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Original research

Investigation of associations between ABO blood group and the severity of COVID-19 in patients admitted to a referral hospital, northern Iran

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus is the third strain of coronavirus with a possible zoonotic origin, which has been labeled deadly since the beginning of the new millennium. Due to various factors affecting the morbidity and mortality of coronavirus disease 2019 (COVID-19) and its various clinical syndromes, in this study we examined the relationship between the ABO blood group and the severity of COVID-19 patients. In this cross-sectional study, the required information was obtained by studying all records of patients with COVID-19 admitted to Razi Hospital in Rasht from April to May 2020. Information in patients' records including age, gender, clinical signs, blood type, high-resolution computed tomography (HRCT) findings, and nasopharyngeal tests was collected. In total, 548 cases were studied; of which 305 patients were male and 243 patients were female. The mean and standard deviation of patients' age was 58.15 ± 0.7 years. PCR test was performed for 195 patients. ABO positive/negative blood group was not significantly associated with disease severity in patients with COVID-19. The results of the present study showed that gender, age, history of underlying disease, disease severity, and ABO blood group were not significantly associated with disease severity.

Keywords: ABO blood group, Coronavirus, COVID-19, Outcome

1. Introduction

In December 2019 in Wuhan, China, cases of pneumonia of unknown etiology with features such as pyrexia, radiological symptoms of acute respiratory distress, decreased or normal white blood cell count, lymphopenia, and failure to respond to antibiotic treatment after 3 to 5 Days were identified [1, 2]. COVID-19 was created by a corona beta virus now known as SARS-CoV-2. SARS-CoV-2 bears a 79% sequence similarity to SARS-CoV, which was prevalent from 2002 to 2003 [3, 4]. It is also an RNA virus that is covered by an envelope-like structure [5]. The coronavirus causes disease in humans, some mammals, and birds. Many studies consider its origin to be a bat [6]. The virus is transmitted through droplets in the air and direct contact with contaminated objects and touching the nose, eyes, and ears, as well as from person to person [7]. The virus

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may have symptoms including fever, cough, sputum, sore throat, respiratory problems, gastrointestinal problems, and headache [8]. The most important side effects of COVID-19 include acute respiratory syndrome, secondary infections, cardiovascular damage, and liver dysfunction. In the elderly and patients with underlying disorders such as diabetes, cardiovascular disease, lung disease, etc., the mortality rate due to the virus has increased [9, 10]. No biological biomarkers have been identified to predict COVID-19. ABO blood groups are carbohydrate epitopes found on the surface of human cells. Determinants of blood groups A and B are the Galα1-3- (Fucα1,2) -Galβ trisaccharide components, GalNAcα1-3- (Fucα1,2) - Galβ- - while Fucα1,2-Galβ- as the antigen is blood group O. Blood groups remain important as important and effective genetic factors in different generations and their relationship with many diseases has been proven. Past studies have shown that Norwalk virus and hepatitis B are sensitive to blood type, and it is also reported that people with blood type O are less likely to develop SARS-CoV. As a result, the risk of viral infections is associated with the type of ABO blood type [11, 12]. Anti-A antibody inhibits the adhesion of S protein of SARS-CoV cells to the ACE2 cell line [13]. Due to the similarity of nucleic acid sequences and similarity of angiotensin 2 (ACE2) converting enzyme binding between SARS-CoV and SARS-CoV-29-11, low sensitivity of blood group O and high sensitivity of blood group A in COVID-19 with the presence of antibodies Anti-blood group, especially anti-A antibody in the blood is associated [14].

In general, there may be other mechanisms associated with the type of blood clot with COVID-19 that further studies are needed to substantiate these hypotheses [15].

Given that if the type of blood type ABO is associated with COVID-19, the type of blood type is known as a biological biomarker in the susceptibility of this virus. In this study, the relationship between the ABO blood group and the severity and outcome of patients with COVID-19 admitted to Razi Hospital from March 1998 to May 1999 was investigated.

