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Coronavirus Pandemic

The association of ABO blood group distribution and clinical characteristics in patients with SARS-CoV-2

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Abstract

Introduction: SARS-COV-2, the novel severe acute respiratory syndrome coronavirus, has become a life-threatening public health crisis. This kind of pandemic is frightening the world with clinical, psychological, and emotional distress and leading to an economic slowdown. To explore any association between the ABO blood type and the susceptibility to coronavirus disease 2019 (COVID-19), we compared ABO blood group distribution among 671 COVID-19 patients with the local control population.

Methodology: The study was conducted in Blood Bank Hospital in Erbil, Kurdistan Region, Iraq. The ABO-typed blood samples were obtained from 671 patients infected with SARS-CoV-2 between February and June 2021.

Results: Our results demonstrated that the risk of SARS-COV-2 was higher for patients with blood group A than those with not-A blood type patients. Of the 671 patients with COVID-19, 301 had type A (44.86%), 232 had type B (34.58%), 53 had type AB blood (7.9%), and 85 had type O (12.67%).

Conclusions: We concluded that the Rh-negative blood type has a protective effect on SARS-COV-2. Our results also indicate that the decreased susceptibility of individuals with blood group O and the increased susceptibility of individuals with blood group A to COVID-19 could be linked to the presence of natural anti-blood group antibodies, particularly anti-A antibody, in the blood. However, there might be other mechanisms that require further study.

Key words: COVID-19; SARS-CoV-2; ABO blood group; clinical characteristics.

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Introduction

The coronavirus disease 2019 (COVID-19) is a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease was discovered in December 2019 in Wuhan, Hubei province. Soon after the World Health Organization (WHO) declaration about the pandemic, scientists believed that COVID-19 might have a zoonotic origin and is closely related to the original SARS-CoV [1]. The ABO blood type was discovered over 100 years ago, leading to the development of blood transfusion. However, corresponding antigens are expressed in many cell types in addition to the red blood cells [2]. Researchers have reported the association between blood types and viruses such as rotavirus, noroviruses, dengue virus, Norwalk virus, and hepatitis B virus and found that blood groups have links to certain viral infections [3,4]. It has also been reported that individuals with blood type O are less likely to be infected with SARS coronavirus [5]. In addition to the differences in the economic, behavioral, and social response to the epidemic between countries, genetic factors can also play a role. Thus, immediately after the beginning of the epidemic, a publication from Wuhan, China, reported a greater risk of infection for people with blood type A, and a lower risk for people with blood group O [6].

The Landsteiner's ABO blood groups are carbohydrate epitopes found on the surface of human cells. Antigenic determinants of blood types A and B are trisaccharide groups GalNAcα1–3-(Fucα1,2)-Galβ- and Galα1–3-(Fucα1,2)-Galβ-, while the antigen of O blood type is Fucα1,2-Galβ- [7]. Scientists believe that male COVID-19 cases outnumbered female cases, and men usually have a more serious illness or a critical sickness status. Furthermore, males have been shown to have 2.4 times more risk of death than females [8,9]. Positive and negative Rh blood types are correlated

Table 1. Relationship between the blood type distribution and gender.

Blood Type	Observed frequency	%	Male (%)	Female (%)
A	301	44.86	255 (84.72)	46 (15.28)
AB	53	7.90	40 (24.53)	13 (75.47)
B	232	34.58	196 (84.48)	36 (15.52)
O	85	12.67	72 (84.71)	13(15.29)
Total	671	100%	563 (83.9)	108 (16.1)

with a very small number of diseases compared to ABO, as ABO Rh type is crucial for type compatibility and response. For instance, hemolytic disease of the newborn baby is a real concern when Rh is mismatched between mother and offspring [10]. Recently scientists concluded that the Rh blood type is associated with COVID-19 and Rh negative has a protective role [11]. Therefore, this work aims to investigate the association between the ABO blood group and susceptibility to SARS-CoV-2.

