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Association of ABO blood group with susceptibility to SARS-CoV-2 infection in Rupandehi district of Nepal

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Abstract

Objectives: Recent studies after the outbreak of coronavirus disease 2019 have shown an association of the ABO blood group to the susceptibility of severe acute respiratory syndrome coronavirus 2 infection. Anti-A and anti-B antibodies, carbohydrate clustering, interleukin-6 levels and host transmembrane protease serine subtype 2 were suggested to cause the variable susceptibility of severe acute respiratory syndrome coronavirus 2 infection to the ABO blood groups. This study aims to find the association of the ABO blood group with severe acute respiratory syndrome coronavirus 2 infection susceptibility in Nepal.

Methods: Population-based matched case–control study was conducted from October 2021 to February 2022 in Rupandehi district of Nepal. A total of 1091 reverse transcription-polymerase chain reaction confirmed coronavirus disease 2019 cases and 2182 controls were included in the study by convenient sampling method.

Results: A statistically significant association of severe acute respiratory syndrome coronavirus 2 infection was observed for the blood group AB between cases and controls (11.5% vs 8.5%; odds ratio = 1.4, 95% confidence interval = 1.10–1.78). However, there was no association of severe acute respiratory syndrome coronavirus 2 infection for blood group A (26.7% vs 28.23%; odds ratio = 0.93, 95% confidence interval = 0.79–1.09), B (26.9% vs 29.84%; odds ratio = 0.86, 95% confidence interval = 0.73–1.02) and O (34.9% vs 33.41%; odds ratio = 1.07, 95% confidence interval = 0.92–1.25).

Conclusion: This study reported slightly more susceptibility to severe acute respiratory syndrome coronavirus 2 infection among individuals with blood group AB.

Keywords

ABO blood group, coronavirus disease 2019, disease susceptibility, severe acute respiratory syndrome coronavirus 2

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Introduction

The World Health Organization (WHO) declared severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as a worldwide health emergency on 30 January 2020 after a steep incline in cases was observed globally.[1] A total of 120,383,919 cases have been confirmed and 2,664,386 deaths have been recorded till 18 March 2021.[2] The first case of coronavirus disease 2019 (COVID-19) was officially reported in Nepal on 13 January 2020.[3] According to the WHO country office, there were more than 200,000 COVID-19 cases in Nepal till January 2021.[4]

Studies have reported that blood group A has a higher susceptibility to SARS-CoV-2 infection.[5–9] However, recent

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Table 1. Characteristics of the participants (n = 1091).

Characteristics	Case		Control	
	n	% (95% CI)	n	%
ABO blood group				
A	291	26.7 (24.1–29.4)	616	28.2
B	293	26.9 (24.2–29.6)	661	29.8
AB	126	11.5 (9.7–13.6)	186	8.5
O	381	34.9 (32.1–37.8)	729	33.4
Total	1091	100.0	2182	100.0

CI: confidence interval.

studies from various locations have shown contrasting results and some have failed to show any association.[10–13] It is speculated to be a result of potentially numerous factors including ABO antibodies, levels of interleukin-6, carbohydrate clustering, and transmembrane proteases.[5,14–16] This study aims to explore the possible association of ABO blood group and SARS-CoV-2 susceptibility in Nepal.

Methods

Study design

This case–control study was conducted from October 2020 to February 2021 in Rupandehi district of Nepal.

The sample size was calculated using G*Power version 3.1 software considering effect size = 0.1, alpha error probability = 0.05, power = 80%, and degree of freedom = 3. A total of 1091 cases and 2182 controls were selected in the study using convenient sampling method, and this sample size was sufficient as calculated using this power sampling.

A list of COVID-19 cases was taken from the District Health Office, Rupandehi, Nepal. During the study period, 2544 cases were reported in the district, of which 1091 cases who knew their ABO blood group were selected for this study.

The cases were contacted by telecommunication by the researchers and data including age, gender, ABO blood group, duration of symptoms, hospital stay and intensive care unit (ICU) stay were collected after obtaining informed verbal consent from the participants. A total of 2182 controls were selected from 6377 apparently healthy blood donors recorded at Blood Bank of Red Cross Society in Rupandehi district during the same time period. Cases were matched with controls by age (±5 years) and gender in the ratio of 1:2. The ABO blood grouping was done by the Tile method.

Inclusion and exclusion criteria

Individuals from the age 18 to 60 years old confirmed with reverse transcription-polymerase chain reaction (RT-PCR) for SARS-CoV-2 infection were included as cases. Apparently healthy blood donors were included as controls. Cases with unclear data sources of ABO blood grouping and blood donors for convalescent plasma therapy were excluded from the study.

