CHAPTER

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Correlation between blood type and SARS-CoV-2 infection susceptibility: A literature review

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ABSTRACT
The pandemic caused by SARS-CoV-2 is one outbreak that affects human health worldwide. Since the first confirmed case, several people have been infected across the globe and many have unfortunately lost their lives due to complications caused by Covid-19. Several studies have been published on the subject since the disease emerged, and among these, studies correlating blood type and levels of infection by SARS-Cov-2. The purpose of this work is to collect works published on the subject, during the period of 2020 and 2021, and to investigate whether it is possible to prove the existence or non-existence of this correlation. Articles were searched in 3 databases, and reaching a final number of 44 analyzed articles. Concluding a greater susceptibility to infection in individuals of type A and group O being considered protective against infection.

Keywords: Covid-19, Blood type, SARS-CoV-2, ABO.

1 INTRODUCTION

1.1 THEORETICAL REFERENCE

The blood type is defined according to the nature of the antigen present on the surface of the erythrocyte cell membrane, which is a macromolecular structure that can be made up of proteins, glycoproteins or carbohydrates that perform various functions in the cell, such as structural, transport, anchoring, enzymatic, and regulation of the complement system (BONIFÁCIO and NOVARETTI, 2009; TORMEY and HENDRICKSON, 2019).

Currently, about 360 types of erythrocyte antigens are recognized, 322 of which are grouped into 36 blood groups (STORRY et al., 2019). The antigens that have the greatest clinical importance are those that are part of the ABO system, the first of which was described in 1900 by the Austrian pathogolist Karl Landsteiner, followed by the Rh factor (GIANGRANDE, 2000; THORNTON and GRIMSLEY, 2019) and connect to a precursor coupled to the erythrocyte membrane, the H antigen, fundamental for the characterization of the ABO system.

From a genetic point of view, the ABO locus is located on the long arm of chromosome 9 (9q34.1-q34), has 3 alleles: A, B and O. The A allele encodes a glycosyltransferase, an enzyme that adds a N molecule terminally -acetylgalactosamine to the H antigen, originating the A antigen on the erythrocyte membrane, and thus the A blood type. The B allele, on the other hand, by the action of the same enzyme, encodes the insertion of a D-galactose molecule at the end of the H antigen, forming the

B antigen and the respective B blood type. Individuals who express the presence of both alleles present the two sugars incorporated in the H antigen and consequently are recognized as having the AB blood type. While the O allele has the enzyme glycosyltransferase inactive, not encoding any antigen, so that individuals with this condition express only the H antigen on the erythrocyte membrane, thus being devoid of A and B antigens and recognized as having the O blood type (BETHESDA, 2005).

In the early 1990s, for the first time, the possibility was raised that these ABO group antigens were somehow related to some infections caused by microorganisms, since, according to research carried out by Borén et al., the presence of ABO group antigens Lewis blood (especially Le^b), in the cells of the gastrointestinal tract would act as receptors for the bacterium Helicobacter pylori, facilitating the entry of this germ into this tissue, enhancing the infection process (BORÉN et al., 1993).

In 2003, another study on the same subject was published, but correlating blood antigens to an infection caused by the Norwalk virus. In this bias, the author theorizes that this virus binds to the H antigen, which is an important part of blood antigens, especially in individuals with blood group O, increasing susceptibility to infection (LINDESMITH et al., 2003).

In 2005, the first correlation between blood antigens and the SARS-CoV virus, a respiratory virus derived from bats, was performed. After an increase in the number of infections by this virus in Hong Kong, the author takes into account the two works mentioned above and investigates whether these infections could be related to blood type. Research has shown that the number of infected blood type O was significantly lower when compared to other blood types among the patients studied (CHENG et al., 2005)

Three years later, the first work appears that theorizes the specific role of protein S (also known as “Spike”), a membrane protein characteristic of the coronavirus that is responsible for binding and its entry into the host cell, correlating with blood types during the viral infection process (GUILLON et al., 2008).

In December 2019, cases of pneumonia without proven causes began to appear in the Wuhan region, China (ZHU et al., 2020). In February 2020, a new strain of coronavirus was identified as the cause, henceforth called “SARS-Cov-2” or “novel coronavirus”.

SARS-CoV-2 is a positive-sense, single-stranded RNA virus (+ssRNA), belonging to the B lineage of the genus Beta-coronavirus of the Coronaviridae family (NAQVI et al., 2020). The virus uses membrane receptors to enter the host cell, more precisely the Angiotensin-Converting Enzyme 2 (ACE2 or ACE2) receptor (YAN et al., 2020), which is present in various tissues such as the trachea, kidneys, small intestine, pancreas, blood vessels and other tissues, however, the tropism of the virus is greater in the lungs (LIU, J. et al., 2021).

According to the studies developed by Hatmal et al. (2020), because it has a slightly more different and stable way of binding and entering host cells, SARS-Cov-2 is more infective and more virulent. The most common manifestations of infection by this virus are respiratory symptoms such as fever, dry cough, and even dyspnea. More severe cases even present sepsis, secondary infections and even multiple organ failure (HUANG et al., 2020).

In March 2020, the World Health Organization, considering the growing trend in the number of new cases of the disease and the number of deaths, raised the infection by this virus to a pandemic status, something that would profoundly change the lives of practically all the people of the world and causing millions to die (CHAMS et al., 2020).

With the emergence of Covid-19, a disease caused by the infection caused by SARS-Cov-2 and, due to the enormous impact it caused in the health area, in addition to the social and psychological disorders caused by the pandemic, it did not take long for researchers and industries to Pharmaceutical companies put the maximum effort into obtaining information about this virus and especially how to combat it (CIOTTI et al., 2022).

Due to its great structural similarity with the other types of coronavirus already studied, works such as Guillion's were soon cited and the possibility was raised that the correlation between blood types and infection could also occur in this new coronavirus.

On the other hand, since then, there has been much controversy surrounding this correlation, as several studies categorically claim susceptibility to infection considering blood type, whereas other authors make a counterpoint. Considering these arguments, the purpose of this work was to carry out a bibliographical review based on works published on this subject, during the period of 2020 and 2021, and to investigate whether it is possible to prove the existence or not of a correlation between blood type and the process of SARS-Cov-2 infection

2 JUSTIFICATION

With the emergence of the first cases of Covid-19 in China, a long race began to investigate and try to better understand the mechanisms of action of SARS-CoV-2. As a relationship between blood types and other coronaviruses has already been previously established by some works, the question whether this relationship would also extend to the new coronavirus immediately arose. In this context, the justification of the present work is to investigate what has already been published on the subject and to analyze whether there already exists, in fact, a concrete answer for the existence or not of this correlation, in addition to knowing how this could help in the fight against this virus causing such a negative impact on the world stage in recent years.

3 OBJECTIVE

3.1 MAIN GOAL

To carry out an investigation among the works already published if the blood type increases the susceptibility to the development of the Covid-19 disease, caused by SARS-CoV-2. Also, if confirmed, investigate at which point in the disease this correlation occurs.

3.2 SPECIFIC OBJECTIVES

- Search for works that talk about the correlation between Covid-19 and blood types in reliable databases.
- Perform filtering and organization of these articles.
- • Discuss what was found in these works and demonstrate whether this correlation is real, in addition to being significant.

4 METHODOLOGY

4.1 DATA SOURCES AND RESEARCH STRATEGY

A systematic search was carried out for articles published between January 2020 and December 2021 in the PubMed, Science Direct and LitCovid databases, using the following descriptors: “Covid-19”, “SARS-CoV-2”, “ABO” and “blood group”, separated only by a comma. There were no language or region restrictions.