2. Materials and Methods

2.1 Study design

In this cross-sectional analytical study, after obtaining permission from the Ethics Committee in University Research at Guilan University of Medical Sciences (Ethical code: IR.GUMS.REC.1399.116) in the molecular and clinical diagnosis laboratory of Guilan University of Medical Sciences in Rasht from April to May 2020, so that after referring to the evidence of patients' records including age, sex, clinical symptoms, history of underlying diseases, blood type, HRCT findings and nasopharyngeal test to determine the relationship between blood type with severity and outcome of COVID-19were collected. After collecting information, the data were entered into SSPS software version 22 for analysis. Data collection tools were recorded as a checklist containing patient information including age, sex, clinical symptoms, history of underlying diseases, blood type, disease severity, and disease outcome.

2.2 qRT-PCR analysis

The nucleic acid was extracted from all samples of patients with the Sansure Biotech Inc kits. Amplification was done using Bio-Rad Real-Time PCR Machine. Concerning the Sansure PCR kit, there was a fundamental step for reverse transcription 30 mins, 50°C, for cDNA pre-denaturation step 1 min, 95°C, next 15 secs, 95°C at 45 cycles and denaturation, annealing, and an elongation 30 secs, 60°C, and definitely, for instrument cool down to step 10 secs, 25°C.

2.3 High-resolution CT (HRCT) test

Positive HRCT chest decisions for COVID-19 were described as ground-glass opacities in the typical subpleural location. The CT scan was performed in one breath-hold to decrease thoracic movement. The slice thickness is 1 to 3 mm. Images were collected by the whole thorax. Proposed parameters to reduce the radiation dose were Kvp: 100-120, mAs: 50-100, Pitch: 0.8-1.5, Thickness: 1-3 mm.

2.4 Statistical analysis

After collecting the data, the information was entered into SPSS software version 22. To describe quantitative variables of mean and standard deviation and qualitative variables were described as numbers and percentages. Statistical tables and graphs are also used to describe the data. Chi-square and Fisher tests were used to examine the relationship between variables. The error level was also considered 5%. Finally, logistic regression was used to model the data.

3. Results

The descriptive characteristics of the patients with COVID-19 studied in the study are as follows: Out of 548 patients with COVID-19, 305 (55.7%) were male and 243 (44.3%) were female. Their mean age was 58.15 ± 0.7 years, of which 273 (49.8%) were in the age group of fewer than 58.15 years and 275 (50.2%) were in the age group of more than 58.15 years. Also, the youngest person was 16 years old and the oldest person was 98 years old.

In overall, 157 (28.6%) A + blood group, 13 (2.4%) A-, 87 (15.9%) B +, 11 (2%) B-, 40 patients (7.3%) were AB +, 1 patient (0.2%) was AB-, 204 patients (37.2%) were O + and 35 patients (6.4%) were O-. In the more general classification, 170 people (31%) were blood group A, 98 people (17.9%) were blood group B, 41 people (7.5%) were blood group AB and 239 people (43.6%) were blood group O. 195 (35.6%) of them were PCR tested which 77 (14.1%) were positive. 521 (95.1%) were HRCT tested, of which 521, 514 (98.6%) were positive and 7 (1.4%) were negative. 234 (42.7%) had O2 saturation above 93% and 314 (57.3%) had O2 saturation below 93%.

Of the 548 patients with COVID-19 studied, 314 (57.3%) with a fever, 374 (68.2%) with a cough, 209 (38.1%) with muscle pain, 354 (64.6%) with respiratory distress, (8.9%) with decreased level of consciousness, 43 (7.8%) had olfactory reduction, 39 (7.1%) with a decrease in taste, 7 (1.3%) with headache, 1 (0.2%) with chest pain, 2 (0.4%) with abdominal pain, 5 (0.9%) with nausea, 3 (0.5%) had vomiting, 2 (0.4%) with diarrhea, 17 (3.1%) with cancer, 9 (1.6%) with hepatitis, 120 (21.9%) with diabetes, 17 (3.1%) with blood diseases, 13 (2.4%) with an immunodeficiency, 3 (0.5%) with pregnant, 114 (20.8%) with cardiovascular disease, 51 (9.3%) with renal failure, 13 (2.4%) were on dialysis, 34 (6.2%) with asthma, 40 (7.3%) with lung disease, 23 (4.2%) with diseases of the nervous system, 77 (14.1%) with hypertension, 57 (10.4%) with other diseases, 308 (56.2%) with at least one underlying disease and 240 (43.8%) had no underlying disease, 30 (5.5%) were intubated and 518 (94.5%) were intubated, the severity of the disease was 231 (42.2%) moderate, 287 (52.4%) severe and 30 (5.5%) severe, 456 (83.2%) were discharged and 92 (16.8%) died.

