Major Article

Analysis of blood type for SARS-CoV-2 and correlation for disease acquisition in various sociodemographic groups including women of childbearing age

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Background: Multiple studies have occurred to determine if a patient's blood type, Rhesus factor (Rh), and sociodemographic attributes contribute to contracting SARS-CoV-2. True association remains unknown.

Methods: Inclusion criteria included in-patients who were tested for SARS-CoV-2 with blood type assessed. Study endpoints combined ABO, Rh and all-cause inpatient mortality (ACIM) with testing positivity. Pregnancy status was one of several secondary endpoints evaluated. A logistic regression analysis was used to estimate association.

Results: Of the 27,662 patients who met inclusion criteria, Type A blood was associated with increased positivity [1.01 (1.0-1.21), P = .03]. Type B [1.10 (0.99-1.23), P = .08] and AB [0.98 (0.81-1.19), P = .84] showed no association. When evaluating ACIM, type A [1.18 (0.91-1.52), P = .22], B [1.13 (0.82- 1.56), P = .480], and AB [1.06 (0.62-1.81), P = .839] were not associated with increased mortality. The female subgroup was less likely to test positive [0.88 (0.82-0.986), P = .002]. Black patients demonstrated a higher likelihood of positivity when compared to White [1.96 (1.79-2.14), P < .001]. Non-pregnant women exhibited a 2.5 times greater likelihood of testing positive [2.49 (2.04-3.04), P < .001].

Conclusions: This study confirms results of previous research which showed SARS-Co-V-2 positivity related to blood type. It also confirms more recent research demonstrating inequities related to acquisition of SARS-CoV-2 for certain sociodemographic groups. Larger studies are warranted to confirm and further explore novel pregnancy findings.

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The role sociodemographic and genetic factors play in susceptibility to SARS-CoV-2 transmission and disease progression still remains unclear. Initial studies from Italy, Spain, China and Denmark have implied that, in contrast to blood type O, those individuals with blood type A were associated with an increased vulnerability to SARS-CoV-2.[1-3] However, more recent research conducted in the United States did not show a correlation between blood type and SARS-CoV-2.[4-7] While there is limited data supporting how genetics and sociodemographic variables contribute to susceptibility, one current study found race to be a contributing factor.[7] The purpose of this case-control study was to explore if blood type and socio-demographic factors contribute to SARS-CoV-2 susceptibility and mortality. It is notably one of the first investigations to examine the relationship between pregnancy status and disease acquisition.

METHODS

This IRB approved, case-controlled study was conducted at the Jefferson University Hospitals located in New Jersey and Pennsylvania from March 2020 through March 2021. Inclusion criteria included all admitted adult patients, ages 18 years and older, who were tested for SARS-CoV-2. Patients were excluded if they did not have a recorded blood type upon admission. For patients who had multiple tests for SARS-CoV-2, the first test with a positive result was used and all others excluded. Primary study end points combined ABO blood type and Rh with likelihood of testing positive and all-cause inpatient mortality (ACIM). Secondary end points included age, gender, race, and body mass index (BMI). There was a subgroup analysis focused on women of childbearing age and pregnancy status.

Statistical analysis

Association amongst patient characteristics with blood type, SARS-CoV-2 test positivity, and mortality were analyzed using Chi squared and Fisher's exact test for discrete variables while the continuous variables were analyzed with ANOVA and unpaired t-test. Logistic regression analysis was used to estimate the association of blood type with testing positive for SARS-CoV-2 and mortality, adjusting for baseline characteristics that were associated with blood type including age, race, and gender. A subgroup analysis was conducted on women of childbearing age (13-49). These analyses were performed using SAS v9.4 (SAS Institute, Cary, NC). All p-values are two-sided and p-values less than 0.05 were considered significant. Odds ratios (OR) were utilized and confidence intervals (CI) were set at 95%.

