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Research Paper

Frequency of ABO Blood Groups in Patients With COVID-19 Referred to Ali Ibn Abi Taleb Hospital in Rafsanjan in 2020

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ABSTRACT

Background and Aim: The Coronavirus causes severe contamination and disease by targeting cell antigens. This study aimed to evaluate the frequency of ABO blood groups in patients with COVID-19.

Materials and Methods: A total of 343 patients with COVID-19 hospitalized in Ali Ibn Abi Taleb in Rafsanjan City, Iran, in the first half of 2020 were selected upon their availability. The study included a demographic checklist, blood group, pulmonary involvement by high-resolution CT scan, and severity of the disease based on clinical symptoms. Chi-square tests and logistic regression were used to analyze data with a 0.05 significant level.

Results: Of 343 patients studied, 108 patients (31.5%) had blood group B, 102 patients (29.7%) blood group O, 98 patients (28.6%) blood group A, and 35 patients (10.2%) had blood group AB. Regression analysis showed that disease severity in patients with blood group O was 31.9% compared to patients with blood group A. Also, in comparison to blood group A, the pulmonary involvement in patients with blood group B was 16%, blood group AB was 20.6% more, and blood group O was 39.8% less.

Conclusion: The non-significant odds of COVID-19 severity were lower in blood group B and higher in blood group O in comparison to blood group A. Also, the severity of pulmonary involvement was lower in blood group O and higher in blood group AB in comparison to blood group A.

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1. Introduction

On October 8, 2019, many cases of pneumonia appeared with an uncertain cause in Wuhan, China [1]. The continuous outbreak of this pneumonia was reported about a new coronavirus called acute respiratory syndrome of coronavirus 2 [2]. The disease spread rapidly from Wuhan, China to other areas, as reported internationally. On February 12, 2020, the World Health Organization (WHO) named the disease that originated from the new coronavirus, corona virus 2019 (COVID-19) [3]. After purifying the virus, the lavage of the patients was diagnosed with genomic sequence and analysis of genetic sequences; the corona family of the virus characterized the virus closely related to acute respiratory syndrome and the Middle East respiratory syndrome virus [4]. After entering the body, the COVID-19 virus targets the lung tissue and affects the lungs by connecting branches on its spherical coating to the receptor called ACE (ACE2 receptor), which is located on a series of pulmonary cells [5] So far, various risk factors for COVID-19 disease have been reported; Meanwhile, age has been reported as an important factor in the incidence and damping of the disease. Regarding the age distribution, 87% of the patients are between 30 and 79 years old [5]. Underlying diseases, such as high blood pressure, diabetes, heart disease, cerebrospinal arteries [6], and other risk factors, can be male and smoking [7]. Recent studies have shown that phenotypes of blood groups are an important genetic factor in some diseases. The ABO system is the most important blood group system located on the surface of red blood cells with its antigens on the outer membrane of red blood cells. The surface of many other cells in the body, such as epithelial, nerve, platelets, and vascular endothelium, is also located [8].

The RH system is also an important system of blood groups and is only found in red blood cells. Several clinical evidence of the role of the ABO system in various diseases such as blood, digestive and cardiovascular diseases, and some cancers are found [9]. On the other hand, there is evidence of the effect of ABO on the risk factors of vascular thrombosis. Also, the increase in Von Willebrand factor has been raised as a risk factor in cardiovascular diseases [10]. Meanwhile, some recent studies have indicated the relationship between the blood group and the risk of COVID-19 disease. On the other hand, in some studies, it was found that the blood group was not strongly associated with a higher risk of infection, but the level of serum antibodies against certain blood groups was significantly associated with the risk of COVID-19 disease [11]. Regarding the role of blood groups on the incidence of some diseases especially COVID-19, the importance of recognizing the risk factors and predisposition to COVID-19 disease and the potential impact of blood groups on the clinical outcome of COVID-19 (mortality, discharge, and length of hospital stay), this study aimed to investigate the frequency of blood groups in patients with COVID-19 at Ali ibn Abi Taleb Hospital in Rafsanjan.

