Relation between ABO and RhD and prevalence and severity of COVID-19 disease

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Abstract

Backgrounds:

This study aims to determine the relation between ABO and RhD and the prevalence and severity of COVID-19 disease.

Methods:

Data of 495 SARS-CoV-2 infected patients admitted to hospitals were collected. The ABO and RhD were determined for each patient to detect any possible relation between the prevalence of SARS-CoV-2 infection and each blood group. The patients were followed up to determine oxygen saturation and surveillance outcome (died or improved) to detect any possible relation between the severity of COVID-19 disease and each blood group.

Results:

A+ blood group was found to have a percentage of 32.3%, O+ to have a percentage of 30.3%, B+ to have a percentage of 21.2%, and AB+ to have a percentage of 10.1%. 19% of all the patients died. 20% of the dead patients were with O+ blood group, 60.5% were with A+ blood group, 10% with B+ blood group and 5% were with O- blood group.

The mean ± SD oxygen saturation on hospital admission was 94.2 ± 6.2% for the patients with O+ blood group, 91.06 ± 7.5% for the patients with A+ blood group, 92.8 ± 6.9% for the patients with B+ blood group, 93.4 ± 3.5% for the patients with AB+ blood group, and 94.5 ± 5.9% for the patients with O- blood group.

Conclusion:

Blood group A+ was the most common in the COVID-19 patients followed by O+ then B+ then AB+. Patients with blood group A+ had the worst oxygen saturation at hospital admission and had a higher mortality rate.

Keywords: COVID-19; ABO blood groups; Rh blood groups

Introduction

The most commonly affected people by COVID-19 are those who suffer from respiratory or cardiovascular diseases,[1, 2] hypertensive and diabetic patients.[3-5] There are some biological parameters such as C-reactive protein (CRP), ferritin, D-dimer, and Lactate dehydrogenase (LDH) that can be considered as **predictive** of the severity of COVID-19, but no biomarker indicates the risk of COVID-19 disease.[6, 7] Blood types are qualitative characteristics that are not affected by the environment, and each phenotype is a reflection of the genetic composition. Blood groups are genetically recorded and their antigens may be a risk factor for some diseases and a preventive factor for other diseases.[8-11] Previous studies reported that some viral infections e.g. hepatitis B and some types of cancer are linked to the ABO blood group.[8-11] Hence, the ABO and rhesus (Rh) blood groups may help in predicting the risk for COVID-19 disease.[12] It was reported that the SARS-CoV-2 infection rate was found **to be lower** in blood group O.[13] This observation (the protective effect of group O) although repeatedly reported by several studies is still controversial.

Although many studies have reported that there is an association between RhD blood group and susceptibility to COVID-19 infection, a new study reported that RhD+ is associated with a risk of high infection and rate of mortality among COVID-19 patients [14]

The present study aims to determine any possible relation between ABO and RhDand the prevalence and severity of COVID-19 disease.

Methods

This retrospective study was performed at Beni-suef university hospital after the study protocol was approved by the Research Ethical Committee of Beni-Suef University and following the Declaration of Helsinki.

A total of 495 patients with laboratory-confirmed SARS-CoV-2 infection with reverse transcription-polymerase chain reaction (RT-PCR), were admitted to the hospital from December 2020 to May 2021.

Patients' written informed consent was obtained, or consent was obtained from a legal representative if they were unable to provide consent.

The ABO and RhD were determined for each patient in order to be able to analyze any possible relation between the prevalence of COVID-19 disease and each blood group. Oxygen saturation is one of the parameters measured for the patients' follow-up and monitoring. It was measured by arterial blood gas analyses. The measured values were correlated with the blood group, and related to the severity of the disease and the clinical course of the patients (death or improvement).

