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ORIGINAL RESEARCH

Lack of Association of the ABO Blood Group with COVID-19 Risk and Severity in Hospitalized Patients in Louisville, KY

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Abstract

Introduction: The potential association of the ABO blood group with the risk of COVID-19 and its severity has attracted a lot of interest since the start of the pandemic. While a number of studies have reported an increased risk associated with blood type A and a reduced risk with type O, other studies have not found a significant effect. This study aimed to define the prevalence of different ABO blood groups in hospitalized COVID-19 patients in the Louisville, KY area and to investigate whether an association exists between the blood group and disease severity.

Methods: This was a retrospective observational study of 380 patients with SARS-CoV-2 infection hospitalized to eight of the adult hospitals in the city of Louisville. Patients were divided into four different groups according to their ABO blood type. Demographic characteristics and clinical variables, including laboratory data as well as clinical outcomes were compared.

Results: Type O was the most common blood group among the hospitalized patients (51%) followed by type A (31%), B (14%) and AB (4%). The observed blood group distribution among the patients was not significantly different from the distribution expected when compared to a population of similar racial/ethnic composition. No significant associations were found between the blood group and comorbidities, inflammatory biomarkers as well as with recorded outcomes, including the mortality rate and the length of the hospital stay.

Conclusions: The data from hospitalized patients in Louisville is not consistent with the ABO blood group having a significant effect as a risk or severity factor for COVID-19, but it is representative of its prevalence among different racial/ethnic populations.

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Introduction

As of January 27, 2021, there have been more than 99 million confirmed cases of COVID-19, including over 2.15 million deaths around the world.[1] COVID-19 can exhibit a wide variety of clinical presentations, ranging from asymptomatic cases to very severe and critical cases with acute respiratory distress syndrome (ARDS), septic shock, multiorgan failure and death.[2–5] Therefore, it is important to study the demographic, clinical and genetic factors that allow the identification of people at increased risk of suffering serious manifestations. Age, sex, hypertension, diabetes, and chronic vascular and respiratory diseases have already been identified as important risk factors for the severity of COVID-19.[2–6]

Efforts to understand the etiology and pathophysiology of the disease have led to the examination of other coronaviruses, including SARS coronavirus (SARS-CoV-1) and the Middle East respiratory syndrome coronavirus (MERS-CoV). Interestingly, several studies on SARS-CoV-1 suggested a relationship between infection risk and blood type, with blood type O being somewhat protective against the virus.[7, 8] Consistent with such findings, several recent reports have also suggested the existence of an association between ABO blood types and COVID-19 risk.[9–11] For example, several groups in China reported an over-representation of individuals with blood group A and an under-rep-

resentation of those with blood group O among hospitalized patients with COVID-19 compared to blood group distribution in the regions of Wuhan and Shenzen.[9–11] The results suggest a higher risk for individuals with blood type A to contract the disease and a lower risk for individuals with blood type O. However, most of these reports did not find a significant association with disease severity or mortality.[12] Later, a report based on a Genome-Wide Association study (GWAS) reported a significant association of two loci, 3p21.31 and 9q34.2, the latter encoding the blood group ABO antigens, with the risk of COVID-19 among hospitalized patients in Italy and Spain. Agreeing with previous reports, this study found again a higher risk for blood type A and lower for type O (13).

However, the matter of the association of the ABO blood group with risk or severity of COVID-19 has not been definitively settled, as several studies have reported divergent or conflicting results. For example, a study of over 14,000 individuals tested in the New York Presbyterian Hospital System reported a slightly increased infection prevalence among patients with non-O blood types. Moreover, when compared with patients with blood type O, the risk of intubation was decreased for patients with blood type A but increased in those of blood groups AB and B, and while the risk of death was decreased for those with blood types A and B, it was increased for those with blood type AB.[14] Furthermore, Latz et al. [15] found no significant association of blood group with peak levels of inflammatory markers or outcomes in COVID-19 patients. Multivariate analyses found that individuals with Rh+ blood were more likely to test positive and that those with blood types AB and B, but not A, were more likely to test positive compared with type O (15). In another study, Leaf et al. did find an over-representation of type A blood and an under-representation of type O blood among 3,239 critically ill COVID-19 patients, but this was true only for non-Hispanic white patients, and not for Blacks or Hispanics (16). Finally, in a study of 428 COVID-19 patients at the University of Cincinnati Hospital System, Mendy et al. did not find an association of blood group with hospitalization or disease severity (17).

