Medical Laboratory Journal
Online ISSN: 2538-4449
Golestan University of Medical Sciences

Evaluating Association between ABO Blood Groups and COVID 19

Original Article

Bhumika Gupta
(DNB PATHOLOGY), Department of Pathology, Government Institute of Medical Sciences, Greater Noida, U.P, India

Shivani Kalhan
(MD PATHOLOGY), Department of Pathology, Government Institute of Medical Sciences, Greater Noida, U.P, India

Shalini Shukla
(MD PATHOLOGY), Department of Pathology, Government Institute of Medical Sciences, Greater Noida, U.P, India

Shalini Bahadur
(MD PATHOLOGY), Department of Pathology, Government Institute of Medical Sciences, Greater Noida, U.P, India

Gyanendra Singh
(MD PATHOLOGY), Department of Pathology, Government Institute of Medical Sciences, Greater Noida, U.P, India

Rambha Pathak
(MD COMMUNITY MEDICINE), Department of Community Medicine, Government Institute of Medical Sciences, Greater Noida, U.P, India

Corresponding author: Dr Shalini Bahadur
Email: shalini.bahadur2008@rediffmail.Com
Tel: +919373009344

Received: 2021/07/20
Revised: 2021/09/02
Accepted: 2021/09/08

DOI: 10.29252/mlj.15.6.1

ABSTRACT

Background and objectives: Coronavirus disease 2019 (COVID-19) is a pandemic caused by SARS-CoV-2 virus that has taken a toll on people all over the world. Previous studies have demonstration association of ABO blood groups with increased susceptibility to various conditions such as infection with *Helicobacter pylori*, Hepatitis B virus and Norwalk virus and even SARS-CoV-1. In this cross-sectional study, we investigated the association between ABO blood groups and COVID-19 in a tertiary care hospital in western Uttar Pradesh, India.

Methods: The study included data from 500 SARS-CoV-2-positive patients who were referred to the hospital. Diagnosis of COVID-19 was made using RT-PCR. Data including demographic information, comorbidities, ABO blood group, Rh factor, clinical severity as well as the need for assisted ventilation, ICU admission and plasma therapy were collected from patients' medical records. The Pearson's correlation, chi square and Fischer exact tests were used to analyze data at significance of 0.05.

Results: Frequency of COVID-19 was highest in blood group B (34.8%) and lowest in blood group AB (11.2%). Furthermore, patients with blood group A had significantly more severe form of COVID-19 when compared to patients with other blood groups. The frequency of ICU admission, assisted ventilation and plasma therapy was significantly higher in patients with blood group A than in patients with other blood groups.

Conclusion: Our results suggest that patients with blood group A are at higher risk of developing severe COVID-19 infection that may require assisted ventilation and ICU admission. Hence, these patients might require more vigilant surveillance and aggressive treatment measures. Further studies are required to validate these findings.

Keywords: ABO Blood-Group System, COVID-19, Disease Susceptibility, SARS-CoV-2.

INTRODUCTION

It has been a year since the World Health Organization announced coronavirus disease 19 (COVID-19) a worldwide pandemic (1). So far, there have been 221 million confirmed cases and 4.5 million deaths due to COVID-19 as of September 5th 2021 (2). Various institutions across the globe have been successful in production of potent vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, but the RNA virus keeps mutating and is capable of re-infecting indiv
iduals (3,4). It has strained the healthcare system and testing resources, making it difficult to identify and prioritize individuals who are at greater risk of infection. Several factors and comorbidities including sex, age, hypertension, diabetes, cardiovascular and respiratory diseases are associated with COVID-19 mortality and morbidity (5,6)

Previous studies have identified the association between ABO blood groups and a number of infections, including *Helicobacter pylori* (7), Hepatitis B virus (8), Norwalk virus (9), *Plasmodium falciparum* (10) and *Neisseria gonorrhoeae* (11). This is due to the *ABO* gene polymorphisms. It has been also shown that individuals with blood group may be less susceptible to SARS-CoV-1 infection. Given that SARS-CoV-1 and SARS-CoV-2 share the same functional receptor, angiotensin-converting enzyme 2 receptor (ACE2) (13,14), it can be assumed that blood groups may also determine susceptibility to SARS-CoV-2 infection. Recent studies have demonstrated an association between blood groups and COVID-19. It has been found that the prevalence of COVID19 is slightly higher among non-O blood groups (15-19). It has been also reported that the Rh negative phenotype is associated with lower risk of severe COVID-19 (20). In this cross-sectional study, we evaluated association between ABO blood groups and COVID-19.

