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Original Article

The Probable Association between Blood Groups and Prognosis of COVID-19

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Abstract

Background: We aimed to verify the association between blood group systems and prognosis of SARS-Cov-2 disease.

Methods: In this cross-sectional study, 329 patients infected with SARS-Cov-2 diagnosed based on their COVID-19 RT-PCR results and chest CT scans, were enrolled in the study. These patients were admitted to Kamkar Arab Nia Hospital, Qom, Iran from March to June 2020. Their blood groups and RH were determined, and demographic characteristics and clinical signs of patients were recorded. The patients' temperature and peripheral capillary oxygen saturation levels (SpO2) were measured. Finally, the duration of hospitalization, intubation, and death rate were also analyzed.

Results: The results of the patients' blood group analysis were as follows: 129(39.2%) patients had A type, 66(20.1%) B type, 21(6.4%) AB type, and 113(34.3%) O type. Of 329 patients, 297 (90.3%) had Rh antigen. The dead cases were higher in O blood type at 13 cases (11.5%). Considering the positive and negative rhesus antigen, 31 (10.4%) and 1 (3.1%) were dead respectively, but the difference was not statically significant**.** As for the A group, the mean of admission duration (8.4±6.1 days) was not significantly different from the B group (8.8 ±7.2 days). AB group with a mean (7.4 ±4.4 days) was not significantly different from the O group (7.8 ± 5.4 days). There was no significant difference in the duration of hospitalization in RH patients, positive or negative. B blood group showed a significant association with the time interval to return to normal oxygen levels.

Conclusion: Blood type was not associated with COVID-19 death rate, nor was it associated with admission duration. B blood group showed a significant association with the time interval to return to normal oxygen levels.

Keywords: SARS-Cov-2; Blood Group Antigens; Iran

Introduction

Coronaviruses are the RNA viruses that trigger flu-like manifestation in the respiratory system (1). This family induce mild symptoms of human coronavirus manifestations along with HCoV-229E and HCoV-OC43 on the respiratory system, then the mutated family member reveal fur-

ther possible effects to damage the alveoli and contribute to edema and sever acute respiratory disease. "Since the 1970 the replication and pathogenesis mechanism of different coronaviruses have been studded" (2).

Severe acute respiratory syndrome coronavirus (SARS-COV or SARS-CoV-1) first occurred in Japan and some other countries in 2002, affecting the 8,000 people with a mortality rate of 10 percent (3, 4). The SARS epidemic was monitored, but the MERS-COV showed the potential ability to spread among 27 countries with a higher rate of mortality than SARS-COV1, more than 35% (5).

The clinical feature varied from asymptotic to cough, dyspnea, myalgia, chills, and headache (6, 7). In some of these cases, the gastrointestinal involvement, such as nausea, vomiting, anorexia, has been recorded (8, 9). In some patients (27-70%), the kidney transplant was performed (10).

A rapid increase in the mortality rate in Wuhan, China, at the end of December warned of a potential respiratory pandemic. Gradually, a novel form of coronavirus affected other countries so called SARS-CoV-2 causing COVID-19 (11-13).

In comparison of SARS-CoV-2 with other types, it has the lowest mortality rate (3.4%), but this pandemic condition resulted from the rapid transmission human to human because of the mutation in the surface glycoprotein (S) which links to angiotensin-converting enzyme 2 (ACE-2) (14).

The first patient with positive nasopharyngeal COVID-19 RT-PCR in Iran was detected on February 7, 2020 (15). Many studies investigated the risk factors of this novel coronaviruses. Male patients, age more than 65, the history of chronic diseases such as diabetes, chronic obstructive pulmonary disease (COPD), hypertension and cardiovascular diseases are mentioned (16).

