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The Effects of Blood Group Types on the Mortality and Survival of Patients with COVID-19 Infection

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Abstract

Background: Identifying patient characteristics that may contribute to significant complications and mortality is essential.
Objectives: This study was conducted to evaluate the mortality and survival of patients with COVID-19 by blood type.
Methods: This study was performed on 644 patients with COVID-19 by a retrospective cohort method using recorded data of patients admitted to Farabi and Golestan-Kermanshah hospitals. The data were extracted from patients' records through a researcher-made checklist. Logistic regression and Cox regression models were utilized in STATA software version 14 to analyze the data.
Results: About 74.53% of patients were male, and the average age was 52.55 ± 16.9 years. The prevalence of blood groups was 22.67%

(n = 146) O, 11.49% (n = 74) AB, 24.38% (n = 157) B, and 41.46% (n = 267) A, respectively. Approximately 69.05% of patients were in the intensive care unit, 37.27% experienced intubations, and 18.94% died. The results showed that the chance of death in blood group AB, B, and A was 1.05 (P = 0.910) times, 2.09 (P = 0.022) times, and 2.29 (P = 0.005) times higher than in blood group O. In addition, the survival of patients with blood group A was lower than other blood groups (P = 0.001).

Conclusions: Based on the results, blood groups O and B had a protective role against the death of COVID-19. Blood type O also required less intubation but was hospitalized longer.

Keywords: ABO Blood Groups, COVID-19, Mortality, Survival Clinical Characteristics, Infection

1. Background

Coronavirus (COVID-19) is an acute respiratory illness caused by the new RNA virus, acute respiratory syndrome, and coronavirus SARS-CoV-2 (1, 2). The number of people with COVID-19 worldwide has increased significantly since the first report of SARS-CoV-2 patients in Wuhan, China, in December 2019 (3-5). A large wave of COVID-19 generated by SARS-CoV-2 variants has been experienced in 2022 (Delta, Lambda, Mo, and Omicron). Approximately 80% of people infected with SARS-CoV-2 were at a mild to moderate state. The remaining 20% may reach a severe clinical stage for about one week, and 5% of all individuals will develop intubation or death (3, 6). Identifying the patients' characteristics that may lead to significant complications and mortality is essential. Knowing about vulnerable populations will lead to implementing prevention strategies, prognosis tools, and

potential treatment options in the future (7). Research has shown that elderly (65 years and above) with an underlying disease, such as high blood pressure, chronic kidney disease, obesity, and diabetes, are at increased risk for the disease, as well as higher rates of COVID-19 mortality (8). According to SARS in 2003, Cheng et showed a relationship between ABO blood type al. and post-exposure SARS-CoV-2 infection. Blood type O populations were believed to be less susceptible to SARS. Intrinsic mechanisms were also investigated, showing that human antihistamine antibodies could block the interaction between viruses and cells by binding to the spike (S) protein (9). As a result, efforts have been made to explore further links between patient characteristics and COVID-19. The relationship between blood type and COVID-19 appeared in March 2020 (10). Several brief scientific reports examined the relationship between the ABO group and the risk of SARS-CoV-2 infection during the

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SARS-CoV-2 epidemic in 2019. Meanwhile, studies on the relationship between blood type and coronavirus 2019 have been published. Early reports of Zhao et al. (11) and Li et al. (12) indicated a relationship between the disease and blood type (13). Recently, patients with type A or AB were related to increased risk and severity of the disease, and patients with type B or O were related to decreased disease severity (14). However, other studies have failed to provide evidence of a relationship between blood type and mortality in COVID-19 patients (15, 16).

2. Objectives

According to the different results, a study was conducted through blood type to evaluate the mortality and survival of patients with COVID-19.

3. Methods

3.1. Study Design

This study was accomplished by retrospective cohort method on the recorded data of COVID-19 patients admitted to Farabi and Golestan-Kermanshah hospitals.

