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REVIEW

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The relationship between blood groups and risk of infection with SARS-CoV-2 or development of severe outcomes: A review

Pourya Shokri[1†] | Saeid Golmohammadi[1†] | Maryam Noori[2†] | Seyed Aria Nejadghaderi[1,3] | Kristin Carson-Chahhoud[4,5] | Saeid Safiri[6,7]

[1]School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[2]Student Research Committee, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

[3]Systematic Review and Meta-analysis Expert Group (SRMEG), Universal Scientific Education and Research Network (USERN), Tehran, Iran

[4]Australian Centre for Precision Health, University of South Australia, South Australia, Australia

[5]School of Medicine, University of Adelaide, South Australia, Australia

[6]Tuberculosis and Lung Disease Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

[7]Social Determinants of Health Research Center, Department of Community Medicine, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Correspondence

Dr. Saeid Safiri, Tuberculosis and Lung Disease Research Center, Tabriz University of Medical Sciences, Daneshgah St, Tabriz, Iran. Postal code: 5142954481.
Email: saeidsafiri@gmail.com; safiris@tbzmed.ac.ir

Summary

The outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is considered a global catastrophe that has overwhelmed health care systems. Since initiation of the pandemic, identification of characteristics that might influence risk of infection and poor disease outcomes have been of paramount interest. Blood group phenotypes are genetically inherited characteristics whose association with certain infectious diseases have long been debated. The aim of this review is to identify whether a certain type of blood group may influence an individual's susceptibility to SARS-CoV-2 infection and developing severe outcomes. Our review shows that blood group O protects individuals against SARS-CoV-2, whereas blood group A predisposes them to being infected. Although the association between blood groups and outcomes of COVID-19 is not consistent, it is speculated that non-O blood group carriers with COVID-19 are at higher risk of developing severe outcomes in comparison to O blood group. The interaction between blood groups and SARS-CoV-2 infection is hypothesized to be as result of natural antibodies against blood group antigens that may act as a part of innate immune response to neutralize viral particles. Alternatively, blood group antigens could serve as additional receptors for the virus and individuals who are capable of expressing these antigens on epithelial cells, which are known as secretors, would then have a high propensity to be affected by SARS-CoV-2.

KEYWORDS

ABO blood groups, blood groups, COVID-19, Rh blood groups, SARS-CoV-2

Abbreviations: ACE, Angiotensin-converting enzyme; ACE2, Angiotensin-converting enzyme 2; COVID-19, Coronavirus disease 2019; FUT2, Fucosyltransferase 2; ICU, Intensive care units; MERS-CoV, Middle East respiratory syndrome coronavirus; MeSH, Medical Subject Heading; RBC, Red blood cell; RBD, Receptor binding domain; SARS-CoV, Severe acute respiratory syndrome coronavirus; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

[†]These authors contributed equally to this work as first authors.

1 | INTRODUCTION

In late December 2019, the outbreak of coronavirus disease 2019 (COVID-19) was observed with an unusual pneumonia in Wuhan, China.[1] It rapidly spread worldwide and was declared as a pandemic by the World Health Organization (WHO) on 11 March 2020.[2] Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the current global health crisis, and it has affected more than 143 million individuals and led to almost 3 million deaths across the world as of late April 2021.[3] COVID-19 primarily involves the lower respiratory tract and is characterized through a dry cough, fever, dyspnoea, and bilateral pneumonia.[4] It has been estimated that 23% of infected cases develop severe symptoms and 6% die due to complications of the disease, such as pneumonia and end-organ failure.[5] Advanced age, male sex, and comorbidities such as diabetes, hypertension, and renal disorders are related to the high SARS-CoV-2 infection rate.[6]

The mechanism of SARS-CoV-2 infection mainly depends on spike protein since it utilizes angiotensin-converting enzyme 2 (ACE2) as receptor for cell entry.[7] Several host proteases could help the virus to invade the cells more efficiently.[7] Expression of ACE2 on various human cell surfaces gives SARS-CoV-2 the ability to infect multiple tissues.[8]

The two other zoonotic coronaviruses that have caused epidemic infections in the past two decades are severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV).[9] The long incubation period and highly contagious nature of COVID-19 are purported to be the primary reason for the substantially high death toll, despite the lower case mortality rate of SARS-CoV-2 in comparison with SARS-CoV and MERS-CoV.[10]

For decades, blood group antigens were relegated just to compatibility testing for blood transfusions. However, clinical significance has expanded with relevance in pathogenesis of microorganisms and even providing the first line of defence against infectious agents through corresponding natural antibodies. ABO and Rh blood groups, are among factors that may offer susceptibility or resistance to viral invasion and also influence prognosis of infectious diseases.[11] Understanding the relationship between diseases that have caused pandemics and blood groups could be a useful risk factor to aid prediction of outcomes and establish efficient measures in combating the disease spread with respect to blood group distributions.

In this review, we sought to describe the relationship between blood groups and risk of infection with SARS-CoV-2 and developing unfavourable outcomes.

2 | METHODS

We searched PubMed database to identify publications from peer-reviewed journals. We used Medical Subject Heading (MeSH) terms, including 'ABO Blood-Group System,' 'Rh-Hr Blood-Group System,' 'SARS-CoV-2,' and 'COVID-19' in combination with other free terms such as 'COVID-19,' 'SARS-CoV-2,' '2019-nCoV,' 'ABO blood types,' 'ABO factor,' 'ABO phenotype,' 'blood group,' 'Rhesus Blood Group System,' 'Rh factor,' 'antigen D,' and 'blood group antigens.' Also, medRxiv (https://www.medrxiv.org/) was searched for pre-prints articles with 'blood group AND COVID-19' key words. The search was conducted on March 11, 2021 and no search filters on publication type, language, time period, and other fields were implemented. Reference lists of all relevant publications were manually screened to identify further qualified studies.

3 | BLOOD GROUP ANTIGENS AND DISEASES

There are a number of carbohydrates and proteins on human red blood cell (RBC) membranes that are known as blood group antigens.[12] According to the World Blood Transfusion Association, about 341 antigens have been identified and categorized into 41 blood group systems.[13] ABO blood group system, as discovered by Landsteiner, is the most important blood group system.[14] The sequential additions of carbohydrates to an oligosaccharide backbone resulted in formation of three antigens, including A, B, and H.[15] Adding a terminal residue to the oligosaccharide backbone, creates the H antigen which then acts as a precursor for formation of A and B antigens.[15] ABO gene encodes two glycosyltransferase enzymes that attach N-acetylgalactosamine or D-galactose to H antigen to produce A and B antigens, respectively.[15] In the case of no glycosyltransferase expression, the H antigen serves as an O phenotype.[15] Group O is the most frequent blood group globally, followed by group A, B, and then AB.[16] However, the distribution of these phenotypes widely varies in different populations and is mostly attributed to epidemics that have occurred in the past, so blood groups that were more resistant against disease tended to be naturally selected over time.[17]

