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A STUDY OF ABO BLOOD GROUP AND ANTICOVID ANTIBODY TITER IN SYMPTOMATIC COVID-19 DISEASE

Dr. Naveen KM[1*], Dr. Raman M Hulinaykar[2], Dr. Virupaksha Kl[3], Dr. Naveen K[4]

[1]*Assistance professor Department of general medicine Siddaganga Medical College & Research Institute.*
[2]*Professor Department Of General Medicine Shridevi Medical College*
[3]*Professor Department Of General Medicine Shridevi Medical College*
[4]*Professor Department Of General Medicine Shridevi Medical College.*

Correspondence:
Dr Naveen KM

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Abstract

Background: COVID-19, an emerging infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a pandemic in March 2020 by WHO. The disease presents with variable clinical severity ranging from mild symptoms to severe respiratory failure. Understanding the factors influencing disease severity and immune response remains crucial for managing this global health crisis. The ABO blood group system has been implicated in susceptibility and severity of various infectious diseases, but limited studies have examined its relationship with COVID-19 outcomes and antibody response. ***Objective:*** To study the correlation of ABO blood group and anti-COVID antibodies with severity of COVID-19 in symptomatic patients. ***Methods:*** A hospital-based cross-sectional study was conducted including 70 COVID-19 positive patients (confirmed by RT-PCR or rapid antigen test) attending follow-up clinic. Blood group determination and anti-COVID antibody measurement using ELISA were performed between 3 to 6 months post-infection. Patients were categorized into mild, moderate, and severe disease based on revised standard operating procedures. Data was analyzed using chi-square test with p-value <0.05 considered statistically significant. ***Results:*** The median age was 41 years with male predominance (65.7%). Blood group B was most common (45.7%), followed by O (25.7%), A (24.3%), and AB (4.3%). Severe disease was observed in 14.3% of patients, most commonly in blood group O (27.8%). Anti-COVID antibodies were detected in 50% of patients overall, with highest positivity in blood group A (58.8%) and O (55.6%). All severe COVID-19 patients showed anti-COVID antibodies, compared to 65.6% of moderate and only 14.3% of mild cases. The most common symptom was cough (40%), and patients with antibodies more frequently presented with fever, fatigue, dyspnea, headache, and diarrhea (p<0.05). ***Conclusion:*** ABO blood group may influence COVID-19 severity, with blood group O patients showing maximum disease severity despite decreased susceptibility to infection. Antibody response correlates with disease severity, with all severe cases demonstrating antibody positivity. These findings suggest that ABO blood group could be one of the factors influencing COVID-19 clinical outcomes.

Keywords: Pandemic; Anti-COVID antibodies; ABO blood group; COVID-19 disease; Disease severity

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INTRODUCTION

COVID-19, an emerging infectious disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), was first identified in December 2019 when several cases of pneumonia of unknown etiology were noted in Wuhan city, Hubei province, Central China. The cases were initially reported in patients who worked or lived around the local Huanan Seafood wholesale market starting December 8, 2019. The disease spread rapidly, infecting more than 12,000 people in China and 82 confirmed cases worldwide by January 2020, prompting WHO to declare the SARS-CoV-2 outbreak as a Public Health Emergency of International Concern on January 30, 2020.[16] Subsequently, it was declared a pandemic in March 2020 by WHO. Globally, as of December 23, 2022, there have been 651 million confirmed cases of COVID-19, including 6.6 million deaths reported to WHO, with a total of 130 million vaccine doses administered as of December 21, 2022.[1]