3.2. Sample Size and Sampling Method

This study was conducted on patients with COVID-19 between March 2021 and January 2022 who were selected by convenient sampling. The inclusion criteria were patients with a minimum age of 18 years and a maximum age of 85 years old with positive PCR test results. The exclusion criteria included incomplete information recorded in the patient's files and having concomitant diseases such as hepatitis, AIDS, influenza, and tuberculosis.

3.3. Data Collection Tools and Methods

A researcher-made checklist was used to collect data. The checklist includes demographic information (gender, smoking status, intubation, underlying disease), symptoms of COVID-19 disease (fever and chills, muscle aches, shortness of breath, weakness, and lethargy), blood type (O, A, AB, and B), as well as the patient's condition (death/discharge), which was extracted from the patient's file.

3.4. Data Analyzing

Mean and standard deviation were used to describe quantitative data, and frequency and percentage were used to describe qualitative data. Kaplan-Meyer method was used to determine the survival rate (mean survival time). The rank logarithm test was used to identify variables affecting patient survival time to fit the best model with survival data. The generalized Cox model included all variables with a P-value of less than 0.25. The response variable was the number of hospitalization days. The appropriate model was fitted using the stepwise method by eliminating the effect of confounders. The risk ratio and 95% confidence interval were calculated for factors related to the survival of patients with COVID-19. The Logistic regression model was used to determine the chances of factors related to patient mortality. The collected data were analyzed using STATA software version 14. The significance level of statistical tests was considered 0.05.

4. Results

The present study was performed on 644 patients with COVID-19 with ABO blood group. About 22.67% (n = 146) had blood type O, 11.49% (n = 74) AB, 24.38% (n = 157) B, and 41.46% (n = 267) A. In addition, 74.53% (n = 480) of the patients were male. Blood group A had the highest prevalence of blood group among men (n = 220, 45.83%). There was a significant relationship between gender and blood group (P = 0.001). The mean \pm standard deviation of patients, age was 52.55 \pm 16.9 years. In general, the mean number of hospitalization days was 7.736 \pm 6.32 days, with blood group O with the longest hospital stay at 7.50 \pm 10.08 days compared to other blood groups (Table 1).

The logistic regression model was used to determine the chances of death of patients regardless of their blood type. The results showed that men casualties were 0.85 times more than women (OR = 0.85, 95% CI = 0.55, 1.33). In addition, the rate of death was 1.03 with a one-year increase in age (OR = 1.03, 95% CI = 1.02, 1.04). The death rate of patients with blood groups AB, B, and A compared to blood group O were 1.05, 2.09, and 2.09, respectively. Patients admitted to the ICU were 1.53 times more likely to die than patients in other wards (OR = 1.53, 95% CI = 0.97, 2.41). Moreover, patients who were intubated were 3.12 times more likely to die than patients without intubation (OR = 3.12, 95% CI = 1.82, 5.32). The death rate of patients per day of hospitalization was 1.03 times higher (OR = 1.03, 95% CI = 1.01, 1.05) (Table 2).

