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Use of ABO blood groups and co-morbidities as predictors of mortality in COVID-19 patients

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Abstract. – OBJECTIVE: This study aimed to investigate the mortality relationship between COVID-19 and ABO blood groups and comorbid diseases. The aim of this study was to determine whether ABO blood groups and comorbid diseases can be used as a prognostic factor for hospitalization.

PATIENTS AND METHODS: This retrospective study included patients aged ≥ 18 years presenting to the adult emergency COVID-19 outpatient clinic. COVID-19 patients were divided into four stages according to their clinical status: mild, moderate, severe, and critical. Those with the comorbid disease were classified as Group I, and those without comorbid disease were classified as Group II.

RESULTS: Of the 384 patients included in the study, 190 (49.5%) were male and 194 (50.5%) were female, with a mean age of 47.3 ± 18.4 years. The clinical data of the patients were scanned from the hospital automation system. Although the risk of transmission was higher, especially in people with A blood type, this rate was lower in the O blood group. The clinical course of the disease was more severe and the mortality rates were higher in the AB blood group ($p < 0.001$). In the hospital, 35 people who were treated for COVID-19 disease died.

CONCLUSIONS: Certain ABO blood types and comorbid diseases were important risk factors for COVID-19 and were associated with mortality. We found that some ABO blood groups and comorbid diseases are associated with COVID-19 and may be important risk factors. While the risk of transmission of COVID-19 is high in blood group A, we think that the clinical course of COVID-19 may be more severe and the death rate higher in blood group AB.

Key Words:
COVID-19, ABO blood groups, Comorbid diseases, Mortality.

Introduction

The new coronavirus disease (COVID-19) continues to spread rapidly around the world despite many preventive measures. According to the WHO's COVID-19 pandemic data, as of May 1, 2021, over 153 million confirmed cases and 3.2 million associated deaths have been reported[1]. To date, the lack of any drug treatment that could be effective for COVID-19 has led to high mortality rates. The causes of the high mortality rates because of COVID-19 are currently being investigated. In most patients, the clinical course is mild or moderate, while in 5% of patients, it is more severe, and these patients may develop respiratory failure, kidney failure, sepsis, or multiple organ failure[2]. The hypoxic state that develops as a result of lung damage and respiratory failure causes worsening of the clinical course of the disease and mortality as a result of multi-organ failure in these patients[3].

Important known risk factors for COVID-19 are age, smoking, diabetes, hypertension, and chronic cardiovascular and respiratory diseases[4-6]. Many studies[7-9] have been conducted investigating the existence of a relationship between ABO blood groups and COVID-19 disease. While some studies[7] stated that the risk of transmission, clinical course, and death was significant, some studies[8,9] reported no significant relationship.

Especially in some COVID-19 patients, the clinical course progresses, and these patients may die within a few days. Can some known types of ABO blood group and comorbid diseases help predict the prognosis of COVID-19? If this patient group is followed and treated more carefully, it can contribute to the recovery of patients. It would be meaningful to investigate this issue. We aimed to examine the relationship between COVID-19 and ABO blood groups and comorbid diseases and to investigate their effects on mortality. We investigated whether ABO blood groups and comorbid diseases could be prognostic markers for COVID-19.

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Patients and Methods

Study Design and Clinical Severity Classification of COVID-19

We applied PCR tests to patients whose clinical status was compatible with COVID-19 and who had symptoms. The first positive or the first negative test was selected in people who had over one test during the disease period. We performed chest tomography on patients with rales, Rhonchus, decreased breath sounds, and shortness of breath on physical examination. Based on the clinical status of the patients, FM findings, and lung involvement in chest computed tomography (CT), we divided the patients into four stages: mild, moderate, severe, and critical.

Stage I (Mild Type)

Pulmonary examination was normal in patients with a good general condition and symptoms, such as headache, sore throat, dry cough, subfebrile fever, and malaise. The patient did not require a chest CT scan. We isolated the patients from their homes.

Stage II (Intermediate Type)

Patients had COVID-19, rail, and ronkus on FM in their clinic. Chest CTs were consistent with those of mild pneumonia. These patients were admitted to wards reserved for COVID-19 patients at the hospital.

