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THE RELATIONSHIP BETWEEN BLOOD GROUPS AND COVID DISEASE IN TULCEA COUNTY

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Abstract: Human OAB blood-type antigens exhibit alternative phenotypes and genetically derived glycoconjugate structures that are located on the red cell surface which play an active role in the cells' physiology, pathology, and cellular molecular recognition. The OAB blood group system is associated with several parameters of healthy aging and disease development. The aim of our studies was to define the possible relationship between the blood group mosaic and the ability to allow the attachment of the SARS-CoV-2 virus due to antigens present on erythrocytes. The number of those infected with COVID-19 is 0.1% lower among those with blood group O and 0.5% higher among those infected with A compared to the area average, and for those with B, we have 1.2% more infected. However, for those in AB, the difference is significant contrary to theories, with 1.6% less infected compared to the area average. The results of our study cannot fully support theories suggesting the protective capacity of blood type O and that individuals with blood types A, B, and AB have a higher risk of contracting COVID-19 and/or making it more severe of the disease. Regarding the Rh system, our results show that the number of people Rh positive infected with the SARS-CoV-2 virus was 2.3% higher than Rh negative meaning that there is protection in individuals who do not possess the Rh antigen, possibly because the virus uses the antigen D to enter the host cell.

Keywords: blood groups, sars-cov-2 virus, COVID disease, Tulcea county.

INTRODUCTION

The infection with SARS-cov-2, newly appeared at the end of 2019 in the Wuhan region of China and spread rapidly becoming a pandemic, with a very large number of deaths. This virus generated a lot of interest in scientific research to find ways to stop its entry and development and how it invades and evolves inside the cells of the host organism, causing the disease. A special interest was given to research for preventing or mitigating the disease thereby avoiding the death of the host and reducing the sequelae.

In the past, investigations revealed an association between the OAB blood group and host susceptibility to infectious diseases caused by certain viral families (Coronaviridae, Retroviridae or Hepadnaviridae and influenza virus) (Zhang et al., 2019; Golinelli et al., 2020; Liu N, et al. 2021).

The relationship between the ABO blood group and the occurrence of COVID-19 was recently studied, showing that individuals belonging to blood group O are less susceptible to SARS-CoV-2 infection compared to those in the non-O group (Golinelli et al., 2020; Liu N, et al. 2021; Franchini et al., 2021; Wu et al., 2020; Guti´errez-Valencia et al., 2021). The studies carried out have a high level of heterogeneity, and have been performed in different populations, finding contradictory results. The distribution of OAB blood groups varies among the different geographic regions, races, and ethnicities.

Our life habits, environment, living and working conditions, the degree of exposure to the SARS-CoV-2 virus in terms of quantity or duration, the degree of health of our body or the percentage in which it is tarred by the pre-existence of chronic or acute diseases, at the time of coming into contact with this virus, certainly plays an important role in our risk of contracting the SARS-CoV-2 virus and in the severity of the COVID disease that will develop (Taylor et al., 2021; Hermel *et al*., 2021

In addition to all this, it has been suggested that blood group antigens but also their complementary anti-A, anti-B, and anti-H antibodies (in the case of the Bomby phenotype) could play important roles in the attachment of pathogens to host cells on the one hand, but also, in immune resistance to this virus. Also important are the levels of Von Willebrand factor and clotting factors that the blood contains, which are also influenced by blood group.

In this context, the question remains about how human blood groups could influence the susceptibility of organisms to contact the disease or the ability to resist it, but also the risk of developing serious complications with intubation and even death.

The aim of our studies is to define the relationship that might exist between the mosaic of blood groups and phenotypes that a human body possesses and the ability to allow the attachment of the SARS-CoV-2 virus and the degree of possible severity it could reach due to the antigens present on the cells, on the one hand, their complementary antibodies and their ability to defend the body, but also the levels of coagulation factors and Von Willebrand factor that differ within the OAB system, group O having lower levels of clotting factors than non-O blood groups.