2. Materials and Methods

This study was performed cross-sectionally and analytically. The statistical population consisted of all patients with COVID-19 referring to Ali ibn Abi Taleb Hospital in Rafsanjan in the first 6 months of 2020. Using Shiryazdi et al. [12] sample size formula, the sample for the present study was estimated 350 COVID-19 patients. The inclusion criteria were informed consent to participate in the study and a definitive diagnosis of COVID-19 based on a positive PCR test. The exclusion criterion was defects in the hospital record.

After obtaining the approval of the ethics committee (IR.RUMS.REC.1399.272) and explaining the objectives of the study and obtaining patients' informed consent, the researcher, attending the patients' bedside, completed a checklist including age, gender, occupation, previous medical history, and blood group information through interviews and case studies. According to the ninth national version of the COVID-19 Diagnosis and Treatment Guide [13], a radiologist evaluated the severity of pulmonary involvement using high-resolution CT scan (HRCT).

Overall, the findings in HRCT pulmonary COVID-19 patients can be seen (with various grades): Patchy ground-glass opacities, crazy paving appearance, patchy consolidations with surrounding ground-glass halo, and patchy consolidations with and without air-bronchogram. Peripheral stripe-like opacity may also be seen after a few days since the onset of symptoms. Generally, findings in the peripheral parts of the lung are the most common. Depending on the degree of involvement of each lobe, a score is assigned to that lobe: 0=No involvement; 1=involvement less than 25%; 2=involvement 26%-50%; 3=involvement 51%-75%; and 4=over 76% involvement. The lobe's involvement can be ground-glass opacity, consolidation, or nodules. The sum of the scores assigned to the lobes is added together. Eight scores are average involvement, and

more than 8 are considered severe involvement. The severity of the disease was also considered according to the ninth national version of COVID-19 Diagnosis and Treatment Guide: stage one (mild) fever of fewer than 38 degrees, sore throat with or without dry cough, chills, headache, losing the sense of taste and smell, nausea, vomiting, anorexia, diarrhea, body aches, weakness, and fatigue [13]. These symptoms can be different for each person, and the patient can have one or more of the symptoms. The vital signs are stable at this stage, and the oxygen saturation level is above 93%. Stage two or the respiratory phase is characterized by respiratory symptoms such as asthma, pain, pressure in the chest, etc. with or without fever equal to/greater than 38°C, the level of oxygen saturation between 99%-93%, and pulmonary involvement less than 50%. The symptoms of the second phase (severe respiratory phase) include the rapid development of respiratory symptoms, especially aggravated asthma, a rate of breathing of 30 breaths per minute, oxygen saturation level less than 90%, the percentage of the fraction of inspired oxygen less than 300 mmHg, and pulmonary

Table 1. Frequency distribution of research variables by blood group in patients with COVID-19

Variables	Groups	No. (%)					P
		Blood Group				Total	
		A (n=98)	B (n=108)	AB (n=35)	O (n=102)		
Gender	Female	50(0.51)	50(3.46)	18(4.51)	47(4.51)	165(1.48)	0.850
	Man	48(0.49)	58(7.53)	17(6.48)	55(9.53)	178(9.51)	
Job	Free	28(6.28)	25(1.23)	12(3.34)	36(3.35)	101(4.29)	0.459
	Governmental	32(7.32)	41(0.38)	11(4.31)	26(5.25)	110(1.32)	
	Unemployed	38(8.38)	42(9.38)	12(3.34)	40(2.39)	132(5.38)	
Drug use	Yes	9(2.9)	8(4.7)	1(9.2)	12(8.11)	30(7.8)	0.399
	No	89(8.90)	100(6.92)	34(1.97)	90(2.88)	313(3.91)	
Smoking	Yes	10(2.10)	10(3.9)	4(4.11)	7(9.6)	31(0.9)	0.802
	No	88(8.89)	98(7.90)	31(6.88)	95(1.93)	312(0.91)	
Underlying disease	Yes	40(8.40)	50(3.46)	17(6.48)	52(0.51)	159(4.46)	0.541
	No	58(2.59)	58(7.53)	18(4.51)	50(0.49)	184(6.53)	
The severity of pulmonary involvement	>25	34(7.34)	31(7.28)	13(1.37)	45(1.44)	123(9.35)	0.529
	26-50	44(9.44)	55(9.50)	14(0.40)	44(1.43)	157(8.45)	
	51-75	14(3.14)	15(9.13)	5(3.14)	7(9.6)	41(0.12)	
	<76	6(1.6)	7(5.6)	3(6.8)	6(9.5)	22(4.6)	
Outcome of the disease	Discharge	43(9.43)	60(6.55)	15(9.42)	59(8.57)	177(6.51)	0.454
	Death	14(3.14)	12(1.11)	5(3.14)	14(7.13)	45(1.13)	
	Intubation	0	1(9.0)	0	0	1(3.0)	
	Outpatient	41(8.41)	35(4.32)	15(9.42)	29(4.28)	120(0.35)	
Severity of the disease	Mild	41(8.41)	35(4.32)	15(9.42)	29(4.28)	120(0.35)	0.382
	Medium	43(9.43)	60(6.55)	15(9.42)	59(8.57)	177(6.51)	
	Intense	14(3.14)	13(0.12)	5(3.14)	14(7.13)	46(4.13)	