Variables	Total	Blood Type				
		0	AB	В	Α	- r-value
X						0.001
Female	164 (25.47)	44 (26.83)	26 (15.85)	47 (28.66)	47 (28.66)	
Male	480 (74.53)	102 (21.25)	48 (10.0)	110 (22.92)	220 (45.83)	
noking						0.912
Yes	6 (0.93)	1 (16.67)	1 (16.67)	2 (33.33)	2 (33.33)	
No	638 (99.07)	145 (22.73)	73 (11.44)	155 (24.29)	265 (41.54)	
tobasion						0.003
Yes	69 (15.94)	13 (13.27)	3 (4.35)	12 (17.39)	41 (59.42)	
No	364 (84.06)	85 (23.35)	48 (13.19)	98 (26.92	133 (36.54	
nderlying disease						0.776
Yes	277 (37.27)	47 (20.70)	29 (12.78)	55 (24.23)	96 (42.29)	
No	382 (62.73)	92 (24.08)	45 (11.78)	94 (24.61)	151 (39.53)	
ard						0.001
Non-ICU	199 (30.95)	27 (13.57)	18 (9.05)	83 (41.71)	71 (35.68)	
ICU	444 (69.05)	119 (26.80)	56 (12.61)	73 (16.44)	196 (44.14)	
gue						0.016
Yes	224 (34.78)	60 (26.79)	30 (13.39)	60 (26.79)	74 (33.04)	
No	420 (65.22)	86 (20.48)	44 (10.48)	97 (23.10)	193 (45.95)	
uscle pain						0.216
Yes	196 (30.43)	51 (26.02)	26 (13.27)	49 (25.0)	70 (35.71)	
No	448 (69.57)	95 (21.21)	48 (10.71)	108 (24.11)	197 (43.97)	
ortness of breath						0.582
Yes	473 (73.45)	107 (22.62)	56 (11.84)	109 (23.04)	201 (42.49)	
No	171 (26.55)	39 (22.81)	18 (10.53)	48 (28.07)	66 (38.60)	
eakness and lethargy						0.518
Yes	139 (21.58)	28 (20.14)	16 (11.51)	30 (21.58)	65 (46.76)	
No	505 (78.42)	118 (23.37)	58 (11.49)	127 (25.15)	202 (40.00)	
ath						0.011
Yes	122 (18.94)	17 (13.93)	9 (7.38)	34 (27.87)	62 (50.82)	
No	522(81.06)	129 (24.71)	65 (12.45)	123 (23.56)	205 (39.27)	
ge (y)	52.55 ± 16.9	51.95 ± 18.8	55.51±17.6	55.51 ± 17.6	51.25 ± 16.2	0.088
II	25.73 ± 3.21	24.72 ± 1.99	26.24 ± 3.13	26.24 ± 3.1	25.89 ± 3.6	0.004
mperature	37.01 ± 0.80	36.75±0.69	37.07± 0.81	37.07 ± 0.81	37.12 ± 0.86	0.003
BC	8.48 ± 6.27	7.99 ± 3.82	8.30 ± 3.98	8.30 ± 3.98	9.14 ± 8.49	0.122
DW .	14.07 ± 1.89	13.85 ± 1.86	14.15 ± 2.05	14.15 ± 2.05	14.18 ± 1.93	0.317
b	12.51 ± 1.86	12.57 ± 1.87	12.51 ± 1.81	12.51± 1.81	12.36 ± 1.87	0.316
mph	18.76 ± 11.4	18.89 ± 11.2	18.86 ± 11.7	18.86 ± 11.7	17.98 ± 11.30	0.384
r	1.23 ± 0.94	1.12 ± 0.65	1.24 ± 0.65	1.24 ± 0.65	1.24 ± 0.88	0.760
he time in hospitalization	6.32 ± 7.73	7.5 ± 10.08	6.11±7.34	6.11±7.34	5.59 ± 4.37	0.088

Abbreviation: SD, standard devotion. ^a Values are presented as mean \pm SD or No (%). ^b P-values were calculated by one-way ANOVA and Fisher's exact test or χ^2 test for the categorical variables; P < 0.05 was considered significant.