The COVID-19 PCR test involved three main stages:

1- Collecting the sample from patient's nose using a soft-tipped swab. The swab was placed inside the nostrils or deeper into the nasal cavity and then sealed in a tube and sent to a lab for analysis.
2- Extracting the genetic material by isolating the genetic material from the rest of the sample.
3- PCR Amplification by using a PCR machine called a thermal cycler and the genetic material was targeted through cycles of heating and cooling. This process creates millions of copies of a segment of the SARS-CoV-2 virus's genetic material in the test tube. A fluorescent light is produced if the virus is present, and the PCR machine detects this signal. Then this signal was analyzed with software to determine a positive test result.

Statistical analysis:

Data were analyzed using IBM SPSS advanced statistics version 22 (SPSS Inc., Chicago, IL). Numerical data were expressed as mean and standard deviation or median and range as appropriate. Qualitative data were expressed as frequency and percentage. Comparison between groups was performed using the ANOVA test. A p-value <0.05 was considered significant.

Results

The frequency of ABO and Rh blood groups for the COVID-19 patients and surveillance outcome is shown in Figure 1 and the percentage of gender in each ABO blood group for the COVID-19 patients is shown in Figure 2. The frequency of ABO and RhDof the COVID-19 patients and surveillance outcome (died or improved) are shown in Table1.

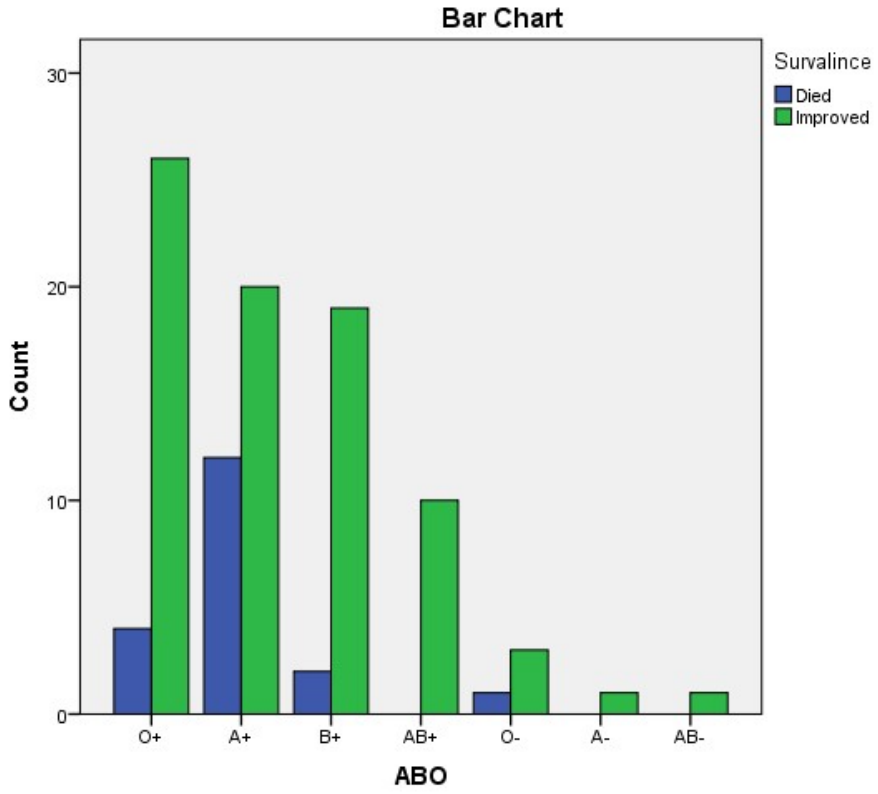

Figure 1: The frequency of ABO and Rh blood groups for the COVID-19 patients and surveillance outcome