involvement more than 50% in HRCT. Step three or the inflammation exacerbation phase -acute is characterized by symptoms of respiratory failure despite non-invasive oxygen therapy, oxygen saturation level less than 88%, signs of shock, and multi-organ failure. In this study, patients of the third group were included. Finally, the data were analyzed using SPSS software version 22 by chi-square tests, t-test, analysis of variance, Mann-Whitney U, and Kruskal-Wallis tests. Logistic regression was used to calculate the odds ratio based on blood group; a blood group was considered a reference. The raw odds ratio of COVID-19 was determined based on serological results among individuals with different blood groups. The impacts of confounding variables such as age, gender, occupation, history of drug use, history of smoking, and the presence of underlying disease were adjusted. The significance level for all tests was considered at 0.05%.

3. Results

In this study, 343 individuals with a Mean±SD age of 55.35±17.23 years (range=23-298 years) were studied. Mean±SD weight was 73.26±13.03 kg, mean length of hospital stay was 4.03±4.52 days, Mean±SD lymphocyte count was 1100.65±882.57, Mean±SD CRP 44.04±73.66, the Mean±SD of involvement severity was 1.89±0.85, and the Mean±SD of disease severity

Table 2. Frequency distribution of research variables in terms of Rh in patients with COVID-19

Variables	Groups	No. (%)			P
		Rh		Total	
		Positive (n=36)	Negative (n=307)		
Gender	Female	13(1.36)	152(5.49)	165(1.48)	0.128
	Man	23(9.36)	155(5.50)	178(9.51)	
Job	Free	17(2.47)	84(4.27)	101(4.29)	0.037
	Governmental	7(4.19)	103(6.33)	110(1.32)	
	Unemployed	12(3.33)	120(1.39)	132(5.38)	
Drug use	Yes	4(1.11)	26(5.8)	30(7.8)	0.596
	No	32(9.88)	281(5.91)	313(3.91)	
Smoking	Yes	3(3.8)	28(1.9)	31(0.9)	0.876
	No	33(7.91)	279(9.90)	312(0.91)	
Underlying disease	Yes	21(3.58)	138(0.45)	159(4.46)	0.128
	No	15(7.41)	169(0.55)	184(6.53)	
Severity	>25%	9(0.25)	114(1.37)	123(9.35)	0.326
	26-50%	17(2.47)	140(6.45)	157(8.45)	
	51-75%	7(4.19)	34(1.11)	41(0.12)	
	<76%	3(3.8)	19(2.6)	22(4.6)	
Outcome	Discharge	18(0.50)	159(8.51)	177(6.51)	0.662
	Death	7(4.19)	38(4.12)	45(1.13)	
	Intubation	0	1(3.0)	1(3.0)	
	Outpatient	11(6.30)	109(5.35)	120(0.35)	
Severity of the disease	Mild	41(8.41)	109(5.35)	120(0.35)	0.512
	Medium	43(9.43)	159(8.51)	177(6.51)	
	Intense	14(3.14)	39(7.12)	46(4.13)	

Table 3. Relationship between COVID-19 disease severity (mild, moderate, and severe) based on the regression model

