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ABO blood groups among Coronavirus disease 2019 patients

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ABSTRACT

Introduction: Susceptibility to some infectious diseases has been associated with blood group phenotypes. Coronavirus disease 2019 (COVID-19) is a new infectious disease caused by a novel corona virus designated Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) which has spread rapidly around the world.
The objective of this study was to determine if the susceptibility or severity to COVID-19 was associated with ABO blood group distribution among the affected countries.
Materials and methods: This retrospective study of COVID-19 disease was based on data from 105 countries collected on the 13th of April 2020 and analysed by SPSS software version 16.0. Spearman correlation coefficient and Kruskal Wallis test were used to assess for associations between ABO blood group with COVID-19.
Results: The results indicated that individuals of blood group A are at increased risk of infection by SARS-CoV-2 virus and severity of COVID-19 disease. Blood groups B and O were less likely to be infected and the disease evolves less severe.
Conclusions: The results are discussed in relation to the host-parasite interactions that might contribute to susceptibility to these infections.

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1. INTRODUCTION

Blood group phenotypes have been reported to be associated with increased susceptibility to some infectious diseases [1, 2]. Blood group B is associated with a lower risk of Hepatitis B virus (HBV) infection while blood group O is at higher risk of HBV infection in endemic areas [3, 4]. Blood group O is associated with disease due to *Norwalk* virus infection while blood group B shows resistance to the infection [5]. The P/Gb3 blood group antigen is correlated with susceptibility to Human Immunodeficiency Virus (HIV) infection [6]. Blood groups A and B were over represented among patients with influenza (H1A1) compared with groups O and AB [7], and the higher susceptibility of influenza A and B were observed with blood group AB [8, 9].
COVID-19 is a new infectious disease caused by the novel corona virus (SARS-CoV-2) that has spread rapidly around the world [10, 11]. Corona viruses are RNA viruses, two-thirds of RNA genome encode viral polymerase (RNA dependent RNA polymerase), RNA synthesis materials, and two non-structural polyproteins that are not involved in host response modulation (ORF1a-ORF1b). The other one-third of the genome encodes four structural proteins spike (S), envelope (E), membrane (M) ve-nucleocapsid (N), and other helper proteins [12, 13].

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Table 1. COVID-19 in 32 Asian Countries on the 13th of April 2020 and the distribution of ABO blood group in these countries

