COVID-19 and blood groups: A six-months observational study in Ferrara, Italy

Salvatore Greco,[1] Nicolò Fabbri,[2] Alessandro Bella,[1] Beatrice Bonsi,[1] Alessandra Violi,[1] Valeria Fortunato,[1] Maurizio Govoni,[3] Giuseppe Graldi,[3] Angelina Passaro[1,4]

[1]Department of Translational Medicine, University of Ferrara; [2]Department of General Surgery, Ospedale del Delta, Lagosanto; [3]Blood Transfusion Service, University Hospital of Ferrara Arcispedale Sant'Anna, Cona; [4]Medical Department, Unit of Internal Medicine, University Hospital of Ferrara Arcispedale Sant'Anna, Cona, Italy

Abstract

The current literature still gives a little information about the relationships between the ABO blood group system and the immune response to the virus or the different disease outcomes. Hypothesizing the presence of a predisposition by some blood groups to COVID-19, we searched for differences between patients towards the different outcomes of disease. We enrolled 330 inpatients with a diagnosis of COVID-19, determining both their ABO blood group system and Rh factor, collecting demographic, clinical and laboratory data. We searched for relationships with COVID-19 outcomes within an observation period of 180 days (Intensification of Care - IoC, In-hospital death, 180-days mortality). The most frequent ABO blood group was A (45.8%); a minor part was represented by group O (38.8%), B (11.5%), AB (3.9%). As for the Rh factor, 86.7% of patients were Rh-positive. There were no significant differences between blood groups and Rh factors as for age, length of hospital stays (LoS), or Charlson Comorbidity Index (CCI), nor we found significant relationships between the ABO groups and COVID-19 outcomes. A significant relation was found between AB group and IoC (p=0.03) while as for the Rh factor, the patients with Rh factor positive died with less frequency during the stay (p=0.03). Cox regression analyses showed substantial differences in the survival functions concerning the Rh factors.

The Rh factor seems to be involved in the 180-day prognosis. The survival functions of patients with Rh factor positive show, in fact, significantly better curves when compared to those with Rh factor negative.

Introduction

Since the spread of Coronavirus Disease 19 (COVID-19) breakthrough in January 2020, many studies have analyzed the characteristics of SARS Coronavirus 2 (SARS-CoV-2). The novel coronavirus associated pneumonia has rapidly become a clinical concern worldwide because of the high contagiousness of the virus itself and as of March 2021, more than 116 million patients have been found with SARS-CoV-2 infection confirmed with at least one oro- and naso-pharyngeal positive swab; the global mortality rate is about 2.2% worldwide.

The pathogenesis of the severe form of COVID-19 is still poorly understood but a higher mortality rate is strongly associated with older age and male sex.[1,2] Patients usually presented with 1 or more comorbidities such as hypertension, diabetes and cardiovascular diseases even if it is still not clear how such illnesses determine the progression of severe COVID-19.[3–5] Clinical manifestations of COVID-19 include fever, cough, arthralgia, myalgia, asthenia, headache, upper respiratory tract symptoms and digestive symptoms (such as nausea, diarrhea, and vomit). The first presentation can be, though, very heterogeneous: up to 80% of patients will have mild influenza-like symptoms, while up to 15% of patients will outset with a severe form of pneumonia. The acute respiratory distress syndrome (ARDS) linked to SARS-CoV-2 infection and consequent to the cytokine storm, remains the first cause of death in patients with COVID-19.[6]

Some researchers have sought for relationships between this viral infection and patients' blood group. Their studies were based on the fact that some viruses such as rotavirus, noroviruses, dengue virus, Norwalk virus and hepatitis B virus showed with blood group.[7–10] Moreover, other studies on SARS-CoV demonstrated the existence of a relationship between infection risk and blood types, suggesting how the blood group O was somehow protective against SARS-CoV-1 infection.[11,12]

A recent multicenter case-control study, conducted in Italy and Spain on 1980 patients hospitalized with severe COVID-19, has contributed to detect a susceptibility locus on chromosome 3 which could describe involvement of the ABO blood group system in COVID-19.[13]

How the blood group interferes with immune system answers in SARS-CoV-2 infections remains unclear; the main goal of this study is to examine the existing relationships between the ABO blood group system and the Rh factors with the possible outcomes of patients hospitalized for COVID-19 including a six-months observation period since hospital admission.

