

Original Article

The association of ABO blood type with the risk and severity of COVID-19 infection

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Abstract: Background: There is conflicting data in the literature about the association of ABO blood type and susceptibility to COVID-19 infection. Moreover, very few studies have examined the effect of blood type on severity of COVID-19 infection. Methods: This was a retrospective, single-center analysis of adult patients with COVID-19 infection who were hospitalized between March 8th to July 31st, 2020 at a regional tertiary care hospital. All patients who were hospitalized with a diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and had a documented ABO blood type were enrolled in this analysis. Aims of this study were to examine the prevalence of ABO blood types in patients with COVID-19 infection and to determine the frequency of severe COVID-19 infection among ABO blood types. Results: A total of 227 cases were identified. Our cohort had a mean age of 63.3 years and 60% were males. The most common blood type was O (49%) followed by A (36%), which was similar to the prevalence of ABO blood types in our regional population. Moreover, there was no significant difference in the frequency of severe COVID-19 infection between ABO blood types (O: 50%, A: 53%, B: 56%, AB: 57%; P=0.93), or any additional outcomes including in-hospital mortality rate (P=0.72), need for ICU admission (P=0.66), ICU free days at day 28 (P=0.51), hospital free days at day 28 (P=0.43), or need for acute renal replacement therapy (P=0.09). Conclusion: We did not find an increased susceptibility of any blood type to COVID-19 infection, nor was there an increased risk of severe COVID-19 infection in any ABO blood types.

Keywords: Severe acute respiratory syndrome coronavirus 2, SARS-CoV-2, coronavirus disease 2019, COVID-19, ABO, blood type, ABO blood group

Introduction

COVID-19 infection caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has become a global pandemic affecting 30 million people worldwide, and over 6 million people in the U.S. alone as of September 16, 2020 [1]. COVID-19 most often presents as a lung infection with symptoms varying widely from flu-like illness to acute respiratory distress syndrome (ARDS) [2, 3]. Emerging data in the literature suggests an association between ABO blood type and the risk of COVID-19 infection. However, there is conflicting data in the literature regarding the association of ABO blood type and the prevalence of COVID-19

infection. A few studies have suggested a higher prevalence of infection amongst individuals with blood type A, and a lower prevalence amongst blood type O [2, 4, 5]; whereas a more recent study from the United States showed higher risk of COVID-19 infection with blood types B and AB and lower with blood type O, and found no correlation found with blood type A [6]. A few studies also have examined the association between blood type and severity of COVID 19 infection and found no difference in frequency of severe COVID-19 infection or 28-day mortality in COVID-19 patients [4, 6].

Our study examines the distribution of different ABO blood types in patients with COVID-19

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infection as well as the frequency of severe COVID-19 infection in different ABO blood types. We also compared outcomes in different ABO blood types.

Patients and methods

This was a retrospective, single-center analysis of adult patients admitted to a regional tertiary care hospital in upstate New York, USA. American College of Surgeons (ACS) COVID-19 Registry was used to identify patients with COVID-19 infection admitted to Albany Medical Center. This study was approved by the Institutional Review Board at Albany Medical Center. Patients with COVID-19 infection were enrolled between March 8th to July 31st, 2020. COVID-19 infection was diagnosed via Reverse Transcription Polymerase Chain Reaction (RT-PCR) from a nasopharyngeal swab in all patients.

Selection criteria

We included all adult patients (age >18 years) hospitalized with COVID-19 infection, who had a documented ABO blood type available in hospital records. We excluded those without a documented ABO blood type. We used the regional American Red Cross data (Western New York) to obtain the ABO blood type distribution for the control group. We compared the prevalence of ABO blood type of the control group with the COVID-19 infected hospitalized patients.

Data collection

The data collection was obtained by chart review of our hospital electronic medical records of COVID-19 patients. The following data was obtained: Demographics-age, sex, race/ethnicity, body mass index (BMI); Comorbidities-coronary artery disease, chronic obstructive pulmonary disease, asthma, diabetes mellitus, end-stage renal disease (ESRD), and smoking history; Admission laboratory parameters-inflammatory markers ferritin, C-reactive protein (CRP), D-dimer, lactate dehydrogenase (LDH), and white blood cell (WBC) count; Treatment received-antibiotics, steroids, and convalescent plasma; Outcome-frequency of severe COVID-19 (Severe COVID-19 was defined as present when there is in-hospital mortality, or requirement of ICU stay or mechanical ventilation or acute dialysis), in-hospital mortality,

ICU-free days at day 28, and hospital-free days at day 28. Patients who remained in ICU or hospital longer than 28 days or who died while in ICU or hospital were given zero free days.

