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Association of IgE elevation with blood group in COVID-19 patients

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ABSTRACT

Aim : All parameters that are thought to be efficient in getting sick and follow-up of the disease should be investigated because of COVID-19 disease has serious consequences. The aim of this study was to investigate whether there is a relationship between the AB0 blood group with Rh factor systems and the frequency of catching COVID-19 infection and between IgE elevation according to blood groups and COVID-19 positivity.

Material and Method: Blood groups and IgE levels of the control group (2690 patients) were compared retrospectively with 7300 patients who were admitted to our hospital between March 10, 2020, and March 31, 2021, and confirmed as COVID-19 positive with viral ribonucleic acid reverse transcriptase-polymerase chain reaction (RT-PCR).

Results: It was found that among the blood groups, the highest COVID-19 positivity belonged to the A blood group (46.17%) and the lowest belonged to the AB blood group (9.04%). The increase in IgE elevation was found statistically significant in COVID-19 positive patients (P<0.001) when compared to the control group(P<0.001). All blood groups, except AB Rh (-), had a statistically significant increase in IgE level when blood groups were evaluated together with Rh factors (P<0.001).

AB Rh (-) blood group had an increase in IgE level that is not statistically significant (P=0.171).

Conclusion: The results of this study showed that the risk of COVID -19 disease may be associated with the AB0 blood group and Rh factor systems, and high IgE level may be observed in patients during the disease. Therefore, investigation of IgE levels may be beneficial in the follow-up of COVID-19 patients

Keywords: COVID-19, blood group, IgE

INTRODUCTION

Before the emergence of severe acute respiratory syndrome (SARS), the human coronaviruses were responsible for causing 15-30% of common cold cases. Coronaviruses are a family of RNA (ribonucleic acid) viruses that can cause infection in humans and a wide variety of animal species (1). In December 2019, an outbreak of severe acute respiratory syndrome coronavirus 2 infections, named coronavirus disease 2019 (COVID-19), was reported in Wuhan, China. COVID-19 virus has rapidly spread worldwide and has been accepted as a pandemic by the World Health Organization (WHO) (2). Clinical courses of COVID-19 were divided into three categories: asymptomatic cases, moderate cases, and severe cases. It has been reported that the mortality rate is 2-3 percent in patients with severe clinical symptoms. However, this is not seen in every patient and it varies according to the clinical presentation of the patient (mild or asymptomatic) and geographical location (3,4). Male sex, age over 60 years, diabetes, high blood pressure, lung diseases, cancer, immune system weakness are risk factors for severe COVID-19 (4,5).

The blood group is determined by the AB0 gene located on the long arm of chromosome 9 (9q34). Blood groups designate according to the presence or absence of A and B antigens produced by A and B variant alleles (6). Many studies have explored the association between AB0 and Rh blood groups and cardiovascular diseases, malignancies, and paralysis. In these studies, it has been found that the risk of disease increased in some blood groups (7,8). It has

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been suggested that the blood group have been correlated with COVID-19 disease susceptibility and the severity of the clinical course. Previous studies have shown various and contradictory results (9, 10)

Immunoglobulins (Ig) are specific molecules that bind to antigens. The IgE like other Ig (IgG, IgA, IgM, and IgD) is composed of two light chains and two heavy chains. Compared to other immunoglobulins, the IgE monomer is consists of four constant regions. The weight of IgE is 190 kDa, correspondingly, which is higher than IgG (150 kDa). The heavy chain is epsilon. Receptors are found on mast and basophil cells in the Epsilon chain. Serum concentrations of IgE are lower compared with IgG concentrations. The half-life of free IgE in the serum is approximately 2 days while IgE bound to mast cells can last for around two weeks (11). IgE is also called "allergic antibody"; plays a major role in the pathogenesis of allergic diseases and it is an important initiator of the humoral response. High IgE serum level is not always related to allergy. There are many clinical conditions associated with an increased IgE serum level (12). IgE has an important role in response to parasitic diseases (protozoa and helminths) and antitumor immunity (13). IgE serum level increases from birth, ranged up to 200 IU/mL until the age of 15 years and then decreases rapidly. IgE serum level is lower than 100 IU/mL for adults (12]). Humoral and cellular immune responses work together against viral infections but the humoral response is easier to determine under laboratory conditions than the cellular response (14). With this approach, humoral immunity investigates for the rapid diagnosis of diseases most virology laboratories (15). RT-PCR analysis is the gold standard for detecting infection in the diagnosis of COVID-19. Among the laboratory findings, lymphopenia occurred most frequently while thrombocytopenia, leukopenia and elevated levels of C-reactive protein (CRP) can also be observed. It has been reported that elevations of alanine aminotransferase, aspartate aminotransferase, creatine kinase, and D-dimer are less commonly observed. Laboratory abnormalities are more obvious in severe patients in comparison to non-severe patients (16,17).

