

The Impact of Blood Group Phenotypes on COVID-19 Severity and Mortality in Duhok Province: a Prospective Cross-sectional Study

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Abstract

Objectives: This study aimed to determine the frequency of blood group types among COVID-19 patients and to investigate its potential association with disease severity and patient outcomes.

Methods: This prospective cross-sectional study was conducted from February to July 2022 in three different healthcare facilities in the Duhok region. All confirmed PCR confirmed COVID-19 patients were classified into: mild, moderate, severe, and critical cases. Information on demographic, clinical, and laboratory characteristics were collected using a standardized questionnaire. All patients were subjected to ABO blood grouping. The statistical calculations were performed by JMP Pro 14.3.0. A *P* value of < 0.05 was considered significant.

Results: The study comprised of 404 patients. The age range of the patients varied from 16 to 100 years with a male predominance (204, 50.5%). Out of the total patients, 250 (61.88%) had mild-moderate course, while 154 (38.12%) had severe-critical course. The most frequent blood group was O (164, 41.58%), followed by blood group A (121, 29.95%). There was no significant difference in the distribution of the Rh factor among the studied subjects (*P* = 0.426). There was a significant increase in disease severity and worse outcome with increasing age (*P* = <0.0001). Considering blood group types, there were no significant differences between blood group types with COVID-19 severity and patients' outcome.

Conclusions: Individuals with blood group O may have a higher risk of contracting COVID-19. Advanced age is a crucial predictor of disease severity and poor outcomes. There were no significant association between blood group types with COVID-19 severity and patients' outcome. However, further research is needed to confirm these findings and determine the underlying mechanisms behind any potential association between blood groups and COVID-19 susceptibility, severity, and outcome.

Keywords: COVID-19; severity, outcome, blood group

Introduction

Coronavirus disease (COVID-19), caused by novel coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has rapidly spread around the world, leading to a global pandemic. The virus is transmitted primarily through respiratory droplets, but aerosol, direct contact with contaminated surfaces, and fecal-oral transmission were also reported during the COVID-19 epidemic.¹ As of April 12, 2023, the virus has infected over 750 million people and caused more than 6.5 million deaths worldwide.²

COVID-19 has a broad range of clinical severity and often lacks specific symptoms. Most patients experience mild or no symptoms and recover well, while a minority can develop severe-critical disease and potentially fatal complications, resulting in death.³

Various risk factors have been implicated in the susceptibility, severity and mortality in patients with COVID-19 infections, for e.g. gender, age, and comorbid diseases.⁴ However, other factors such as environment, hormones, and blood group phenotypes have suggested to play an important role too.⁵

There is conflicting evidence regarding the link between blood group typing and susceptibility to COVID-19, as well as its outcomes.⁶ Numerous studies have reported that individuals of any blood group are susceptible to contracting SARS-CoV-2 infection, without any particular preference for a specific blood group.⁷ However, other investigators found that individuals with certain blood group phenotypes may be more or less susceptible to the disease.⁸ A study from China found that patients with blood group A had a higher risk of

COVID-19 infection and developing severe disease, while blood group O had a lower risk.⁵ Another study from USA found that blood group B and AB were more likely to acquire the virus so did those with Rh positive blood type, while blood group O was less likely.⁹

The exact mechanism behind this association is not clear yet, but some investigators have suggested that blood group antigens may interact with the SARS-CoV-2 virus in a way that affects the severity of the disease.⁵ These factors may play an important role in the pathogenesis of COVID-19 and subsequently developing a treatment.

While several studies have investigated demographic, clinical, and laboratory characteristics of COVID-19 in Duhok province,^{10,11} the relationship between ABO typing and COVID-19 infection has not been explored yet. Therefore, the objective of this study was to determine the frequency of blood group types among COVID-19 patients and to investigate its potential association with disease severity and patient outcomes.

Patients and Methods

Setting

The study was conducted in three different healthcare facilities in the Duhok region. The first facility was the Duhok COVID-19 hospital, which includes 50 ward beds and 20 ICU beds and focuses on severe, critical, and complicated cases. The second facility was Lalav infectious diseases hospital, a 100-bed hospital that mainly manages moderate to severe cases. The third facility was the Zakho COVID-19 center,

located in Zakho emergency hospital, which consists of 48 beds and primarily manages moderate to severe cases. More severe cases are referred to the Duhok COVID-19 hospital.

