Relationship between the ABO Blood Group and the COVID-19 Susceptibility

Jiao Zhao[1,#], Yan Yang[2,#], Hanping Huang[3,#], Dong Li[4,#], Dongfeng Gu[1], Xiangfeng Lu[5], Zheng Zhang[2], Lei Liu[2], Ting Liu[3], Yukun Liu[6], Yunjiao He[1], Bin Sun[1], Meilan Wei[1], Guangyu Yang[7,*], Xinghuan Wang[8,*], Li Zhang[3,*], Xiaoyang Zhou[4,*], Mingzhao Xing[1,*], Peng George Wang[1,*]

[1]School of Medicine, The Southern University of Science and Technology, Shenzhen, People's Republic of China

[2]National Clinical Research Center for Infectious Diseases, The Second Affiliated Hospital School of Medicine, Southern University of Science and Technology; Shenzhen Third People's Hospital, Shenzhen, People's Republic of China

[3] Department of Infectious Diseases, Wuhan Jinyintan Hospital, Wuhan, People's Republic of China

[4]Renmin Hospital of Wuhan University, Wuhan 430060, People's Republic of China

[5]Department of Epidemiology, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, People's Republic of China

[6]School of Statistics, East China Normal University, Shanghai, People's Republic of China

[7]School of Life Sciences and Biotechnology, Shanghai Jiao Tong University, Shanghai, People's Republic of China

[8]Department of Urology, Zhongnan Hospital of Wuhan University, Wuhan, People's Republic of China

[#]These authors contributed equally

*Corresponding

Peng Wang

Email: wangp6@sustech.edu.cn

Abstract

To explore any relationship between the ABO blood group and the COVID-19 susceptibility, we compared ABO blood group distributions in 2,173 COVID-19 patients with local control populations, and found that blood group A was associated with an increased risk of infection, whereas group O was associated with a decreased risk.

Key Words: ABO blood group, coronavirus, SARS-CoV-2, COVID-19, disease susceptibility

INTRODUCTION

The novel coronavirus SARS-CoV-2, causing the new infectious disease COVID-19, has spread widely around the world. Current clinical observation suggest that people's age and gender are two risk factors in the susceptibility to COVID-19[1]. Older people and men are more susceptible to infection and development of more severe disease. However, no biological markers have been identified to predict the susceptibility to COVID-19 so far. Landsteiner's ABO blood types are carbohydrate epitopes that are present on the surface of human cells. The antigenic determinants of A and B blood groups are trisaccharide moieties GalNAcα1-3-(Fucα1,2)-Galβ- and Galα1-3-(Fucα1,2)-Galβ-, while O blood group antigen is Fucα1,2-Galβ-. While blood types are genetically inherited, the environment factors can potentially influence which blood types in a population will be passed on more frequently to the next generation. Susceptibility of viral infection has been found to be related to ABO blood group. For example, Norwalk virus and Hepatitis B have clear blood group susceptibility[2,3]. It was also reported that blood group O individuals were less likely to become infected by SARS coronavirus[4]. Here, we investigated the relationship between the ABO blood type and the susceptibility to COVID-19 in patients from three hospitals in Wuhan and Shenzhen, China.

METHODS

We collected and ABO-typed blood samples from 1,775 patients infected with SARS-CoV-2 and 206 deceased cases (came from 1,775 patients) at the Jinyintan Hospital in Wuhan, Hubei province, China. Another 113 and 285 patients with COVID-19 were respectively recruited from Renmin Hospital of Wuhan University, Hubei province and Shenzhen Third People's Hospital, Guangdong province, China. The diagnosis of COVID-19 was confirmed by a positive real-time reverse transcriptase polymerase-chain-reaction test of SARS-CoV-2 on nasal and pharyngeal swab specimens from patients. Two recent surveys of ABO blood group distribution of 3,694 non-COVID-19 people from Wuhan City and 23,386 non-COVID-19 people from Shenzhen City were used as comparison controls for the Wuhan and Shenzhen patients with COVID-19, respectively[5-6]. Statistical analyses were performed using 2-tailed χ^2. Data from different hospitals were meta-analyzed using random effects models, with calculation of odds ratio (OR) and 95% confidence interval (*CI*). Statistical analyses were performed using SPSS software (version 16.0) and STATA software (version 13).

