

# Association of the ABO blood group with SARS-CoV-2 infection in a community with low infection rate

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## Vox Sanguinis

### Abstract

**Background and objectives** Reports on the association of the ABO phenotypes with infection by the SARS-CoV-2 virus have mostly come from countries with high infection rates. This study examined the possible association between SARS-CoV-2 infection and the ABO phenotype in Black Africa.

**Materials and methods** This report is from a single centre where both asymptomatic and symptomatic patients were quarantined. At the time of this report, Oyo State, Nigeria had carried out 15 733 tests of which 3119 were positive for the virus with 1952 recoveries and 37 deaths. The ABO distribution of patients was compared with that of a blood donor population.

**Results** Of the 302 participants, 297 (98%) had their blood group determined, asymptomatic and symptomatic individuals were 123 (40.7%) and 179 (59.3%) respectively. Blood group O was significantly less represented among the patients ( $P < 0.01$ ) while blood groups B and AB were significantly more represented ( $P < 0.01$ ,  $P = 0.03$  respectively). Patients with anti-B (groups A and O) were significantly less represented than those without anti-B (B and/or AB): B and AB ( $P < 0.001$ ), B ( $P = 0.002$ ), AB ( $P = 0.01$ ). There was no difference in the blood group distribution of symptomatic and asymptomatic patients ( $\chi^2$  (3,  $N = 302$ ) = 2.29;  $P = 0.51$ ), but symptomatic patients with anti-A (groups B and O) were more represented than asymptomatic patients with anti-A ( $\chi^2$  4.89;  $P = 0.03$ ).

**Conclusion** The higher prevalence of blood group O and more potent beta haemolysins (anti-B antibodies) are likely reasons for the lower infectivity by the SARS-CoV-2 virus and severity of COVID-19 disease in the community.

**Key words:** antibodies, blood group, COVID-19, haemolysin, isoagglutinins, serology.

Received: 26 October 2020,  
revised 24 December 2020,  
accepted 27 December 2020

## Introduction

The ABO blood group antigens are present on cellular elements in the blood and body secretions. This could

explain why it has been associated with some diseases especially those of the respiratory and gastrointestinal tracts [1]. COVID-19, a disease resulting from SARS-CoV-2 viral infection, reportedly affects most systems of the body; it is also linked to the ABO blood group phenotypes [2]. Most studies have reported protection from blood group O but susceptibility of group A [2–5]. GWAS confirmed these findings and an association signal which

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coincides with the ABO blood group locus. [6] There is evidence to suggest that the anti-A antibodies present in the serum rather than the blood group itself could be responsible for the association [7, 8]. Infection rates and fatality from COVID-19 have been low in most African countries [9] where blood group O is more prevalent than other ABO blood group phenotypes in the population [10–12]. We therefore explore the likelihood that the low infection rates may be deduced from this.

## Methods

This study was conducted at an Infectious Diseases Centre situated in Ibadan, the capital of Oyo state, Nigeria. The estimated population of Ibadan, the capital of Oyo State, is about six million. At the time of compilation of this report, Oyo State in South Western Nigeria had carried out 15 733 tests and of this number, 3119 were confirmed positive for the SARS-CoV-2 virus with 1952 recoveries and 37 deaths. Asymptomatic individuals were identified contacts of confirmed positive cases who also tested positive to the virus. In accordance to the guidelines of the Nigeria Centre for Disease Control (NCDC), asymptomatic individuals who tested positive for SARS-CoV2 and considered unable to appropriately self-isolate because of poor living conditions were quarantined and observed in the isolation centres until negative. This is to prevent the spread of the disease. This prospective data were therefore obtained from both asymptomatic and symptomatic individuals, and the study was carried out between 27th April 2020 and 30th August 2020, and the positivity rate was 19.8%.

COVID-19 testing was performed by Real-Time Polymerase Chain Reaction on nasopharyngeal and oropharyngeal swabs collected into Viral Transport Media. Briefly, within 2 h of collection, viral RNA was extracted from the nasopharyngeal and throat swabs using QIAamp viral RNA mini kit (Qiagen, Hilden, Germany) according to manufacturer's instructions. A commercial real-time RT-PCR kit (BGI, Europe) which detects the open reading frame 1ab (ORF1ab) was used for the real-time RT-PCR assay. The total reaction volume was 30 $\mu$ L, and the reaction was set up according to manufacturer's protocol. The reaction procedure was 50°C for 20 min, 95°C for 10 min, followed by 40 cycles of 95°C for 15 s and 60°C for 30 s. Threshold cycle (Ct value) greater than 38 indicated a positive sample. Each run cycle included known positive and negative control as well as the internal control.

