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Blood Type and Susceptibility of SARS-Cov 2 Infection

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Keywords

blood group, SARS-CoV 2 susceptibility, risk of severe COVID-19, blood typing.

Abstract

Introduction. It has been established by various authors that the frequency of distribution of ABO group antigens is directly related to the epidemic, infectious diseases such as plague, cholera, and measles. Epidemics and pandemics alter the genegeography characteristic of blood groups.

Material and methods. We study a total of 447 blood samples, 333 (age range 8-87 years) of which belonged to an infected and post-infected patient with SARS-Cov 2. A healthy control group of 114 individuals was also used for the study. The materials were taken from Kobuleti Central Hospital "Beaumonde" Clinical Laboratory (Adjara Region, Georgia republic, South Caucasus). The study also included volunteers who were infected with SARS-Cov 2 and recovered. Materials were collected in the 28/01/2021- 30/04/2021time interval.

All blood samples were processed on the basis of the Immunogenetics laboratory of the Biology Department of Batumi Shota Rustaveli State University (BSU) and Microbiology Laboratories of BAU Batumi International University (Georgia Republic). We used anti-A, anti-B, and anti-AB monoclonal antibodies for ABO blood typing.

Result. The ABO system blood group is unequally distributed in the control and Sarc-Cov2 infected patients groups. The unequal distribution mainly refers to the O (I) and A (II) groups. The A (II) group is found in the infected patient's group in almost 13.7% more cases than in the healthy control group. O (I) phenotypic group is 16.4% less present in patients compared to the healthy control group (The $\chi 2$ is 9.134. P-value - .027561). The results are significant at $p < .05$.

Conclusion. In the current study, compared with the ABO blood group distribution of healthy controls in the Adjara region (Georgia republic), the SARS-CoV-2 infection rate was higher in the A blood group. O (I) blood group show low susceptibility to SARS-CoV-2 infection. Our results are in agreement with other scientific studies. We think that the results of the study will make a certain contribution to the meta-analysis of this issue.

1. Introduction

Blood group antigens are ancient genetically determined biomarkers, which developed several million years ago. The blood group antigens distribution pattern is not equal for different populations. The different frequencies of these antigens are depending on various environmental factors. Among them, most selectivity factors are infectious diseases caused by several microorganisms and viruses [1].

The blood group antigens are the special carbohydrates or glycoprotein. They are located on the membrane of red blood cells. They play a significant role in the cell's normal physiology and

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pathology [2]. Red blood cell antigens are not primary gene products. The specific glycosyltransferase enzymes are the primary gene products. The glycosyltransferase enzymes take a role in the attachment of different carbohydrate molecules to the primary chain[3][4][5].

It has been established by various authors that the frequency of distribution of ABO antigens is directly related to the epidemic, infectious diseases such as plague, cholera, and measles. Epidemics and pandemics alter the gene geography of blood groups. There were reported that blood group antigens are the cellular receptors for microorganisms and viruses [3][6][7][8][9][10].

The spread of SARS-CoV 2 is a new challenge of the world, which is a respiratory virus that spreads very easily and in some cases has complications that can even be fatal[11][12][13][14][15].The "SARS-CoV-2" virus nameis given by the International Committee on Taxonomy of Viruses [16].

There are potential risk factors that affect susceptibility SARS-CoV-2 infection and Covid-19 disease progression.Numerous medical and sociodemographic risk factors for infection and complicating of Covid-19 disease have been identified[17][18][19][20][21].

Detection of additional risk factors further increased the degree of prevention. Peripheral blood markers, in particular erythrocyte group antigens, are important in this regard.

The current study aims to investigate the relationship between blood groups and the SARS-CoV 2 susceptibility orCovid 19 disease severity.Various studies have shown that the lowest incidence SARS-CoV-2 infection was in people with group O, while in other groups the infection rate was quite high[22].The first similar studies were conducted on the example of the Chinese population. J. Li, X. Wangandand coauthors suggested that A bloodgroup distributionwas higher in the SARS-CoV-2 infected patients than in healthy controls.On the other side theO blood group in patients was lower distributed than in the control groups[23]. The spain population studyshowed amore highrisk ofSARS-CoV 2 infection among A blood group persons than other groups patients.The authors suggestedthatO blood group have protective effect[24].