The primary objective of our study was to examine the distribution of ABO blood types in hospitalized patients with COVID-19 infection. Our secondary objective was to compare the frequency of severe COVID-19 infection in various ABO blood types. Additional objectives were to compare the in-hospital mortality, ICU admission, ICU-free days at day 28, hospital-free days at day 28, mechanical ventilation, and acute hemodialysis among different blood types.

Statistical analysis

The continuous data were summarized by the mean and standard deviation (SD) or median and interquartile range (IQR) or range as appropriate. Statistical inference is by Kruskal-Wallis (KW) non-parametric test with significance accepted at $P < 0.05$. Categorical data were presented as numbers and percentages with inference by Fisher's exact test. Minitab statistical software version 19 and R program version 3.6.1 were used.

Results

There were 371 COVID-19 patients admitted during the study period of March 8th to July 31st, 2020. We excluded 144 COVID-19 patients who lacked a documented ABO blood type. A total of 227 patients were included in the study after fulfilling the inclusion criteria. Study subjects were divided into four groups based on their documented blood type. We did not have a sufficiently large enough sample size to sub-categorize each blood type into positive or negative Rhesus factor. Out of 227 included patients, 112 (49.3%; 95% CI: 42.8 to 55.8%) were blood type O, 83 (36.6%; CI: 30.3 to 42.8%) were type A, 25 (11.0%; CI: 6.9 to 15.1%) were type B and 7 (3.1%; CI: 0.8 to 5.3%) were type AB. These percentages are not statistically different from our regional ABO blood type percentages obtained from the Red Cross (O: 54.5%, A: 32.3%, B: 10.1% and AB: 3.1%).

Patient characteristics

Our cohort had a mean age of 63.3 years and 60% were males. **Table 1** shows the compari-

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Table 1. Characteristics and outcomes of patients with COVID-19 infection according to ABO phenotype

Characteristic	All (N=227)	Blood Type O (N=112; 49.3%)	Blood Type A (N=83; 36.6%)	Blood Type B (N=25; 11.0%)	Blood Type AB (N=7; 3.1%)	P-value
Demographics						
Age (years)	63.3, 65, (55-75)	60.7, 62, (51-72)	67.3, 67.0, (55-80.5)	60.9, 69, (49-74)	66.4, 69, (64.5-72.5)	0.04
Male N (%)	135 (59.5%)	75 (67.0%)	42 (50.6%)	14 (56.0%)	4 (57.1%)	0.14
Race N (%)						<0.01
White	122 (53.7%)	50 (44.6%)	58 (69.6%)	10 (40%)	4 (57.1%)	
Black	52 (22.9%)	36 (32.1%)	9 (10.8%)	6 (24%)	1 (14.3%)	
Asian	10 (4.4%)	5 (4.5%)	2 (2.4%)	3 (12%)	0 (0.0%)	
Hispanic	18 (7.9%)	11 (9.8%)	7 (8.4%)	0 (0.0%)	0 (0.0%)	
Body Mass Index	29.2, 28.5, (24.3-39.1)	29.1, 28.6, (24.7-31.2)	29.6, 28.2, (23.7-32.8)	28.5, 28.4, (25.8-32.2)	29.5, 29.1, (25.2-34.8)	0.98
Comorbidities, N (%)						
COPD	32 (14.1%)	15 (13.4%)	11 (13.3%)	6 (24.0%)	0 (0.0%)	0.42
Asthma	26 (11.5%)	16 (14.3%)	9 (10.8%)	1 (4.0%)	0 (0.0%)	0.50
Diabetes Mellitus	88 (38.8%)	44 (39.3%)	28 (33.7%)	11 (44.0%)	5 (71.4%)	0.24
ESRD	12 (5.3%)	6 (5.4%)	4 (4.8%)	2 (8.0%)	0 (0.0%)	0.88
Hypertension	135 (59.5%)	63 (56.3%)	49 (59.0%)	18 (72.0%)	5 (71.4%)	0.50
CAD	56 (24.7%)	29 (25.9%)	20 (24.1%)	7 (28.0%)	0 (0.0%)	0.54
Smoking History	50 (22.0%)	29 (25.9%)	13 (15.7%)	4 (16.0%)	4 (57.1%)	0.04
Inflammatory Markers						
LDH (IU/L)	327.2, 273.5, (206.8-408.5)	340.1, 273.5, (209.5-417.0)	298.4, 282.5, (205.5-353.0)	315.1, 271.0, (237.0-414.0)	445.3, 309.0, (217.0-410.5)	0.86
Ferritin (ng/mL)	698.6, 410.5, (184.0-902.0)	808.6, 439.0, (223.0-920.8)	503.2, 336.0, (182.8-771.3)	809.7, 484.0, (329.0-1067.0)	770.4, 432.0, (154.5-937.5)	0.25
C-Reactive Protein (mg/L)	123.8, 96.2, (33.6-182.2)	133.1, 94.6, (30.7-220.9)	109.2, 87.7, (29.9-147.3)	119.7, 111.7, (44.0-166.1)	135.7, 135.3, (57.9-180.0)	0.77
D-dimer (mg/L)	9.5, 1.6, (0.8-6.7)	9.1, 1.7, (0.8-5.7)	10.3, 1.5, (0.8-10.0)	4.9, 1.4, (0.9-4.2)	22.2, 10.8, (0.9-16.6)	0.72
Therapy Provided - N (%)						
Antibiotics	183 (80.6%)	90 (80.4%)	66 (79.5%)	20 (80.0%)	7 (100%)	0.76
Steroids	99 (43.6%)	50 (44.6%)	31 (37.3%)	13 (52.0%)	5 (71.4%)	0.23
Anticoagulants	48 (21.1%)	25 (22.3%)	14 (16.9%)	7 (28.0%)	2 (28.6%)	0.50
Convalescent Plasma	92 (40.5%)	42 (37.5%)	32 (38.6%)	13 (52%)	5 (71.4%)	0.20