ABO blood group had no significant relationship with the severity of the disease in patients with COVID-19 (P = 0.216).

ABO blood group was not significantly associated with disease severity in patients under 58 years of age with COVID-19 using the Fisher test (P = 0.279).

Also, the ABO blood group had no significant relationship with the severity of the disease in patients over 58 years of age with COVID-19 using the Fisher test (P = 0.717) (Table 1).

ABO blood group was not significantly associated with disease severity in male patients with COVID-19 using the Fisher test (P = 0.229).

Also, the ABO blood group had no significant relationship with the severity of the disease in female patients with COVID-19 using the Fisher test (P = 0.882).

ABO blood group had no significant relationship with disease severity in patients with the underlying disease with COVID-19 using the Fisher test (P = 0.691).

Table 1. Distribution of disease severity in patients with COVID-19 by ABO blood group by age

Variable		Disease severity			Total	P-Value
		Medium	Intense	Serious		
Under 58 years	A	26 (32.1%)	51 (63%)	4 (4.9%)	81	0.279
	B	25 (45.5%)	29 (52.7%)	1 (1.8%)	55	
	AB	9 (37.5%)	12 (50%)	3 (12.5%)	24	
	O	50 (44.2%)	58 (51.3%)	5 (4.4%)	113	
Total		110 (40.3%)	150 (54.9%)	13 (4.8%)	273	
Over 58 years	A	35 (39.3%)	48 (53.9%)	6 (4.7%)	89	0.717
	B	21 (48.8%)	20 (46.5%)	2 (4.7%)	43	
	AB	5 (29.4%)	11 (64.7%)	1 (5.9%)	17	
	O	60 (47.6%)	58 (46%)	8 (6.3%)	126	
Total		121 (44%)	137 (49.8%)	17 (6.2%)	275	

Table 2. Distribution of disease severity in patients with COVID-19 by ABO blood group by an underlying disease.

Variable		Disease severity			Total	P-Value
		Medium	Intense	Serious		
Underlying disease	A	36 (37.5 %)	53 (55.2%)	7 (7.3 %)	96	0.691
	B	26 (48.1%)	27 (50%)	1 (1.9%)	54	
	AB	9 (45%)	10 (50%)	1 (5%)	20	
	O	64 (46.4%)	66 (47.8%)	8 (5.8%)	138	
Total		135 (43.8%)	156 (50.6%)	17 (5.5%)	308	
without underlying disease	A	25 (33.8%)	46 (62.2%)	3 (4.1%)	74	0.223
	B	20 (45.5%)	22 (50%)	2 (4.5%)	44	
	AB	5 (23.8%)	13 (61.9%)	3 (14.3%)	21	
	O	46 (45.5%)	50 (49.5%)	5 (5%)	101	
Total		96 (40%)	131 (54.6%)	13 (5.4%)	240	

Also, the ABO blood group had no significant relationship with the severity of the disease in patients without underlying disease with COVID-19 using the Fisher test (P = 0.223) (Table 2).

ABO positive/negative blood group had no significant relationship with disease severity in patients with COVID-19 using the Fisher test (P = 0.228).

4. Discussion

In our study, among the patients, a PCR test was performed on 195 patients, of which 77 had a positive PCR and a definite case of COVID-19.

In the study by Hu et al., The results showed that among those in close contact with a definite case of COVID who were examined and their PCR results were positive, 20.8% had a short interval, and 50% had positive CT findings, while 20.8% of these cases were never symptomatic; these populations were significantly younger [16].