Similar data was given in the Danish population example. M. B. Barnkob and coauthors identify that ABO blood group antigens are the risk factor for SARS-CoV-2 infection. The total 7422 Danish individuals study shows the reduced prevalence of SARS-CoV-2 infection in the O blood group. On the other side authors not found any relationship between hospitalization or death from COVID-19 and blood group [25].

Canada population study showedanti-A antibodies protective effect against SARS-CoV-2 infection.Data indicate thatCOVID-19 patients with A or AB blood group are at increased risk for mechanical ventilationrequirement than patients with O or Bblood group[26].

The data for Arab Community studyshowedthatSARS-CoV-2 infected persons majority were A blood group and in most cases, the saturation range of oxygen was 90–100%, O blood group persons infected rate was reduced, but on the other side oxygen saturation range were less and equaled 70–80%. The A blood group persons in most cases did not require artificial respiration. Patients who required artificial respiration in most cases were persons with the O blood group. The B blood group patients in the lowest percentage experienced myalgia, they needed more than three weeks to recover. Based on this data O blood group people had a low chance for SARS-CoV-2 infection, but they need more treatment periods in hospital and also artificial respiration is a more needed procedure for them compared to the other blood groups[27].

As already mentioned studies have shown that patients with different blood types have different complications of Covid19 disease. Many studies suggested that blood type may affect the risk of severe COVID-19. 14,112 individuals tested for SARS-CoV-2 from the New York-Presbyterian hospital system were used as study materials for finding possible associations between ABO and Rh blood types and SARS-CoV-2 infection, intubation, and also death. The authors found an increased prevalence of SARS-CoV-2 infection among persons with non-O blood types. The intubation risk was little decreased for persons with A blood

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group and slightly increased in the persons, which have AB and B blood types, compared with O blood type. The study showed also that death risk was increased in persons with AB blood type. The proportion of death was less in A and B blood type cases[23].

However, we also find alternative studies. The study, which looked at 107796 individuals in the USA population, showed that blood types were not correlated with SARS-CoV-2 susceptibility or Covid-19 disease severity. Similarly, B and AB types weren't correlated with worse outcomes compared to O blood type [19].

Similar data are given from Christopher A. Latzandand coauthors [28]. The authors were evaluated the association of hospitalization, intubation, and death with blood type. They did not find an association between ABO blood type and inflammatory markers. There was no correlation between clinical outcomes of the severity of covid19 disease and ABO blood type. Also, ABO blood type was not related to the risk of intubation and/or death in patients with COVID-19.

2. Research materials and methods

We study a total of 447 blood samples, 333 of which belonged to a patient post-infected with SARS-CoV 2. A control group of 114 individuals was also used for the study. People in the control group did not have an infection reported during the study, in most cases, they were in contact with the SARS-CoV 2infected persons (family members, friends, classmates, roommates, and etc.) but they were not infected in the studying period. At the same time, they were not vaccinated.

A large proportion of the studying patients (n = 236) are female, while 98 individuals are male. The materials were taken from Kobuleti Central Hospital "Beaumonde" Clinical Laboratory (Adjara Region, Georgia republic, South Caucasus).

The study also included volunteers who were infected with SARS-CoV-2 and recovered. The age range of the SARS-CoV 2infectedand post infected persons is 8-87 years. Prior to data collection, patients were provided with information about the current study. They were informed of the purpose of the study and substantiated in writing their consent to participate in the study. Materials were collected in the 28/01/2021- 30/04/2021time interval. The research has been duly approved by the research ethics committee from the Batumi Shota Rustaveli State University (BSU).

A special bilingual (Georgian and English) questionnaire was prepared for the patients involved in the study. The questionnaire included various items (name, surname; gender, address; date of birth; personal contact information; height, weight, etc.). Study participants went through the interview phase and at the end of the questionnaire they recorded their writing consent.

All blood samples (patient, control) were processed on the basis of the Immunogeneticslaboratory of the Biology Department of Batumi ShotaRustaveli State University (BSU) and Microbiology Laboratories of BAU, Batumi International University (Georgia Republic).