Table 1
Individual characteristics for SARS-CoV-2 positivity

Blood Type	A	AB	B	O	Total	P value
Total N,%	9227 (33.4%)	1260 (4.6%)	4218 (15.2%)	12957 (46.8%)	27,662	
Age (mean, SD)	57.3 (19.0)	57.3 (19.3)	55.5 (19.2)	56.1 (19.3)	56.3 (19.2)	<0.001
Gender						0.002
Male	43%	45%	41%	41%	42%	
Female	57%	55%	59%	59%	58%	
*BMI mean, (SD)	29.5 (8.8)	27.6 (8.9)	29.5 (7.9)	29.1 (7.6)	29.3 (8.1)	0.798
Not Obese	61.6%	75%	57.6%	61.8%	61%	
Obese*	38.4%	25%	42.4%	38.2%	39%	
Race						<0.001
White	70%	59.4%	47.1%	57.2%	60%	
Black	20.6%	30.7%	38.9%	31%	28.7%	
Other	9.3%	9.8%	14%	11.8%	11.3%	

*Obese defined as Body Mass Index (BMI) $\geq$ 30 kg/m^2
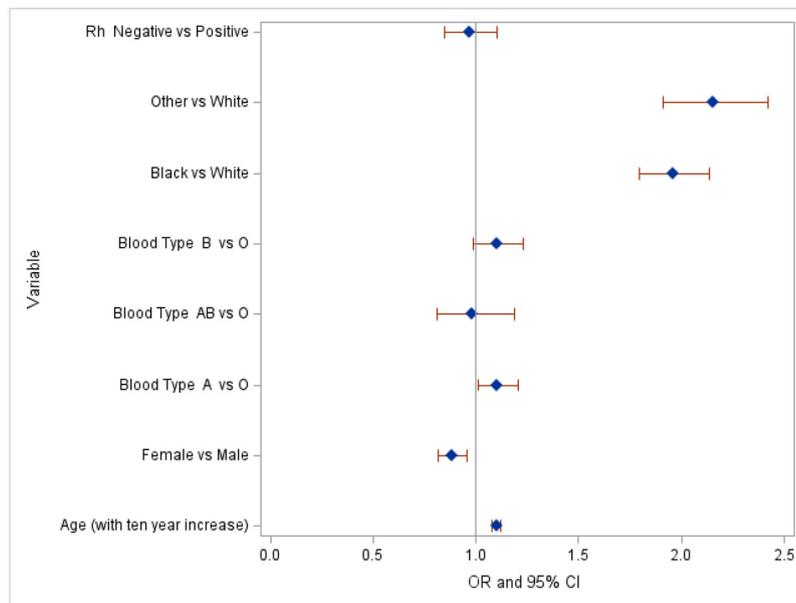

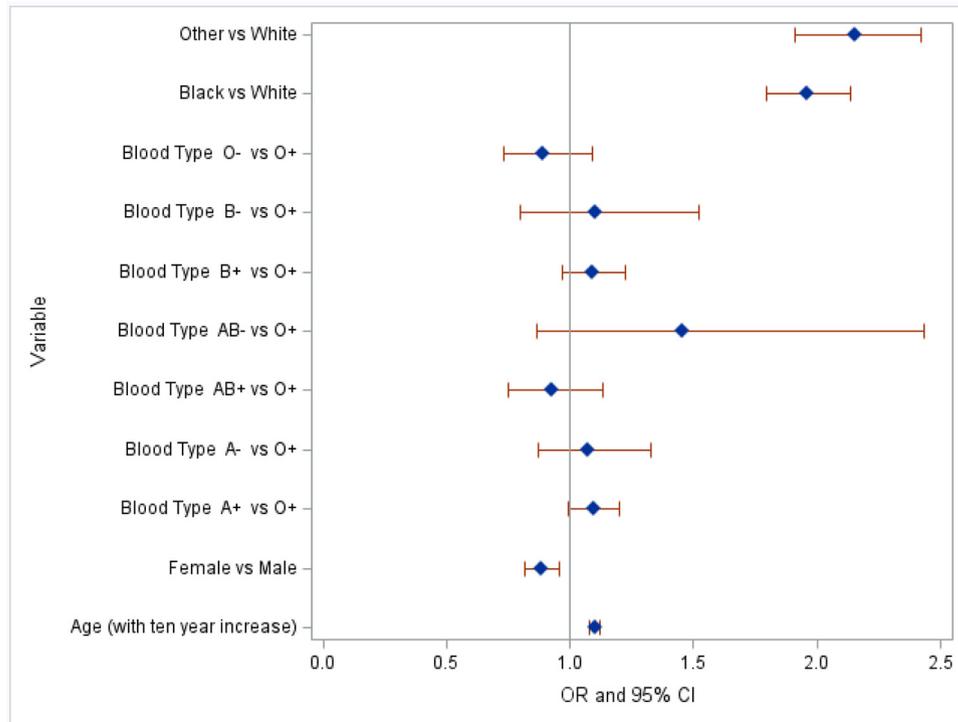**Fig 1.** Odds of testing positive for SARS CoV2 by blood type*.

