Osmangazi Tıp Dergisi
Osmangazi Journal of Medicine 2023;

Araştırma Makalesi / Research Article

Evaluation of the Relationship Between ABO Blood Group Distribution and Clinical Features in Long-Term COVID-19 Patients: A Retrospective Study

Uzun Dönem COVID-19 Hastalarında ABO Kan Grubu Dağılımı ile Klinik Özellikler Arasındaki İlişkinin Değerlendirilmesi: Retrospektif Bir Çalışma

[1]Yaşar Bildirici, [2]Anıl Uçan, [3]Şebnem Eker Güvenç, [4]Uğur Bilge

[1] Eskisehir City Hospital, Department of Pediatrics, Eskişehir, Turkey

[2] Eskisehir City Hospital, Department of Internal Medicine, Eskişehir, Turkey

[3] Eskisehir City Hospital, Department of Family Medicine, Eskişehir, Turkey

[4] Eskisehir Osmangazi University, Department of Family Medicine, Faculty of Medicine, Eskisehir, Turkey

Abstract

This study investigates the associations of ABO blood groups on long-term COVID patients who applied to the COVID-19 Follow-up Center. New co-morbidities after COVID-19 were also evaluated. Methods: This study was designed retrospectively with patients admitted to COVID-19 Follow-up Center between December 13, 2020, and November 1, 2021. The study sample consisted of 502 patients divided into four groups according to their blood types. Patients were analyzed according to their symptoms and our findings after COVID-19 by blood group variable. Newly diagnosed co-morbidities were recorded from patient's files, and the drug history of the patients was investigated A total of 502 COVID-19 patients were retrospectively analyzed, and the mean age was 55.5(±13.2) years. Patients were predominantly female (263/502) (52.4%). While long-term COVID-19 symptoms were observed in 76.9% of the patients, extreme fatigue (46.2%) and ongoing shortness of breath (32.9%) were observed most frequently. No relationship was found between other prolonged symptoms of the disease and blood groups except heart palpitation with blood groups A and B compared to AB and O (p=0.048) . In addition, there was no significant difference in the ongoing symptoms and inflammatory parameters like C-Reactive Protein and Lymphocyte count. This study demonstrated no difference between blood types and long-term COVID-19 patients' clinical features.
Keywords: COVID-19; ABO Blood Group; Signs and Symptoms

Özet

Bu çalışma, COVID-19 İzlem Merkezine başvuran uzun süreli COVID hastalarında kan grupları arasındaki ilişkilerin araştırılmasını amaçlamaktadır. COVID-19 sonrası yeni komorbiditeler de değerlendirilmiştir. Bu çalışma, 13 Aralık 2020 ile 01 Kasım 2021 tarihleri arasında COVID-19 İzlem Merkezi'ne başvuran hastalar ile retrospektif olarak tasarlandı. Çalışmanın örneklemini, kan gruplarına göre 4 gruba ayrılan 502 hasta oluşturdu. Hastalar kan grubu değişkenine göre COVID-19 sonrası semptomlarına ve bulgularına göre analiz edildi. Hasta dosyalarından yeni tanı konulan ek hastalıklar kaydedildi ve hastaların ilaç öyküsü araştırıldı. Toplam 502 COVID-19 hastası retrospektif olarak incelendi ve yaş ortalaması 55,5(±13,2) idi. Hastaların çoğunluğunu kadınlar oluşturmaktaydı (263/502) [%52.4]. Hastaların %76,9'unda uzun süreli COVID-19 semptomları görülürken, en sık aşırı yorgunluk (%46,2) ve devam eden nefes darlığı (%32,9) görüldü. Uzun süreli COVID semptomları değerlendirildiğinde, AB ve O'ya kıyasla A ve B kan grupları ile ilişkili tek semptom kalp çarpıntısıydı (p=0,048). Hastaların kan grupları ile hastalığın semptomları ve seyri arasında anlamlı bir ilişki bulunmadı. Ayrıca devam eden semptomlarda ve C-Reaktif Protein ve lenfosit sayımı gibi inflamatuar parametrelerde anlamlı fark yoktu. Bu çalışma, kan grupları ile uzun süreli COVID-19 hastalarının klinik özellikleri arasında fark olmadığını göstermiştir.
Anahtar Kelimeler: COVID-19; ABO kan grubu sistemi; Belirti ve bulgular