4.2 STUDY SCREENING AND DATA EXTRACTION

The “EndNote X9” software was used to manage the process of sorting the articles found in the search, acting in the identification and removal of duplicates. In addition, all articles were manually reviewed in order to reduce the risk of additional duplicates.

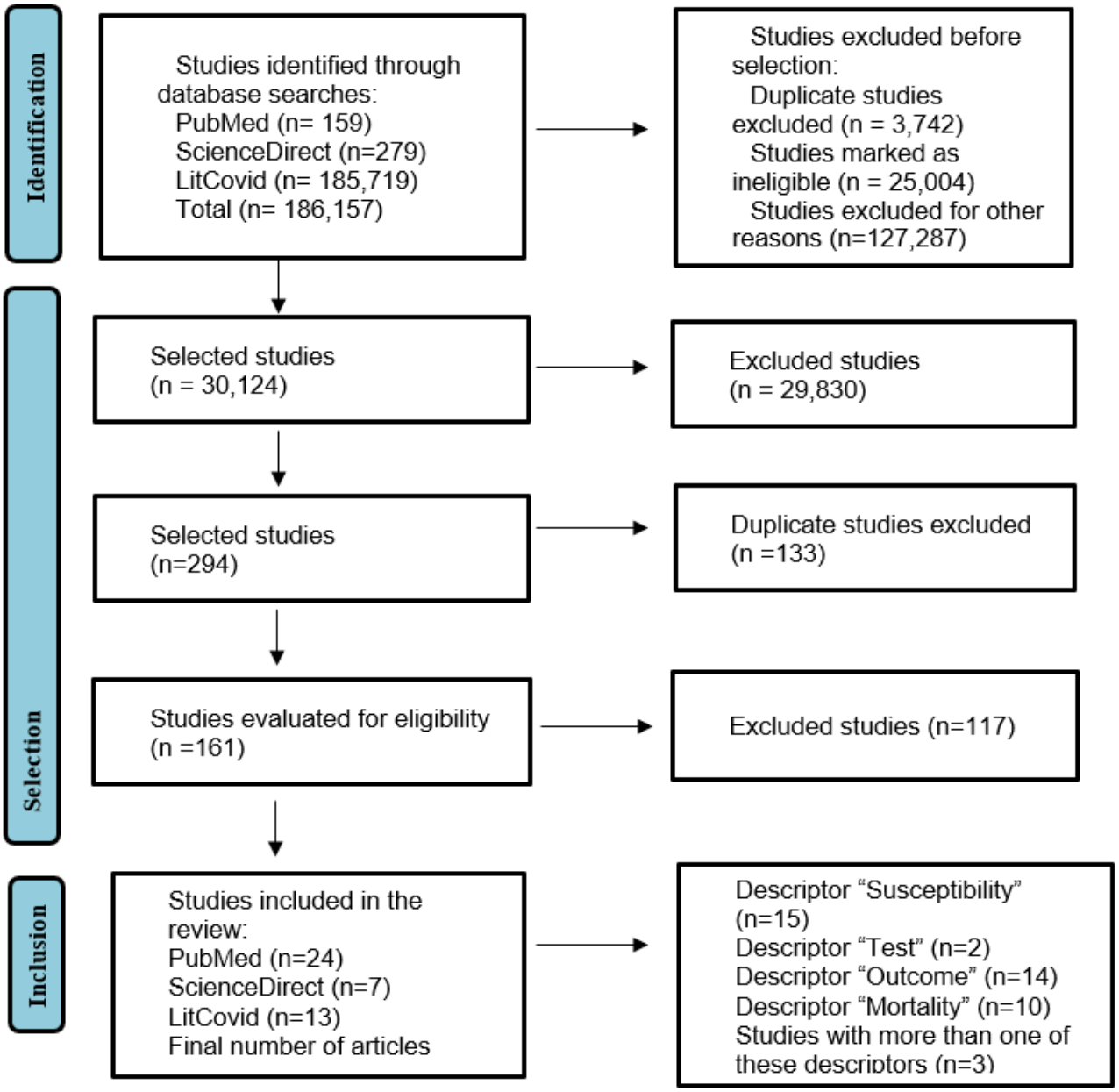
4.3 SELECTION CRITERIA (INCLUSION/EXCLUSION)

After eliminating duplicates, the exclusion criteria used were, in order: articles that did not fit the purpose of this work, articles that did not have at least one of the descriptors present in their titles and articles without a full text available for access.

5 DISCUSSION OF THE RESULTS

Upon initial research in the 3 cited databases, the total number of articles found was 186,157. After applying the inclusion and exclusion criteria shown in Figure 1, the final number of articles worked on in this review was established as 44.

Figure 1: Study selection flowchart adapted from Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISM) (PAGE et al., 2021)



O The first cut performed was the presence of duplicate articles within this initial number. The second cut took place in order to reduce the considerable number of articles retrieved from the databases using the chosen descriptors. In this way, we chose to redo the search in the "LitCovid" database, which brought a greater number of articles in the initial search, and to use only the descriptors "blood group" and "ABO". The justification is the fact that this database is specific to articles related to Covid-19, and after analysis, we could see that many of the articles filtered in the initial search only spoke about Covid-19 in general, and were not associated with the theme. With this cut, 25,004 articles were marked as ineligible.

The second and third cuts were made in order to exclude articles that were not related to the theme of this work. In this case, the vast majority consisted of articles that dealt only with the infection by the coronavirus, without correlating it with blood groups, therefore becoming ineligible.

Despite the third cut, analyzing the remaining 30,124 articles, it can be seen that some articles still only had Covid-19 or the SARS-CoV-2 virus as their subject, and did not talk about the association with blood type. For this reason, a fourth cut was applied, searching only the descriptors “blood group” and “ABO”, and reaching a number of 294 articles. To be sure of the veracity of the cut, all titles of all 29,673 excluded articles were checked manually and it was found that they did not talk about blood group or ABO group, therefore, they did not fit the theme. Of this number of 294 articles, a fifth cut was made to remove duplicates again, reaching a number of 161 articles evaluated for eligibility.

All these 161 articles fit the theme of this work, but because there is still a significant number of articles for analysis and because they do not fit the maximum number of references required for publication, a new cut methodology was applied. The idea for this section was to provide a general notion of the correlation between blood type and SARS-CoV-2 infection, that is, to demonstrate whether this correlation is significant at all stages, from susceptibility to infection, probability from positive tests, the development of the disease, to mortality. With that, 4 new descriptors were applied: “susceptibility”, “test”, “outcome” and “mortality”, reaching a final number of 44 articles included in this bibliographic review.

Among the selected articles, twenty-eight of them are classified as retrospective studies, six are bibliographic reviews, five letters to the editor, two case-control studies, one epidemiological, one cohort and one survey based on a questionnaire. It was possible to perceive a great variation in relation to the total number of patients analyzed in the works, with the smallest number of samples being 46, and the largest 4,968 patients.

Among the articles that mentioned an average age of the patients studied, a variation from 7.9 to 77 years can be observed. Male and female patients were also quantified in some of the studies, in addition to the percentage of patients who died during the surveys. The percentage of blood types, as well as the prevalence among them, was also collected and is shown in Table 1, which follows below.

Table 1: Characteristics of selected studies. NI: Not reported.

