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Association Between ABO Blood Groups and Clinical Characteristics, Severity, and Outcomes of COVID-19 Patients

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ABSTRACT

Background: COVID-19, caused by SARS-CoV-2, presents a wide spectrum of clinical manifestations and severity, from asymptomatic infection to severe illness and death. Various host factors, such as age, comorbidities, and genetic factors such as blood group, may affect susceptibility and outcomes of patients. Elucidating the relationship between blood groups and COVID-19 may help in identifying patients who are at increased risk for severe outcomes.

Objective: To assesses associations with clinical characteristics, severity, and outcomes among confirmed COVID-19 patients.

Methodology: The study was designed as a hospital-based cross-sectional study in which 180 confirmed COVID-19 cases and their blood groups were identified among adults admitted to Sheikh Zayed Hospital, Rahim Yar Khan. Data was analyzed using SPSS software version 26.0.

Results: The mean age of the study cases was 48.5 ± 15.1 years, and 60% were males. The distribution of the blood groups was B (35%), O (30%), A (25%), and AB (10%). Hypertension was more common in group A (51.1%, p=0.04). ICU admission was more common in AB (33.3%), A (24.4%), and O (12.9%, p=0.05). Higher mortality was observed in AB (22.2%) and A (17.7%) than O (7.4%), but it was statistically insignificant (p=0.07).

Conclusion: ABO blood groups have been found to be associated with the severity and outcome of COVID-19. Blood groups A and AB have a poor outcome, while blood group O has a protective effect. ABO blood grouping may be a useful tool for the management of COVID-19.

Keywords: COVID-19; SARS-CoV-2; ABO Blood Group; Disease Severity; Clinical Outcomes

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Introduction

The pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also referred to as coronavirus disease 2019 (COVID-19), is a major public health concern worldwide since its emergence in Wuhan City, China, in late 2019.[1,2] The disease has already affected millions of people across the globe and caused significant morbidity and mortality. The disease spectrum varies widely in COVID-19, ranging from an asymptomatic or mild upper respiratory tract infection to severe pneumonia, acute respiratory distress syndrome (ARDS), multi-organ failure, and even death.[3] Various host factors have been implicated in the disease susceptibility and outcome in COVID-19. These include age, gender, and co-morbid conditions such as hypertension, diabetes mellitus, cardiovascular disease, and obesity. Recent studies have indicated that genetic factors such as ABO blood groups may also play an important role in the susceptibility to SARS-CoV-2 infection and the outcome in COVID-19.

The ABO blood group system, first identified by Karl Landsteiner in 1901, is considered to be the most important blood group system in human beings.[4,5] This blood group system has four main blood groups: A, B, AB, and O, depending on the presence or absence of A and B antigens on the surface of red blood cells. Traditionally, ABO blood groups have been related to the incidence of various infectious and non-infectious diseases. For example, blood group O has been related to a reduced incidence of severe malaria and cardiovascular diseases, whereas blood group A has been related to a greater susceptibility to certain viral infections.[6] However, the exact mechanisms underlying this relationship remain to be determined; it is believed that immunological factors such as naturally occurring antibodies to A and B blood groups, as well as alterations in coagulation profiles, which are particularly important in COVID-19 due to hypercoagulability, play a crucial role in this relationship.

However, it is also emerging that people with blood group A may be at a greater risk of contracting SARS-CoV-2 infection and developing severe forms of the disease, while people with blood group O may be at a lower risk.[7,8] Various theories have been put forward for the above. One theory is that there is a possible interaction of anti-A antibodies with the receptor-binding domain of the SARS-CoV-2 spike protein, which may inhibit viral attachment and infection in people with blood group O. Another theory is that people with different blood groups may express different levels of angiotensin-converting enzyme 2 (ACE2), the viral receptor for SARS-CoV-2. Furthermore, it is also possible that ABO blood groups may affect the immune response, production of inflammatory cytokines, and thrombotic tendency, which may affect the prognosis of COVID-19 patients.

The role of ABO blood groups in COVID-19 is an important aspect that is clinically relevant and may be useful in identifying those at increased risk of severe disease and in the efficient allocation of resources for prevention. Several studies have noted differences in the presentation, laboratory features, severity, and outcome in COVID-19 patients across different ABO blood groups. For example, differences in laboratory markers such as inflammation, coagulation, and organ failure have been noted across different ABO groups, implying that the disease may not only be affected by the blood groups but also the disease process itself. However, the studies have been inconsistent in their findings across different populations.

The present study attempts to comprehensively explore the clinical characteristics of COVID-19 patients according to their ABO blood group, such as demographic characteristics, symptoms, laboratory data, disease severity, and outcome. To evaluate if ABO blood groups have any influence on the clinical presentation, severity, or outcomes of COVID-19 among hospitalized patients can contribute to further knowledge about factors that affect SARS-CoV-2 infection. Knowing this association can help physicians use blood group system as a predictive tool to determine how severe the disease may progress, which is helpful in the global fight against COVID-19.

