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The relationship between the severity of COVID-19 pneumonia and ABO blood groups

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ABSTRACT

Aims: It is known that the distribution of ABO blood groups creates significant differences in viral infections and that blood group type can also be used as a biomarker to predict the risk of SARS-CoV-2 infection. In this study, we aimed to investigate the relationship between disease severity and blood groups in patients diagnosed with COVID-19 pneumonia.

Methods: Designed as a retrospective cohort study, our study included patients who were admitted to the Pulmonology Department of Kütahya Health Sciences University Evliya Çelebi Training and Research Hospital for inpatient treatment with a diagnosis of COVID-19 pneumonia between 31.03.2020 and 30.09.2020 and sociodemographic characteristics, blood group, Rh status, admission information, and CT findings were recorded from electronic patient records. Blood group characteristics were examined in the categorization based on the radiologically defined severity classification of COVID-19 pneumonia.

Results: The study group consisted of 93 males (47.2%) and 104 females (52.8%). Regarding blood type distribution, 50 (25.4%) patients had type O, 105 (53.3%) had type A, 26 (13.2%) had type B, and 16 (8.1%) had type AB. The blood group distribution according to the Rh factor was 25 (12.7%) Rh (-) and 172 (87.3%) Rh (+). No statistically significant difference was found in the distribution of COVID-19 pneumonia severity on chest computed tomography (CT) based on blood groups (p=0.200). No statistically significant difference was found in the relationship between COVID-19 pneumonia severity on chest CT and the Rh factor (p=0.283). On the other hand, when the relationship between the Rh factor and COVID-19 severity was examined, it was found that patients in the Rh (-) group had a higher rate of intensive care unit (ICU) admission (p=0.001), a higher rate of high-flow oxygen requirement during follow-up (p=0.030), and a higher mortality rate (p=0.02) compared to the Rh (+) group.

Conclusion: We have determined that there is no association between ABO blood group distribution characteristics and the severity of COVID-19 pneumonia, but there may be a prognostic association between the Rh factor and the severity of COVID-19.

Keywords: COVID-19, pneumonia, ABO blood group, Rh, SARS-CoV-2

INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic began in December 2019 as a cluster of patients with pneumonia of unknown origin linked to a seafood market in Wuhan, China, and spread throughout the Wuhan region.[1] Despite strict measures taken to control the viral outbreak, the disease continued to spread across China, straining hospital resources and healthcare workers.[2] SARS-CoV-2 continued to spread through human-to-human transmission and rapidly evolved into a global emergency.[3,4]

The gold standard for COVID-19 diagnosis is reverse transcription polymerase chain reaction (RT-PCR) using nasopharyngeal and oropharyngeal swabs.[5] However, while RT-PCR is highly specific, it is a test with varying levels of sensitivity.[6] Low sensitivity and false-negative rates highlight the importance of medical imaging; while chest X-rays are more practical, computed tomography (CT) has been shown to be superior in the diagnostic evaluation of COVID-19.[7]

To date, numerous factors have been identified that may be associated with poor prognosis and outcomes following COVID-19 infection, including gender, race, ethnicity, age, obesity, and pre-existing medical conditions.[8] In addition to these studies, blood type has also been investigated as a risk factor for COVID-19.

Although several studies have investigated the association between ABO blood groups and chest CT severity in COVID-19 patients, data from Turkish cohorts specifically evaluating radiologically defined pneumonia severity classifications-as categorized by Turkish Ministry of Health adult treatment guidelines-remain limited. The aim of

the present study is to contribute to this body of evidence by examining blood type characteristics in relation to radiologically and clinically defined COVID-19 severity in a Turkish tertiary care setting.

