O was found associated with lower rates ($p = 0.005$). Lymphocyte count was found lower ($p = 0.035$) and rate of lung parenchymal involvement was higher ($p = 0.003$) in patients with Rh antigen. It was found that a higher percentage of patients with B BG required treatment in the intensive care unit (ICU) compared to other ABO BGs ($p = 0.015$). These results suggest a higher risk of Covid-19 contraction in the population with BG A and lower risk for BG O population while indicating poorer prognosis for patients with BG B.

**Keywords:** covid-19, ABO BGs, Rh antigen, prognosis

## 1. Introduction

The new type of coronavirus which was emerged in China's Wuhan city in 2019 was named Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), and the disease it caused was called Coronavirus Disease 2019 (Covid-19) (1, 2). It shows a wide spectrum of clinical manifestations from asymptomatic to severe acute respiratory failure and death (3). A definitive treatment is yet to come.

One of the issues investigated regarding Covid-19 disease is its relationship with blood groups (BGs). Evidence exists that BGs play a key role in infectious diseases. In studies to date, the O allele was thought to act as a potential selective factor, affecting susceptibility to various pathogens of diseases such as malaria, Helicobacter pylori and cholera infections. A and B antigens are purportedly can be used as receptors by microorganisms (4). Rotavirus positive cases were found more common in cases with BG A while less common in cases with BG B (5,6). A study of animals with SARS-CoV infection revealed that when ACE2 expressing cells in the Chinese hamster ovary are transfected with the S protein, the S protein / ACE 2-

dependent adhesion of these cells to an ACE 2 expressing cell line is specifically inhibited by monoclonal or human native anti-A antibodies (7).

The observed relation of BG antigens to infections provoked interest regarding their probable role in rapidly spreading Covid-19. Despite many studies conducted on the prognosis, mortality and risk factors, there are limited data regarding the relationship of BGs and Covid-19. In this study, we aimed to compare the risk of contraction and prognostic features of the disease between different BGs.

## 2. Materials and Method

This was a retrospective cross-sectional study carried out in patients who referred to Umraniye Training and Research Hospital Covid-19 outpatient clinics. Inclusion criteria of the patients in the study were referral to Covid-19 outpatient clinics from April 15, 2020 to May 15, 2020, being 18 years or older, having BG information on hospital's records and having a definite diagnosis with a positive Covid-19 RT-PCR Test.

In this context, 365 patients were included in the study as the "Covid-19 Patient" group. In a study conducted in 2019, the frequency and distribution of BGs of patients thought to represent the Istanbul population was determined (8). These patients were included in our study as a control group and served as the basis for comparison of ABO and Rh rates. (8). History of the patients was analyzed retrospectively, as well as hematological" parameters like complete blood and Cero Reactive Protein (CRP) and thoracic tomography (TT). Intensive care admissions and survival of the patients were looked for. Based on these data, the prevalence and prognosis of the disease in each BG were evaluated. In 22 of 365 subjects,

*Correspondence: eminpala72@gmail.com

only Covid-19 RT-PCR test was performed without further examination. TT could not be performed in 3 patients due to pregnancy.

### 2.1. Statistical analysis of data

The data were analyzed by SPSS 25.0 software (SPSS, Inc, Chicago, IL, USA). Distribution of the data was tested using Kolmogorov Smirnov test. Besides descriptive statistical methods; t-test for parametric data, One Way Anova Test, Mann Whitney U test and Kruskal Wallis H test for non-parametric data were used. Chi-Square test was used to evaluate categorical data. Correlation analysis was used while analyzing quantitative data and significance was assumed as $p<0.05$ for all tests.

**Table 1**. Risk of disease acquisition in COVID-19 cases and controls

| | Covid-19 N (%) | Control N (%) | P | Relative Risk | Odds ratio | Confidence Interval 95% |
|---|---|---|---|---|---|---|
| **Group O** | 98 (26.8) | 41878 (33.79) | **0.005** | 0.720 | 0.719 | 0.570-0.906 |
| **Group A** | 191 (52.3) | 54289 (43.81) | **0.001** | 1.406 | 1.408 | 1.146-1.729 |
| **Group B** | 51 (14.0) | 18854 (15.21) | 0.509 | 0.905 | 0.905 | 0.673-1.217 |
| **Group AB** | 25 (6.8) | 8879 (7.16) | 0.815 | 0.953 | 0.953 | 0.634-1.431 |