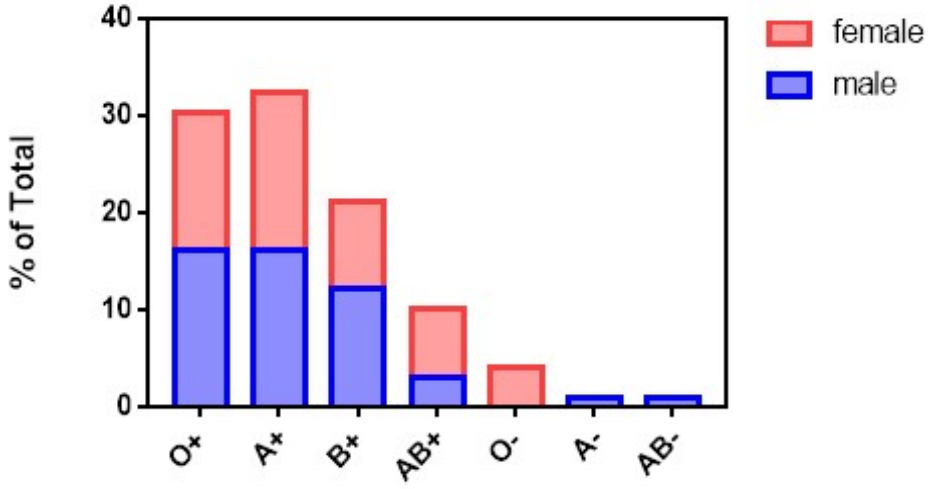

Figure 2: Gender in each ABO blood group for the COVID-19 patients

Table 1: The frequency of ABO and RhD blood groups for the COVID-19 patients and surveillance outcome

Blood group	Died [n (%)]	Improved [n (%)]
O	25 (14.7%)	145 (85.3%)
A	60 (36.4%)	105 (63.6%)
B	10 (9.5%)	95 (90.5%)
AB	0 (0%)	55 (100%)
Rh D (+)	90 (19.4%)	375 (80.6%)
Rh D (-)	5 (16.7%)	25 (83.3%)

The distribution of ABO groups between the deceased and the recovered patients was significantly different (more A, less O in the deceased; p <0.001), but that the distribution of the RhD antigen was not different (p=0.717; NS). A total of 495 (49.5% men, 50.5% women) patients with confirmed SARS-CoV-2 infection were included in this study, (400 ; 80.8%) of them were discharged alive from the hospital and (95 ; 19.2%) were died. The percentages of hypertension and diabetes mellitus, which were the most common chronic diseases found in study patients, were 15%, and 18%, respectively. These co-morbid factors were observed mostly in the patients who died.The A+ blood group was found to have a percentage of 32.3%, O+ to have a percentage of 30.3%, B+ to have a percentage of 21.2%, and AB+ to have a percentage of 10.1%. The O-blood group was found to have a percentage of 4%, A- with a percentage of 1%, and AB- to have a percentage of 1%.

19% of all the patients died. 20% of the dead patients were with the O+ blood group, 60.5% were with the A+ blood group, 10% with the B+ blood group, and 5% were with the O- blood group.

The percentage of gender in each ABO blood group for the died COVID-19 patients is shown in Figure 3, and the percentage of co-morbidities in each ABO blood group for the died COVID-19 patients is shown in Figure 4 The mean oxygen saturation for the COVID-19 patients is shown in Table 2.

The mean ± SD oxygen saturation on hospital admission was 94.2 ± 6.2% for the patients with the O+ blood group, 91.0 ± 7.5% for the patients with the A+ blood group, 92.8 ± 6.9% for the patients with the B+ blood group, 93.4 ± 3.5% for the patients with the AB+ blood group, and 94.5 ± 5.9 for the patients with the O- blood group. There was no significant difference in oxygen saturation variation between any two blood groups in the study except between A+ and O+ blood groups where there was a significant difference in oxygen saturation variation between them (p < 0.001). The relation between variation in oxygen saturation of each group and the other groups is shown in table 3. The mean oxygen saturation for the ABO and RhD blood groups is shown in table 4