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We also want to know if therapeutic decisions must and can take into account the blood groups and phenotypes that the COVID-19 patient possesses.

Therefore, the objective of our study was to analyze if an association exists between the OAB blood group and COVID-19 infection and severity according to data from the Tulcea County population.

MATERIAL AND METHODS

The authors state that they have obtained appropriate institutional review board approval and have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations.

The data required for our biomedical analysis was obtained with the consent of the management of the Emergency County Hospital "Sfântul Evangelist Luca" in Tulcea, having the approval to collect information about diseases and the blood groups OAB and Rh registered as being related to them.

The extraction of data regarding blood groups and possible diseases associated with them as well as the areas where they come from, was done using the Hippocrates application of the hospital without using the personal data: name, CNP of the subjects tested for OAB and Rh.

The tested subjects were people admitted to the Tulcea County Hospital for various conditions, presented to the Emergency Reception Unit, Tulcea due to accidents, mothers who gave birth in the Tulcea County Hospital's maternity ward, and who had a positive COVID test.

RESULTS

In this study were taken into the statistical calculation subjects tested OAB and Rh, in the years 2020, 2021, and 2022 and confirmed with COVID in Tulcea County Hospital.

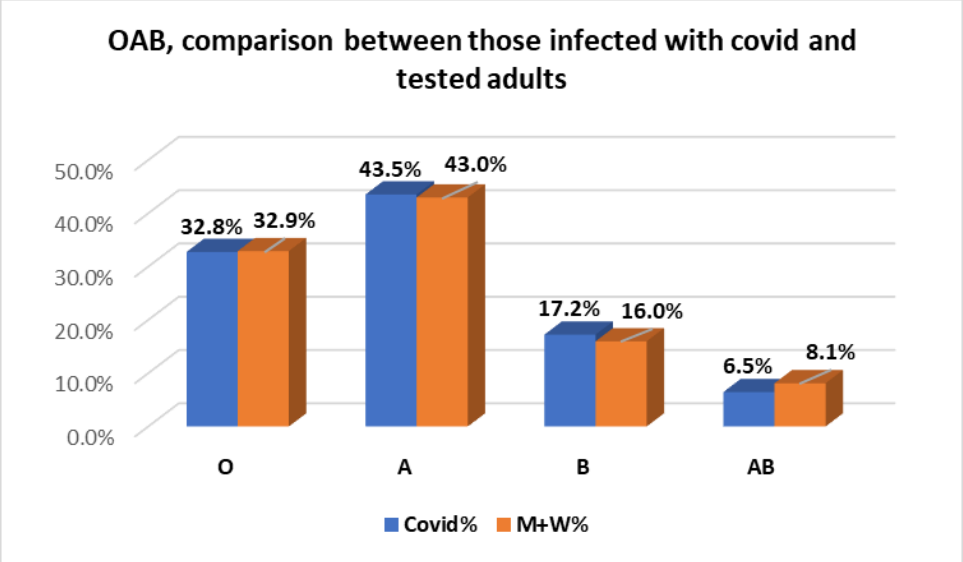

Fig. 1. Relationship between the total of adults tested for the OAB blood group system and those infected with SARS-CoV-2 in Tulcea County Hospital (2020 - 2022).

Relationship between the total of adults tested for OAB blood group system and those infected with SARS-CoV-2

As shown in Figure 1, in the case of blood group O, the percentages of those infected, compared to the total number of adults tested, are very close: 32.8%/32.9%, with 0.1% less for those infected with COVID-19.

For blood group A, 43.5%/ versus 43%, represents 0.5% more infected with represent than in all adults. Blood group B comprised 17.2% versus 16% with 1.2% more infected with SARS-cov-2.

