

## RESEARCH ARTICLE

# SARS-CoV-2 and mutation RT-qPCR test positivity correlation with ABO and Rh blood types

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**Abstract**

Studies show that there may be a relationship between ABO blood type and SARS-CoV-2 transmission. It was aimed to determine by investigating the blood type of patients whose one-step reverse transcription and real-time polymerase chain reaction (RT-qPCR) test were positive for SARS-CoV-2. ABO and Rh blood types of individuals whose RT-qPCR test was positive for SARS-CoV-2 were examined and an evaluation was made to identify whether there was a relationship between them or not. The blood type data of 44,928 SARS-CoV-2 positive RT-qPCR test results have been obtained. 17,656 (39.29%) were delta, 8048 (17.91%) were alpha, 800 (1.78%) were beta, and 3000 (6.67%) were omicrons while 15,424 (34.33%) SARS-CoV-2 positive mutation was found to be negative. Our study suggests that O and Rh (-) blood types may provide protection against delta, AB and Rh (+) blood types may hinder omicron infection while A and Rh (+) blood types may be more vulnerable to alpha and delta while B and Rh (+) are more sensitive to beta mutation. The molecular mechanism underlying the relationship between blood types and SARS-CoV-2 infection needs further molecular studies and multi-centered studies.

**Keywords**

ABO blood type, COVID-19, Rh blood type, RT-qPCR, Sars-CoV-2

## 1 | INTRODUCTION

The virus named SARS-CoV-2 by the World Health Organization (WHO) due to its resemblance to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) caused a global pandemic. This disease which constitutes a pandemic has been termed as Coronavirus disease-2019 (COVID-19) by WHO.<sup>1,2</sup> Although the pathogenesis of COVID-19 and the associated respiratory failure are not fully understood, risk factors for hypertension, diabetes, obesity, and cardiovascular diseases have been reported as well as advanced age and male gender.<sup>3,4</sup>

Blood group antigens can provide a protective effect against infectious organisms by trapping them through receptors or altering the immune response in the form of anti-ABO antibodies.<sup>5,6</sup> In a study, it was shown that although the rosette of *Plasmodium falciparum* isolates decreased in individuals belonging to blood type

O, erythrocytes adhered to the vascular endothelium by being infected rapidly and caused severe damage due to vaso-occlusion in individuals other than blood group O.<sup>7</sup> In another study, it was shown that individuals of blood type O were infected with a high rate of *Vibrio cholerae* strains.<sup>8</sup> Data from the 2003 SARS-CoV-1 outbreak showed that healthcare workers with blood type O were less likely to develop this disease.<sup>9</sup> In the literature, there are studies showing that patients with blood type O phenotype can be protected from COVID-19 infection whereas individuals with A blood type may be at higher risk as well as studies showing that there is no relationship with blood types.<sup>10-14</sup> However, ABO blood type is known to be associated with angiotensin-converting enzyme (ACE) activity and response in cases with essential hypertension. It is understood that patients with COVID-19 are encoded by two different genetic clusters which include ACE-2 receptor function, immune system, and ABO blood type.<sup>15</sup> Blood types other than O have increased ACE

activity and more risk of cardiovascular disease (hypertension) while blood type O samples have lower ACE levels and a lower risk of cardiovascular disease.<sup>11</sup>

The A allele of ABO blood type has been associated with an increased risk of developing cardiovascular disease as reported in several studies. Antigen A can protect P-selectin and intracellular adhesion molecule-1 from enzymatic cleavage by promoting stronger and longer binding of leukocytes to them on the vessel wall. More adhesion molecules attached to endothelial cells increase adhesion and inflammation while decreasing circulation. As a result, individuals with blood type A are more likely to develop cardiovascular diseases and predisposition to coagulation when exposed to stresses such as viral infection.<sup>16</sup> In this study, it was aimed to determine the relationship between ABO blood type differences and PCR positivity by investigating the blood types of patients whose RT-qPCR test was positive for SARS-CoV-2.

## 2 | MATERIALS AND METHODS

The study was performed by retrospectively scanning the Laboratory Management Information System (LIMS) of the General Directorate of Public Health after obtaining the approval of permission from Ankara Yıldırım Beyazıt University Yenimahalle Training and Research Hospital Ethics Committee (Date: April 13, 2022 and Decision No: 2022-23). The study was in accordance with the Declaration of Helsinki and its later amendments as revised in 2013. Our study was carried out between August 1, 2021 and December 31, 2021 on the samples brought to Ankara Provincial Health Directorate Molecular Diagnosis Laboratory by the contact tracing teams. ABO and Rh (D) blood types of individuals whose RT-qPCR test was positive for SARS-CoV-2 with the Bio-Speedy SARS-CoV-2 Emerging Plus kit were investigated and a retrospective evaluation was made to determine whether there was a relationship between them or not. The inclusion criteria of the study were adult age groups ( $65 \geq$  and  $\geq 18$  years of age) and all patient groups except pregnancy. SARS-CoV-2 mutation results of 44 928 cases with positive SARS-CoV-2 RT-qPCR and ABO blood type data of these cases were scanned via LIMS.

