Study of ABO Blood Group Susceptibility to Coronavirus Disease - COVID-19

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Abstract

Background: The pandemic outbreak of COVID-19 highlighting the zoonotic cross-over link in the present century has provoked an emergency worldwide. Recent experimental evidence supporting the proposition of ABO blood grouping and its susceptibility in certain blood group individuals has created interest among researchers to explore more.

Aim: The aim of this study is to find the susceptibility of "ABO" blood group in COVID-19-positive cases.

Objectives: Association of ABO blood group patterns with COVID-19-positive cases.

Materials and Methods: A cross-sectional, observational study design was conducted among 728 confirmed positive COVID-19 admitted to the tertiary health care center in Maharashtra from June 01, 2020 to August 31, 2020. The inclusion criteria were COVID-19-positive cases confirmed by positive real-time reverse transcriptase-polymerase chain reaction test of severe acute respiratory syndrome coronavirus 2. We collected the demographic details, associated clinical symptoms and ABO blood groups from all the patients. The data collected were subjected to statistical analysis.

Results: The most common blood group affected was B + (35.5%) followed by A + (26.10%), AB + (20.60%) and O + (11.18%) and the least common was AB- (0.96%), O- (1.51%), A- (1.65%) and B- (1.79%).

Conclusions: ABO blood grouping can be used as one of the simplest yet efficient markers for COVID-19. Blood group B Rh-positive and A Rh-positive were the most prevalent blood group types in patients with COVID-19.

Keywords: 2019 novel coronavirus disease, ABO blood group, spike glycoprotein, susceptibility

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INTRODUCTION

Currently, the coronavirus emerging from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)/ COVID-19 virus in Wuhan, Hubei Province, China, has been declared as Pandemic disease by the World Health Organization (WHO). Also known as (SARS-CoV-2, SARS2 and 2019-nCoV), this epidemic is spreading widely across the globe like a wildfire. Recent reports

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have highlighted the role of zoonotic links, cross-species transmission (CST) and spillover conjuncture between animals (bats, poultry, snakes and marmots) and human transmission before acquiring direct human-to-human contact.[1-3] This CST agent (virus and its virions) further causes severe respiratory illness leading to pneumonia, multi-organ failure and cardiac arrest.[4,5]

Karl Landsteiner, in 1900, discovered the phenomena of red blood cell (RBC) agglutination, which is a well-documented hypothesis. The dynamic association between the blood group and diseases has been studied from the early 1900s because human blood group antigens can serve as receptors for various pathogens. Even a minute variation in structure can induce antibody productions as a part of the defense mechanism. These oligosaccharide structures with glycosyltransferase enzymes and sugar moiety found on various cell surfaces and body secretions can be mimicked by pathogens and act as a predisposing factor for disease progression.[6] Based on this phenomenon, a study was conducted to assess the relationship between the ABO blood group and the COVID-19 susceptibility among the Chinese populations. The results inferred that blood Group O individuals were at low risk, and blood Group A was at high risk to COVID-19 infection.[7] Considering this, the present study aims to study the relation of ABO blood group in COVID-19 cases among the Indian population and correlate its susceptibility pattern among the various blood groups.

MATERIALS AND METHODS

After clearance from the ethical committee with Designated Protocol no 340/2019–2020, we conducted a time-bound, cross-sectional and observational study from June 01, 2020 to August 31, 2020, at Krishna Institute of Medical Sciences, Karad, Western Maharashtra, India. For the course, we rationalized that there are an association, linkage and high susceptibility between specific blood group individuals and COVID-19-positive cases. We calculated the total sample size of about 728. All the patients with COVID-positive cases confirmed by positive real-time reverse transcriptase-polymerase chain reaction test (RT-PCR) of SARS-CoV-2 on nasal and pharyngeal swab specimens were enrolled in the study. Ethical considerations were fulfilled by obtaining verbal informed consent from all the participants who fit the study inclusion criteria. No threat or pressure was imposed on the participants who denied participation in the study. The confidentiality of all the participants was maintained. The demographic details, travel history and associated symptoms were noted. Clinical confirmation of positive cases was done using RT-PCR