ABO phenotypes are a common target of epidemiological studies since they are genetically determined traits and the frequency of their distribution varies noticeably across ancestry groups.[18] Accordingly, multiple investigations have been conducted to identify the possible relationship between blood groups as genetic risk factors for various human diseases, especially infectious diseases.[11] A relationship between blood groups and diseases was first postulated in 1917 to investigate an association between ABO blood types and tuberculosis.[19] Since then, many studies have supported the hypothesis that blood groups could be related to the risk of occurrence and progression of several diseases, including cardiovascular disorders, diabetes, neurological diseases, and cancers of the gastrointestinal system.[20,21] In the case of infectious diseases, it has been shown that individuals with blood group O are at higher risk of being infected with norovirus, HBV, Vibrio cholerae, and dengue virus.[22–26] Conversely, individuals with non-O blood groups were at higher risk of severe *Plasmodium falciparum* infection than those with blood group O.[27] Moreover, the efficacy of infectious disease related vaccines may be influenced by blood group distribution in the target population.[28,29]

The mechanism in which blood group antigens may confer susceptibility or protection from infectious agents or influence the evolution of diseases have yet to be elucidated. However, there is some underlying evidence to suggest that blood group antigens may play a key role as receptors and/or cofactors for several infectious agents[11,30] including Norwalk virus and *Helicobacter pylori* which interact with ABO antigens to successfully bind with gastric mucosa.[31,32] Furthermore, various pathogens are capable of expressing blood group antigens identical or cross-reactive epitopes on their surfaces.[11] Therefore, natural antibodies against ABO antigens may act as part of innate immunity that can attenuate infection.[11]

The next general blood group category is the Rhesus (Rh) system, determined by the presence or absence of Rh or D antigen. Unlike the ABO system, Rh phenotypes are associated with few diseases, most of which are haemolytic diseases of newborns that occur as a consequence of Rh mismatching between mother and offspring.[33]

4 | BLOOD GROUPS AND RISK OF CONTRACTING WITH SARS-CoV-2

The initial idea of a relationship between blood groups and coronavirus infections refers to 2005, where Cheng et al. examined the association of ABO blood groups and risk of SARS-CoV infection on 45 health care staff who were not protected by relevant equipment in exposure to affected patients.[34] The comparison revealed that individuals with blood group O had a lower risk of infection compared to non-O blood groups (odds ratio [OR] = 0.18; 95% confidence interval [CI]: 0.04–0.81; p = 0.03).[34] Given that the epidemic was controlled rapidly, the former finding was not sufficiently debated nor corroborated by further research at the time. More investigations are now underway to better understand if there is the same association between blood groups and the emerging virus, due to SARS-CoV-2 and SARS-CoV sequences being very similar and given that both utilize ACE2 for cell entry.[35]

A recent Italian-Spanish genome-wide association study found that polymorphisms at two susceptibility loci, including 9q34.2 and 3p21.31, contributed to SARS-CoV-2 induced respiratory failure that was significant at the genome-wide level.[36] The ABO gene resides on 9q34.2 locus, which suggests that the ABO blood group system has potential implications for SARS-CoV-2 infection.[36]

Several reports have come to a conclusion that O blood group subjects are at lower odds of testing positive for COVID-19, whereas those with non-O blood groups, particularly group A, have higher susceptibility to the infection.[35–53] For instance, in a French study by Gallian et al. including 998 samples collected from blood donors, the seroprevalence values of SARS-CoV-2 neutralizing antibodies were lower in group O donors compared with other blood groups (1.32% vs. 3.86%; p = 0.014).[46] A previous systematic review and meta-analysis of seven studies demonstrated that patients with COVID-19 were more likely to have blood group A (OR = 1.23; 95% CI: 1.09–1.40) and less likely to have blood group O (OR = 0.77; 95% CI: 0.67–0.88).[49] In addition, a retrospective cohort study using the data of 14,112 individuals tested for SARS-CoV-2, reported that patients with Rh negative phenotype presented 2.7% lower risk of initial infection (Risk ratio [RR] = 0.85; 95% CI: 0.73–0.96).[54] Similarly, a large cohort enrolling 225,386 confirmed COVID-19 cases by PCR testing showed that patients with blood group O and negative Rh phenotype were less represented as compared to other blood groups (RR = 0.74; 95% CI: 0.66–0.83).[55]

Moreover, populations living in endemic malaria regions appear to have a lower incidence of COVID-19.[56,57] One potential explanation for this restricted spread is high prevalence of blood group O in malaria-endemic regions, which have been selected due to protective effects against *Plasmodium falciparum*.[27,58] Therefore, since O blood group carriers are somewhat resistant to SARS-CoV-2 infection, reduced spread of the infection would reasonably be expected in these regions.[59,60]

It is noteworthy to mention that the impact of blood groups on COVID-19 may differ by race/ethnicity. In a study including 2,033 COVID-19 patients in the United States of America (USA), the distribution of O phenotype was lower than expected and A phenotype was over-represented in White patients, while among Black and Hispanic patients the observed and expected ABO phenotype distribution showed no significant difference.[61] This is in concordance with a previous observation that blood group A in White patients was associated with developing acute respiratory failure syndrome after severe sepsis or major trauma, unlike Black patients.[62]

Although all studies in this area have been performed on adult patients, NCT04682912 is recruiting approximately 2,000 children under the age of 18 years who were documented positive for SARS-CoV-2 through PCR assay in order to examine the possible link of blood groups with SARS-CoV-2 infection in such groups of patients.[63]

5 | SECRETOR STATUS OF BLOOD GROUP ANTIGENS AND SARS-CoV-2 INFECTION

ABO blood group antigens are expressed not only on erythrocytes but also widely distributed along the mucosal membrane of the gastrointestinal tract, respiratory and reproductive systems, and in their secretions.[64] Expression of such antigens on epithelial cell surfaces and secretions is genetically determined by *FUT2* gene, encoding fucosyltransferase 2 enzyme.[65] Based on synthesis of this enzyme, approximately 80% of the population are 'secretor' and 20% are 'non-secretors'.[65] Expression of blood group antigens on mucosal cells have raised some questions about whether the interactions with infectious agents play a role on entry processes of pathogens. In this case, it was shown that in non-secretors, lack of blood type antigen expression on mucosal cells offers some degree of protection from several pathogens, which then potentially bind to these antigens on mucosal surfaces.[65–67]

Recently, it has been shown that the receptor binding domain (RBD) of SARS-CoV-2 spike protein exhibited only low-level affinity for binding to A, B, and H antigens on RBCs but, when exposed to blood group antigens expressed on respiratory epithelial cells, a high

affinity was found toward binding to blood group A antigen in comparison with B and H antigens.[68] Consistently, Valenti et al. determined that in non-O blood group patients affected by SARS-CoV-2, non-secretor phenotype was significantly associated with reduced need of mechanical ventilation and intensive care unit (ICU) admission as compared to secretor phenotypes (OR = 0.57; 95% CI: 0.37–0.87; $p = 0.007$), whereas it did not reach statistical significance for blood group O patients.[69] Therefore, secretor phenotype in group A carriers may play a fundamental role in SARS-CoV-2 invasion to host respiratory cells and further progression of the disease. However, this conclusion may be challenged by a previous study in which no correlation was found between *FUT2* gene and COVID-19 prevalence nor mortality.[70] Thus, clarifying the exact role of secretor status on SARS-CoV-2 infection requires further investigations.