Prompted by the contrasting conclusions of several reports, we undertook this study with the aim of examining the association between the ABO blood groups and the risk and severity of COVID-19 using data from 380 hospitalized patients in the Louisville, KY, area.

Methods

Study Design, Subjects, and Setting

This was a retrospective study including 380 patients with a diagnosis of SARS-CoV-2 infection and blood group data, who were hospitalized in any of the eight adult hospitals in the City of Louisville, KY. The study group was part of a larger study of hospitalized COVID-19 patients that started on March 5, 2020 and ended on July 1, 2020.[18]

Human Subjects Protection

The study was approved by the Institutional Review Board (IRB) at the University of Louisville Human Subjects Research Protection Program Office (IRB number 20.0257) and by the research offices at each participating hospital. The study was exempt from informed consent.

Data Collection

Data were abstracted from hospital electronic medical records. Collected data included patient age; sex; race/ethnicity; body mass index; medical and social history; physical examination findings; laboratory findings, including blood type, chest radiographs and chest CT findings; medications; intensive care unit (ICU) admission; and need for invasive mechanical ventilation (IMV). Race/ethnicity was categorized as Black, Hispanic, non-Hispanic white (white, NH), Asian and Other.

Study Definitions

SARS-CoV-2 infection: A patient hospitalized with a positive SARS-CoV-2 reverse transcriptase polymerase chain reaction (RT-PCR) from a nasopharyngeal swab or other respiratory sample.

SARS-CoV-2 Community Acquired Pneumonia (CAP) with ARDS: A patient with SARS-CoV-2 CAP with evidence of acute respiratory distress syndrome (ARDS) defined as bilateral opacities on a chest radiograph or computed tomographic (CT) scan not fully explained by cardiac failure or fluid overload with PaO2/FiO2 ≤300 mmHg on ventilator settings that include positive end-expiratory pressure (PEEP) ≥5 cm H2O. [20]

Cardiac and cardiovascular events: The following cardiac or cardiovascular events that were present at the time of admission or developed during hospitalization were collected: development of heart failure, cardiac arrest, cardiogenic shock, acute myocardial infarction, pulmonary edema, new arrhythmia, acute worsening of a chronic arrhythmia, cerebrovascular accident, pulmonary embolism, myocarditis, and deep vein thrombosis.

Septic Shock: Defined by persisting hypotension requiring vasopressors to maintain a mean arterial pressure of 65 mm

Hg or higher and a serum lactate level greater than 2 mmol/L (18 mg/dL) despite adequate volume resuscitation.[19]

Clinical outcomes: Binary outcomes evaluated included need for IMV, admission to ICU, septic shock, ARDS, and death. Time-to-event outcomes evaluated included time to hospital discharge, time to initiation of mechanical ventilation, time to ICU admission, time to septic shock, time to ARDS, and time to death.

Laboratory results: Laboratory data included in this study included the first recorded results obtained within 24 hrs. of hospital admission for each patient. Laboratory results included Hematology data (WBC, neutrophil, lymphocyte and platelet counts and erythrocyte sedimentation rate [ESR]); immunological an biochemical inflammatory markers (IL-6, C-reactive protein [CRP], Ferritin, Procalcitonin, D-dimer, Troponin, Brain natriuretic peptide [BNP], blood urea nitrogen [BUN]; respiratory data (PaO2/FiO2) and relative viral load data (PCR Ct values for SARS-CoV-2 N1 gene).

Blood group distribution

National blood group distribution data was obtained from the American Association of Blood Banks Technical Manual. [20] The "Expected" total blood group distribution of the study population based on race/ethnicity was calculated by multiplying each group's relative representation in the patient population (non-Hispanic White [.48], Black [.33], Hispanic [.12], Asian [.03], Other [.03]) by the respective ABO blood type distribution data (%) for each race/ethnic group in the U.S. according to the American Red Cross [21] and then adding them together. For the "Other" group, an average of the other groups was used.