Objective

To assesses associations with clinical characteristics, severity, and outcomes among confirmed COVID-19 patients.

Methodology

The current study is a hospital-based cross-sectional study conducted in Sheikh Zayed Hospital, Rahim Yar Khan. In this study, a non-probability consecutive sampling technique was used to select a total of 180 patients with confirmed cases of COVID-19 infection. Adult patients aged 18+ years with laboratory confirmation of COVID-19 infection by reverse transcription polymerase chain reaction (RT-PCR) and with known blood group information were included in the study. Patients with incomplete clinical data and known hematological disorders were excluded.

The data collection was done retrospectively from the hospital's medical records using a structured proforma. The data on demographic variables, such as age and gender, ABO blood groups (A, B, AB, and O), symptoms of fever, cough, dyspnea, and fatigue, as well as comorbid conditions of hypertension, diabetes mellitus, and cardiovascular disease, were recorded. The laboratory parameters of C-reactive protein, D-dimer, and complete blood counts, as well as radiological findings of chest X-ray and computed tomography scans, were also

recorded. The severity of disease was classified as mild, moderate, severe, and critical according to standard clinical criteria, and the outcomes of the disease, such as recovery, ICU admission, mechanical ventilation, and death, were recorded.

All the data collected was entered and analyzed using the statistical software, Statistical Package for Social Sciences (SPSS) 26.0. To determine if there is an association between ABO blood groups and clinical characteristics, as well as disease severity, the Chi-square test was used. A p-value of less than or equal to 0.05 was considered statistically significant. Institutional ethical clearance for the study was obtained, and confidentiality of the patients was maintained.

Results

The study comprised 180 patients with an average age of 48.5 years ± 15.1 years. The majority of the patients (39.4%) were in the age group of 41-60 years, followed by 31.1% in the 18-40 years age group and 30.0% in the age group of more than 60 years. Males were predominant in the study with 60.0% of male patients, whereas 40.0% were females. Most of the patients were from urban areas, with 58.3% of the total, followed by 41.6% of rural patients. In the study, 33.3% were smokers, and 66.6% were non-smokers. In terms of body mass index, 41.1% of the patients were overweight or obese, while 58.8% of the patients had a BMI of less than 25 (Table 1).

Table 1. Demographic Characteristics of Study Population (n=180)

Variable	Frequency (%)
Age (years)	
Mean Age	48.5 ± 15.1
18–40 years	56 (31.1%)
41–60 years	71 (39.4%)
>60 years	53 (30.0%)
Gender	
Male	108 (60.0%)
Female	72 (40.0%)
Residence	
Urban	105 (58.3%)
Rural	75 (41.6%)
Smoking Status	
Smokers	60 (33.3%)
Non-Smokers	120 (66.6%)
Body Mass Index (BMI)	
≥25 (Overweight/Obese)	74 (41.1%)
<25	106 (58.8%)

Table 2. Distribution of ABO Blood Groups by Gender (n=180)

Blood Group	Male (n=108)	Female (n=72)	Total (n=180)
A	27 (25.0%)	18 (25.0%)	45 (25.0%)
B	39 (36.1%)	24 (33.3%)	63 (35.0%)
AB	12 (11.1%)	6 (8.3%)	18 (10.0%)
O	30 (27.7%)	24 (33.3%)	54 (30.0%)
Total	108 (100%)	72 (100%)	180 (100%)

The majority of males and females belonged to blood group B, with 36.1% and 33.3%, respectively. The second highest blood group was blood group O, with slightly more females (33.3%) than males (27.7%). The distribution of blood group A was similar for both males and females (25.0%). The least common blood group was blood group AB, with 11.1% of males and 8.3% of females. The distribution of ABO blood groups was almost similar for males and females. No significant variation was noted (Table 2).

Fever and cough were found to be more common in all ABO blood groups, but there was no significant difference. Dyspnea was more common in blood groups A (71.1%) and AB (72.2%) when compared with blood group O (42.5%). The association was found to be statistically significant at p=0.05. Hypertension was more common in blood group A (51.1%). The difference was statistically significant at p=0.04. Fatigue and diabetes were more common in blood groups A and AB, but this was not statistically significant. Blood groups A and AB were found to have more severe clinical features when compared with blood group O (Table 3).