These could to some extent support the theory of Peter Arend, 2021 regarding the protective capacity of blood type O against various infections and COVID-19 and the greater availability of individuals with blood type A and B to become infected and develop the disease. On the other hand, with blood group AB, we have 1.6% less infected with SARS-CoV-2: 6.5% compared to 8.1% in all tested adults. This does not support Arend's 2021 theory that, due to the presence of A and B antigens and the absence of anti-A and/or anti-B antibodies, the AB blood group is the most immunologically disadvantaged in the face of infection by various pathogens and infection COVID, blood group O is the most protected.

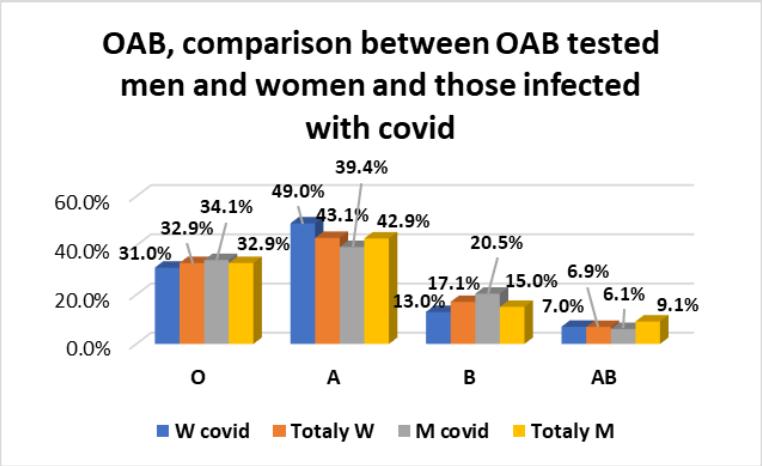

Fig. 2. Relationship between the total of adults tested for the OAB blood group (men and women), and those infected with SARS-CoV-2 (men and women) in Tulcea County Hospital (2020- 2022).

Relationship between the adults tested for OAB blood group (men and women), and those infected with SARS-CoV-2 (men and women)

From Figure 2 it can be seen that women with blood group O (31%) got sick with COVID-19 3.1% less than men with blood group O (34.1%).

Women with blood group A (49%) more by 9.6 % than men with blood type A (39.4%) and those with blood type B (13%) less than men with blood type B (20.5%) by 7.5% Women with blood type AB (7%) were infected with 0.9% more than AB men (6.1%).

Women with blood group O got sick with COVID-19 (31%) 1.9% less than the percentage of women in the study (32.9%) and men (34.1%) 1.2% more than the percentage of men with blood type O in the study (32.9%).

Women with blood type A were more affected by COVID-19 by 5.9% compared to the average of women in the study, totaling 49% compared to 43.1% and men with blood type A were more resistant (39.4%) by 3.5% compared to the 42.9% average for men in the area.

Women with blood type B had 13%, 4.1% better COVID defense than the area average of 17.1% and men with blood type B were 20.5%, 5.5% more susceptible compared to an average of 15%.

In group AB, the percentages of infected women are almost equal to the average of the studied group of 6.9%, the increase being only 0.1%, and men with blood group AB (6.1%) have 3% less than the average of men from the studied group of 9.1%, as can also be seen in the graph in Fig. 2.

Relationship between the total of adults tested for the Rh blood group and those infected with SARS-CoV-2

The results in Figure 3 show that in the situation of the Rh blood group system, of the 232 subjects infected with COVID-19 and Rh 206 tested, 88.8% were Rh + against 86.5% area percentage and 26, 11.2% Rh- against 13.5 % area percentage. There were 2.3% more Rh+ subjects infected with COVID than the area average (88.8%/86.5%), which may suggest that the D antigen may function as a receptor for the attachment of the SARS-CoV-2 virus, and the absence of the antigen D was protective against COVID infection.