Statistical analysis

The data were entered in Excel and analyzed using the Statistical Package for Social Sciences version 20. Data were expressed in percentage, mean value, standard deviation (SD), median and interquartile range (IQR). Chi-square test was used to determine the association of SARS-CoV-2 infection in ABO blood groups. The odds ratio (OR) at 95% confidence interval (CI) was presented to show the strength of association. A p-value of less than 0.05 was considered statistically significant.

Ethical consideration

This study was approved by the Ethical Review Board (ERB) of Nepal Health Research Council (NHRC) (reference no. 517/2020). The data were obtained from the cases via telecommunication after obtaining informed verbal consent. The verbal consent was approved by ERB of NHRC. The list of blood donors was obtained after receiving permission from Blood Bank of Red Cross Society, Rupandehi, Nepal. Anonymized data of the blood donors were used with general consent from blood donation process.

Results

A total of 1091 cases and 2182 controls were included in this study. Majority of the cases and controls were males (65.4%) in comparison to females (34.6%). Among the cases, the most common ABO blood group was O and the least common was blood group AB (Table 1). The mean age for the COVID-19 cases was 36.92 (SD = 10.75) years.

The majority of the cases (80.4%) were symptomatic and a few cases (19.6%) were asymptomatic who were in close contact with COVID-19 cases. Blood group A had the highest (82.5%) and blood group B had the least (77.8%) symptomatic cases. The median duration of symptoms self-reported by the cases was 7 days (IQR = 4–12). A total of

Table 2. Distribution and duration of symptoms among the cases in accordance with ABO blood group.

Characteristics	ABO blood group				
	A, n (%)	B, n (%)	AB, n (%)	O, n (%)	Total, n (%)
Symptomatic	240 (82.5)	228 (77.8)	99 (78.6)	310 (81.4)	877 (80.4)
Asymptomatic	51 (17.5)	65 (22.2)	27 (21.4)	71 (18.6)	214 (19.6)
Duration of symptoms (days)					
1–3	44 (15.1)	51 (17.4)	23 (18.3)	52 (13.6)	170 (15.6)
4–10	127 (43.6)	115 (39.2)	50 (39.7)	183 (48)	475 (43.5)
>10	69 (23.7)	62 (21.2)	26 (20.6)	75 (19)	232 (21.3)
Duration of hospital stay (days)					
1–3	4 (1.4)	3 (1.0)	1 (0.8)	3 (0.8)	11 (1.0)
4–10	11 (3.8)	6 (2.0)	5 (4.0)	12 (3.1)	34 (3.1)
>10	19 (6.5)	14 (4.8)	6 (4.8)	13 (3.4)	52 (4.8)
Duration of ICU stay (days)					
1–3	1 (0.3)	0 (0.0)	1 (0.8)	1 (0.3)	3 (0.3)
4–10	3 (1.0)	4 (1.4)	3 (2.4)	2 (0.5)	12 (1.1)
>10	2 (0.7)	3 (1.0)	0 (0.0)	4 (1.0)	9 (0.8)

ICU: intensive care unit.

Table 3. ABO blood group distribution difference between case and control groups.

ABO blood groups				
	A	B	AB	O
Control, n (%)	616 (28.2%)	651 (29.8%)	186 (8.5%)	729 (33.4%)
Case, n (%)	291 (26.7%)	293 (26.9%)	126 (11.5%)	381 (34.9%)
χ^2	0.88	3.15	7.72	0.74
p-value	0.35	0.08	0.005	0.39
OR	0.93	0.86	1.40	1.07
95% CI	0.79–1.09	0.73–1.02	1.10–1.78	0.92–1.25

OR: odds ratio; CI: confidence interval.

97 (8.9%) cases were admitted to hospitals and the median duration of hospital stay was 12 days (IQR = 7–14.5). Among the admitted cases, 24 (2.4%) were admitted to the ICU and the median duration of stay was 12 days (IQR = 7–15) (Table 2).

The proportion of blood group AB among the cases infected with SARS-CoV-2 was higher in comparison to the controls (11.5% vs 8.5%), and this association was found to be statistically significant (OR = 1.40, 95% CI = 1.10–1.78). There was no association of susceptibility of SARS-CoV-2 with blood group A (OR = 0.93, 95% CI = 0.79–1.09), blood group B (OR = 0.86, 95% CI = 0.73–1.02) and blood group O (OR = 1.07, 95% CI = 0.92–1.25) (Table 3).

