

Association between ABO blood groups and risk of SARS-CoV-2 pneumonia

In December 2019, a cluster of acute respiratory illness caused by a novel coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) occurred in Wuhan, China.^{1,2} Epidemiological and clinical characteristics, risk factors for mortality of patients infected with SARS-CoV-2, and risk factors in the susceptibility to SARS-CoV-2 included age and chronic disease have been reported.³⁻⁶ However, the use of biological markers to predict the susceptibility to SARS-CoV-2 has not been well described. So far, only one study has reported that ABO blood groups were associated with the susceptibility to SARS-CoV-2.⁷ In the present study, after eliminating other confounding risk factors (including age, gender and comorbidities), we further investigated and confirmed the association of ABO blood groups and risk of SARS-CoV-2 pneumonia in patients from the Central Hospital of Wuhan, as well as two hospitals in Wuhan, China.

Patients diagnosed with SARS-CoV-2 who died or were discharged between February 1 and March 25, 2020, were included in this retrospective cohort study. The study was approved by the Ethics Committee of the Central Hospital of Wuhan, and the need for informed consent was waived.⁸ Epidemiological information, clinical data, underlying comorbidities, CT images of lungs, laboratory findings and clinical outcomes were extracted from electronic medical records. The blood group distribution data of the other two hospitals (Wuhan Jinyintan Hospital and Renmin Hospital of Wuhan University) and healthy controls in Wuhan came from the paper published online.⁷ Data were expressed as percentages (%). We used chi-squared tests or Fisher's exact tests in order to compare the various groups.

The ABO blood group in 265 patients infected with SARS-CoV-2 from the Central Hospital of Wuhan showed a distribution of 39.3 %, 25.3 %, 9.8 % and 25.7 % for A, B, AB and O, respectively (Table I). The proportion of blood group A in patients infected with SARS-CoV-2 was significantly higher than that in healthy controls (39.3 % vs. 32.2 %, $P = 0.017$),⁷ while the proportion of blood group O in patients infected with SARS-CoV-2 was significantly lower than that in healthy controls (25.7 % vs. 33.8 %, $P < 0.01$).

We next investigated whether age, gender and chronic disease influence the ABO blood group distribution (Table I). The results showed that, among blood group A (43.6 % vs. 32.2 % in controls, $P < 0.01$) and blood group O (22.2 % vs. 33.8 % in controls, $P < 0.01$), patients over 60 years of age were consistent with all the above patients. Similarly, we

also found that A (42.5 % vs. 32.2 %, $P = 0.021$) and O (23.0 % vs. 33.8 %, $P = 0.016$) distribution of blood groups in male patients was consistent with all the above patients. In all chronic diseases, we found that the proportion of hypertension (41.7 % vs. 32.2 %, $P = 0.031$) and hepatitis (85.7 % vs. 32.2 %, $P < 0.01$) in blood group A was much higher than that in the control group; however, there is currently no literature supporting that hypertension and hepatitis increase the risk of infection of SARS-CoV-2. In dead patients, we found no differences between blood types.

Finally, we integrated the data of the three hospitals in Wuhan for analysis (Table II).⁷ We still find that the proportion of blood group A in patients infected with SARS-CoV-2 was significantly higher than that in healthy controls (38.0 % vs. 32.2 %, $P < 0.001$), while the proportion of blood group O in SARS-CoV-2 infected patients was significantly lower than in healthy controls (25.7 % vs. 33.8 %, $P < 0.001$). The distribution ratio of blood type A and O between various ages and genders was almost consistent with the trend of all patients.

In this study, we demonstrated that blood group A patients were at higher risk of hospitalization following SARS-CoV-2 infection, while blood group O patients had lower risk, which suggested that the ABO blood type could be used as a biomarker to predict the risk of SARS-CoV-2 infection.

