Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

COVID-19 and the ABO blood group connection

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), causing the current pandemic of COVID-19, is genetically similar to SARS-CoV that caused the SARS outbreak in 2002. Recently, next-generation sequencing of SARS-CoV-2 showed a 99·98 % sequence identity across 9 patients. SARS-CoV-2 showed 79 % similarity to SARS-CoV, with a comparable receptor-binding domain (ACE2) on modeling [1].

Susceptibility of certain viral infections has been linked to antigenic determinants of ABO blood groups. Cheng et al. showed linkage of SARS coronavirus infection with ABO blood groups, where individuals with blood group O were less likely to become infected, compared to non-O blood group individuals (OR 0·18) [2].

Data from Wuhan, China, the first epicenter of COVID-19 pandemic, shows ABO blood group linkage with COVID-19 infections [3]. Zhao et al. compared ABO blood groups of controls from the general population with 2173 COVID-19 patients from three hospitals in Wuhan region. Across all three hospitals, blood group A was associated with a higher risk for COVID-19 (OR 1·21; P = 0·027) compared with non-A blood groups, whereas blood group O was associated with a significantly lower risk for the infection (OR 0·67; P < 0·001) compared with non-O blood groups [3].

Another observational study on data from New York Presbyterian hospital system, on 1559 individuals tested for SARS-CoV-2 with known blood type, also showed similar results. In SARS-CoV-2 positive cases, there was a high proportion of blood group A, with a low proportion of blood group O [4].

With regards to the case fatality rate, as mentioned by Zhao et al., blood group A was also linked to higher mortality risk in contrast to blood group O (OR 1·482; P = 0·008), the latter was associated with a lower mortality risk compared with non-O blood groups (OR 0·660; P = 0·014) [3].

Zietz & Tatonetti mentioned the significance of this association in only Rh-positive blood types[4]. But what is important to note, is that the association of blood type is not explainable by other risk factors e.g. obesity, diabetes mellitus and other comorbidities [4].

The linkage and effects of blood groups have been hypothesized using different facts:

For one, blood groups are dictated by sugars, and coronaviruses in the cattle have surface proteins that bind to sugars. It might be of value to consider the extra sugar N-acetyl galactosamine, on the surface of blood group A cells [5], possibly suggesting more pathogen contact. This sugar is missing on blood group O cells [5].

The association of the spike (S) protein of SARS-CoV-2, a transmembranal protein, has been shown with ACE2 protein that acts as its cellular receptor [6]. As suggested in the past for SARS-CoV [7], the adhesion of Spike protein to the ACE2 receptor on the host cell surface may be inhibited by the presence of anti-A antibody. Although this may be true for blood group B and blood group O, it does not explain blood group AB, that even without anti-A antibody does not have a higher susceptibility to this infection.

SARS-CoV-2 replicates in respiratory & gastrointestinal epithelium [8], that can synthesize A or B glycan antigens, depending on the phenotype. If the S protein of an A, B, or AB group induvial carries respective glycan antigens, it is possible that binding of the respective antibodies can block the interaction between S protein and ACE2, thereby offering complete or incomplete protection [9]. Thus, infectivity between ABO groups can presumably be predicted e.g. the virus produced in an individual with blood group B will be carrying antigen B and has a higher chance of infecting a person with blood group B or AB, as compared to blood group A or O. This can explain the least number of cases in blood group O that contains both antibody-A and antibody-B. It is also believed that once the infection is fully established, it then replicates in the individual's epithelial cells and thus exhibits that individual's antigen, rendering the individual's antibodies ineffective [9].

Another possible explanation for the relatively protective characteristic of blood group O is that during the evolutionary phenotype formation, epitopes are exposed to the ancestral, non-immune immunoglobulin IgM & its highly anti-glycan ABO isoagglutinin activities [10]. These activities of IgM are downregulated by phenotypic glycosylation in the non-O groups. Blood group O maintains the isoagglutinins and the power of ancestral IgM, the vanguard of immunity [10].

Whether these hypotheses hold true or whether the association is insignificant, is still not clear. However, the association between blood groups & other infections in the past cannot be ignored [5]. As more research data is pouring in every day, blood group should be registered for every infected individual for future correlations on larger sets of data. Large scale, international, collaborative studies on ABO linkage to the prevalence and mortality of COVID-19 can be a way forward in understanding the pathophysiology of the virus.

Another implication to consider is the use of convalescent plasma in COVID-19 patients. Ever since Casadevall and Pirofski suggested that convalescent sera from recovered COVID-19 individuals may be an option for treating high-risk COVID-19 patients and possibly for prophylaxis of infection in individuals at high risk of COVID-19 disease [11], and the emergency investigational new drug (eIND) approval by the FDA [12], clinical trials for the use of convalescent plasma to treat COVID-19 have bloomed. With 60 clinical trials currently registered [13], ABO-compatibility must be mandated in any protocol as such.

Author credits

FZZ: Selected information and compiled into a manuscript
ARZZ: Worked on history of ABO link in other viral diseases
SMA: Worked on SARS-CoV-2 behavior
SZAZ: Conceptualized & finalized the manuscript

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Why is this manuscript important?

Many viral diseases have shown an association with ABO blood groups in the past. SARS-CoV, being one of them, showed a positive association with blood group A with a high number of positive cases in blood group A. Blood group O, on the other hand, had a lesser incidence of infection compared to other groups. Since two studies in pre-print from China and USA have shown a similar pattern for SARS-CoV-2, we hypothesize a link connecting ABO blood groups to SARS-CoV-2. We believe this link must be explored for a better understanding of the pathophysiology of COVID-19, as well as for the safety of the ongoing convalescent plasma therapy clinical trials.

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