India experienced one of the highest COVID-19 infection rates globally, with over 25 million confirmed cases and an escalating death toll. The first case was identified on January 30, 2020, in Kerala in a student who had returned from Wuhan, China. Since March 2020, there has been a significant upsurge in the spread of infection.[16] The coronavirus outbreak caused a major public catastrophe and evolved into a global concern. The virus can spread from person to person

and was named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) due to its characteristic appearance in electron microscopy.[14] Humoral immunity, especially neutralizing antibodies, are thought to play a vital role in acquiring protection against SARS-CoV-2 infection. Studies have shown that the receptor binding domain of the viral spike protein is a highly targeted site in COVID-19 patients. Some experimental models indicate that adaptive transfer of neutralizing monoclonal antibodies reduces mortality and viral burden. However, in severe cases, it has been observed that antibodies may trigger immunopathogenic events and demonstrate higher antibody titers compared to mild symptomatic patients.[4]The incidence of previous infections including SARS-CoV in 2002-2003 and MERS-CoV in 2012 demonstrated that transmission from animal to human and person-to-person transmission are possible with novel coronaviruses.[15]

The ABO blood group system, discovered in 1900, has been extensively studied for its role in various diseases. Humans have four different types of ABO blood groups—A, B, AB, and O—based on agglutination patterns. A and B antigens are present on red blood cells, while corresponding antibodies are absent in the sera. These antigens are expressed on the surface of RBCs, and the human ABO gene, weighing 18 kilobases and consisting of 7 coding exons, is located on chromosome 9. The genes for A and B encode A and B transferases due to amino acid substitution caused by nucleotides. O genes are not active as they do not produce functional enzymes. Many studies have found that ABO blood group plays an important role in various diseases such as cardiovascular, oncological, and some infectious and non-infectious diseases.[2] Only a few studies have examined the relationship between SARS-CoV-2 and blood groups. Studies have shown that individuals with blood group A are more susceptible to COVID-19, while blood group O appears protective.[3]However, there are insufficient studies on blood groups and antibody titers in different clinical categories of COVID-19 disease, which prompted the present investigation.

MATERIALS AND METHODS

A hospital-based cross-sectional study was conducted over 18 months. The study included confirmed COVID-19 cases by RT-PCR or Rapid Antigen Test who attended the COVID-19 follow-up clinic after 6 months. Patients aged 18-60 years were included in the study. Patients with previously known chronic systemic illnesses such as ischemic heart disease, chronic obstructive pulmonary disease, interstitial lung disease, chronic kidney disease, and persons on immunosuppressant therapy were excluded from the study.

Sample size was calculated using Cochrane's formula considering the proportion of A blood group in positive COVID-19 patients according to a study by Qian Fan, Wei Zhang et al.[2] With a precision level of 0.12, prevalence (p) of 0.43, q=0.57, and Z value of 1.96 at 95% confidence limit, the calculated sample size was 66, which was rounded to 70 patients. Stratified random sampling method was employed for patient selection.

After obtaining ethical committee clearance from the institution and informed consent from patients fulfilling inclusion and exclusion criteria, data collection was initiated. A pre-designed proforma, which was internally validated, was used to collect information on all needed variables. Patients were categorized into mild, moderate, and severe COVID-19 cases based on the revised standard operating procedure for admission and management of COVID-19 positives.[10,11]Each patient's blood group was recorded. Antibody titers were tested in each patient by enzyme-linked immunosorbent assay (ELISA) between 3 to 6 months post-infection, and levels of antibody titers were compared among various categories of COVID-19 patients.

The collected data was entered and analyzed using Epi info-7 software. Percentages and proportions were calculated for qualitative data. Chi-square test was performed to assess statistical significance, with p-value less than 0.05 considered statistically significant. Correlation between different blood groups and antibody titers with severity of COVID-19 was evaluated.

RESULTS

The study included 70 COVID-19 positive patients with ages ranging from 19 to 72 years and a median age of 41 years. Male patients comprised 65.7% (n=46) of the study population compared to 34.3% (n=24) female patients.