We used anti-A, anti-B and anti-AB monoclonal antibodies for blood typing(Figure 1).During study we used as forward as reversed immunoserologicalmethods. The principle of the mentioned methods is based on erythrocyte groupspecificantigen-antibody agglutination reaction. Agglutination was assessed with the naked eye, and in some cases there was used the optic microscopy to detect as false as weak agglutinationreaction (Figure 2).

Figure 1.Immunoserological express method used in the study using monoclonal antibodies.

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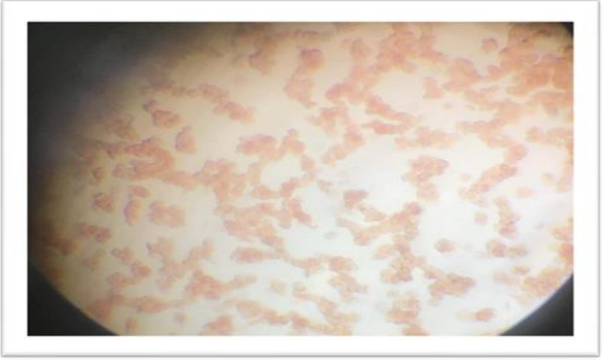


Figure 2. Fixation of agglutination in the field of view of a optic microscope.

3. Results

A. ABO phenotypic group and susceptibility of SARS-Cov 2 infection

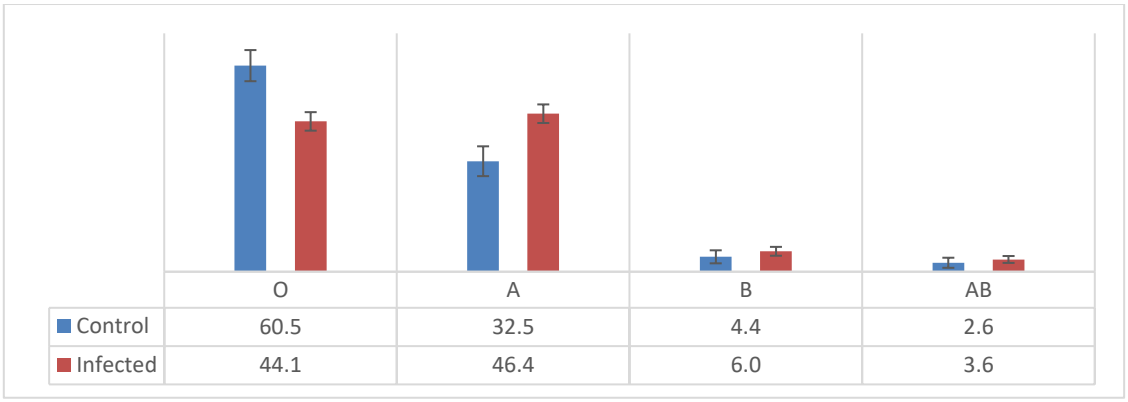
The blood groups of people infected or postinfected with SARS-Cov 2 were studied (n=333). The distribution characteristics of the ABO group system of the infected were compared with the healthy control group involved in the study, which numbered a total of 114 individuals.

The blood group ABO system is unequally distributed in the healthy control and Sarc-Cov2 infected patients group, in particular the distribution of blood group in the SARS-Cov 2 infectedpatient group is as follows: O (I) - 44.1%; A (II) - 46.2%; B (III) - 6% and AB (IV) - 3.6%.

In the control group the prevalence of ABO blood groups are as follows: O (I) - 60.5%; A (II) - 32.5%; B (III) - 4.4% and AB (IV) - 2.6% (Figure 3).

As can be seen from the figure (Figure 3) below, the unequal distribution mainly refers to the O (I) and A (II) phenotypic groups. The A (II) phenotypic group is found in the infected patient's group in almost 13.7% more cases than in the healthy control group. This difference indicates the susceptibility of the A (II) phenotypic group to SARS-CoV 2 infection. We also can say that the A (II) blood group is a high-risk group for SARS-CoV 2 infection.

If we compare the prevalence of the O (I) phenotype in infected and healthy people, we find that they are infected with low frequency. As can be seen from the figure (Figure 3) the O (I) phenotypic group is 16.4% less present in patients compared to the control group, which indicates a low susceptibility to SARS-CoV-2 infection in this blood group.The $\chi 2$is 9.134.P-value - .027561. The results are significant at p <.05.