The antigens of the ABO blood group system are intricate carbohydrate molecules on the outer surface of red blood cells membrane (17). The early publication on blood group and infection disease, related ABO blood type was published in 1917 with tuberculosis (18). Several viral diseases have shown the role of ABO antigens in disease susceptibility and vulnerability such as in Hepatitis B, Ebola, and influenza. Many patients had O phenotype in the COVID-19 epidemic (19). Latz et al. in a study including 7648 COVID19 patients reported that A blood type was more prone to the SARS-CoV-2 virus (20).

We aimed to investigate the relationship between blood groups and COVID19 patients who referred to Kamkar-Arab Nia Hospital, Qom, Iran from March to June 2020.

Methods

This cross-sectional analysis involved 329 patients who had referred from March 1st to June 31st to Kamkar-Arab Nia Hospital, Qom, Iran diagnosed with COVID-19 based on the findings of their positive nasopharyngeal RT-PCR test and their chest CT scans.

Ethical considerations

This study was approved by the Ethics Committee of the Qom University of Medical Sciences (IR.MUQ.REC.1399.123).

Bedridden patients or intubation in the time of admission were excluded later. General data, i.e., age, gender, underlying disease were documented. In addition, COVID-19 symptoms were recorded. After collecting samples for routine blood tests, the blood groups and RH were also determined. Then, the temperatures and peripheral capillary oxygen saturation levels (SpO2) were obtained. Considering SpO2≥93% and T<37.3 °C as normal, patients with impaired cases were followed until the time of returning to normal levels. This duration was a criterion in patient's general condition prognosis. Intubation during hospitalization was also considered. Following the patient discharge, number of days that patients spent in the hospital were recorded as other criteria for prognosis. Eventually, the death cases were documented and the correlation with ABO blood group and Rh antigen were evaluated.

For statistical analysis, a simple linear regression was calculated to predict the duration of reach

93% O_2 saturation based on the blood type. We run a logistic regression to estimate the possibility of counting deaths in each blood group. The Chi-square test was calculated comparing the death with blood group. To test the differences in means for hospitalized duration and blood group the ANOVA was used. For comparing the mean of Rh antigens and time of hospitalization, the *t* independent test was utilized. In all tests, *P*-value less than 0.05 (typically ≤ 0.05) was considered statistically significant.

Results

From 329 patients, 167(50.8%) were male. The ages varied from 15 to 99 yr (mean=64.7 ±18.5). The hospitalization duration range was from 1 to 38 days (mean = 8.2 ±6 d). Thirty-two (9.7%) of patients died because of the disease. The common symptoms of patients are shown in Table 1. In addition, the past medical history of patients are shown in Table 2. The mean body temperature (T) (± standard deviation) was 37.16±0.87 °C. The mean first SpO2 level (± standard deviation) was 90.47±7.08 ranging from 40% to 99%.

Table 1: Common symptom among patients infected with COVID-19 in Qom, Iran

Variable	*%*
Fever	38.3
Chill	27.7
Cough	46.4
Weakness	24.3
Sputum	7.3
Dyspnea	58.7
Myalgia	20.1
Diarrhea	8.2
Nausea	10.6
Vomiting	7.0
Abdominal Pain	2.4

The results of the patients' blood group and Rh analysis, death rate and, the mean of admission duration in each blood groups and Rh are shown in Table 3. The dead cases were higher in O blood type as 13 cases (11.5%).

Table 2: Medical history among patients infected with COVID-19 in Qom, Iran

Medical history	*%*
Diabetes mellitus	25.8
Hypertension	39.8
Chronic obstructive pulmonary disease (COPD)	5.5
Asthma	4.8
Liver disease	1.5
Cerebrovascular accident (CVA)	5.2
Epilepsy	1.2
Alzheimer	3.3
Coronary heart disease (CHD)	12.5
Heart failure	6.1
Cancer	1.2
Chemotherapy	0.3
Hypothyroidism	1.8
End stage renal disease (ESRD)	4.3
Chronic kidney disease(CKD)	3.3
Kidney transplant	0.9
Smoking	2.1
Addiction	3.3