Coincidentally, previous studies found that ABO blood type distribution also had significant differences in other viral infections. Chen *et al.* reported that blood group O individuals were less likely to become infected by SARS coronavirus,⁹ Batool *et al.* found that blood group O might have some influence in protecting against blood-transmitted infection, and people having blood group A were more prone to contract hepatitis B and HIV.¹⁰ Jing *et al.* found that blood group B was associated with a lower risk of HBV infection.¹¹ Guillon *et al.* reported that the S protein/angiotensin-converting enzyme 2-dependent adhesion of these cells to an angiotensin-converting enzyme 2 expressing cell line was specifically inhibited by human natural anti-A antibodies, which might block the interaction between the virus and its receptor.¹² This could explain why blood group A is susceptible, while blood group O is not. However, there may be other factors that need further study.

In summary, based on our research, and confirmed by reported data, people with blood group A had a significantly higher risk of SARS-CoV-2 infection, whereas blood group O

Table I. The ABO blood group distribution in patients infected with SARS-CoV-2 and healthy controls in Wuhan.

	Blood Group			
	A	B	AB	O
Controls (Wuhan Area, <i>n</i> = 3694), %	1188 (32.3 %)	920 (24.9 %)	336 (9.1 %)	1250 (33.8 %)
Central Hospital of Wuhan (<i>n</i> = 265), %	104 (39.3)	67 (25.3)	26 (9.8)	68 (25.7)
χ^2	5.645	0.019	0.152	7.447
<i>P</i>	0.017	0.891	0.696	< 0.01
Age distribution (<i>n</i> = 265), %				
Less than 40 years (<i>n</i> = 69)	24 (34.8)	17 (24.6)	8 (11.6)	20 (29.0)
χ^2	0.213	0.003	0.509	0.714
<i>P</i>	0.644	0.959	0.476	0.398
Between 41–59 years (<i>n</i> = 79)	29 (36.7)	20 (25.3)	8 (10.1)	22 (27.9)
χ^2	0.732	0.007	0.099	1.242
<i>P</i>	0.392	0.933	0.753	0.265
Over 60 years (<i>n</i> = 117)	51 (43.6)	30 (25.6)	10 (8.6)	26 (22.2)
χ^2	6.752	0.033	0.041	6.871
<i>P</i>	< 0.01	0.856	0.839	< 0.01
Gender distribution (<i>n</i> = 265), %				
Male (<i>n</i> = 113)	48 (42.5)	30 (26.6)	9 (8.0)	26 (23.0)
χ^2	5.323	0.158	0.170	5.771
<i>P</i>	0.021	0.691	0.680	0.016
Female (<i>n</i> = 152)	56 (36.8)	37 (24.3)	17 (11.2)	42 (27.6)
χ^2	1.462	0.025	0.764	2.521
<i>P</i>	0.227	0.875	0.382	0.112
Chronic disease, %				
Cerebrovascular disease (<i>n</i> = 55)	19 (34.6)	15 (27.3)	6 (10.9)	15 (27.3)
χ^2	0.141	0.162	0.215	1.045
<i>P</i>	0.707	0.687	0.643	0.307
Coronary heart disease (<i>n</i> = 51)	18 (35.3)	14 (27.5)	7 (13.7)	12 (23.5)
χ^2	0.226	0.174	1.296	2.393
<i>P</i>	0.634	0.676	0.255	0.122
Heart failure (<i>n</i> = 16)	2 (12.5)	6 (37.5)	1 (6.3)	7 (43.8)
χ^2	2.826	1.349	0.000	0.699
<i>P</i>	0.093	0.245	1.000	0.403
Hypertension (<i>n</i> = 115)	48 (41.7)	26 (22.6)	10 (8.7)	31 (27.0)
χ^2	4.668	0.315	0.022	2.367
<i>P</i>	0.031	0.575	0.883	0.124
Diabetes (<i>n</i> = 66)	26 (39.4)	19 (28.8)	4 (6.1)	17 (25.8)
χ^2	1.552	0.522	0.726	1.895
<i>P</i>	0.213	0.470	0.394	0.169
Digestive disorder (<i>n</i> = 90)	33 (36.7)	26 (28.9)	7 (7.8)	23 (25.6)
χ^2	0.816	0.744	0.185	2.700
<i>P</i>	0.366	0.389	0.667	0.100
COPD (<i>n</i> = 11)	4 (36.4)	4 (36.4)	1 (9.1)	2 (18.2)
χ^2	0.089	0.769	0.000	0.604
<i>P</i>	0.766	0.380	1.000	0.437
Solid tumour (<i>n</i> = 27)	13 (48.2)	8 (29.6)	1 (3.7)	5 (18.5)
χ^2	3.134	0.320	0.405	2.815
<i>P</i>	0.077	0.572	0.525	0.093
Chronic renal disease (<i>n</i> = 41)	15 (36.6)	12 (29.3)	2 (4.9)	12 (29.3)
χ^2	0.364	0.708	0.439	0.379
<i>P</i>	0.546	0.400	0.508	0.538
Hepatitis (<i>n</i> = 7)	6 (85.7)	1 (14.3)	0 (0)	0 (0)
χ^2	6.883	0.422	0.032	2.224
<i>P</i>	< 0.01	0.516	0.858	0.136