Distribution of ABO Blood Groups and Disease Severity

Blood group B was the most common (45.7%, n=32), followed by blood group O (25.7%, n=18), blood group A (24.3%, n=17), and blood group AB was least common (4.3%, n=3). Among the total COVID-19 patients, 45.7% (n=32) had moderate disease, 40% (n=28) had mild disease, and 14.3% (n=10) had severe disease (Table 1). The severity of disease was most common in blood group O patients (27.8%, n=5), followed by blood group A (23.5%, n=4) and blood group B (4%, n=1). Notably, blood group AB patients presented only with mild and moderate disease without any severe cases (Table 2, Fisher's Exact Test = 7.694, p=0.243).

Clinical Presentation

The most common symptom among patients was cough (40%, n=28), followed by headache (34.29%, n=24), dyspnea and sputum production (31.43%, n=22 each). The least common presentation was anosmia (12.86%, n=9). In severe disease, cough with sputum production (n=9) was the most common symptom, followed by dyspnea and myalgia (n=8 each), while only 2 patients presented with fever (Table 3).

TABLE 1: Distribution of COVID-19 patients according to ABO blood group and severity

Blood Group	Mild n (%)	Moderate n (%)	Severe n (%)	Total n (%)
A	5 (29.4)	8 (47.1)	4 (23.5)	17 (24.3)
B	12 (48.0)	12 (48.0)	1 (4.0)	25 (35.7)
AB	5 (50.0)	5 (50.0)	0 (0.0)	10 (14.3)
O	6 (33.3)	7 (38.9)	5 (27.8)	18 (25.7)
Total	**28 (40.0)**	**32 (45.7)**	**10 (14.3)**	**70 (100.0)**

Fisher's Exact Test = 7.694, p = 0.243

TABLE 2: Age distribution and disease severity

Age Group (years)	Mild n (%)	Moderate n (%)	Severe n (%)	Total n (%)
18-32	13 (46.4)	7 (21.9)	0 (0.0)	20 (28.6)
33-47	11 (39.3)	10 (31.3)	1 (10.0)	22 (31.4)
48-62	1 (3.6)	11 (34.4)	7 (70.0)	19 (27.1)
63-77	3 (10.7)	4 (12.5)	2 (20.0)	9 (12.9)
Total	**28 (100.0)**	**32 (100.0)**	**10 (100.0)**	**70 (100.0)**

Fisher's Exact Test = 22.574, p = 0.000

TABLE 3: Clinical symptoms and disease severity

Symptoms	Mild n (%)	Moderate n (%)	Severe n (%)	p-value
Fatigue	4 (14.3)	14 (43.8)	3 (30.0)	0.037
Dyspnea	6 (21.4)	17 (53.1)	8 (80.0)	0.002
Cough	24 (85.7)	27 (84.4)	9 (90.0)	1.000
Sputum production	19 (67.9)	19 (59.4)	9 (90.0)	0.238
Headache	11 (39.3)	25 (78.1)	4 (40.0)	0.004
Myalgia	7 (25.0)	24 (75.0)	8 (80.0)	0.000

TABLE 4: Anti-COVID antibody distribution by blood group and disease severity

Category	Antibody Positive n (%)	Antibody Negative n (%)	Total n (%)	p-value
By Blood Group				
A	10 (58.8)	7 (41.2)	17 (100.0)	0.706
B	11 (44.0)	14 (56.0)	25 (100.0)	
AB	4 (40.0)	6 (60.0)	10 (100.0)	
O	10 (55.6)	8 (44.4)	18 (100.0)	
By Disease Severity				
Mild	4 (14.3)	24 (85.7)	28 (100.0)	<0.001
Moderate	21 (65.6)	11 (34.4)	32 (100.0)	
Severe	10 (100.0)	0 (0.0)	10 (100.0)	

Anti-COVID Antibody Distribution

Among all COVID-19 patients, 50% (n=35) tested positive for anti-COVID antibodies while the other 50% (n=35) tested negative. Anti-COVID antibodies were present in significant titers in 50% of both male and female patients (p=0.05). Among patients with blood group A, 58.8% (10 of 17) had antibodies present, followed by 55.6% (10 of 18) with blood group O, 43.8% (14 of 32) with blood group B, and 33.3% with blood group AB (Table 4, Fisher's Exact Test = 1.544, p=0.706).