All Data are presented as Mean, Median, IQR; unless otherwise indicated. P-values are calculated based on Kruskal-Wallis test for all variables measured on a continuous scale. P-values for Categorical data are calculated with Fisher's exact test. Severe COVID-19 was defined as present when there is in-hospital mortality, or requirement of ICU stay or mechanical ventilation or acute dialysis.

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Table 2. Frequency of severe COVID-19 infection and outcome in ABO blood types

	All (N=227)	Blood Type O (N=112)	Blood Type A (N=83)	Blood Type B (N=25)	Blood Type AB (N=7)	P-value
Severe COVID-19*	118 (52.0%)	56 (50.0%)	44 (53.0%)	14 (56.0%)	4 (57.1%)	0.93
In-hospital Mortality	45 (19.8%)	20 (17.9%)	20 (24.1%)	4 (16.0%)	1 (14.3%)	0.72
Required ICU	108 (47.6%)	53 (47.3%)	39 (47.0%)	12 (48.0%)	4 (57.1%)	0.66
Mechanical ventilation	69 (30.4%)	41 (36.6%)	16 (19.3%)	8 (32.0%)	4 (57.1%)	0.02
Required Dialysis	17 (7.5%)	13 (11.6%)	2 (2.4%)	2 (8.0%)	0 (0.0%)	0.09
ICU-free days at day 28	19.2, 27, (10-28)	19.3, 28, (10-28)	19.3, 27, (7-28)	19.4, 28, (13-28)	14.6, 18, (0-28)	0.86
Hospital-free days at day 28	11.5, 13.0, (0.0-21)	12.0, 13.5, (0-21)	11.7, 14.0, (0-22)	11.1, 12.0, (0-19)	4.9, 1.0, (0.0-12)	0.43

All Data are presented as Mean, Median, IQR; unless otherwise indicated. P-values are calculated based on Kruskal-Wallis test for all variables measured on a continuous scale. P-values for Categorical data are calculated with Fisher's exact test. *Severe COVID-19 was defined as present when there is in-hospital mortality, or requirement of ICU stay or mechanical ventilation or acute dialysis.

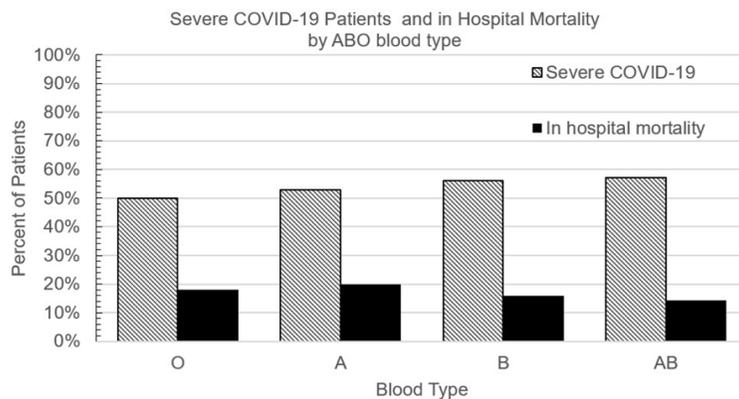


Figure 1. Percentage of COVID-19 patients with severe COVID-19 infection and in-hospital mortality by ABO blood type.

son of baseline characteristics, admission laboratory values, and therapy received in the four different blood types. Blood type O was the most prevalent blood type and was predominantly African American. Patients with blood types A and AB were slightly older in age compared to the remaining blood types ($P=0.04$). All blood types were similar in terms of medical comorbidities except smoking was more prevalent in the blood type AB ($P=0.04$). There was no significant difference in the level of inflammatory markers at hospital admission between the four blood types. In addition, there was no significance difference between the medical treatment they received.