Correspondence: Angelina Passaro, Department of Translational Medicine, University of Ferrara, and Medical Department, University Hospital of Ferrara Arcispedale Sant'Anna, Via Aldo Moro, 8 – 44124, Cona, Ferrara, Italy.
Tel.: +39.0532.236291.
E-mail: psn@unife.

Key words: Coronavirus, COVID-19, blood group, ABO, Rh factor.

Acknowledgements: We would like to dedicate our sincere thanks to all the members of the medical staff that is still participating in the fight against this pandemic, to all the extremely skillful and valuable nursing staff members as well as our assistance personnel, every day working on the frontline. Special thanks to the directors of the Internal Medicine Units where our research took place: Giovanni Zuliani MD, PhD, director of the "University Internal Medicine" department of "Arcispedale S.Anna" in Cona (Fe), Roberto Manfredini MD, PhD, director of the "Clinical Medicine" department of "Arcispedale S.Anna" in Cona (Fe) and Stefano Parini, MD, director of the "Internal Medicine" department of "Ospedale del Delta" in Lagosanto (Fe).

Contributions: SG, NF, AB, BB: acquisition, analysis and interpretation of data; drafting the article. AV, VF: acquisition and analysis of data. MG, GG: revising the article critically for important intellectual content. AP: the conception and design of the study; drafting the article and revising it critically for important intellectual content, final approval of the version to be submitted.

Conflict of interest: The authors declare no potential conflict of interest.

Funding: None.

Ethics approval: Received.

Received for publication: 12 April 2021.
Accepted for publication: 25 May 2021.

Hematology Reports 2021; 13:9177
doi:10.4081/hr.2021.9177

Materials and Methods

Study design and subjects' enrollment

This is a multicenter, retrospective cohort study. We enrolled 330 adult inpatients (≥18 years old), consecutively hospitalized in our two main Hospitals: Arcispedale "S.Anna" in Cona (Fe) and "Ospedale del Delta" in Lagosanto (Fe), by 13 June 2020. They were diagnosed with SARS-CoV-2 infection, determined by at least one viral RNA detection at oro- and naso-pharyngeal swab. The 330 patients had all origins from northern Italy and there was no consanguinity among them.

The ABO blood group and the Rh factor were both determined with the Type&Screen determination or, if already determined during previous hospital stays, they were taken by the electronic registries of the Blood Transfusion Service. The observation period did not stop at the time of hospital dismission but went on (in the case of survival) until the 180th days since hospital admission.

We followed STROBE guidelines (Strenghtening the Reporting of Observational Studies in Epidemiology) for reporting observational studies as for the compilation of this manuscript.

The local Ethics Committee approved the protocol of this study (code: 520/2020/Oss/AOUFe).

Statistical analysis

Data analyses were performed by using SPSS 26.0 (IBM SPSS Statistics, IBM Corporation) software. The normal distribution of the continuous variables was analyzed using Kolmogorov-Smirnov and Shapiro-Wilk tests. Variables not normally distributed were log-transformed before entering the parametric statistical analyses. Categorical variables were summarized by using frequencies and percentages, and continuous data were presented as mean± standard deviation (SD). The Mann-Whitney U test was used for continuous variables, and the $\chi 2$ test or the Fisher exact test was used for categorical variables. The Bonferroni correction for multiple comparisons was used when necessary.

The Cox regression analyses were performed for describing the survival curves of the groups of patients according to the blood group or to their Rh factor.

A multivariate logistic regression analysis was performed for evaluating the predictive role of the variables that were found to be significantly different between groups in the univariate analyses. All $p<0.05$ are considered statistically significant.

