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The impact of ABO blood groups on SARS-CoV 2 infection susceptibility and prognosis

Elif Torun Parmaksız, MD[1],
Ergün Parmaksız, MD[2],
Coşkun Doğan , MD[1],
Nesrin Kıral, MD[1],
Ali Fidan, MD[1],
Sevda Cömert, MD[1].

[1] Kartal Dr Lütfi Kırdar City Hospital, Departmant of Chest diseases, Istanbul, Turkey.

[2] Kartal Dr Lütfi Kırdar City Hospital, Departmant of Nephrology, Istanbul, Turkey.

Correspondence:
Elif Torun Parmaksız, MD
Kartal Dr Lütfi Kırdar City Hospital, Departmant of Chest diseases, Istanbul, Turkey.
email: dreliftorun@yahoo.com

Background and aim: Severe acute respiratory syndrome coronavirus SARS-CoV-2 is the causative agent of the global pandemic coronavirus disease 2019 (COVID-19). We aimed to investigate the susceptibility to Covid 19 infection and severity and outcomes of the disease with respect to different ABO blood groups.

Material & methods: A total of 568 subjects admitted with Covid-19 infection are retrospectively evaluated. The demographic data, clinical characteristics, radiological and laboratory findings, ABO and RH blood groups and outcomes of the disease are recorded.

Results: The mean age of 297male (52.3%) and 271 female (47.7%) subjects was 58.11 ±17.14 years(19-95). The distribution of Covid patients with respect to ABO blood groups is as follows: blood group A 46.7%(n=164), blood group O 28.9% (n=265), blood group B 15.3% (n=87) and blood group AB 9.2 %(n=52). Hypertension was the most frequent comorbidity in all blood groups. The duration of hospital stay is significantly longer in subjects with blood group A and intensive care unit (ICU) admission rates were significantly higher in blood groups A and AB.

Conclusion: A blood group tends to be more commonly infected with SARS-CoV-2 while blood group O patients have lower risk. ABO and Rh blood groups can be considered as a biomarker to predict the risk of SARS-CoV-2 infection susceptibility and fatality.

Keywords: Covid 19; blood groups; SARS-coV-2

Introduction

A public health crises has first emerged in the city of Wuhan, Hubei province in China in December 2019. This was a viral infection caused by a novel enveloped RNA betacoronavirus named as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Subsequently, the rapid surge in the number of coronavirus disease 2019 (COVID-19) cases has turned out to be a global problem. The world has previously experienced respiratory tract virus infections such as influenza A virus subtypes H1N1 and H5N1, SARS-CoV1, MERS-CoV and Ebola. However, this new coronovirus, the SARS-CoV2 has caught most of the world unprepared. Due to highly contagious nature and rapid human to human transmission, it has spread worldwide and the World Health Organisation (WHO) has declared COVID-19 as a global pandemic on March 11, 2020 [1]. This is the date when the first confirmed Covid-19 case in our country was reported. Covid-19 may emerge in a wide spectrum of clinical presentations ranging from mild symptoms to severe pneumonia and respiratory failure. Which biomarkers predict the susceptibility to COVID-19 and the severity of the infeciton are not clearly elucidated. In the current study, we aimed to investigate the predisposition to Covid 19 infection as well as severity and outcomes of the disease with respect to different ABO blood groups.

Material & Methods

In this single-centre study we recruited adult Covid-19 patients who were admitted to our clinics. Covid-19 diagnosis was based on contact history, clinical presentation, signs and symptoms and laboratory and radiological data.

The demographic data including age and gender, clinical characteristics and comorbidities of all patients were recorded. All subjects had been computerized tomography (CT) scanned on admission and radiological findings were recorded. Laboratory test results on admission were recorded. These included complete blood count, renal function tests, hepatic function tests, D-dimer, ferritin, CRP and ABO Rh blood groups. The medications used, duration of hospital stay and clinical outcomes were recorded.

Throat-swab specimens from the oropharynx and nasopharynx were obtained from all patients at admission and were put in viral-transport medium. SARS-CoV-2 was confirmed by real-time RT-PCR (reverse transcriptase polymerase-chain-reaction) test . The local Medical Research Ethics Committee approved the study. All patients had signed informed consent.

Statistical analyses were performed using SPSS software (version 17.0) The associations between blood groups (ABO and Rh) and comorbidities and gender were evaluated by using logistic regressions of risk factors on blood groups. Chi-square test was used to find out whether blood group distributions differed between the compared populations. To compare A blood group-vs-non-A blood groups and Rh positive and negative groups, we reported p-values from Fisher's exact test (two-sided), odds ratio and odds ratio confidence intervals.