RESULTS

The ABO blood group in 3,694 people in Wuhan displayed a percentage distribution of 32.2%, 24.9%, 9.1% and 33.8% for A, B, AB and O, respectively, while the 1,775 patients with COVID-19 from Wuhan Jinyintan Hospital showed an ABO distribution of 37.8%, 26.4%, 10.0% and 25.8% for A, B, AB and O, respectively. The proportion of blood group A among patients with COVID-19 was significantly higher than that among the control group, being

37.8% in the former vs 32.2% in the later ($P < 0.001$). The proportion of blood group O in patients with COVID-19 was significantly lower than that in control group, being 25.80% in the former vs 33.84% in the later (P < 0.001, Table 1). These results showed associations between ABO blood groups and COVID-19 susceptibility. The COVID-19 risk significantly increased for blood group A (OR 1.279, 95% *CI* 1.136~1.440) and decreased for blood group O (OR 0.680, 95% *CI* 0.599~0.771) (Table 1).

A similar distribution pattern of higher risk for blood group A and lower risk for blood group O was observed in the deceased patients. Specifically, the proportions of blood groups A, B, AB and O in the 206 deceased patients were 41.3%, 24. 3%, 9.2% and 25.2%, respectively. Blood group O was associated with a lower risk of death compared with non-O groups, with an OR of 0.660 (95% *CI* 0.479~0.911, $P = 0.014$) (Table 1). To the contrary, blood group A was associated with a higher risk of death compared with non-A groups, with an OR of 1.482 (95% *CI* 1.113~1.972, $P = 0.008$) (Table 1).

We next examined 113 patients with COVID-19 from another hospital in Wuhan City, the Renmin Hospital of Wuhan University, and found a similar risk distribution trend of ABO blood groups for the infection. Specifically, compared with non-O groups, blood group O were associated with a lower risk of infection, with an OR of 0.644 (95% *CI* 0.418~0.993, $P = 0.045$) (Table 1). Compared with non-A blood groups, blood group A displayed a relatively higher risk (OR=1.396; 95% *CI* 0.952~2.048) than those observed in patients from Wuhan Jinyintan Hospital, although the associations did not reach statistical significance likely due to the small sample size.

The ABO blood group in 23,368 people in Shenzhen displayed a percentage distribution of 28.8%, 25.1%, 7.3% and 38.8% for A, B, AB and O, respectively. Analysis of 285 patients

with COVID-19 from Shenzhen showed proportions of blood groups A, B, AB and O to be 28.8%, 29.1%, 13.7% and 28.4%, respectively. Similarly, a significantly lower risk of infection was associated with blood group O (OR 0.627; 95% *CI* 0.484~0.812). Additionally, we found that blood group AB had an increased risk of infection in this group of patients (OR 2.008; 95% *CI* 1.427~2.824) (Table 1).

Figure 1 shows the estimates of ORs of the risk of ABO blood groups for COVID-19 on the pooled data from the three hospitals by random effects models. Again, the results showed that blood group A was associated with a significantly higher risk for COVID-19 (OR 1.21; 95% *CI* 1.02~1.43, *P* = 0.027) compared with non-A blood groups, whereas blood group O was associated with a significantly lower risk for the infection (OR 0.67; 95% *CI* 0.60~0.75, *P* < 0.001) compared with non-O blood groups. Compared with other ABO blood groups, AB blood group (OR 1.48, 95% *CI* 0.97~2.24) and B blood group (OR 1.09, 95% *CI* 0.98~1.22) seemed to have a relatively higher risk of infection, although the associations did not reach statistical significance.

DISCUSSION

In this study, we found that ABO blood groups displayed different association risks for the infection with SARS-CoV-2 resulting in COVID-19. Specifically, blood group A was associated with an increased risk whereas blood group O was associated with a decreased risk. These findings are consistent with similar risk patterns of ABO blood groups for other coronavirus infection found in previous studies. For example, Cheng *et al.* reported that the SARS-CoV infection susceptibility in Hong Kong was differentiated by the ABO blood group

systems[4]. The authors found that compared with non-O blood group hospital staff, blood group O hospital staff had a lower chance of getting infected. Patrice *et al.* found that anti-A antibodies specifically inhibited the adhesion of SARS-CoV S protein-expressing cells to ACE2-expressing cell lines[7]. Given the nucleic acid sequence similarity[8] and receptor angiotensin-converting enzyme 2 (ACE2) binding similarity between SARS-CoV and SARS-CoV-2[9-11], the lower susceptibility of blood group O and higher susceptibility of blood group A for COVID-19 could be linked to the presence of natural anti-blood group antibodies, particularly anti-A antibody, in the blood. This hypothesis will need direct studies to prove. There may also be other mechanisms underlying the ABO blood group-differentiated susceptibility for COVID-19 that require further studies to elucidate. In the 285 patients from Shenzhen, we also found that blood group AB had an increased risk of infection. This result needs to be confirmed given the small size of this cohort of patients. After submission of our study, another study by Michael *et al*. using observational data on 1,559 SARS-CoV-2-tested individuals came online, reporting that the odds for SARS-CoV-2 infection was significantly increased for blood group A and decreased for blood group O. This reproduced our findings of the associations between the ABO blood group and the COVID-19 status[12].