6 | BLOOD GROUPS AND PROGNOSIS OF COVID-19

The majority of studies concluded that ABO blood groups cannot influence the outcomes of COVID-19 and are not associated with mortality.[17,39,41,50,51,60,71–78] However, those few studies that found a relationship between blood groups and evolution of COVID-19 were almost consistent in their results, reporting a higher risk of unfavourable outcomes in non-O blood groups compared to blood group O.

Evaluating the relationship between blood groups and risk of severe disease or death, Ray et al., have enrolled 225,556 cases of COVID-19.[55] They reported that blood group O and Rh negative carriers represented lower risk of developing sever outcomes or death as compared to non-O blood groups (adjusted RR = 0.87; 95% CI: 0.78–0.97) and Rh positive (aRR: 0.82; 95%CI: 0.68-0.96) individuals, respectively.[55] In a systematic review and meta-analysis of five studies, a statistically significant association has been found in the case of blood group A and a higher risk of mortality due to SARS-CoV-2 infection, while no association was observed in other blood groups.[37] Takagi et al. performed a meta-regression analysis on data of 101 nations, with blood group distribution data available online.[79] In addition to blood group proportions, total number of confirmed COVID-19 cases and deaths in these nations in a whole population of ~7 billion were almost 9 million and 450,000, respectively.[79] It showed that blood group O was independently associated with lower SARS-CoV-2 mortality ($p = 0.02$).[79] The data of all the studies evaluating this association are summarized in Table 1.

7 | THE POSSIBLE MECHANISMS UNDERLYING THE ASSOCIATION BETWEEN BLOOD GROUPS AND SARS-CoV-2 INFECTION

The inherent mechanisms explaining protection from or predisposition to SARS-CoV-2 infection are not yet clear, although there are multiple possibilities.

7.1 | ABO antigens as receptors for SARS-CoV-2 cell entry

Viral interaction with ACE2 for facilitating cell entry might be possible with other host molecules such as blood group antigens, which in turn affect the susceptibility of different blood type carriers to getting infected by SARS-CoV-2. A recent in vitro study indicated that when the SARS-CoV-2 exposed to ABO antigens expressed on respiratory epithelial cells, the RBD showed a significant preference for binding to A antigen compared to B and H antigens ($p < 0.001$). This highlights the potential role of A antigen expressing on epithelial cells over the development of SARS-CoV-2 infection.[68]

7.2 | Antibodies against ABO antigens and neutralization of SARS-CoV-2 particles

In 2008, Guillon et al. demonstrated that the adhesion of SARS-CoV spike protein to ACE2 could be inhibited by natural anti-A antibodies.[88] The same can be extended to SARS-CoV-2.[89] Thus, one might assume that both blood group O and B should provide protection, while numerous studies revealed that blood group B do not alter the risk of acquiring COVID-19.[38,49,90] For instance, Gerard et al. indicated that subjects with anti-A antibody (i.e. blood groups O and B) were significantly under-represented in COVID-19 in comparison with A and AB ($p < 0.001$), A ($p < 0.001$), or AB ($p = 0.032$).[91] Then, they examined the hypothesis if there is a difference between group O and B anti-A antibody.[91] As a result, the prevalence of group O carriers was significantly lower, whereas the prevalence of group B carriers was significantly higher in COVID-19 patients ($p < 0.001$), suggesting that anti-A from O blood groups are more protective than anti-A from B.[91] Differences in the nature of anti-A antibodies from O and B are responsible for the predominant immunoglobulin isotypes of anti-A antibody, being IgG in blood group O and IgM in blood group B.[89,92] A beneficial aspect of this theory would be implicated in convalescent plasma therapy, so that donors with higher titres of natural antibody based on their blood group could be recruited selectively in order to optimize the treatment.[89]

7.3 | ABO blood group phenotypes and SARS-CoV-2 progression

Blood group O is associated with a lower risk of unfavourable outcomes in patients with COVID-19.[55,79,80] A possible explanation may be attributed to lower levels of von Willebrand and VIII factors in blood group O individuals which may lead to decreased risk of cardiovascular diseases.[93–96] Coagulopathy and vasculopathy features of COVID-19 are reported to be substantial contributors to development of acute respiratory distress syndrome.[97] Therefore, lower risk of disease progression shown in blood group O patients is

TABLE 1 Associations between blood groups and COVID-19 unfavourable outcomes in recent studies

First author	Country	Study design	Age (Mean or Median)	Gender (% female)	Number of COVID-19 participants	Adjustment	Outcomes
Hoiland et al.[40]	Canada	Retrospective cohort	68	35.7	95	Yes Sex Age Comorbidities	(i) A greater proportion of A or AB patients required mechanical ventilation compared with O or B patients (adjusted HR = 1.76; 95% CI: 1.17–2.65; $p = 0.007$). (ii) A greater proportion of A or AB patients required CRRT compared with O or B patients (adjusted HR = 3.75; 95% CI; 1.28–10.9; $p = 0.02$) (iii) Median ICU length of stay was longer in A or AB patients (13.5 days) than in O or B patients (9 days; $p = 0.03$), but there were no differences in the probability of ICU discharge after adjustment (adjusted HR = 0.63; 95% CI: 0.39–1.03; $p = 0.06$).
						No	ICU admission white blood cell count ($p = 0.02$), highest recorded value for fibrin D-dimer ($p = 0.05$), AST ($p = 0.02$), ALT ($p = 0.01$), and highest recorded value for serum creatinine ($p = 0.03$) were lower in O or B patients than in A or AB patients.
Muñiz-Diaz et al.[80]	Spain	Case-control study	69	40.9	965	Yes Sex Age Comorbidities	Risk of mortality in group A individuals was higher than in group O individuals (OR = 1,75; 95% CI: 1.22–2.51; $p = 0.00$)
						No	(i) Patients with blood group A have a higher risk of death than the rest of the ABO blood groups (OR = 1.35; 95% CI: 1.03–1.78; $p = 0.029$). (ii) Patients with blood group O showed a lower risk of death than non-O blood group patients (OR = 0.75; 95% CI: 0.56–0.99; $p = 0.044$)
Mannan et al.[81]	Bangladesh	Cross-sectional	40	25	1021	No	A significant relationship was found between blood groups and being symptomatic or asymptomatic (p 0.009).
Kim et al.[82]	South Korea	Retrospective cohort	49	49	2840	No	COVID-19 patients with blood type A were more prone to progress severe outcomes ($p < 0.001$).
El-Shitany et al.	Egypt and Saudi Arabia	Cross-sectional	33	84	726	No	(i) Blood group O showed the highest percentage of patients who experienced an oxygen saturation range of 70%–80% ($p = 0.025$) (ii) Blood group O and A showed the highest and lowest percentage of patients who required artificial respiration ($p = 0.05$ and $p = 0.05$, respectively)