Correspondence:
Anıl UÇAN
Eskisehir City Hospital, Department of Pediatrics, Eskişehir, Turkey
e-mail: anil-ucan@hotmail.com

Received 09.01.2023 Accepted 09.02.2023 Online published 20.02.2023

Bildirici Y, Ucan A, Eker Güvenc S, Bilge U, Evaluation of the Relationship Between ABO Blood Group Distribution and Clinical Features in Long-Term COVID-19 Patients: A Retrospective Study, Osmangazi Journal of Medicine, 2023;45(2):290-300
Doi: 10.20515/otd.1230770

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in December 2019 in Wuhan, China, as a cause of severe morbidity and mortality. A year later, in December 2020, more than 65 million confirmed cases and more than 1.5 million deaths were reported globally (1). Nowadays, the pandemic reached 608 million cases worldwide as of September 19, 2022 (2). From the onset of the pandemic to the present, in the prediction of disease progression, proven specific biomarkers has not been revealed. Examining the relationship between human blood groups and infectious diseases has been used as a marker from the past to the present (3,4). Several studies on SARS-CoV-1 have shown a relationship between the risk of infection and blood type. O blood group is protective against disease (5). A recent study found a possible relationship between blood group A and COVID-19 infection and mortality, while it was associated with a lower risk of infection and death for group O (6). In addition, another study found that blood group A is more likely to test COVID-19 positive (7). ABO antibody titer is hypothesized to impact the severity of the disease and its complications (8). Group O carriers were substantially less common than group B carriers in COVID-19 patients (p 0.001), indicating that anti-A from O blood groups is more protective than anti-A from B, as previously reported in a study (9). A systematic review and meta-analysis study observed higher mortality in patients with blood type A compared to non-A blood groups in the study (10).

However, studies on the severity and frequency of complications during follow-up are limited. In the long-term patient follow-ups of COVID-19, a need has arisen for the chronic period of clinical management of the disease, possible complication detection, and timely intervention, thus minimizing the uncertainties that COVID-19 patients may experience (11).

This study investigates the associations between ABO blood groups and clinical features in long-term COVID-19. We also aimed to evaluate the clinical outcomes and complications of the disease. Database created in our center will provide clinicians very valuable information about the future of the follow-up process of COVID-19 patients, full of uncertainty, and the evaluation of severe long-term consequences of the disease.

2. Materials and Methods

Study Partıcipants

The archive records of 502 patients between December 13, 2020, and November 1, 2021, who were diagnosed with COVID-19 at the Eskişehir City Hospital and admitted to the COVID-19 Follow-up center were analyzed retrospectively. A prospective COVID-19 register was created for each SARS-CoV-2 positive patient admitted to the COVID-19 hospital. ABO blood types, which had previously been identified through serological testing in a lab accredited by the Ministry of Health, were obtained from the patient's national identification card. The patient characteristics, laboratory-confirmed blood types, height, weight, co-morbidities (histories of cardiovascular disease, diabetes, hypertension, chronic obstructive lung disease, and other), smoking status, symptoms at diagnosis(fatigue, fever, cough, sore throat, chest pain, shortness of breath, loss of taste and smell, myalgia, headache, loss of appetite, expectoration) and follow-up symptoms associated with long-term COVID-19, follow-up chest X-RAY, treatment of disease(antiviral, antibiotics, steroid, IVIG or other therapies), Intensive Care Unit (ICU) transfer, follow-up dates, and laboratory values were recorded. Related co-morbidities were analyzed as binary variables and included cardiovascular disease (history of coronary artery disease and stroke history), diabetes mellitus, hypertension, and chronic obstructive lung disease (COPD). The blood group of patients analysis result in our database were obtained by e-Pulse application. The e-Pulse is a personal health record system that the Turkish Ministry of Health integrated all the information systems of all health institutions. E-Pulse is an application that people can access their laboratory results, medical images, prescription and medication details, emergency information, diagnosis details,

reports and health records that contain all the examination details via desktop and mobile platforms. People can also share their medical records with their doctor(s) and relatives within specific regulations. The exclusion criteria were inadequate diagnosis, CT images, and missing follow-up records. Thirteen patients from the study were excluded because their blood group information was not evaluated reliably or they couldn't be reached to obtain their information. The clinical outcome was determined as the need for ICU.