Methodology

Study design

The current study involved ABO-typed blood samples from 671 patients infected with SARS-CoV-2 at Blood Bank Hospital in Erbil, Kurdistan Region (KRG), Iraq, between February 2021 and June 2021. The diagnosis of COVID-19 was declared by a positive real-time reverse transcriptase polymerase chain reaction test (RT-PCR) of SARS-CoV-2 on nasopharyngeal swab specimens from patients. Each patient's ABO type was obtained from the ABO blood group database. Therefore, the case cluster consisted of individuals from Erbil with a known blood type who were diagnosed with SARS-CoV-2 between February 2021 and June 2021 and discharged from the hospital. This data was combined with data on clinical characteristics which was obtained from electronic medical records and statistical computations were performed.

The medical records of 671 COVID-19 patients were divided into four groups, A, B, AB and O, according to the ABO blood groups. The ABO blood type distribution of 671 patients was analyzed, and the pathology and clinical characteristics of all patients with SARS-CoV-2 were analyzed. The proportion of Blood Type in each category of KRG population (expected proportions) is the same as in-patient sample (observed proportions).

Statistical analysis

We explored the ABO blood group distribution and clinical characteristics of COVID-19 patients by using Minitab 17 statistic software [12]. Data were analyzed with the Chi Square test which is a statistical hypothesis test to determine the goodness of fit of whether a variable belongs to a particular distribution. It is often used to determine whether sample data represent the entire population. $p < 0.05$ was considered statistically significant.

Ethical approval

The study was conducted in Blood Bank Hospital in Erbil, Kurdistan Region, Iraq, in collaboration with the Department of Medical Microbiology, Faculty of Sciences and Health, Koya University, Iraq. The Ethical Committee of the Faculty of Science and Health, Koya University, Iraq, approved the study. The participants were divided into two sections: the COVID-19 cases cluster, with 671 participants and the control group.

Results

A total of 671 patients were consecutively enrolled in the present study; all the patients were found SARS-CoV-2 RT-PCR positive. Among the patients, 563 (83.9%) were men, and 108 (16.1%) were women (Table 1). The highest number of samples belonged to blood group A (301; 44.86%; 95% CI 0.410505; 0.487117), followed by B (232; 34.58%; 95% CI 0.309767; 0.383102), O (85; 12.67%; 95% CI 0.102452; 0.154239) and AB (53; 7.9%; 95% CI 0.059724; 0.102045) (Table 2). On the other hand, the

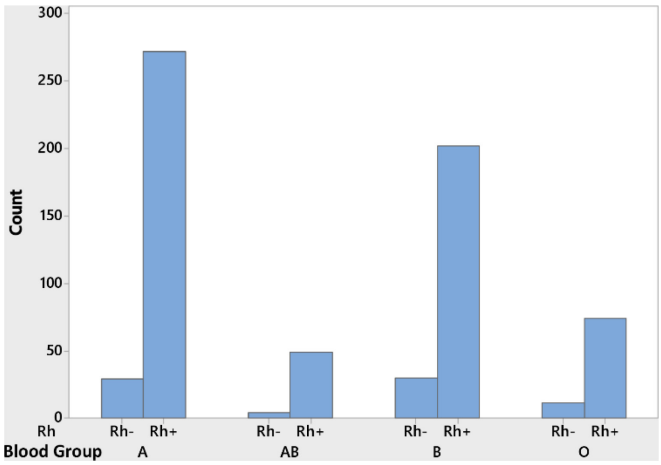
Table 2. Frequency of the ABO blood type distribution in patients with COVID-19 and expected control.