The severity of the disease showed statistical significance with ABO blood groups (p=0.04), with blood groups A and AB having more patients with severe and critical conditions, while blood group O patients were more likely to have mild conditions. The patients admitted to ICU were more with blood group AB (33.3%), followed by blood group A (24.4%), while the least were with blood group O (12.9%). There was a significant difference (p=0.05). The patients with mechanical ventilation were more with blood groups A and AB, showing statistical significance (p=0.04). Even though patients with blood groups AB (22.2%) and A (17.7%) had more mortality when compared to blood group O (7.4%), it did not show statistical significance (p=0.07). Patients with blood groups A and AB were more likely to have severe conditions with poor clinical outcomes when compared to patients with blood group O (Table 4).

Discussion

The current study aimed at evaluating the clinical characteristics of patients with COVID-19 in association with their ABO blood groups, which indicated a significant association between the types of blood groups and the severity of the disease. The study indicated that patients with blood groups A and AB tend to have severe disease manifestations with poor clinical outcomes, while patients with blood group O tend to have mild manifestations of the disease.

In this study, the average age of the patients was found to be 48.5 ± 15.1 years, with the majority of the patients from the 41–60 years age group, which could be due to the increased occurrence of co-morbid conditions and decreased immune response with advancing age. The majority of the patients in this study were males (60%), which is consistent with the previous studies that found more males to be infected with COVID-19 than females and suggested that males are more susceptible to severe COVID-19 infection than females due to various factors such as immune response, hormonal factors, and increased exposure to various risk factors such as smoking. A study by Twitchell (2022) found that males are more likely to get severe COVID-19 outcomes than females due to various factors.[9]

In the present study, it was observed that the distribution of ABO blood groups was such that the B blood group was the most prevalent, followed by the O, A, and AB blood groups. It is also noteworthy that the distribution of blood groups was almost the same in males and females, thus establishing the fact that gender does not play an important role in the distribution of blood groups. On the contrary, in a study done by Sun et al., (2022) on the distribution of ABO blood groups in the Chinese population, among 23 million, showing the order O > A > B > AB. Geographical variation was also seen in this study, with the O gene showing an increase from north to south, while the B gene showed a decrease.[10] The study by

Anyiam (2023), despite having 2,388 blood donors in Ekiti State, Nigeria, showed that blood group O was the most prevalent (78.2%), while blood group AB was the least prevalent (0.9%). In addition, 94.7% were Rh positive, with a total HIV prevalence of 0.81%.[11]

As far as the clinical characteristics are concerned, fever and cough were the most common presenting symptoms in all the blood groups, as supported by the well-established clinical presentation of COVID-19. However, dyspnea was found to be more common in patients with blood groups A and AB in comparison to those with blood group O. Dyspnea is known to be a severity indicator, and the higher incidence of dyspnea in patients with blood groups A and AB may indicate that these patients are more likely to experience severe respiratory complications during the course of the disease. Hypertension was also found to be more common in patients with blood group A, and hypertension is known to be a risk factor for severe COVID-19. While a study by Guzman-Esquivel et al., (2023), showed that severe symptoms of acute COVID-19, such as myalgias, tachycardias, and antibiotic use, are associated with an increased risk of long COVID-19, with education level and blood group B/AB conferring risk of type 2 diabetes, whereas O+ blood group is associated with a lower risk.[15]

Another significant finding of this study was the association between disease severity and ABO blood groups. Patients in blood groups A and AB had more severe and critical disease, while those in blood group O had mild disease. This finding is in accordance with other international studies that found more susceptibility and severity in blood group A and mild disease in blood group O. The proposed mechanism for this effect is that natural anti-A antibodies are present in blood group O individuals, and this could interfere with the binding of SARS-CoV-2 to cell receptors, thus reducing disease severity.

Similarly, a study conducted by Hoiland (2020) found that critically ill COVID-19 patients with blood groups A and AB were found to be more likely to need mechanical ventilation and CRRT and had longer ICU stays than those with groups O and B. This implies that the COVID-19 illness may be worse for individuals with blood groups A and AB. However, the reason for this is not clear.[16] Additionally, a study done by Abegaz (2021) found that individuals with blood group A have a higher association

Table 3. Clinical Characteristics According to ABO Blood Groups

Clinical Feature	A (n=45)	B (n=63)	AB (n=18)	O (n=54)	p-value
Fever	39 (86.6%)	54 (85.7%)	17 (94.4%)	45 (83.3%)	0.88
Cough	37 (82.2%)	51 (80.9%)	16 (88.8%)	42 (77.7%)	0.91
Dyspnea	32 (71.1%)	36 (57.1%)	13 (72.2%)	23 (42.5%)	0.05*
Fatigue	33 (73.3%)	42 (66.6%)	12 (66.6%)	28 (51.8%)	0.09
Hypertension	23 (51.1%)	27 (42.8%)	8 (44.4%)	19 (35.1%)	0.04*
Diabetes	22 (48.8%)	26 (41.2%)	9 (50.0%)	17 (31.4%)	0.08

protection against long COVID-19.[12] In a study by Su et al., (2022), the ABO blood group types were shown to affect susceptibility to respiratory infections, with A, B, and AB blood types conferring a higher risk of upper respiratory tract infections, and blood types A and B conferring a lower risk of influenza and pneumonia.[13]