Stage III (Severe Type)

The general condition of the patients was serious, and there was respiratory distress in their clinics. The respiratory rate was ≥ 30 breaths/min, oxygen saturation in room air was ≤93%, and partial pressure of oxygen/fraction of inspired oxygen (PaO_2 / FiO_2) < 300 mmHg. Chest CT showed lung involvement in many foci and areas compatible with pneumonia. While these patients were first treated in the wards, they were transferred to the ICU after their clinical conditions deteriorated.

Stage IV (Critical Type)

Respiratory failure requiring mechanical ventilation (respiratory rate ≥ 35 breaths/min, oxygen saturation <90% in room air, PaO_2 / FiO_2 <200 mmHg), shock, and other organ failures. We admitted these patients to the ICU.

Comorbid Disease Condition

We divided the patients into two groups according to whether or not they had comorbid diseases. Those with comorbid diseases were classified as Group I, and those without comorbid diseases were classified as Group II.

This single-center retrospective study was conducted at the Van Yuzuncu Yil University Faculty of Medicine Hospital between March 1 and October 31, 2020. Patients aged ≥ 18 years who visited the adult emergency COVID-19 outpatient clinic were included in the study. We excluded patients younger than 18 years of age and whose blood groups were unknown from the study. The clinical data of the patients were scanned from the hospital automation system. Vaccine application data were got from the e-nabız application of the Ministry of Health of the Republic of Turkey.

The clinical prognosis worsens as the clinical course of the COVID-19 progress from stage I to IV according to the severity of the disease. The distribution of ABO blood groups according to the disease stage of COVID-19 and their relationship with clinical prognosis and mortality were investigated. The presence of comorbid diseases, their effects on the clinical prognosis of COVID-19, and their relationship with mortality were investigated.

This study was conducted following the principles of the Declaration of Helsinki principles. This study was approved by the Ministry of Health of the Republic of Turkey (2020-05-15T09_06_00) and the University Ethics Board (B.30.2. YYU0.01.00.00/93, 06.24.2020).

Statistical Analysis

Descriptive statistics for continuous variables are expressed as mean ± standard deviation, while categorical variables are expressed as numbers and percentages. One-way analysis of variance was used to compare group averages in terms of continuous variables. Duncan's multiple comparison tests were used to determine the different groups after the analysis of variance. The chi-squared test was used to determine the relationship between the groups and categorical variables. The statistical significance level was set at 5% in the calculations, and the SPSS statistical package program (Armonk, NY, USA) was used in the calculations. The value of $p < 0.05$ is considered statistically significant.

Results

Of the 384 patients included in the study, 190 (49.5%) were male and 194 (50.5%) were female, with a mean age of 47.3 ± 18.4 years. The mean age

Table I. According to the gender of the patients; distribution of blood types, PCR test results, and hospitalization services.

		Male n, (%)	Female n, (%)	Total n, (%)
Number of patients		190, 49.5%	194, 50.5%	384, 100.0%
Blood Groups	A	96, 25.0%	89, 23.2%	185, 48.2%
	B	25, 6.5%	34, 8.9%	59, 15.4%
	O	66, 17.2%	69, 18.0%	135, 35.2%
	AB	3, 0.8%	2, 0.5%	5, 1.3%
PCR Test	Positive	58, 15.1%	42, 10.9%	100, 26.0%
	Negative	103, 26.9%	113, 29.4%	216, 56.3%
	Not tested	29, 7.6%	39, 10.2%	68, 17.7%
Hospitalized Service	ICU	27, 7.0%	21, 5.5%	48, 12.5%
	Service- ICU	13, 3.4%	10, 2.6%	23, 6.0%
	Service	65, 16.9%	69, 18.0%	134, 34.9%
Isolation at home		85, 22.1%	94, 24.5%	179, 46.6%

Abbreviations: PCR: Polymerase Chain Reaction, ICU: Intensive Care Unit.
Service-ICU: Patients admitted to the intensive care unit due to worsening of their condition.