Blood groups	Univariate			Multivariate		
	OR	%95 Confidence Interval	P=0.399	OR	%95 Confidence Interval	P=0.798
A	Ref	-	-	Ref		
B	1.288	2.177-0.762	0.344	1.203	2.067-0.700	0.504
AB	0.966	2.024-0.461	0.927	1.137	2.450-0.527	0.743
O	1.517	2.586-0.889	0.126	1.319	2.287-0.761	0.324
Rh			0.334			0.519
Rh-	Ref	-	-	Ref		
Rh+	0.721	1.401-0.371	0.799	0.799	1.583-0.403	0.519

Table 4. Relationship between pulmonary involvement severity (less than 25%, 26%-50%, 51%-75%, more than 76%) based on the regression model

Blood groups	Univariate			Multivariate		
	OR	%95 Confidence Interval	P=0.132	OR	%95 Confidence Interval	P=0.061
A	Ref	-	-	Ref		
B	1.181	1.971-0.708	0.523	1.160	1.942-0.692	0.573
AB	0.998	2.056-0.485	0.996	1.206	2.509-0.580	0.616
O	0.648	1.093-0.384	0.104	0.602	1.024-0.354	0.061
Rh			0.083			0.519
Rh-	Ref	-		Ref	-	-
Rh+	0.056	1.077-0.296	0.083	0.799	1.583-0.403	0.519

was 1.78±0.66. Among the 343 subjects, 108 (31.5%) had blood group B, 102 (29.7%) O, 98 (28.6%) A, and 35 (10.2%) had blood group AB. The frequency distribution of research variables by blood group is given in Tables 1 and 2. As seen, the frequency distribution of gender (P=0.850), occupation (P=0.459), drug use (P=0.399), smoking (P=0.802), underlying disease (P=0.541), severity of pulmonary involvement (P=0.529), disease outcome (P=0.454) and severity of disease (P=0.382) were not significant according to blood group (Table 1).

Also, of these, 36 (10.5%) were Rh-negative, and 307 (89.5%) were Rh-positive. Among other factors, only the frequency distribution of occupations in the Rh group was significant (P=0.037) (Table 2).

As shown in Table 3, in the univariate condition, the blood group (P=0.399) and Rh (P=0.334) had no statistically significant relationship with the severity of COVID-19 disease. Also, in multivariate conditions, the relationship between the blood group (P=0.798) and Rh (P=0.519) with the severity of COVID-19 disease was not statistically significant. Compared to patients with blood group A, the odds of severe disease in patients with blood group B were 1.288 times higher. Also, patients with blood group O had 1.517 times higher odds of developing a more severe form of the disease than patients with blood group A. However, the odds of more severe disease in patients with blood group AB was about 0.4 less than that of blood group A. According to Table 4, in the univariate condition, the blood group (P=0.132) and Rh (P=0.083) had

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no statistically significant relationship with the severity of pulmonary involvement. Also, in multivariate conditions, the relationship between the blood group (P=0.061) and Rh (P=0.519) had no significant relationship with the severity of pulmonary involvement. Patients with blood group B are 1.181 times more likely to have more pulmonary involvement than patients with blood group A. Also, Rh-positive patients are 0.056 times more likely to have less pulmonary involvement than Rh-negative patients.

4. Discussion

This study aimed to evaluate the frequency of ABO blood groups in patients with COVID-19 in Ali Ibn Abi Taleb Hospital in Rafsanjan in the first half of 2020. Of 343 subjects, 31.5% had blood group B, 29.7% had blood group O, 28.6% had blood group A, and 10.2% had blood group AB. In the study by Li et al. 39.3% of patients had blood group A [2] and Dai et al. showed that people with blood group O were far less likely to develop COVID-19 than other blood groups. People with blood group A, especially patients with a history of cardiovascular problems such as high blood pressure are more likely to progress to severe cases of COVID-19 [12]. Hessami et al. named blood group A the most prevalent blood group among people with COVID-19. Blood group O was also found to play a protective role in reducing COVID-19 incidence [13]. Zietz et al. found that blood group A had the highest and blood group O had the lowest ratio among COVID-19 patients [14]. Fernandez-Botran et al. found a statistically significant relationship between blood groups and the risk of COVID-19 disease. The results of this study showed that blood group O has a protective role against COVID-19 disease, which is probably due to the lower incidence of thrombotic and cardiovascular events among these individuals [15]. Zhang et al. also found a statistically significant relationship between blood groups and the risk of COVID-19 [16]. In a study by Alkout et al., blood group A was found to play a predisposing role to COVID-19. It was also found that there was a statistically significant relationship between the severity of the disease and blood groups so people with blood group A are much more prone to more severe disease than other blood groups [17].