## 3. Results

Three hundred sixty-five patients (210 female and 155 male) between the ages of 18-89 years (mean age= 45.5 ± 15.9 years) participated in the study. According to BGs, the mean ages of O, A, B, AB were 45 ± 15.6, 45 ± 15.7, 48 ± 16.9 y, 43 ± 15.9 years, respectively. While BG A predominated in the study group with 52.3%; 26.8% had BG O, 14.0% had BG B and 6.8% had BG AB. While 86.6% of the patients have the Rh antigen, 13.4% were in the Rh-negative. When we compared the BG rates of the Covid-19 patients with the control group; the rate of BG A in subjects was significantly higher compared to controls (52.3% versus 43.81%, p = 0.001), whereas BG O rate in subjects was significantly lower (26.8% vs 33.79%, p = 0.005) (Table 1). As for Rh antigen, cases and controls seemed similar (Table 1).

Values of CRP, White Blood Cells (WBC), Neutrophile (Nt), Lymphocyte (Ly) and Neutrophile to Lymphocyte Ratio (NLR) were separately compared between ABO and Rh BGs. No significant difference was found except Ly value, which was significantly lower in the Rh-positive group (p = 0.035) (Table 2).

**Table 2.** Comparison of hematological parameters in ABO and Rh blood groups

| | | Mean±SD | Median | Min-Max | P |
|---|---|---|---|---|---|
| **CRP** | **Group 0** | 2.0±3.8 | 0.4 | 0.1-25.5 | 0.129** |
| | **Group A** | 2.0±3.3 | 0.8 | 0.1-24.7 | |
| | **Group B** | 2.6±3.6 | 0.9 | 0.1-15.1 | |
| | **Group AB** | 1.7±3.0 | 0.3 | 0.1-13.1 | |
| **WBC (x1000/mm$^3$)** | **Group 0** | 6.18±2.55 | 5.63 | 2.06-19.29 | 0.671** |
| | **Group A** | 6.37±2.63 | 5.91 | 3.05-25.64 | |
| | **Group B** | 6.44±2.22 | 6.10 | 2.96-13.68 | |
| | **Group AB** | 6.49±2.19 | 6.03 | 2.72-12.35 | |
| **NEU (x1000/mm$^3$)** | **Group 0** | 3.82±2.15 | 3.38 | 1.16-14.86 | 0.227** |
| | **Group A** | 4.12±2.40 | 3.75 | 1.35-24.30 | |
| | **Group B** | 4.28±2.07 | 3.69 | 1.60-12.10 | |
| | **Group AB** | 4.22±1.95 | 3.92 | 1.01-10.50 | |
| **LY (x1000/mm$^3$)** | **Group 0** | 1.74±0.76 | 1.67 | 0.36-3.94 | 0.652* |
| | **Group A** | 1.65±0.70 | 1.51 | 0.36-4.11 | |
| | **Group B** | 1.58±0.61 | 1.50 | 0.34-3.20 | |
| | **Group AB** | 1.77±0.74 | 1.49 | 0.64-3.43 | |
| **NLR** | **Group 0** | 2.61±1.87 | 2.04 | 0.60-11.88 | 0.351** |
| | **Group A** | 3.08±3.11 | 2.36 | 0.51-35.22 | |
| | **Group B** | 3.42±3.58 | 2.37 | 0.90-24.00 | |
| | **Group AB** | 2.85±1.84 | 2.35 | 0.72-7.19 | |

*One Way ANOVA, ** Kruskall Wallis H Tes

Relationship between TT findings of patients with Covid-19 according to ABO and Rh BGs is shown in Table 3. No significant difference was found between ABO BGs in terms of lung involvement. However, Rh-positive patients had significantly higher lung involvement (Relative Risk = 1.408, Odds Ratio = 2.538, 95% Confidence Interval = 1.347-4.784, p = 0.003) (Table 3).

Relationship between intensive care admissions according to ABO BGs is shown in Table 4. The rate of admission to the intensive care unit was significantly higher in patients with BG B (Relative Risk = 3.078, Odds Ratio = 3.365, 95% Confidence Interval = 1.199-7.835, p = 0.015), while no significant difference was found according to Rh antigen. When we analyzed the relationship between the number of days of stay in the Intensive Care Unit (ICU) due to COVID 19 according to the ABO and Rh BGs, no significant difference was found (Table 4).