test (Bio-Rad CFX96) and applying the clinical and laboratory staging systems. We classified the instances based on clinical and laboratory staging systems as Stage 1: Mild (Early Infection)-Groups A, B and C; Stage IIa: Moderate (Pulmonary Involvement without Hypoxia)-Group D; Stage IIb: Moderate (Pulmonary Involvement with Hypoxia)-Group E; Stage III: Severe (Systemic Hyperinflammation with Cytokine Storm)-Group F. We further investigated biochemical parameters on the classified group. Individuals with known blood groups were noted, and those who were not aware of the blood group were subjected to the standard ABO blood grouping method as given by Karl Landsteiner. A simple random sampling method and lottery method of blinding participants were employed to avoid selection and performance bias. The data collected were subjected to statistical analysis using the Statistical package of social sciences.

RESULTS

A total of 728 COVID-positive cases were included, of which 61% were males and 39% were females. All the values were expressed in mean and standard deviation (SD). Statistical analysis was performed using the Chi-square test. The mean age group was 40.37 (SD ± 18.36). Of total 728 patients, 190 (26.10%) were A +; 12 (1.65%) were A-; 259 (35.5%) were B +; 13 (1.79%) were B-; 86 (11.81%) were O +; 11 (1.51%) were O-; 150 (20.60%) were AB + and 7 (0.96%) were AB-. The percentage distribution of ABO blood grouping with COVID-19 is shown in Figure 1. The highest percentage involved was B + blood group patients with 35.5% and the least being AB- with 0.96%. The Chi-square test was applied. The *P* was found to be <0.001, indicating that the B blood group was statistically prevalent than other blood groups in the present population with COVID-19 disease.
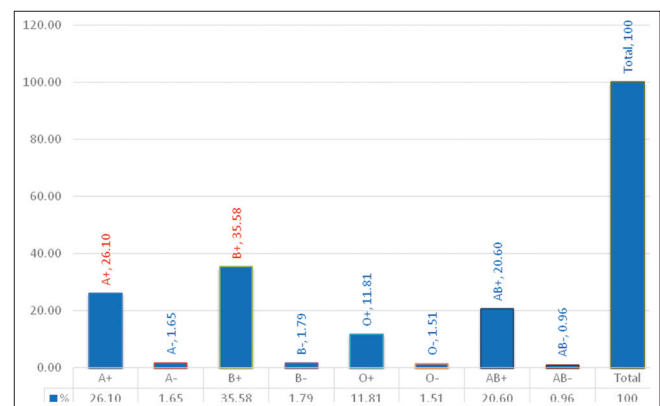
Figure 1: Frequency distribution of blood groups in COVID-19 patients

DISCUSSION

Blood group antigens are the most common target for epidemiological study as they are polymorphic traits inherited in different populations and among other individuals.[8] Being considered part of innate immunity, these dynamic entities have always proved interested among researchers for their direct role in various infectious diseases. Equipped with receptor moiety and membrane microdomains, they promote and "grease the wheels" for colonization, invasion and signal transduction for microorganisms. The symbiotic relationship between the blood groups and microbes, including the virus, has reopened the mystery for future research. Recently, few factual hypotheses have linked the strong affinity of spike protein of coronavirus with sugar moiety-N-acetylgalactosamine present on the cattle RBCs, inferring that A blood group individuals bear an extra sugar molecule, are more susceptible to this zoonotic CST infection.[8,9] Based on this phenomenon, we undertook a study to see an association, linkage, and high susceptibility between specific blood group individuals and COVID-19-positive cases among the Indian population.

This study found that ABO blood groups display an association and connection with COVID-19-positive cases. Precisely, the proposition of blood Group B + was highest with 35.58% of admitted patients, and the proportion of AB- displayed the lowest percentage of about 0.96%. This difference in the proportion of susceptibility of positive cases of COVID-19 among blood groups in the Indian population showed significant discordance with a previous documented study conducted by Jiao *et al.* from the Chinese community (2173 positive cases)[7] and Zietz *et al.* from New York population (1559 positive cases).[9]