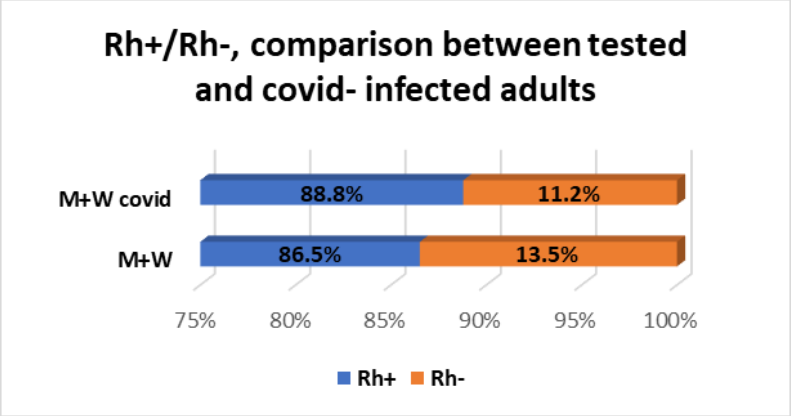

Fig. 3. Relationship between the total of adults tested for the Rh blood group and those infected with SARS-CoV-2 in Tulcea County Hospital (2020 - 2022).

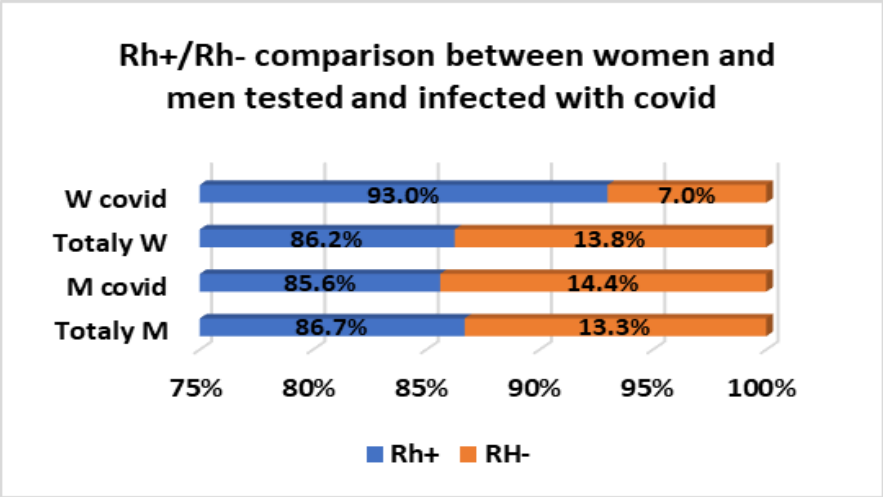

Fig. 4. Relationship between women and men tested for Rh blood system and those infected with SARS-CoV-2 in Tulcea County Hospital (2020 - 2022).

Relationship between women and men tested for Rh blood system and those infected with SARS-CoV-2

Compared to the area average, as it appears from Fig 4, there were 1.1% more Rh- men infected with COVID: 14.4/13.3, and, respectively, less Rh+ (85.6%/86.7%). On the other hand, as far as the ladies are concerned, the situation is much reversed: 93% infected with Rh+ COVID compared to 86.2%, the average of the area. We have 6.8% less Rh- infected (7%) than the area average of 13.8%. It seems that in the case of the female sex, the lack of D antigen acted as a protective factor.

Relationship between the total of adults tested for OAB and Rh blood group system and those infected with SARS-CoV-2

Combining the two GS systems (Fig 5) we have the following results: O+ 31.5% COVID against 28.8% area average, O-1.3% COVID against 4.1% area average, A+ 36.6% COVID against 37.1% area average, A- 6.9% COVID vs. 5.9% area average, B+ 14.7% COVID vs. 13.6% area average, B- 2.6% COVID vs. 2.4% area average, AB+ 6.0% COVID vs. Area average of 7.0%, AB- 0.4% COVID vs. 1.2% area average.