MATERIAL AND METHOD

For this study, permission was obtained from the Presidency of the Non-interventional Researches Ethics Committee of Fırat University Faculty of Medicine (Date: 18.11.2021, Decision No: 2021//12-21). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Nose and throat swabs were collected from 7300 patients who were admitted to the emergency department with clinical complaints or COVID-19 contacts between March 2020, and March 2021, and they were confirmed as COVID-19 positive by RT-PCR BİORAD (Qiagen, Germany). The blood group and Rh factor of these patients were determined by a gel card system (Grifols Eflexis Diana, Spain). IgE levels were quantified with the nephelometry method by using the IMMAGE 800 (Beckman Coulter) and levels of 165 IU/ml or above were considered high. In this study, 2690 patients with known blood groups and levels of IgE who were admitted to our hospital were identified as a control group. The IgE levels according to blood group and Rh factor of the COVID-19 positive patients were compared with the control group. Data were analyzed using IBM SPSS version 20.0. The chi-square test was used to compare the IgE elevation in terms of blood types and Rh positivity among COVID-19 positive and negative groups. Results of the study were analyzed using frequency distributions and percentages. Chi-square results were shown in table format with the p-value.

RESULTS

Blood types and IgE levels of 7300 patients who were diagnosed with COVID-19 and the control group were compared retrospectively. Of the 7300 COVID-19 positive patients, 63,01% (4600) were men and 36.98% (2700) were women. In the control group of 2690 patients, 1360(50.55%) were men and 1330(49.44%) were women. The positivity of COVID-19 was found statistically significant in male patients compared to the control group (P<0.001). It was observed that the highest blood group was A with 46.17% and the lowest was AB blood group with 9.04%. It was found that the increase in IgE level according to Rh (+) blood factors was statistically significant among COVID-19 positive patients with IgE elevation compared to the control group(P<0.001). The increase in IgE elevation was found statistically significant in COVID-19 positive patients (P<0.001) when compared to the control group according to Rh (-) blood factor. No statistically significant increase in IgE level was observed difference between Rh factor groups (P=0,621). In **Table 1**, the distribution of IgE level of COVID-19 positive patients according to blood group and Rh factor was shown.

Blood groups according to Rh (+) and Rh (-) factors compared to the control group, all blood groups except AB Rh (-) had a statistically significant increase in IgE level(P<0.001). COVID-19 patients with AB Rh (-) blood group had an increase in IgE level compared to the control group that is not statistically significant (P=0,117). In **Table 2**, elevations of IgE level compared with all blood groups according to Rh(+) factor and Rh(-) factors.

Table 1. Distribution of IgE elevations according to blood group, Rh factors

	Patient		IgE		Control		IgE		Total		p
	n	%	n	%	n	%	n	%	n	p	
A	3400	46.57	850	25	1280	47.54	210	16.40	1060	<0.001	<0.001
0	1970	26.98	660	33.50	640	23.79	120	18.75	780	<0.001	
B	1270	17.39	520	40.94	550	20.44	140	25.45	660	<0.001	
AB	660	9.04	160	24.24	220	8.17	30	13.63	190	0.001	
Rh+	6530	89.45	1910	29.24	2320	86.24	480	20.68	2390	<0.001	0.621
Rh-	770	10.54	280	36.36	370	13.75	20	5.40	300	<0.001	

Table 2. Comparison of IgE elevations with blood groups according to Rh (+) and Rh(-) factor

	Patient		IgE		Control		IgE		Total		p
	n	%	n	%	n	%	n	%	n	p	
A Rh +	3030	41.50	730	24.09	1080	40.14	210	19.44	940	0.002	<0.001
0 Rh +	1800	24.65	600	33.33	570	21.18	120	21.05	720	<0.001	
B Rh +	1120	15.34	450	40.17	490	18.21	130	26.53	580	<0.001	
AB Rh +	580	7.94	130	22.41	180	6.69	20	11.11	150	0.001	
A Rh -	370	5.06	120	32.43	200	7.43	0	0	120	<0.001	<0.001
0 Rh -	170	2.32	60	35.29	70	2.60	0	0	60	<0.001	
B Rh -	150	2.05	70	46.66	60	2.23	10	16.66	80	<0.001	
AB Rh -	80	1.09	30	37.5	40	1.48	10	25	40	0.171	