## 2.1 | Statistical analysis

SPSS v23 software was used for statistical analysis. Blood types and SARS-CoV-2 positivity rates were evaluated using the crosstab. Differences between the mutation groups were compared using the  $\chi^2$  and Fisher tests. Mutation rates based on blood types were evaluated with the binomial test. Cases, where the  $p$  value was below 0.05, were considered statistically significant.

## 3 | RESULTS

Blood type information of 44.928 SARS-CoV-2 positive RT-qPCR test results between August 1, 2021 and December 31, 2021 was obtained from LIMS. 59.69% ( $n = 26.820$ ) of the patients were female and 40.31% ( $n = 18.108$ ) of the patients were male while the mean age was  $63.6 \pm 14.4$  years. Of these positive results, 17.656 (39.29%) were delta mutation, 8048 (17.91%) were alpha mutation, 800 (1.78%) were beta mutation, 3000 (6.67%) were omicron mutation while 15.424 (34.33%) was SARS-CoV-2 positive mutation-negative. ABO and Rh (D) blood type distribution of the patients' age, gender, and RT-qPCR test SARS-CoV-2 mutation results are provided in Table 1. ABO and Rh (D) blood type percentages of healthy blood donors in Ankara and Turkey along with the percentages of ABO and Rh (D) blood types whose RT-qPCR test was positive for SARS-CoV-2 in our study are given in Table 2 together with the literature review.<sup>17,18</sup>

In our study, it was observed that type A blood has the most SARS-CoV-2 mutation positivity in the distribution of SARS-CoV-2 positive mutation rates according to blood types since it was the most common blood type in our country. In addition, although the AB blood type is the least common blood type in our country, the rate of positivity increased rapidly as the L452R mutation became widespread. The positivity of the second common blood type in our country, O type, started to decrease as the L452 mutation became widespread. The SARS-CoV-2 positivity rate of Rh (D) (+) blood type increased in alpha mutation. SARS-CoV-2 positivity of the Rh (D) (-) blood type is more common in cases where there is no mutation.

**TABLE 1** ABO and Rh (D) blood type distribution of RT- qPCR test SARS-CoV-2 mutation results

Mutation	ABO blood type												
	Total	A		B		O		AB		Rh+		Rh-	
		n	%	n	%	n	%	n	%	n	%	n	%
Positive	29 504	13 196	44.72%	6498	22.02%	5859	19.85%	3951	13.39%	20 525	69.56%	8979	30.43%
Alpha	8048	4040	50.20%	1528	18.99%	1640	20.38%	840	10.44%	6496	80.72%	1552	19.28%
Beta	800	248	31.00%	304	38.00%	160	20.00%	88	11.00%	704	88.00%	96	12.00%
Delta	17 656	7664	43.41%	3848	21.79%	3448	19.53%	2696	15.27%	10 857	61.49%	6799	38.51%
Omicron	3000	1244	41.47%	818	27.27%	611	20.37%	327	10.90%	2468	82.27%	532	17.73%
Negative	15 424	6074	39.38%	4032	26.14%	2933	19.02%	2385	15.46%	9376	60.79%	6048	39.21%

Region	Reference	A (%)	B (%)	O (%)	AB (%)	Rh+ (%)	Rh- (%)
Ankara	This study	42.89%	23.44%	19.57%	14.10%	66.55%	33.45%
Ankara	17, 18	44.62%	15.45%	32.24%	7.69%	88.13%	11.87%
Turkey	17, 18	41.88%	15.26%	34.92%	7.93%	85.02%	14.98%

**TABLE 2** ABO and Rh (D) blood type percentages of healthy blood donors in Ankara and Turkey, and ABO and Rh (D) blood type percentages whose RT-qPCR test was positive for SARS-CoV-2

## 4 | DISCUSSION

RT-qPCR tests are actively being studied by laboratories determined by the TR Ministry of Health to identify "B.1.1.7 (alpha)", "E484K (beta, gamma, zeta, eta, theta, iota)," "L452R (delta, epsilon, kappa)," and "B.1.1.529 (Omicron)" mutations in SARS-CoV-2 positive patients in our country.<sup>19</sup> Studies show that there may be a relationship between ABO blood type and SARS-CoV-2 transmission as well as risk factors such as age and gender.<sup>2-5</sup> Our study suggests that having O and Rh (D) (-) blood types may be protective in L452 mutation, while A and Rh (D) (+) blood types may be more sensitive to alpha mutation and L452 mutation.