Fig 2. Odds of testing positive by blood type and Rh.

RESULTS

A total of 27,662 patients who had been tested for SARS-CoV-2 infection were included in the study. Of these patients, 42% were male, mean age was 56.3 [19.2] years [SD] and 60% were of white race. Average BMI was 29.3 [8.1] kg/m^2 [SD] and 39% of patients were considered obese. Further demographic characteristics of the studied population and ABO blood group associations are seen in Table 1. Overall, blood type O (-) was found to have the lowest number of positive tests. ACIM was the highest in blood group A (-) and lowest in O (+). Blood type A was associated with an increased odds of positivity [1.01 (1.0-1.21), P = .03] as seen in Figure 1. However, blood types B and AB did not show an association. Analysis of blood type in combination with Rh revealed no association with increased positivity when compared with blood type O (+) (Fig 2). Additionally, females

were less likely to test positive than males [(0.88 (0.82-0.98), P = .002)], and black patients were more likely to test positive than white patients [(1.96 (1.79-2.14), P < .001)].

Analysis of results women of childbearing age

In the subgroup of women of childbearing age, the associations of age, race, blood type, and pregnancy status with COVID positivity was examined (Table 2). Race and pregnancy status were associated with COVID positivity (P < .001 in both cases). Race showed an association with pregnancy status in women who were COVID + (P < .001) and COVID − (P < .001). Likewise, COVID positivity was associated with race in both non pregnant (P < .001) and pregnant (P < .001) patients. Pregnancy status was associated with categorical age in women who were both COVID + (P < .001) and COVID - (P < .001). For women who were not pregnant, COVID positivity was associated with age (P = .023). In a multivariable analysis adjusted for age and race (Fig 3), none of the blood types were associated with increased positivity when compared with blood type O. As in the overall study population, black race was associated with increased testing positivity when compared with white race [(2.07 (1.72-2.50), P < .001)] in this cohort as well. Moreover, pregnant patients were less likely to test positive for SARS-CoV-2 than non-pregnant patients (OR non-pregnant vs. pregnant=2.49 (2.05-3.05), P < .001).

Limitations

One identified study limitation is that BMI data was not consistently available for all patients in the study. Therefore, we could not control for BMI in the logistic regression model. Also, this is a case-control study in which the cases and controls were recruited from an in-patient setting. This has the potential to produce selection bias as hospital patients may have characteristics different than the general, non-hospitalized community. Immunization status was not a factor in this study as vaccinations were not available to the general public, including our study population, until April of 2021.Therefore,