of the patients admitted to the ICU was 67.2 ±13.1 years, the median age was 71 years, and the ICU stay was 12.2 ± 14.4 days. According to the sex of the patients included in the study, the distribution of blood groups, PCR test results, and hospitalized services is shown in Table I. In our COVID-19 patients, the relationship between ABO blood groups and clinical severity of the disease, recovery, and mortality rates was significant ($p<0.001$). When we examined our COVID-19 patients according to ABO blood groups, the transmission rates were higher, especially in people with A blood type, while this rate was lower in people with the O blood group. The clinical course of the disease and the mortality rates were significant in COVID-19 patients ($p<0.001$). The relationship between ABO blood groups and mortality according to the clinical stages of COVID-19 (I-II-III and IV) is shown in Table II. The total number of patients who died of COVID-19 was 48. While 35 (9.1%) of these deceased patients were being treated in the hospital, 13 (3.4%) died for another reason after being transferred to another center or discharged. The recovery and death rates of patients with COVID-19 according to ABO blood groups and hospitalized wards are shown in Table III. There was a significant correlation between PCR positivity and mortality in COVID-19 patients with comorbid diseases. The recovery and mortality rates according to lung involvement and PCR test in COVID-19 patients are shown in Table IV. In our study, the most common comorbid diseases accompanying COVID-19 patients were, in order of frequency: diabetes mellitus 44 (11.5%), hypertension 35 (9.1%), cancer 35 (9.1%), chronic obstructive pulmonary disease 20 (5.2%), heart failure 10 (2.6%).

Discussion

The coronavirus disease (COVID-19) pandemic has resulted in a very high number of deaths. The most important findings of this study were a significant relationship between COVID-19 and ABO blood groups, comorbid diseases, PCR test positivity, lung involvement in lung CT and mortality ($p<0.001$). People with blood group A had a higher risk of contracting COVID-19, whereas those in the O blood group had a lower risk of contracting COVID-19. We found that the mortality rate because of COVID-19 was higher in the AB blood group.

Many studies[7-9] have investigated the relationship between COVID-19 and blood types. One study compared COVID-19 patients to a healthy control group. It was found to be 57% in the A blood type, 38% in the control group, 24.8% in the O blood type, and 37.2% in the control group in COVID-19 patients ($p<0.001$)[10]. They found that people with blood type A had a high risk of COVID-19 and people with blood type O had a low risk of the disease[10,11]. In another study[12] of 187 COVID-19 patients, the distribution of ABO by blood groups was: A 69 (36.90%), B 63 (33.69%), O 41 (21.92%), and AB 14 (7.49%). A blood group was the most common, AB blood group was the least. Another study[13] found that people with blood type O had a significantly lower risk of contracting COVID-19. In a study investigating the relationship between ABO blood groups and the clinical course, severity, and mortality of COVID-19, the risk of hospitalization of COVID-19 patients was evaluated, and it was found that this rate was higher in in-

Table II. Distribution of ABO blood groups according to COVID 19 clinical stages I-II-III and IV, their relationship with recovery and mortality.

COVID-19 clinical situations		Blood Groups				Total (n, %)	*p*-value
		A (n, %)	B (n, %)	0 (n, %)	AB (n, %)		
Stage I	Recovering	78, 20.3%	35, 9.1%	63, 16.4%	0, 0.0%	176, 5.8%	0.001*
	Deaths	3, 0.8%	0, 0.0%	0, 0.0%	0, 0.0%	3, 0.8%	
	Total	81, 21.1%	35, 9.1%	63, 16.4%	0, 0.0%	179, 46.6%	
Stage II	Recovering	58, 15.1%	17, 4.4%	53, 13.8%	0, 0.0%	128, 33.3%	
	Deaths	4, 1.0%	1, 0.3%	1, 0.3%	0, 0.0%	6, 1.6%	
	Total	62, 16.2%	18, 4.7%	54, 14.1%	0, 0.0%	134, 34.9%	
Stage III	Recovering	8, 2.0%	0, 0.0	1, 0.3%	1, 0.3%	10, 2.6%	
	Deaths	9, 2.3%	2, 0.5%	2, 0.5%	0, 0.0%	13, 3.4%	
	Total	17, 4.4%	2, 0.5%	3, 0.8%	1, 0.3%	23, 6.0%	
Stage IV	Recovering	11, 2.9%	2, 0.5%	9, 2.3%	0, 0.0%	22, 5.8%	
	Deaths	14, 3.7%	2, 0.5%	6, 1.6%	4, 1.0%	26, 6.8%	
	Total	25, 6.5%	4, 1.0%	15, 3.9%	4, 1.0%	48, 12.5%	