Table I. (Continued)

	Blood Group			
	A	B	AB	O
Deaths ($n = 57$), %	20 (35.1)	15 (26.3)	8 (14.0)	14 (24.6)
χ^2	0.220	0.060	1.644	2.162
P	0.639	0.807	0.200	0.141

COPD, chronic obstructive pulmonary disease.

Table II. The ABO blood group distribution in patients infected with SARS-CoV-2 from three Wuhan hospitals.

	Blood Group			
	A	B	AB	O
Controls (Wuhan Area, $n = 3694$), %	1188 (32.2)	920 (24.9)	336 (9.1)	1250 (33.8)
Three Wuhan Hospitals ($n = 2153$), %	819 (38.0)	561 (26.1)	219 (10.2)	554 (25.7)
χ^2	20.859	0.953	1.833	36.445
P	<0.001	0.329	0.176	<0.001
Age distribution ($n = 2153$), %				
Less than 40 years ($n = 342$)	124 (36.3)	95 (27.8)	29 (8.5)	94 (27.5)
χ^2	2.395	1.372	0.145	5.688
P	0.122	0.241	0.704	0.017
Between 41–59 years ($n = 784$)	304 (38.8)	196 (25.0)	79 (10.1)	205 (26.2)
χ^2	12.739	0.003	0.740	17.439
P	<0.001	0.956	0.390	<0.001
Over 60 years ($n = 1027$)	391 (38.1)	270 (26.3)	111 (10.8)	255 (24.8)
χ^2	12.617	0.818	2.749	30.034
P	<0.001	0.366	0.097	<0.001
Gender distribution ($n = 2153$), %				
Male ($n = 1143$)	451 (39.5)	305 (26.7)	110 (9.6)	277 (24.2)
χ^2	20.749	1.461	0.291	37.271
P	<0.001	0.227	0.590	<0.001
Female ($n = 1010$)	368 (36.4)	256 (25.4)	109 (10.8)	277 (27.4)
χ^2	6.549	0.082	2.664	14.878
P	0.010	0.774	0.103	<0.001

Three Wuhan hospitals: the Central Hospital of Wuhan, Wuhan Jinyintan Hospital and Renmin Hospital of Wuhan University.

had a significantly lower risk of SARS-CoV-2 infection. People with blood type A should strengthen protection to reduce the risk of infection; however, people with blood type O should not take the virus lightly, and must still take precautions to avoid increasing the risk of infection. The underlying molecular mechanism of our findings will need further study.

Funding information

This study was supported by the Health and Family Planning Commission of Wuhan City (WX18M02).

Conflict of interest

No reports.

Authors' contribution

Conceived and designed the experiments: J.L., M.Y. and A.D. Performed the experiments: J.L., X.W. and A.D. Analysed the

data: J.L., X.W., J.C. and A.D. Wrote the paper: J.L. J.L. and X.W. contributed equally.

Juyi Li^{1,†} 
 Xiufang Wang^{2,†}
 Jian Chen³
 Yi Cai²
 Aiping Deng¹ 
 Ming Yang⁴ 

¹Department of Pharmacy, Key Laboratory for Molecular Diagnosis of Hubei Province, The central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei,

²Department of Pain, The central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei,

³Department of Information, The central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei and

⁴Department of Plastic surgery, Hospital Dean's Office, The central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China.

E-mails: dapyxb@163.com (A. D.); 2217137592@qq.com (M. Y.)