First author and year	Country	Kind of study	Total Sample	Age Average	Women (%)	Male (%)	Deaths (%)	Type A (%)	Type B (%)	Type AB (%)	Type O (%)	Prevalence
AL-ANSARI *et al.* (2021)	Saudi Arabia	Retrospective	90	58	28 (31.1)	62 (68.9)	20 (22.2)	20 (22.2)	24 (26.7)	5 (5.6)	41 (45.6)	O>B>A>AB

(ALMADHI *et al.*, 2021)	Bahrain	Retrospective	2334	NI	NI	NI	NI	513 (21.9)	644 (27.5)	117 (5.0)	1060 (45.4)	O>B>A>AB
(AL-YOUHA *et al.*, 2021)	kuwait	Retrospective	3.305	42	1.017 (30.8)	2.288 (69.2)	151 (4.6)	843 (25.5)	956 (28.9)	281 (8.5)	1225 (37.1)	O>B>A>AB
(ANSARI-LARI e SAADAT, 2021)	Iran	letter to the editor	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
(AYATOLLAHI *et al.*, 2021)	Iran	Retrospective	1.554	56.6	740 (47.6)	814 (52.4)	287 (18.5)	472 (30.4)	436 (28.1)	112 (7.3)	534 (34.4)	O>A>B>AB
(BARI *et al.*, 2021)	Pakistan	Retrospective	66	7.9	28 (42.4)	38 (57.6)	0	17 (25.8)	23 (34.9)	1 (4.3)	25 (37.9)	O>B>A>AB
(BEHBOUDI *et al.*, 2021)	Iran	Retrospective	148	55.4	68 (45.9)	80 (54.1)	51 (34.5)	38 (26)	52 (35.6)	16 (10.9)	40 (27.5)	B>O>A>AB
(BHATTACHARJEE *et al.*, 2020)	India	Literature review	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
(CHEGNI *et al.*, 2020)	Iran	Letter to the Editor	94	NI	21 (22.3)	73 (77.7)	94 (100)	34 (44.7)	17 (22.4)	4 (5.3)	21 (27.6)	A>O>B>AB
(COLUK *et al.*, 2021)	Türkiye	Retrospective	211	NI	NI	NI	NI	101 (47.9)	32 (15.2)	9 (4.2)	69 (32.7)	A>O>B>AB
(COVALI *et al.*, 2021)	Romania	Retrospective	46	27.8	46 (100)	0	NI	24 (52.2)	10 (21.7)	3 (6.5)	9 (19.6)	A>B>O>AB
(FAN *et al.*, 2020)	China	case-control	105	56.8	50 (47.6)	55 (52.4)	NI	45 (42.8)	28 (26.7)	9 (8.5)	23 (21.9)	A>B>O>AB
(FAROUG MOHAMED *et al.*, 2021)	Sudan	Retrospective	100	NI	44 (44)	56 (56)	NI	30 (30)	15 (15)	9 (9)	46 (46)	O>A>B>AB
(GÖKER et al., 2020)	Türkiye	Retrospective	186	42	86 (46.2)	100 (53.8)	NI	106 (57)	20 (10.8)	14 (7.5)	46 (24.8)	A>O>B>AB
(GOLINELLI, 2021)	Italy	letter to the editor	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
(HALIM *et al.*, 2021)	Bangladesh	Retrospective	771	NI	NI	NI	NI	288 (37.35)	134 (17.38)	204 (26.5)	145 (18.81)	A>AB>O>B
(ISHAQ *et al.*, 2021)	Pakistan	Retrospective	1.067	47.8	355 (33.2)	712 (66.7)	113 (10.5)	202 (18.9)	295 (27.6)	49 (4.5)	521 (48.8)	O>B>A>AB
(KABRAH, ABUZERR, *et al.*, 2021)	Saudi Arabia	Retrospective	285	44.5	145 (50.9)	140 (49.1)	4 (1.4)	81 (28.4)	43 (15.1)	11 (3.9)	150 (52.6)	O>A>B>AB

(KABRAH, KABRAH, *et al.*, 2021)	Saudi Arabia	Literature review	16 estudos	NI	NI	NI	NI	NI	NI	NI	NI	NI
(KERBAGE *et al.*, 2021)	Lebanon	case-control	404	64	154 (32.5)	320 (67.5)	NI	172 (42.6)	53 (13.1)	24 (6)	155 (38.3)	A>O>B>AB
(KIM *et al.*, 2021)	USA	Literature review	9 estudos	NI	NI	NI	NI	NI	NI	NI	NI	NI
(KOMAL *et al.*, 2021)	Pakistan	Questionnaire-based research	305	30	99 (32.4)	206 (67.5)	NI	77 (25.4)	101 (33.1)	51 (16.7)	76 (24.9)	B>A>O>AB
(KUMAR *et al.*, 2021)	USA	Retrospective	3.563	67	1.675 (47)	1.888 (53)	NI	1.301 (36.5)	377 (10.6)	133 (3.7)	1.752 (49.2)	O>A>B>AB
(LATZ *et al.*, 2020)	USA	Retrospective	1.289	56.6	872 (67.7)	417 (32.3)	89 (6.9)	440 (34.2)	201 (15.6)	61 (4.7)	587 (45.5)	O>A>B>AB
(LEHRER e RHEINSTEIN, 2021)	USA	Retrospective	720	58	351 (48.8)	369 (51.2)	76 (10.5)	323 (44.9)	66 (9.2)	23 (3.2)	308 (42.8)	A>O>B>AB
(LEVI *et al.*, 2020)	Brazil	letter to the editor	2.037	NI	NI	NI	NI	816 (40.1)	237 (11.6)	71 (3.5)	913 (44.8)	O>A>B>AB
(LIU, N. *et al.*, 2021)	China	Literature review	10 estudos	NI	NI	NI	NI	NI	NI	NI	NI	NI
(MAHMUD *et al.*, 2021)	Bangladesh	Retrospective	438	39.8	180 (41.1)	258 (58.9)	5 (1.3)	144 (32.8)	148 (33.7)	52 (11.9)	94 (21.5)	B>A>O>AB
(MATZHOLD *et al.*, 2021)	Austria	Retrospective	336	77	187 (55.3)	151 (44.7)	78 (23)	151 (44.9)	54 (16.1)	31 (9.2)	100 (29.8)	A>O>B>AB
(MAY *et al.*, 2021)	USA	Letter to the Editor	165	57	65 (39)	100 (61)	32 (19)	56 (34)	30 (18)	8 (5)	71 (43)	O>A>B>AB
(MUÑIZ-DIAZ *et al.*, 2021)	Spain	Cohort	854	45	516 (60.5)	338 (39.5)	NI	403 (47.1)	65 (7.6)	32 (3.7)	354 (41.4)	A>O>B>AB
(NALBANT *et al.*, 2021)	Türkiye	Retrospective	313	57.7	145 (46.3)	168 (53.7)	0	147 (47)	44 (14)	22 (7)	99 (32)	A>O>B>AB
(PADHI *et al.*, 2020)	India	Retrospective	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
(PAUL *et al.*, 2020)	USA	Retrospective	249	70	128 (51.4)	121 (48.6)	118 (47.3)	87 (35)	43 (17.2)	9 (3.7)	110 (44.2)	O>A>B>AB
(RANA *et al.*, 2021)	India	Epidemiological	2.586	NI	NI	NI	NI	774 (29.9)	1.081 (41.8)	183 (7)	548 (21.1)	B>A>O>AB