Results

From March 15 to June 13, 2020, 330 patients were hospitalized in our two main hospitals of Ferrara province dedicated to COVID inpatients. All of them received a laboratory diagnosis of SARS-CoV-2 infection, confirmed by at least one viral RNA detection at the oro- and naso-pharyngeal swab.

We determined both their ABO groups and Rh factors, describing then all demographic, anamnestic and clinical characteristics of the inpatients. First, we tried to check whether statistically significant differences between the groups of patients existed in terms of age, length of stay (days) and Charlson Comorbidity Index (CCI) calculated for every inpatient: this index is considered one of the best ways of categorizing comorbidities of patients and it was based on the International Classification of Diseases (ICD) diagnosis codes found in administrative data, such as hospital abstracts data.

The most frequent ABO blood group, in our cohort of patients, was type A, with a total of 151 cases (45.8%), 128 patients were type O (38.8%), 38 type B (11.5%) and 13 were type AB (3.9%). These numbers do not differ from those of Northern Italy blood group register (Gimema foundation data, https://www.gimema.it/diffusione-dei-gruppi-sanguigni/), where the most prevalent blood group is A (44%), followed by group O (40%), group B (11%) and group AB (5%).

As for the Rh factor, 286 patients were Rh-positive (86.7%), while 44 (13.3%) were Rh-negative and these percentages are similar to those of our Country (85% for Rh-positive *vs*. 15% of Rh-negative, Gimema foundation data, https://www.gimema.it/diffusione-dei-gruppi-sanguigni/). The mean age of the whole population was 74±16 years and we found no significant differences between groups in terms of age. We analyzed then the length of stay, LoS, (mean time 21±16 days), finding no differences between groups for ABO blood group and Rh factor (Tables 1 and 2).

We searched then for relationships between the ABO groups and the main outcomes of SARS-CoV-2 infection

Table 1. Demographic, anamnestic and clinical data of patients divided for AB0 blood group.

Blood group (N=330)	N. (%)	Age (years ± SD)	Min-max	LoS (days ± SD)	Min-max	CCI (points)	Min-max	P value α	P value β	P value π
Type O	128 (38.8)	74±16	19-96	22±16	1-80	2.3±2.4	0-11	0.56	0.84	0.23
Type A	151 (45.8)	74±15	24-97	21±15	1-92	2.0±2.3	0-11	0.56	0.84	0.23
Type B	38 (11.5)	76±16	29-97	20±18	1-75	2.7±2.4	0-8	0.56	0.84	0.23
Type AB	13 (3.9)	79±17	40-97	22±20	6-77	2.9±2.4	0-8	0.56	0.84	0.23
Total	330	74±16	19-97	21±16	1-92	2.3±2.3	0-11	0.56	0.84	0.23

With "LoS" it is meant the duration of hospital stay. "CCI" represents the Charlson Comorbidity index. α=age differences between ABO groups; β=LoS differences between ABO groups; π=CCI differences between ABO groups.

Table 2. Demographic, anamnestic and clinical data of patients divided for Rh factor.

Rh (N=330)	N. (%)	Age (years ± SD)	Min-max	LoS (days ± SD)	Min-max	CCI (points)	Min-max	P value α	P value β	P value π
+	286 (86.7)	74±16	24-97	22±2	1-92	2.2±2.4	0-11	0.32	0.16	0.79
-	44 (13.3)	76±15	19-97	18±2	2-63	2.3±2.3	0-9	0.32	0.16	0.79
Total	330	74±21	19-97	21±2	1-92	2.3±2.3	0-11	0.32	0.16	0.79

With "LoS" it is meant the duration of hospital stay. "CCI" represents the Charlson Comorbidity index. α=age differences between Rh groups; β=LoS differences between Rh groups; π=CCI differences between Rh groups.

