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SHORT COMMUNICATION

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# Histo-blood group A is a risk factor for severe COVID-19

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## Abstract

**Objectives:** Evaluate the impact of ABO histo-blood group type on COVID-19 severity.

**Background:** ABO histo-blood type has been associated with different outcomes in infectious diseases. It has also shown a higher proportion of type A patients with SARS-CoV-2. In this observational study, extracted from an ongoing clinical trial on the efficacy of convalescent plasma transfused in COVID-19 patients, we describe the impact of ABO blood type on the risk of developing severe COVID-19.

**Materials and Methods:** Seventy-two consecutive patients (37 type A, 23 type O, 11 type B, 1 type AB) with severe (respiratory failure) COVID-19 were included. Control group was composed of 160 individuals randomly selected from the same populational basis.

**Results:** Blood group A was overrepresented (51.39%) in the patient group in relation to the control group (30%), whereas blood group O was less represented (31.94%) in patient than in control group (48%). Odds ratio (A vs. O) was 2.581 (1.381–4.817), CI 95%; $p = 0.004$. Also, blood group A patients appeared to have more severe disease, given by the scores of the Sequential Organ Failure Assessment and Simplified Acute Physiologic Score 3 ($p = 0.036$ and $p = 0.058$, respectively).

**Conclusion:** Histo-blood type A is associated with a higher risk of developing severe COVID-19 in relation to blood type O.

KEYWORDS
ABO blood group, COVID-19, SARS-CoV-2

## 1 | INTRODUCTION

The ABO histo-blood group consists of three main alleles, the codominants A and B and the recessive O, controlled by a single gene located in chromosome 9q34. The biologic functions of the antigens A and B and the antibodies anti-A and anti-B are mostly unknown. Some traits are associated with specific blood types. For instance, blood type O individuals present lower von Willebrand factor (VWF) and coagulation factor (F) VIII plasma levels compared to non-O blood type subjects, which is also the explanation for the association with lower risk of venous thrombosis[1] and higher risk of haemorrhage observed in blood type O individuals.[2]

ABO blood type has also been associated with different outcomes in some infectious diseases. Group O patients with malaria by *Plasmodium falciparum* have better outcomes than group A patients.[3] Also, blood type A is associated with increased risk for acute respiratory

  

**TABLE 1** Baseline and clinical characteristics of study cohorts

| | Group A (37) | Group O (23) | *p* value |
|---|---|---|---|
| Age (years), mean ± SD | 60.19 ± 13.53 | 56 ± 15.78 | 0.279 |
| Male (%) | 23 (62.16) | 13 (56.52) | 0.788 |
| Comorbidities | | | |
| Hypertension | 24/37 (64.86%) | 16/23 (69.57%) | 0.783 |
| Diabetes mellitus | 21/37 (56.76%) | 10/23 (43.48%) | 0.427 |
| BMI ($kg/m^2$) ± SD | 33.25 ± 8.733 | 33.51 ± 7.306 | 0.91 |
| Renal replacement therapy | 11/32 (34.4%) | 7/18 (38.9%) | 0.768 |
| SAPS-3 score, mean ± SD | 65.17 ± 15.05 | 56.95 ± 16.21 | 0.058 |
| SOFA score, mean ± SD[a] | 10.5 ± 3.917 | 8.1 ± 4.154 | 0.036 |
| $PaO_2/FiO_2$ ratio, median (range)[a] | 111.7 (50.0–421.3) | 169.8 (64–366.7) | 0.141 |

Abbreviations: BMI, body mass index; SAPS-3 score, Simplified Acute Physiology Score 3; SOFA, Sequential Organ Failure Assessment.
[a]SOFA score and $PaO_2/FiO_2$ ratio were assessed on admission to the study. The time from symptoms onset till the admission to the study did not differ between groups (data not shown).

**TABLE 2** Distribution of ABO blood group in patients and in controls

| Blood group | Patients (72) | Controls (160) | *p* value |
|---|---|---|---|
| O | 23 (31.94%) | 77 (48%) | 0.004[a] |
| A | 37 (51.39%) | 48 (30%) | |
| B | 11 (15.28%) | 28 (18%) | |
| AB | 1 (1.39%) | 5 (3%) | |

[a]Comparison between types O and A only.

distress syndrome following trauma or sepsis.[4] However, other studies failed to establish a correlation between blood type and mortality in adult patients with acute hypoxaemic respiratory failure secondary to severe sepsis or major trauma under mechanical ventilation.[5]

It has been hypothesised that group O confers a relative protection against SARS-CoV-1 infection.[6] In this study, blood group O healthcare professionals were less susceptible to infection than non-group O individuals. This finding may be attributed to the interference of anti-A antibodies on virus–receptor interaction.[7] More recently, Zhao and colleagues were the first to show that the proportion of blood group A patients infected with SARS-CoV-2 was higher than that observed in healthy subjects (39.3% vs. 32.3%, $p = 0.017$).[8] Additional studies confirmed the association between blood group A and COVID-19 infection.[9–11] However, another study failed to establish an association between blood group and susceptibility to SARS-CoV-2 infection.[12] Herein, we describe the impact of ABO blood type on severe cases of COVID-19 in a population with a high genetic admixture.

## 2 | MATERIALS AND METHODS

This is an observational study in which the data were extracted from an ongoing clinical trial on the efficacy and safety of convalescent plasma administered to patients diagnosed with severe COVID-19 admitted to an intensive care unit (ICU).