Discussion

The most prevalent blood group among general population in Nepal is O (35%–36%) which is followed by A (29%–34%), B (27%) and AB (4%–9%), respectively.[17–19] Similarly, blood group O (35%) was the most and AB (12%) was the least prevalent among the cases in this study. The blood group distribution in this study was similar to the general population in the country. Comparable blood group distribution was also found in similar studies conducted in China and the United States. However, in the Chinese study, there was an association of COVID-19 disease with blood group A, and in the American study, there was no association of COVID-19 disease with the ABO blood group, which is contrary to this study.[5,20] Slightly different blood group distribution was observed in a study conducted in Pakistan where the most prevalent blood group was B and the least was AB. The study found a significant association of COVID-19 disease with blood groups B and AB.[21] The results showed that blood group AB was significantly associated with SARS-CoV-2 infection, whereas blood groups A, B and O did not show any association. To our best knowledge, this study is the first of its kind in Nepal that examines the association of ABO blood groups with susceptibility to SARS-CoV-2.

The findings showed the highest susceptibility to SARS-CoV-2 among blood group AB (OR = 1.40; CI = 1.10–1.78), which is in accordance with the findings conducted in Massachusetts, USA[10] and Shenzhen, China.[5] Higher

susceptibility of infection among blood group AB was also reported from Saudi Arabia[11] and Lebanon,[22] but the association was not statistically significant.

Contrary to this study, a study conducted by Zietz et al.[20] revealed higher risk of SARS-CoV-2 infection in blood group B (OR = 1.04, 95% CI = 0.92–1.16) and A (OR = 1.02, 95% CI = 0.93–1.12) and lower risk in blood group AB (OR = 0.91, 95% CI = 0.74–1.10) compared to blood group O. Similarly, a study among 1775 patients with COVID-19 from Wuhan showed the highest risk in blood group A (OR = 1.28, 95% CI = 1.34–1.44) and the lowest risk among blood group O (OR = 0.68, 95% CI = 0.60–0.77).[5] A meta-analysis by Franchini et al.[23] which included 21 studies showed individuals with blood group O had lower susceptibility to SARS-CoV-2 infection compared to non-O blood group (OR = 0.81, 95% CI = 0.75–0.86).

The higher levels of interleukin-6 in blood group O may contribute to the lower risk of SARS-CoV-2 infection.[14,24] The higher titer of anti-A and anti-B antibodies have been speculated to provide protective role against SARS-CoV-2 virus by neutralizing its proteins.[25] Antigens A and B in ABO blood groups induce carbohydrate clustering which increases the likelihood of the spike proteins of SAR-CoV-2 to bind with angiotensin-converting enzyme (ACE2) and cluster of differentiation 147 receptors of the host cells.[15] These hypotheses may explain the higher susceptibility seen in blood group AB. Some studies proposed that host transmembrane protease serine subtype 2 helps in mobilization of serine in spike protein, which might have a role in ABO group modulation for SARS-CoV-2 infection.[16,26]

The glycosylated spike (S) protein of SARS-CoV binds to receptors of ACE2 which is inhibited by anti-A antibody. Zhao et al.[5] and Guillon et al.[27] observed that anti-A antibodies block the adhesion of S protein to ACE2 receptors. Inhibition by natural anti-A antibodies may explain the relatively lower susceptibility of blood group B observed in this study.

There are some limitations to this study. First, it was conducted in a single district of western part of Nepal and hence cannot be generalized. Second, selection bias may have occurred as cases and control were selected conveniently. Third, controls were blood donors who were not tested with RT-PCR for COVID-19. Fourth, the variant of SARS-CoV-2 was not determined among the cases.

Conclusion

Individuals with blood group AB were more susceptible to SARS-CoV-2 infection. The blood groups A, B, and O showed no association with susceptibility to SARS-CoV-2 infection. Blood group B has the least susceptibility to SARS-CoV-2 infection. Prospective, multi-institutional and larger studies may be required to conclude the association of ABO blood group with susceptibility to SARS-CoV-2 infection.

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Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Ethical approval

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Informed consent

Verbal consent was obtained from the cases included in the study in accordance with the ethical approval obtained from Nepal Health Research Council. Minors were not included in this study. Verbal informed consent was taken as the data were collected via telecommunication to minimize the risk of spreading SARS-CoV-2 infection. The method of obtaining consent verbally was approved by Nepal Health Research Council.

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References

1. Velavan TP and Meyer CG. The COVID-19 epidemic. *Trop Med Int Health* 2020; 25(3): 278–280.
2. World Health Organization. Coronavirus disease (COVID-19), https://www.who.int/emergencies/diseases/novel-coronavirus-2019 (accessed 18 March 2021).
3. Bastola A, Sah R, Rodriguez-Morales AJ, et al. The first 2019 novel coronavirus case in Nepal. *Lancet Infect Dis* 2020; 20(3): 279–280.
4. Pandav R, Samuel R, Khan S, et al. Situation Update #38—Coronavirus Disease 2019 (COVID19). WHO Country Office for Nepal, 2021. Report No.: 38, https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200227-sitrep-38-covid-19.pdf
5. Zhao J, Yang Y, Huang H, et al. Relationship between the ABO blood group and the COVID-19 susceptibility. *Clinical Infectious Disease* 2020; 19: 54–63.
6. Li J, Wang X, Chen J, et al. Association between ABO blood groups and risk of SARS-CoV-2 pneumonia. *Br J Haematol* 2020; 190(1): 24–27.
7. Cheng Y, Cheng G, Chui C, et al. ABO blood group and susceptibility to severe acute respiratory syndrome. *JAMA* 2005; 293(12): 1447–1451.