(Intensification of Care, In-hospital death, Six-months mortality): the first statistically significant relationship was between the AB group and the IoC (p value=0,03): however, this could be influenced by the small size of the sample and of the lack of patients with AB group who needed an IoC during their hospital stay. The same analyses were performed for the Rh factor, finding that there was a significant difference between the groups of patients, indicating in particular that the patients with Rh factor negative had greater in-hospital mortality rates (p=0.03). No sex-related difference between groups towards the three disease outcomes chosen (data not shown). The predictive role by the Rh factor towards the in-hospital mortality was investigated through a logistic regression analysis that showed how the strongest factor able to predict the death of patients within the hospital stay was age (OR=1.06; 95% CI 1.04-1.09, p<0.001).

Lastly, we performed COX regression analyses to analyze whether the four ABO blood groups and the Rh factors could somehow determine a difference in terms of mortality after a period of observation of 180 days.

In particular, Figure 1 shows the survival curves of the four different populations where the ABO group was determined: in the box a of the Figure 1 there is no adjustment for any of the patients' characteristic, while the box b, on the right, shows the same survival curves adjusted for age and CCI. No clear differences are evidenced by the analysis for ABO blood-group.

We did the same with the Rh factors (Figure 2, box a and box b), but in this case we found an evident difference in the survival functions of the two groups of patients: those with Rh factor positive, in fact, survived longer than the patients with Rh factor negative, and the results was con-

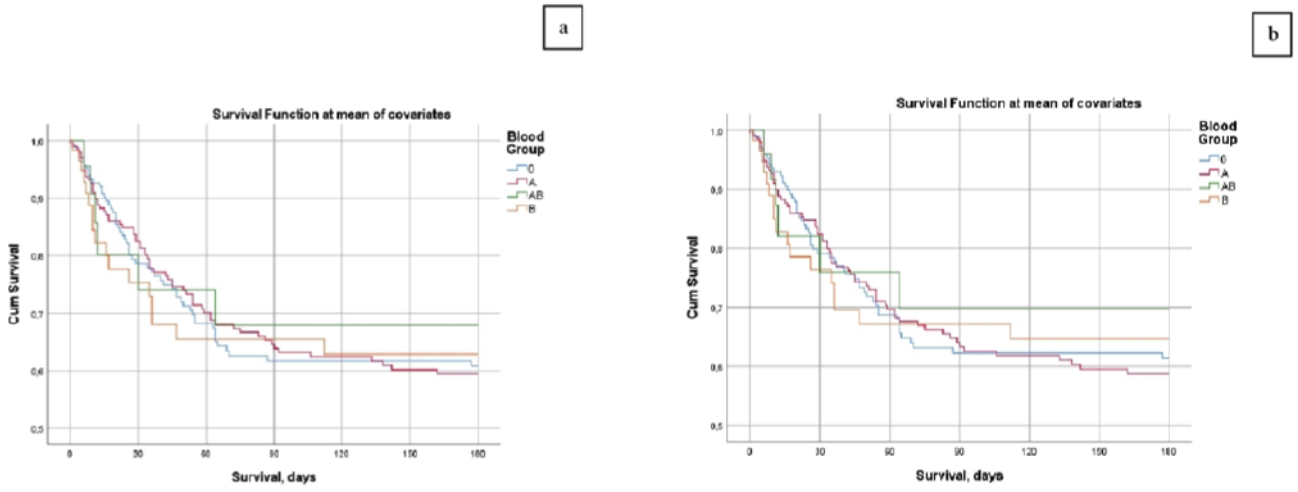

Figure 1. Box a: Cox regression analysis, survival at the 180th day since the first positive viral RNA detection in the four populations (Group O=blue curve; Group A= red curve; Group B= orange curve; Group AB= green curve). Box b: Cox regression analysis, survival at the 180th day since the first positive viral RNA detection in the four populations (Group O=blue curve; Group A= red curve; Group B= orange curve; Group AB= green curve) adjusted for age and CCI (Charlson Comorbidity Index).

