

Association between ABO blood groups and rhesus antigen and susceptibility to COVID-19 in the Yazd hospital

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Abstract

Blood group antigens are one of the most important antigens in humans that have an impact on susceptibility to disease and may be used as a prognosis factor in different diseases such as COVID-19. The study aimed to investigate the relationship between ABO blood groups and Rhesus antigen and susceptibility to COVID-19. The clinical data of 398 subjects were used in the investigation collected from 148 cases vs. 250 controls. This information was obtained from Shahid Sadoughi Hospital of Yazd (IRAN) University. Blood groups and outcomes were assessed using statistical tests for four populations: COV + vs. COV- and COV +/deceased vs. COV +/live. Out of a total of 148 COVID-19 patients, 80 (54/1%) were male, 68 (45/9%) were female. Among these patients, 33 (22/6%) had type A+, 44 (30/1%) had type B+, 13 (8/9%) had type AB+, and 36 (24/7%) had type O+. On the other hand, out of 148 patients, 126 (86/3%) had positive blood types, and 20 (13/7%) had negative blood types. As a result, no significant difference was found in the relationship between ABO blood groups and RH type and susceptibility to COVID-19 (p-value = 0.392 and p-value = 0.847, respectively). Other data showed a significant difference between patients group with other parameters such as age (p-value<0.001) and gender (p-value<0.001). Although in this study there was no association between blood type and RH type with COVID-19, findings of the association between age and gender can confirm the results of previous studies.

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Keywords: Age, blood groups, COVID-19, gender, rhesus antigen

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Introduction

The COVID-19 infectious disease, caused by the novel coronavirus (SARS-CoV-2), first emerged in late December 2019 in Wuhan, China, and progressed to become a worldwide pandemic [1,2]. The virus can present with a variety of mild to severe clinical symptoms, which can involve the respiratory tract, gastrointestinal system, kidneys, and olfactory system;

some carriers, however, are asymptomatic [3]. There are different genetic factors or underlying disease pathologies, such as cardiovascular disease, diabetes, and COPD, which may contribute to the varying symptomatology [4]. Blood group is one factor that has been shown in literature as a potential contributory factor to the morbidity and mortality of COVID-19 [5]. There are two divisions for blood groups, including the main blood groups ABO and the sub-blood group Rh (antigen Rhesus) [6]. Antigens, which determine blood types, can be proteins or polysaccharides [7]. Interestingly, these blood group antigens can act as receptors for bacteria, parasites and viruses. Thus, the importance of these antigens in viral pathogenesis is found in the attachment phase of viral infection [8]. Among the different blood groups, A has been proposed as a high-risk blood type for COVID-19, while non-A blood groups, including blood group O, have a lower risk of COVID-19 [9]. However, there is still limited information in this regard, because, in addition, the Rhesus antigen found on some blood groups may also be a factor in the course of the infection of this virus(9). Therefore, we performed a study examining the role of blood group, and the presence or absence of the rhesus antigen has on the progression of COVID-19 infection. This study is the first study of its kind in Asia to account for the presence or absence of the Rh antigen within the various blood groups. The results of this study through comparing the course of patient recovery with blood group and presence or absence of Rh factor is important to further the understanding and guide future research and treatment into this novel virus.

Method

A retrospective case-control study was implemented in the period from 1st April 2020 to 5th July 2020, with a total of 398 subjects (148 cases vs. 250 controls). All subjects were patients from Shahid Sadoughi Hospital of Yazd (IRAN) University, one of the hospitals considered for the treatment of COVID-19 patients in the area. We extracted blood types for SARS-CoV-2-tested individuals using laboratory results recorded in the Shahid Sadoughi hospital HIS system. This included 148 individuals infected with SARS-CoV-2 and 250 healthy people with identified blood types who were tested for SARS-CoV-2 with nasopharyngeal and pharynx swab test (either a positive or negative result). Persons with only one positive SARS-CoV-2 lab test were accepted as COV+, even if another test was negative. We assessed the correlation between blood groups and outcomes using four pairs of populations: COV + vs. COV- and COV+/Deceased vs. COV+/Alive.

Result

In total, 148 COVID-19 patients and 250 non-COVID-19 patients were studied. Descriptive analysis of the data (Tables 1 and 2) showed that the majority of the COVID-19 patients were male (54.1%), while the majority of non-COVID-19 patients were female (70.4%). Most COVID-19 and non-COVID-19 patients had B+ (30.1%) and O+ (30%) blood types, respectively. Both groups had a similar percentage of RH ± blood type, with RH + accounting for the most patients. In both groups, the majority of patients recovered their health (Tables 3 and 5). However, COVID-19 patients had a much higher percentage of death compared to non-COVID-19 patients, 34.5% vs. 6.4%, respectively. COVID-19 patients were 55.40 years old on average and this value was 36.41 years old for non-COVID-19 patients.