Even though fatigue and diabetes mellitus were more common in blood groups A and AB, they were not statistically significant. However, there is a possible relationship between blood groups and increased burden of disease. As a study by Meo (2016) revealed that blood group B is associated with a higher risk of type 2 diabetes, whereas blood group O is associated with a lower risk.[14] In addition, a study by Mandal (2018) revealed that AB and A blood groups are associated with a slightly higher relative with cancer. On the other hand, groups B and AB are associated with infections and cognitive disorders. Group O has a lower risk of disease but is more susceptible to infections like cholera and tuberculosis.[17]

In addition, differences in the expression of angiotensin-converting enzyme 2 (ACE2), which is the main receptor for SARS-CoV-2, may be involved in this association. It has been hypothesized that people with different ABO blood groups may have different expression or activity of the ACE2 receptor, which could be involved in SARS-CoV-2 infection. In addition, according to a study done by Zhang (2021), blood type O has been shown to be less susceptible to COVID-19 due to anti-A antibodies, which can prevent the virus's spike protein from binding to ACE2 receptors, thus preventing infection and/or reducing the

Table 4. Disease Severity and Outcomes by ABO Blood Groups

Variable	A (n=45)	B (n=63)	AB (n=18)	O (n=54)	p-value
Disease Severity					
Mild	11 (24.4%)	17 (26.9%)	5 (27.7%)	21 (38.8%)	0.04*
Moderate	11 (24.4%)	21 (33.3%)	4 (22.2%)	17 (31.4%)	
Severe	14 (31.1%)	16 (25.3%)	5 (27.7%)	11 (20.3%)	
Critical	9 (20.0%)	9 (14.2%)	4 (22.2%)	5 (9.2%)	
ICU Admission	11 (24.4%)	13 (20.6%)	6 (33.3%)	7 (12.9%)	0.05*
Mechanical Ventilation	8 (17.7%)	9 (14.2%)	3 (16.6%)	7 (12.9%)	0.04*
Mortality	8 (17.7%)	7 (11.1%)	4 (22.2%)	4 (7.4%)	0.07

severity of symptoms.[18] Another study done by Arend (2021) noted that blood type O has been shown to be less susceptible to SARS-CoV-2 because it does not have A/B antigens, thus allowing anti-A and anti-B IgM antibodies to remain active, thus preventing the virus from binding to the receptors, while non-O blood groups have A/B antigens, which reduces this innate antibody response, thus making them more susceptible to SARS-CoV-2 infection.[19]

Moreover, it has been established that ABO blood groups play a role in coagulation, with non-O blood groups (A, B, and AB) being associated with hypercoagulability due to higher levels of von Willebrand factor and factor VIII. This is particularly significant in COVID-19, as it has been established that thrombotic complications play a significant role in the severity and mortality of COVID-19 patients. This is supported by a study done by Ward (2020), which established that blood group O has a lower risk of thrombosis due to 25% lower plasma levels of von Willebrand factor (VWF) and that VWF in O blood group is easily cleaved by ADAMTS13 metalloprotease. ABO blood groups play a significant role in platelet function, with blood group O showing reduced platelet-VWF interaction, thus lowering the risk of thrombosis.[20]

The findings of this study are significant in clinical practice. Blood group could be used as a potential risk factor for disease severity in COVID-19 patients. Clinicians could benefit from this finding in managing COVID-19 patients. Patients in blood groups A and AB should be closely monitored and managed to prevent disease progression. However, more studies are recommended to further understand this association and to validate this finding in large cohorts and multiple centers. More research is recommended to explore this association and to understand the biological mechanism behind this association.

Limitations

This study has several limitations. First, the non-probability consecutive sampling method may introduce selection bias, as only admitted patients were included. Second, the single-center design limits generalizability to other populations and healthcare settings. Third, the small sample size, particularly for blood group AB (n=18), reduces statistical power and increases the width of confidence intervals; therefore, findings for AB group should be interpreted with caution. Fourth, the retrospective design relies on medical record accuracy and completeness. Fifth, we did not perform multivariate adjustment for potential confounders such as age, gender, comorbidities, and smoking status. Finally, causality cannot be inferred from this cross-sectional design.

Conclusion

The current study proves the presence of a correlation between ABO blood groups and the clinical characteristics and outcomes of patients with COVID-19. Blood groups A and AB have shown a correlation with disease severity and outcomes, while blood group O seems to have a protective effect. The potential usefulness of ABO blood grouping in the clinical management of patients with COVID-19 is evident.

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