(Continues)

TABLE 1 (Continued)

First author	Country	Study design	Age (Mean or Median)	Gender (% female)	Number of COVID-19 participants	Adjustment	Outcomes
							(iii) Blood group B showed the lowest percentage of patients who experienced myalgia ($p = 0.039$) (iv) Blood group B showed the lowest percentage of patients who needed 3 weeks or more to recover ($p = 0.045$)
Kotila et al.[83]	Nigeria	Cross-sectional	38.8	33.1	302	No	Patients with blood group O and B were more presented in symptomatic COVID-19 group than asymptomatic group ($p = 0.03$).
Ad'hiah et al.[84]	Iraq	Case-control	49.8	40.3	300	Yes Sex Age	Significantly increased risk of death in COVID-19 cases was associated with groups A (OR = 14.60; 95% CI: 2.85–74.88; $p = 0.001$), AB (OR = 12.92; 95% CI: 2.11–79.29; $p = 0.006$), A + AB (OR = 14.67; 95% CI: 2.98–72.33; $p = 0.001$), and A + B + AB (OR = 9.67; 95% CI: 2.85–74.88; $p = 0.005$).
Aktimur et al.[42]	Turkey	Retrospective cohort	53.3	50.8	179	No	(i) Duration of ICU stay was longer in patient with blood group A ($p = 0.013$). (ii) Mortality was higher in patients with group A ($p = 0.027$).
Belaouni et al.[43]	Morocco	Cross-sectional	35.13	0	242	No	Covid-19 patients with blood group AB were more at risk of developing headache ($p < 0.001$),
Zalba Marcos et al.[85]	Spain	Retrospective cohort	70.9	36	226	Yes Sex Age	Group B and AB developed more thrombosis ($p = 0.012$), required more admission to the ICU ($p = 0.037$), and had elevated fibrinogen level ($p = 0.005$).
Ray et al.[55]	Canada	Retrospective cohort	53.8	71	225,556	Yes Sex Age Area-level income quintile Rurality Local health integration network	(i) Patients with blood type B were at higher risk for severe illness or death than type A (adjusted RR = 1.21; 95% CI: 1.04–1.40) (ii) Patients with blood type O were at lower risk for severe illness or death than all others types (adjusted RR = 0.87; 95% CI: 0.78–0.97) (iii) Patients with Rh- blood type were at lower risk for severe illness or death than Rh + blood type (adjusted RR = 0.82; 95% CI: 0.68–0.96) (iv) Type O blood with negative Rh phenotype versus other blood types was protective against SARS-CoV-2 positivity without severe illness or death (adjusted OR = 0.72; 95% CI: 0.63–0.83) and also SARS-CoV-2 positivity with severe illness or death (adjusted

TABLE 1 (Continued)

First author	Country	Study design	Age (Mean or Median)	Gender (% female)	Number of COVID-19 participants	Adjustment	Outcomes
						Comorbidities	OR = 0.84; 95% CI: 0.65–1.08).
Kibler et al.[86]	France	Retrospective cohort	82 ± 8.4	68.2	22	Yes Sex Age Comorbidities	Blood group A versus other blood groups were associated with COVID-19 severity (hospitalization and/or death) (OR = 8.27; 95% CI: 1.83–37.43; $p = 0.006$).
Schetelig et al.[87]	Germany	Cross-sectional	50	66.9	6919	Yes Sex Age BMI Comorbidities	Blood group B was associated with a higher risk of severe respiratory infections (OR = 1.24; 95% CI: 1.01–1.53; $p = 0.038$) and hospitalizations (OR = 1.78; 95% CI: 1.18–2.68; $p = 0.006$) compared to blood group O.
Takagi et al.[79]	101 nations across the world	Cross-sectional	-	-	6.8 billion	Yes Age Comorbidities Tobacco and alcohol use Life expectancy at birth Medical doctor/nursing/midwifery personnel density GDP/GNI per capita–PPP Annual PM2.5 concentration Daily ambient ultraviolet radiation	Blood group O ($p = 0.022$) were associated with lower mortality.
						No	(i) Blood group B ($p = 0.004$) and O ($p < 0.001$) were associated with lower mortality.(ii) Blood group A ($p = 0.001$) was associated with higher mortality.
Pahdi et al.[59]	33 states and union territories in India	Cross-sectional	-	-	-	No	An inverse association was revealed between blood group O and COVID-19 death per million ($r = -0.370$; $p = 0.033$) and a positive correlation of blood group B with COVID-19 mortality rate ($r = 0.687$; $p < 0.0001$)

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019; GDP, gross domestic product; GNI, gross national income; HR, hazard ratio; ICU, intensive care unit; OR, odds ratio; PPP, purchasing; RR, risk ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

assumed to be a result of this phenomenon.[98,99] Moreover, it was reported that levels of angiotensin-converting enzyme (ACE), which is responsible for converting angiotensin I to angiotensin II, is lower in blood group O carriers.[100] Angiotensin II could promote inflammatory responses and also induce high blood pressure.[101] Therefore, low levels of ACE in group O patients infected with SARS-CoV-2 may be accompanied by presentation of milder symptoms.

8 | BLOOD GROUP DISTRIBUTIONS AND DYNAMIC OF COVID-19 PANDEMIC

To examine the relationship between dynamics of COVID-19 pandemic and distribution of blood groups, Liu et al. analysed a large data set from WHO and Johns Hopkins University, representing nearly 5.4 billion people across the world.[102] They identified that infection case growth factor and death case growth factor per day were positively associated with proportion of individuals with blood group A.[102] In order to assess other parameters related to the dynamic of the COVID-19 pandemic, countries were divided into two groups based on a known higher (⩾30%) and lower (<30%) proportion of blood group A.[102] At initiation of the exponential phase of the COVID-19 pandemic, there was no difference in infection cases between these two groups, while the number of infections and deaths 26 days after the beginning of the pandemic were significantly higher for countries with high proportions of individuals with blood group A.[102] In addition, death cases doubling time per day was significantly shorter for higher blood group A countries ($p < 0.05$).[102] While the impact of confounder variables was not considered in this study, it provided valuable results on association of blood groups and the dynamic of the COVID-19 pandemic.[102]

9 | COVID-19 PANDEMIC AND AN ONGOING INCREASE IN THE RATE OF PUBLICATIONS

Since the initiation of COVID-19 pandemic, there has been a great deal of concern regarding rapid expansion of low-quality research and investigations. This is especially evident in literature attempting to identify a possible link between blood types and susceptibility to COVID-19 or risk of developing severe outcomes. The effect of cofounding variables such as age, sex, ethnicity, genetic variations, and underlying comorbidities are often neglected, meaning associations that have been discovered using this approach are somewhat questioned. In this regard, Delanghe et al. found a significant correlation between A allele and both COVID-19 prevalence and mortality in univariate analysis, but A allele lost its significance when genetic variants, including polymorphisms of ACE and complement component 3 (C3) were added to the multivariate regression model. This suggesting that the role of blood groups in COVID-19 appear to be secondary to other variables rather than independent.[70]

Moreover, in the case of blood group comparison between infected and non-infected individuals, a great number of studies obtained the control population from blood donors that are typically recruited from people in group O due to their universal compatibility, therefore it may have resulted in overestimation of O carriers in control groups.[103] Consequently, the results of such studies should be interpreted with great caution.