Some studies have reported a higher risk of infection in blood groups A [20, 21] and AB [22, 23]. In the last two studies [18, 19], an analysis was performed to modulate the effect of age and gender variables, but in none of these studies [18-20] modulation of the effect of confounding variables of underlying diseases, smoking, contact with COVID-19 patient and, travel to high-risk areas was not done. Fan et al. identified blood group A as a risk factor for COVID-19 in women [21]. In this study, 89.5% of patients with COVID-19 were Rh-positive. Esref et al. found that Rh-negative has a protective role, and Rh-positive has a predisposing role against COVID-19 disease [22]. In Takagi's study, no correlation was found between Rh-positive blood groups and COVID-19 infection [23].

The results of the current study, which examined the association between blood group and COVID-19 infection, revealed that compared to blood group A, the severity of COVID-19 disease in individuals with blood group O was 31.9%, blood group B 20.3%, and blood group AB 13.7% higher. Also, compared to blood group A, pulmonary involvement in people with blood group AB was 20.6%, blood group B 16% higher, and blood group O was 39.8% less. In this regard, Rouhanizadeh et al. found that the risk of COVID-19 infection in people with blood group O was significantly lower compared to other blood groups (30%) [24]. As we know, the exact cause of death of some patients with COVID-19 is not known. Some cite clot formation and cardiovascular disease as a reason for increased mortality. On the other hand, cardiovascular diseases, which can be a risk factor for the severity of COVID-19 [25], are more prevalent in people with non-O blood groups [26]; therefore, they can be considered confounding factors and affect the results of the study. It should be noted that the method of conducting studies is one of the possible reasons for the difference in results [22].

In some studies, the evaluation of COVID-19 infection was based on a positive PCR test [19, 20, 27] or positive PCR test and clinical signs [21, 28], and the selection of the control group included the total population of the area before the occurrence of COVID-19 [18, 27], normal population with negative antibody test [19], or individuals with negative PCR test without clinical signs [22]. Therefore, this variation is not ineffective in selecting the case group and the control for the heterogeneity between the results. In this study, the definitive diagnosis of COVID-19 was based on a positive PCR test, but the CT scan findings were also used. It is noteworthy that blood group antigens (hematopoietic-blood antigens) are found on the surface of red blood cells and in other body cells, including mucosal surfaces and body secretions [29, 30]. These antigens can act as receptors or cofactors for the virus, altering the tendency of the virus to enter the cell [27, 31] or, as a false receptor, preventing it from attaching to the cell [32]. As the virus multiplies in the epithelial cells, the blood group antigens sent in those cells may also appear on the virus's surface [33].

Blood group antibodies can also be considered part of the innate immune system against enveloped viruses, including SARS-CoV-2 [34], which carry blood group antigens. Therefore, these antibodies in blood group O can prevent the virus from attaching to its receptor. In this study, the checklist was completed based on patients' reports; so, caution should be exercised in generalizing the results.

5. Conclusion

This study showed that the odds of disease severity were lower in blood group B and blood group O but higher in blood group A, although these odds were not significant. Also, the severity of pulmonary involvement was lower in blood group O and higher in blood group AB than in blood group A, which was not significant. However, caution should be exercised in generalizing the results according to the sample size, geographical discussion, and sampling method.

Ethical Considerations

Compliance with ethical guidelines

The Ethics Committee of Rafsanjan University of Medical Sciences approved this study (Code: IR.RUMS.REC 1399,272).

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Authors' contributions

All authors have contributed to the present research department's design, implementation, and writing.

Conflict of interest

The authors declared no conflict of interest.

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