*Statistically significant at 5% level of significance.

dividuals with blood group A[14]. In a study conducted in Wuhan, the distribution of 206 patients who died of COVID-19 by A, B, AB, and O blood types was determined to be 41.3%, 24.3%, 9.2%, and 25.2%. Those with blood type A had a higher risk of death, whereas those with blood type AB had a lower risk of death[15]. In their meta-analysis, they investigated whether there was an association between ABO blood types and COVID-19 disease in terms of risk of infection, intubation, and death. They found that people with blood type A have a higher risk of contracting COVID-19, whereas people with blood type O have a lower risk of contracting COVID-19[16,17]. In the studies we have examined, COVID-19 is most common in people with blood type A. In some studies, the O blood group was the least common, while in others, the AB blood group was the least common. The blood group with the highest incidence in the community was group A. Therefore, COVID-19 was most commonly seen in group A. In our study, the transmission of COVID-19 was most common in blood group A and at least in blood group O. However, deaths because of COVID-19 were the most common in blood group AB and the second most common death in blood group A. The reason for the difference in the results is the low incidence of AB in the general population. Deaths because of COVID-19 should be calculated based on the number of patients in each blood group. Therefore, the result was low when the total number of patients included in the study was compared with those in the AB blood group. Therefore, we believe they have made errors in the calculations. In our study, there were five patients with AB blood type, and all of

Table III. The recovery and death rates of patients with COVID-19 by ABO blood groups and hospitalized wards.

		In the same blood group			In all patients		*p*-value
		Recovering (%)	Deaths (%)	Total (%)	Recovering (%)	Deaths (%)	
ABO Blood Groups	A	155, 83.8%	30, 16.2%	185, 100%	40.4%	7.8%	0.001*
	B	54, 91.5%	5, 8.5%	59, %100	14.1%	1.3%	
	0	126, 93.3%	9, 6.7%	135, 100%	32.8%	2.3%	
	AB	1, 20.0%	4, 80.0%	5, 100%	0.3%	1.0%	
Hospitalized	ICU	22, 45.8%	26, 54.2%	48, %100	5.7%	6.8%	0.001*
	ICU-SERVICE	10, 43.5%	13, 56.5%	23, 100%	2.6%	3.4%	
	SERVICE	128, 95.5%	6, 4.5%	134, 100%	33.3%	1.6%	
Outpatient		176, 98.3%	3, 1.7%	179, 100%	45.8%	0.8%	
	Total	336, 87.5%	48, 12.5%	384, 100%	87.5%	12.5%	

Abbrevations: ICU-Service: Patients admitted to the intensive care unit due to worsening of their condition.
ICU: Intensive Care Unit, *Statistically significant at 5% level of significance.

Table IV. Recovery and mortality rates according to lung involvement and PCR test in COVID-19 patients.

		Recovering (n=336, %)	Ex (n=48, %)	Total (n=384, %)	*p*-value
CHEST CT	Lung involvement (+)	118, 30.7%	43, 11.2%	161, 41.9%	0.001*
	Lung involvement (-)	153, 39.8%	4, 8.3%	157, 40.9%	
	No chest CT	65, 16.9%	1, 0.3%	66, 17.2%	
PCR TEST	Positive	77, 20.1%	23, 6.0%	100, 26.0%	0.001*
	Negative	191, 49.7%	25, 6.5%	216, 56.3%	
	Not tested	68, 17.7%	0, 0.0%	68, 17.7%	
Total		336, 100.0%	48, 100.0%	384, 100.0%	

Abbreviations: CT: Computed Tomography, PCR: Polymerase Chain Reaction.
*Statistically significant at 5% level of significance.

them were admitted to the ICU. Only one person recovered and four people died. There are also studies in which different results have been got.