†Juyi Li and Xiufang Wang contributed equally.

Keywords: ABO blood groups, infection, markers, pneumonia, SARS-CoV-2

First published online 26 May 2020
doi: 10.1111/bjh.16797

References

- Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. *New Engl J Med.* 2020;**382**:727–33.
- 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. *The Lancet.* 2020;**395**:1054–62.
- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *New Engl J Med.* 2020;**382**:1708–20.
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA.* 2020;**323**(11):1061.
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet.* 2020;**395**:507–13.
- Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *Lancet Respirat Med.* 2020;**8**:e21.
- Zhao J, Yang Y, Huang H, Li D, Gu D, Lu X, et al. Relationship between the ABO Blood Group and the COVID-19 Susceptibility. medRxiv preprint. 11 March, 2020.
- Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis.* 2020;**20**:425–34.
- Cheng Y, Cheng G, Chui CH, Lau FY, Chan PK, Ng MH, et al. ABO blood group and susceptibility to severe acute respiratory syndrome. *JAMA.* 2005;**293**:1450–1.
- Batool Z, Durrani SH, Tariq S. Association Of Abo And Rh Blood Group Types To Hepatitis B, Hepatitis C, Hiv And Syphilis Infection, A Five Year' Experience In Healthy Blood Donors In A Tertiary Care Hospital. *J Ayub Med College, Abbottabad : JAMC.* 2017;**29**:90–2.
- Jing W, Zhao S, Liu J, Liu M. ABO blood groups and hepatitis B virus infection: a systematic review and meta-analysis. *BMJ open.* 2020;**10**:e034114.
- Guillon P, Clement M, Sebille V, Rivain JG, Chou CF, Ruvoen-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**:1085–93.

More on 'Association between ABO blood groups and risk of SARS-CoV-2 pneumonia'

We read with interest the recent report from Li *et al.*¹ describing an association between ABO blood groups and risk of SARS-CoV-2 pneumonia. In an initial study of 265 patients with COVID, the authors observed that blood group O individuals were significantly underrepresented amongst patients who required hospitalization for severe COVID-19 infection ($P < 0.01$). Conversely, blood group A was significantly more common in patients with severe COVID-19 compared to the local population ($P = 0.017$). Subsequently, in a larger validation cohort that included 2 153 patients with COVID-19, this ABO effect was reproduced with blood group O again being associated with a significant protective effect ($P < 0.001$). In keeping with these data, another independent study ($n = 2 173$) also reported that blood group O was associated with reduced susceptibility to severe COVID-19.² Since the pathogenesis underlying COVID-19 remains poorly understood, we believe that these novel findings provide interesting insights into biological mechanisms that may contribute to interindividual differences in COVID-19 susceptibility.

The importance of ABO blood group in blood transfusion and clinical transplantation is well established. In addition, multiple studies have shown that ABO blood group is an important independent risk factor for cardiovascular disease and venous thromboembolism (VTE).^{3,4} In particular, risk of

thrombosis is significantly reduced in blood group O compared to non-O individuals. More recent data have defined biological mechanisms through which ABO modulates thrombotic risk.^{5–7} Given the accumulating evidence demonstrating that COVID-19 is associated with a significant coagulopathy^{8,9} and that microthrombi disseminated through the lung vasculature contribute to acute respiratory distress syndrome (ARDS),^{10,11} the association between ABO blood group and COVID-19 susceptibility is of particular interest.

Although ABO(H) blood group carbohydrate structures are traditionally considered red blood cell antigens, they are actually expressed on a range of other cell types, including endothelial cells (EC) and platelets.¹² In addition, covalently-linked ABO(H) determinants are also present on a number of plasma glycoproteins, including von Willebrand factor (VWF), and factor VIII (FVIII).¹³ Importantly, the ABO(H) sugars on VWF have been shown to influence its biological activity. First, plasma VWF levels are 20–30% lower in normal blood group O individuals compared to non-O subjects.⁵ These reduced VWF levels are due to the fact that group O VWF has a significantly reduced plasma half-life compared to non-O VWF (10.0 compared to 25.5 h).¹⁴ Since FVIII circulates in high-affinity complex with VWF, plasma FVIII:C levels are also significantly reduced in blood group