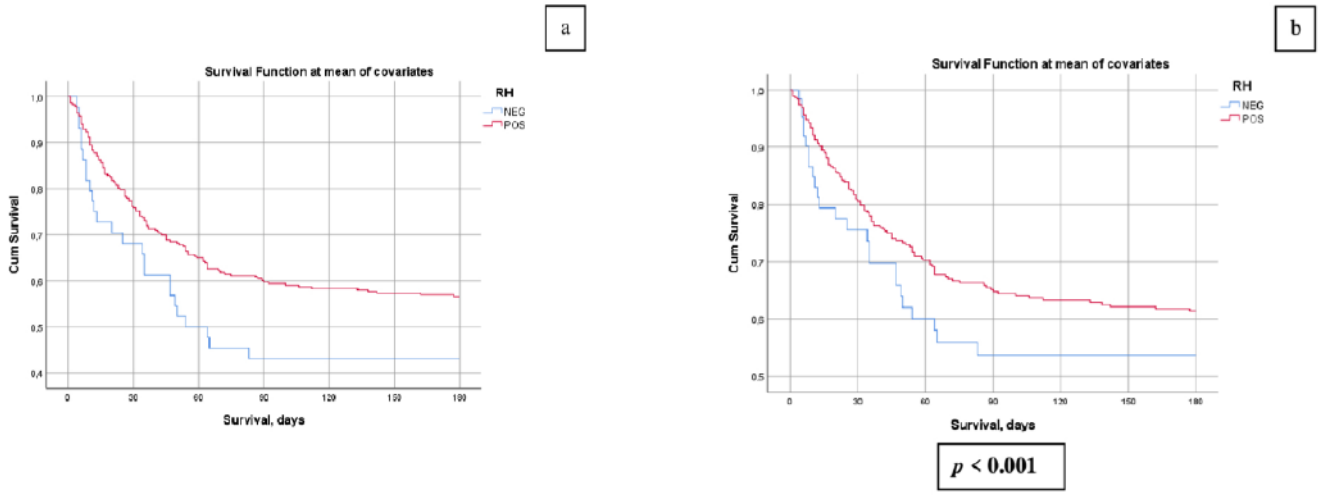

Figure 2. Box a: Cox regression analysis, survival at the 180th day since the first positive viral RNA detection in the two populations (Rh neg= blue curve; Rh pos= red curve). Box b: Cox regression analysis, survival at the 180th day since the first positive viral RNA detection in the two populations (Rh neg= blue curve; Rh pos= red curve) adjusted for age and CCI (Charlson Comorbidity Index).

firmed even in the analysis with the adjustment for age and CCI (p value between groups' survival functions <0.001).

Discussion

Recently, Ellinghaus *et al*.[13] hypothesized that the ABO blood group system could somehow determine different outcomes in the patients with COVID-19. They detected a novel susceptibility locus at a chromosome 3p21.31 gene cluster and confirmed a potential involvement of the ABO blood group system in COVID-19. In their work, group O was found to be somehow protective towards COVID-19 complications.

Wu *et al*.,[14] in a recent meta-analysis, found that blood group A was associated with a higher risk for acquiring COVID-19, whereas blood group O was associated with a lower risk. Zietz *et al.*,[15] in their study on 14,112 individuals tested for SARS-CoV-2 infection, found slightly increased infection prevalence among non-O types. The risk of intubation was decreased among A-group patients and increased among patients with AB and B groups, compared with type O; moreover, the risk of death was increased for type AB and decreased for types A and B. They also estimated Rh-negative blood type to have a protective effect for all three outcomes. Similar results were found by Zhao *et al*. in their study of more than 3,500 subjects.[16]