Statistical Analysis

Patient characteristics were calculated for cases based on blood type. Continuous variables were reported as medians and interquartile ranges, and categorical variables were reported as frequencies and percentages. Assessment for significant differences in patient characteristics between blood groups was conducted using Mann-Whitney U tests and Chi-square tests of independence. Chi-square tests of homogeneity were utilized to identify potential differences in blood type proportions between national data and hospitalized SARS-CoV-2 patients in Louisville, KY, as well as any differences in expected versus observed blood type distribution. P-values < 0.05 were used to denote significance for all tests conducted. Statistical analysis was performed using R Studio Version 3.6.1.

Results

Demographics and Blood Groups

The demographic characteristics of the patients in the study and the ABO blood group distribution is shown in **Table 1**. Blood group O was the most prevalent among the hospitalized patients (51%), followed by group A (31%), B (14%) and AB (5%). The median age of the overall population (n=380) was 63 years [IQR: 44,74] and 57% of the patients were male. There were no statistically significant differences in the age of the patients or sex distribution among the groups. Overall, the patient population identified as 48% non-Hispanic white (white, NH), 33% Black, 12% Hispanic, 3% Asian and 3% Other.

Table 1. Demographic characteristics and blood groups

Variable	All	A	AB	B	O	p-value
n (%)	380 (100)	116 (31)	19 (5)	52 (14)	193 (51)	
Age* (years)	63 [44, 74]	66 [53, 76]	64 [52, 68]	61 [44, 74]	60 [41,72]	0.133
Sex						0.869
Male (%)	218 (57)	70 (32)	11 (5)	30 (14)	107 (49)	
Female (%)	162 (43)	46 (28)	8 (5)	22 (14)	86 (53)	
Race/Ethnic Group**						
White, NH	183 (48)	66 [36]	6 [3]	22 [12]	89 [49]	
Black	125 (33)	35 [28]	10 [8]	22 [18]	58 [46]	
Hispanic	47 (12)	9 [19]	1 [2]	3 [6]	34 [72]	
Asian	13 (3)	3 [23]	2 [15]	4 [31]	4 [31]	
Other	12 (3)	3 [25]	0 [0]	1 [8]	8 [67]	

*median [IQR]

Values in parentheses denote the percentage of the total population in the **All column. Values in brackets under the four different blood group columns denote the percentage of each blood group for each racial/ethnic group.

Included in **Table 1** are the distribution of each blood type in each of the racial/ethnic groups. Our data recorded a higher relative prevalence (by percentage) of blood type O among the Hispanic patients (72%) and higher relative prevalence of blood type A in non-Hispanic White patients (36%), while the relative prevalence of blood types B and AB was higher in Black and Asian patients.

Observed vs. Expected Blood Group Distributions

At first inspection, the higher prevalence of blood group O (51%) compared to that of group A (31%) in our patient population seemed opposite to what other studies had previously reported. Taking into consideration that individuals from Black, Hispanic and other minorities are over-represented among hospitalized COVID-19 patients compared to the general population and the variability in the prevalence of different blood groups among different racial/ethnic groups, we decided to investigate whether the blood group distribution observed in our patient population was influenced by its racial/ethnic composition. [21,22] To this effect, we calculated the "expected" prevalence of each blood type by multiplying the percentage of each racial/ethnic group in our patient population by the reported blood group distribution in each one (see Materials and Methods). These numbers (expected distribution) were then compared with the actual (observed) blood group distribution in our study (**Table 2**). No statistically significant differences were found for the overall distribution.