Countries	Total Cases	Active N (%)	Death N (%)	Recovered N (%)	Blood group (%)			
					A	B	O	AB
Armenia	1067	786 (73.7)	16 (1.5)	265 (24.8)	50	13	31	6
Bahrain	1361	763 (56.1)	7 (0.51)	591 (43.4)	20.7	23.7	51.7	3.9
Bangladesh	1012	924 (91.3)	46 (4.5)	42 (4.2)	22.4	35.2	33.2	9.2
Cambodia	122	31 (25.4)	0 (0)	91 (74.6)	28	19	48	5
China	82249	1170 (1.4)	3341 (4.1)	77738 (94.5)	28	19	48	5
Hong Kong	1013	575 (56.8)	4 (0.4)	434 (42.8)	26.3	25.5	41.8	6.4
India	10541	8978 (85.2)	358 (3.4)	1205 (11.4)	21.4	39.9	29.3	9.4
Indonesia	4839	3954 (81.7)	459 (9.5)	426 (8.8)	26	29	37	8
Iran	73303	22735 (31.0)	4585 (6.3)	45983 (62.7)	30	24.7	37.5	7.8
Iraq	1378	583 (42.3)	78 (5.7)	717 (52.0)	27.7	28.3	35.7	8.3
Israel	11868	9751 (82.2)	117 (1.0)	2000 (16.9)	38	19	35	8
Japan	7645	6703 (87.7)	143 (1.9)	799 (10.5)	40	20	30.1	9.9
Kazakhstan	1179	1023 (86.8)	14 (1.2)	142 (12.0)	32	26	33	9
Lebanon	641	540 (84.2)	21 (3.3)	80 (12.5)	38.8	11.2	46.1	3.9
Macao	45	35 (77.8)	0 (0)	10 (22.2)	26.3	25.5	41.8	6.4
Malaysia	4987	2427 (48.7)	82 (1.6)	2478 (49.7)	30.5	27.5	34.5	7.5
Mongolia	93	86 (92.5)	1 (1.1)	6 (6.5)	28	11	56	5
Myanmar	62	56 (90.3)	4 (6.5)	2 (3.2)	24	33	36	7
Nepal	16	15 (93.7)	0 (0)	1 (6.3)	28.5	27.3	35.5	8.7
North Korea	854	772 (90.4)	38 (4.5)	44 (5.2)	31.2	30.3	27.2	11.3
Pakistan	5716	4242 (74.2)	96 (1.7)	1378 (24.1)	23.3	38	28.8	9.9
Philippine	5223	4593 (87.9)	335 (6.4)	295 (5.7)	23	25	46	6
Saudi Arabia	4934	4064 (82.4)	65 (1.3)	805 (16.3)	25.9	18	51.8	4.3
Singapore	2918	2323 (79.6)	9 (0.3)	586 (20.1)	24.6	24.8	44.5	6.1
South Korea	10564	2808 (26.6)	222 (2.1)	7534 (71.3)	34	27	28	11
Syria	25	18 (72)	2 (8)	5 (20)	33	15	48	4
Taiwan	393	263 (66.9)	6 (1.5)	124 (31.6)	26	23.9	44.1	6
Thailand	2613	1167 (44.7)	41 (1.6)	1405 (53.8)	17	37	41	5
Turkey	61049	55796 (91.4)	1296 (2.1)	3957 (6.5)	42.5	15.8	33.7	8
UAE	4521	3644 (80.6)	25 (0.6)	852 (18.9)	24	22.9	48.4	4.7
Vietnam	265	97 (36.6)	0 (0)	168 (63.4)	22	31	42	5
Yemen	1	1 (100)	0 (0)	0 (0)	29.6	16.5	51.5	2.4

The first step of corona virus infection is the interaction between human cells with S Protein [13]. The receptor binding domain (RBD) in SARS-CoV-2 S protein attaches to Angiotensin-converting enzyme 2 (ACE2) as host receptor [14]. It needs to be cleaved in two sites called S protein priming by transmembrane protease serine 2 (TMPRSS2) to enter the cell and replicate [15-17].

It has been reported that severe acute respiratory syndrome coronavirus (SARS-CoV) is less likely to infect people with blood group O compared with other blood groups [18], and a recent study of ABO blood group susceptibility of infection by SARS-CoV-2 from three hospitals in China (Wuhan and Shenzhen) indicated individuals of blood group A are more susceptible to COVID-19 compared with non-A blood groups. In contrast, people of blood group O appeared to be less susceptible to the COVID-19 disease [19].

The aim of this study was to determine if there was an association between group A and COVID-19 among other countries similar to the data reported from China.

2. MATERIALS AND METHODS

The Worldmeter website (www.worldmeter.info) was used to collect data on COVID-19 cases for 105 countries on the 13th of April 2020. The website listed numbers of cases in five categories. Total cases were the figures reported for the total cumulative counts of laboratory confirmed infections. Active cases were the total number minus deaths and those who recovered. Recovery was defined based on various criteria: resolution of symptoms and two negative tests for the virus within 24 hours; resolution of symptoms with no recurrence within 14 days; discharge from hospital. Deaths were the cumulative number of confirmed cases. A subset of cases defined as critical was analysed separately [20].

Data on ABO blood groups for the countries was obtained from (https://en.m.wikipedia.org/wiki/Blood_type_distribution_by_country). Data for these countries in six geographical regions are listed in Tables 1-6 [21].