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Table 2. Characteristics and Results of the Crude	Logistic Regression for the Outcom	$ne(n=644)^{a}$			
Variables	Total	Death	Unadjusted		
-			OR (95%Cl)	P-Value [®]	
Sex		()		0.499	
Female	164 (25.47)	34 (20.73)	1 (Ref.)		
Male	480 (74.53)	88 (18.33)	0.85 (0.55, 1.33)		
Blood type					
0	146 (22.67)	17 (11.64)	1 (Ref.)		
AB	74 (11.49)	9 (12.16)	1.05 (0.44, 2.48)	0.910	
В	157 (24.38)	34 (21.66)	2.09 (1.11, 3.94)	0.022	
А	267 (41.46)	62 (23.22)	2.29 (1.28, 4.09)	0.005	
Smoking				0.886	
No	638 (99.07)	121(18.97)	1 (Ref.)		
Yes	6 (0.93)	1(16.67)	0.85 (0.09,7.38)		
Entobasion				0.001	
Yes	69 (15.94)	32 (46.38)	1 (Ref.)		
No	364 (84.06)	79 (21.70)	3.12 (1.82, 5.32)		
Underlying disease				0.001	
Yes	227 (37.27)	63 (27.75)	1 (Ref.)		
No	382 (62.73)	55 (14.40)	2.28 (1.51, 3.42)		
Ward				0.067	
Non-ICU	444 (69.05)	92 (20.72)	1 (Ref.)		
ICU	199 (30.95)	29 (14.57)	1.53 (0.97, 2.41)		
Ague				0.003	
Yes	224 (34.78)	28(12.50)	1(Ref.)		
No	420 (56.22)	94 (22.38)	0.49(0.31, 0.78)		
Muscle pain				0.001	
Yes	196 (30 43)	20 (10 20)	1(Ref)		
No	448 (69 57)	102 (22 77)	0.38(0.23, 0.64)		
Shortness of breath	440 (05.57)	102 (22.77)	0.50 (0.25, 0.04)	0.220	
Vas	472 (72.45)	05 (20.08)	1(Def)	0.220	
Ne	475 (26 55)	25 (20.08)	124(0.02.214)		
	1/1(20.55)	27 (15.79)	1.34 (0.83, 2.14)	0.001	
weakness and ictuargy	(21 50)	(2, (22, 22))	(D-f)	0.001	
Yes	139 (21.58)	42 (30.22)	1 (Ref.)		
No	505(78.42)	80 (15.84)	2.30 (1.49, 3.54)		
Age (y)	52.55 ± 16.9	60.07±17.01	1.03 (1.02, 1.04)	0.001	
BMI	77.96 ± 3.21	25.97 ± 3.98	1.03 (0.96, 1.09)	0.367	
Temperature	37.01± 0.80	36.99± 0.71	0.98 (0.74, 1.29)	0.871	
WBC	8.48 ± 6.27	9.22 ± 4.08	1.01 (0.99, 1.04)	0.198	
RDW	14.07±1.89	14.65 ± 2.35	1.19 (1.08, 1.31)	0.001	
Hb	12.51 ± 1.86	12.38 ± 1.83	0.95 (0.86, 1.06)	0.423	
Lymph	18.76 ± 11.4	15.57±11.14	0.96(0.94, 0.98)	0.001	
Cr	1.23 ± 0.94	1.35 ± 1.47	1.13 (0.95, 1.35)	0.154	
The time in hospitalization	6.32 ± 7.73	8.00 ± 9.66	1.03 (1.01, 1.05)	0.012	

 a Values are presented as mean \pm SD or No (%). $4^{\,b}$ P-value $<\,$ 0.05 was considered significant.

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Figure 1 reports the unadjusted Cox regression model and Kaplan-Meyer diagram to compare the hospitalization period with recovery or death status in the ABO blood group. In the Kaplan-Meyer diagram, blood groups O and AB had higher survival rates than blood groups A and B, which showed a significant difference in the log-rank test (P = 0.001). The results of the Cox regression model showed that patients with blood group B had 2.16 and 2.43 times shorter survival time than those with blood group O, which was significant (P = 0.001, Figure 1). Patients with blood type A were 1.68 times shorter than those with blood type A and blood type B was 1.26 times shorter survival time than those with blood type other than B. In addition, the life expectancy of patients with blood groups AB and O was longer than those with blood groups other than AB (Figure 1).