(RAHIM *et al.*, 2021)	pakistan	Retrospective	1.935	39.7	607 (31.4)	1.328 (68.6)	NI	523 (27)	694 (35.9)	490 (11.8)	228 (25.3)	B>A>O>AB
(SAINZ BUENO *et al.*, 2021)	Spain	Retrospective	1.287	NI	786 (30.3)	1.800 (69.7)	317 (12.2)	544 (42.3)	154 (12)	54 (4.2)	535 (41.6)	A>O>B>AB
(SERTBAS *et al.*, 2021)	Türkiye	Retrospective	3.551	57.5	1.651 (47.8)	1.854 (52.2)	798 (22.4)	1.673 (44.1)	548 (15.8)	279 (7.7)	1.051 (32.4)	A>O>B>AB
(SHIBEEB e KHAN, 2021)	Qatar	Literature review	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
(SZYMANSKI *et al.*, 2021)	USA	Retrospective	4.968	62.1	2.562 (51.6)	2.406 (48.4)	1.146 (23.1)	1.473 (29.6)	846 (17)	204 (4.1)	2.445 (49.2)	O>A>B>AB
(TAMAYO-VELASCO *et al.*, 2021)	Spain	Retrospective	108	71.5	40 (52.9)	33 (47.1)	17 (23.3)	59 (54.6)	10 (9.3)	4 (3.7)	35 (32.4)	A>O>B>AB
(SILVA-FILHO *et al.*, 2020)	Brazil	Literature review	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
(YAYLAC1 *et al.*, 2020)	Türkiye	Retrospective	397	47.1	221 (55.7)	176 (44.3)	29 (7.3)	201 (50.6)	55 (13.9)	21 (5.3)	119 (30.3)	A>O>B>AB
(ZHAO *et al.*, 2021)	China	Retrospective	2.173	NI	NI	NI	206 (9.4)	797 (36.7)	577 (26.5)	232 (10.7)	567 (26)	A>B>O>AB

With regard to the country where the studies were conducted, we have articles published in the Americas, Africa, Europe and Asia, seven of them in the United States of America, five in Turkey, four in Iran and Pakistan, three in India, Spain, China and Saudi Arabia, two in Brazil and Bangladesh, and one in Sudan, Romania, Qatar, Lebanon, Kuwait, Italy, Bahrain and Austria. The prevalence of blood types presented in each country was calculated and can be seen in Table 2.

Table 2: Distribution of blood groups by country.

Country	**A(%)**	**B(%)**	**AB(%)**	**O(%)**	**Prevalence**
Saudi Arabia	27%	17.9%	4.2%	51%	O>A>B>AB
Austria	44.9%	16.1%	9.2%	29.8%	A>O>B>AB
bahrain	21.9%	27.5%	5.0%	45.4%	O>B>A>AB
Bangladesh	35.8%	23.3%	20.3%	19.8%	A>B>AB>O
Brazil	40.1%	11.6%	3.5%	44.8%	O>A>B>AB
China	37%	26.5%	10.5%	25.9%	A>B>O>AB
Spain	69.4%	15.9%	6.2%	63.8%	A>O>B>AB

USA	33.6%	14.3%	4%	48.1%	O>A>B>AB
India	29.9%	41.8%	7%	21.1%	B>A>O>AB
Iran	30.2%	28.1%	7.3%	33.1%	O>A>B>AB
kuwait	25.5%	28.9%	8.5%	37.1%	O>B>A>AB
Lebanon	42.6%	13.1%	6%	38.3%	A>O>B>AB
Pakistan	24.2%	33%	17.5%	25.2%	B>O>A>AB
Romania	52.2%	21.7%	6.5%	19.6%	A>B>O>AB
Sudan	30%	15%	9%	46%	O>A>B>AB
Türkiye	47.8%	15%	7.4%	29.7%	A>O>B>AB

Of the 44 publications analyzed in this work, 29 claimed that there was some level of correlation between blood type and Covid-19 infection and 15 argued against this association. Thus, some facts were hypothesized; if there is such a connection, at what moment does it manifest itself? Is it possible for a person to be more susceptible or not to be infected by SARS-Cov-2? In the possibility of positive tests? During some point in the development of the infection? Or does it influence mortality, once the patient becomes infected? The responses presented in the studies included in this work are shown in Table 3.

Table 3: Correlation results between the studies included.

	Yes	**No**
Susceptibility	14	2
Test	1	1
Development	6	9
Mortality	8	3
Total	29	15

5.1 ABOUT SUSCEPTIBILITY

Most works on the correlation between blood type and Covid-19 infection will deal directly with the part before the patient is properly infected by the virus, that is, if an individual's blood type can make him more vulnerable or even act as a protection against SARS-CoV-2 infection at the cellular level.

Some of the articles argue that the blood type does not influence this phase of the infection process (BEHBOUDI et al., 2021; KABRAH, ABUZERR, et al., 2021), however, as mentioned in Table 3, most of them state that there is some kind of correlation.

The results found vary about which blood type acts in this part of susceptibility, but most of them bring that: Blood type A is more likely to have its cells infected by the virus and blood type O has greater mechanisms of protection against this entry.

To enter the host cell, SARS-CoV-2 uses its S transmembrane glycoprotein (or spike). This S protein contains two subunits, S1 and S2, with S2 generally binding to the ACE2 receptor for cellular entry.

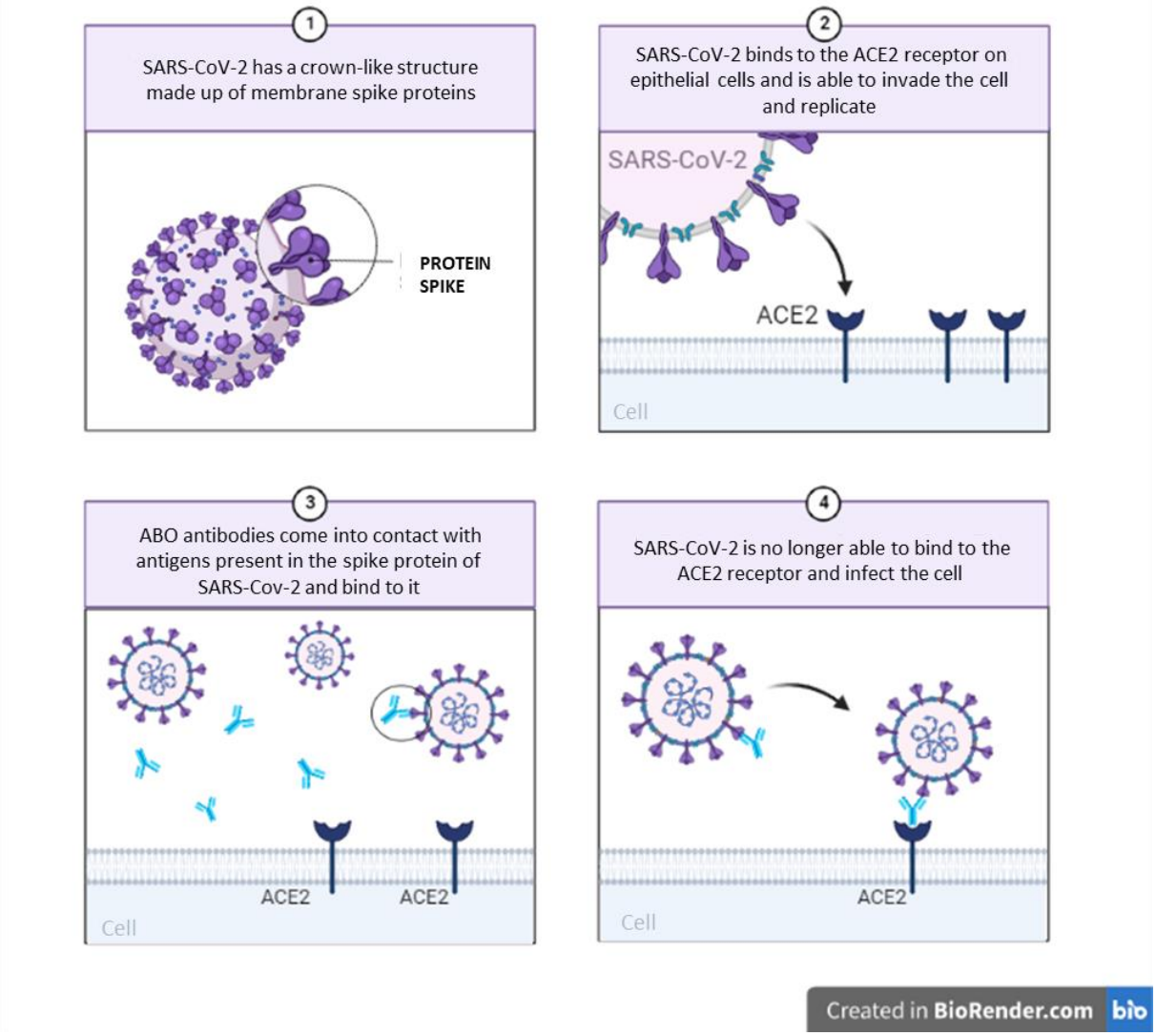
A study conducted by Brazilians from the Federal University of Bahia raises the hypothesis that the greater susceptibility found in type A can be explained by carbohydrate-carbohydrate interactions, however S1 binds to proteins containing sialic acid, such as CD147, which is also considered a SARS-CoV-2 entry receptor into the host cell. The hypothesis from this work is that the A antigen, mainly, stimulates the modulation of receptors containing sialic acid in the cell membrane through carbohydrate-carbohydrate interactions, which can maximize the binding of protein S in the cell membrane and consequently its entry in the host cell (SILVA-FILHO et al., 2020).