The relation between blood group and death rate was not statically significant (*P*= 0.854). In addition, the relation between Rh antigen and death rate was not statically significant (*P* = 0.185).
The mean of admission duration was not significantly different (*P*=0.652). There was not a significant different in the scores for Rh positive and Rh-negative mean (*P*=.111) with hospitalization duration. Linear regression analysis showed significant difference between the time interval to return to normal oxygen levels between blood groups (O blood group: ref, A blood group: *P*=0.161, B blood group: *P*=.026, AB blood group: *P*=.176). B blood group showed a significant association with the time interval to return to normal oxygen levels (*P*=.026). However, there was no significant difference in the time interval to return to normal oxygen levels between Rh antigen groups (Rh negative: ref, Rh-positive: *P*=.222).

Table 3: The results of the patients' blood group and Rh, death rate and, mean of admission duration analysis

Variable	*N*	*Percent*	*Death rate N (%)*	*Mean of admission duration D*
A	129	39.2	12 (9.3)	8.4 ± 6.1
B	66	20.1	5 (7.6)	8.8 ±7.2
AB	21	6.4	2 (9.5)	7.4 ±4.4
O	113	34.3	13(11.5)	7.8 ± 5.4
Rh +	297	90.3	31 (10.4)	8.4 ±6.1
Rh-	32	9.7	1(3.1)	6.6 ±4.4

Discussion

In this cross-sectional study, the number of people with blood type A, infected with COVID-19 was higher. Blood group (A) difference appears able to increase the risk of disease by as much as 39% (21). There is disagreement on the relations of blood groups with infectious diseases (18). Several studies have shown the effect of blood type O on the severity of diseases such as malaria, *Helicobacter pylori* and severe cholera (22-24). SARS-CoV-2 shows a positive association with blood type A with a large number of positive cases in blood type A(25).

In a study on 2,173 patients with COVID 19 in Wuhan, China, people with blood type A were more susceptible to develop the disease (26). The O blood group protects from SARS-CoV-2 effects and demographic features as well as risk factors did not confound the finding (27). For many years, there has been debate about the relationship between blood type and the incidence of various diseases, including carcinomas (28), liver disease (29, 30) and infectious diseases (31). Blood type is a significant factor in disease prognosis, especially on viral diseases (32). In a study that examined the vulnerability and prognosis of ABO blood type to Ebola virus infection, type B showed a higher risk of infection and death (33). In recent decades, O blood group was more vulnerable to the influenza virus and that the H1 antibody titer after vaccination was higher in O blood type (34). Regarding the discussion on the interaction of this novel coronavirus and blood type ABO, COVID-19's lower prevalence in blood groups B and O was due to the presence of antibody against antigen A, which appears to need further studies investigating the effect of this antibody (35). In a study in France, 998 samples from blood donors were tested and people with O blood types were less likely to become infected with the coronavirus (36).

Blood type is not a factor in coronavirus infection but it can cause the severity of this disease (37). ABO polymorphisms can significantly contribute to virus transmission (38). In one study about the association between SARS-CoV-2 infection and ABO blood group polymorphism, on 7503 positive SARS-CoV-2 cases and 2962160 controls were done. The results showed that people who were positive for SARS-CoV-2 were more likely to have blood type A and less likely to have blood type O (39). People with blood type A were at higher risk for SARS-CoV-2, and blood type O was associated with a lower risk. Blood type was almost correlated with the clinical features of patients with COVID-19 (25).

In our result, the number of blood groups A and O was close to each other (A: 39.2%, O: 34.3%). The association of hospitalization duration and blood group was not significantly different ($P>0.05$). We found a significant relationship between B blood group and time to reach O_2 saturation 93% ($P<0.05$). Based on the logistic regression, there was no significant association between the blood type and death rate. ($P>0.05$). Our observation was the result of a 329 population so to generalize the study, a research with wider population need to be considered.

Conclusion

Blood type was not associated with COVID-19 death rate, nor was it associated with admission

duration. B blood group showed a significant association with the time interval to return to normal oxygen levels.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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