Several pathophysiological mechanisms have been proposed to explain the possible association existing between ABO type and SARS-CoV-2 infection and the review by Goel *et al*.[17] summarizes them all: anti-A and/or anti-B antibodies, expressed in group O patients, would bind to A and/or B antigens of the viral envelope, thus preventing from infection. The circulating antibodies would be able, in this case, to reach the virus even on the cell surfaces in other districts such as the gastrointestinal tract. Another possible protective role could be represented by the S protein of SARS-CoV-2: it is conceivable that SARS-CoV-2 S protein, and in particular the A antigen of its surface, could be bound by human anti-A antibodies, which could consequently block the interaction between the virus and the angiotensin-converting enzyme 2 receptor (ACE2R), thereby preventing entry into the lung epithelium. As for the predisposing factors towards infection, there would be an increase in angiotensin-converting enzyme 1 (ACE-1) activity, observed in group A patients. Similarly, these patients would experience more coagulation-related cardiovascular complications because of their higher levels of VWF and factor VIII.

Other different proposed mechanisms would involve the ABH glycans on SARS-CoV-2 S protein surface, able to enhance binding to ACE2 or, according to other currents of thought, to serve as alternative receptors for SARS-CoV-2 itself, favouring the infection.

However, a multi-institutional, retrospective review by Latz *et al.* on 7,648 symptomatic patients tested for SARS-CoV-2 infection, showed that there was no association between ABO blood type and COVID-19 disease severity (defined as intubation or death); furthermore, there were no significant associations between the blood type and the need for hospitalization, the proning requirement while intubated or for any of the inflammatory markers reviewed in the study.[18]

Our experience was limited to the territory of a province in Northern Italy, Ferrara, that typically has a high prevalence of elderly subjects. During the first phases of the pandemic, our territory was characterized by a small number of cases compared with the neighboring provinces and several possible explanations were given, even if the reason behind this phenomenon is still unclear. First, Ferrara is geographically out of the "Via Emilia", one of the longest commercial ways of the Northern Italy and this could partially explain the exiguous number of total infections of the territory (if compared to the mean number of infections in Italy), because of the minor interactions between people during the previous phases of SARS-CoV-2 diffusion. The old age of the inhabitants, often guests of retirement homes, together with the intrinsic predisposition by these patients towards infectious diseases, could explain instead the high prevalence of COVID-19 cases in this setting.

An important topic to take into consideration is that Ferrara, together with Rovigo, that is another neighboring city in the Po river delta's area, is historically an area of former malaria endemic. Apart from the similarities between COVID-19 and malaria in the clinical presentation of the disease[19] and in the possible complications of both illnesses (ARDS, septic shock and multi-organ failure), it could be interesting to underline that the spread of SARS-CoV-2 virus is particularly reduced in malarial areas.[20]

Moreover, the province of Ferrara, flagellated in the last centuries until the 1960s by the malarial epidemic, together with other Italian areas, was recently studied by some researchers who tried to understand why it showed positive rates for COVID-19 far lower than in the rest of the Emilia Romagna region.

Some researchers and experts suggested that this situation could be in part caused by the micro-climate present in this area, even if this is still to be confirmed by solid data and needs to be further investigated.[21]

We chose as study population the patients hospitalized between March and June 2020. First, we searched for differences in terms of age, length of stay and Charlson Comorbidity Index between patients with different groups (Table 1);

Table 3. Relationships between COVID-19 outcomes (IoC= Intensification of Care. in-hospital death. six-months mortality) and both AB0 blood group and Rh factors. P values between groups are on the right: α=Intensification of Care *vs* No Intensification of Care; β=In-hospital death *vs* In-hospital survival; Ω=six-months mortality vs six-months survival.

Blood group (N=330)	IoC (N=87), %	In-hospital death (N=91), %	Six-months mortality (N=149), %	P value α	P value β	P value Ω
Type O (N=128)	34 (26.6)	34 (26.6)	58 (45.3)	0.95	0.74	0.96
Type A (N=151)	41 (27.2)	37 (24.5)	68 (45.0)	0.77	0.25	0.97
Type B (N=38)	12 (31.6)	15 (39.5)	17 (44.7)	0.44	0.08	0.96
Type AB (N=13)	0 (0)	5 (38.5)	6 (46.2)	*0.03*	0.37	0.94
Rh (N=330)						
Pos (N=286)	72 (25.2)	73 (25.5)	124 (43.4)	0.21	*0.03*	0.10
Neg (N=44)	15 (34.1)	18 (40.9)	25 (56.8)			

Rh groups.