Furthermore, there is a significant structural similarity between protein S subunit 1 and a part of the A antigen of epithelial cells, which may also lead to this interaction and influence on susceptibility (WU et al., 2021).

The protective factor related to blood type O is raised by Yamamoto et al., remembering that ABO antigens are present not only in erythrocytes, but also in several other cells, such as the epithelial cells of the respiratory tract. So, when the virus invades that cell, it replicates and when it leaves the cell, it uses parts of the host cell's own membrane to create its membrane. In doing so, the virus may end up incorporating parts of the ABO antigens into its S protein, creating epitopes. When leaving this cell and trying to infect other cells of other hosts, these epitopes can be recognized by natural blood antibodies of this new individual.

Type O people have both Anti-A and Anti-B antibodies in their plasma, that is, following this line, they are the ones with the greatest capacity to recognize these epitopes in viruses that previously infected individuals of types A, B or AB and act accordingly. as neutralizers of these viruses, preventing their entry into the cell and consequent infection, at a certain level acting in a protective manner (YAMAMOTO et al., 2021). This information was compiled by the authors of this work, who proposed an illustrative scheme of this idea (Figure 2).

Figure 2: The protective power of blood antibodies against SARS-Cov-2 infection.



5.2 TEST

The correlation between blood types and SARS-CoV-2 infection has mixed results when it comes to test positivity. In the study carried out by Coluk and collaborators, 211 patients with flu symptoms were selected and then the PCR test was performed to detect SARS-CoV-2, in addition to the categorization of the blood group and Rh of the participants. After statistical analysis, no significant correlation was found between blood types and patients who tested positive (COLUK et al., 2021).

In the work conducted by Nalbant and collaborators, where a retrospective analysis of 313 patients who were tested was performed and a 4.1 times greater chance of positivity in the test was found in patients from group O when compared to other blood groups within this analyzed population (NALBANT et al., 2021).

5.3 DEVELOPMENT

Once someone is infected with SARS-CoV-2, can their blood type have any influence on disease progression? In an attempt to answer this question, some works have analyzed the presence or absence of aggravating factors in the clinical picture, such as the need for mechanical ventilation, use of vasopressors, what are the blood levels of infection and thromboembolism markers, need for intubation, need for ICU admission, among others (KUMAR et al., 2021).

The results found converge with each other. In a study conducted solely on infected children, it was found that type A was significantly associated with complications and consequent admission to the ICU and the need to use respirators.(BARI et al., 2021). Another study, this time done only with pregnant women positive for Covid-19, associated a lower risk of symptoms in patients with Rh+ and also found a greater association between blood group A and cases of hemorrhage and premature rupture of the placenta (SAINZ BUENO et al., 2021).

Most of the studies showed that type A can lead to a predisposition to increase the severity of the infection and type O can act in a protective way, but the results found are not statistically significant (GÖKER et al., 2020; KIM et al. al., 2021).

A study carried out in Bangladesh, conducted with patients admitted to the ICU, brings a more radical view: type A people had more clinical symptoms such as leukocytosis, increased serum ferritin levels and a greater need for oxygen supplementation when compared to patients of type A. other blood types (HALIM et al., 2021)

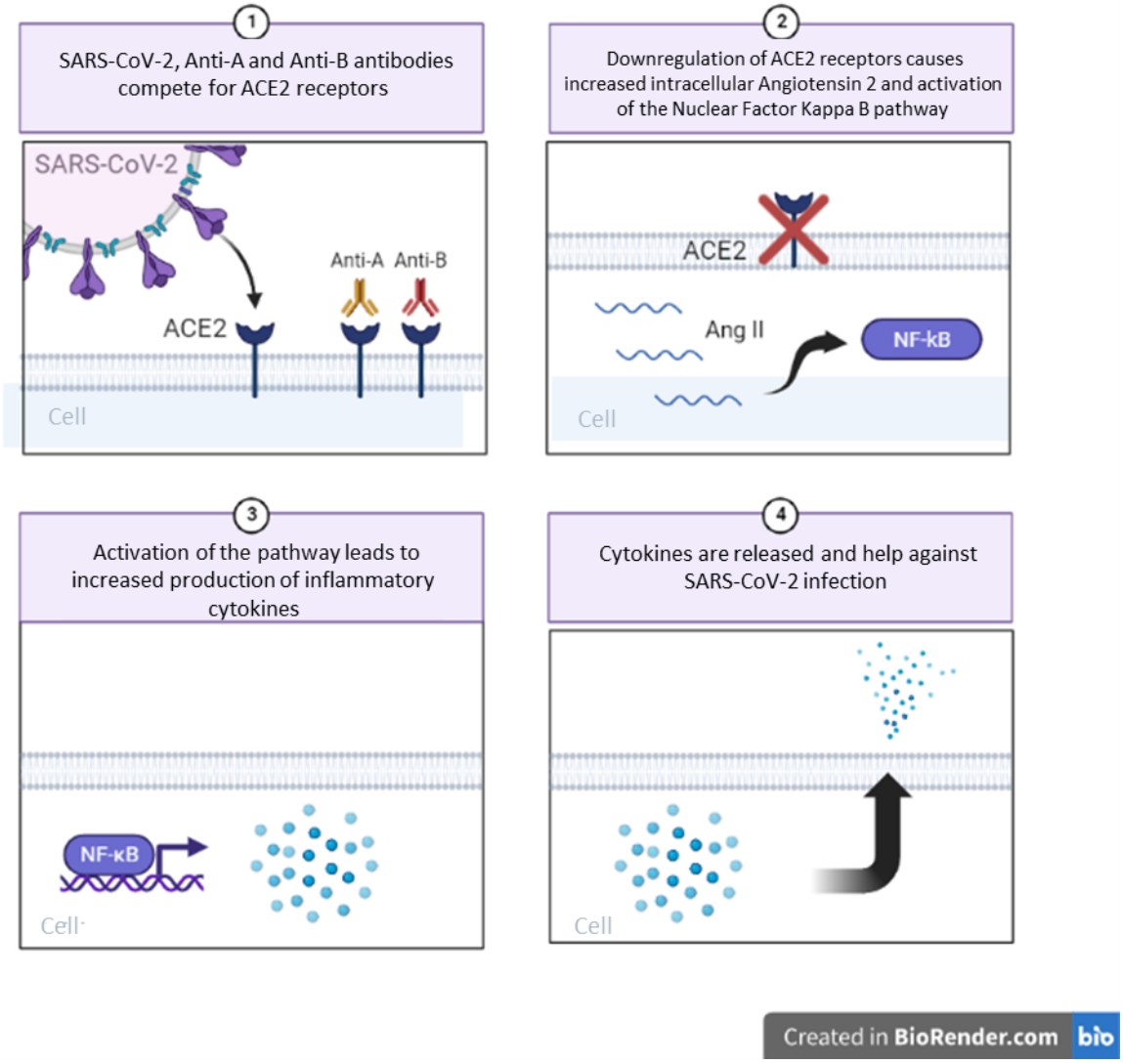
Another study from Bangladesh did not find significant differences in the progression of the disease in those infected, but detected that patients with blood type A had a late seroconversion when compared to patients with other blood groups, that is, patients with blood type A took longer to create antibodies against Covid-19, when infected by SARS-CoV-2 (MAHMUD et al., 2021).