Taken together, if we assume that there is a real connection between blood groups and SARS-CoV-2 infection, then it might be helpful in risk stratification of a target population to prioritize vaccination programs for the most susceptible groups. It should also be taken into account that individuals with blood group A must strengthen protection for minimizing their exposure to the virus. However, this finding does not guarantee O blood carriers become fully protected, hence, they should still observe precaution to avoid increasing the risk of SARS-CoV-2 infection. Furthermore, biological differentiation as the basis for policy decisions need to be weighed against ethical and social implications in a real-world public health setting. On a larger scale, countries with higher proportions of individuals with blood group A could consider implementing restriction measures more actively and earlier, while if the proportion of people with blood type O is predominant, a less intensive and slower restriction strategy could be implemented due to the reduced dynamic of COVID-19.

10 | CONCLUSION

Although the association between blood groups and outcomes of COVID-19 is not certain, it is speculated that non-O blood group carriers with COVID-19 are at higher risk of developing severe outcomes. The interaction between blood groups and SARS-CoV-2 infection is hypothesized to be as result of natural antibodies against blood group antigens. Also, the severity of disease and disease complications may be influenced by secretor status and ABO antibody titer. Further preclinical and clinical studies are warranted to draw a precise conclusion on the association between blood groups and SARS-CoV-2 infection.

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No conflict of interest declared.

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P.S., S.G., M.N., and S.A.N. prepared the first draft of the manuscript; K.C.C. and S.S. critically revised and edited the manuscript; S.S. supervised this project. All authors reviewed and approved the final version of the manuscript.

ORCID

Seyed Aria Nejadghaderi https://orcid.org/0000-0002-8692-9720
Saeid Safiri https://orcid.org/0000-0001-7986-9072

REFERENCES

1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020;382:727-733. https://doi.org/10.1056/NEJMoa2001017
2. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. *Acta Biomed Atenei Parm*. 2020;91:157-160. https://doi.org/10.23750/abm.v91i1.9397
3. *WHO Coronavirus Disease (COVID-19) Dashboard*. https://covid19.who.int/ [29 January 2021].
4. Adhikari SP, Meng S, Wu Y-J, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. *Infectious diseases of poverty*. 2020;9:1-12.
5. Li J, Huang DQ, Zou B, et al. Epidemiology of COVID-19: a systematic review and meta-analysis of clinical characteristics, risk factors, and outcomes. *J Med Virol* 2021;93:1449-1458. https://doi.org/10.1002/jmv.26424
6. Rashedi J, Mahdavi Poor B, Asgharzadeh V, et al. Risk factors for COVID-19. *Infez Med*. 2020;28:469-474.
7. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. 2020;181:271-280. https://doi.org/10.1016/j.cell.2020.02.052
8. Kochi AN, Tagliari AP, Forleo GB, Fassini GM, Tondo C. Cardiac and arrhythmic complications in patients with COVID-19. *J Cardiovasc Electrophysiol*. 2020;31:1003-1008. https://doi.org/10.1111/jce.14479
9. De Wit E, Van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. *Nat Rev Microbiol*. 2016;14:523, 534.
10. Lu L, Zhong W, Bian Z, et al. A comparison of mortality-related risk factors of COVID-19, SARS, and MERS: a systematic review and meta-analysis. *J Infect*. 2020;81:e18-e25. https://doi.org/10.1016/j.jinf.2020.07.002
11. Cooling L. Blood groups in infection and host susceptibility. *Clin Microbiol Rev*. 2015;28:801-870. https://doi.org/10.1128/cmr.00109-14
12. Czerwiński M. Blood groups–minuses and pluses. do the blood group antigens protect us from infectious diseases? *Postepy Hig Med Dosw*. 2015;69:703-722. https://doi.org/10.5604/17322693.1158795
13. Cismaru CA, Cismaru GL, Nabavi SF, et al. Multiple potential targets of opioids in the treatment of acute respiratory distress syndrome from COVID-19. *J Cell Mol Med*. 2021;25:591-595. https://doi.org/10.1111/jcmm.15927
14. Landsteiner K. Zur Kenntnis der antifermentativen, lytischen und agglutinierenden Wirkungen des Blutserums und der Lymphe. *Zentralbl Bakteriol*. 1900;27:357-362.
15. Daniels G. *Human Blood Groups*. Malden: Blackwell Science; 2002.
16. *Blood Type Frequencies by Country Including the Rh Factor*. http://www.rhesusnegative.net/themission/bloodtypefrequencies/
17. Aljanobi GA, Alhajjaj AH, Alkhabbaz FL, Al-Jishi JM. The relationship between ABO blood group type and the COVID-19 susceptibility in Qatif Central Hospital, eastern Province, Saudi Arabia: a retrospective cohort study. *OJIM* 2020;10(02):232-238. https://doi.org/10.4236/ojim.2020.102024
18. Bodmer W. Genetic characterization of human populations: from ABO to a genetic map of the British people. *Genetics*. 2015;199:267-279. https://doi.org/10.1534/genetics.114.173062
19. Garratty G. Blood groups and disease: a historical perspective. *Transfus Med Rev*. 2000;14:291-301. https://doi.org/10.1053/tmrv.2000.16228
20. Kamil M, Al-Jamal HAN, Yusoff NM. Association of ABO blood groups with diabetes mellitus. *Libyan J Med*. 2010;5. https://doi.org/10.3402/ljm.v3405i3400.484710.3402/ljm.v5i0.4847
21. Huang JY, Wang R, Gao Y-T, Yuan J-M. ABO blood type and the risk of cancer–findings from the Shanghai cohort study. *PLoS One*. 2017;12, e0184295. https://doi.org/10.1371/journal.pone.0184295
22. Liao Y, Xue L, Gao J, Wu A, Kou X. ABO blood group-associated susceptibility to norovirus infection: a systematic review and meta-analysis. *Infect Genet Evol* 2020;81:104245. https://doi.org/10.1016/j.meegid.2020.104245
23. Jing W, Zhao S, Liu J, Liu M. ABO blood groups and hepatitis B virus infection: a systematic review and meta-analysis. *BMJ open*. 2020;10.
24. Hashan MR, Ghozy S, El-Qushayri AE, Pial RH, Hossain MA, Al Kibria GM. Association of dengue disease severity and blood group: a systematic review and meta-analysis. *Rev Med Virology*. 2020:e2147.
25. Harris JB, Khan AI, LaRocque RC, et al. Blood group, immunity, and risk of infection with Vibrio cholerae in an area of endemicity. *IAI*. 2005;73:7422-7427. https://doi.org/10.1128/iai.73.11.7422-7427.2005
26. Ruvoën-Clouet N, Belliot G, Le Pendu J. Noroviruses and histo-blood groups: the impact of common host genetic polymorphisms on virus transmission and evolution. *Rev Med Virol* 2013;23:355-366. https://doi.org/10.1002/rmv.1757
27. Degarege A, Gebrezgi MT, Ibanez G, Wahlgren M, Madhivanan P. Effect of the ABO blood group on susceptibility to severe malaria: a systematic review and meta-analysis. *Blood Rev* 2019;33:53-62. https://doi.org/10.1016/j.blre.2018.07.002
28. Lee B, Dickson DM, deCamp AC, et al. Histo-blood group Antigen phenotype determines susceptibility to genotype-specific rotavirus infections and impacts measures of rotavirus vaccine efficacy. *J Infect Dis*. 2018;217:1399-1407. https://doi.org/10.1093/infdis/jiy054
29. Clemens JD, Sack DA, Harris JR, et al. ABO blood groups and cholera: new observations on specificity of risk and modification of vaccine efficacy. *J Infect Dis*. 1989;159:770-773. https://doi.org/10.1093/infdis/159.4.770
30. Cooling L. Blood groups in infection and host susceptibility. *Clin Microbiol Rev*. 2015;28:801-870. https://doi.org/10.1128/cmr.00109-14
31. Huang P, Farkas T, Marionneau S, et al. Noroviruses bind to human ABO, Lewis, and secretor histo-blood group Antigens: identification of 4 distinct strain-specific patterns. *J Infect Dis*. 2003;188:19-31. https://doi.org/10.1086/375742
32. Aspholm-Hurtig M, Dailide G, Lahmann M, et al. Functional adaptation of BabA, the H. pylori ABO blood group antigen binding adhesin. *Science*. 2004;305:519-522. https://doi.org/10.1126/science.1098801
33. Anstee DJ. The relationship between blood groups and disease. *Blood* 2010;115:4635-4643. https://doi.org/10.1182/blood-2010-01-261859