Information obtained from all patients managed at the centre included demographics, presenting symptoms and premorbid ailments. The blood group was obtained as part of the laboratory work up for all patients. The ABO phenotype was carried out by tile grouping, the method

used during emergency for ABO blood group determination in our setting. The tile grouping done during emergency situations are thereafter confirmed by tube grouping in the hospital setting. Confirmation by tube grouping was not done in this instance because the blood group determination was for record purpose and not for blood transfusion. Blood donors of a teaching hospital in a neighbouring state in South Western Nigeria, a city about 140km from the study centre, served as controls [13].

## Statistical analysis

The ABO frequencies of the patients were compared with that of the blood donors. The presenting symptoms were coded as respiratory, gastrointestinal and various combinations including respiratory and gastrointestinal. In addition, the participants were categorized into symptomatic and asymptomatic cases. A cross tabulation of the coded symptoms was carried out with the four ABO phenotypes and with the blood group coded as 'O' and 'non-O' blood group. The coded symptoms were also compared with the blood group coded as presence of anti-A antibody in the serum (blood groups O and B) and absence of these antibodies (blood groups A and AB). Chi-squared test was used to compare the association of the frequencies of the ABO of the participants with that of the blood donors and also to test for association between the coded blood groups and symptoms. Logistic regression was used in a model to test if age, gender or the different coded blood groups could predict the likelihood of an infected person developing symptoms. The level of significance for all the tests was set at 5%. Data were entered and analysed using STATA version 13 (StataCorp, College Station, Texas, USA).

## Results

A total of 302 participants were analysed, of which 179 (59.3%) were symptomatic and 123 (40.7%) were asymptomatic. There were 202 (66.9%) males and 100 (33.1%) females with a mean age of  $38.8 \pm 16.1$  years. Five of the participants did not have their blood group recorded and were excluded from the analyses. Respiratory symptoms were experienced by 70 (39.1%) participants, gastrointestinal symptoms by 21 (11.7%) participants while 6 (3.4%) experienced both. Blood group O was significantly less represented among the patients ( $P < 0.01$ ) compared with donor controls while blood groups B and AB were significantly more represented ( $P < 0.01$ ,  $P = 0.03$  respectively). There was no significant difference between the A phenotype among the COVID-19 patients and the donor population ( $P = 0.28$ ). (Table 1). A comparison of those

**Table 1** ABO Phenotypes of COVID-19 patients in an Isolation Centre in Nigeria compared with a Blood Donor Population Distribution

ABO blood group	COVID-19 patients (N = 302)	Donor population (N = 9138)	$\chi^2$	P
A	58 (19.1%)	2098 (23%)	1.19	0.28
AB	17 (5.6%)	307 (3.3%)	4.85	0.03
B	77 (25.3%)	1771 (19.4%)	19.72	<0.01
O	145 (47.7%)	4962 (54.3%)	23.61	<0.01

Five COVID-19 patients did not have their blood groups recorded.

with or without corresponding antibodies (A or B) in their sera showed that, patients with anti-B (groups A and O) were significantly less represented than those without anti-B (B and/or AB): A and AB ( $P < 0.001$ ), B ( $P = 0.002$ ), AB ( $P = 0.01$ ). However, patients with anti-A showed no significant difference compared with those without anti-A except for the AB population which showed more infection rate ( $P = 0.04$ ) (Table 2). The ABO distribution of symptomatic and asymptomatic patients is shown in the Figure 1. There was no significant difference between the blood group distribution between symptomatic and asymptomatic patients ( $\chi^2$  (3, N = 302) = 2.29;  $P = 0.51$ ) but symptomatic patients with anti-A (groups B and O) were more represented than asymptomatic patients with anti-A ( $\chi^2$  4.89;  $P = 0.03$ ). There was no difference between symptomatic and asymptomatic patients with anti-B (Table 3). Blood group was not associated with whether the patients had respiratory ( $\chi^2$  (1, N = 302) = 1.03;  $P = 0.31$ ) or gastrointestinal symptoms ( $\chi^2$  (1, N = 302) = 1.6;  $P = 0.2$ ). Age modestly predicted if a patient infected with SARS-CoV-2 would become symptomatic (OR 0.98 (95%CI 0.96, 0.99;  $P = 0.01$ ). Gender, blood group or blood group recoded as 'O' and 'non-O' showed no association in the model ( $P = 0.98$ ;  $P = 0.96$ ;  $P = 0.61$  respectively).