Perhaps the work that brings a more concrete answer to this association is a study carried out in Spain, where they demonstrated a better prognosis in patients with blood type O. The explanation for this prognosis is that in addition to Anti-A and Anti-B antibodies present in the serum of these patients, they compete with the SARS-CoV-2 virus for the ACE-2 receptor. 2 and consequent entry into cells leads to a “downregulation” of ACE-2 receptors, as a form of cell defense.

This fact would cause an increase in intracellular angiotensin 2, which in abundance activates the Nuclear Factor Kappa B (NF-kB) pathway, triggering an increase in the production of several inflammatory cytokines, which act as an extra protection for patients with this type blood throughout the infection process, which may be responsible for an up to two times lower risk of need for mechanical ventilation (TAMAYO-VELASCO et al., 2021). For further clarification criteria, based on

the idea proposed by the authors mentioned above, a proposed interaction mechanism was proposed, according to figure 3

Figure 3: The protective power of downregulation of ACE2 receptors in type O individuals



5.4 MORTALITY

When it comes to the influence of blood type on the ability of SARS-CoV-2 infection, and the development of Covid-19 to lead the patient to death, the works that address this subject and that consider that this correlation does exist have brought biased results. The vast majority were studies that had a number of patients studied who died and their blood types were surveyed. Depending on which blood group was most frequently present among these patients, it was found that this group had a correlation with mortality from Covid-19.

It is important to point out that none of the works brings a theory or explanation about how this correlation occurs and how the blood type can lead to the death of those infected, in addition to being essential to remember that several factors can be responsible for a certain blood type being in greater

quantity in a certain population, such as ethnicity, geolocation, among others. As is the case of the work done by Padhi and collaborators, which argues for a greater susceptibility to death in patients with blood type B, investigated in a group of patients from India (PADHI et al., 2020). In a study carried out in New York City, United States, the most reported blood type among patients who died is type A (SZYMANSKI et al., 2021).

Even the articles that raise this correlation fail to bring statistically significant data, therefore, the works studied do not establish a correlation between blood types and the mortality of patients infected by Covid-19.

5.5 ROLE OF RACE AND GEOGRAPHIC REGION IN THIS CORRELATION

As can be seen in Table 2, the prevalence of a blood type changes from country to country, which can be explained by genetic inheritance. If a study is conducted on individuals of only one race, it may end up creating a skewed result.

This concern is raised by some studies included in this review, such as a study conducted in Pakistan, which found that people with blood type B are more susceptible to infection by SARS-CoV-2. However, Pakistan is part of one of the only regions in the world where there is a higher prevalence of people with blood type B (RAHIM et al., 2021).

Likewise, a study conducted with pregnant women in Romania shows that the largest number of infected women were type A, but the authors themselves already correlate this with the higher prevalence of this type among the Romanian population, and consider the result not significant. (COVALI et al., 2021).

Therefore, it is important to emphasize that there is a need to conduct research involving a population of patients that is multiracial, with the objective of considering possible racial disparities and differences in the prevalence of blood types when analyzing the correlation with SARS-CoV infection. -2 (PAUL et al., 2020).

As much as a correlation exists and can be proven, the progression of the disease will depend on several other factors that may be implicit, such as the patient's age, presence or absence of comorbidities, among others, which may play important roles.

One of the most recognizable consequences of aging is the decline of the immune system. Older people are not considered immunosuppressed, but the vast majority of them do not respond to antigens as quickly as younger people. In addition, the likelihood that these individuals are undergoing treatments with drugs that are immunosuppressive increases with age, making these patients more vulnerable to infections and the development of Covid-19 (MONTECINO-RODRIGUEZ et al., 2013).

The same goes for patients with certain diseases that inhibit the immune system, such as cancer, for example, as well as patients with some milder comorbidities, but which may still influence the onset of the disease, as is the case mainly of arterial hypertension, due to its relationship with the renin angiotensin aldosterone system and the ACE2 receptor, the main cell entry receptor used by SARS-CoV-2 and which is also the target of several drugs for hypertension, which can lead to an increase in the risk and development of infection in these patients (SAVOIA et al., 2021).

Circumstances like these mean that the clinical effects of the correlation between the ABO group and susceptibility, development and mortality by Covid-19 can be easily masked, which may explain the reason for so much controversy surrounding the existence or not of an association (YAMAMOTO et al., 2021).

6 CONCLUSION

The pandemic caused by SARS-CoV-2 is an outbreak that affects human health. Since the first confirmed case, several people have been infected across the globe and many have unfortunately lost their lives due to complications caused by Covid-19. Several studies have been published on the subject since the disease emerged, and among these, studies correlating blood type and levels of SARS-Cov-2 infection.

The data found in the works contemplated in this review suggest a greater susceptibility of type A to infection and a greater protective effect both in susceptibility and in the development of the disease in individuals of type O. However, these correlations are not significant for the development of the disease. They exist, but they are not enough to be decisive in the process of infection by Covid-19.

The studies discussed here have several factors that should be considered, such as the role of race and genetic inheritance in the reliability of the results found, the lack of studies with greater miscegenation of the participating patients, in addition to the results found without statistical significance.

The correlation between blood types and Covid-19 infection exists, but it does not prove to be clinically significant and needs more research on the subject to elucidate this association and what its exact mechanisms are.

REFERENCES

Al-ansari, r. Y. Et al. Abo in correlation to the requirement of mechanical ventilation and mortality in critically ill patients with covid-19. J hematol, 2021.