The simple and multiple Cox regression model results showed that men's survival time was 0.96 times more than women (OR = 0.96, 95% CI = 0.64, 1.44). In addition, the survival time decreases 1.02 times for one year older (OR = 1.02, 95% CI = 1.01, 1.03). Patients admitted to the ICU had 1.56 times less survival time than patients admitted to other wards (OR = 1.56, 95% CI = 1.02, 2.37). Moreover, intubated patients had a longer lifespan of 1.37 times longer than patients who were not intubated (OR=1.37, 95% CI = 0.91, 2.09) (Table 3).

5. Discussion

Since the advent of COVID-19, different results have been reported regarding the correlation between blood type, mortality, and survival rates among infected individuals. The relationship between COVID-19 and ABO blood type has been a controversial area and an active research topic worldwide.

In this study, the frequency of blood groups was A (41.46%), B (24.38%), O (22.67%), and AB (11.49%), respectively. A case-control study conducted in Wuhan, China, in 2020 on 105 positive cases of COVID-19 and 103 controls showed the prevalence of blood groups A (42.8%), B (26.8%), AB (8.57%) and O (21.9%) (17). A study by Yan Cheng et al. on 256 hospitalized patients with COVID-19 showed that blood groups were A (25%), B (24%), AB (4%) and O (47%) (18). In addition, a study conducted in South America in 2020 on people with COVID-19 showed that most patients had blood type O (49%), followed by A (27%), B (19%), and AB (7). Since different studies have been performed on diverse populations with different genotypes, the difference in frequency of blood groups in different studies may be due

to the study population.

The present study showed that the mean age of people with COVID-19 is 52.55 ± 16.9 years, which showed a significant relationship between age, morbidity, and mortality (P = 0.001). Researchers have also found that age and gender are associated with susceptibility or severity of SARS-CoV-2 infection (19). In other studies, it has been proved that aging results in a higher mortality rate, and the risk of death in people over 50 years is 3.77 times higher than in people under 50 years (20). A study by Nikolic-Zurgich on aging and the immune system showed that immunity is a set of age-related changes that affect the immune system and lymphatic organs and increase vulnerability to infectious diseases over time. As a result, older people are more prone to mortality and complications associated with infectious diseases (21). Age is a significant predictor of morbidity and mortality, which is unsurprising. As a result, specific preventive and therapeutic measures must be implemented in the elderly population.

Women were involved more than men with the disease and lost their lives as a consequence. A study conducted in Massachusetts was also consistent with the present study (22). A survey of 120 people with COVID-19 in Mexico found that the risk of mortality in men was 1.74 times higher than in women but did not show a significant relationship (20). A study by Katharine E on patients with COVID-19 showed that male gender and aging were significantly related to death (7).

People with blood type A were more susceptible to SARS-CoV-2 infection. In the first report, Zhao et al. stated that SARS-CoV-2 tended to infect people with blood type A among people with different blood types, and type O was less infected (11). The results of other studies also showed that people with blood type A are more prone to infectious diseases than other blood groups, which was consistent with the present study (23). Another study showed a significant relationship between COVID-19 disease and blood type A, which was not observed in other blood groups (17). Other studies have suggested that people with blood type A may be at increasing risk for infection, and type O may be protective (16, 24). Determining why blood type A populations are more susceptible to the SARS-CoV-2 virus is complex. In fact, in most cases, the cause of some diseases in a particular blood type is still unclear.

The blood group types among patients with COVID-19, blood groups A and B with increasing risk of death compared with blood type O, were correlated. A study by James Szymanski et al. in New York on 6574 patients with



Figure 1. Cox unadjusted regression model and Kaplan-Meier plot comparing the survival time (in days) between the blood type groups. Time survival: Duration of hospital stay. Statistically significant P-value < 0.05 for a difference between groups.