Patients from 18 to 80 years of age with severe (respiratory failure) COVID-19, admitted to four hospitals, were included in this study. All patients were intubated at some moment during in-hospital care. Also, all patients required vasopressor medication at some point during admission, and all of them were also treated with corticosteroids (methylprednisolone or dexametasone) during their stay in ICU. Exclusion criteria were disseminated cancer or other conditions believed to significantly reduce short-term life expectancy. The control group for the ABO typing was composed of individuals randomly selected from city neighbourhoods according to their representation, as shown by local population-based serological surveys, and control groups for RhD were first-time blood donors at our institution. Also, we applied two scores of disease severity that predicts mortality in ICU. The Simplified Acute Physiologic Score 3 (SAPS-3) and the Sequential Organ Failure Assessment (SOFA) are scores that employs clinical and laboratory variables to predict mortality in severely ill patients. Although the SAPS-3 is calculated within the first 24 h of admission to the ICU, the SOFA can be used in the admission and every 48 h to reassess the risk of mortality. Higher score indicates higher risk of death.

ABO blood type was determined using standard serologic methods and was performed only after inclusion in this study. We performed descriptive statistics and Fisher's exact test was employed to analyse categorical variables. Continuous variables were evaluated for normality and then tested with Student's *t* test or Mann–Whitney *U* test, as appropriate. Comparison was performed between blood groups O and A only, as the groups B and AB were much less represented. The study was approved by the Institutional Ethics Committee and written informed consent was obtained from all participants.

## 3 | RESULTS

We included in the study 72 consecutive patients with COVID-19, confirmed by RT-PCR, and 160 control subjects (Table 1). The A and

O blood groups had similar baseline (age, sex distribution and body mass index) and clinical characteristics (comorbidities and renal replacement therapy), except for SAPS-3 and SOFA scores, which was higher in blood group A patients than in blood group O ($p = 0.058$; $p = 0.036$, respectively) (Table 1). The distribution of ABO blood groups in patients and in controls is listed in Table 2. Blood group A was an overrepresented patient group in comparison with control group, with an odds ratio of 2.581 (95% CI: 1.381–4.817) ($p = 0.004$). Finally, 4 (5.55%) of the 72 participants were RhD-negative, whereas this characteristic was observed in 12.75% (246 out of 1930) of the population, with an odds ratio of 2.483 (95% CI: 0.9357–6.375) ($p = 0.07$).

## 4 | DISCUSSION

Our study has shown that blood group A predisposes to severe COVID-19, at least in relation to blood group O. More than half the patients with respiratory failure were admitted to ICU at the hospitals, and the patients who participated in this study are of blood A type, a higher proportion than that observed in the general population of the same region. Previous studies suggested that blood group A individuals are more susceptible to infection.[8–10] Besides being more represented in ICU, group A patients seem to be more likely to develop more severe COVID-19, with higher SAPS-3 and SOFA, which, we think, is in accordance with the finding of a higher frequency of blood group A patients in ICU, a supposition that needs to be confirmed at the end of the convalescent plasma study, when the mortality rate in both groups of patients can be compared. Also, group A patients presented a slightly higher percent of male genre, not statistically significant; however, we could not exclude the possibility of a selection bias, as it is known that male patients are supposed to have a worse prognosis. An important observation here is that the population in the region (state of São Paulo) where this study was developed is considered to present a high degree of genetic admixture (Europeans, Africans, Amerindians and Asians), a characteristic probably not common in other countries, such a China, United States, and Europe.

One possible explanation for this finding is the higher plasma levels of VWF and blood coagulation factor VIII (FVIII), a characteristic associated with a higher risk of thrombosis in non-O blood group, such as A type, in relation to group O subjects.[1,13] VWF is a glycoprotein that acts as a molecular bridge between platelets and subendothelial components following a vascular injury. As well as this, VWF modulates inflammation through several mechanisms, such as leukocyte recruitment, resulting in enhancement of the inflammatory process.[14] Another possible explanation is that anti-A antibodies (present in blood type O individuals, but not in blood group A) may interfere with the interaction of SARS-CoV-2 with target cell, as previously demonstrated for SARS-CoV-1.[7] These hypotheses need to be addressed in further studies.

It is also interesting to note that patients from both groups had a high (and similar) mean of body mass index, which is not surprising, as it has been extensively shown that obesity is an important risk factor for COVID-19 severity.

Finally, it seems possible that absence of expression of RhD antigen could be associated with some protection against severe COVID-19; however, sample size is not large enough to derive any conclusion on this issue.

We acknowledge the limitations of our study. For example, the number of patients is relatively small. However, a positive point is that the control group can be considered to be highly representative of the local population.

In conclusion, we have shown that individuals of blood type A are at a higher risk of developing severe COVID-19 in relation to individuals of blood type O, a finding that could quite possibly guide clinicians to adopt more precocious therapeutic and vigilant risk measures for patients of this blood type.

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### CONFLICT OF INTEREST

The authors have no competing interests.

### AUTHOR CONTRIBUTIONS

**Pedro M. M. Garibaldi**: writing; review and editing; data collection. **Luciana C. Oliveira**: writing; review and editing; data collection. **Benedito A. da Fonseca**: writing; review and editing. **Maria A. Martins**: writing; review and editing. **Carlos H. Miranda**: writing; review and editing. **Carlos E. L. Almado**: writing; review and editing. **Dante M. Langhi**: writing; review and editing. **Renato N. Gilio**: writing; review and editing; data collection. **Leonardo C. Palma**: writing; review and editing. **Bruno B. M. Gomes**: writing; review and editing; data collection. **Camila Bottura**: writing; review and editing; data collection. **Larissa C. Barrientto**: writing; review and editing; data collection. **Camila D. Donadel**: writing; review and editing; data collection. **Rodrigo T. Calado**: writing; review and editing. **Gil C. De Santis**: Conceptualization; writing; review and editing (lead); data collection, analysis.

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