34. Cheng Y, Cheng G, Chui CH, et al. ABO blood group and susceptibility to severe acute respiratory syndrome. *Jama*. 2005;293:1450-1451. https://doi.org/10.1001/jama.293.12.1450-c
35. Zhou P, Yang X-L, Wang X-G, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020;579:270-273. https://doi.org/10.1038/s41586-020-2012-7
36. Ellinghaus D, Degenhardt F, Bujanda L, et al. Genomewide association study of severe covid-19 with respiratory failure. *N Engl J Med*. 2020;383:1522-1534. https://doi.org/10.1056/NEJMoa2020283
37. Liu N, Zhang T, Ma L, et al. The impact of ABO blood group on COVID-19 infection risk and mortality: a systematic review and meta-analysis [published online ahead of print December 8, 2020]. *Blood Rev*. 2020:100785. https://doi.org/10.1016/j.blre.2020.100785
38. Pourali F, Afshari M, Alizadeh-Navaei R, Javidnia J, Moosazadeh M, Hessami A. Relationship between blood group and risk of infection and death in COVID-19: a live meta-analysis. *New Microbes and New Infections*. 2020;37:100743. https://doi.org/10.1016/j.nmni.2020.100743
39. Abdollahi A, Mahmoudi-Aliabadi M, Mehrtash V, Jafarzadeh B, Salehi M. The novel coronavirus SARS-CoV-2 vulnerability association with ABO/Rh blood types. *Iran J Pathol*. 2020;15:156-160. https://doi.org/10.30699/ijp.2020.125135.2367
40. Hoiland RL, Fergusson NA, Mitra AR, et al. The association of ABO blood group with indices of disease severity and multiorgan dysfunction in COVID-19. *Blood Adv*. 2020;4:4981-4989. https://doi.org/10.1182/bloodadvances.2020002623
41. Barnkob MB, Pottegård A, Støvring H, et al. Reduced prevalence of SARS-CoV-2 infection in ABO blood group O. *Blood Adv*. 2020;4:4990-4993. https://doi.org/10.1182/bloodadvances.2020002657
42. Aktimur SH, Sen H, Yazicioglu B, Gunes AK, Genc S. The assessment of the relationship between ABO blood groups and Covid-19 infection. *Uhod*. 2020;30:121-125.
43. Belaouni M, Malki E, Bahraouy RE, et al. ABO-RH blood group and risk of Covid-19 in a moroccan population. *medRxiv*. 2020:2002. https://doi.org/10.1101/2020.12.02.20242180
44. El-Shitany NA, El-Hamamsy M, Alahmadi AA, et al. The impact of ABO blood grouping on COVID-19 vulnerability and seriousness: a retrospective cross-sectional controlled study among the Arab community. *IJERPH*. 2021;18, 276. https://doi.org/10.3390/ijerph18010276
45. Franchini M, Glingani C, Del Fante C, et al. The protective effect of O blood type against SARS-CoV-2 infection. *Vox Sang*, 116, 249, 250.2020. https://doi.org/10.1111/vox.13003
46. Gallian P, Pastorino B, Morel P, Chiaroni J, Ninove L, de Lamballerie X. Lower prevalence of antibodies neutralizing SARS-CoV-2 in group O French blood donors. *Antivir Res*. 2020;181:104880. https://doi.org/10.1016/j.antiviral.2020.104880
47. Aljanobi GA, Alhajjaj AH, Alkhabbaz FL, Al-Jishi JM. The relationship between ABO blood group type and the COVID-19 susceptibility in Qatif Central hospital, eastern Province, Saudi arabia: a retrospective cohort study. *OJIM*. 2020;10:232-238. https://doi.org/10.4236/ojim.2020.102024
48. Göker H, Aladağ-karakulak E, Demiroğlu H, et al. The effects of blood group types on the risk of COVID-19 infection and its clinical outcome. *Turk J Med Sci*. 2020;50:679-683. https://doi.org/10.3906/sag-2005-395
49. Golinelli D, Boetto E, Maietti E, Fantini MP. The association between ABO blood group and SARS-CoV-2 infection: a meta-analysis. *PLoS One*. 2020;15, e0239508. https://doi.org/10.1371/journal.pone.0239508
50. Latz CA, DeCarlo C, Boitano L, et al. Blood type and outcomes in patients with COVID-19. *Ann Hematol*. 2020;99:2113-2118. https://doi.org/10.1007/s00277-020-04169-1
51. Solmaz İ., Araç S. ABO blood groups in COVID-19 patients; cross-sectional study. *Int J Clin Pract*, 75. 2020:e13927. https://doi.org/10.1111/ijcp.13927
52. Wu Y, Feng Z, Li P, Yu Q. Relationship between ABO blood group distribution and clinical characteristics in patients with COVID-19. *Clin Chim Acta*. 2020;509:220-223. https://doi.org/10.1016/j.cca.2020.06.026
53. Zalba Marcos S, Antelo ML, Galbete A, Etayo M, Ongay E, García-Erce JA. Infection and thrombosis associated with COVID-19: possible role of the ABO blood group. *Med Clínica Engl Ed*. 2020;155:340-343. https://doi.org/10.1016/j.medcli.2020.06.020
54. Zietz M, Zucker J, Tatonetti NP. Associations between blood type and COVID-19 infection, intubation, and death. *Nat Commun*. 2020;11:5761. https://doi.org/10.1038/s41467-020-19623-x
55. Ray JG, Schull MJ, Vermeulen MJ, Park AL. Association between ABO and Rh blood groups and SARS-CoV-2 infection or severe COVID-19 illness. *Ann Intern Med*, 174, 308, 315.2021. https://doi.org/10.7326/m20-4511
56. Muneer, A, Kumari, K, Tripathi, M, Srivastava, R, Mohmmed, A, Rathore, S. Comparative analyses revealed reduced spread of COVID-19 in malaria endemic countries [published online ahead of print May 14, 2020]. *BMJ*.
57. Sargin G, Yavaşoğlu Sİ., Yavasoglu I. Is coronavirus disease 2019 (COVID-19) seen less in countries more exposed to Malaria? *Med hypotheses*. 2020;140:109756. https://doi.org/10.1016/j.mehy.2020.109756
58. Cserti CM, Dzik WH. The ABO blood group system and Plasmodium falciparum malaria. *Blood*. 2007;110:2250-2258. https://doi.org/10.1182/blood-2007-03-077602
59. Padhi S, Suvankar S, Dash D, et al. ABO blood group system is associated with COVID-19 mortality: an epidemiological investigation in the Indian population. *Transfus Clinique Biol*. 2020;27:253-258. https://doi.org/10.1016/j.tracli.2020.08.009
60. Taha SAH, Osman MEM, Abdoelkarim EAA, et al. Individuals with a Rh-positive but not Rh-negative blood group are more vulnerable to SARS-CoV-2 infection: demographics and trend study on COVID-19 cases in Sudan. *New Microbes and New Infections*. 2020;38:100763. https://doi.org/10.1016/j.nmni.2020.100763
61. Leaf RK, Al-Samkari H, Brenner SK, Gupta S, Leaf DE. ABO phenotype and death in critically ill patients with COVID-19. *Br J Haematol*. 2020;190:e204-e208. https://doi.org/10.1111/bjh.16984
62. Reilly JP, Meyer NJ, Shashaty MGS, et al. ABO blood type A is associated with increased risk of ARDS in whites following both major trauma and severe sepsis. *Chest*. 2014;145:753-761. https://doi.org/10.1378/chest.13-1962
63. *Blood Types in Children with COVID-19*. https://www.clinicaltrials.gov/ct2/show/NCT04682912 [March 22, 2021 2021].
64. Navas EL, Venegas MF, Duncan JL, Anderson BE, Chmiel JS, Schaeffer AJ. Blood group antigen expression on vaginal and buccal epithelial cells and mucus in secretor and nonsecretor women. *J Urology*. 1993;149:1492-1498. https://doi.org/10.1016/s0022-5347(17)36425-x
65. Kelly RJ, Rouquier S, Giorgi D, Lennon GG, Lowe JB. Sequence and expression of a candidate for the human secretor blood group α (1,2)Fucosyltransferase gene (FUT2) homozygosity for an enzyme-inactivating nonsense mutation commonly correlates with the non-secretor phenotype. *J Biol Chem*. 1995;270:4640-4649. https://doi.org/10.1074/jbc.270.9.4640