Data Sources and Study Size

All patients who met the inclusion criteria during the specified date range were included. The study group at the Eskisehir City Hospital examined the patient's medical records. From electronic medical records, data on clinical features were collected using data collecting forms. Data sources were obtained from patient history and records. A team of doctors with the appropriate training examined the data.

Laboratory Parameters

Laboratory findings were categorized as normal, high or low based on the following reference values: haemoglobin (female: 12.4-16.1 g/dl, male: 13.9-17.7 g/dl), lymphocyte count: 1.07-3.12x103/µL), platelets: 150-450 103/µL, CRP N: <5 mg/L, Ferritin: 22-322 ng/mL, D-Dimer: 0-550 µg/L. All the laboratory data were recorded during COVID-19 Follow-up Center admission.

A reverse transcriptase-polymerase chain reaction was used to screen for SARS-CoV-2 using a sample from a nasopharyngeal swab. The patient's sample underwent viral analysis and real-time (Q) PCR tests. Using vNAT solution, the RNA was extracted (Bioeksen, Istanbul, Turkey). The Rotor-Gene Q (Qiagen), LightCycler 480 (Roche), and Biospeedy SARSCoV-2 RT-qPCR kit (Bioeksen) were used for all reactions. Targeting the RdRp (RNA-dependent RNA polymerase) gene fragment reverse transcription (RT) and rt PCR (QPCR) are carried out by the kit in a single step (RT-QPCR). Software programs LightCycler 480, and Rotor-Gene Q were used to evaluate the data.

Long-Term Covid-19 Symptoms

We evaluated symptoms occurring in the first 4 weeks after diagnosis. Complaints of the patients were evaluated with literature for association with COVID-19. These complaints are; extreme tiredness, shortness of breath, chest pain or tightness, problems with memory and concentration, insomnia, heart palpitations, dizziness, pins and needles, joint pain, depression and anxiety, tinnitus or earaches, feeling sick, diarrhea, stomach aches, loss of appetite, a high temperature, cough, headaches, sore throat, changes to sense of smell or taste and rashes. Some unspecified complaints are categorized as 'Other'.

Covid-19 Follow-Up Centers

As the pandemic progressed, the need for follow-up of the unknown long-term results of the COVID-19 disease arose (12). The Ministry of Health of the Republic of Turkey has also started a study to detect the long term effects of COVID-19. Certain pilot centers have been selected to establish COVID-19 Follow-Up Centers across the country. In this project, 10 academics from various fields of expertise were appointed, the current situation analysis was made by these experts, and the scientific justifications presented strengthened the establishment of COVID-19 Follow-Up Centers. Our center has started to work as a 2nd pilot center, the information system module to be used has been completed, and it has become operational on December 13 2020.

Ethics

The study was approved by both the Turkish Ministry of Health and the ethics committee at Eskişehir Osmangazi University Faculty of Medicine (approval number 2020/259) and carried out in compliance with the Declaration of Helsinki principles and all applicable regulations. Due to the retrospective nature of the study and because no identifying

information relating to participants was included, written informed consent was waived. All experimental protocols were conducted according to the Strengthening of the Reporting of Observational Studies in Epidemiology guidelines.

Statistical Analysis

Continuous data are given as Mean ± Standard Deviation. Categorical data are given as a percentage (%). Shapiro Wilk's test was used to investigate the suitability of the data for normal distribution. One-way analysis of variance (One-Way ANOVA) was used for cases with three or more groups to compare normally distributed groups. The Kruskal-Wallis H test was used for cases with three or more groups that did not conform to the normal distribution. Fisher Exact Chi-Square analyses were used to analyze the created cross tables, and Cramer's V values were calculated for the level of relationship between categorical data. IBM SPSS Statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) programs were used in the analysis. A value of $p<0.05$ was accepted as a criterion for statistical significance.

3. Results

A total of 502 COVID-19 patients followed up after their hospitalization in the COVID-19 Follow-Up Center took part in the study. Two hundred and thirthy nine (47.6%) of the patients were male, and 263 (52.4%) were female.