MATERIALS AND METHODS

The study included data from 500 SARS-CoV-2-positive patients who were referred to a tertiary hospital affiliated to the Government Institute of Medical Sciences, Greater Noida, India.

Diagnosis of COVID-19 was made using RT-PCR. Data including demographic information, underlying comorbidities, ABO blood type, Rh factor and clinical severity were collected from patients' medical records (21).

Other information including the need for ICU admission, assisted ventilation, plasma therapy and disease outcome were also collected.

Continuous variables were expressed as mean ± standard deviation and categorical variables were expressed in proportions. The collected data were further stratified into groups on the basis of presence or absence of comorbidities. Data analysis was done in SPSS 15 using the Pearson's correlation, Chi square and Fischer exact tests. All analyses were carried out at significance of 0.05.

RESULTS

Most patients were male (70.8%) and in the 21-30 years age range. The mean age of the patients was 41.99 ±15.76 years. Male patients presented with significantly more severe form of COVID-19 compared to females ($p<0.004$) (Table 1).

According to the results, frequency of COVID-19 was highest in blood group B (34.8%) and lowest in blood group AB (11.2%). Furthermore, patients with blood group A had significantly more severe form of COVID-19 when compared to patients with other blood groups (Table 1).

The data were further stratified based on the presence of comorbidities.

The results showed that patients of type A blood group had a more severe form of COVID-19.

Table 1-The association of ABO blood groups with clinical severity

3/ Gupta and colleagues		Clinical severity		P-value
		Moderate	Severe	
SEX. Female	125(85.6%)	14(9.5%)	7(4.79%)	0.004
Male	253(71.4%)	70(19.7%)	31(8.7%)	
Age (years)				
0-10	4(100%)	0	0	
11-20	18(100%)	0	0	
21-30	114(93.44%)	6(4.9%)	2(1.63%)	
31-40	102(84.2%)	16(13.2%)	3(2.47%)	
41-50	51(67.1%)	18(23.68%)	7(5.32%)	
51-60	57(64%)	19(21.34%)	13(14.6%)	
61-70	27(50.9%)	17(32.07%)	9(16.98%)	
71-80	2(15.3%)	7(53.8%)	4(30.7%)	
81-90	3(75%)	1(25%)	0	
Blood groups				
A vs non-A	88(67.6%)	28 (21.5%)	14 (10.7%)	0.04
AB vs non-AB	41 (73.2%)	9(16.07%)	6(10.7%)	0.64
B vs non-B	136(78.1%)	29(16.6%)	9(5.1%)	0.316
O vs non-O	113(80.7%)	18(12.8%)	9(6.4%)	0.243
Rh factor (-)	23(82.14%)	3(10.7%)	2(7.14%)	0.707
(+)	355(75.2%)	81(17.16%)	36(7.6%)	
Blood groups of patients with comorbidities	27	19	10	0.633
A vs non-A	8	5	18	0.448
AB vs non-AB	30	18	57	0.898
B vs non-B	34	13	55	0.311
O vs non-O				
Blood groups of patients without comorbidities	61	9	4	0.023
A vs non- A	33	4	1	0.897
AB vs non-AB	106	11	0	0.176
B vs non-B	79	5	1	0.373
O vs non-O				

The frequency of ICU admission, assisted ventilation and plasma therapy was significantly higher in patients with blood type A than in patients with other blood types (Table 2).

Table 2- Frequency of ICU admission, assisted ventilation and plasma therapy in patients with different blood groups

Variables	Blood group A/non-A	P-value	Variables	Blood group B/non-B	P-value
ICU admission	42/80	0.0146	ICU admission	38/84	0.330
Assisted Ventilation	42/80	0.0146	Assisted Ventilation	38/84	0.330
Plasma therapy	21/31	0.012	Plasma therapy	10/42	0.012
Recovered (n=495) Dead (n=5)	129/366 1/4	0.758	Recovered (n=495) Dead (n=5)	173/322 1/4	0.485
Variables	Blood group AB/non-AB	P-value	Variables	Blood group O/non-O	P-value
ICU admission	15/107	0.659	ICU admission	27/95	0.096
Assisted Ventilation	15/107	0.659	Assisted Ventilation	27/95	0.096
Plasma therapy	7/45	0.584	Plasma therapy	14/38	0.855
Recovered (n=495) Dead (n=5)	54/439 2/3	0.040	Recovered (n=495) Dead (n=5)	139/356 1/4	0.688

No correlation was found between Rh factor and severity of COVID-19, ICU admission, assisted ventilation and plasma therapy (Table 3). Out of 500 patients, 495 recovered and only five deaths were recorded. The outcome of disease had no significant association with the ABO blood group and Rh factor.