METHODS

Ethics

This study was conducted with the approval of the Ethics Committee for Non-interventional Clinical Researches at Kütahya University of Health Sciences (Date: 17.09.2020, Decision No: 2020/14). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design

Our study, designed as a retrospective cohort study, included patients who were radiologically suspected of having COVID-19 between 31.03.2020 and 30.09.2020 and were diagnosed with COVID-19 pneumonia following a positive RT-PCR result, and who were hospitalized for treatment at Pulmonology Department of KSBÜ Evliya Çelebi Training and Research Hospital. The patients' electronic records were reviewed to document sociodemographic characteristics, blood type, Rh status, clinical information, and chest CT findings. Patients radiologically suspected of having COVID-19 and/or those with positive RT-PCR results were classified as COVID, while patients without findings consistent with COVID-19 on chest CT and/or with negative RT-PCR results were classified as Non-COVID. These patients were further divided into three groups based on chest CT findings: mild-moderate and severe-very severe. Radiological criteria: CT findings were classified according to the severity criteria defined in the Turkish Ministry of Health COVID-19 Adult Treatment Guidelines (2020). Cases without radiological evidence of severe pneumonia on CT were classified as 'mild pneumonia'; cases with bilateral diffuse pulmonary involvement were classified as 'severe pneumonia'; and patients who subsequently met intensive care criteria during ward follow-up were reclassified as 'very severe pneumonia. Chest CT images were evaluated by two experienced pulmonologists working in the clinic, both with direct clinical experience in COVID-19 management during the study period. In cases of discordant radiological classification between the two evaluating physicians, consensus was reached through discussion. Blood group characteristics were examined in the categorization based on the severity classification of radiologically defined COVID-19 pneumonia.

Inclusion Criteria

Patients aged 18 years or older with radiological findings consistent with COVID-19 pneumonia and a confirmed COVID-19 diagnosis based on PCR test, Total Antibody Test, Anti-SARS-CoV-2 IgM and/or IgG, and who were hospitalized for treatment at the Pulmonology Department of KSBÜ Evliya Çelebi Training and Research Hospital with a diagnosis of COVID-19 pneumonia between 31.03.2020 and 30.09.2020 were included in our study.

Exclusion Criteria

Individuals under 18 years of age who were admitted to the Pulmonology Department of KSBÜ Evliya Çelebi Training and Research Hospital between 31.03.2020 and 30.09.2020 with a confirmed diagnosis of COVID-19 pneumonia but without pulmonary involvement, as well as patients who were diagnosed with COVID-19 pneumonia after consultation but treated as outpatients and/or sent to quarantine without hospitalization, were excluded from our study.

Data Collection

Certain data from electronic patient records reviewed by the researchers were transferred to a prepared data form without identifying information. The flowchart is shown in **Figure**. The data form included patients' sociodemographic characteristics, blood type and Rh status, and laboratory parameters such as CRP, D-dimer, ferritin, fibrinogen, and lymphocyte counts. Chest CT findings were evaluated by pulmonologists working in the clinic, and patients were divided into 3 groups. Based on the adult treatment guidelines prepared by the Ministry of Health, patients were classified according to the severity of involvement on their admission CT scans: cases without radiological findings of severe pneumonia were classified as 'mild pneumonia,' and patients with bilateral diffuse pneumonia on CT were classified as 'severe pneumonia,' and patients admitted with a diagnosis of severe COVID-19 pneumonia whose treatment was managed on the ward but who later met intensive care criteria and required intensive care monitoring were classified as 'very severe pneumonia.' Blood group characteristics were examined in this categorization based on the classification.

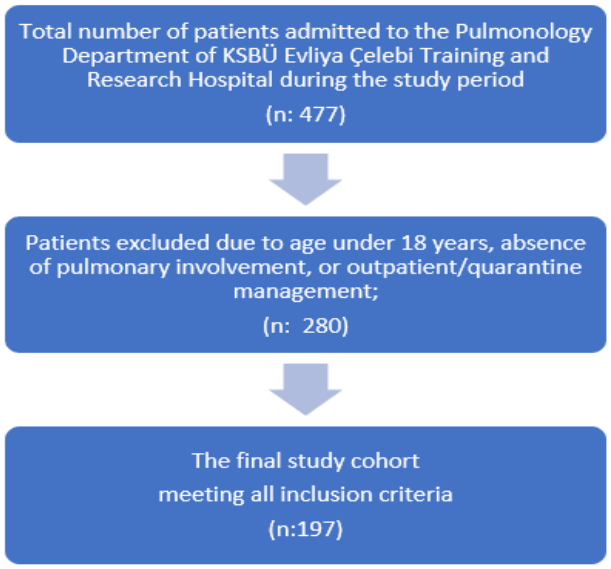

Figure. Flowchart of patient selection. Of 477 patients admitted during the study period, 280 were excluded according to the predefined exclusion criteria. The final study cohort consisted of 197 patients who met all inclusion criteria