As there were reports from three hospitals in China

Table 2. COVID-19 in 37 European Countries on the 13th of April 2020 and the distribution of ABO blood group in these countries

Countries	Total Cases	Active N (%)	Death N (%)	Recovered N (%)	Blood group (%)			
					A	B	O	AB
Austria	14119	6102 (43.2)	384 (2.8)	7633 (54.1)	44	14	36	6
Belgium	31119	20094 (64.6)	4157 (13.4)	6868 (22.1)	40	10.1	45	4.9
Bosnia	1080	823 (76.2)	39 (3.6)	218 (20.2)	43	14	36	7
Bulgaria	695	579 (83.3)	35 (5.0)	81 (11.6)	44	15	33	8
Croatia	1650	1225 (74.2)	25 (1.5)	400 (24.2)	42	18	34	6
Cyprus	662	585 (88.4)	12 (1.8)	65 (9.8)	43.8	12	39.1	5.1
Czech. Republic	6059	5385 (88.9)	147 (2.4)	527 (8.7)	42	18	32	8
Denmark	6496	3976 (61.2)	285 (4.4)	2235 (34.4)	44	10	41	5
Estonia	1373	1227 (89.3)	31 (2.3)	115 (8.4)	35.3	23.7	33.8	7.2
Finland	3161	2802 (88.6)	59 (1.87)	300 (9.5)	41	18	33	8
France	136779	94094 (68.8)	14967 (10.9)	27718 (20.3)	44	10	42	4
Germany	130072	58678 (45.1)	3194 (2.4)	68200 (52.4)	43	11	41	5
Greece	2145	1777 (82.8)	99 (4.6)	269 (12.5)	37.9	13	44.4	4.7
Hungary	1512	1268 (83.9)	122 (8.1)	122 (8.07)	40	19	32	9
Iceland	1711	770 (45.0)	8 (0.5)	933 (54.5)	32	10.6	55	2.4
Ireland	10647	10257 (96.3)	365 (3.4)	25 (0.2)	31	11	55	3
Italy	195516	103616 (53.0)	20465 (10.5)	35435 (18.1)	42	9	46	3
Latvia	657	636 (96.8)	5 (0.8)	16 (2.43)	37	20	36	7
Liechtenstein	79	23 (29.1)	1 (1.3)	55 (69.6)	43.5	11.8	40	4.7
Lithuania	1070	945 (88.3)	24 (2.2)	101 (9.4)	39	13	43	5
Luxemburg	3292	2723 (82.7)	69 (2.1)	500 (15.2)	43	11	41	5
Malta	384	337 (87.8)	3 (0.8)	44 (11.5)	45.5	8	43	3.5
Moldova	1847	1677 (90.8)	36 (1.9)	134 (7.3)	37.8	20.6	33.5	8.1
Netherlands	26551	23478 (88.4)	2823 (10.6)	250 (0.9)	42	8	47	3
Norway	6605	6439 (97.5)	134 (2.03)	32 (0.5)	49	8	39	4
Poland	7049	6180 (87.7)	251 (3.6)	618 (8.8)	38	17	37	8
Portugal	16934	16122 (95.2)	535 (3.2)	277 (1.63)	46.6	7.7	42.3	3.4
Romania	6879	5496 (79.9)	332 (4.8)	1051 (15.3)	43	16	33	8
Russia	21102	19238 (91.2)	170 (0.8)	1694 (8.0)	35.8	23.2	32.9	8.1
Serbia	4054	3569 (88.0)	85 (2.1)	400 (9.9)	42	15	38	5
Slovakia	835	726 (86.9)	2 (0.2)	107 (12.8)	42	18	32	8
Slovenia	1220	1012 (82.9)	56 (4.6)	152 (12.4)	40	15	38	7
Spain	172541	86981 (50.4)	18056 (10.5)	47504 (27.5)	43	10	44	3
Sweden	10948	9648 (88.1)	919 (8.4)	381 (3.5)	44	12	38	6
Switzerland	25688	10850 (42.2)	1138 (4.4)	13700 (53.3)	47	8	41	4
Ukraine	3372	3155 (93.6)	98 (2.9)	119 (3.5)	40	17	37	6
United Kingdom	88621	76948 (93.6)	11329 (12.8)	344 (0.4)	39	10	47	4

indicating individuals of blood group A are more susceptible to COVID-19 compared with non-A blood groups [19], this retrospective study was carried out to determine if there was a similar pattern in other populations. The statistical analyses were performed with SPSS software version 16.0. Spearman correlation coefficient was used for the relationship of ABO blood group with COVID-19 disease outcome and Kruskal Wallis test for non-parametric data to compare the distribution of ABO and COVID-19 disease outcome in the six geographical areas.