Regarding the COVID-19 patients, it took, on average, 4 days after the admission date to get the test results. Each COVID-19 patient was hospitalized for approximately 11 days on average. Table 6 displays the duration of stay in the hospital for each blood type in COVID-19 patients. As can be seen, patients with B+ blood type had the highest stay in the hospital with 13.11 days on average, and the minimum stay belonged to negative blood types. However, ANOVA did not find any significant relationship between blood type and duration of stay (p -value = 0.362).

Fisher's Exact Test did not find any significant relationship between sex and two important types of release (death vs. recovery) for the COVID-19 patients (p -value = 0.489). However, a significant relationship was found between age and types of release using t -test (mean difference = 8.594+/-3.592, p -value = 0.018).

TABLE 1. Age

		Minimum	Maximum	Mean	Std. Deviation
COVID-19	Age Valid N (listwise)	0	94	55.40	22.103
Non-COVID-19	Age Valid N (listwise)	1	93	36.41	19.811

TABLE 2. Sex

		Frequency	Percent	
COVID-19	Valid	Male	80	54.1
		Female	68	45.9
Non-COVID-19	Valid	Male	74	29.6
		Female	176	70.4

TABLE 3. Sort of release

			Frequency	Percent
COVID-19	Valid	Death	51	34.5
		Recovery-Partial Recovery	89	60.1
		Other	8	5.4
Non-COVID-19	Valid	Death	16	6.4
		Recovery-Partial Recovery	169	67.6
		Other	65	26.0

TABLE 4. Blood groups

			Frequency	Percent
COVID-19	Valid	A+	33	22.6
		B+	44	30.1
		AB+	13	8.9
		O+	36	24.7
		A-	5	3.4
		B-	8	5.5
		AB-	3	2
		O-	4	2.8
		24.8		
Non-COVID-19	Valid	A+	62	24.8
		B+	65	26.0
		AB+	12	4.8
		O+	75	30.0
		A-	11	4.4
		B-	15	6
		AB-	1	0.4
		O-	9	3.6

TABLE 5. RH

			Frequency	Percent
COVID-19	Valid	positive	126	86.3
		negative	20	13.7
Non-COVID-19	Valid	positive	214	85.6
		negative	36	14.4

TABLE 6. Duration of hospitalization

Blood type	Mean duration of stay in hospital
A+	9.64
B+	13.11
AB+	8.85
O+	11.81
A-	7
B-	7.5
AB-	10
O-	4.5

Age, gender, blood type, RH type and type of release were then compared between the groups (COVID-19 and non-COVID-19). Using t-test, we found out that mean of age is significantly different between the two groups (p-value<0.001) with COVID-19 patients to be on average 9 years older (Table 1). Logistic regression showed that gender is significantly different between the two groups (p-value<0.001), with men, to be 2.798 times more likely to get the COVID-19 (OR = 2.798).

Blood type and RH type were not statistically related to the COVID-19/non-COVID-19 outcome (p-value = 0.392 and p-value = 0.847, respectively). By discarding the ‘other’ type of release, this factor was significantly related to the COVID-19/non-COVID-19 (p-value<0.001), that is, death was 6.053 times more likely to occur in the COVID-19 group than the non-COVID-19 patients.

Discussion

Blood group antigens are one of the most important antigens in humans that can be used as a prognosis factor in different diseases. Different studies have been conducted on the effectiveness of blood types on the risk of viral infections. Also, several studies have been designed around the world on the impact of blood groups on COVID-19 infection. There is data on ABO blood groups’ role in contamination to these pathogens and the severity of diseases, but this is not what we saw for COVID-19 [10–12]. Furthermore, probably there are some blind areas that were hidden from scientists. In contrast to our outcomes, Zhao et al.’s study in Wuhan showed that Chinese people with A blood group are more sensitive to COVID-19 infection [13], but there is controversy in their outcomes [14,15]. Like our study outcomes, Latz et al. study revealed that ABO blood type and RH have no relation with COVID-19 infection nor its different burdens and outcomes [14]. That study was the first study before our study that assessed the effect of RH antigen on COVID-19 infection. On the other hand, the GÖKER et al. study demonstrated that although there is a relationship between blood group and COVID-19 infection, there is no association between these antigens and disease outcome [15]. In contrast, Wu study revealed that there is a significant relationship between blood group A and increased risk of COVID-19 infection, death or recovery time [16]. However, in the present study, patients with the B blood group remained longer in the hospital, but this difference was not significant. Although the association of blood type with disease outcomes and disease severity has been established in some diseases, this was not the case with COVID-19. This study is consistent with other studies on the role of age and sex in COVID-19 outcomes and showed that infection in males occurs approximately 2.8 more times, and younger individuals recover faster than older people [17]. Some of the limitations in our study are related to the limited sample size, and geographic homogeneity of COVID-19 patients, due to the relatively low infection rate in Yazd city. Other underlying diseases may affect the research outcomes. Also, patients considered as control might be infected with

COVID-19 in the future. Since this study is the first study in the west of Asia, it could cover the geographic limitation, which has been presented in previous studies. Also the present study is the first study that assessed time of recovery in different blood groups and RH. On the other hand, this study is the second study that evaluated RH as an independent factor that can be effective on outcomes of disease, including recovery, death and also recovery time course.