Table 2. Observed and Expected* blood group distributions among hospitalized COVID-19 patients

Race/Ethnic Group**	Fraction of Total	A	AB	B	O
White, NH	.48	36 (40)	3 (4)	12 (11)	49 (45)
Black	.33	28 (26)	8 (4)	18 (19)	46 (51)
Hispanic	.12	19 (31)	2 (2)	6 (10)	71 (57)
Asian	.03	23 (28)	15 (7)	31 (25)	31 (40)
Other	.03	25 (32)	0 (4)	8 (13)	67 (51)
Overall**	**1.00**	**31 (33)**	**5 (4)**	**14 (14)**	**51 (48)**

* Based on data for blood group distribution by racial/ethnic group according to the American Red Cross (21). Observed and (expected) percentages of each blood group are given for each racial/ethnic group.

**Overall expected blood group distribution calculated as indicated in *Materials and Methods*. Comparison of observed vs. expected overall distributions did not show statistically significant differences (p>0.05)

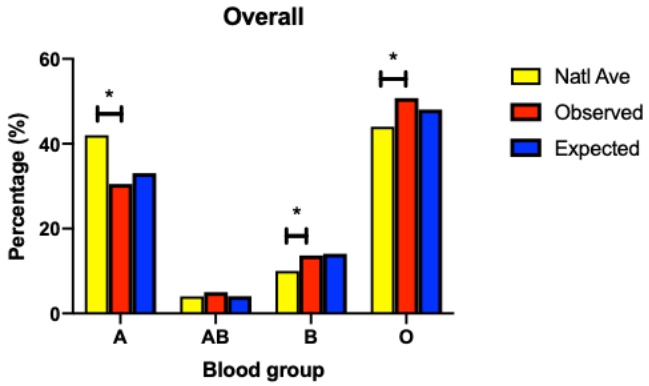

Figure 1. Comparision of Observed blood group frequencies with the National U.S. average and Expected frequencies based on Racial/Ethnic distribution in the Louisville Metro area. *p<0.05

In order to show the importance of comparing the results observed in the patient population against a population of similar racial/ethnic composition, **Figure 1** compares the overall observed blood group distribution with a) the National U.S. average data [20], and b) the expected overall distribution calculated in **Table 2**. As shown, while there were no statistically significant differences between the observed and expected distributions in any of the four blood groups, the observed distributions were significantly different from the "average" U.S. distribution for blood groups A, B and O.

Comorbidities and Blood Groups

Since many comorbidities have been established as risk factors for COVID-19 severity [4–8], we compared the prevalence of comorbidities by blood group (**Table 3**). As expected, based on previous reports, the most common comorbidities among the hospitalized patients were hypertension (52%), diabetes (33%) and hyperlipidemia (36%). Statistical analysis showed that there were no significant differences in the prevalence of comorbidities among the different groups, with the exception of the higher BMI and more prevalent hypertension in patients with blood type AB.

Table 3. Comorbidities and blood groups

Variable	All	A	AB	B	O	p-value
n	380 (100)	116 (31)	19 (5)	52 (14)	193 (51)	
BMI (median [IQR])	30 [24.37]	29 [24,35]	37 [32,42]	27 [22,35]	31 [25,37]	0.012
Smoking History						0.411
Never	265 (62)	69 (59)	13 (68)	30 (58)	123 (64)	
Current	40 (11)	17 (15)	0 (0)	4 (8)	19 (10)	
Former	105 (28)	30 (26)	6 (32)	18 (35)	51 (26)	
Alcohol abuse (%)	29 (8)	8 (7)	2 (11)	6 (12)	13 (7)	0.646
Heart failure (%)	67 (18)	18 (16)	1 (5)	10 (19)	38 (20)	0.390
CV accident (%)	64 (17)	20 (17)	2 (11)	8 (15)	34 (18)	0.925
Renal disease (%)	83 (22)	26 (22)	4 (21)	13 (25)	40 (21)	0.896
ERSD/Dialysis (%)	34 (9)	10 (9)	3 (16)	6 (12)	15 (8)	0.507
Diabetes (%)	126 (33)	36 (31)	8 (42)	21 (40)	61 (32)	0.502
Liver Disease (%)	10 (3)	4 (3)	0 (0)	3 (6)	3 (2)	0.297
Cirrhosis (%)	6 (2)	3 (3)	0 (0)	0 (0)	3 (2)	0.594
Asthma (%)	36 (9)	11 (9)	1 (5)	4 (8)	20 (10)	0.858
COPD (%)	57 (15)	16 (14)	4 (21)	3 (6)	34 (18)	0.158
CA disease (%)	66 (17)	26 (22)	2 (11)	7 (13)	31 (16)	0.326
Hypertension (%)	199 (52)	69 (59)	14 (74)	30 (58)	86 (45)	0.011
Myoc. Infarct. (%)	28 (7)	13 (11)	0 (0)	2 (4)	13 (7)	0.166
Atrial Fibrillation (%)	39 (10)	15 (13)	2 (11)	4 (8)	18 (9)	0.639
Deep Vein Thr. (%)	21 (6)	5 (4)	1 (5)	4 (8)	11 (6)	0.847