## 4. Discussion

In our study, we found that those with BG A are at higher risk for Covid-19 contraction, while this risk is lower for BG O. It was observed that higher percentage of patients with BG B required ICU.

**Table 3: Relationship between ABO and Rh blood groups and Tomography findings**

| | CT Involvement | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Yes | | No | | | | | |
| | N | % | N | % | p | Relative Risk | Odds rario | Confidence interval 95% |
| **Group O** | 63 | 26.3 | 28 | 28.0 | 0.658 | 1.031 | 1.110 | 0.658 – 1.874 |
| **Group A** | 126 | 52.5 | 50 | 50.0 | 0.674 | 0.970 | 0.905 | 0.567 – 1.443 |
| **Group B** | 33 | 13.8 | 15 | 15.0 | 0.763 | 1.030 | 1.107 | 0.572 – 2.143 |
| **Group AB** | 18 | 7.5 | 7 | 7.0 | 0.872 | 0.978 | 0.978 | 0375-2.297 |
| **Total** | 240 | 100.0 | 100 | 100.0 | | | | |
| **Chi-Square** | | | | | | | | |
| **Rh Negative** | 24 | 10.0 | 22 | 22.0 | | | | |
| **Rh Positive** | 216 | 90.0 | 78 | 78.8 | **0.003** | 1.408 | 2.538 | 1.347 – 4.784 |
| **Total** | 240 | 100.0 | 100 | 100.0 | | | | |
| **Chi-Square** | | | | | | | | |

**Table 4: Relationship between ABO and Rh blood groups and intensive care unit admissions**

| | Admission to Intensive Care Unit | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Yes | | No | | | | | |
| | N | % | N | % | p | Relative Risk | Odds rario | Confidence interval 95% |
| **Group O** | 4 | 22.2 | 94 | 27.1 | 0.650 | 0.778 | 0.769 | 0.247-2.395 |
| **Group A** | 6 | 33.3 | 185 | 53.8 | 0.980 | 0.445 | 0.438 | 0.161-1.193 |
| **Group B** | 6 | 33.3 | 45 | 13.0 | **0.015** | 3.078 | 3.356 | 1.199-7.835 |
| **Group AB** | 2 | 11.1 | 23 | 6.6 | 0.463 | 1.700 | 1.761 | 0.381-8.129 |
| **Total** | 18 | 100.0 | 347 | 100.0 | | | | |
| **Chi-Square** | | | | | | | | |
| **Rh Negative** | 2 | 11.1 | 47 | 13.5 | | | | |
| **Rh Positive** | 16 | 88.9 | 300 | 86.5 | 0.768 | 0.99 | 0.798 | 0.178-3.582 |
| **Total** | 18 | 100.0 | 347 | 100.0 | | | | |
| **Chi-Square** | | | | | | | | |

**Table 5: Length of stay in ICU in terms of days according to ABO blood groups**

| | | Length of stay, days | | | | |
|---|---|---|---|---|---|---|
| | | Mean±SD | Min | Max | Median | p |
| **ICU stay*** | **Group O** | 11.50±5.26 | 4.00 | 16.00 | 13.00 | 0.941* |
| | **Group A** | 12.00±6.96 | 6.00 | 25.00 | 10.00 | |
| | **Group** B | 11.83±10.63 | 3.00 | 29.00 | 7.00 | |
| | **Group AB** | 15.50±0.71 | 15.00 | 16.00 | 15.50 | |
| **ICU stay*** | **Rh Negative** | 10.00±5.66 | 6.00 | 14.00 | 10.00 | 0.621** |
| | **Rh Positive** | 12.50±7.62 | 3.00 | 29.00 | 11.00 | |

***Kruskall Wallis H Test,**Man-Whitney U Test**

Other studies have yielded similar results to ours. Fan et al. reported that the rate of having Covid-19 infection among those with BG A was significantly higher (5). Li et al. found that the rate of BG A was significantly higher in patients infected with SARS-CoV-2 compared to healthy controls, while the rate of BG O was significantly lower (8). Another study reported that BG A was associated with a significantly higher risk for COVID-19, whereas BG O was associated with lower risk (9). Wu et al. have found that the proportion of patients with BG A in the COVID-19 group was significantly higher than that in the control group, whereas the proportion of patients with type O blood in COVID-19 was significantly lower (10). Our study supports other studies in the literature in terms of the rate of ABO BGs in patients with COVID-19 infection.