Al-youha, s. A. Et al. The impact of abo blood groups on clinical outcomes and susceptibility to covid-19: a retrospective study in an unselected population. Transfusion, v. 61, n. 5, p. 1631-1641, may 2021. Issn 0041-1132 (print) 0041-1132.

Almadhi, m. A. Et al. The effect of abo blood group and antibody class on the risk of covid-19 infection and severity of clinical outcomes. Sci rep, 2021.

Ansari-lari, m.; saadat, m. The morbidity and mortality of covid-19 are associated with abo and rh blood groups. Eur j prev cardiol, v. 28, n. 11, p. E26-e28, sep 20 2021. Issn 2047-4873 (print) 2047-4873.

Ayatollahi, a. A. Et al. Association between blood groups and covid-19 outcome in iranian patients. Future virol, aug 2021. Issn 1746-0794 (print) 1746-0794.

Bari, a. Et al. Association of blood groups with the severity and outcome of covid-19 infection in children. J coll physicians surg pak, v. 30, n. 1, p. S57-s59, jan 2021. Issn 1022-386x.

Behboudi, e. Et al. Association between abo blood groups and rhesus antigen and susceptibility to covid-19 in the yazd hospital. New microbes new infect, 2021.

Bethesda. Bethesda handbook of clinical hematology. Philadelphia: lippincott williams & wilkins, 2005. Isbn 0781747155.

Bhattacharjee, s.; banerjee, m.; pal, r. Abo blood groups and severe outcomes in covid-19: a meta-analysis. Postgrad med j, 2020.

Bonifácio, s. L.; novaretti, m. C. Z. Funções biológicas dos antígenos eritrocitários. Revista brasileira de hematologia e hemoterapia, v. 31, n. 2, p. 104-111, 2009. Issn 1516-8484.

Borén, t. Et al. Attachment of helicobacter pylori to human gastric epithelium mediated by blood group antigens. Science, v. 262, n. 5141, p. 1892-5, dec 17 1993. Issn 0036-8075 (print) 0036-8075.

Chams, n. Et al. Covid-19: a multidisciplinary review. Front public health, v. 8, p. 383, 2020. Issn 2296-2565 (print) 2296-2565.

Chegni, h. Et al. Is there a link between covid-19 mortality with genus, age, abo blood group type, and ace2 gene polymorphism? Iran j public health, 2020.

Cheng, y. Et al. Abo blood group and susceptibility to severe acute respiratory syndrome. Jama, v. 293, n. 12, p. 1450-1, mar 23 2005. Issn 0098-7484.

Ciotti, m. Et al. The covid-19 pandemic: viral variants and vaccine efficacy. Crit rev clin lab sci, v. 59, n. 1, p. 66-75, jan 2022. Issn 1040-8363.

Coluk, y. Et al. Association of blood subgroups with pcr test positivity and lung involvement in patients with covid-19. Cureus, v. 13, n. 3, p. E14172, mar 29 2021. Issn 2168-8184 (print)

2168-8184.

Covali, r. Et al. Sars-cov-2 infection susceptibility of pregnant patients at term regarding abo and rh blood groups: a cohort study. Medicina (kaunas), v. 57, n. 5, may 14 2021. Issn 1010-660x (print) 1010-660x.

Fan, q. Et al. Association between abo blood group system and covid-19 susceptibility in wuhan. Front cell infect microbiol, v. 10, p. 404, 2020. Issn 2235-2988.

Faroug mohamed, m. Et al. Susceptibility of blood groups infection with covid-19 disease among sudanese patients suffering from different chronic diseases. Pak j biol sci, v. 24, n. 7, p. 815-820, jan 2021. Issn 1028-8880.

Giangrande, p. L. The history of blood transfusion. Br j haematol, v. 110, n. 4, p. 758-67, sep 2000. Issn 0007-1048 (print) 0007-1048.

Göker, h. Et al. The effects of blood group types on the risk of covid-19 infection and its clinical outcome. Turk j med sci, v. 50, n. 4, p. 679-683, jun 23 2020. Issn 1300-0144 (print) 1300-0144.

Golinelli, d. On the association between the abo blood group and covid-19 susceptibility. Blood transfus, v. 19, n. 1, p. 89-90, jan 2021. Issn 1723-2007 (print) 1723-2007.

Guillon, p. Et al. Inhibition of the interaction between the sars-cov spike protein and its cellular receptor by anti-histo-blood group antibodies. Glycobiology, v. 18, n. 12, p. 1085-93, dec 2008. Issn 0959-6658 (print) 0959-6658.

Halim, m. R. Et al. Abo blood group and outcomes in patients with covid-19 admitted in the intensive care unit (icu): a retrospective study in a tertiary-level hospital in bangladesh. J multidiscip healthc, 2021.

Hatmal, m. M. Et al. Comprehensive structural and molecular comparison of spike proteins of sars-cov-2, sars-cov and mers-cov, and their interactions with ace2. Cells, v. 9, n. 12, dec 8 2020. Issn 2073-4409.

Huang, c. Et al. Clinical features of patients infected with 2019 novel coronavirus in wuhan, china. Lancet, v. 395, n. 10223, p. 497-506, feb 15 2020. Issn 0140-6736 (print) 0140-6736.

Ishaq, u. Et al. Association of abo blood group with covid-19 severity, acute phase reactants and mortality. Plos one, 2021.

Kabrah, s. M. Et al. Susceptibility of abo blood group to covid-19 infections: clinico-hematological, radiological, and complications analysis. Medicine (baltimore), v. 100, n. 52, p. E28334, dec 30 2021. Issn 0025-7974 (print) 0025-7974.

Kabrah, s. M. Et al. Systematic review and meta-analysis of the susceptibility of abo blood group to covid-19 infection. Transfus apher sci, v. 60, n. 4, p. 103169, aug 2021. Issn 1473-0502 (print) 1473-0502.

Kerbage, a. Et al. Impact of abo and rhesus blood groups on covid-19 susceptibility and severity: a case-control study. J med virol, 2021.

Kim, y. Et al. Relationship between blood type and outcomes following covid-19 infection. Seminars in vascular surgery, v. 34, n. 3, p. 125-131, 2021/09/01/ 2021. Issn 0895-7967. Disponível em: < https://www.sciencedirect.com/science/article/pii/s0895796721000405 >.

Komal, a. Et al. Analyses of abo blood groups with susceptibility and symptomatic variations of covid-19 infection, a questionnaire-based survey. Apmis, 2021.

Kumar, g. Et al. Does abo blood groups affect outcomes in hospitalized covid-19 patients? J hematol, 2021.

Latz, c. A. Et al. Blood type and outcomes in patients with covid-19. Ann hematol, v. 99, n. 9, p. 2113-2118, sep 2020. Issn 0939-5555 (print) 0939-5555.

Lehrer, s.; rheinstein, p. H. Abo blood groups, covid-19 infection and mortality. Blood cells mol dis, v. 89, p. 102571, jul 2021. Issn 1079-9796 (print) 1079-9796.

Levi, j. E. Et al. Lack of association between abo blood groups and susceptibility to sars-cov-2 infection. Vox sang, 2020.

Lindesmith, l. Et al. Human susceptibility and resistance to norwalk virus infection. Nat med, v. 9, n. 5, p. 548-53, may 2003. Issn 1078-8956 (print) 1078-8956.

Liu, j. Et al. Sars-cov-2 cell tropism and multiorgan infection. Cell discov, v. 7, n. 1, p. 17, mar 23 2021. Issn 2056-5968 (print) 2056-5968.