	O	A	B	AB
Control	60.5	32.5	4.4	2.6
Infected	44.1	46.4	6.0	3.6

*The $\chi 2$is 9.134. P-value - .027561.

Figure 3. Distribution characteristics of the ABO system in the SARS-CoV-2 infected patients and healthy control group.

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B. ABO blood group and Covid-19 disease

We wondered how the phenotypic groups of the ABO system were distributed in mild, moderate, and severe types of Covid-19 disease. In our study, the disease was categorized in 310 patients (23 patients could not be categorized due to incomplete and/or inaccurate data, so their information was not analyzed at this stage).

As can be seen from the figure below (Figure 4), the majority of studying patients (46.1%) are with moderate Covid19 disease, followed by a milder category with 32,8% prevalence. 14.5% of the studying patients are considered severe category patients, some of them needed resuscitation treatment (Figure 4).

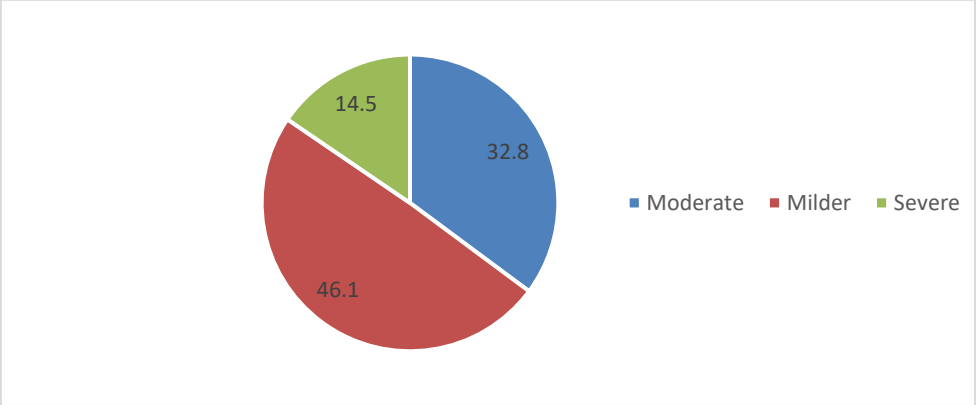

Figure 4.Categorization of patients according to covid-19 disease complexity (n = 310).

If we look at the table below(Table 1) we will see that in moderate, milder, and severe Covid- 19 disease patients the distribution of blood group characteristics is heterogeneous, namely: the distribution of ABO system groups in mild and severe forms is as follows: A> 0> B> AB. In both categories, the highest prevalence has the A (II) phenotypic group. A large proportion of severe patients have blood group characteristics. Based on the total number, their proportion is 7,47 ± 1,5%, which is 3,9% lower than resuscitation patients with 0 (I) blood group. The 0 (I) blood group proportion in the severe category of Covid19 is 3,5 ± 1,0% (Table 1).

Table1. The prevalence of ABO blood group system in mild, moderate, and severe patients

Infected group	Severity of covid 19 disease	Mild	Moderate	Severe
Blood group	O	13,5±1,9	24,8±2,5	3,5±1,0
	A	17,1±2,1	21,9±5,5	7,4±1,5
	B	2,3±0,9	2,3±0,9	1,6±0,5
	AB	2,3±0,9	0,3±0,3	1,0±0,6

*$\chi^2$12.4042; p-value is .053535.

In this case, the $\chi^2$is 12.4042. The p-value is .053535. Which is almost corresponding to the coefficient of confidence p <.05. However, we believe that research in this area should be continued in order to obtain more valid conclusions.

C. Age categorization inSars-Cov 2 infected patients

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Age is known to be one of the risk factors for Sars-cov 2 infection[29][30]. In particular, it is known that the chances of infection and disease complications are high in patients over 60 years of age[26]. It is well known that the immune response varies with age[30][31][32].

We tried to see the peculiarities of blood group redistribution in terms of age. In particular, we have identified patients in two age groups, those ≥ 60 and those ≤60. The number of patients ≥60 is 254, while ≤60 there are 79. A total of 333 individuals were analyzed.