Table 1. shows some of the main characteristics of the patients. When all patients were evaluated, the mean age was 55.5 years (SD±13.2). While long-term COVID-19 symptoms were observed in 76.9% of the patients, extreme fatigue (46.2%) and ongoing shortness of breath (32.9%) were observed most frequently. Heart palpitations were more frequent in individuals with blood groups A and B than AB and O when long-term COVID symptoms were assessed (p=0.048). No progression was detected in the patient's follow-up chest X-rays compared to the X-rays during hospitalization. However, the findings persisted in 66 (29.7%) patients. Almost all patients (96%) received Favipiravir treatment during hospitalization. No significant relationship was found between the patient's blood groups and the disease's symptoms and course (Table 1). When the inflammatory markers of the disease and blood groups were compared, no significant difference was found (Table 2). Blood group A was the most common among the patients who applied, with a percentage of 44%. Newly diagnosed comorbid disease after COVID infection was observed in 56.9% of the patients. Hypertension (35.2%) and diabetes (23.3%) were observed most frequently. No significant difference was observed when blood groups and co-morbidity status were compared (p=0.553). Blood groups and newly diagnosed diseases after COVID-19 were compared (Table 3). Diagnoses appeared to be unaffected by blood groups. (p=0.168). When all treatments were compared, no significant relationship was found between blood groups and treatment requirements during the disease (p=0.791). A comparison of blood groups and baseline characteristics of the patients is given in Tables 1 and 2.

Table 1. Clinical characteristics of the patients according to their blood groups

	Blood Types									
	A		AB		B		O		Cramer's V	p-value (95% Cl)
	n	%	n	%	n	%	n	%		
Gender										
Male	107	47.6%	22	52.4%	31	41.9%	79	49.1%	0.054	0.696 (0.684-0.707)
Female	118	52.4%	20	47.6%	43	58.1%	82	50.9%		
Co-morbidities	134	59.6%	24	57.1%	37	50.0%	91	56.5%	0.065	0.553 (0.547-0.573)

Diabetes	166	73.8%	32	76.2%	61	82.4%	126	78.3%	0.073	0.447 (0.455-0.480)
Hypertension	83	36.9%	14	33.3%	21	28.4%	59	36.6%	0.056	0.733 (0.722-0.744)
Coroner Artery Disease	26	11.6%	5	11.9%	10	13.5%	14	8.7%	0.054	0.681 (0.669-0.693)
COPD	12	5.3%	0	0.0%	5	6.8%	11	6.8%	0.080	0.355 (0.342-0.367)
Symptoms in Admission	191	84.9%	37	88.1%	63	85.1%	129	80.1%	0.070	0.532 (0.519-0.545)
Fatigue	104	46.2%	23	54.8%	40	54.1%	68	42.2%	0.089	0.262 (0.250-0.273)
Fever	23	10.2%	2	4.8%	6	8.1%	16	9.9%	0.054	0.770 (0.760-0.781)
Cough	72	32.0%	13	31.0%	18	24.3%	46	28.6%	0.059	0.651 (0.638-0.663)
Loss of taste and smell	2	0.9%	0	0.0%	1	1.4%	2	1.2%	0.036	0.906 (0.898-0.913)
Sore throat	24	10.7%	7	16.7%	8	10.8%	25	15.5%	0.075	0.415 (0.403-0.428)
Chest pain	3	1.3%	1	2.4%	1	1.4%	1	0.6%	0.045	0.594 (0.582-0.607)
Expectoration	1	0.4%	1	2.4%	1	1.4%	1	0.6%	0.064	0.342(0.330- 0.355)
Shortness of Breath	28	12.4%	6	14.3%	12	16.2%	21	13.0%	0.038	0.833 (0.823-0.843)
Myalgia	29	12.9%	3	7.1%	9	12.2%	31	19.3%	0.106	0.152 (0.143-0.162)
Loss of Appetite	9	4.0%	2	4.8%	1	1.4%	10	6.2%	0.077	0.394 (0.382-0.407)
Headache	6	2.7%	1	2.4%	4	5.4%	2	1.2%	6	0.280 (0.268-0.291)
Long COVID-19 symptoms	173	76.9%	35	83.3%	63	85.1%	135	83.9%	0.092	0.263 (0.252-0.275)
Extreme tiredness	104	46.2%	22	52.4%	39	52.7%	81	50.3%	0.053	0.717 (0.705-0.728)
Shortness of Breath	74	32.9%	22	52.4%	29	39.2%	54	33.5%	0.115	0.091 (0.083-0.098)
Chest pain or tightness	34	15.1%	3	7.1%	15	20.3%	21	13.0%	0.091	0.262 (0.250-0.273)
Problems with memory and concentration	33	14.7%	8	19.0%	17	23.0%	37	23.0%	0.102	0.142 (0.133-0.151)
Insomnia	26	11.6%	8	19.0%	13	17.6%	19	11.8%	0.081	0.331 (0.319-0.343)
Heart palpitations	28	12.4%	2	4.8%	9	12.2%	8	5.0%	0.126	0.045 (0.040-0.051)
Dizziness	10	4.4%	2	4.8%	5	6.8%	9	5.6%	0.037	0.826 (0.816-0.835)
Pins and needles	5	2.2%	2	4.8%	2	2.7%	3	1.9%	0.050	0.600 (0.587-0.612)
Joint pain	68	30.2%	11	26.2%	26	35.1%	51	31.7%	0.048	0.784 (0.773-0.795)
Depression and anxiety	1	0.4%	1	2.4%	0	0.0%	3	1.9%	0.083	0.278 (0.266-0.289)
Tinnitus or earaches	1	0.4%	0	0.0%	1	1.4%	5	3.1%	0.105	0.154 (0.144-0.163)
Feeling sick, diarrhea, stomach aches, loss of appetite	12	5.3%	1	2.4%	3	4.1%	17	10.6%	0.115	0.119 (0.111-0.127)
A high temperature, cough, headaches, sore throat, changes to sense of smell or taste	61	27.1%	12	28.6%	20	27.0%	47	29.2%	0.022	0.974 (0.970-0.978)
Rashes	6	2.7%	1	2.4%	3	4.1%	8	5.0%	0.058	0.647 (0.635-0.659)
Other	57	25.3%	12	28.6%	21	28.4%	36	22.4%	0.052	0.707 (0.695-0.718)
Control Chest XRAY										
Similar	66	29.7%	8	19.0%	16	22.2%	46	28.7%	0.080	0.392 (0.380-0.405)
Regression	156	70.3%	34	81.0%	56	77.8%	114	71.3%		