Correlation between Severity and Antibody Response

All patients with severe disease (100%, n=10) showed anti-COVID antibodies, while 65.6% (n=21) of moderate cases and only 14.3% (n=4) of mild cases had detectable antibodies (Table 4). Patients who tested positive for anti-COVID antibodies presented more frequently with fever, fatigue, dyspnea, headache, and diarrhea compared to those who tested negative for antibodies, and these differences were statistically significant (p<0.05).

DISCUSSION

The present hospital-based cross-sectional study included 70 patients who tested positive for COVID-19 by RT-PCR or Rapid Antigen Test and attended follow-up after 6 months. The median age was 41 years (range 19-72 years), which was comparable to other studies, though Harapan et al.[16]reported a slightly higher median age of 49 years. Male predominance was observed in our study (65.7%), contrasting with the study by Harapan et al.[16] which reported 62.1% female patients. Blood group B was most common (45.7%) in our study, while AB was least common (4.3%), which differs from population-based cohort studies^(2,3) that reported blood group O as most prevalent. In our study, moderate disease was most common (45.7%), followed by mild (40%) and severe disease (14.3%). Severe disease was predominantly found in blood group O patients (27.8%) (Table 1), which aligns with findings by Dal MS et al.[24]who reported severe COVID-19 in 40.82% of O blood group patients and mild disease predominantly in AB positive patients.

The association between O blood group and severe disease despite lower susceptibility suggests complex immunological mechanisms that warrant further investigation.

Regarding antibody response, 50% of our study participants showed anti-COVID antibodies at 6 months follow-up, considerably lower than the 85.6% reported by Harapan et al.[16] in RT-PCR positive patients. This discrepancy may reflect variations in timing of antibody testing, disease severity distribution, or individual immune response variability. Blood group B patients showed maximum antibody positivity (31.43%), while AB blood group showed least positivity (Table 4). Importantly, all severe COVID-19 patients (100%) demonstrated anti-COVID antibodies, compared to 65.6% of moderate cases and only 14.3% of mild cases, suggesting a strong correlation between disease severity and antibody response. This finding is consistent with observations by Gozalbo-Rovira et al.[4]who noted higher antibody titers in severe cases, though they did not find this association statistically significant. The clinical presentation in our study revealed cough as the most common symptom (40%), and patients with detectable antibodies more frequently presented with fever, fatigue, dyspnea, headache, and diarrhea ($p<0.05$), indicating that symptomatic severity correlates with robust antibody production.

Several mechanisms have been proposed to explain ABO blood group associations with COVID-19 outcomes.[17]The receptor-binding domain of SARS-CoV-2 spike protein may share sequence similarity with ancient lectin family known to bind blood group antigens. Anti-A antibodies present in non-A blood groups could potentially block viral attachment to ACE2 receptors, providing protective effects. Additionally, differences in blood group antigen expression can influence host susceptibility to various pathogens through mechanisms involving lectin binding, toxin neutralization, and evasion of host clearance mechanisms.[22,23]These immunological variations may explain why blood group O individuals, despite having lower susceptibility to infection, experience greater disease severity when infected.

CONCLUSION

This study demonstrates that ABO blood group may influence COVID-19 severity and immune response. Blood group B was most prevalent among symptomatic COVID-19 patients, while blood group O patients exhibited maximum disease severity despite decreased overall susceptibility to infection. Fifty percent of COVID-19 patients demonstrated detectable anti-COVID antibodies at 6 months post-infection. Blood group B patients showed maximum antibody positivity, while AB blood group showed least antibody response. A strong correlation was observed between disease severity and antibody presence, with all severe cases demonstrating antibody positivity compared to only 14.3% of mild cases. These findings suggest that ABO blood group could be one of several factors influencing COVID-19 clinical outcomes and immune response. Further multicentric studies with larger sample sizes are warranted to validate these findings and elucidate the underlying immunological mechanisms.

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