Liu, n. Et al. The impact of abo blood group on covid-19 infection risk and mortality: a systematic review and meta-analysis. Blood reviews, v. 48, p. 100785, 2021/07/01/ 2021. Issn 0268-960x. Disponível em: < https://www.sciencedirect.com/science/article/pii/s0268960x20301351 >.

Mahmud, r. Et al. Association of abo blood groups with presentation and outcomes of confirmed sars cov-2 infection: a prospective study in the largest covid-19 dedicated hospital in bangladesh. Plos one, v. 16, n. 4, p. E0249252, 2021. Issn 1932-6203.

Matzhold, e. M. Et al. Lewis and abo histo-blood types and the secretor status of patients hospitalized with covid-19 implicate a role for abo antibodies in susceptibility to infection with sars-cov-2. Transfusion, v. 61, n. 9, p. 2736-2745, sep 2021. Issn 0041-1132 (print) 0041-1132.

May, j. E. Et al. Questioning the association between abo type and outcomes in patients with covid-19. Ann hematol, v. 100, n. 12, p. 3081-3082, dec 2021. Issn 0939-5555 (print) 0939-5555.

Montecino-rodriguez, e.; berent-maoz, b.; dorshkind, k. Causes, consequences, and reversal of immune system aging. J clin invest, v. 123, n. 3, p. 958-65, mar 2013. Issn 0021-9738 (print) 0021-9738.

Muñiz-diaz, e. Et al. Relationship between the abo blood group and covid-19 susceptibility, severity and mortality in two cohorts of patients. Blood transfus, v. 19, n. 1, p. 54-63, jan 2021. Issn 1723-2007 (print) 1723-2007.

Nalbant, a. Et al. Association of abo blood group and age with covid-19 positive test. Rev assoc med bras (1992), v. 67suppl 1, n. Suppl 1, p. 46-50, 2021. Issn 0104-4230.

Naqvi, a. A. T. Et al. Insights into sars-cov-2 genome, structure, evolution, pathogenesis and therapies: structural genomics approach. Biochim biophys acta mol basis dis, v. 1866, n. 10, p. 165878, oct 1 2020. Issn 0925-4439 (print) 0925-4439.

Padhi, s. Et al. Abo blood group system is associated with covid-19 mortality: an epidemiological investigation in the indian population. Transfusion clinique et biologique, v. 27, n. 4, p. 253-258, 2020/11/01/ 2020. Issn 1246-7820. Disponível em: < https://www.sciencedirect.com/science/article/pii/s124678202030118x >.

Paul, s. Et al. Abo blood type and outcomes in a diverse covid-19 infected population. Blood, v. 136, p. 27-28, 2020/11/05/ 2020. Issn 0006-4971. Disponível em: < https://www.sciencedirect.com/science/article/pii/s000649711873437x >.

Rahim, f. Et al. Abo / rh-d blood types and susceptibility to corona virus disease-19 in peshawar, pakistan. Pak j med sci, v. 37, n. 1, p. 4-8, jan-feb 2021. Issn 1682-024x (print)
1681-715x.

Rana, r.; ranjan, v.; kumar, n. Association of abo and rh blood group in susceptibility, severity, and mortality of coronavirus disease 2019: a hospital-based study from delhi, india. Front cell infect microbiol, v. 11, p. 767771, 2021. Issn 2235-2988.

Sainz bueno, j. A. Et al. Association of abo and rh blood groups with obstetric outcomes in sars-cov-2 infected pregnancies: a prospective study with a multivariate analysis. European journal of obstetrics & gynecology and reproductive biology, v. 264, p. 41-48, 2021/09/01/ 2021. Issn 0301-2115. Disponível em: < https://www.sciencedirect.com/science/article/pii/s0301211521003432 >.

Savoia, c.; volpe, m.; kreutz, r. Hypertension, a moving target in covid-19: current views and perspectives. Circ res, v. 128, n. 7, p. 1062-1079, apr 2 2021. Issn 0009-7330 (print) 0009-7330.

Sertbas, m. Et al. Association of blood groups on the risk of covid-19 infection, morbidity, and mortality. North clin istanb, 2021.

Shibeeb, s.; khan, a. Abo blood group association and covid-19. Covid-19 susceptibility and severity: a review. Hematology, transfusion and cell therapy, 2021/09/14/ 2021. Issn 2531-1379. Disponível em: < https://www.sciencedirect.com/science/article/pii/s2531137921001346 >.

Silva-filho, j. C.; melo, c. G. F. D.; oliveira, j. L. D. The influence of abo blood groups on covid-19 susceptibility and severity: a molecular hypothesis based on carbohydrate-carbohydrate interactions. Medical hypotheses, v. 144, p. 110155, 2020/11/01/ 2020. Issn 0306-9877. Disponível em: < https://www.sciencedirect.com/science/article/pii/s0306987720322581 >.

Storry, j. R. Et al. International society of blood transfusion working party on red cell immunogenetics and blood group terminology: report of the dubai, copenhagen and toronto meetings. Vox sang, v. 114, n. 1, p. 95-102, jan 2019. Issn 0042-9007 (print) 0042-9007.

Szymanski, j. Et al. Abo blood type association with sars-cov-2 infection mortality: a single-center population in new york city. Transfusion, 2021.

Tamayo-velasco, á. Et al. Can the cytokine profile according to abo blood groups be related to worse outcome in covid-19 patients? Yes, they can. Front immunol, v. 12, p. 726283, 2021. Issn 1664-3224.

Thornton, n. M.; grimsley, s. P. Clinical significance of antibodies to antigens in the abo, mns, p1pk, rh, lutheran, kell, lewis, duffy, kidd, diego, yt, and xg blood group systems. Immunohematology, v. 35, n. 3, p. 95-101, sep 2019. Issn 0894-203x (print) 0894-203x.

Tormey, c. A.; hendrickson, j. E. Transfusion-related red blood cell alloantibodies: induction and consequences. Blood, v. 133, n. 17, p. 1821-1830, apr 25 2019. Issn 0006-4971 (print) 0006-4971.

Wu, s.-c. Et al. The sars-cov-2 receptor-binding domain preferentially recognizes blood group a. Blood advances, v. 5, n. 5, p. 1305-1309, 2021. Issn 2473-9529. Disponível em: < https://doi.org/10.1182/bloodadvances.2020003259 >. Acesso em: 11/24/2022.

Yamamoto, f.; yamamoto, m.; muñiz-diaz, e. Blood group abo polymorphism inhibits sars-cov-2 infection and affects covid-19 progression. Vox sang, v. 116, n. 1, p. 15-17, jan 2021. Issn 0042-9007 (print) 0042-9007.

Yan, r. Et al. Structural basis for the recognition of sars-cov-2 by full-length human ace2. Science, v. 367, n. 6485, p. 1444-1448, mar 27 2020. Issn 0036-8075 (print)
0036-8075.

Yaylaci, s. Et al. The effect of abo and rh blood group antigens on admission to intensive care unit and mortality in patients with covid-19 infection. Rev assoc med bras (1992), v. 66suppl 2, n. Suppl 2, p. 86-90, 2020. Issn 0104-4230.

Zhao, j. Et al. Relationship between the abo blood group and the coronavirus disease 2019 (covid-19) susceptibility. Clin infect dis, v. 73, n. 2, p. 328-331, jul 15 2021. Issn 1058-4838 (print) 1058-4838.

Zhu, n. Et al. A novel coronavirus from patients with pneumonia in china, 2019. N engl j med, v. 382, n. 8, p. 727-733, feb 20 2020. Issn 0028-4793 (print) 0028-4793.