Study Design and Patients

This study is a prospective cross-sectional investigation conducted in the Duhok province, Kurdistan Region, Iraq, from February to July 2022. All PCR confirmed COVID-19 patients who agreed to participate in the study were included, while those who were diagnosed based on laboratory tests other than PCR or radiological images were excluded. Enrolled patients provided informed consent, and information on demographic, clinical, and laboratory characteristics were collected using a standardized questionnaire. The ethical committee of the Directorate General of Health (DGOH) in Duhok, Iraqi Kurdistan approved the study (Reference number: 1342022-2-12).

Classification of Disease Severity

COVID-19 patients were classified in accordance to National Institutes of Health COVID-19 Treatment Guidelines³

(1) **Mild type:** Patients who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell). On the other hand, dyspnea or abnormal chest imaging should not be present.

(2) **Moderate type:** Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO_2) $\geq 94\%$ on room air at sea level.

(3) **Severe type:** Individuals who have $SpO_2 < 94\%$ on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) < 300 mm Hg, a respiratory rate > 30 breaths/min, or lung infiltrates $> 50\%$.

(4) **Critical type:** Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

Laboratory Investigations

COVID-19 diagnosis was conducted using Real-Time Polymerase Chain Reaction (RT-PCR) on the upper respiratory tract specimens of all patients. Additionally, blood samples were collected from each patient and analyzed using the standard ABO blood typing method, as previously described.¹²

Statistical Analysis

The demographic characteristics of the COVID-19 patients were presented in mean and Sta. deviation or number and percentage. The associations of demographic characteristics and blood groups with disease severity and patients' outcomes were examined in Pearson chi-squared tests. The null hypothesis was rejected in a P -value < 0.05 . The statistical calculations were performed by JMP Pro 14.3.0 (https://www.jmp.com/en_us/home.html).

Results

The demographic, clinical and blood group characteristics of the COVID-19 is demonstrated in Table 1. The study comprised of 404 patients. The age range of the patients varied from 16 to 100 years, with a male predominance (50.5%). Out

of the total patients, 250 (61.88%) had mild-moderate course, while 154 (38.12%) had severe-critical course (Table 1).

Table 2 presents the frequency distribution of ABO blood grouping among COVID-19 patients. Among the 404 patients, the highest frequency was observed in blood group O, with 168 individuals (41.58%), followed by blood group A, with 121

Table 1. Demographic, clinical and blood group characteristics of the COVID-19 patients

Characteristics (n = 404)	Statistics	
	Numbers	Percentages
Age (16–100 yrs)	Mean: 48.54	SD: 19.67
Age category (16–100 yrs)		
16–19	5	1.24
20–29	71	17.57
30–39	83	20.55
40–49	61	15.1
50–59	66	16.34
60–69	48	11.88
70–79	32	7.92
80–89	27	6.68
90–100	11	2.72
Gender		
Male	204	50.5
Female	200	49.5
Disease severity		
Mild-moderate	250	61.88
Severe-critical	154	38.12
Patient outcome		
Recovered	369	91.34
Dead	35	8.66
Blood group		
A–	3	0.74
A+	118	29.21
AB–	1	0.25
AB+	22	5.45
B–	6	1.49
B+	86	21.29
O–	11	2.72
O+	157	38.86

Table 2. Prevalence of ABO blood groups and Rh susceptibility with COVID-19

Blood group	Total no. (%)	Rh–	Rh+	P value
A	121 (29.95)	3 (2.48)	118 (97.52)	0.426
B	92 (22.77)	6 (6.52)	86 (93.48)	
O	168 (41.58)	11 (6.55)	157 (93.45)	
AB	23 (5.69)	1 (4.35)	22 (95.65)	
Total	404 (100)	21 (5.2)	383 (94.8)	

individuals (29.95%). On the other hand, blood group AB patients were the least prevalent, accounting for only 5.69% of the cases. The Chi-square test showed that there was no significant difference in the distribution of the Rh factor among the studied subjects ($P = 0.426$).

Table 3 presents the association between blood groups with disease severity and patient outcomes among COVID-19 patients. The table highlights a significant increase in disease severity and worse outcome with increasing age. Considering blood group types, there were no significant differences between blood group types with COVID-19 severity and patients' outcome.