The intriguing relationship between ABO BGs and Covid-19 suggested whether the Rh antigen will also have an impact on the risk of Covid-19. Abdollahi et al. could not find a significant difference in terms of the presence of Rh antigen and having Covid-19 infection (11). Latz et al. found a rate of Covid-19 positivity significantly higher in people with Rh-positive BG (12). In a study including 227 patients with positive PCR test and 165 cases whose CT findings favored of Covid-19, it was found that Rh positivity was significantly higher in patients diagnosed with Covid-19 (13). In this study, we could not find a statistically significant relation between Rh antigen and Covid-19.

We also compared the CRP levels in ABO and Rh BGs in terms of prognosis. Patients with BG B had the highest mean CRP values while those with BG AB had the lowest, but no significant difference was found between ABO BGs. Besides, while the mean CRP values were increased in the Rh-positive group, the difference was not significant either. Similarly, Latz et al. found no significant difference in CRP values between ABO BGs (12).

Hematological parameters such as WBC, Nt, and Ly are also important markers showing the prognosis in Covid-19 disease. Fan et al. have conducted an analysis that included Covid-19 patients regardless of the severity of the disease and the control group and showed that the WBC values wasn't significantly different between the two groups, the rate of neutrophils was significantly higher in the Covid-19 group, and the lymphocyte count and lymphocyte ratio were significantly lower than the control group. In the same study, they compared ABO BGs with lymphocyte numbers of Covid-19 patients and showed that although the lymphocyte count was lower in individuals with A BG compared to other ABO BGs, the difference wasn't statistically significant (6). Latz et al. showed in their study that there was no statistically significant difference in WBC value between ABO BGs (13). In our study, when we compared ABO BGs regarding WBC and neutrophil counts, no statistically significant difference was found. When we compared the WBC and neutrophil counts regarding the Rh groups, there was no significant result here, either. When the ABO BGs were compared according to the lymphocyte count, there was no statistically significant difference, although the mean lymphocyte count was lower in individuals with B BG compared to other ABO BGs. On the other hand we found that the lymphocyte values were significantly lower in the Rh-positive group compared to the Rh-negative group.

One of the important prognostic markers of Covid-19 disease is NLR. In a study NLR was found to be significantly higher in patients with clinically severe disease compared to the non-severe group (14). In their retrospective cohort study involving 245 patients, Liu et al. have found that higher NLR was significantly associated with an increased risk of all-cause mortality during hospital stay (15). Nalbant et al. compared Covid-19 patients with a control group without Covid-19 and found that the NLR value was significantly higher in the

Covid-19 group compared to the control group (16). In our study, we compared NLR in BGs as a prognostic marker. Although B BG has the highest NLR among ABO BGs and O BG the lowest NLR, the difference between ABO BGs was not statistically significant. In Rh BGs, despite the NLR was higher in the Rh-positive group compared to the Rh-negative group, the difference was not statistically significant.

TT is an important imaging tool in Covid-19 disease. Although RT-PCR is the gold standard in diagnosis, the high rate of false negativity has increased the importance of TT which has a sensitivity of 98%. It is of great importance not only in diagnosis, but also in monitoring the progression of pneumonia and evaluating the effectiveness of treatment (17). Therefore, we have included TT in our study and compared TT involvement in different BGs. In ABO BGs, 52.5% of the patients with TT involvement had A BG and 7.5% of them had AB BG but no statistically significant difference was found between any ABO BGs in terms of TT involvement. When we examined the relationship between TT involvement and Rh antigen status, we found that the TT involvement of Rh-positive patients was statistically significantly higher than Rh-negative patients. In this case, the significantly higher TT involvement of Rh-positive patients compared to Rh-negative patients may indicate that the Rh antigen may be important in the course of the disease.