Statistical Analysis

The data from the study were analyzed using the SPSS 25.0 software package. Descriptive statistics were presented as counts and percentages for categorical variables, and as means and standard deviations for numerical variables. The Chi-square test was used to compare categorical variables. Since the data did not follow a normal distribution, the Mann-Whitney U test and the Kruskal-Wallis test were applied to compare measured values between groups. Statistical significance was set at $p<0.05$.

RESULTS

Our study included 93 male (47.2%) and 104 female (52.8%) patients. No significant differences were observed between the genders in the study group. The mean age of the patients was 57.8±16.4 years (mean±SD). The mean length of hospital stay was 17.9±21.3 days.

In the blood group analysis, A Rh-positive A (+) was the most common blood group (91 patients, 46.2%), followed by O Rh-positive O (+) (43 patients, 21.8%). 23 patients (11.7%) were AB (+); 15 patients (7.6%) were B (+); 14 patients (7.1%) were A (–); 7 patients (3.6%) were O (–); 3 patients (1.5%) were AB (–); and only 1 patient (0.5%) was in the B (–) group. A total of 25 patients (12.7%) were Rh (–), while 172 patients (87.3%) were Rh (+). Some characteristics of the patients are shown in **Table 1**.

Table 1. Selected patient characteristics

Characteristics	Number (n)	Percent (%)
Gender		
Male	93	47.2
Female	104	52.8
Blood group		
O	50	25.4
A	105	53.3
B	26	13.2
AB	16	8.1
Rh factor		
Rh-	25	12.7
Rh+	172	87.3
COVID severity at CT (n=190)		
Non-COVID	21	11.1
Mild and moderate	87	45.7
Severe and very severe	82	43.2
Need for HFNO during inpatient follow-up (n=145)*		
No	139	95.9
Yes	6	4.1
ICU admission during follow-up (n=156)		
No	132	84.6
Yes	24	15.4
IMV (n=129)		
No	118	91.5
Yes	11	8.5
NIMV (n=135)		
No	112	83.0
Yes	23	17.0
Elevation of liver function tests during follow-up		
No	158	80.2
Yes	39	19.8

CT: Computed tomography, *HFNO: High flow nasal oxygen, ICU: Intensive care unit, IMV: Invasive mechanical ventilation, NIMV: Non-invasive mechanical ventilation

Based on the severity of COVID-19, no findings suggestive of COVID-19 were detected on the chest CT scans of 21 patients (11.1%). Mild and moderate COVID-19 findings were detected in 87 patients (45.7%), and severe and very severe COVID-19 findings were detected in 82 patients (43.2%). No significant differences were found between blood groups and chest CT findings or COVID-19 severity. When patients were divided into two groups based on Rh status Rh (+) and Rh (–), no significant differences were found in chest CT severity. The relationship between patients' blood groups and certain case characteristics is shown in **Table 2**, and the relationship between Rh groups and certain case characteristics is shown in **Table 3**.

During the hospital stay, the need for high-flow oxygen therapy developed in 6 patients (4.1%). Although no significant difference was observed in the analysis conducted for blood groups A, B, O, and AB, when patients were divided into 2 groups according to Rh status Rh (-) and Rh (+). The rate of high-flow oxygen requirement during inpatient follow-up was found to be statistically significantly higher in the Rh (-) group compared to the Rh+ group (p=0.030).

During inpatient follow-up, 24 patients (15.4%) were transferred to the intensive care unit. Although no significant difference was observed in the analysis conducted for blood groups A, B, O, and AB, when patients were grouped by Rh status (Rh- and Rh+), the rate of transfer to the intensive care unit (ICU) during inpatient follow-up was found to be statistically significantly higher in the Rh- group compared to the Rh+ group (p=0.001).