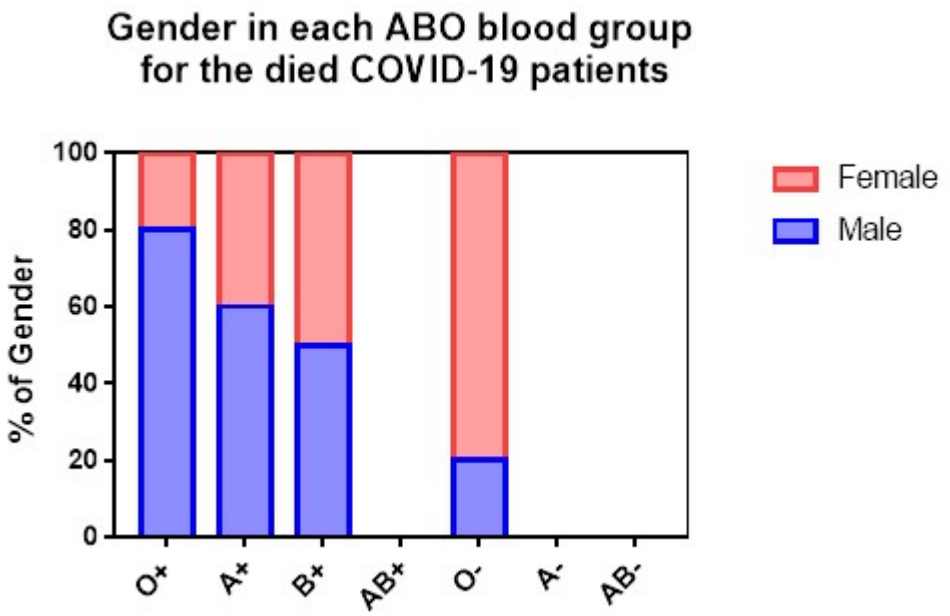

Figure 3: Gender in each ABO blood group for the died COVID-19 patients

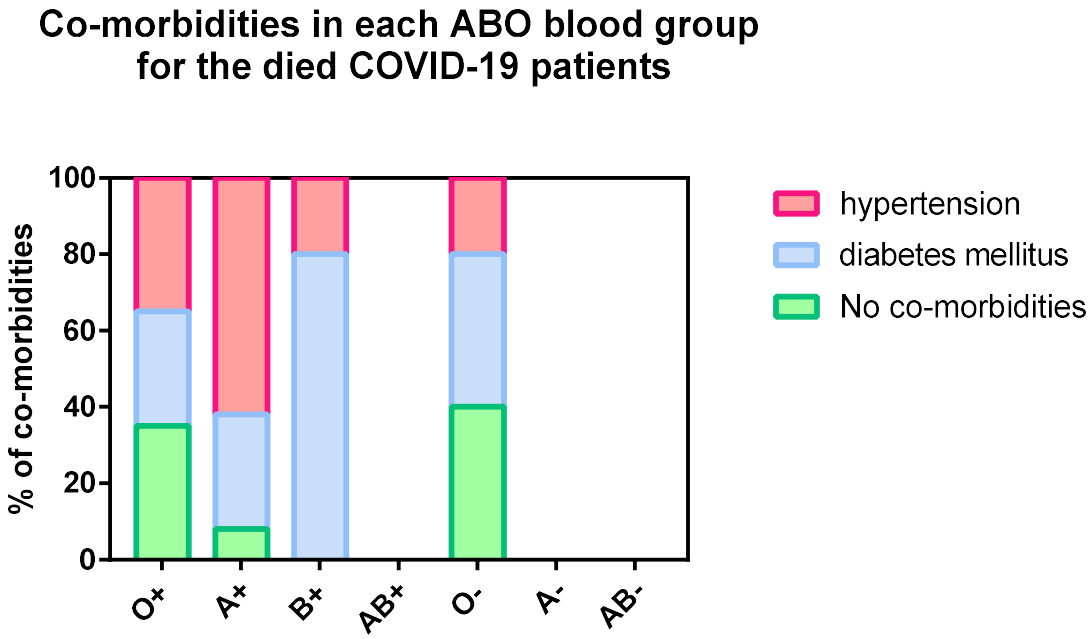

Figure 4: Co-morbidities in each ABO blood group for the died COVID-19 patients

Table 2: Mean oxygen saturation for each blood group

Blood group	No.	Mean ± SD(%)	Std. Error	Minimum
O+	150	94.2±6.2	0.51	75.00
A+	160	91±7.5	0.6	76.00
B+	105	92.8±6.9	0.67	71.00
AB+	50	93.4±3.5	0.5	88.00
O-	20	94.5±5.9	1.3	85.00
A-	5	96±0.0	0.0	96.00
AB-	5	98±0.0	0.0	98.00
Total	495	92.7±6.7	0.3	71.00