Clinical manifestations of patients infected with SARS-CoV-2 can range from mild, nonspecific symptoms to severe pneumonia with organ dysfunction (17). Therefore, the rate of admission to the intensive care unit is important in determining the severity of the disease and clinical course. In our study, when we compared the BGs and the rates of admission to the intensive care unit, we found that among ABO BGs, the rate of admission to the intensive care unit was significantly higher in patients with B BG. There was no statistically significant relationship between the presence of Rh antigen and admission to the intensive care unit. When we compared the days of stay in the intensive care unit, there was no statistically significant difference between both ABO BGs and the presence of Rh antigen and prolonged intensive care unit stay. May et al. have reported that 98 patients needed admission to intensive care unit in the follow-up of 165 patients admitted for inpatient care in their hospitals, and that there was no significant difference between ABO BGs of the patients getting inpatient care and patients admitted to the intensive care unit (18). In their study, Yaylacı et al. have reported that there was no statistically significant relationship between ABO BGs and admission to the intensive care unit, and that they found a statistically significant relationship between having Rh antigen and the rate of admission to the intensive care unit (19). In another study it was observed that there was no statistically significant difference between ABO BGs regarding the rate of patients admitted to the intensive care unit, but in the comparison between A or AB BGs (A + AB) and O or B BGs (O + B), it was observed that the A + AB group stayed longer in the intensive care unit and the difference was statistically significant (20). We think that different results between these studies may be related with the fact that there were no Rh-negative patients in the study of Yaylacı et al.

For mortality rates according to BGs, Latz et al. have reported that there was no significant relationship between ABO BGs and mortality rates in their study (12). Yaylacı et al. reported that there was no significant difference in the mortality rate between ABO BGs, but despite absence of mortality in the Rh-negative group patients mortality rate was significantly higher in Rh-positive group (19). Zietz et al. reported that they did not detect a significant relationship between BG and death due to Covid-19 in their study (20). Ray et al. have reported that O BG among ABO BGs and Rh-negative patients have a lower risk of mortality (21). In their study, Zhao et al. found that those with A BG had a higher risk of mortality compared to those other than A BG, while those with BG O had a lower risk of mortality than those other than BG O (9). In our study, 42.9% of the patients who died had B BG. Although we could not find a statistically significant difference in mortality between different ABO BGs, the mortality rate in group B patients was found to be very close to being statistically significantly higher. We think that we could not reach a statistically significant value due to the low number of patients included in our study and the low number of cases that resulted in mortality. Indeed, in our study, the rate of admission to intensive care, which is the main factor affecting mortality, was found to be significantly higher in group B patients. Again, although it did not reach a significant level, NLR, one of the important predictive markers of prognosis, was highest in group B patients. In the light of all these results, we can assume that in group B patients, Covid-19 infection has a more severe course and their prognosis is worse.

Covid-19 disease can progress with different clinical findings in people with similar backgrounds and descriptive features. The reasons for this difference have occupied the minds since the beginning of the epidemic. In this context, there are various hypotheses that many genetic and histopathological features, including HLA tissue antigens, may be the answer to different clinical course. The issue that blood groups may also be one of the reasons for the different clinical response of individuals to Covid-19 disease has been found in the literature for the last 1 year. However, the number of publications answering this question is limited in the literature and according to our search, there is only one publication in our country whose case number is limited (19). In this context, we think that our study contributes to the clarity of other studies that report limited and contradictory results examining the relationship between blood types and the prognosis of covid-19 disease. In addition, we think that the existence of only one publication from Turkey in this field increases the importance of our study.

Our study had some limitations. The relatively high false-

negative rate of the Covid-19 RT-PCR test and absences of BG information in hospital records limited the number of the study group. This situation restricted ability to attain statistically significant values, especially in mortality analyzes.

Results of our study are suggestive of the higher risk for BG A and lower risk for BG O of contracting Covid-19. The rate of admission to intensive care was significantly higher in BG B patients, indicative of a worse prognosis. Larger-scale clinical studies investigating the relationship between BGs and Covid-19 are needed to confirm these results.

**Conflicts of Interest**

There is no conflict of interest to declare.

**Acknowledgments**

None to declare.

**Ethical Approval**

This study was approved by the Ethics Committee of University of Health Sciences Turkey (date: 10.07.2020, No. 2020.07.10-39). The study was conducted in accordance with the principles of the Declaration of Helsinki.

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