DISCUSSION

Several research has been done on the susceptibility to infection between the pathogenesis of COVID-19 disease and blood groups. AB0 blood groups have been reported to be associated with many diseases such as type 1 diabetes, autoimmune diseases, rheumatic diseases, dengue fever, multiple sclerosis, hepatitis B and psoriasis (18,19). It has been shown that SARS-CoV infects individuals according to AB0 blood groups and can synthesize AB0 antigens in pneumocytes, the enterocytes of the small intestine, and kidney distal tubular epithelial cells (20). Antibodies of the AB0 system were suggested to hinder the interaction between SARS CoV spike protein and angiotensin-converting enzyme 2 (ACE 2) (21). There is no study on the use of biological markers to predict susceptibility to COVID-19. SARS CoV has surface proteins that bind to sugars. It has been postulated that individuals with blood group A are more susceptible to COVID-19 infection due to N-acetyl galactosamine, on the surface of blood group A cells (22). AB0 blood groups of 265 patients infected with COVID-19 were retrospectively analyzed, and the blood groups of the patients were group as follows: A in 39.3%, group B in 25.3%, group AB in 9.8%, and group 0 in 25.7%. Compared to the control group, the rate of those with blood group A was reported to be significantly higher (39.3% vs. 32.3%, P=0.017) while those with blood group 0 was significantly lower (25.7% vs. 33.8%, P<0.001) (23). Wu et al. (24). reported that the risk of getting infected by COVID-19 in a blood group A individual was significantly higher than that in other blood groups while in a 0 blood group individual had a much lower risk of getting infected by COVID-19 Arac et al. (25) reported that blood group A was dominant compared to other blood groups especially blood group 0 among COVID-19 patients,their results indicated that no statistically significant difference exists between COVID-19 patients and healthy individuals in terms of the AB0 blood group system. Gur et al. (26) found that the ratio of blood group A was higher 48.6% vs. 42.8% and blood group 0 28.2% vs. 33.7% had a lower ratio compared to Turkey's average in COVID-19 patients. In addition, they stated that the percentages of patients with A Rh+ and A Rh- blood groups were significantly higher than Turkey's average 42.1% vs. 37.8%, and 6.5% vs. 5% . In the study, the blood group A (46.57%) is highly frequent among COVID-19 patients, while blood group AB(9.04%) is the lowest. Abdollahi et al. (27) and Bhandari et al. (28) have not determined any correlation between Rh positivity and susceptibility to COVID-19. Latz et al. (29). and Zietz et al. (30) found that individuals in Rh (+) blood type had a higher risk for COVID-19 infection. Although the rates of Rh-positive patients were higher than the rates of Rh-negative patients among COVID-19 patients (89,45%,10,54%) compared to the control group (%86,24,%13,75), we observed no statistically significant difference between Rh type and risk of COVID-19 infection (P=0,612). Kirisci et al. (31) indicate that the COVID-19 disease affected men more than women (OR= 2.091) (p=0.0001) . Similarly, in our study, we detected a statistically significant association between gender and the prognosis of COVID-19, and men had a higher risk than women.

The increase in IgE level is generally observed with allergic diseases. However, the elevation of IgE level is also seen in some diseases such as malignancies,

immunodeficiency syndromes, skin diseases, inflammatory diseases, and infections. Parasitic infections are a primary cause of raised IgE levels among infectious diseases. IgE elevation can be seen with some parasitic infections such as Entamoeba, Giardia, Ascaris. IgE elevation can also be seen with viral diseases. Infectious mononucleosis due to Epstein-Barr virus (EBV) infection presents fever, pharyngitis, cervical lymph node enlargement, and fatigue. Increased IgE levels may take weeks or months to normalize after infection (32). A multicenter study has demonstrated that cytomegalovirus (CMV) and EBV seropositivity are much higher in allergic individuals compared with nonallergic individuals (33). Another study determined a high total IgE in Human Immunodeficiency Virus (HIV) infected children, independent of the activation and aggravation of HIV infection (34). It has been hypothesized that IgE serum level elevation in HIV infection results from increased polyclonal stimulation of B lymphocytes. Due to the fact that COVID-19 is a viral infection, our study demonstrated a statistically significant increase in IgE level among all blood groups compared to control groups (P<0.001). Blood groups according to Rh factors compared to control group, all blood groups except AB Rh (-) had a statistically significant increase in IgE level(P<0.001). There was no statistically significant increase in AB Rh(-) blood group with IgE level compared to the control group (P=0,117).

CONCLUSION

In our study, we investigate if there is an association between the AB0 blood group according to Rh factors and IgE elevation in COVID-19 patients confirmed with PCR. Our study demonstrated that total IgE level, except for AB Rh (-) patients, increased significantly in COVID-19 patients. All parameters of COVID-19 infected patients in the general population worldwide should be evaluated and examined with serological approaches.

ETHICAL DECLARATIONS

Ethics Committee Approval: For this study, permission was obtained from the Presidency of the Non-interventional Researches Ethics Committee of Fırat University Faculty of Medicine (Date: 18.11.2021, Decision No: 2021//12-21).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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