Table 3: Relation between variation in oxygen saturation of each group and the other groups

Dependent Variable	(I) ABO	(J) ABO	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
O2sat	O+	A+	3.57	.74	.000	1.37	5.77
		B+	1.4	.83	.62	-1.06	3.87
		AB+	0.77	1.06	.99	-2.4	3.93
		O-	-.33	1.55	1	-4.94	4.27
		A-	-1.8	2.97	.99	-10.6	6.97
		AB-	-3.8	2.97	.85	-12.6	4.97
	A+	O+	-3.57*	.74	.000	-5.77	-1.37
		B+	-2.17	.82	.11	-4.6	.26
		AB+	-2.8	1.06	.11	-5.94	.33
		O-	-3.9	1.5	.15	-8.5	.69
		A-	-5.4	2.97	.53	-14.2	3.39
		AB-	-7.4	2.97	.16	-16.2	1.39
	B+	O+	-1.4	.83	.62	-3.87	1.06
		A+	2.17	.82	.12	-.26	4.6
		AB+	-.64	1.12	.99	-3.97	2.69
		O-	-1.74	1.6	.93	-6.46	2.99
		A-	-3.23	2.99	.93	-12.1	5.63
		AB-	-5.23	2.99	.58	-14.1	3.63
	AB+	O+	-.77	1.07	.99	-3.93	2.39
		A+	2.8	1.06	.11	-.33	5.94
		B+	.64	1.12	.99	-2.69	3.97
		O-	-1.1	1.73	.99	-6.22	4.02
		A-	-2.6	3.06	.98	-11.68	6.48
		AB-	-4.6	3.06	.74	-13.68	4.48
	O-	O+	.33	1.56	1	-4.28	4.95
		A+	3.9	1.55	.16	-.69	8.5
		B+	1.73	1.6	.93	-2.99	6.46
		AB+	1.1	1.73	.99	-4.02	6.22
		A-	-1.5	3.27	.99	-11.19	8.18
		AB-	-3.5	3.27	.93	-13.18	6.18
	A-	O+	1.83	2.97	.99	-6.97	10.64
		A+	5.4	2.97	.53	-3.39	14.2
		B+	3.23	2.99	.93	-5.63	12.1
		AB+	2.6	3.06	.98	-6.48	11.69
		O-	1.5	3.27	.99	-8.18	11.19
		AB-	-2	4.13	.99	-14.25	10.25
	AB-	O+	3.83	2.97	.85	-4.98	12.64
		A+	7.41	2.97	.16	-1.39	16.2
		B+	5.24	2.99	.58	-3.63	14.1
		AB+	4.6	3.06	.74	-4.48	13.69
		O-	3.5	3.27	.93	-6.19	13.19
		A-	2	4.13	.99	-10.25	14.25

*. The mean difference is significant at the 0.05 level.

Table 4: Mean oxygen saturation for the ABO and RhD blood groups

Blood group	Oxygen saturation (Mean)	Oxygen saturation (Std. Deviation)	Oxygen saturation (Std. Error of Mean)
O	94.21	6.246	1.071
A	90.76	7.529	1.311
B	92.76	7.021	1.532
AB	93.82	3.763	1.135
Rh D (+)	92.54	6.804	0.7055
Rh D (-)	95.33	5.317	2.171

Discussion

Similar to other studies, the study examined any possible relation between blood group and the prevalence and severity of COVID-19 disease, the frequency of the A+ blood group was found to be higher than the other blood groups in COVID-19 disease patients and the RhD+ was also found with a higher frequency than the RhD- among the COVID-19 patients. [7, 15, 16] However, the study of Mawaddah et.al, showed that the frequency of the O blood group had a higher SARS-CoV-2 infection incidence.[17] The difference in blood group antigens may affect the individual susceptibility to several infections.[15, 18] Blood group antigens can have a direct role in viral infection by acting as a cofactor and aid the viral adherence or entrance to the host cell by organizing the cellular membrane microdomains. Therefore, the blood group antigens may affect the immunological response to several infections.[15, 18]