During follow-up in the ward, 14 patients died (7.1%), while 183 patients were discharged. In the analysis conducted according to blood groups A, B, O, and AB, no significant difference was found in mortality rates among the groups. However, when grouped as Rh (-) and Rh (+), a higher mortality rate was observed in the Rh (-) group (p=0.020).

DISCUSSION

COVID-19 first emerged in December 2019 in Wuhan, China, with cases of pneumonia of unknown origin; this disease, caused by SARS-CoV-2, quickly spread from person to person and evolved into a global pandemic.[1-4] COVID-19, declared as a pandemic by the World Health Organization, can present with a wide clinical spectrum ranging from mild upper respiratory symptoms to severe pneumonia, acute respiratory distress syndrome (ARDS), and multiple organ failure.[8]

The gold standard for COVID-19 diagnosis is RT-PCR testing using nasopharyngeal and oropharyngeal swabs; however, due to the variable sensitivity of this test and rates of false negative results, the diagnostic value of imaging methods has come to the fore.[5,6] In this context, chest CT is recognized as a superior method compared to chest X-rays for the diagnosis and severity assessment of COVID-19 pneumonia.[7] While factors such as advanced age, male gender, obesity, and comorbid chronic diseases have been identified as factors negatively affecting the clinical course of the disease,[8] research has begun to investigate the effects of genetic markers, such as blood type, on disease severity in order to fully explain inter-individual differences in prognosis.[9,10]

Our study examined the relationship between the severity of pneumonia and blood groups in patients diagnosed with

Table 2. The relationship between blood groups and certain characteristics of the cases

Characteristics	Group O n (%)	Group A n (%)	Group B n (%)	Group AB n (%)	p-value*
Gender					
Male	25 (50)	46 (43.8)	13 (50)	9 (56.3)	0.741
Female	25 (50)	59 (56.2)	13 (50)	7 (43.8)	
Follow-up result					
Discharge	48 (96)	97 (92.4)	23 (88.5)	15 (93.8)	0.688
Death	2 (4)	8 (7.6)	3 (11.5)	1 (6.3)	
COVID severity at CT (n=190)					
Non-COVID	8 (17)	7 (6.7)	2 (8.3)	4 (26.7)	0.200
Mild and moderate	19 (40.4)	53 (51)	10 (41.7)	5 (33.3)	
Severe and very severe	20 (42.6)	44 (42.3)	12 (50)	6 (40)	
Need for HFNO during inpatient follow-up (n=145)					
No	36 (97.3)	71 (95.9)	21 (95.5)	11 (91.7)	0.865
Yes	1 (2.7)	3 (4.1)	1 (4.5)	1 (8.3)	
ICU admission during follow-up (n=156)					
No	33 (86.8)	70 (86.4)	18 (81.8)	11 (73.3)	0.584
Yes	5 (13.2)	11 (13.6)	4 (18.2)	4 (26.7)	
IMV (n=129)					
No	34 (100)	57 (90.5)	18 (85.7)	9 (81.8)	0.141
Yes	0 (0)	6 (9.5)	3 (14.3)	2 (18.2)	
NIMV (n=135)					
No	32 (91.4)	54 (80.6)	18 (85.7)	8 (66.7)	0.221
Yes	3 (8.6)	13 (19.4)	3 (14.3)	4 (33.3)	
Elevation of liver function tests during follow-up					
No	42 (84)	87 (82.9)	16 (61.5)	13 (81.3)	0.084
Yes	8 (16)	18 (17.1)	10 (38.5)	3 (18.8)	

*p-values were calculated using the appropriate statistical tests. A p-value <0.05 was considered statistically significant. CT: Computed tomography, HFNO: High flow nasal oxygen, IMV: Invasive mechanical ventilation, NIMV: Non-invasive mechanical ventilation

COVID-19. No association was found between radiological severity on chest CT and blood groups or the Rh factor. ICU transfer, need for high-flow oxygen therapy and death during follow-up were significantly more common in the Rh (-) group.