As can be seen from the figure below (Figure 5), the distribution of ABO system antigens is unequally represented in these two groups. An interesting profile is presented in the group of ≤ 60s. In particular, a large part of this group has Ablood group. It is known from the literature that various diseases, especially thromboembolism, are an increase in this group of people, which is one of the main complications for COVID-19 disease. The association is caused by variability in VWF and factor VIII levels according to group affiliation. The number of these plasma proteins responsible for blood clotting increases the risks of thromboembolism. Numerous literature sources indicate that the levels of VWF and VIII factors are significantly higher in the case of group A, especially in other groups, especially in group O[33][34]. The change in this factor also varies with age.

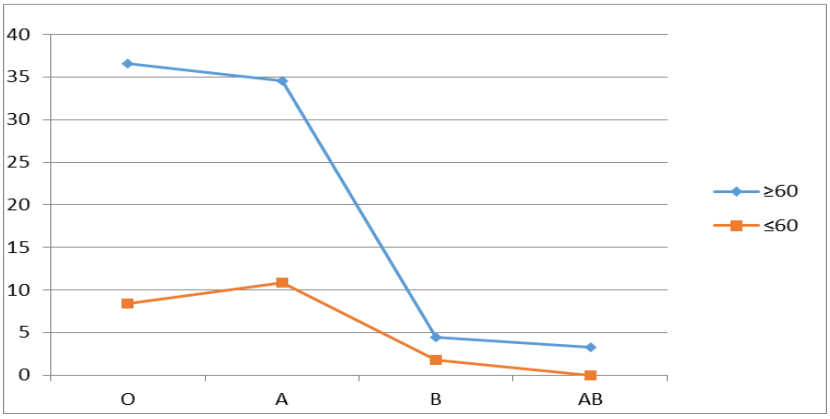

Figure 5.Distribution of ABO system antigens in different age groups.

4. Discussion

The peculiarities of the ABO system phenotypic distribution in the SARS-Cov 2infected patients were also compared with the regional characteristics of Adjara (Georgia republic)[35], As well as we used the data of the blood donors of one of the clinics in the Adjara region [36].

From Table 2 it can be seen the distribution characteristics of the ABO system are unequal in all four groups. The distribution of ABO system groups in all comparable groups (Healthy control, regional distribution, and blood donors) is similar to the O> A> B> AB pattern. Three comparable groups exhibit a more or less similar profile. The difference between the prevalence of phenotypes O and A in all three groups is at least 11% (healthy control - 24.5%, regional distribution - 11.2%, blood donors – 15,37%), while for the infected patient group this profile is slightly different and looks like so: A> O> B> AB. Group A phenotype predominates in the infected group (Table 2). $\chi 2$ statistic is 27.1471. p-value equals .001323. The result is significant at $p < .05$.

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Table 2Distribution of ABO blood group system phenotypes in different groups

Blood group	patients		Control		Regional distribution		Blood donors	
	N	%	N	%	N	%	N	%
O	147	44,1±2,7	69	60,5±4,4	238	47,6±2,2	504	49,95±1,5
A	154	46,2±2,7	37	32,5±4,3	182	36,4±2,1	349	34,58±1,4
B	20	6±1,2	5	4,4±1,8	57	11,4±1,4	109	10,8±0,9
AB	12	3,6±1	3	2,6±1,4	21	4,2±0,8	47	4,6±0,6
Total	n=333	100%	n= 114	100%	n=498	100%	n=1009	100%
$\chi 2$	27.1471							
p-value	.001323							
The result is significant	p <.05.							

An interesting picture is shown according to the distribution characteristics of the A (II) phenotypic group. In all three comparable groups, the prevalence of the A (II) phenotype group is almost identical with 2-4% variations (healthy control - 32.5%, regional distribution - 36.4%, blood donors - 34.58%), while in the infected patient group prevalence of A (II) phenotype is a significant increase and reaches 46.2%.

The prevalence of A (II) Phenotypic group increased by 13.7% times in the infected patient group compared to the healthy control group, 9.8% times increase compared to the regional indicator, and 11.62% times increase compared to the blood donors (Table 1). In all cases, the result is significant at p <.05. The results of our study are consistent with studies in different populations and once again support the view that group O blood group carriage indicates a low chance of Sars-Cov 2 infection, while group A carries are a high risk of infection status [37][38][28][22][23][24][25][26][27].