In summary, we report a link between COVID-19 susceptibility and the ABO blood group. Specifically, people with blood group A have a higher risk whereas people with blood group O have a lower risk for SARS-Cov-2 infection. This study may have potential clinical implications given the current COVID-19 crisis: (1) People with blood group A might need particularly strengthened personal protection to reduce the chance of infection; (2) SARS-CoV-2-infected patients with blood group A might need to receive more vigilant surveillance and aggressive treatment; (3) It might be helpful to introduce ABO blood typing in both

patients and medical personal as a routine part of the management of SARS-CoV-2 and other coronavirus infections, to help define the management options and assess risk exposure levels of people. Whether this relationship between the ABO blood group and SARS-CoV-2 infection also holds in asymptomatic infections remains to be investigated. Moreover, other factors, such as chronic preexisting medical conditions that could potentially affect the chance and severity of SARS-CoV-2 infection were not addressed in the present study due to insufficient information, which limits the significance of the study. Therefore, it would be premature to use this study to guide clinical practice at this time. However, the findings in this study are important and provocative and should encourage further studies to verify.

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Author contributions statement

P.G.W and G.Y.Y conceived, designed and supervised the overall study. P.G.W, M.X, G.Y.Y, L.Z, and X.Y.Z supervised and administered the project. L.Z, H.P.H and T.L collected and verified ABO blood types of patients from Wuhan Jinyintan Hospital. X.Y.Z and D.L collected and verified ABO blood types of patients from Renmin Hospital of Wuhan University. Z.Z, L.L and Y.Y collected and verified ABO blood types of patients from Second Affiliated Hospital, Southern University of Science and Technology. Y.J.H, B.S, M.L.W, X.H.W collected and verified the data. D.F.G, X.F.L, Y.K.L, Z.J, M.X, and P.G.W analyzed the data. P.G.W, J.Z, G.Y.Y and M.X, wrote and revised the paper. All authors read and approved the final manuscript. This study received approval from the Research Ethics Committees of the participating institutions.

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Conflict of interest

All authors declare that they have no conflicts of interest.

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Figure Legend

Figure 1. Meta-analysis of the risk of ABO blood groups for COVID-19 in three hospitals.

The X-axis represents the point estimate of odds ratio and corresponding 95% confidence interval; the Y-axis represents the source of study patients. OR, odds ratio. CI, confidence interval.

Table 1. The ABO blood group distribution in patients with COVID-19 and normal controls.

	Blood Group			
	A	B	AB	O
Controls (Wuhan Area)				
3694	1188 (32.2%)	920 (24.9%)	336 (9.1%)	1250 (33.8%)
Wuhan Jinyintan Hospital				
Patients				
1775	670 (37.8%)	469 (26.4%)	178 (10.0%)	458 (25.8%)
$\chi 2$	16.431	1.378	1.117	35.674
P	**<0.001**	0.240	0.291	**<0.001**
OR	1.279	1.083	1.114	0.680
95%CI	1.136~1.440	0.952~1.232	0.920~1.349	0.599~0.771
Deaths				
206	85 (41.3%)	50 (24.3%)	19 (9.2%)	52 (25.2%)
$\chi 2$	6.944	0.015	0.000	6.102
P	**0.008**	0.903	1.000	**0.014**
OR	1.482	0.966	1.015	0.660
95%CI	1.113~1.972	0.697~1.340	0.625~1.649	0.479~0.911
Renmin Hospital of Wuhan University				
113 patients	45 (39.8%)	25 (22.1%)	15 (13.3%)	28 (24.8%)
$\chi 2$	2.601	0.318	1.815	3.640
P	0.107	0.573	0.178	0.045
OR	1.396	0.857	1.530	0.644
95%CI	0.952~2.048	0.546~1.344	0.878~2.664	0.418~0.993
Controls (Shenzhen area)				
23386	6728 (28.8%)	5880 (25.1%)	1712 (7.3%)	9066 (38.8%)
Patients from Shenzhen Third People's Hospital				
285	82 (28.8%)	83 (29.1%)	39 (13.7%)	81 (28.4%)
$\chi 2$	0.000	2.160	15.729	12.278
P	1.000	0.142	**<0.001**	0.001
OR	1.000	1.223	2.008	0.627
95%CI	0.773~1.294	0.946~1.582	1.427~2.824	0.484~0.812

CI, confidence interval; OR, odds ratio; **P* value was calculated by 2-tailed $\chi 2$

Figure 1