Blood Type	Observed frequency		Expected frequency		Difference (Observed-Expected)	95% CI (confidence interval)
Category	N	%	N	%	(Observed-Control)	%
A	301	44.86	208.88	31.13	+92.12	41.0505; 48.7117
AB	53	7.90	51.80	7.72	+1.2	5.9724; 10.2045
B	232	34.58	160.84	23.97	+71.16	30.9767; 38.3102
O	85	12.67	249.48	37.18	-164.48	10.2452; 15.4239
Total	671	100%	671	100%	0.00	

O blood group had the highest prevalence (249.48; 37.18%) in the control group, followed by the A blood group (208.88; 31.13%), B (160.84; 23.97%), and AB (51.8; 7.72%). Overall, blood type A had a higher possibility of testing positive than other blood types, while all other blood types, and specifically the AB blood type, showed a decrease in risk (Table 2). Our null hypothesis was that the proportion of blood type in each category in KRG population (expected proportions) was the same as with the patient sample (observed proportions) (Table 2)

Individuals negative for Rh were at decreased risk, while Rh-positive individuals were at high risk for COVID-19 infection at 11.03% and 88.97%, respectively (Figure 1). The patients had fever, cough, headache, sore throat, chest pain and fatigue at the time of admission (Table 3). In terms of symptom distribution, cough was more common in patients with certain blood types; 70.76% type A patients, 72.84% type B patients, 75.47% type AB patients and 62.35% type O patients had cough. Fatigue, headache, and sore throat are also associated with the risk of SARS-CoV-2 at 62.89%, 39.79%, and 31.45%, respectively. Only 23.4% of the patients had chest pain (Table 3). The ABO blood group distribution was also related to fever, patients with fever had type A (75.75%), B (60.78%), AB (66.04%) and O (52.94%) blood types (Table 3).

Figure 1. Association of ABO Rh blood group with risk of SARS-COV-2 infection.



Discussion

In this study, we found that the ABO blood group distribution was associated with the occurrence of COVID-19 symptoms of fever, cough, headache, sore throat, chest pain and fatigue. No significant difference was observed between the other blood group patients *(p* > 0.05). This indicated that blood type might influence the clinical characteristics of patients with SARS-CoV-2. The distribution of human blood type varied with the races, and it has been correlated as a genetic risk factor for different virus diseases, such as the severe acute respiratory syndrome (SARS) outbreak in 2003 and malignancies [13].

To better understand COVID-19, we investigated whether blood groups are associated with the risk of COVID-19 infection. Overall, we concluded modest but consistent risk differences among blood groups. Our

Table 3. Association between ABO blood group distribution and clinical characteristics in patients with COVID-19.

Factors	COVID-19 All %	ABO blood type				*p* value
		A	B	AB	O	
Rh						
+	597 (88.97)	272 (90.37)	202 (87.07)	49 (92.45)	74 (87.06)	0.48
-	74 (11.03)	29 (9.63)	30 (12.93)	4 (7.55)	11 (12.94)	
Fever						
Yes	449 (66.92)	228 (75.75)	141 (60.78	35 (66.04)	45 (52.94)	
No	222 (33.08)	73 (24.25)	91 (39.22)	18 (33.96)	40 (47.06)	0.00
Cough						
Yes	475 (70.79)	213 (70.76)	169 (7284)	40 (75.47)	53 (62.35)	0.27
No	196 (29.21)	88 (29.24)	63 (27.16)	13 (24.53)	32 (37.65)	
Headache						
Yes	267 (39.79)	130 (43.19)	94 (40.52)	18 (33.96)	25 (29.41)	0.10
No	404 (60.21)	171 (56.81)	138 (59.48)	35 (66.04)	60 (70.59)	
Sore throat						
Yes	211 (31.45)	118 (39.20)	54 (23.28)	20 (37.74)	19 (22.35)	0.00
No	460 (68.55)	183 (60.80)	178 (76.72)	33 (62.26)	66 (77.65)	
Chest pain						
Yes	157 (23.40)	69 (22.92)	60 (25.86)	13 (24.53)	157 (23.40)	0.47
No	514 (76.00)	232 (77.08)	172 (74.14)	40 (75.47)	514 (76.60)	
Fatigue						
Yes	422 (62.89)	208 (69.10)	139 (59.91)	16 (30.19)	59 (69.41)	0.00
No	249 (37.11)	93 (30.90)	93 (40.09)	37 (69.81)	26 (30.59)	

