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ABO Blood Groups and susceptibility to Covid19 in African Population

[1]A Sall, [1]BD Sanon, [2]MB Diakhaby, [1]A Drame, [1]D Samb, [3]L Fortes, [4]M Seck, [4]BF Faye, [4]AO Toure, [4]S Diop

[1]Laboratory of Hematology, Dalal Jamm Hospital. Dakar-Senegal

[2]Laboratory of Virology, Dalal Jamm Hospital. Dakar-Senegal

[3]Epidemic Treatment Center, Dalal Jamm Hospital. Dakar-Senegal

[4]National Blood Transfusion Center. Dakar-Senegal

Corresponding Author: A Sall, Laboratory of Hematology, Dalal Jamm Hospital. Dakar-Senegal.

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Abstract

Background: SARS-CoV-2 infection is characterized by high contagiousness, morbidity and mortality which are accompanied by various biological changes, particularly hematological changes. Its association with blood groups has been revealed by several authors. Our overall goal was to find a link between ABO blood groups and COVID-19 in African population

Patients and Methods: We conducted a prospective, descriptive and analytical study carried out in the epidemic treatment center and the hematology laboratory of the Dalal Jamm hospital in Dakar. All patients aged over 18 years, and tested positive for SARS-CoV-2 infection by molecular biology, were included. Clinical data was provided by attending physicians.

The complete blood count was performed on NX1500 (Sysmex Japan) and blood grouping was done on the Ortho device (Ortho, Clinical Diagnostic, USA).

The data were compiled using the Microsoft Excel. Statistical analyses were performed on SPSS. The confidence interval of 95% was used for the estimations and statistical tests were considered significant when the p-value was below 0.05

Results: A total of 259 patients were recruited including 157 males and 102 females with a mean age of 56.7 years. The comorbidities were dominated by high blood pressure (28.46%) and diabetes (13.08%). The non-severe forms represented almost three-quarters of our population. The distribution of ABO groups in our population showed a predominance of group O (49.57%) followed by groups A (28.21%), B (17.09%) and AB (5.13%) (O> A> B> AB). This same formula was found

in our reference sample. However, blood group A was more represented in our population compared to that of reference with a difference at the limit of significance (p = 0.055). Regarding blood groups according to clinical forms, we found that group A had twice the risk of developing a severe form [OR = 1.95; CI = 1.06-3.57; p-0.032] while the O group would be protective [OR = 0.76; CI = 0.59-0.89; p-0.02]. This trend was however lost on multivariate analysis.

Conclusion: Our study revealed that blood group A was linked to the severity of COVID-19 but this result remains to be confirmed with much larger sampling.

Keywords: ABO blood groups; SARS-CoV-2 infection; Clinical forms

Introduction

After the SARS outbreaks in 2003 in China and the MERS-CoV outbreak in 2012 in the Middle East, the world faced a new coronavirus: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The pneumonia caused by SARS-CoV-2 has been called coronavirus disease 2019 (COVID-19).

Very quickly, several studies suggested that advanced age and male sex were 2 risk factors for susceptibility to COVID-19 [1,2]. Additionally, people with cardiovascular disease, respiratory disorders, or diabetes were more prone to developing severe disease.

Another risk factor was then revealed: the ABO blood group. One of the first studies carried out in Wuhan, China, had suggested that there was an association between blood group A and COVID-19 [3]. Other authors have reported that patients with blood group A had a higher risk of acquiring SARS-CoV-2 infection compared to non-A groups; while group O patients had a significantly lower risk of infection [4]. However, other authors had found a high risk for blood groups B and AB [5,6].In addition to its association with SARS-CoV-2 infection, ABO blood groups are believed to be linked to the severity of the disease. Authors had revealed that patients with blood groups A and AB had a higher risk of developing a severe form compared to other groups [5,7].Faced with these contradictory results, we set ourselves the objective of researching in an African population, on the one hand, the link between ABO blood groups and susceptibility to COVID-19, on the other hand the impact of ABO blood groups on the severity of the disease.

Patients and Methods

We performed a prospective case-control study that took place over a period of 6 months (January-June 2021) at the Dalal Jamm hospital in Dakar. This hospital housed the largest covid19 treatment center in Senegal. This included patients hospitalized with a SarsCov2 infection documented by RTPCR, over 18 years of age and having signed the free and informed consent form. Patients with respiratory distress without molecular biology evidence were not included. The controls consisted of healthy blood donors recruited from the Dakar blood transfusion center during the same study period. For each patient, we studied age, sex, comorbidities, clinical signs. The clinical signs allowed us to classify the patients into 2 groups:

- Patients with a non-severe form (mild and moderate clinical forms)
- Patients with a severe form (serious and severe clinical forms)

The biological parameters studied were, the complete blood count performed on XN1500 *(Sysmex, Japan)* and the ABO blood group. To do this, a tube sample containing EDTA was taken from each patient. The blood typing was carried out using the globular method

of Beth Vincent for the search for antigens on the surface of red blood cells and that of Simonin for the search for antibodies in the serum. Each test was done by 2 different technicians and a perfect match of the 2 methods was required for the validation of a blood grouping.