In a multicenter retrospective study, they examined 1,289 patients who tested positive for COVID-19. The distribution of patients according to blood group was as follows: blood group A, 440 (34.2%); blood group B, 201 (15.6%); blood group AB, 61 (4.7%); and blood group O, 587 (45.5%). However, in this study, no significant relationship was found between the ABO blood group and the clinical course of COVID-19, especially in terms of intubation and mortality. Unlike other studies, they found that people with O blood type were more likely to develop COVID-19 (45.5%)[8]. However, they determined that people with blood type A had a lower risk of both intubation and death than those with blood type O. They also found that people with the AB blood type had a higher risk of both intubation and death. Individuals with type B blood have a higher risk of intubation and a lower risk of death[16]. In this study, the course of COVID-19 in people with A and O blood groups represents a situation contrary to the existing literature[8]. The clinical course of COVID-19, especially in people with AB blood groups, differs from that reported in the literature. A meta-analysis by Wu et al[11] found that the prognosis of COVID-19 is more severe in individuals with the AB blood type. In these studies, the clinical course of COVID-19 was more severe, and the mortality rate was higher, especially in the AB blood group, which supports our results. In our study, the distribution of deaths caused by COVID-19 according to blood groups and the number of people in each blood group are as follows. A Blood group 30/185 (16.2%), B blood group 5/59 (8.5%), O blood group 9/135 (6.7%), and AB blood group 4/5 (80%).

The clinical course may be more severe in COVID-19 patients with comorbid diseases, and mortality rates may increase in these individuals. In a study conducted in Wuhan, China, 51% of 99 patients with COVID-19 were diagnosed with chronic diseases. Death has occurred in some patients because of the development of acute respiratory distress syndrome (ARDS), acute respiratory failure, and other serious complications[18]. In another study[19], the rate of people with one or more chronic diseases, such as chronic lung disease, diabetes mellitus, cardiovascular disease, cerebrovascular disease, kidney disease, and obesity, was found to be 79% among people with COVID-19. The Chinese Centers for Disease Control and Prevention reported an overall case fatality rate of 2.3% in 44,672 patients who were positive for COVID-19. The most common accompanying chronic diseases were cardiovascular disease 10.5%, diabetes 7.3%, and hypertension 6%, which were higher[2]. In Italy, Nevola et al[20] the most common comorbid diseases in their study are hypertension 55.8%, type 2 diabetes 2%, chronic renal failure 36.5%, COPD 14.9%, ischemic heart disease 19.9% , and active neoplasia (3.8%). In our study, the most common chronic diseases were diabetes mellitus (11%), cancer (9.4%), CVD (8.9%), and COPD (7.6%). We found a correlation between COVID-19 and comorbid diseases, with the clinical course of the disease and mortality rates.

Limitations

We did not study the Rh factor in the ABO blood groups of patients included in the study. The low number of patients with AB blood group in the total number of patients included in the study.

Conclusions

According to our results, the risk of contracting COVID-19 was higher in people with blood type A, while it was lower in people with blood type O. Although the number of people with AB blood type in society is small, according to our data, the clinical course of COVID-19 was more severe and the mortality rate was higher in people with AB blood type. People with blood type A had the second-highest death rate. We found that the clinical course of COVID-19 in COVID-19 patients with comorbid diseases is severe and associated with higher mortality. Therefore, we think that ABO blood groups and comorbid diseases can be used as prognostic markers for COVID-19.

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Conflict of Interest

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

Ethics Approval

This study was conducted in accordance with the Declaration of Helsinki principles. For this study, the Ministry of Health of the Republic of Turkey (2020-05-15T09_06_00) and the University Ethics Board (B.30.2.YYU0.01.00.00/93, 06.24.2020) approval received.

Informed Consent

The patients were informed and consent was obtained.

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