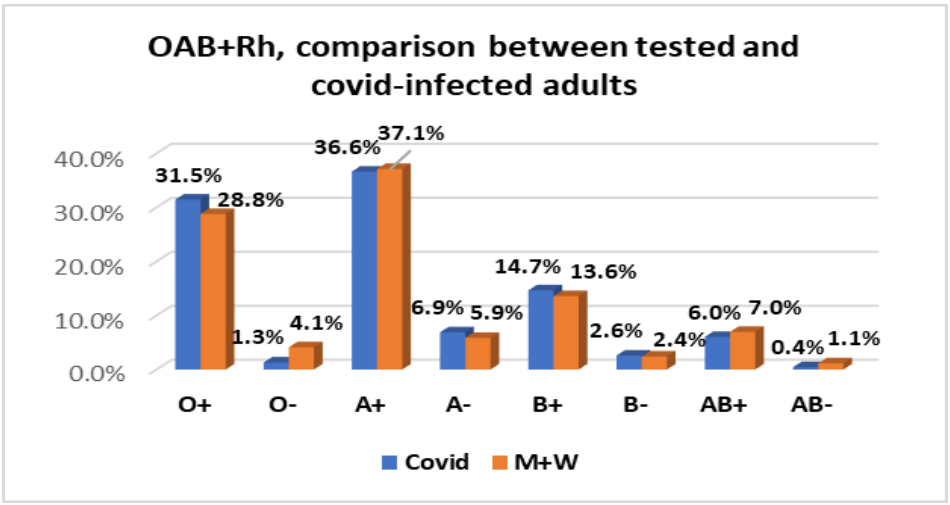

Fig. 5. Relationship between the total of adults tested for OAB and Rh blood group system and those infected with SARS-CoV-2 in Tulcea County Hospital (2020- 2022).

It is noted that the most protected blood group is O- which has 2.8% less than the area average and this is in a rare blood group which in the area average has only 4.1%. In AB- we have a difference of 0.8% less infected with COVID-19 from a percentage of 1.2% of the area average, which is quite a lot.

Although, according to Peter Arend's theory from 2021, we would have expected to have more infections and more severe conditions among subjects with blood group system AB+ and AB-, they recorded lower values of the number of COVID-19 infected (6% /7% for AB+ and 0.4%/1.2% for AB).

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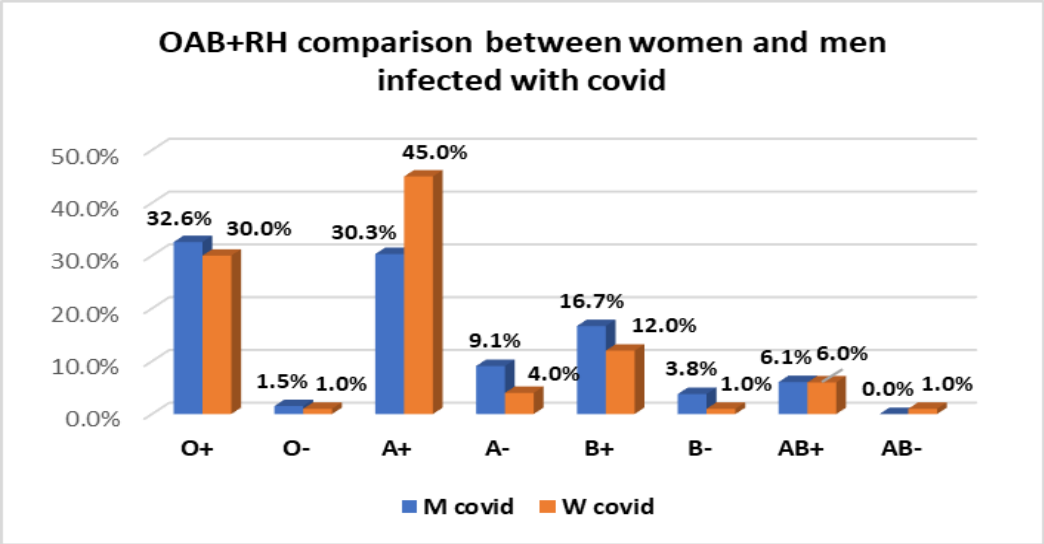

Fig. 6. Relationship between women and men tested for OAB and Rh blood groups and infected with SARS-CoV-2 in Tulcea County Hospital (2020 - 2022).