In a study conducted in Turkiye, blood group A was the most common, followed by blood group O, among patients diagnosed with COVID-19.[11] Consistent with the literature, our study demonstrated that the most common blood group among individuals diagnosed with COVID-19 was A Rh(+), followed by O Rh(+).

A study examining the relationship between ABO blood groups and COVID-19 infection reported that individuals with blood group A are more susceptible to the infection, while blood group O may offer protection against it.[9] In a study investigating whether the ABO and Rh blood group systems contribute to susceptibility to COVID-19, no significant differences were observed with respect to ABO blood group.[10] In our study as well, in line with the literature, the highest number of patients was found in the A blood group. Although it has been found that individuals with blood type A are more susceptible to COVID-19 compared to those with blood type O, a study revealed that individuals with blood type A have a lower risk of intubation and death compared to those with blood type O.[12] In a different study, it was reported that individuals with blood type O have a lower risk of severe illness and death compared to other blood groups.[13] In another study by Arent and colleagues,[14] the risk of COVID-19 was found to be higher in individuals with blood type A; additionally, blood type A was found to be more protective against moderate/severe symptoms. Studies in the literature regarding the relationship between COVID-19 and blood type show variability. In our study, however, when the relationship between ABO blood groups and the risk of intubation and death was examined, no significant differences were found among the groups.

In a study examining the Rh factor, it was shown that Rh (-) individuals have a lower risk of infection compared to Rh (+) individuals.[12] This finding was also observed in a study reporting that Rh (+) individuals are more likely to test positive for SARS-CoV-2.[13] The same study reported that being Rh (+) is associated with a higher likelihood of a positive PCR test, as well as higher risks of intubation and death.[13] In another study by Zietz and colleagues,[12] it was shown that COVID-19 patients with the Rh (-) blood type had lower risks of infection, intubation, and death. Similarly, another study demonstrated that individuals with the Rh (-) blood group, particularly those with the O (-) blood group, are less susceptible to SARS-CoV-2 infection.[15] In a different study, no intensive care admissions or mortality were observed in patients with the Rh (-) blood group, while admission rates to the ICU were found to be significantly higher in the Rh (+) group, and no significant association was reported between

Table 3. Relationship between Rh groups and certain characteristics of the cases

Characteristics	Rh (-) group n (%)	Rh (+) group n (%)	p-value*	OR (95% CI)
Gender				
Male	12 (48)	81 (47.1)	1.000	0.96 (0.42-2.23)
Female	13 (52)	91 (52.9)		
Follow-up result				
Discharge	20 (80)	163 (94.8)	0.020*	4.53 (1.38-14.86)
Death	5 (20)	9 (5.2)		
COVID severity at CT (n=190)				
Non-COVID	3 (13)	18 (10.8)	0.273	
Mild and moderate	7 (30.4)	80 (47.9)	0.382	0.53 (0.12-2.23)
Severe and very severe	13 (56.5)	69 (41.3)	0.860	1.13 (0.29-4.40)
Need for HFNO during inpatient follow-up (n=145)				
No	16 (84.2)	123 (97.6)	0.030*	7.69 (1.43-41.4)
Yes	3 (15.8)	3 (2.4)		
ICU admission during follow-up (n=156)				
No	12 (57.1)	120 (88.9)	0.001*	6.00 (2.17-16.60)
Yes	9 (42.9)	15 (11.1)		
IMV (n=129)				
No	12 (80)	106 (93)	0.119	3.31 (0.77-14.19)
Yes	3 (20)	8 (7)		
NIMV (n=135)				
No	13 (81.3)	99 (83.2)	0.736	1.14 (0.30-4.38)
Yes	3 (18.8)	20 (16.8)		
Elevation of liver function tests during follow-up				
No	21 (84)	137 (79.7)	0.790	0.96 (0.42-2.23)
Yes	4 (16)	35 (20.3)		