Part of the SARS-CoV spike (S)-1 domain has been found to show a high affinity for ACE-2.<sup>20</sup> Anti-A antibodies have been found to specifically inhibit the adhesion of cells expressing the SARS-CoV S protein to cell lines expressing ACE-2. Guillon et al. determined that blood type O showed lower sensitivity and blood type A showed higher sensitivity considering the nucleic acid sequence similarity and receptor ACE-2 binding similarity between SARS-CoV and SARS-CoV-2.<sup>21</sup>

In a genome study involving de novo genotyping in patients diagnosed with COVID-19, the authors identified two new gene clusters on chromosome 3p21.31. In the same study, it was determined that one of the gene clusters contains genes related to both ACE-2 functionality and immune response, while the other cluster encodes genes for the ABO blood type, confirming the potential effect of the ABO blood type system in COVID-19. Moreover, it was concluded that the 3p21.31 locus in which the human chromosome gene cluster is located, is more prone to COVID-19 sensitivity in individuals with severe disease. Accordingly, it has been found that patients with blood type A have a high COVID-19 risk whereas individuals with blood type O are protected.<sup>15</sup> On the other hand, Boudin et al. detected COVID-19 cases in 76% of 1769 (young and healthy) crew members upon disembarking affected by the epidemic with clinical symptoms and/or polymerase chain reaction test positivity. They stated that there was no significant relationship between SARS-CoV-2 infection and ABO and Rh (D) types.<sup>22</sup>

In the study of Focosi et al., in which they evaluated the seropositivity of SARS-CoV-2 antinucleocapsid immunoglobulin G seropositivity in 7.713 cases including healthy blood donors, they could not detect increased seropositivity in blood type A compared to blood type O. They emphasized that hospital environment contains only the most severe presentations of COVID-19, so results tend to be biased.<sup>23</sup> A limiting factor for our study was the fact that

the samples of individuals with contact or complaints were brought to our laboratory by the contact tracing teams and individuals who were not in contact or had no symptoms were not tested.

Zietz et al. found a higher prevalence between the A and B blood types and lower levels in the AB blood type in a study involving 13,059 patients in the USA when they compared the prevalence of COVID-19 with blood type O. Blood type AB was found to be at high risk for both intubation and death while the risk for both outcomes was lower in blood group A than in type O. Individuals with Rh (-) were at low risk for both intubation and death which is consistent with a lower risk of initial infection.<sup>24</sup> Leaf et al. found the frequency of COVID-19 infection for Caucasians to be higher in blood type A than in blood type O while there is no significant difference in blood types of Hispanics in their study including the intensive care units of 67 hospitals in the USA.<sup>25</sup> Jawdat et al. reported that blood type B is a risk for COVID-19 disease and blood type O may protect from COVID-19 infection in their study.<sup>10</sup>

O and Rh (D) (-) blood types may provide protection against delta mutation, AB and Rh (D) (+) blood types may hinder omicron infection while A and Rh (D) (+) blood types may be more vulnerable to alpha mutation and delta mutation and B and Rh(D) (+) are more sensitive to beta mutation based on the findings of our study.

## 5 | CONCLUSION

In conclusion, although people with all blood types have an equal risk of COVID-19 infection, the molecular mechanism underlying the relationship between blood types and SARS-CoV-2 infection needs further molecular studies and multicenter studies. Further studies are needed to determine the biological mechanisms considering the current findings and other risk factors of blood types.

### AUTHOR CONTRIBUTIONS

Conceptual design, literature survey, data collection, processing, and interpretation are carried out by Burcu Gürer Giray. Gökçe Güven Açıık contributed to literature search. The manuscript was drafted, revised, and edited by Burcu Gürer Giray. All authors read and approved the final manuscript.

### CONFLICT OF INTEREST

The authors declare no conflict of interest.

### DATA AVAILABILITY STATEMENT

Research data are not shared.

## ETHICS STATEMENT

The study was performed by retrospectively scanning the Laboratory Management Information System (LIMS) of the General Directorate of Public Health after obtaining the approval of permission from Ankara Yıldırım Beyazıt University Yenimahalle Training and Research Hospital Ethics Committee (Date: April 13, 2022 and Decision No: 2022-23). The study was conducted in accordance with the Declaration of Helsinki Principles. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki and its later amendments as revised in 2013. Written informed consent was obtained from the parents. The participant has consented to the submission of the case report to the journal.

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