3. RESULTS

Tables 1-6 summarise the data on COVID-19 cases and ABO blood groups by geographical region. The mean percentage of each ABO blood group distribution by region included in the analyses. Latin America has a significantly higher proportion of blood group O (59.4%) compared with Africa (49%), Australasia (47%), USA and Canada (45%), Asia (40%), and Europe (40%) ($X^2 = 47.36$, df = 5, $p < 0.0001$). The USA and Canada have a higher proportion of blood group A (42%) compared with Europe (41%), Australasia (37%), Africa (29%), Asia (29%) and Latin America (27%) ($X^2 = 57.19$, df = 5, $p < 0.0001$). Asia has a significantly higher proportion of blood group B (24%). Compared with Africa (18%), Europe (14%), Latin America (11%), Australasia (12%) then USA and Canada (10%) ($X^2 = 49.91$, df = 5, $p < 0.0001$). Asia had the highest proportion of AB (7.1%) compared with Europe (6%), Africa (4%), Australasia (4%), USA and Canada (4%) and

Latin America (3%) (X^2 = 46.38, df = 5, p < 0.0001).

Table 3. COVID-19 in 15 African Countries on the 13th of April 2020 and the distribution of ABO blood group in these countries

Countries	Total Cases	Active N (%)	Death N (%)	Recovered N (%)	Blood group (%)			
					A	B	O	AB
Cameroon	848	738 (87)	12 (1.4)	98 (11.6)	40	12.4	44.2	3.4
Egypt	2190	1437 (65.6)	164 (7.5)	589 (26.9)	26	13	57	4
Ethiopia	82	65 (79.3)	3 (3.7)	14 (17.1)	30	22	42	6
Ghana	566	554 (79.3)	8 (1.4)	4 (0.7)	18.9	19.7	58.3	3.1
Ivory Coast	626	531 (84.8)	6 (0.9)	89 (14.2)	23.5	23.5	48.5	4.5
Kenya	208	159 (76.4)	9 (4.3)	40 (19.2)	26.2	22.2	47.4	4.2
Libya	26	16 (61.5)	1 (3.9)	9 (34.6)	33.1	12.8	48.9	5.2
Mauritania	7	4 (57.1)	1 (14.3)	2 (28.6)	28.3	18.6	49.1	4.0
Mauritius	324	273 (84.3)	9 (2.8)	42 (12.9)	27	26	40	7
Morocco	1838	1502 (81.7)	126 (6.8)	210 (11.4)	32.9	15.8	46.8	4.5
Nigeria	343	242 (70.6)	10 (2.9)	91 (26.5)	23.1	21.3	52.9	2.7
South Africa	2272	1835 (80.8)	27 (1.2)	410 (18.1)	37	14	45	4
Sudan	29	21 (72.4)	4 (13.8)	4 (13.8)	29.5	16	51.5	3
Uganda	54	47 (87.0)	0 (0)	7 (12.9)	40	11	45	4
Zimbabwe	17	14 (82.4)	3 (17.7)	0 (0)	19	15	65	1

While analyses of the ABO blood group distribution indicated there were significant differences among the six regions, analysis of their association with COVID-19 in 105 countries indicated there were significant correlations between group A and infections (Table 7).

Table 4. COVID-19 in 15 Latin American Countries on the 13th of April 2020 and the distribution of ABO blood group in these countries