We used the gel filtration column agglutination technique on the Ortho automatic blood typing machine (Ortho Clinical Diagnostics, USA).

Our study was approved by the Research Ethics Committee (REC) of the Faculty of Medicine, Pharmacy and Odontology of the University Cheikh Anta Diop in Dakar (UCAD) and all patients signed a free and informed consent before participating in the study.

Data were collected using Microsoft Excel Spreadsheet and then transferred to SPSS v.20 software for data management and statistical analysis. Continuous variables were described as mean with standard deviation or as median with inter quartile range if the variable was not normally distributed. Qualitative variables were described as proportion. For the bivariate analysis, difference between means was tested using the student t-test or the Mann–Whitney non-parametric depending on the normality assumption. Association between categorical variables was performed using the Pearson chi-square test or the Fisher exact test. The estimations were done within a 95 % confidence level and the entire statistical tests were significant when the p value was below the threshold level of 0.05.

Results

A total of 259 patients infected with SARS-CoV 2 were recruited during the study period. Patients with a severe form represented just over a quarter of the study population and there were 191 patients with a non-severe form.

The mean age of the patients was 56.7 years [18 to 95 years]. This age was much greater in patients with a severe form of the infection compared to other patients (69 vs 56, p <0.001). Patients over 60 years of age represented 73.5% of patients with a severe form against only 24% for patients with mild infection (p <0.001).

The sex ratio of our study population was 1.5. This male predominance was found regardless of the clinical form; however, no link was found between male sex and disease severity (p = 0.15) (Table 1).

The most frequent comorbidities found in our patients were hypertension (28.5%), followed by the combination of diabetes and hypertension (18.5%), but 20% of patients presented no morbidity. The severe form of the infection was, however, clearly associated with diabetes (p = 0.008).

Table 1: Epidemiological data of patients.

Clinical Forms Parameters	Sévère (n=68)	Not sévère (n=191)	P value
Epidemiological Data			
Médiane Age (IQR)	69 (59-75)	56 (40-68)	<0.001
Age Groups (years)			
18-44 45-59 >=60	4 (5.88%) 14 (20.58%) 50 (73.52%)	62 (32.46%) 46 (24.08%) 46 (24.08%)	<0.001
Sex			

Females	23 (34.33%)	79 (41.36%)	0.15
Males	45 (65.67%)	112 (58.64%)	

The distribution of blood groups O, B and AB was almost similar in the 2 groups (patients and controls). A difference was however noted for blood group A which was more frequent in patients infected with SarsCov2 with 28.2% than in healthy blood donors with 23.5%; with a difference at the limit of significance (p = 0.055) (Table 2).

Table 2: Distribution of ABO blood groups in patients and healthy blood donors

ABO Blood groups	Patients (N=234)	Controls (Blood donors) (N=19486)	P-value
A	66 **(28.21%)**	4586 (23.53%)	0.055
AB	12 (5.13%)	799 (4.10%)	0.255
B	40 (17.09%)	3857 (19.79%)	0.870
O	116 (49.57%)	10244 (52.57%)	0.840

Regarding the bivariate analysis of the distribution of ABO blood groups according to clinical forms, we found that blood group A was associated with the severe form of the infection. Blood group A doubled the risk of developing a severe form (OR = 1.95; CI = 1.06 - 3.57; p = 0.032) while blood group O would be rather protective (OR = 0.76; CI = 0.59 - 0.89; p = 0.002). No difference was found for B and AB blood groups (Table 3).

Table 3: Distribution of blood groups according to clinical forms.

Clinical Forms Groupe ABO	Sévère (N=68)	Not sévère (N=166)	OR* (CI*95%)	p- value
Group not A	42 (61.76%)	126 (75.90%)	Réf	Réf
Group A	26 (38.24%)	40 (24.10%)	1.95 (1.06 – 3.57)	0.032*
Group not AB	67 (98.53%)	155 (93.37%)	Réf	Réf
Group AB	1 (1.47%)	11 (6.63%)	0.21 (0.02 – 1.66)	0.18
Group not B	54 (79.41%)	140 (84.34%)	Réf	Réf
Group B	14 (20.59%)	26 (15.66%)	1.39 (0.67 – 2.87)	0.44
Group not O	41 (60.29)	77 (46.39%)	Réf	Réf
Group O	27 (39.71)	89 (53.61%)	0.76 (0.59 – 0.89)	0.02*

*OR: odds ratio; *CI: Confidence Interval

Multivariate analysis was performed with adjustment for several variables such as age, sex, clinical form, clinical signs, Neutrophils to lymphocyte ratio (NLR) (Table 4). Although a trend seems to show that group A is associated with the penetrance of covid 19 (AOR = 2.23; CI 95% = 0.801 - 6.21; p = 0.085), it was not significant.

Table 4: Multivariate Analysis.