Severity and outcome

There was no significant difference between ABO blood types and the prevalence of severe COVID-19 infection (O: 50%, A: 53%; B=56% and AB=57%; $P=0.93$) (Table 2; Figure 1). There was also no significant difference in the

in-hospital mortality ($P=0.72$), ICU-free days at day 28 ($P=0.86$), and hospital-free days at day 28 ($P=0.43$) among different ABO blood types (Table 2).

Discussion

In our analysis of 227 patients with COVID-19 infection, blood type O had the highest prevalence, followed by blood type A. However, the higher prevalence of COVID-19 in blood type O was likely to be accounted for by the higher prevalence

of blood type O in our regional population. This suggests that a particular blood type does not increase the susceptibility to COVID-19 infection. There also was no significant difference in frequency the of severe COVID-19 infection among ABO blood types. Additionally, there was no difference in in-hospital mortality, ICU-free days at day 28, and hospital-free days at day 28 among ABO blood types.

Blood type antigens may be involved in infection either directly or indirectly. They may play a direct role as receptors or co-receptors for microorganisms or they may act indirectly by modifying host susceptibility or facilitating cell adhesion or intracellular uptake. Associations have been identified between blood type and susceptibility to certain microorganisms [7], such as *Plasmodium falciparum* (blood type O confers resistance to severe malaria) [8, 9], *Helicobacter pylori* (increased susceptibility with blood type O and decreased likelihood of infection with blood type B and AB) [10] and

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Noroviruses (blood type O was more susceptible to *Norovirus* infection, and the rest of the blood types did not affect the susceptibility) [11]. Previous study by Cheng and colleagues, reported that patients with blood type O had decreased susceptibility to severe acute respiratory syndrome coronavirus-1 (SARS-CoV-1) [12]. Subsequently Guillon and colleagues hypothesized that decreased susceptibility to blood type O might have been due to the impact of anti-A antibodies on the interaction between the SARS-CoV-1 spike protein with angiotensin converting enzyme-2 cellular receptor [13].

Limited data is available on the association between blood type and COVID-19 infection, including susceptibility, severity of infection, and outcomes. Investigators from China, Europe, and United States showed that patients with blood type A may be at higher risk of infection whereas blood type O may be protective [5, 14]. However, a more recent study from the United States showed higher risk of COVID-19 infection with blood types B and AB and lower risk with blood type O, and no association found with blood type A [6]. Few authors suggested that Blood type O and B may be protective against COVID-19 infection due to the circulating anti-A antibodies, particularly IgG anti-A in blood type O individuals [15]. In our study, we found that blood type O had the highest prevalence, followed by blood type A. This finding was similar to the prevalence of ABO blood type in our regional population, which suggest that a particular blood type does not provide immunity to the COVID-19 infection.

Few studies have examined the association between ABO blood types and severity of COVID-19 infection. Most studies found no difference in frequency of severe COVID-19 infection or in-hospital mortality in COVID-19 [4, 6]. One study found that in a cohort of critically ill patients, there was significantly ($P=0.02$) more requirements for mechanical ventilation in patients with blood types A and AB [16]. Our findings concur with results from previous studies, and demonstrate no significant difference in prevalence of severe COVID-19 infection among ABO blood types, in-hospital mortality, ICU-free days at day 28, and hospital-free days at day 28.

Our study has several limitations. It is a single-center, retrospective, observational study with

a relatively small sample size which would limit the statistical power for the detection of small differences in outcome measures. Data on ABO blood types was unavailable for approximately 38% of the patients. Regional Red Cross data was used as a control group for the comparison of ABO blood types, which may not be representative of the general population [17]. We could not subcategorize blood types by Rhesus factor positivity because of small sample size.

Conclusion

In conclusion, we did not find increased susceptibility to COVID-19 infection in any particular ABO blood type. Additionally, ABO blood type had no effect on the frequency of severe COVID-19 infection, in-hospital mortality, ICU-free days at day 28, and hospital-free days at day 28.

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Disclosure of conflict of interest

Dr. Feustel received funding as a statistical consultant for Transonic Systems and is a Scientific advisor with shares in Penrose TherapeuTx, LLC. The remaining authors have disclosed that they do not have any potential conflicts of interest.

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