CV: Cardiovascular; ERSD: End stage renal disease; CA: Coronary Artery

Biomarkers and Blood Groups

Because laboratory data might give an indication of differences in disease severity, a number of hematological, immunological and biochemical markers were investigated in the different blood groups. **Table 4** summarizes information on the levels of the different markers obtained within 24 hrs. of hospital admission. No statistically significant differences in any of the laboratory markers, including the relative viral load measured by the Ct value in the PCR test, were found among the different blood groups.

Table 4. Inflammatory markers and blood groups

Variable	All	A	AB	B	O	p-value
n	380 (100)	116 (31)	19 (5)	52 (14)	193 (51)	
Blood cells (cells x 10^3/mL)						
WBC	7 [5,10]	7 [5,10]	6 [4,8]	7 [5,9]	7 [5,10]	0.287
Neutrophils	5 [3,8]	5 [4,8]	4 [2,6]	5 [3,7]	5 [3,8]	0.269
Lymphocytes	1 [1,1]	1 [1,2]	1 [1,1]	1 [1,1]	1 [1,2]	0.948
Platelets	195 [155,250]	201 [160,253]	202 [158,258]	184 [139,235]	194 [156,254]	0.625
Other biomarkers						
ESR (mm/hr)	52 [30,77]	60 [31,92]	60 [44,69]	72 [19,100]	44 [32,71]	0.759
IL-6 (pg/mL)	61 [31,135]	79 [41,168]	47 [29,122]	67 [48,154]	54 [24,98]	0.297
CRP (mg/mL)	76 [36,176]	86 [42,191]	71 [45,139]	58 [29,169]	74 [40,172]	0.388
Procalcitonin(ng/mL)	0.14 [0.05,0.57]	0.16 [0.05,0.97]	0.14 [0.05,0.48]	0.15 [0.08,0.53]	0.12 [0.05,0.53]	0.860
D-dimer (ng/mL)	919 [496,1957]	845 [481,1962]	681 [441,1240]	1145 [748,2850]	903 [496,1813]	0.424
BNP (pg/mL)	123 [39,628]	292 [41,671]	73 [63,187]	484 [386,2180]	92 [36,383]	0.275
Troponin (ng/mL)	0.02 [0.01,0.05]	0.01 [0.01,0.07]	0.02 [0.01,0.04]	0.02 [0.01,0.03]	0.01 [0.01,0.05]	0.965
Ferritin (ng/mL)	372 [140,836]	322 [137,809]	288 [140,561]	585 [164,1368]	360 [146,714]	0.121
BUN (mg/dL)	18 [11,33]	19 [12,32]	21 [14,25]	18 [11,41]	18 [11,31]	0.758
PaO2/FiO2 ratio	249 [131,354]	230 [129,350]	288 [216,312]	276 [185,360]	257 [129,357]	0.864

All markers represent median [IQR]

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; BNP: Brain natriuretic peptide; BUN: Blood urea nitrogen; PaO2: Partial pressure of oxygen; FiO2: fraction of inspired oxygen; N1: SARS-CoV-2 N1 gene

Outcomes and Blood Groups

The outcomes and length of hospital stay were compared among the different blood groups (**Table 5**). Overall, the mortality rate was 20%, while the length of hospital stay ranged from 4-16 days [IQR]. Consistent with the results of the laboratory markers, there were no statistically significant differences among blood groups for any of the recorded outcomes, including the mortality rate and the length of hospital stay.