8. Noor A, Tashfeen S, Akhtar F, et al. Association of COVID-19 with ABO blood groups in tertiary care center of Pakistan. *PAFMJ* 2020; 70(1): S251–S255.
9. Kabrah SM, Kabrah AM, Flemban AF, et al. Systematic Review and Meta-analysis of the Susceptibility of ABO Blood Group to COVID-19 Infection. *Transfus Apher Sci* 2021; 60(4): 45–78.
10. Latz CA, DeCarlo C, Boitano L, et al. Blood type and outcomes in patients with COVID-19. *Ann Hematol* 2020; 99(9): 2113–2118.
11. Aljanobi GA, Alhajjaj AH, Alkhabbaz FL, et al. The relationship between ABO blood group type and the COVID-19 susceptibility in Qatif central hospital, Eastern Province, Saudi Arabia: a retrospective cohort study. *Open J Intern Med* 2020; 10(2): 232–238.
12. Levi JE, Telles PR, Scrivani H, et al. Lack of association between ABO blood groups and susceptibility to SARS-CoV-2 infection. *Vox Sang* 2021; 116(2): 251–252.
13. Boudin L, Janvier F, Bylicki O, et al. ABO blood groups are not associated with risk of acquiring the SARS-CoV-2 infection in young adults. *Haematologica* 2020; 105(12): 2841–2843.
14. Pourali F, Afshari M, Alizadeh-Navaei R, et al. Relationship between blood group and risk of infection and death in COVID-19: a live meta-analysis. *New Microbes New Infect* 2020; 37: 100743–100748.
15. Zhang Y, Garner R, Salehi S, et al. Association between ABO blood types and coronavirus disease 2019 (COVID-19), genetic associations and underlying molecular mechanisms: a literature review of 23 studies. *Ann Hematol* 2021; 100(5): 1123–1132.
16. Arend P. Why blood group A individuals are at risk whereas blood group O individuals are protected from SARS-CoV-2 (COVID-19) infection: a hypothesis regarding how the virus invades the human body via ABO(H) blood group-determining carbohydrates. *Immunobiology* 2021; 226(3): 152027.
17. Shrestha L, Malla U and Mahotra NB. ABO and Rh blood groups and their ethnic distribution in a teaching hospital of Kathmandu, Nepal. *JNMA J Nepal Med Assoc* 2013; 52(190): 311–315.
18. Sah J, Pant D, Shrestha V, et al. Distribution of ABO, Rhesus blood groups and hemoglobin concentration among the school students of Deurali VDC, Kaski, Nepal. *Int J of Pharm Bio Sci* 2013; 4(3): 10–16.
19. Pramanik T and Adhikari P. Trend of blood group distribution among the different ethnic groups of Kathmandu Valley. *Nepal Med Coll J* 2006; 8(4): 248–249.
20. Zietz M, Zucker J and Tatonetti NP. Testing the association between Blood Type and COVID-19 infection, intubation, and death. *Nat Commun* 2020; 11(1): 5761–5766.
21. Rahim F, Amin S, Bahadur S, et al. ABO/Rh-D blood types and susceptibility to corona virus disease-19 in Peshawar, Pakistan. *Pak J Med Sci* 2021; 37(1): 4–8.
22. Khalil A, Feghali R and Hassoun M. The Lebanese COVID-19 cohort; a challenge for the ABO blood group system. *Front Med* 2020; 7: 585341.
23. Franchini M, Cruciani M, Mengoli C, et al. ABO blood group and COVID-19: an updated systematic literature review and meta-analysis. *Blood Transfus* 2021; 19(4): 317–326.
24. Naitza S, Porcu E, Steri M, et al. A genome-wide association scan on the levels of markers of inflammation in Sardinians reveals associations that underpin its complex regulation. *Plos Genet* 2012; 8(1): e1002480.
25. Deleers M, Breiman A, Daubie V, et al. Covid-19 and blood groups: ABO antibody levels may also matter. *Int J Infect Dis* 2021; 104: 242–249.
26. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell* 2020; 181(2): 271–280e8.
27. Guillon P, Clément M, Sébille V, 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): 1085–1093.