Table 4. Binary logistic regression analysis between variables towards the in-hospital mortality.

Variable	OR	95% CI (lower-upper)	P value
Rh factor	0.53	0.26-1.07	0.08
Age	1.06	1.04-1.09	*<0.001*
Sex (M)	0.69	0.40-1.18	0.18
CCI	1.09	0.97-1.22	0.13

"OR" = Odds Ratio; "CI" = 95% Confidential interval; "CCI" = Charlson Comorbidity index.

then we considered the Rh factor as the main variable of the analysis, trying to find relationships with the clinical and anamnestic characteristic of patients, without any significant result (Table 2). Finally, we searched for relationships between the blood groups and the three COVID-19 main outcomes (IoC, in-hospital death, six-months mortality, Table 3), doing the same with the Rh factors.

The first statistically significant relationship found was between the AB blood group and in-hospital mortality (p=0.03) but it is clearly affected by the small size of sample (13 patients). Moreover, no patients with AB group died or needed an intensification of care during the hospital stay, making it very difficult to get to any conclusion about the real role of this blood group in determining a different outcome for SARS-CoV-2 infection, as for our cohort of patients.

The Cox regression analyses performed for the four blood groups confirmed that there were no substantial differences in terms of mortality within an observation period of 180 days, even when an adjustment for age and CCI was made (Figure 1, box a and b).

The second statistically significant relationship concerned the differences between the groups of patients with Rh factor positive and negative in terms of in-hospital mortality rate: in particular, those with Rh factor negative seemed to have worse outcomes within the hospital stay (40.9% vs. 25.5%, p=0.03). This aspect was more evident in the survival curves performed through the Cox regression analyses that showed how the patients with Rh factor positive had better outcomes within 180 days, also in the case of adjustment for age and CCI (Figure 2, box a and b, p <0.001).

Our data would partially agree with the study by Ray *et al*.[22] on more than 220,000 patients from Canada; these researchers found that the adjusted relative risk for severe COVID-19 in patients with Rh factor negative was 0.82 (95% CI, 0.68-0.96). However, differently from this population-based cohort study we did not find any significant relationship with ABO group. A possible explanation of this could be found in the relatively small dimensions of the sample under examination. It is possible, in fact, that the extension of the analyses to a greater number of subjects would have improved the significance of the results concerning the ABO blood groups systems, as it happened for the other studies cited above.

The only multivariate analysis performed, concerned the Rh factor of patients that was found to be significantly different between the groups of patients survived or dead within the hospital stay. The variables chosen for the analysis were age, sex and CCI, together with the Rh factor and we found age to be the strongest factor able to determine the in-hospital stay was age, as now all the studies about COVID-19 have shown.

Apart from the small size of the sample, this work has all the limitations of retrospective studies and, above all, it was not possible to perform any kind of genetic analysis that could allow us to get to different conclusions. Moreover, we could not collect the data about the subjects with SARS-CoV-2 infection who were not hospitalized, so that we could only count on the data of the inpatients. To partially overcome the limit of the small size of the sample, we decided in fact to extend the period of observation to six months, differently from most studies that have shorter follow-up time periods, often because of the difficulties in collecting data from patients after hospital dismission.

Many aspects of SARS-CoV-2 infection are still far to be fully understood and, among them, the relationship between blood groups is probably among the most interesting ones. It is still unclear whether a strong genetic predisposition to COVID-19 exists, and it is still to be defined whether a particular blood group or the positivity of the Rh factor could substantially affect the disease outcomes.

We believe that studies like ours, especially with long observation periods, can give a better point of view towards all the COVID-19 outcomes.