66. Raza MW, Blackwell CC, Molyneaux P, et al. Association between secretor status and respiratory viral illness. *BMJ*. 1991;303:815-818. https://doi.org/10.1136/bmj.303.6806.815
67. Blackwell CC, James VS, Davidson S, et al. Secretor status and heterosexual transmission of HIV. *BMJ*. 1991;303:825-826. https://doi.org/10.1136/bmj.303.6806.825-a
68. Wu S-C, Arthur CM, Wang J, et al. The SARS-CoV-2 receptor-binding domain preferentially recognizes blood group A. *Blood Advances*. 2021;5:1305-1309. https://doi.org/10.1182/bloodadvances.2020003259
69. Valenti L, Villa S, Baselli G, et al. Association of ABO blood group and secretor phenotype with severe COVID-19. *Transfusion*. 2020;60:3067-3070. https://doi.org/10.1111/trf.16130
70. Delanghe JR, De Buyzere ML, Speeckaert MM. C3 and ACE1 polymorphisms are more important confounders in the spread and outcome of COVID-19 in comparison with ABO polymorphism. *Eur J Prev Cardiolog*. 2020;27:1331-1332. https://doi.org/10.1177/2047487320931305
71. Dzik S, Eliason K, Morris EB, Kaufman RM, North CM. COVID -19 and ABO blood groups. *Transfusion*. 2020;60(8):1883–1884. https://doi.org/10.1111/trf.15946
72. Yang Z, Liu J, Zhou Y, Zhao X, Zhao Q, Liu J. The effect of corticosteroid treatment on patients with coronavirus infection: a systematic review and meta-analysis. *J Infect* 2020;81:e13-e20. https://doi.org/10.1016/j.jinf.2020.03.062
73. May JE, McGwin G, Jr., Gangaraju R, et al. Questioning the association between ABO type and outcomes in patients with COVID-19. *Ann Hematol*. 2020:1-2. https://doi.org/10.1007/s00277-020-04348-0
74. Mahallawi WH, Al-Zalabani AH. The seroprevalence of SARS-CoV-2 IgG antibodies among asymptomatic blood donors in Saudi Arabia. *Saudi J Biol Sci*, 28, 1697, 1701.2021. https://doi.org/10.1016/j.sjbs.2020.12.009
75. Khalil A, Feghali R, Hassoun M. The Lebanese COVID-19 cohort; A challenge for the ABO blood group system. *Front Med*. 2020;7:585341. https://doi.org/10.3389/fmed.2020.585341
76. Göker H, Aladağ-karakulak E, Demiroğlu H, et al. The effects of blood group types on the risk of COVID-19 infection and its clinical outcome. *Turk J Med Sci*. 2020;50:679-683. https://doi.org/10.3906/sag-2005-395
77. Bhandari P, Durrance RJ, Bhuti P, Salama C. Analysis of ABO and Rh blood type Association with acute COVID-19 infection in hospitalized patients: a superficial association among a multitude of established confounders. *J Clin Med Res*. 2020;12:809-815. https://doi.org/10.14740/jocmr4382
78. Zeng X, Fan H, Lu D, et al. Association between ABO blood groups and clinical outcome of coronavirus disease 2019: evidence from two cohorts. *medRxiv*. 2020. 2020.2004.2015.20063107. https://doi.org/10.1101/2020.04.15.20063107
79. Takagi H. Down the rabbit-hole of blood groups and COVID-19. *Br J Haematol*. 2020;190:e268-e270. https://doi.org/10.1111/bjh.17059
80. Muñiz-Diaz E, Llopis J, Parra R, et al. Relationship between the ABO blood group and COVID-19 susceptibility, severity and mortality in two cohorts of patients. *Blood Transfus*. 2021;19:54-63. https://doi.org/10.2450/2020.0256-20
81. Mannan A, Mehedi HMH, Chy NUHA, et al. A multi-centre, cross-sectional study on coronavirus disease 2019 in Bangladesh: clinical epidemiology and short-term outcomes in recovered individuals. *New Microbes and New Infections*. 2021;40:100838. https://doi.org/10.1016/j.nmni.2021.100838
82. Kim YH, Ko Y-H, Kim S, Kim K. How closely is COVID-19 related to HCoV, SARS, and MERS?: Clinical comparison of coronavirus infections and identification of risk factors influencing the COVID-19 severity using common data model (CDM). *medRxiv*. 2021. 2020.2011.2023.20237487. https://doi.org/10.1101/2020.11.23.20237487
83. Kotila TR, Alonge TO, Fowotade A, Famuyiwa OI, Akinbile AS. Association of the ABO blood group with SARS-CoV-2 infection in a community with low infection rate. *Vox Sang*. 2021. https://doi.org/10.1111/vox.13077
84. Ad'hiah AH, Allami RH, Mohsin RH, Abdullah MH, AJR AL-Sa, Alsudani MY. Evaluating of the association between ABO blood groups and coronavirus disease 2019 (COVID-19) in Iraqi patients. *Egypt J Med Hum Genet*. 2020;21(1):50. https://doi.org/10.1186/s43042-020-00097-x
85. Zalba Marcos S, Antelo ML, Galbete A, Etayo M, Ongay E, García-Erce JA. Infection and thrombosis associated with COVID-19: possible role of the ABO blood group. *Med Clínica Engl Ed*. 2020;155:340-343. https://doi.org/10.1016/j.medcli.2020.06.020
86. Kibler M, Dietrich L, Kanso M, et al. Risk and severity of COVID-19 and ABO blood group in transcatheter aortic valve patients. *Jcm*. 2020;9, 3769. https://doi.org/10.3390/jcm9113769
87. Schetelig J, Baldauf H, Wendler S, et al. Severity of respiratory infections due to SARS-CoV-2 in working population: age and body mass index outweigh ABO blood group. *medRxiv*. 2021:20226100. 2020.2011.2005. https://doi.org/10.1101/2020.11.05.20226100
88. Guillon P, Clément M, Sébille V, et al. Inhibition of the interaction between the SARS-CoV spike protein and its cellular receptor by anti-histo-blood group antibodies. *Glycobiology*. 2008;18:1085-1093. https://doi.org/10.1093/glycob/cwn093
89. Focosi D. Anti-A isohaemagglutinin titres and SARS-CoV-2neutralization: implications for children and convalescent plasma selection. *Br J Haematol*. 2020;190:e148-e150. https://doi.org/10.1111/bjh.16932
90. Wu B-B, Gu D-Z, Yu J-N, Yang J, Shen W-Q. Association between ABO blood groups and COVID-19 infection, severity and demise: a systematic review and meta-analysis. *Infect Genet Evol*. 2020;84:104485. https://doi.org/10.1016/j.meegid.2020.10448
91. Gérard C, Maggipinto G, Minon JM. COVID-19 and ABO blood group: another viewpoint. *Br J Haematol*. 2020;190:e93-e94. https://doi.org/10.1111/bjh.16884
92. Stussi G, Huggel K, Lutz HU, Schanz U, Rieben R, Seebach JD. Isotype-specific detection of ABO blood group antibodies using a novel flow cytometric method. *Br J Haematol*. 2005;130:954-963. https://doi.org/10.1111/j.1365-2141.2005.05705.x
93. Vasan SK, Rostgaard K, Majeed A, et al. ABO blood group and risk of thromboembolic and arterial disease: a study of 1.5 million blood donors. *Circulation*. 2016;133:1449-1457.discussion 1457. https://doi.org/10.1161/circulationaha.115.017563
94. Schleef M, Strobel E, Dick A, Frank J, Schramm W, Spannagl M. Relationship between ABO and Secretor genotype with plasma levels of factor VIII and von Willebrand factor in thrombosis patients and control individuals. *Br J Haematol*. 2005;128:100-107. https://doi.org/10.1111/j.1365-2141.2004.05249.x
95. Dentali F, Sironi A, Ageno W, et al. Non-O blood type is the commonest genetic risk factor for VTE: results from a meta-analysis of the literature. *Semin Thromb Hemost*. 2012;38:535-548. https://doi.org/10.1055/s-0032-1315758
96. Wu O, Bayoumi N, Vickers MA, Clark P. ABO(H) blood groups and vascular disease: a systematic review and meta-analysis. *J Thromb Haemostasis*. 2008;6:62-69. https://doi.org/10.1111/j.1538-7836.2007.02818.x
97. McGonagle D, O'Donnell JS, Sharif K, Emery P, Bridgewood C. Immune mechanisms of pulmonary intravascular coagulopathy in COVID-19 pneumonia. *Lancet Rheumatology*. 2020;2:e437-e445. https://doi.org/10.1016/s2665-9913(20)30121-1
98. Klok FA, Kruip MJHA, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19.