It was reported previously to explain the higher frequency of A blood group than the other blood groups in COVID-19 patients,[19] that the interaction of COVID-19 virus S spike protein and the Angiotensin-converting enzyme 2 receptors may be inhibited and disrupted by the anti A antibodies found in persons with non A blood groups which act, to some extent, as a protective mechanism.[16]

In this study, the frequency of RhD+ in COVID-19 patients was higher than the frequency of RhD-. A previous study referred to that a possible protection from COVID-19 virus by the RhD- blood group, however, no definite rational was concluded from this study.[15] Also, it was observed in this study that AB+ was less frequent in COVID-19 patients compared to the other positive blood group. [20]

Hypertension and diabetes mellitus was found in this study as the most common risk factors for COVID-19 severity. That was similar to the study of Mawaddah et.al. [17] It is known that having any of these comorbidities is a worrying prognostic factor in patients with pneumonia.[21] Severe acute respiratory syndrome coronavirus (SARS-CoV-2) may cause pneumonia, acute lung injury (ALI),[22, 23] or acute respiratory distress syndrome (ARDS)[24, 25] which may lead to pulmonary fibrosis or death.[26] The lung injury leads to hypoxemia which is regarded as the indication for needing oxygen therapy [27, 28] and detected by measuring oxygen saturation in blood. [29, 30]

The severity of infection in this study was compared between the blood groups by detecting the mean oxygen saturation for each blood group on hospital admission and detecting the percentage of mortality in each blood group. A+ blood group has the worst prognosis in this study as it was associated with a higher percentage of mortality and the worst oxygen saturation on hospital admission compared to other blood groups. That was similar to a study conducted in Wuhan[31] and that reported in the study of Hakan et.al.[16] However, a previous study showed that most of the dead cases were in the none A blood group and reported that A blood group was associated with a lower number of death cases. [17] This study explained that by the higher incidence of hypertension among the cases of none A blood group.[17, 32] That indicates the high effect of some comorbidities on the severity and mortality rate in COVID-19 patients,[33, 34] despite the protective mechanism of blood group antigens in none A blood group patients.[35, 36] In contrast to our study also, there was a meta-analysis study that showed that the AB blood group was highly associated with death among COVID-19 patients. [37]

The risk of thrombosis increases highly in patients with blood group A therefore, they are more likely to develop pulmonary embolism. [38, 39] Studies have shown previously that pulmonary embolism, which develops in COVID-19 patients, is associated with acute respiratory syndrome in these patients; therefore, it is important to use prophylactic anticoagulants in the treatment protocol according to COVID-19 treatment guidelines especially for patients with A blood group.[40-42] In this study, it was found that the mortality rate in males more than females. That may explained by the biological differences in men's and women's immune systems that may impact our ability to fight infections such as SARS-2-CoV-2. Also, females are generally more resistant to infections than men, which may be mediated by a variety of factors including sex hormones and high expression of coronavirus receptors (ACE 2) in men, as well as lifestyle factors such as higher levels of smoking and drinking in men compared to women. Furthermore, women are more responsible than men when it comes to the Covid-19 pandemic. This may have a reversible impact on the implementation of preventive measures such as frequent hand washing, the use of a face mask, and stay-at-home orders.[43]

Conclusion

The blood group A+ was the most common in the COVID-19 patients then O+ then B+ then AB+. Patients with blood group A+ had the worst oxygen saturation at hospital admission and had a higher mortality rate. Patients with blood group A should use prophylactic anticoagulants according to COVID-19 treatment guidelines as they are at more risk for pulmonary micro thrombosis than other groups. Group A patients should therefore benefit from special preventive therapeutic measures because of their greater sensitivity to the consequences of infection.

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