Table 3- Association of disease severity with the Rh factor

Variables	Rh factor		P-value
	Negative (n=28)	Positive (n=472)	
Clinical presentation			
Mild	23(82.14%)	355(75.2%)	0.707
Moderate	3(10.7%)	81(17.16%)	
Severe	2(7.14%)	36(7.6%)	
ICU admission	5(17.8%)	117(30.9%)	0.406
Plasma therapy	3(10.71%)	49(10.3%)	1.000
Assisted ventilation	5(17.8%)	117(30.9%)	0.406
Recovered	28(100%)	467(98.9%)	
Dead	0	5(1.05%)	1.00

Frequency of comorbidities was also studied in relation to ABO blood groups. Based on the results, asthma was significantly more common among patients with blood group AB (Table 4).

Table 4- Association of comorbidities with the ABO blood groups

Variables	Blood group				P-value
	A	AB	B	O	
Number of patients (%)	130(26%)	56(11.2%)	174(34.8%)	140(28.0%)	
Diabetes	30(23.07%)	6(10.7%)	35(20.11%)	36(25.7%)	0.125
Hypertension	24(18.41%)	5(44.64%)	30(17.2%)	28(20.0%)	0.313
Hypothyroidism	7(5.38%)	4(5.74%)	10(5.74%)	9(6.42%)	0.958
CAD	4(3.07%)	1(1.78%)	3(1.72%)	4(2.85%)	0.869
TB	2(1.53%)	0	0	1(0.71%)	0.261
Asthma	2(1.53%)	4(7.14%)	2(1.14%)	1(0.71%)	0.017
COPD	1(1.53%)	1(1.78%)	2(1.14%)	0	0.614
Malaria	1(1.53%)	0	0	1(0.71%)	0.623

CAD: Coronary artery disease; TB: Tuberculosis; COPD: Chronic obstructive pulmonary disorder.

DISCUSSION

In this study, we investigated association of COVID-19 incidence and severity with blood groups in 500 patients admitted to a hospital in India. The results showed that male patients outnumbered female patients and had more severe form of the disease. These findings are in line with findings of two previous studies (16, 22). The reason for lower frequency and severity of COVID-19 in females is not clear, but the female sex hormones might be responsible for the altered immune response. It was demonstrated that male mice were more prone to SARS-CoV-1 infection than female mice. Ovariectomized female mice also had increased mortality rates. It was claimed that the estrogen receptor signaling might have protective against SARS-CoV-1 infection (23). Advanced age is a known risk factor for COVID-19 (5,6), which was also confirmed in our study. Patients with advanced age and comorbidities had more severe symptoms. Besides gender and age, the ABO blood groups may be used as a suitable indicator of COVID-19 risk and severity. In the present study, COVID-19 was significantly more severe in patients with blood group A than in patients with other blood groups. In agreement with our results, in a study conducted by Zhao et al. on 2173 confirmed COVID-19 cases from three hospitals in China, the risk of severe COVID-19 was higher in patients with type A blood than in patients with non-A type blood (15). Similar results were obtained from another study in China (16) and a study in Canada (17). Blood type A was significantly associated with the need for ICU admission, assisted ventilation and plasma therapy, which is consistent with findings of Hoiland et al. (17). However, Zietz et al. reported a lower risk of intubation amongst patients with blood type A and a higher risk among patients with types AB and B compared to those with blood type O (16). Other studies also concluded that the blood type O was associated with decreased risk of COVID-19, which is inconsistent with our findings.