Countries	Total Cases	Active N (%)	Death N (%)	Recovered N (%)	Blood group (%)			
					A	B	O	AB
Argentina	2277	1664 (73.1)	98 (4.3)	515 (22.6)	34.7	8.8	53.8	2.7
Bolivia	354	320 (90.4)	28 (7.9)	6 (1.7)	32.2	10.6	55.9	1.3
Brazil	23723	19389 (81.7)	1355 (5.7)	2979 (12.6)	42	10	45	3
Chile	7525	5076 (67.5)	82 (1.1)	2367 (31.5)	8.8	3.4	86.7	1.1
Colombia	2852	2421 (84.9)	112 (3.9)	319 (11.2)	28.8	3.0	66.4	1.8
Cuba	726	584 (80.4)	21 (2.9)	121 (16.7)	36.3	11.2	49.4	3.1
Dominican	16	8 (50)	0 (0)	8 (50)	28.5	18.3	49.9	3.3
Ecuador	7529	6577 (87.4)	355 (4.7)	597 (7.9)	14.7	7.4	77.4	0.5
El Salvador	149	118 (79.2)	6 (4.0)	25 (16.8)	24	11.7	63	1.3
Guinea	319	302 (94.7)	0 (0)	17 (5.3)	22.5	23.9	48.9	4.7
Honduras	407	374 (91.9)	26 (6.4)	7 (1.7)	28.7	8.4	60.2	2.7
Jamaica	73	50 (68.5)	4 (5.5)	19 (26.0)	25	21	50.5	3.5
Mexico	5014	2718 (54.2)	332 (6.6)	1964 (39.2)	27.5	8.9	61.8	1.8
Peru	9784	6926 (70.8)	216 (2.2)	2642 (27)	18.9	8.1	71.4	1.6
Venezuela	189	70 (37.0)	9 (4.8)	110 (58.2)	30	6	62	2

The analyses of the data for ABO blood group distributions and numbers of COVID-19 cases in 105 countries on the 13th of April 2020 indicated there was a significant positive correlation between blood group A and the total number of COVID-19 cases (r_s = 0.329, p < 0.001). Groups B (r_s = -0.252, p < 0.010) and O (r_s= - 0.231, p < 0.018) were significantly negatively correlated with the total number of COVID-19 cases; there was no significant correlation with AB (r_s = 0.089, p < 0.366).

There was a significant positive correlation between the active cases and group A (r_s= 0.331, p < 0.001). In contrast, groups B (r_s = -0.229, p < 0.019) and O (r_s = -0.266, p < 0.006) were significantly negatively correlated. There was no significant correlation with AB (r_s = 0.103, p< 0.298).

Critical cases, defined as requiring ICU facilities, were positively correlated with blood group A (r_s= 0.365, p < 0.0001); however, they were negatively correlated with blood group B (r_s= -0.357, p < 0.0001). There was no significant correlation with O (r_s = -0.133, p < 0.176) or AB (r_s = 0.003, p < 0.977).Deaths due to COVID-19 in 105 countries were negatively correlated with blood group B (rs = -0.242 p < 0.013), but not with the other groups: A, r_s = 0.094 p < 0.338; O, r_s = 0.105, p < 0.285; AB, r_s = -0.142 p < 0.150. Among individuals who recovered, there were insignificant positive correlations with blood group O (r_s = 0.089 p < 0.368) and B (r_s = 0.041 p < 0.676) and insignificant negative correlations with blood group A (r_s =

- 0.090 p < 0.362) and AB (r_s = -0.044 p < 0.657).

Table 5. COVID-19 in 4 Australasian Countries on the 13th of April 2020 and the distribution of ABO blood group in these countries

Countries	Total Cases	Active N (%)	Death N (%)	Recovered N (%)	Blood group (%)			
					A	B	O	AB
Australia	6400	2741 (42.8)	61 (1.0)	3598 (56.2)	38	10	49	3
Fiji	16	16 (100)	0 (0)	0 (0)	34	17	44	5
New Zealand	1366	729 (53.4)	9 (0.7)	628 (46)	38	11	47	4
Papua New Guinea	2	2 (100)	0 (0)	0 (0)	38	10	49	3

Table 8 summarises the mean value of total and active cases for each geographical area. The USA and Canada have a significantly higher proportion of total cases with the mean total cases (306430) compared with other areas: Europe (25528); Asia (9754); Latin America (3816);

Table 6. COVID-19 in Canada and United States on the 13th of April 2020 and the distribution of ABO blood group in these countries

Countries	Total Cases	Active N (%)	Death N (%)	Recovered N (%)	Blood group (%)			
					A	B	O	AB
Canada	25680	17144 (66.8)	780 (3.04)	7756 (30.2)	42	9	46	3
USA	587173	526581 (89.7)	23644 (4.0)	36948 (6.3)	42	10	44	4

Australasia (1946); Africa (629) (total cases; X^2 = 27.26, df = 5, p < 0.0001; active cases; X^2 = 29.53, df = 5, p < 0.0001).The statistical analysis on the mean percentage of critical cases indicated that Europe has a significantly higher percentage compared with other areas, followed by the USA and Canada, Latin America, Asia, Australasia and Africa (X^2 = 30.92, df = 5, p < 0.0001).