Treatment										
Favipiravir	216	96.0%	40	95.2%	70	94.6%	151	93.8%	0.045	0.757 (0.746-0.768)
Hydroxychloroquine	12	5.3%	1	2.4%	4	5.4%	12	7.5%	0.060	0.707 (0.695-0.719)
Deksametazon	57	25.3%	10	23.8%	15	20.3%	43	26.7%	0.048	0.778 (0.767-0.788)
Pulse Steroid	25	11.1%	4	9.5%	15	20.3%	13	8.1%	0.124	0.068 (0.062-0.075)
Enoxaparin	135	60.0%	25	59.5%	40	54.1%	86	53.4%	0.089	0.341 (0.329-0.353)
Acetylsalicylic acid	6	2.7%	0	0.0%	2	2.7%	3	1.9%	0.052	0.822 (0.812-0.832)
Human Plasma	11	4.9%	3	7.1%	2	2.7%	10	6.2%	0.057	0.630 (0.618-0.643)
IVIG	10	4.4%	2	4.8%	4	5.4%	5	3.1%	0.040	0.788 (0.777-0.798)
Tosilizumab	5	2.2%	0	0.0%	2	2.7%	3	1.9%	0.047	0.858 (0.849-0.867)
Levofloxacin	70	31.1%	18	42.9%	26	35.1%	44	27.3%	0.092	0.233 (0.22-0.244)
Ceftriaxone	20	8.9%	3	7.1%	5	6.8%	15	9.3%	0.034	0.959 (0.954-0.964)
ICU	23	10.2%	9	21.4%	8	10.8%	18	11.2%	0.009	0.510 (0.497-0.523)

Note: p< 0.05 is statistically significant.
Abbreviations: Cl, confidence interval; COPD, Chronic Obstructive Pulmonary Disease; IVIG, Intravenous Immunoglobulin Therapy; ICU, intensive care unit

Table 2. Comparison of basic characteristics and laboratory values of patients according to blood groups