Relationship between women and men tested for OAB and Rh blood groups and infected with SARS-CoV-2

As shown in Fig 6, in the case of the group O+, we have 2.6% more men who have the COVID disease: 32.6% against 30% women, O- 1.5% men 0.5% more than 1% women, A+ 30, 3% men 14.7% less than 45% women, A- 9.1% men, 5.1% more than 4% women, B+ 16.7% men 4.7% more than 12 % female, B- 3.8% male 2.8% more than 1% female, AB+ 6.1% male, only 0.1% more than 6% female and AB- 0 male and 1% female.

DISCUSSION

In summary, we report a relationship between susceptibility to COVID-19 and OAB blood type. Specifically, people with blood type A have a higher risk, while people with blood type O have a lower risk of infection with SARS-Cov-2. This study may have potential clinical implications, given the current COVID-19 crisis: (1) people with blood type A may need particularly enhanced personal protection to reduce the chance of infection; (2) Patients infected with SARS-CoV-2 with blood type A may need more vigilant surveillance and aggressive treatment; (3) it may be useful to administer OAB blood to both patients and healthcare workers as a routine part of the management of SARS-CoV-2 and other coronavirus infections, to help define management options and assess exposure levels at the risk of people. (Zhao et al., 2021).

Antibodies anti-A of group O are more protective than those in group B. This observation is probably related to the fact that the predominant isotype of anti-B/anti-A immunoglobulin in group A and B serum is IgM and in group O serum is IgG, an already known aspect that has been well demonstrated by flow. Cytometry.

In conclusion, this way of analyzing the data strongly suggests that the presence of anti-A antibodies in serum, and more specifically anti-A IgG, should be considered a more significant factor than the blood group itself, insofar as the relationship between susceptibility to COVID-19 and blood groups OAB is concerned. (Gerard et al., 2020).

Ig M are mainly restricted to the blood due to their high molecular weight, however, Ig G can readily operate in various body fluids and occasionally on the surface epithelium. The epithelial surface is the most important checkpoint for viral entry into the upper respiratory tract (Abdelmasih et al., 2020). We suggest that blood groups may act as a risk factor for the development of thromboembolic events and thus could be used for risk assessment in COVID-19. We can conclude, at the diagnostic level, that OAB blood groups can potentially be used for risk stratification of patients affected by COVID-19, to anticipate the deterioration of patients at high risk of complications. At a therapeutic level, plasma from normal individuals with blood type O could replace the use of convalescent serum for the treatment of COVID-19 (Abdelmasih et al., 2020).

Coagulopathy associated with COVID-19 should be carefully managed in non-group 0 hypertensive patients as critically ill patients, as such an association could lead to an increased risk of adverse outcomes such as cardiac injury and death from inflammation and hyper-coagulation mechanisms. Therefore, we speculate that targeted anticoagulant therapies should be introduced early in the treatment of these high-risk, COVID-19 patients, namely hypertensive individuals with a non-0 blood group, to reduce cardiac injury and death (Sardu et al., 2020).

Given the high levels of vWF and factor VIII, we strongly suggest higher, possibly therapeutic doses of anticoagulation in these patients (Escher et al., 2020).

Based on our research and confirmed by the reported data, people with blood group A had a significantly higher risk of infection with SARS-CoV-2, while blood group O had a significantly lower risk of infection with SARS-CoV-2. People with blood group A should strengthen protection to reduce the risk of infection; however, people with blood type O should not take the

virus lightly and should still take precautions to avoid increasing the risk of infection. (Li et al., 2020).

There is little evidence that the severity of COVID-19 depends on the OAB blood type of the infected person. On the other hand, in terms of susceptibility to SARS-CoV-2 infection, individuals with blood group A may be at greater risk compared to individuals with blood group O (Bullerdiek et al., 2022). Knowledge of a patient's OAB phenotype should not directly influence therapeutic decisions (Bullerdiek et al., 2022).