Table 7. Distribution of ABO blood groups among the six geographical regions

Region	N	Blood group (%)			
		A	B	O	AB
USA and Canada	2	42	10	45	4
Europe	37	41	14	40	6
Asia	32	29	24	40	7.1
Latin America	15	27	11	59.4	3
Australasia	4	37	12	47	4
Africa	15	29	18	49	4
Chi- Square		*57.19*	*49.91*	*47.36*	*46.38*
Df		*5*	*5*	*5*	*5*
P value		*0.0001*	*0.0001*	*0.0001*	*0.0001*

4. DISCUSSION

Individuals of blood group A were over represented among those infected with the new coronavirus SARS-CoV-2 compared with non-A blood group. There were significantly fewer individuals of blood group O among the infected patients. [19], and in another study the odds of COVID-19 positive versus negative test results were increased in blood groups A and decreased in blood groups O [22]. The current study indicated that blood group A was correlated with infection by SARS-CoV-2 and more among those with severe COVID-19 disease. Blood groups B and O had negative correlations with infections due to SARS-CoV-2. Group B was negatively correlated with deaths from COVID-19 disease.

The USA, Canada and Europe have the highest numbers of SARS-CoV-2 infections compared with other regions. This observation might reflect in part the higher proportion of blood group A.

SARS-CoV-2 shares a highly similar gene sequence and behaviour pattern with SARS-CoV [23]. Both interact with Angiotensin-converting enzyme2 (ACE2) to enter the host cell [14, 24]. A previous study with both monoclonal and human natural anti-A antibodies blocked the interaction between the S protein and ACE2 receptor providing [25]. Recent observation indicate that subjects with anti-A in serum are significantly less represented in the COVID-19 group than those lacking anti-A [26]. If anti-A inhibits binding of the virus to its receptor, it might reduce density of colonisation.

These observations require further studies to define epidemiological factors linked with COVID-19 disease such as nutrition, age, population density, personal hygiene and strength of health care system which influence the spread of the disease [27], assessing the association of ABO blood group among COVID-19 cases and disease severity with respect to ethnic groups in each country, while study in the effects of anti-A on interactions between the SARS-CoV-2 virus and host cells in vitro.

5. CONCLUSIONS

This study supports the previous observation and indicted that blood group A contributes to the risk of COVID-19 disease. Groups B and blood group O which have the anti-A isohemagglutinin were negatively associated with SARS-CoV-2 virus infection. More detailed studies of ABO groups among COVID-19 patients for each country

Table 8. COVID-19 disease outcome and the distribution of ABO blood groups in 6 geographical regions on the13th of April 2020

Region	N	Total cases	Active N (%)	Critical* N (%)	Death N (%)	Recovered N (%)
USA and Canada	2	306430	271860 (78.2)	6665 (2.2)	12212 (3.5)	22352 (18.25)
Europe	37	25528	15931 (77.5)	786 (2.3)	2175 (4.3)	5909 (17.4)
Asia	32	9453	4404 (69.4)	204 (1.4)	357 (2.6)	4693 (28.0)
Latin America	15	4063	3107 (74.1)	91 (2.0)	176 (4.0)	780 (21.9)
Australasian	4	1946	872 (74.0)	21 (0.4)	18 (0.4)	1057 (25.5)
Africa	15	629	496 (77.9)	1.13 (0.2)	26 (5.5)	107 (16.6)
Chi- Square		*27.46*	*29.82 (3.01)*	*38.32 (30.2)*	*24 (15)*	*18.22 (3.8)*
Df		*5*	*5*	*5*	*5*	*5*
P value		*0.0001*	*0.0001 (0.699)*	*0.0001 (0.0001)*	*0.0001 (0.01)*	*0.003 (0.58)*

**Critical = subset of active cases requiring intensive treatment.*

and in vitro studies on the effects of Anti-A on interactions between the SARS-CoV-2 virus and host cells are needed.

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