Table 4 provides comparison between each specific blood group in relation to severity and outcomes of COVID-19. For blood group A, B, AB, and O, 64.46%, 63.04%, 69.57%, and 58.33% were classified as mild-moderate disease, respectively. Rh-positive patients had 62.14% mild-moderate disease, while Rh-negative patients had 57.14% mild-moderate disease. The data presented in table indicates no statistically significant differences between ABO blood groups in terms of COVID-19 severity and outcome, with P -value >0.05

Discussion

The distribution of ABO blood typing among COVID-19 patients has been a topic of interest for investigators due to its

potential implications in COVID-19 susceptibility, severity, and mortality.

In our study, blood type O was found to be the most prevalent, followed by blood type A. This finding was consistent with a research conducted in Sulaimaniyah, Iraq, where the frequencies of ABO types followed the pattern of $O > A > B > AB$ and Rh positive $>$ Rh negative.¹³ The outcome of our study contradicts another study in Iraq, which identified blood group A as the most prevalent.¹⁴ However, a neighboring country, Saudi Arabia, reported results consistent with our study, indicating that blood type O (62.4%) was the most common blood group among COVID-19 patients, followed by blood type A (25.2%).¹⁵ Another study conducted in the USA reported that the prevalence of COVID-19 was higher in patients with type O blood (45.5%) compared to those with A blood (34.2%).⁹ This finding was also observed in studies conducted in China⁵ and Pakistan,⁷ where blood group O was found most frequent type. The finding in our study suggests that individuals with blood group O may have higher risk of contracting COVID-19. However, it is important to note that this finding did not provide evidence of a causal relationship between blood groups and COVID-19 susceptibility. On contrary, other literatures reported that individuals with blood group A had a higher risk of COVID-19 infection, while individuals with blood group O had a lower risk of infection.^{9,16,17} However, we believe that

Table 3. Association between blood types and COVID-19 severity and patient outcomes

Characteristics ($n = 404$)	Disease severity		P -value*	Patient outcome		P -value*
	Mild-moderate ($n = 250$)	Severe-critical ($n = 154$)		Recovered ($n = 269$)	Dead ($n = 35$)	
Age category (16–100 yrs)						
16–19	4 (80.00)	1 (20.00)		5 (100)	0 (0.00)	
20–29	66 (92.96)	5 (7.04)		71 (100)	0 (0.00)	
30–39	66 (79.52)	17 (20.48)		83 (100)	0 (0.00)	
40–49	43 (70.49)	18 (29.51)		61 (100)	0 (0.00)	
50–59	44 (66.67)	22 (33.33)	<0.0001	61 (92.42)	5 (7.58)	<0.0001
60–69	16 (33.33)	32 (66.67)		38 (79.17)	10 (20.83)	
70–79	9 (28.13)	23 (71.88)		24 (75.00)	8 (25.00)	
80–89	2 (7.41)	25 (92.59)		22 (81.48)	5 (18.52)	
90–100	0 (0.00)	11 (100.00)		4 (36.36)	7 (63.64)	
Gender						
Male	124 (60.78)	80 (39.22)	0.6466	185 (90.69)	19 (9.31)	0.6388
Female	126 (63.00)	74 (37.00)		184 (92.00)	16 (8.00)	
Blood group						
A–	3 (100)	0 (0.00)	0.4941	3 (100)	0 (0.00)	0.7954
A+	75 (63.56)	43 (36.44)		104 (88.14)	14 (11.86)	
AB–	1 (100.00)	0 (0.00)		1 (100)	0 (0.00)	
AB+	15 (68.18)	7 (31.82)		20 (90.91)	2 (9.09)	
B–	2 (33.33)	4 (66.67)		6 (100)	0 (0.00)	
B+	56 (65.12)	30 (34.88)		80 (93.02)	6 (6.98)	
O–	6 (54.55)	5 (45.45)		11 (100)	0 (0.00)	
O+	92 (58.60)	65 (41.40)		144 (91.72)	13 (8.28)	

* Two-sided P value

Table 4. Association of disease severity and patients' outcomes among patients with different blood groups