Table 5. Outcomes and blood groups

Variable	All	A	AB	B	O	p-value
n	380 (100)	116 (31)	19 (5)	52 (14)	193 (51)	
Septic Shock (%)	61 (16)	20 (17)	2 (11)	9 (17)	30 (16)	0.885
ARDS (%)	70 (18)	23 (20)	3 (16)	8 (15)	36 (19)	0.904
Cardiac events* (%)	47 (12)	14 (12)	2 (11)	3 (6)	28 (14)	0.403
ICU admission	165 (43)	52 (45)	6 (32)	22 (42)	85 (44)	0.749
IMV	114 (30)	36 (33)	5 (31)	13 (29)	60 (36)	0.850
Mortality (%)	76 (20)	22 (19)	4 (21)	12 (23)	38 (20)	0.938
Times (days — median [IQR])						
Hospital stay	8 [4,16]	9 [4,18]	6 [6,11]	8 [4,19]	8 [4,15]	0.495
To Septic Shock	4 [1,7]	4 [1,8]	2 [1,3]	5 [1,6]	4 [2,8]	0.714
To ARDS	3 [1,7]	4 [1,10]	1 [0,2]	5 [3,9]	3 [1,5]	0.296
To ICU admission	1 [0,3]	1 [0,3]	1 [0,2]	0 [0,3]	1 [0,3]	0.716
To IMV	2 [1,4]	2 [1,4]	1 [1,3]	3 [1,5]	2 [1,4]	0.725
To death	11 [6,15]	10 [6,16]	12 [10,12]	8 [6,16]	11 [6,15]	0.973

*Cardiac events include heart failure, cardiac arrest, acute myocardial infarction, cerebrovascular accident and pulmonary embolism.

ICU: Intensive care unit, IMV: Invasive mechanical ventilation.

Discussion

A better understanding of the risk factors involved in the clinical presentation of COVID-19 is crucial and critical given the current pandemic circumstances. Prompted by inconsistencies in the literature regarding the association of the ABO blood group with the risk of suffering from the disease and of its severity, this study investigated the relative frequency of different ABO blood types among hospitalized COVID-19 patients in the Louisville metropolitan area, as well as the potential association of the blood type with disease severity and outcomes. Our data showed that type O was the most common blood group among the hospitalized patients (51%), followed by types A (31%), B (14%) and AB (4%). The observed blood group distribution among the patients was not significantly different from the distribution that would have been expected based on the racial/ethnic composition and without any influence of the blood group. Moreover, no significant associations were found between the blood group and comorbidities, inflammatory biomarkers or recorded outcomes, including the mortality rate and the length of the hospital stay. Thus, our data argues against the blood group being a significant risk factor for the severity of COVID-19.

Several initial reports from China and later from other countries [9–11] concluded that the blood type influences the risk of COVID-19 by comparing the relative frequencies of blood types among COVID-19 patients with those among the general population or blood donors in the same area. In these studies, blood type A was reported to be over-represented while blood type O was under-represented among COVID-19 patients in comparison with the control group, suggesting that individuals with blood type A had an increased risk while those with blood type O had a decreased risk for COVID-19. However, analysis of the blood group distribution in COVID-19 patients in our study showed that blood type O was by far the most common (51%), considerably higher than type A (31%). These data would seem to suggest an over-representation of type O and an under-representation of type A among COVID-19 patients in our area, if compared to the national average U.S. blood group distribution (44% type O and 42% type A).[20] However, two important facts need to be taken into consideration: first, the racial/ethnic breakdown of the COVID-19 patient population in the U.S., including our own data for the Louisville metro area (**Table 2**), show an over-representation of Blacks and Hispanics compared to the national average;[22] second, blood group prevalence varies among different racial/ethnic groups.[21] Thus, we compared our actual "observed" blood group distribution with an "expected" distribution, calculated by taking into account the fraction of each of the major racial/ethnic groups in the overall patient population and the blood group distribution in each (**Table 2** and **Figure 1**). Accordingly, the observed blood group distribution among the COVID-19 patients in our study was very similar to what would be expected in a control group of a similar racial/ethnic composition and assuming no effect of the blood group. While these results suggest that, at least in our study, blood group was not associated with increased risk for COVID-19, they also highlight the importance of taking into consideration the racial/ethnic composition of the population under study.