Based on agglutination law, O blood group individuals with anti-A and anti-B antibodies should be least suspected of any infection. To correlate in-depth on how the O blood group individuals are least suspected, Yamamoto in 2020 said that the coronavirus is a single-stranded RNA virus with four Madrid of proteins, among which spike, i.e., the S protein that facilities interaction with the Angiotensin-converting enzyme (ACE) receptors of respiratory epithelium can synthesize A or B glycan antigens, depending on the phenotype.[8,10] According to the author, the S protein of an A, B or AB group individual carries respective glycan antigens and respective antibodies, can block the interaction between S protein and ACE2, thereby offering complete or incomplete protection. This could further explain why blood group O individuals were least affected. With support for this existing hypothesis, another possible explanation suggested by Arend Peter[11]

was that, during the evolutionary phenotype formation, epitopes were exposed to the ancestral, nonimmune immunoglobulin M and its highly anti-glycan ABO isoagglutinin activities that further downregulated the phenotypic glycosylation in the non-O groups than the O group individuals, thus making the blood group O as universal groundbreakers of immunity.[10]

In the present study, B + individuals with anti-A antibodies were at high risk among the Indian population compared to the Chinese community, which increased the risk of a blood group bearing anti-B antibodies. The hypothesis of additional sugar moiety-N-acetylgalactosamine present in A blood group was considered the precise reason why A blood group was at high risk among the Chinese population and should be reevaluated and quantitatively assessed even in B blood group individuals. To add on, the demographic population variations should be correlated to prove the hypothesis. O blood group concept for coronavirus protection favors Chinese populations, further making their evidence concrete and robust. The disparity lies among the non-O blood groups individuals among the Indian community as shown in our study. Hence future studies with more samples among different communities should be undertaken. Once verified, several clinical implications such as more vigilant surveillance and treatment with extra personnel protection should be given for the blood group individuals who are at more risk than other blood groups.

Correlations between sex and gender differences have also been observed in various infectious diseases in past research. The importance of sex as a variable gained more interest in 2016 when the National Institutes of Health and Sex-Based Gender Medicine reinforced the inclusion of sex as a biological variable in a study design.[12] According to descriptive and observational data from Wuhan, China, about 51% to 66.7% of affected patients were male.[13] The percentage was per other countries such as Italy with 58%. The Economic Survey of India (2020) has also documented that 60% of males are more probing for acquiring COVID-19 than 25% of females. In the present study, 61% were males and 39% were females, making males more susceptible to COVID infections. This interrelationship can be connected to confounding variables such as the habit of smoking, effect of sex hormones and increased ACE 2 activity among males.[13] Schurz and *et al*. hypothesized that the X chromosome is equipped with more immune-related genes than the Y chromosome, making females as supreme power with dynamic immune response. However, at the opposing end, females are more prone to autoimmune diseases due to the overproduction of these genes.[14] Tran *et al*. and Franconi and Campesi have documented that

most of the adverse drug reactions occur more in females because the majority of clinical drug trials were performed on males.[15,16] All these studies emphasize that we focus on even minor vital information that is often neglected during the research study design.

The highest prevalence of smoking among males has also contributed to increased susceptibility for the current COVD-19 pandemic. Approximately about 288 million men in China and 17.6% of males in the USA were smokers compared to 12.6 million women in China and 13.6% females in the USA.[17-19] Controversial studies have documented that the nicotinic acetylcholine receptor (nAChRs) acts as a coreceptor for viral cell entry within the respiratory tract and central nervous system inhibit the binding of SARS-COV-2, thus preventing the adhesion. Changeux *et al.* in 2020 inferred nicotine's use as a protective therapy against COVID-19, preventing the replication of the virus and acting as a positive allosteric modulator for nAChRs. However, there is no empirical evidence proving this hypothesis. Hence, the WHO has strongly recommended further revaluate this hypothesis as nicotine is a drug of abuse and can lead to other complications.[20]

CONCLUSIONS

Blood grouping can be used as one of the most straightforward yet efficient biomarkers for COVID-19. Blood group B Rh-positive and A Rh-positive were the most prevalent blood group types in patients with COVID-19. Furthermore, research should also be focused on including minor parameters such as ABO blood grouping, sex and habits such as smoking and correlate them with disease progression. As documented by our study, males with B + blood groups were at high risk and should be kept under surveillance. Newer precautionary protocols should be developed and formulated on this basis.

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Conflicts of interest
There are no conflicts of interest.

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