Blood group	Disease severity		P-value*	Patient outcome		P-value*
	Mild-moderate (n = 250)	Severe-critical (n = 154)		Recovered (n = 269)	Dead (n = 35)	
Group A						
A	78 (64.46)	43 (35.54)	0.4848	107 (88.43)	14 (11.57)	0.1744
Non-A	172 (60.78)	111 (39.22)		262 (92.58)	21 (7.42)	
Group B						
B	58 (63.04)	34 (36.96)	0.7939	86 (93.48)	6 (6.52)	0.406
Non-B	192 (61.54)	120 (38.46)		283 (90.71)	29 (9.29)	
Group AB						
AB	16 (69.57)	7 (30.43)	0.4346	21 (91.30)	2 (8.70)	0.9955
Non-AB	234 (61.42)	147 (38.58)		348 (91.34)	33 (8.66)	
Group O						
O	98 (58.33)	70 (41.67)	0.2154	214 (90.68)	22 (9.32)	0.577
Non-O	152 (64.41)	84 (35.59)		155 (92.26)	13 (7.74)	
Rh						
Rh-	12 (57.14)	9 (42.86)	0.6461	21 (100)	0 (0.00)	0.2391
Rh+	238 (62.14)	145 (37.86)		348 (90.86)	35 (9.14)	

*Pearson chi-squared tests were performed for statistical analyses.

the higher prevalence of COVID-19 in blood type O in the present study can be explained by the fact that blood type O is more common in our regional population.¹⁸ In general, further prospective research with case control are warranted to better understand the association between blood group types and COVID-19 susceptibility.

Considering risk factors associated with disease severity and mortality, we found that increasing age was associated with disease severity and worse outcome in COVID-19 patients. Several researchers documented this finding.^{10,19,20} This is because older individuals have impaired immunity, reduced production of T cells in the thymus, and an increased prevalence of comorbid diseases such as diabetes mellitus, and hypertension. These factors decrease the ability of the immune system to respond to pathogens, making older individuals more susceptible to severe illness from COVID-19.¹⁹ It is interesting to note that the present study did not find gender to be a significant predictor of severity or mortality in COVID-19 patients, which contrasts with the findings of our previous report where female gender was identified as a predictor of disease severity.¹⁰ Other literatures described male gender as risk factor for severe COVID-19.^{4,21} It is important to keep in mind that the findings of individual studies can vary and are subject to various factors such as sample size, study design, and population characteristics. Further research may be necessary to better understand the relationship between gender and COVID-19 severity and mortality.

This study investigated the potential correlation between the ABO blood group system and COVID-19 severity and outcomes. However, our data did not indicate any significant association between any of the blood groups with the severity and outcome of COVID-19, which contrasts previous study conducted in Sulaimaniyah, Iraqi Kurdistan.¹³ In agreement

to our findings, Ishaq et al. reported no significant association between ABO groups and infection severity or associated death in a retrospective cohort study of 1067 COVID-19 patients.⁷ Several other studies have also reported similar findings. For e.g., a large, multi-institutional, retrospective review found no association between ABO blood type and COVID-19 severity and death.⁹ Likewise, studies from Turkey demonstrated that blood groups did not have significant predictive effects on COVID-19 severity and mortality,^{8,17} and there was no significant difference in the frequency of severe COVID-19 infection among ABO blood types.²² Many studies conducted in countries such as Kuwait,²³ Lebanon,²⁴ China,²⁵ Italy,²⁶ the USA,^{6,9} and France²⁷ have also reported results that were in line with our findings. However, some studies have reported different findings regarding the association between blood types and COVID-19 severity and outcomes. For example, a study in China found that blood group A patients had a higher risk of severity, while blood group O patients had a lower risk.²⁸ Another study in India found that blood group O patients had decreased mortality, while blood group B patients had increased mortality.²⁹ Yet another study in Spain found that blood group A patients had a higher mortality risk, while group O patients had a lower mortality risk.¹⁶ Further study from the USA suggested that individuals with blood group A and AB had a higher risk of severe disease and mortality than those with blood group O or B.³⁰ Nonetheless, limited data is available on the association between blood groups and COVID-19 severity and outcomes, and further research is needed to fully understand the potential association between blood groups and COVID-19 severity and mortality.

This study has several limitations. First, we did not include a control group to determine the exact susceptibility of

individuals with different blood types to COVID-19; second, small sample size; third, observational study that did not prove causation.

In conclusion, individuals with blood group O may have a higher risk of contracting COVID-19. Advanced age is a crucial predictor of disease severity and poor outcomes. There were no significant association between blood group types with COVID-19 severity and patients' outcomes. However, further research is needed to confirm these findings and determine the underlying mechanisms behind any potential association between blood groups and COVID-19 susceptibility, severity, and outcome.

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Conflict of Interest

The authors declare that there is no conflict of interest. ■

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