f able 3. Data Analysis Using the Crude and Adjusted Cox Regression Models (n = 644)							
Variables —	Unadju	isted	Adjusted				
	HR (95%Cl)	P-Value ^a	AHR (95%Cl)	P-Value ^a			
Sex		0.876		-			
Female	1 (Ref.)						
Male	0.96 (0.64, 1.44)						
Smoking		0.916					
No	1 (Ref.)						
Yes	1.11 (0.15, 7.99)						
Entobasion		0.133					
No	1 (Ref.)						
Yes	1.37 (0.91, 2.09)		-				
Underlying disease		0.044		0.882			
No	1 (Ref.)		1 (Ref.)				
Yes	1.45 (1.01, 2.10)		1.03 (0.68, 1.54)				
Ward		0.037		0.135			
Non-ICU	1 (Ref.)		1 (Ref.)				
ICU	1.56 (1.02, 2.37)		1.40 (0.90, 2.18)				
Ague		0.004		0.125			
No	1 (Ref.)		1 (Ref.)				
Yes	0.53(0.34, 0.81)		0.68(0.41, 1.11)				
Muscle pain		0.040		0.519			
No	1 (Ref.)		1 (Ref.)				
Yes	0.60 (0.37, 0.97)		0.83 (0.47, 1.45)				
Shortness of breath		0.993					
No	1 (Ref.)		-				
Yes	0.99 (0.64, 1.53)						
Weakness and lethargy		0.001		0.002			
No	1 (Ref.)		1 (Ref.)				
Yes	1.99 (1.37, 2.90)		1.91 (1.28, 2.85)				
Age (y)	1.02 (1.01, 1.03)	0.001	1.02 (1.01, 1.03)	0.001			
BMI	1.03 (0.97, 1.08)	0.338	-	-			
Temperature	1.04 (0.79, 1.36)	0.752					
WBC	1.01 (0.98, 1.03)	0.526	-	-			
RDW	1.08 (1.01, 1.17)	0.045	1.07 (0.98, 1.16)	0.090			
Hb	0.99 (0.90, 1.09)	0.911	-	-			
Lymph	0.98 (0.96,0.99)	0.048	0.99 (0.97, 1.01)	0.593			
Cr	1.03 (0.91, 1.16)	0.595	-	-			

 a P-value < 0.05 was considered significant.

COVID-19 showed that the risk of death in blood group A (HR = 1.17, CI = 1.02 - 1.33) and blood group B (HR = 1.29, CI = 1.08 - 1.54) increased compared to blood group O (13). A study in Wuhan, China, found that people with COVID-19 in blood type A had a higher risk of death (25). Li et al. found a similar relationship between ABO and COVID-19 at a central hospital in Wuhan, China (12). Other studies have also indicated that non-O blood types are at higher risk for infection and death (26). The present study showed that blood group O was younger than the other blood groups, but there was no significant relationship between age and blood groups. A cohort study conducted at three different hospitals in China showed that people with blood type O had a younger mean age, and this study did not show a significant relationship between age and blood type (10). However, an analysis of African Americans hospitalized in the United States found that people with AB blood type had a lower mean age than other blood groups (18). Therefore, age is a confounding factor for the survival of patients based on blood group. Consequently, checking the survival of patients with COVID-19 based on blood groups in almost the same age groups is suggested.

5.1. Conclusions

Based on the results, there was a significant relationship between the survival rate of patients with COVID-19 and their blood type. Blood group A and blood group B had an increasing risk of death compared to blood group O. On the other hand, most hospitalized patients in the intensive care unit had blood type A. Blood groups A and B also had the highest intubation rate, but blood group O was more hospitalized than other blood groups.

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Footnotes

Authors' Contribution: Ar. N, Za. N contributed to designing the study. Za. N, Ar. N collected the data, and Za analyzed the data. N, Ar. N. The final report and manuscript were written by Ma Sh, Al J, and Za. N, Ar. N. All the authors read and approved the version for submission.

Conflict of Interests: The authors declare there are no competing interests.

Data Reproducibility: The identified datasets of the current study are available from the corresponding author upon reasonable request.

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