**Table 2** Comparisons of the presence/absence of antibodies (anti-A, anti-B) in the serum of patients and donors

	ABO Blood Group	Donor Control, n (%)	COVID-19 Patients, n (%)	$\chi^2$	P
With anti-B	O and A	7060 (77.3)	203 (68.4)	12.88	<0.001
	B and AB	2078 (22.7)	94 (31.6)		
Without anti-B	B	1771 (19.4)	77 (25.9)	9.3	0.002
	AB	307 (3.4)	17 (5.7)	6.6	0.01
With anti-A	O and B	6733 (73.7%)	222 (74.7)	0.17	0.68
	A and AB	2405 (26.3)	75 (25.3)		
Without anti-A	A	2098 (23)	58 (19.5)	1.39	0.24
	AB	307 (3.4)	17 (5.7)	4.11	0.04

## Discussion

The findings of this study showed that blood group O is protective against COVID-19 infection while blood groups B and AB are risk factors. Expectedly, we also noted that patients with anti-B (Blood groups O and A) in their serum were less likely to be infected by the virus and that patients with anti-A (blood groups O and B) were more likely to become symptomatic from the infection. Unlike other studies, we did not find susceptibility of group A to the infection but rather an underrepresentation suggesting a possible protection, though this did not reach a significant level. The male gender was twice more susceptible to infection by the virus than the female gender, similar to the finding of male susceptibility by other studies [14, 15]. Contrary to other studies, the mean age for our patients was 39 years, which is at least a decade younger than found in most studies [14, 15].

The protection conferred by the group O phenotype was reported by studies which compared ABO blood group frequencies in COVID-19 patients with the community blood donor population, and these studies at the same time observed susceptibility to the infection by blood group A [2, 3]. A study which compared ABO frequencies between COVID-19 patients and other hospitalized patients found no significant difference between both groups [16]. The findings of our study differed from other studies by the observation of susceptibility in both groups B and AB rather than in group A only. This observed difference is more likely to be region specific and therefore could be genetic or influenced by environmental factors. We opined that these findings might be similar in other African or Black populations where blood group O is in the majority [10–12]. The findings of no difference between the observed and expected ABO distribution in Blacks and Hispanics (with high blood group O prevalence) compared with Whites where the observed frequency was significantly different from the expected [17] supports this hypothesis. This shows that infection by the virus differed between Blacks and Hispanics with high frequencies of the O phenotype compared with Whites with low O phenotype.

Analysis of the association between ABO distribution and COVID-19 infection by looking at the presence or absence of the corresponding antibodies confirms the difference between our studies and previous published data. Our study found the prevalence in those with anti-B to be significantly different from those without which again is at variance with previous studies which found such a difference between those with and without anti-A [7]. The protection conferred by blood group O has been attributed to circulating anti-A antibodies of the IgG type which could interfere with the virus-cell adhesion process [18]. Similarly, anti-B from group O is often IgG in contrast to

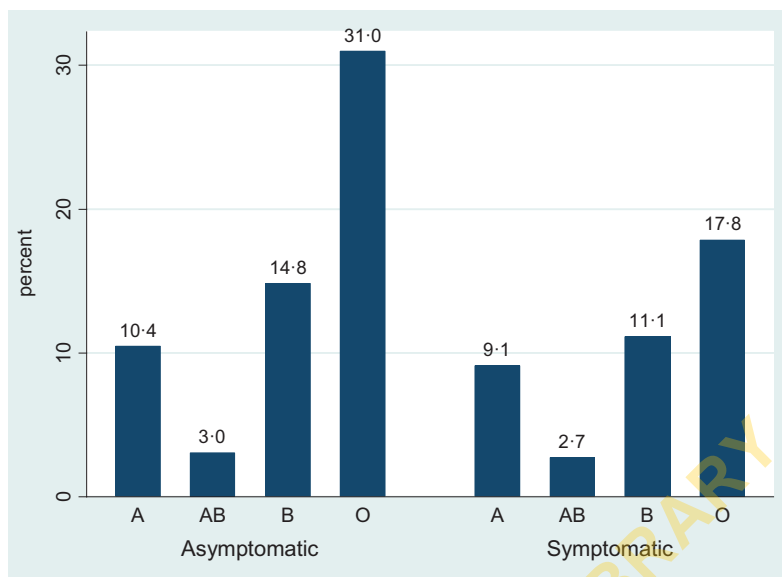


Fig. 1 A comparison of ABO phenotypes between symptomatic and asymptomatic patients with SARS-CoV-2.