	Blood Type	N	Mean	Std. Deviation	Minimum	Maximum	p-value (95% Cl)
Age, years	A	225	55.56	13.229	20	93	0.063
	AB	42	55.10	16.564	26	88	
	B	74	50.68	13.199	20	85	
	O	161	54.82	14.304	24	90	
Weight, Kg	A	225	80.10	14.900	41	125	0.429
	AB	42	79.81	19.407	46	132	
	B	74	76.45	12.172	49	100	
	O	161	79.41	13.893	46	115	
Height, Cm	A	225	166.85	9.245	150	190	0.778
	AB	42	167.64	8.938	150	181	
	B	74	166.23	8.730	150	187	
	O	161	166.40	8.929	149	193	
Hemoglobin (female: 12.4-16.1 g/dL; male: 13.9-17.7 g/dL)	A	225	13.5467	1.48393	7.50	16.70	0.844
	AB	42	13.4667	1.57954	10.20	17.00	
	B	74	13.6716	1.56595	8.40	18.00	
	O	161	13.4466	1.84993	7.60	17.60	
Lymphocyte (N:1.7-7.2x10^3/µL)	A	225	2250.5778	744.12648	680.00	6390.00	0.998
	AB	42	2209.2857	618.67046	930.00	3950.00	
	B	74	2227.9730	607.05663	860.00	3950.00	
	O	161	2248.9441	716.45861	830.00	5150.00	
Platelets (N: 150-450/µL)	A	225	241804.4444	64790.78265	78000.00	491000.00	0.163
	AB	42	254404.7619	75479.94711	125000.00	475000.00	
	B	74	232328.3784	69410.20714	28300.00	422000.00	
	O	161	254484.4720	71905.32887	60000.00	517000.00	
C-Reactive Protein (N: <1.0 mg/dL)	A	225	8.6933	31.62305	.10	376.00	0.665
	AB	42	11.9929	31.54382	.00	137.00	
	B	74	4.1905	9.25745	.10	55.00	
	O	161	8.4735	24.46255	.10	145.30	
Ferritin (N: 22-322 ng/mL)	A	225	104.348	122.0569	.2	880.0	0.924
	AB	42	120.287	144.9614	.2	657.0	
	B	74	106.192	137.1171	.2	640.0	

	O	161	105.462	135.3200	.2	1119.0	
D-Dimer (N: 0-550 µg/L)	A	225	6.8431	88.67018	.10	1330.00	0.081
	AB	42	1.2029	1.45539	.14	5.70	
	B	74	.7457	1.46096	.19	12.10	
	O	161	.8130	2.00658	.10	22.57	

Table 3. Comparison of newly diagnosed diseases after COVID-19 according to blood groups

	Blood Types									
	A		**AB**		**B**		**O**		**Total**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Anxiety	9	4.0%	2	4.7%	7	9.4%	1	0.6%	29	5.7%
Obstructive Sleep Apnea Syndrome	1	0.4%	0	0.0%	1	1.3%	2	1.2%	4	0.7%
Type-2 Diabetes	3	1.3%	2	4.7%	0	0.0%	7	4.3%	12	2.3%
Asthma	0	0.0%	0	0.0%	0	0.0%	2	1.2%	2	0.3%
Depression	5	2.2%	2	4.7%	0	0.0%	5	3.1%	12	2.3%
Erectile Dysfunction	0	0.0%	0	0.0%	0	0.0%	1	0.4%		
Hypothyroidism	3	1.3%	0	0.0%	0	0.0%	0	0.0%	3	0.5%
Hypertension	6	2.6%	0	0.0%	4	5.4%	3	1.8%	13	2.5%
Coronary Artery Disease	0	0.0%	1	2.1%	0	0.0%	1	0.4%	2	0.3%
Congestive Heart Failure	1	0.4%	0	0.0%	1	1.3%	0	0.0%	2	0.3%
Chronic Obstructive Pulmonary Disease	0	0.0%	1	2.1%	0	0.0%	1	0.4%	2	0.3%
Sleep Disorder	2	0.8%	1	2.1%	0	0.0%	0	0.0%	3	0.7%
Venous Insufficiency	0	0.0%	0	0.0%	1	1.3%	0	0.0%	1	0.1%

4. Discussion

This study tried to reveal the relationship between the blood types of hospitalized patients for COVID-19 and long-term symptoms of COVID-19. ABO blood types have been extensively studied in infectious diseases (13,14). Differences in blood group can increase or decrease host susceptibility to many infections (15,16). Blood group antigens may play a direct role in infection by acting as receptors and/ or can act as a receptor for microorganisms, parasites, and viruses (1). Blood types also in the COVID-19 pandemic due to all its unknowns and unpredictability were investigated as a biomarker. The first question in this study sought to establish a connection between blood groups and the characteristic features of COVID-19 and its complications (4,6,7,17). Several reports have shown that blood group A has a lower risk for intubation and hospitalization in the intensive care unit (ICU) (7), while blood group AB and B have an increased risk, in contrast.