Comorbidities such as diabetes, hypertension and cardiovascular disease are known risk factors for COVID-19, which can alter the clinical presentation of the disease (5,6). We divided the patients into different groups based on the presence of comorbidities. The results showed that type A blood group was associated with more severe COVID-19 presentations even in the absence of comorbidities. This further highlights the association between blood type A and COVID-19 severity. A previous study reported that the presence of anti-A antibodies in patients with non-A blood groups could antagonize the interaction between the virus and ACE2 (12). Given that ACE2 acts as the

receptor for both SARS-CoV-1 and SARS-CoV-2 (13,14), it is expected to observe a more severe form of COVID-19 in patients with blood type A. The Rh factor had no association with the clinical presentation of COVID-19, the need for ICU admission and assisted ventilation. Inconsistent with this finding, a study reported that the risk of severe COVID-19 was lower in Rh-negative patients (20). Similarly, Zietz found that Rh-negative patients required less ICU admission.

A limitation of our study was the relatively small sample size. Also, the relationship between asymptomatic COVID-19 patients and ABO blood groups could not be evaluated. It is recommended to conduct future studies with a case-control design and a larger sample size in order to remove any unmeasured confounding factor such as lead time bias.

CONCLUSION

Our results indicate that there is a link between the ABO blood groups and COVID-19 susceptibility. Specifically, patients with blood group A are at higher risk of developing severe COVID-19, which may require assisted ventilation and ICU admission. Hence, these patients might require more vigilant surveillance and aggressive treatment measures.

ACKNOWLEDGMENTS

None.

DECLARATIONS

Funding

The authors received no financial support for the research, authorship and/or publication of this article.

Ethics approvals and consent to participate

Ethics approval was taken from the local authorities.

Conflicts of interest

The authors declare that there is no conflict of interest.

REFERENCES

1. Cucinotta D, Vanelli M. *WHO Declares COVID-19 a Pandemic.* Acta Biomed. 2020 Mar 19; 91(1):157-60. [View at Publisher] [DOI] [PubMed] [Google Scholar]

2. Worldometer. *Reported Cases and Deaths by Country, Territory, or Conveyance. COVID-19 Coronavirus Pandemic.* Available online: https://www.worldometers.info/coronavirus/ (accessed on 5 September 2021)

3. To KK, Hung IF, Ip JD, Chu AW, Chan WM, Tam AR, et al. *COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing.* Clin Infect Dis. 2020 Aug 25:ciaa1275. [View at Publisher] [DOI:10.1093/cid/ciaa1275] [PubMed] [Google Scholar]

4. Van Elslande J, Vermeersch P, Vandervoort K, Wawina-Bokalanga T, Vanmechelen B, Wollants E, et al. *Symptomatic SARS-CoV-2 reinfection by a phylogenetically distinct strain.* Clin Infect Dis. 2020: ciaa1330. [DOI] [PubMed]

5. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. *Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.* Lancet. 2020 Mar;395(10229):1054-62. [View at Publisher] [DOI:10.1016/S0140-6736(20)30566-3] [PubMed] [Google Scholar]

6. Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, et al. *Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis.* J Infect. 2020; 81(2): e16-e25. [View at Publisher] [DOI:10.1016/j.jinf.2020.04.021] [PubMed] [Google Scholar]

7. Borén T, Falk P, Roth KA, Larson G, Normark S. *Attachment of Helicobacter pylori to human gastric epithelium mediated by blood group antigens*. Science. 1993; 262(5141): 1892-5 [View at Publisher] [DOI:10.1126/science.8018146] [PubMed] [Google Scholar]

8. Wang DS, Chen DL, Ren C, Wang ZQ, Qiu MZ, Luo HY, et al. *ABO blood group, hepatitis B viral infection and risk of pancreatic cancer*. Int J Cancer. 2012 Jul 15;131(2):461-8. [View at Publisher] [DOI:10.1002/ijc.26376] [PubMed] [Google Scholar]

9. Lindesmith L, Moe C, Marionneau S, Ruvoen N, Jiang X, Lindblad L, et al. *Human susceptibility and resistance to Norwalk virus infection*. Nat Med. 2003 May;9(5):548-53. [View at Publisher] [DOI:10.1038/nm860] [PubMed] [Google Scholar]

10. Loscertales MP, Owens S, O'Donnell J, Bunn J, Bosch-Capblanch X, Brabin BJ. *ABO blood group phenotypes and Plasmodium falciparum malaria: unlocking a pivotal mechanism.* Adv Parasitol. 2007; 65:1-50. [View at Publisher] [DOI:10.1016/S0065-308X(07)65001-5] [PubMed] [Google Scholar]