Conclusions

In our cohort study, we found no relevant relationships were found for ABO blood group system towards different COVID-19 outcomes such as the intensification of care, the in-hospital death or the 180-day mortality rate. On the contrary, the Rh factor seems to be involved in determining the prognosis of COVID inpatients within 180 days and our analyses showed that the patients with Rh factor positive have better survival functions.

References

1. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054-1062.
2. Li X, Xu S, Yu M, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. J Allergy Clin Immunol 2020;146:110-18.
3. Chen R, Liang W, Jiang M, et al. Risk Factors of Fatal Outcome in Hospitalized Subjects With Coronavirus Disease 2019 From a Nationwide Analysis in China. Chest 2020;158:97-105.
4. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: Prospective observational cohort study. BMJ 2020;369:m1985.
5. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA 2020;323:2052-9.
6. Channappanavar R, Perlman S. Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. Semin Immunopathol 2017;39:529-39.
7. Kalayanarooj S, Gibbons R V., Vaughn D, et al. Blood group AB is associated

with increased risk for severe dengue disease in secondary infections. J Infect Dis 2007;195:1014-7.
8. Hutson AM, Atmar RL, Graham DY, Estes MK. Norwalk virus infection and disease is associated with ABO histo-blood group type. J Infect Dis 2002;185:1335-7.
9. Kazi AM, Cortese MM, Yu Y, et al. Secretor and salivary ABO blood group antigen status predict rotavirus vaccine take in infants. J Infect Dis 2017;215:786-9.
10. Liu J, Zhang S, Liu M, et al. Distribution of ABO/Rh blood groups and their association with hepatitis B virus infection in 3.8 million Chinese adults: A population-based cross-sectional study. J Viral Hepat 2018;25:401-41.
11. Cheng Y, Cheng G, Chui CH, et al. ABO blood group and susceptibility to severe acute respiratory syndrome. JAMA 2005;293:1450-1
12. Cooling L. Blood groups in infection and host susceptibility. Clin Microbiol Rev 2015;28:801-70.
13. Genomewide Association Study of Severe Covid-19 with Respiratory Failure. N Engl J Med. Published online 2020. doi:10.1056/nejmoa2020283
14. Wu BB, Gu DZ, Yu JN, et al. Association between ABO blood groups and COVID-19 infection, severity and demise: A systematic review and meta-analysis. Infect Genet Evol 2020;84:104485.
15. Zietz M, Zucker J, Tatonetti N. Testing the association between blood type and COVID-19 infection, intubation, and death. medRxiv Published online 2020. doi:10.1101/2020.04.08.20058073
16. Zhao J, Yang Y, Huang H, et al. Relationship between the ABO Blood Group and the COVID-19 Susceptibility. Clin Infect Dis 2020. doi:10.1093/cid/ciaa1150
17. Goel R, Bloch EM, Pirenne F, et al. ABO blood group and COVID□19: a review on behalf of the ISBT COVID-19 working group. Vox Sang. 2021;17:vox.13076. doi:10.1111/vox.13076
18. Latz CA, DeCarlo C, Boitano L, et al. Blood type and outcomes in patients with COVID-19. Ann Hematol 2020;99:2113-8.
19. O'Brien D, Tobin S, Brown GV, Torresi J. Fever in returned travelers: Review of hospital admissions for a 3-year period. Clin Infect Dis 2001;33:603-9.
20. Napoli PE, Nioi M. Global Spread of Coronavirus Disease 2019 and Malaria: An Epidemiological Paradox in the Early Stage of A Pandemic. J Clin Med 2020;9:1138.
21. Carta MG, Scano A, Lindert J, et al. Association between the spread of COVID-19 and weather-climatic parameters. Eur Rev Med Pharmacol Sci 2020;24:8226-31.
22. Ray JG, Schull MJ, Vermeulen MJ, Park AL. Association Between ABO and Rh Blood Groups and SARS-CoV-2 Infection or Severe COVID-19 Illness. Ann Intern Med 2021;174:308-15.