result showed that Rh-negative individuals were at lower risk of COVID-19 infection (11.03%) than Rh-positive individuals (88.97%). There were no significant differences among Rh negative and positive individuals (p = 0.482). Our data agreed with Zietz (2020), who reported that SARS-CoV-2 infection was significantly increased for Rh-positive and decreased for Rh-negative [10]. Our statistical analysis showed no significant difference between blood groups and Rh (p > 0.05). Current clinical observation suggests that gender is a risk factor in the susceptibility to COVID-19. Previous studies have reported that usually men are more susceptible to SARS-CoV-2 infection [7]. This is consistent with our study, which demonstrated a greater number of men (83.90%) than women (16.10%) patients among the 671 cases of COVID-19. It has also been reported that MERS-CoV and SARS-CoV occur more frequently in males than females [14,15]. The low susceptibility of females to viral infections might be attributed to the protection from sex hormones and the X chromosome, which play a vital role in the innate immune response to infection [16]. By contrast, it has been recently reported that such gender differences can be attributed to some comorbidities that indirectly increase the risk of infection among males. For example, social isolation, tobacco smoking, alcohol use, and cardiovascular risk factors are mostly associated with the male gender [17].

Red blood cells (RBCs) contain the ABO blood group antigens, which are glycoproteins with high pleomorphic properties. The A and B antigen-encoding genes (two dominant and two recessive alleles) are present on chromosome 9q34.2 [18]. It consists of the A, B, and O alleles, with four genetic phenotypes (A, B, O, and AB blood types) [19]. Differences in blood type antigen expression can increase or decrease host susceptibility to multiple infections. ABO antigens serve as receptors or co-receptors for viruses, making them directly involved in infection. Additionally, many blood group antigens facilitate cell adhesion, signal transduction, or intracellular uptake through the organization of membrane micro-domains [13]. As part of the innate immune system, ABO antibodies act as receptors for different inflammatory responses and immune responses against different microorganisms, including bacteria, enveloped viruses, and parasites [20]. The ABO blood group may also serve as a COVID-19 susceptibility biomarker along with gender and Rh. As a result of our study, we found different associations between ABO blood groups and SARS-CoV-2 infection risks. Specifically, blood group A was related to an increased risk, whereas patients with blood group O had a lower risk, demonstrating that the ABO blood type was associated with SARS-CoV-2 susceptibility. As blood group O individuals have both types of antibodies, they might benefit from better protection than blood group A or B individuals who possess only one of these antibodies and even more so than blood group AB people who have none. According to Kaidarova (2016) and Guillon (2008), anti-A antibodies specifically inhibited the adhesion of SARS-CoV-S-expressing cells to ACE2-expressing cells [21,22]. Given the receptor angiotensin-converting enzyme 2 (ACE2) binding similarity and RNA sequence similarity between SARS-CoV-2 and SARS-CoV [23], the higher risk of blood group A and lower risk of blood group O for SARS-CoV-2 could be connected to the presence of anti-blood group antibodies. Further studies are needed to prove this association. However, there may also be other mechanisms that require further studies to elucidate.

Conclusions

Our study concluded that ABO and Rh blood groups influence the risk of SARS-CoV-2 infection. We found that blood group AB and Rh-negative are at a lower risk of infection in comparison with Rh-positive and non-AB blood types. Our finding revealed that among the confirmed the COVID-19 patients, the ABO blood type distribution might have some impact on the clinical manifestations of SARS-CoV-2. The clinical manifestations after infection included fever, cough, headache, sore throat, and chest pain. Finally, although the blood group of individuals might not be one of the hazard factors for COVID-19, but it was associated with the clinical characteristics of patients with SARS-CoV-2.

Limitations of the study

This study has some limitations. First, only 671 patients with COVID-19 were included in this study, which may have led to a certain bias in the results. This was because the vast majority of patients diagnosed with SARS-CoV-2 were not tested to determine their blood group. Therefore only 671 samples were available at the Blood Bank Hospital in Erbil, Kurdistan Region, Iraq.

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