According to the results of Nikpouraghdam M study with Logistic Regression analysis, age, male gender, and underlying diseases have a significant effect on mortality in COVID-19 patients [17]. In MERS and SARS, men were more affected than women [18]. Women are less likely to be infected due to the X chromosome and sex hormones that affect innate acquired immunity [19].

In the present study, the ABO blood group was not significantly associated with disease severity in patients with COVID-19.

But a 2005 study by Cheng et al., Which looked at the association between ABO blood type and severe acute respiratory infection, reported that SARS-CoV infection is differentiated through ABO blood group systems. They found that people with blood type O had a much lower chance of getting the virus than those without blood type O [20].

Also, a study by Guillon et al. was conducted in 2008 in Hong Kong with the aim of epidemiological analysis of the prevalence of COVID 19 disease. SARS-CoV is reported to proliferate in cells that express histo-blood ABH antigens, and the SARS-CoV glycosylated S protein binds to the angiotensin-converting enzyme 2, which acts as a cellular receptor. In this study, a cell model was used to understand whether natural antibodies to the ABO system could block the interaction of the angiotensin-converting enzyme and protein S. It was also observed that this interaction depended on the adhesion of these cells to a cell line expressing the angiotensin-converting enzyme by normal monoclonal or anti-A antibodies, which may block virus interactions with the receptor and thus protect. To better understand the possible effect of ABO polymorphisms on the epidemiology of SARS, they developed a mathematical model of virus transmission dynamics that considers the protective effect of natural ABO antibodies. This model showed that ABO polymorphisms can play a role in significantly reducing virus transmission and affect the number of infected individuals and the kinetics of the epidemic. Finally, they reported that blood type O showed a lower risk of disease [13].

In our study, according to the results of logistic regression of age variables, cancer, hypertension and the severity of COVID-19 disease is an independent predictor of disease outcome in patients, so patients over 58 years of age compared with patients under 58 years of age. They are years old, their death rate is 3.154 times higher (P = 0.0001) and patients with cancer

have a death rate of 3.707 times higher than patients without cancer (0.025 (P = 0) and patients with hypertension compared to patients without hypertension, the death rate is 2.11 times higher (P = 0.014) and patients whose disease is more severe than other patients, Their death ratio is 3.205 times higher (P = 0.0001).

In various studies such as the meta-analysis by Yang et al. And meta-analysis by Zheng et al., The underlying diseases of diabetes, hypertension, cardiovascular disease, and hyperlipidemia have been associated with a worse prognosis [21]. In some studies, hypertension has been identified as an independent risk factor for severe COVID-19 [22]. It should be noted, however, that hypertension is a common disease worldwide with an incidence of 78% in people aged 65 to 74 in Sweden. After statistically adjusting for age, they found that there was no relationship between blood pressure and mortality [23].

A 2020 study by Zhao et al. Aimed to examine the relationship between ABO and COVID-19 blood groups in 2173 patients admitted to three Chinese hospitals who tested positive. These results showed that blood type A had a higher risk of developing COVID-19 than those without blood type A. While, whereas blood type O showed the lowest risk of contracting the virus. This study was the first to determine the association between ABO and COVID-19 blood type. However, it is a preliminary and limited study that needs further study in this field [24].

The results of the present study showed that among the parameters of age, gender, the severity of COVID-19 disease, blood groups, pregnancy status, cancer, hepatitis, diabetes, blood diseases, immune deficiency disease, cardiovascular disease, insufficiency kidney, dialysis, asthma, lung disease, nervous system disease, hypertension, and other underlying diseases are the only variables of age, cancer, hypertension and the severity of COVID-19 disease.

Authors' contributions

All authors contributed equeally in all parts of manuscript, also read and approved the final version of manuscript.

Conflict of interests

None to declare.

Ethical declarations

The Research Ethics Committee of Guilan University of Medical Sciences has been accepted all processes of the current study (IR.GUMS.REC.1399.116).

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