Blood Groups	Sex		Fever	Dyspnea	Clinical Forms		NLR	AOR	P-value
	Male	Female			Not Severe	Sévère			
O	71 (51.45%)	45 (47.47%)	29 (39.19%)	27 (45.76%)	89 (53.61%)	27 (39.71%)	6.92 ±9.48	Réf	Réf
A	45 (32.35%)	21 (22.11%)	27 (36.49%)	16 (27.12%)	40 (24.10%)	26 (38.24%)	7.12 ± 8.55	2.23 (0.801 – 6.21)	0,085
AB	1 (0.72%)	11 (11.58%)	3 (4.05%)	1 (1.69%)	11 (6.63%)	1 (1.47%)	4.39 ±3.75	0.66 (0.063 – 7.1)	0,73
B	22 (15.94%)	18 (18.95%)	15 (20.27%)	15 (25.42%)	26 (15.66%)	14 (20.59%)	5.16 ±6.5	1.83 (0.53 – 6.28)	0,33

Discussion

COVID-19 is a highly contagious infectious disease. Appeared in China in the city of Wuhan in December 2019, it has spread very quickly across the world, becoming a pandemic since March 11, 2020.

In addition to the risk factors listed in the literature, the ABO blood group could be considered as a risk factor according to several studies with divergent results. It is in this context that we investigated a link between ABO blood groups and susceptibility to SARS-CoV-2 infection in Senegalese population.

The average age was 56.71 years with extremes of 18 to 95 years. Just over half (51.3%) of our patients were over 60 years old as found in most studies [8,9].

A significant association was found between age and severity of SARS-CoV-2 infection (p <0.001). This link could be explained by the weakening of the immune system in the elderly on the one hand and to an increased inflammation which promotes extensive viral replication on the other hand. The prolonged responses to this inflammation therefore cause considerable damage to the lungs and often to other organs.

We found a male predominance with 60.47% and a sex ratio of 1.5. This male predominance has been found in several other studies [10,11]. Are men therefore more susceptible to infection with SARS-CoV-2? According to Grass Elli et al. [12], this predominance of men could be explained by female sex hormones which may play an anti-inflammatory role. They are potential defense agents of the immune system because they are able to: stimulate the production of antibodies and promote the repair of certain respiratory cells. In addition, they are believed to inhibit the ACE2 receptor, which is the pathway for SARSCoV-2 to enter cells. However, no link was found between the gender and the severity of the infection (p = 0.15) unlike the study by Jin et al [13].

In this present study, diabetes was strongly associated with severe infection (p = 0.008). The susceptibility in people with diabetes could be due to the fragility of their innate immunity, both humoral and cellular. In addition, inflammation biomarkers (Il-6, CRP, D-dimer) are higher in diabetic subjects resulting in greater cytokine storm and more rapid disease progression [14].

Regarding blood groups, our population consisted mainly of group O (49.5%) followed by group A (28.21%) while groups B and AB represented only 17.09 and 5.13% (O> A > B> AB). This same formula was found in our reference sample, namely a predominance of group O (52.57%) followed by groups A (23.53%), B (19.79%) and AB (4.10%). However, group A was more represented in patients with covid19 with 28.5% compared to the control population (23.5%) (p-0.055). The latter could be significant if the size of our population were larger.

Danish authors [15] had found a susceptibility for group A (OR = 1.09; 95% CI, 1.04-1, 14) while group O was protective (OR = 0.87; CI at 95%, 0.83-0.91).

Although the majority of studies agree on this same trend, divergent results have been highlighted by other studies such as the one performed on 285 patients with COVID-19 in Shenzhen. The latter had shown an increased risk of infection for the AB group (OR 2.008; CI=1.427 ~ 2.824) [16]. Padhi et al. [17] in India had also found higher probabilities of infection with SARS-CoV-2 for groups B and AB.

We also investigated the link between blood type and disease severity. In our study, blood group A was at higher risk of developing a severe form of the infection [OR = 1.95 (1.06-3.57); p-0.032]. On the other hand, the O group would be protective [OR = 0.7 (0.59-0.89); p-0.02]. No association was observed for groups AB and B.

Our multivariate analysis revealed no association between blood group and clinical forms after adjustment for gender, fever, cough, asthenia, hemoglobin level and NLR ratio. These results were identical to those obtained in the study by Latz et al. [18] who found no correlation between blood group and clinical status after adjustment for gender, race, chronic kidney disease, coronary artery disease, history of stroke and diabetes mellitus.

Several hypotheses have been put forward to explain the mechanism that could link the blood group to SARS-CoV-2 infection. Authors had suggested that the anti-A antibody inhibited the interaction between SARS-CoV-1 and the ACE2 receptor [19]. However, Lu et al. [20] had reported a structural similarity between the receptor binding domains of SARS-CoV-1 and SARS-CoV-2. This shows that the anti-A antibody could inhibit the interaction between SARS-CoV-2 and the host cell.

However, our study has certain limitations: small sampling, population restricted to adults and reference population not recruited under the same conditions as patients.

In perspective, multicenter studies should be conducted to shed light on the mechanisms by which blood groups may promote or worsen SARS-CoV-2 infection.

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