Our results are consistent with other recent studies in the U.S. that have not found an association of blood group with disease severity or outcomes in COVID-19 patients.[15–17] However, the reasons for the discrepancies with those studies where an effect of blood group was found are not completely clear. The relative genetic diversity of the different populations under study, as well as the population chosen as "control" in each case, could be involved. The U.S. population is very diverse, and it is possible that such genetic diversity may mask an effect of blood group or make it more difficult to detect. Moreover, as evidenced by the different conclusions obtained when comparing our observed results with either the national U.S. average or the expected blood group distribution, the use of the appropriate control group is obviously a key factor. One of the main strengths of this study is that the observed ABO blood group distribution is consistent with the racial/ethnic breakdown of our patient population, thus highlighting the well-known fact that the spread of COVID-19 in the U.S. has disproportionately affected minority populations, including African Americans and Hispanics.[22]

Another important issue is that of the potential association of blood group with the severity and mortality of COVID-19. To tackle this question, our study initially analyzed the presence of a variety of comorbidities that may potentially influence the severity of the disease in infected persons, separating our patient population by blood group (**Table 3**). Our data analysis indicated that the prevalence of different comorbidities among patients with different blood groups was not significantly different, thus suggesting no differences in predisposing conditions. The only exception found was that of a higher BMI and more frequent incidence of hypertension in patients with blood type AB. However, these results were likely influenced by the reduced number of patients (n=19) with this blood type, thus precluding any conclusions or generalizations.

Our study also investigated whether patients of different blood groups differed in terms of hematologic, immunologic, biochemical and respiratory markers associated with the severity of the COVID-19 disease. As shown by our results, no statistically significant differences in any of these markers were found among the different patient groups, suggesting no significant effect of the blood group on the severity of the disease. In addition, our study analyzed the incidence

of a variety of disease complications and outcomes among patients of different blood groups, including mortality and length of hospital stay. As shown in **Table 5** and consistent with the results of the inflammatory biomarkers, no significant differences were found among the different groups, indicating, again, no significant association of blood group with the risk of developing severe manifestations of the disease or death.

Although the number of cases included in our study (n=380) is similar to other studies reporting on the association of blood group with COVID-19, it is still relatively small compared to other larger studies. Based on the relatively small number of cases, we chose not to include the Rh blood group to further divide our patient population, as that would have resulted in groups with a very low number of patients for the Rh- blood groups. A further limitation is the fact that our cases included only patients admitted to the hospital, and thus, they are not necessarily representative of the overall population in our community that tested positive for SARS-CoV-2. In this regard, our population would represent those individuals that developed symptoms severe enough to be admitted to the hospital. However, if any of the blood groups had initially had an influence on the risk of infection, we would have expected to see such bias reflected in the patient population admitted to the hospital. Rather, our numbers were consistent with the racial/ethnic distribution of the admitted patients.

In conclusion, our study found no significant differences in the prevalence of the ABO blood type among hospitalized patients with COVID-19 in the Louisville, KY, area when compared to a population of similar racial/ethnic composition. Moreover, our study did not detect significant associations of blood group with a variety of hematologic, immunologic, biochemical and respiratory markers of disease severity, nor with the frequency of different disease outcomes, including mortality.

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Appendix: Center of Excellence for Research in Infectious Diseases (CERID) COVID-19 Study Group

CERID Leadership
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Ruth Carrico, PhD, Director of Epidemiological Research
Leslie Wolf, PhD, Director of Laboratory Research
Steven Gootee, MHI, Director of Research Operations
Emily Just, MA, Director of Administrative Operations

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Data Management & Biostatistics Unit
Stephen Furmanek, MPH *(Lead)*
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Research & Diagnostic Laboratory Unit
Leslie Wolf, PhD *(Lead)*

Biorepository Unit
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Quality Assurance Unit
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