Thrombosis Res. 2020;191:145-147. https://doi.org/10.1016/j.thromres.2020.04.013

99. O'Sullivan JM, Ward S, Fogarty H, O'Donnell JS. More on 'Association between ABO blood groups and risk of SARS-CoV-2 pneumonia. *Br J Haematol*. 2020;190:27-28. https://doi.org/10.1111/bjh.16845
100. Dai X. ABO blood group predisposes to COVID-19 severity and cardiovascular diseases. *Eur J Prev Cardiolog*. 2020;27:1436-1437. https://doi.org/10.1177/2047487320922370
101. Dandona P, Dhindsa S, Ghanim H, Chaudhuri A. Angiotensin II and inflammation: the effect of angiotensin-converting enzyme inhibition and angiotensin II receptor blockade. *J Hum Hypertens*. 2007;21:20-27. https://doi.org/10.1038/sj.jhh.1002101
102. Liu Y, Häussinger L, Steinacker JM, Dinse-Lambracht A. Association between the dynamics of the COVID-19 epidemic and ABO blood type distribution. *Epidemiol Infect*. 2021;149:e19. https://doi.org/10.1017/s0950268821000030
103. Golding J, Northstone K, Miller LL, Davey Smith G, Pembrey M. Differences between blood donors and a population sample: implications for case-control studies. *Int J Epidemiol*. 2013;42:1145-1156. https://doi.org/10.1093/ije/dyt095

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