Results

A total of 568 patients were included in the study; 297 (52.3%) were males and 271(47.7%) were females. The mean age of the subjects was 58.11 ±17.14 years, ranging from 19 to 95 years. The distribution of subjects with respect to ABO and Rh blood groups is demonstrated in Table 1. Nearly half of the cases (46.7%; n=265) had blood group A. A flowchart showing the outcomes of male and female subjects with respect to ABO and RH blood groups takes place in Figure 1. The most frequent comorbidities were hypertension and DM. The distribution of accompanying diseases in different blood groups is shown in Table 2. The mean ages of subjects in different ABO blood groups were similar. The laboratory data did not show significant difference in different blood groups. The length of hospital stay was similar between the groups; however, ICU admission rates were significantly higher in blood groups A and AB (Table 3). As mentioned, blood group A was the most frequent blood group. We compared A group with non-A groups and found out that malignancy was more common in group A subjects with statistical significance. The duration of hospital stay is significantly longer in subjects with blood group A (Table 4)CT findings of

Table 1. The distrubition of subjects with respect to ABO and Rh blood groups.

	n	%	Female/ male (n)	Age (mean±SD)	Total n (%)
0 Rh+	147	25.9	80/67	58.92±18.07	164 (28.9)
Rh-	17	3.0	10/7	63.59±12.88	
A Rh+	232	40.8	105/127	58.56±16.34	265 (46.7)
Rh-	33	5.8	14/19	57.73±19.09	
B Rh+	81	14.3	42/39	54.54±17.69	87 (15.3)
Rh-	6	1.1	2/4	69.33±12.24	
AB Rh+	42	7.4	13/29	56.83±17.32	52 (9.2)
Rh-	10	1.8	5/5	55.20±15.41	

Table 2. Comorbidities

	0	A	B	AB	p
Hypertension	74 (45.1%)	87 (32.8%)	35 (40.2%)	15 (28.8%)	***0.02***
DM	42 (25.6%)	61 (23.0%)	21 (24.1%)	9 (17.3%)	*0.90*
Obstructive lung disease	21 (12.8%)	36 (13.6%)	9 (10.3%)	4 (7.7%)	*0.65*
Cardiovascular disease	28 (17.1%)	52 (19.6%)	12 (13.8%)	12 (23.1%)	*0.12*
Chronic renal failure	14 (8.5%)	13 (4.9%)	1 (1.1%)	1 (1.9%)	***0.05***
Malignancy	12 (7.3%)	29 (10.9%)	3 (3.4%)	3 (5.8%)	*0.14*

Table 3. Comparison of data based on ABO blood groups

	0	A	B	AB	p
Age	59 ± 17	58 ± 16	56 ± 18	57 ± 16	*0.33*
Leucocyte count (n/µl)	7174	7542	7126	6621	*0.55*
Lymphocyte count (n/µl)	1367	1408	1339	1473	*0.75*
Lactate dehydrogenase (U/L)	277	308	281	272	*0.37*
D-dimer (µg/L)	1671	2141	1543	918	*0.16*
Creatinine (mg/dL)	1.16	1.01	1.95	0.82	*0.2*
Ferritin (µg/L)	283	349	481	295	*0,41*
Duration of hospital stay (days)	7.26	8.28	6.37	7.52	*0,1*
ICU admission n (%)	16 (9,8)	42 (15,8)	8 (9.2)	8 (15.4)	***0,001***

Table 4. Comparison of A and non-A blood groups

	A	Non-A	p	OR	95% CI
n	265	303			
Age	58.45	57.81			
Male/female	146/119	151/152	0.23	1.23	0.88-1.71
Hypertension, n (%)	87 (32.8)	124 (40.9)	0.05	0.70	0.50-0.99
DM, n (%)	61 (23.0)	72 (23.8)	0.84	0.95	0.65-1.41
Obstructive lung disease, n (%)	36 (13.6)	34 (11.2)	0.44	1.24	0.75-2.05
Cardiovascular disease, n (%)	52 (19.6)	52 (17.2)	0.51	1.17	0.77-1.80
Chronic renal failure, n (%)	13 (4.9)	16 (5.3)	1.00	0.92	0.43-1.96
Malignancy, n (%)	29 (10.9)	18 (5.9)	***0.03***	1.94	1.05-3.59
Leucocyte count (n/µl)	7542	7065	0.23		
Lymphocyte count (n/µl)	1408	1377	0.64		
Lactate dehydrogenase (U/L)	307.8	277.5	0.07		
D-dimer (µg/L)	2141	1510	0.06		
Creatinine (mg/dL)	1.01	1.33	0.28		
Ferritin (µg/L)	349.5	337.4	0.86		
Duration of hospital stay	8.28	7.05	0.02		