Conclusion

This present study examined the role that blood groups and the presence or absence of Rh factor have on the morbidity and mortality of COVID-19. The results of this study did not find an association between blood groups, or Rh factors and the severity of COVID-19 infection when accounting for morbidity or mortality outcomes. Future studies can take the results of this mediocre study into account when designing a more robust, larger, more generalizable study.

Authors' contribution

Study concept and design: Akram Astani and Emad Behboudi; Analysis and interpretation of data: Vahideh Hamidi and Mohsen Nakhaie; Drafting of the manuscript: Fatemeh Gholizadeh and Yaser Ghelmani; Critical revision of the manuscript for important intellectual content: Javad Charostad; Statistical analysis: Emilia Maria Grala.

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Transparency declaration

All authors declared that they have no conflict of interest.

References

- [1] Wong SH, Lui RN, Sung JJ. Covid-19 and the digestive system. *JJog Hepatology* 2020;35(5):744–8.
- [2] Zandi M, Behboudi E, Soltani S. Role of glycoprotein hemagglutinin-esterase in COVID-19 pathophysiology? *Stem Cell Rev Rep* 2021:1–2.
- [3] Behboudi E, Hamidi-Sofiani V, Zeynali P. Review of therapeutic candidates for the new coronavirus disease (COVID19). *Razi J Med Sci* 2020;27(6): 0–.
- [4] Guo Y-R, Cao Q-D, Hong Z-S, Tan Y-Y, Chen S-D, Jin H-J, et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak—an update on the status. *Militar Med Res* 2020;7(1):1–10.
- [5] Zietz M, Tatonetti NP. Testing the association between blood type and COVID-19 infection, intubation, and death. *MedRxiv* 2020.
- [6] Fan Q, Zhang W, Li B, Li D-J, Zhang J, Zhao F. Association between ABO blood group system and COVID-19 susceptibility in Wuhan. *Front Cell Infect Microbiol* 2020;10.
- [7] Tam AA, Özdemir D, Fakı S, Bilginer MC, Ersoy R, Çakır B. ABO blood groups, Rh factor, and thyroid cancer risk: to 'B' or not to 'B'. *Endocrine Res* 2020;45(2):137–46.
- [8] Anstee DJB. The relationship between blood groups and disease. *J Am Soc Hematol* 2010;115(23):4635–43.
- [9] Zhao J, Yang Y, Huang H-P, Li D, Gu D-F, Lu X-F, et al. Relationship between the ABO blood group and the COVID-19 susceptibility. 2020.
- [10] Cheng Y, Cheng G, Chui C, Lau F, Chan PK, Ng MH, et al. ABO blood group and susceptibility to severe acute respiratory syndrome. *Jama* 2005;293(12):1447–51.
- [11] Harris JB, LaRocque RC. Cholera and ABO blood group: understanding an ancient association. *Am J Trop Med Hygiene* 2016;95(2):263.
- [12] Liumbruno GM, Franchini M. Beyond immunohaematology: the role of the ABO blood group in human diseases. *Blood Transfus* 2013;11(4): 491.
- [13] Zhao J, Yang Y, Huang H-P, Li D, Gu D-F, Lu X-F, et al. Relationship between the ABO blood group and the COVID-19 susceptibility. *medRxiv* 2020.
- [14] Latz CA, DeCarlo C, Boitano L, Png CM, Patell R, Conrad MF, et al. Blood type and outcomes in patients with COVID-19. *Ann Hematol* 2020:1–6.
- [15] Göker H, Karakulak EA, Demiroğlu H, Ceylan ÇMA, Büyükaşık Y, Inkaya AÇ, et al. The effects of blood group types on the risk of COVID-19 infection and its clinical outcome. *Turk J Med Sci* 2020;50(4):679–83.
- [16] Wu Y, Feng Z, Li P, Yu Q. Relationship between ABO blood group distribution and clinical characteristics in patients with COVID-19. *Clin Chim Acta* 2020.
- [17] Tay MZ, Poh CM, Rénia L, MacAry PA, Ng LF. The trinity of COVID-19: immunity, inflammation and intervention. *Nat Rev Immunol* 2020: 1–12.