B (III) blood group distribution is unequal in different studied groups (patients- 6%, healthy control – 4.4%, regional distribution – 11.4 %, blood donor- 10.8%).Based on our data we cannot make any conclusion regarding this issue.

AB (IV) phenotype distribution patterns is slightly similar in all groups, difference is mainly within 2-3% (patients- 3.6%, healthy control – 2.6%, regional distribution – 4,2%, blood donor- 4,6%). Based on our data AB (IV) phenotype group isn't correlated with susceptibility of SARS-Cov infection.

Numerous literary reviews have been made by the authors' groups regarding the association of blood group with SAS-Cov 2 infection [39][40][41]. Authors describe the possible mechanisms of association, the majority of them are based on hypotheses. Some of the authors linked to each other blood groups distribution in the population and regional infection growth rate. It is observed that blood type distribution may play a significant role in geographically heterogenous SARS-Cov 2 infection spreading[41].

Here we should consider one interesting literary review to be published after the meeting of the International Group of Experts on Transfusion Medicine and Hematology. The purpose of the expert meeting was to review the literature by the

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International Society for Blood Transfusion (ISBT) to determine a possible association between ABO type and COVID-19 and to reconcile existing studies to offer some kind of recommendations[40].

Of the many hypotheses proposed, we would like to single out a few that clearly indicate a close link between blood type and susceptibility to SARS-Cov 2 infection. One of the most popular hypotheses is the relationship between blood group-specific natural anti-A and anti-B antibodies and SARS-Cov 2 infection. Based on hypotheses natural blood group-specific anti-A antibodies block and neutralize the Sars-cov 2 virus and prevent it from binding to the angiotensin-converting enzyme 2 (ACE2) protein[39].The degree of infection may also be related to the quantitative rate of natural antibodies. Anti-A and anti-B titers in group O blood donors varies between people based on age and gender [42].On the other side it is known that O (I) group donors have immune anti-A and anti-B antibodies with very high titers[43]. It is possible that people carrying such kindsof antibodies are more protected fromSARS-Cov 2 infection or have a relatively low chance of complicating theCovid 19 disease due to cross-reactivity.

The second plausible hypothesis is related to antigenic mimicry. It has been established that the SARS - CoV - 2 S protein, which is responsible for binding to the cellular receptor, is structurally similar to A antigen and therefore human immune system does not detect the virus as a foreign exogenous factor and does not activate the cellular and humoral immune system against it [40].

Most important is to mentioned ABH histo-blood group antigens. They belong to oligosaccharides, which are present on red blood cells as well as expressed in other tissues of the body, including the respiratory epithelium and body secretions[44]. Their presence on the respiratory epithelium, therefore, indicates additional leverage for the virus to penetrate the cell.

SARS-CoV-2 virus spike protein can facilitate cell entry through RBD and ACE2 interactions. There is some hypothesis that it is possible SARS-CoV-2 RBD interaction with other host molecules, including as well blood group antigens. There is also new evidence that the SARS - CoV - 2 S receptor-binding domain (RBD) may have sequence similarity to the ancient lectin family, which is carbohydrate in nature and is found in plants, fungi, animals, bacteria, and viruses. The SARS -CoV- 2 RBD domain binds to antigen A, which is present on the epithelial cells of the respiratory system. This may explain group A susceptibility to SARS -CoV- 2 infection[44].

As for the complication of the Covid-19 disease, there are some considerations here as well. Thromboembolism is considered to be one of the complications of the Covid 19 disease. The Von Willebrand factor (VWF) and factor VIII level variability taking into account group affiliation. These factors are responsible for blood clotting, and an increase in their number increases the risk of thromboembolism. The levels of VWF and VIII factors are high in the case of antigen A, which makes it even more susceptible to disease complication[45][46][33][47][48].

5. Conclusion

In the current study, compared with the ABO blood group distribution of healthy controls in the Adjara region (Georgia republic), the Sars-CoV 2 infection rate was higher in the A blood group. O (I) blood group show low susceptibility to SARS-CoV-2 infection. Our results are in agreement with other scientific studies. We think that the results of the study will make a certain contribution to the meta-analysis of this issue.

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