The subsequent synthesis of potential antigens A and B requires the presence of antigen H. Antigen H decreases quantitatively in favor of antigens A and B, with AB individuals having the lowest amount of substance H, and group O having the highest amount (Hălmagi & Bichiș, 2019). This fact could mean that as long as an aggressor (virus, bacterium, parasite) can use both A and B but also H antigens for attachment, the blood group to which it belongs would no longer be so important in the OAB system. Antigen H has, thanks to the gene that encodes it, a certain number of antigens. If there are also genes coding for antigens A and/or B, then the substances galactose-transferase and N-acetyl-galactosamine-transferase (Hălmagi & Bichiș, 2019) are fixed on the substrate antigen H, giving rise to antigens A and/or B, only within the limit its presence on the red blood cell. So there will be the same number of antigen receptors in all situations: the absence of antigens A or B, the presence of antigen A or antigen B, or the presence of both antigens A and B, the limit being given by the number of antigens H. The differentiation could be due to the ability of the aggressor to attach only to some of the antigens, as with Plasmodium vivax which cannot attach to red blood cells Fy (a-b-): in Plasmodium vivax infections, mutations in the FY gene that result in red blood cells without the antigen Duffy protects against infection with this strain of malaria (Abegaz, 2021). Anti-A, anti-B, and/or anti-H antibodies have an important influence, however, in the case of the Bombay phenotype. The concentrations of coagulation factors and Von Willebrand Factor present in each blood group could also be important in the severity of the disease.

The concentrations of coagulation factors and Von Willebrand Factor present in each blood group could also be important in the severity of the disease.

We believe that it is good to know the blood groups that the patient with the COVID-19 disease has in order to assess in time the possibility of the need to receive anticoagulants and their dose and to know what to expect in the further evolution of the disease, but and the blood group indicated for the personnel dealing with this patient to reduce the transmissibility of the virus as much as possible, given that the virus replicates in the host's cells giving rise to new viruses of the type of phenotypes that the host has and so it is good that those who come into contact with this patient have antibodies against these viruses. For example, patients with A should be cared for by staff with B or O, those with B by staff with A or O, and those with AB by anyone, and as for those with O, only people who have anti-H antibodies are immune, but this is a very difficult thing because they are only 1% of the world's population being the possessors of the world's rarest blood group, the Bombay phenotype.

COVID-19 infection could be the result of complex interactions of factors that can range from genetic, behavioral, psychological, social status, and environmental risk factors (Ajeneye et al., 2020).

CONCLUSION

As a result of the research carried out in our study, it emerged that:

The number of those infected with COVID-19 is 0.1% lower among those with blood group O and 0.5% higher among those infected with A compared to the area average, and for those with B, we have 1.2% more infected.

However, for those in AB, the difference is significant contrary to theories, with 1.6% less infected compared to the area average.

The results of our study cannot fully support theories suggesting the protective capacity of blood type O and that individuals with blood types A, B, and AB have a higher risk of contracting COVID-19 and/or making it more severe of the disease.

Regarding the Rh system, the number of Rh-positive people infected with Sars-Cov 2 was 2.3% higher than Rh-negative meaning that there is protection in individuals who do not possess the Rh antigen, possibly because the virus uses the antigen D to enter the host cell.

Data from our study indicate complex relationships between the SARS-CoV-2 virus and host blood groups and phenotypes. We believe that a comparative study among their blood donors could also be useful, a study that could clarify many aspects.

AUTHORS CONTRIBUTIONS

Conceptualization: N.V. and B.D.; methodology: N.V., B.D., E.M., T.V.; data collection N.V.; data validation: N.V., B.D., E.M. and T.V.; data processing: V., B.D., E.M. and T.V.; writing—original draft preparation N.V. T.V.; writing—review and editing: N.V.

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CONFLICT OF INTEREST

The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed. No writing assistance was utilized in the production of this manuscript.

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