Table 3 Comparisons of the presence/absence of antibodies (anti-A, anti-B) in the serum of symptomatic and asymptomatic patients

	ABO Blood Group	Symptomatic Patients, n (%)	Asymptomatic Patients, n (%)	$\chi^2$	P
With anti-A	O and B	136 (77.3%)	86 (71.1)	4.89	0.03
	A and AB	40 (22.7)	35 (28.9)		
Without anti-A	A	31 (17.6)	27 (22.3)	1.17	0.28
	AB	9 (5.1)	8 (6.6)	0.46	0.5
With anti-B	O and A	123 (69.9)	80 (66.1)	0.47	0.49
	B and AB	53 (30.1)	41 (33.9)		
Without anti-B	B	44 (25)	33 (27.3)	0.28	0.60
	AB	9 (5.1)	8 (6.6)	0.38	0.54

antibodies from group A or B which are mostly IgM. It is thus likely that as suggested for anti-A, the anti-B from blood group O is more potent against the virus than anti-B from blood group A [7, 19]. Hence, the protection accorded to patients with blood group O would differ from that from blood group A since the anti-B is mostly of the IgM type. This could be an explanation for the non-significant level of protection attributable to patients with blood group A, though it could also be argued that the reason for the non-significant difference is that the study was not sufficiently powered to detect a difference.

Another peculiarity of our study is that it clearly shows that blood group AB is a risk factor for COVID-19 infection, and this difference compared with the blood donor population is statistically significant ( $P = 0.03$ ). It is not surprising that the AB phenotype is susceptible to

infection by the virus since individuals who have the AB blood group lack either anti-A and anti-B. This is also supported by the difference in the level of significance shown to blood group AB by those with anti-A ( $P = 0.04$ ) and those with anti-B ( $P = 0.01$ ) (Table 2). Though other studies showed increased risk of blood group AB to infection and severity of the disease, but these did not reach a statistically significant level [5, 19]. In the review of 28-day mortality which included the different races in the USA, Leaf RK et al reported similar mortality rate across the races but the graph showed a clear increased mortality in Blacks with the AB phenotype [17]. This would further support our hypothesis of the ABO phenotype showing a different trend in the response of Blacks to COVID-19 infection. A response which is likely linked to the higher prevalence of the O blood group and possibly more potent anti-B (haemolysin).

The strength of this study is that 98% of the participants had their blood group documented as well as the availability of information for individuals who were infected by the virus but were asymptomatic. The limitation of the study is the relatively smaller study size, and that it is a study from a single centre in comparison with other related studies. Though the choice of the donor population for this study was from a study carried out in another city which could be a limitation, the city is however in the same geographical location and of the same tribe as our community. The results also are similar to that of another donor population in the eastern part of the country [20] and that of a well-baby clinic from our institution [21] suggesting that the ABO prevalence is

more representative of that of the general population. Furthermore, the selective choice of blood group O as donors, done elsewhere, [16] is not practiced in Nigeria. It is therefore unlikely that the donor population was enriched by group O blood donors.

## Conclusion

This study confirmed the association between ABO phenotypes and COVID-19 infection and the severity of infection. It also confirms the protection of blood group O from infection. However, contrary to other studies, we found that individuals with blood groups B and AB were more susceptible to the disease. The higher prevalence of blood group O and the presence of beta haemolysins which are very potent are possible reasons for a lower infectivity by the SARS-CoV-2 virus and severity of the COVID-19 disease in communities like ours.

## Acknowledgements

The authors acknowledge the support of the Oyo State Government and the Oyo State COVID-19 Task Force

under the chairmanship of Engineer Seyi Makinde FNSE, the Executive Governor of Oyo State, for equipping the Infectious Disease Centre, Olodo with appropriate laboratory facilities including a robust laboratory information system (LIS) all of which made it easy to conduct this study.

## Conflict of interest

The authors have no conflict of interest.

## Author contributions

TOA, AF conceptualized the study; TRK, TOA designed the study; TRK, OIF, ASA analysed and interpreted the data. TRK prepared the first draft, and all authors approved the final draft.

## Funding

The Infectious Disease Centre, Olodo, Ibadan is fully funded by the Government of Oyo State and the patients do not pay for any of the services.

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