11. Foster MT Jr, Labrum AH. *Relation of infection with Neisseria gonorrhoeae to ABO blood groups*. J Infect Dis. 1976 Mar;133(3):329-30. [View at Publisher] [DOI:10.1093/infdis/133.3.329] [PubMed] [Google Scholar]

12. Guillon P, Clément M, Sébille V, Rivain JG, Chou CF, Ruvoën-Clouet N, et al. *Inhibition of the interaction between the SARS-CoV spike protein and its cellular receptor by anti-histo-blood group antibodies*. Glycobiology. 2008; 18(12): 1085-93. [View at Publisher] [DOI:10.1093/glycob/cwn093] [PubMed] [Google Scholar]

13. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. *Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding*. Lancet. 2020; 395(10224): 565-574. [View at Publisher] [DOI:10.1016/S0140-6736(20)30251-8] [Google Scholar]

14. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. *A pneumonia outbreak associated with a new coronavirus of probable bat origin*. Nature. 2020; 579(7798): 270-73. [View at Publisher] [DOI] [PubMed] [Google Scholar]

15. Zhao J, Yang Y, Huang H, Li D, Gu D, Lu X, et al. *Association of ABO blood groups with SARS-COV-2 infection.* Preprint; 2020. [View at Publisher] [DOI:10.21203/rs.3.rs-37570/v1]

16. Zietz M, Zucker J, Tatonetti NP. *Associations between blood type and COVID-19 infection, intubation, and death.* Nat Commun. 2020 Nov 13;11(1):5761. [View at Publisher] [DOI:10.1038/s41467-020-19623-x] [PubMed] [Google Scholar]

17. Hoiland RL, Fergusson NA, Mitra AR, Griesdale DEG, Devine DV, Stukas S, et al. *The association of ABO blood group with indices of disease severity and multiorgan dysfunction in COVID-19.* Blood Adv. 2020 Oct 27;4(20):4981-89. [View at Publisher] [DOI:10.1182/bloodadvances.2020002623] [PubMed] [Google Scholar]

18. Padhi S, Suvankar S, Dash D, Panda VK, Pati A, Panigrahi J, et al. *ABO blood group system is associated with COVID-19 mortality: An epidemiological investigation in the Indian population*. Transfus Clin Biol. 2020; 27(4): 253-58. [View at Publisher] [DOI:10.1016/j.tracli.2020.08.009] [PubMed] [Google Scholar]

19. Bommanavar S, Smitha T. *ABO blood grouping and COVID 19: Is there any correlation in suspectibility?* J Oral Maxillofac Pathol. 2020; 24(2): 212-16. [View at Publisher] [DOI:10.4103/jomfp.JOMFP_240_20] [PubMed] [Google Scholar]

20. Ray JG, Schull MJ, Vermeulen MJ, Park AL. *Association Between ABO and Rh Blood Groups and SARS-CoV-2 Infection or Severe COVID-19 Illness: A Population-Based Cohort Study*. Ann Intern Med. 2021 Mar;174(3):308-15. [DOI:10.7326/M20-4511]

21. Ministry of Health & Family Welfare. *Guidance document on appropriate management of suspect/confirmed cases of COVID-19.* New Delhi: MoHFW, Government of India; 2020.

22. Ad'hiah AH, Abdullah MH, Alsudani MY, Shnawa RMS, Al-Sa'ady AJR, Allami RH, et al. *Association between ABO blood groups and susceptibility to COVID-19: profile of age and gender in Iraqi patients.* Egypt J Med Hum Genet. 2020;21(1):76. [View at Publisher] [DOI:10.1186/s43042-020-00115-y] [PubMed] [Google Scholar]

23. Channappanavar R, Fett C, Mack M, Ten Eyck PP, Meyerholz DK, Perlman S. *Sex-Based Differences in Susceptibility to Severe Acute Respiratory Syndrome Coronavirus Infection*. J Immunol. 2017 May 15;198(10):4046-53. [View at Publisher] [DOI:10.4049/jimmunol.1601896] [PubMed] [Google Scholar

How to Cite:
Gupta B, Kalhan SH, Shukla SH, Bahadur SH, Singh G, Pathak R [Evaluating Association between ABO Blood Groups and COVID 19]. mljgoums. 2021; 15(6): 1-7 DOI: 10.29252/mlj.15.6.1