Table 5. Comparison of Rh positive and negative groups

	Rh (+)	Rh (-)	p	OR	95% CI
n	502	66			
Age	57.87	59.91	0.35		
Male/female	262/240	35/31	0.89	0.96	0.57-1.61
Hypertension, n (%)	186 (37.1)	25 (37.9)	0.89	0.96	0.56-1.63
DM, n (%)	120 (23.9)	13 (19.7)	0.53	1.28	0.67-2.43
Obstructive lung disease, n (%)	65 (12.9)	5 (7.6)	0.31	1.81	0.70-4.68
Cardiovascular disease, n (%)	92(18.3)	12 (18.2)	0.97	1.01	0.51-1.96
Chronic renal failure, n (%)	22 (4.4)	7 (10.6)	0.06	0.38	0.15-0.94
Malignancy, n (%)	43 (8.6)	4 (6.1)	0.63	1.45	0.50-4.18
Leucocyte count (n/µl)	7308	7134	0.69		
Lymphocyte count (n/µl)	1393	1381	0.90		
Lactate dehydrogenase (U/L)	295.37	265.51	0.08		
D-dimer (µg/L)	1899	1027	***0.001***		
Creatinine (mg/dL)	1.17	1.25	0.75		
Ferritin (µg/L)	351.28	287.53	0.34		
Duration of hospital stay	69 (13.8)	5 (7.5)	***0.001***		

all patients were evaluated and were grouped as no radiological involvement, involvement of single lung or involvement of both lungs. The distribution of radiographic findings is demonstrated in Figure 2. In all blood groups, bilateral involvement of the lungs was the predominant feature.

ICU admission rates were 9.8% in blood group O, 15.8% in blood group A, 9.2% in blood group B, 15.4% in blood group AB. Exitus rates were 3.7% in blood group O, 6% in blood group A, 2.3% in blood group B, 5.8% in blood group AB.

The clinical features and laboratory data of Rh positive and negative subjects is demonstrated in Table 5.

Discussion

In this comprehensive research, we observed association between ABO blood groups and Covid 19 infection. Blood group A subjects tends to be more commonly infected with SARS-CoV-2. Consistent with previous studies on SARS-CoV -1 and recent studies on SARS-CoV-2, O blood group seems to be affected less [2-4]. Rh positive and negative subjects with SARS-CoV-2 infection had similar features with respect to demographic data and comorbidities, however Rh-positive cases had significantly higher rates of ICU admission.

Since onset of the outbreak, the factors associated with increased susceptibility have been investigated. The infection exhibits a very wide spectrum of severity. Male gender, age and chronic underlying diseases such as cardiovascular diseases including hypertension, diabetes mellitus, cerebrovascular diseases, immunosuppression are reported to be associated with increased COVID 19 risk for morbidity and mortality. On the other hand, it is also likely that other inborn factors will prove to be relevant to predict the predisposition and severity of the

infection. In a recent study from China, it has been reported that cases having blood group A had a higher susceptibility for SARS-CoV-2 infection and more severe disease whereas risk was lower in blood group O [4].

Viral infection susceptibility and ABO blood group interactions have been investigated for decades. The subjects with blood group O seem to be effected more by Norwalk virus [5] and Helicobacter pylori [6]. Blood group A has been associated with increased risk of susceptibility to severe acute respiratory syndrome [2].

It has been suggested that the ACE2 protein is the SARS-CoV virus receptor and me-diates the transferring enzyme activities. Therewithal, the actual and/or additional host and pathogen binding seems to be an intermediate hybrid O-glycan. O-glycosylation plays a key role in the pathogenesis of coronavirus infections. This involves the formation of hybrid, serologically A-like, O-GalNAcα1-Ser/Thr-R, T nouvelle (Tn) antigenic structures. In blood group O, polyreactive nonimmune or innate immunoglobulin M (IgM) controls the expression and qualities of the syngeneic A-like/Tn structures. The pathogen becomes exposed to the anti-ABO isoagglutinin activities. In the non-O blood groups,on the other hand, the anti-A, B and O-isoagglutinin activities are downregulated by being neutralized through the ABO-phenotype-determining enzymes. Therefore, blood group A is the preferred target for the virus [7].

In a recent study from our city, the distribution of blood groups are as follows: 38.3% A Rh (+), 29.4% O Rh (+), 13.2% B Rh (+), 6.4% AB Rh (+), 5.5% A Rh (-), 4.4% O Rh (-), 2.1% B Rh (-), 0.7% AB Rh (-) [8]. Taking our study population into account, Covid patients had blood groups as follows: 40.8% A Rh (+), 25.9% O Rh (+), 14.3% B Rh (+), 7.4% AB Rh (+), 5.8% A Rh (-), 3% O Rh (-), 1.1% B Rh (-), 1.8% AB Rh (-). It is clearly observed that blood group A is higher in the infected group compared to the whole population, whereas blood group O is lower in the infected group.

There are several limitations of the study. The study population consists of subjects admitted to the hospital. The subjects who presented milder forms of the infection and treated in outpatient's basis are not included. We do not have a control cohort group of healthy subjects from our hospital; however, this may not be a major issue since the distribution of blood groups is compared with the normal population reported previously. The association between Rh positivity and poor prognosis might have the bias of small proportion of Rh-negative cases. Nevertheless, this ratio reflects the whole population.

Certainly, susceptibility to an infection and its severity depend on various factors and solely blood group cannot be predicted as a risk factor. Nobody should take SARS-CoV-2 lightly, but prioritization of the most vulnerable population is essential. Especially blood group A and RH positive subjects should take stronger precautions.

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