Table 2
Demographics for women of childbearing age

|	Total (N = 6904)	COVID Negative (N = 6234)	COVID Positive (N = 670)	P value
Race				<0.001
White, N (%)	2500 (36.2)	2185 (35.1)	315 (47.0)	
Black, N (%)	3165 (45.8)	2943 (47.2)	222 (33.1)	
Other, N (%)	1239 (18.0)	1106 (17.7)	133 (19.9)	
Age, (SD)	33.4 (7.9)	33.4 (7.9)	33.7 (8.1)	0.416
Age (categorical)				0.335
<35, N (%)	3985 (57.7)	3610 (57.9)	375 (56.0)	
≥35, N (%)	2919 (42.3)	2624 (42.1)	295 (42.3)	
Pregnancy Status				<0.001
No, N (%)	4256 (61.7)	3744 (60.1)	512 (76.4)	
Yes, N (%)	2648 (38.4)	2490 (39.9)	158 (23.6)	
Blood Type				
A, N (%)	2188 (31.7)	1982 (31.8)	206 (30.8)	0.886
AB, N (%)	293 (4.2)	267 (4.3)	26 (3.9)	
B, N (%)	1127 (16.3)	1016 (16.3)	111 (16.6)	
O, N (%)	3296 (47.7)	2969 (47.6)	327 (48.8)	
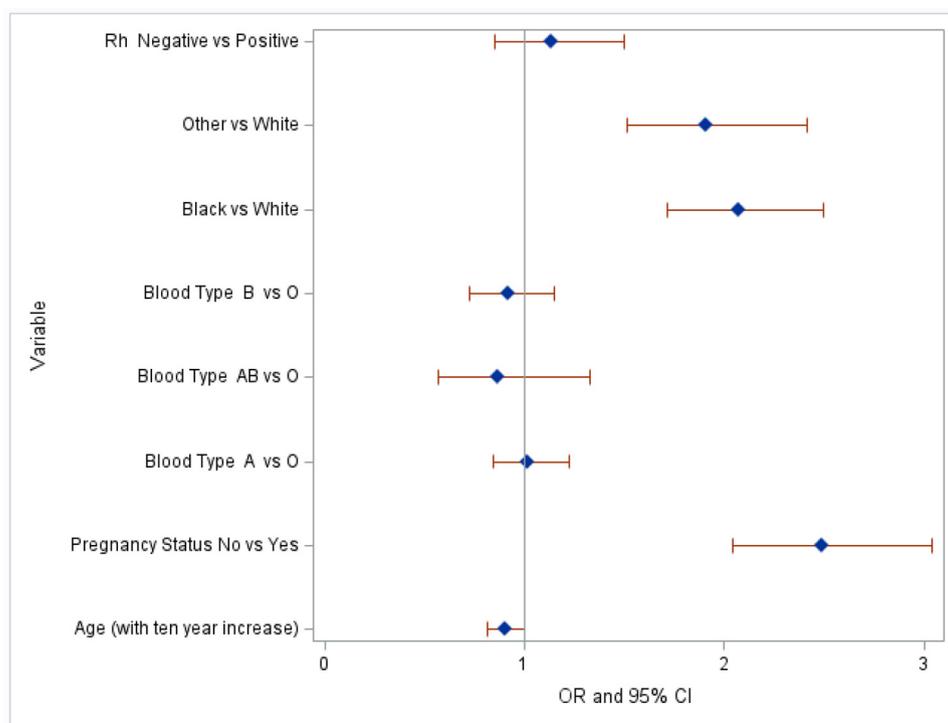
Fig 3. Odds of testing positive for SARS-CoV-2 in women of childbearing age.

immunization status is not relevant, nor considered a limitation for this study.

DISCUSSION

This case-controlled study, consisting of 27,662 patients, supported initial international studies which demonstrated a significant correlation between blood type A and SARS-CoV-2 susceptibility.[1-3] When evaluating subgroups, additional findings demonstrated evidence that females were less likely to test positive for SARS-CoV-2 than men for all age groups. Black patients were more susceptible to SARS-CoV-2 than Whites.[7] The most novel finding of this study is the association of SARS-CoV-2 positivity in women of childbearing age. This research suggests that non-pregnant women were 2.5 times more likely to test positive for SARS-Co-V-2 than pregnant women. This study is the first to identify a correlation between pregnancy status and SARS-CoV-2 positivity and can add to the limited body of knowledge that exists pertaining to this population and SARS-CoV-2. More research is warranted to support this finding and to explore if positivity is affected by physiological, social, or behavioral factors, or influenced by a combination of causes.

References

1. Li J, Wang W. Association between ABO blood groups and risk of SARS-CoV-2 pneumonia. *Br J Haematol*. 2020;190:24−27.
2. Ellinghaus D, Degenhardt F, Bujanda L, et al. Severe Covid-19 GWAS group. Genomewide. Association study of severe Covid 19 with respiratory failure. *N Engl J Med*. 2020;383:1522−1534.
3. Barnkob MB, Pottegard A, Stovring H, et al. Reduced prevalence of SARS-CoV-2 infection in ABO blood group O. *Blood Adv*. 2020;4:4990−4993.
4. Latz CA, DeCarlo C, Boitano L, et al. Blood type and outcomes in patients with COVID-19. *Ann Hematol*. 2020;99:2113−2118.
5. Zietz M, Zucker J, Tatonetti NP. Associations between blood type and COVID-19 infection, intubation and death. *Nat Commun*. 2020;11:5761.
6. Pendu JL, Breiman A, Rocher J, Dion M, Ruvoën-Clouet N. ABO blood types and COVID-19; spurious, anecdotal, or truly important relationships: a reasoned review of available data. *Viruses*. 2021;13:160.
7. Anderson J, May H, Knight S, et al. Association of sociodemographic factors and blood group with risk of COVID in a U.S. population. *JAMA Network*. 2021;4:1−4.