*Chi-square test, OR: Odds ratio, CT: Computed tomography, CI: Confidence interval, HFNO: High flow nasal oxygen, ICU: Intensive care unit, IMV: Invasive mechanical ventilation, NIMV: Non-invasive mechanical ventilation

mortality and Rh antigens.[11] Similar results were obtained in another study, which demonstrated that the Rh (-) blood group is protective, while the Rh (+) blood group is significantly more susceptible to COVID-19.[10] Ray and colleagues[15] reported that the Rh (-) blood group is associated with a lower risk of developing severe COVID-19 infection, suggesting that the Rh (-) blood group may have a protective effect against severe SARS-CoV-2 disease. A separate study by Zietz and colleagues[12] reported similar findings, concluding that COVID-19 patients with a negative Rh factor had a lower likelihood of developing infection, requiring intubation, or dying. In another study examining the relationship between the ABO and Rh blood group systems and COVID-19, it was determined that the Rh factor plays a role in the severity of COVID-19 infection, and it was reported that Rh (+) individuals are more prone to severe infection and complications.[16]

In our study, blood groups and Rh factor were not significantly associated with radiological or clinical severity of COVID-19 pneumonia. To the best of our knowledge, this is the first study to evaluate this relationship. However, the need for high-flow oxygen therapy and ICU transfer was significantly higher in the Rh (-) group.

However, the proportion of patients requiring high-flow oxygen therapy during their hospital stay and the rates of transfer to the ICU during follow-up were found to be significantly higher in the Rh (-) group. In the evaluation based on clinical follow-up results, while no significant difference was observed in mortality rates between the two groups according to blood groups, we found that mortality rates were higher in the Rh (-) group.

Limitations

The main limitation of our study is its retrospective design and the small study population. One of the limitation was that formally validated CT severity scoring system (e.g., CT-SS, CO-RADS, or the RSNA expert consensus classification) was not applied, as the study was designed and conducted during the early pandemic period (2020), when these standardized tools were either newly introduced or not yet widely adopted in our center. Given the retrospective nature of the study and the reliance on electronic patient records, formal blinding of radiological readers to clinical data was not feasible.

A key limitation of this study is that, due to the small sample size, it was not possible to perform a fully adjusted multivariate logistic regression analysis; therefore, the association between the Rh factor and clinical outcomes should not be interpreted independently of potential confounding variables. Although the differences observed between the Rh(-) and Rh(+) groups in terms of HFNO requirements, ICU admissions and mortality rates were statistically significant, these findings must be interpreted with caution given the limited sample size. This is one of the limitations of the study.

Another drawback of our study is that only inpatients were included. Prospective studies with larger populations would be more valuable.

CONCLUSION

This study found no statistically significant association between ABO blood group distribution and the radiological severity of COVID-19 pneumonia on chest CT. However, Rh(-) blood type was associated with significantly higher rates of high-flow nasal oxygen requirement, ICU admission, and in-hospital mortality compared to Rh(+) blood type. These findings suggest a potential prognostic role for the Rh factor in COVID-19 clinical outcomes, though the small Rh(-) subgroup size necessitates cautious interpretation. These results are in contrast to the majority of published studies that report a protective effect of Rh(-) blood type, underscoring the importance of larger, prospective, multicenter studies-ideally with multivariable adjustment-to definitively characterize the relationship between blood group systems and COVID-19 severity.

Our study is the first in the literature examining the relationship between blood type and the severity of COVID-19 pneumonia radiologically and clinically. However, we believe that further studies in larger populations are needed in this regard. There is a need for recent studies examining blood group associations in the context of current variants and post-vaccination populations.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of the Ethics Committee for Non-interventional Clinical Researches at Kütahya University of Health Sciences (Date: 17.09.2020, Decision No: 2020/14).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained. This retrospective study used pre-existing anonymized patient data. No additional intervention was performed, and there was no direct patient contact. The study was approved by the Ethics Committee, and the requirement for written informed consent was waived by the ethics committee.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

Concept: ÜE, ŞEP, FM, DU; Design: ÜE, ŞEP; Control: ÜE, İK; Data Collection and/or Processing: İK, ŞEP, FM, ÖFT; Analysis and/or Interpretation: ÜE, İK, ÖFT; Literature Review: İK, FT, ZYYT; Article Writing: ÜE, İK; Critical Review: All Authors.

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