A population-based cohort study revealed that blood group O is at lower risk of developing progression in COVID-19 (18). Researchers discovered through a meta-analysis that blood group O is a protective factor while blood group A is a partial risk factor for COVID-19

infection (19). This outcome is contrary to that of Mendy et al. (2020), who found blood group variables may not be associated with hospitalization or disease severity in COVID-19 (20).

Data on newly diagnosed diseases after COVID-19 are scarce in the literature. Several reports have shown that Covid-19 confers an increased risk for type 2 diabetes (21). It was reported that COVID-19 can be associated with other abnormalities like potassium disbalance (22). As mentioned in the literature review, COVID-19 can also lead to newly onset hypertension and cardiovascular diseases (23,24). Another source of uncertainty is that blood types can be related to newly diagnosed diseases after COVID-19 infection. ABO blood types and newly diagnosed diseases after COVID-19 were compared, and no significant difference between the two groups was evident. This inconsistency may be due to the limited size of the study. According to our findings, COVID-19 negatively impacts co-morbidities regardless of blood group. So that after the infection, close screening of such patients is essential. Blood pressure, blood glucose, and mental health should be followed up closely.

However, data on blood types and symptom association in COVID-19 are scarce in the literature. A study supported that blood groups are more effective during the disease, but their effect on symptoms at admission is limited (25). Our study showed no evidence of the association between the symptoms at presentation and blood groups. A possible explanation for this might be the study's small sample size. Our findings are contrary to a preprint study. A study found a relationship between the long-term symptoms of the disease and the A blood group (26). These results, however, have demographic limitations and should be confirmed with a large patient series.

The severity of COVID-19 disease has been predicted using various prediction models (27). Several lines of evidence suggest that COVID-19 severity was correlated with elevated levels of inflammatory markers (CRP, D-dimer, and LDH) and WBC (mostly neutrophils) and decreased levels of lymphocytes and platelets (28–30).

Thus far, a prospective observational cohort study has been conducted to identify people at risk of long COVID (31). Previous research has established no significant relationship between blood groups and inflammatory markers of COVID-19 patients (32). Another report has shown that there is no difference in laboratory parameters between long-term COVID-19 and non-long-term COVID-19 (33). Consistent with the literature, no relationship was found between inflammatory markers of the disease and blood groups. These results match those observed in an earlier study (32). It was stated in the same study that blood groups do affect not only inflammatory markers but also the course of the disease. This implies that standard biochemistry and hematological laboratory tests are insufficient to forecast the long-term progression of COVID-19. According to earlier research, inflammatory mediators may enable us to properly predict the severity of COVID-19 problems and monitor subsequent treatment interventions (34).

Contrary to expectations, several reports have shown no association between ABO blood types and the severity of illness. According to a retrospective study conducted in China, researchers did not find any relationship between blood type and disease severity (35). These results were supported by the study of Barnkob et al, one of the largest scales studies (36). No significant results were obtained when ABO blood groups and ICU hospitalizations were compared in a multicentric study of 7648 patients (32). Consistent with the literature, our research found no significant difference between ABO blood types and ICU hospitalization. One possible explanation is that disease progression depends on multiple variables, such as co-morbidity and viral load.

The generalisability of these results is subject to certain limitations. There are 502 hospitalized patients in our sample, which is comparatively small. Another drawback of this study is that it was conducted in a single center. Additional multi-center surveys are required to determine the relationship between

the ABO blood groups and long-term COVID-19 outcomes. These studies may also lay a solid foundation for future research. In this investigation, several patients' laboratory data were also absent, which posed another obstacle to a thorough analysis.

5. Conclusion

Although blood types have a role in the prediction and prognosis of COVID-19, it was seen in our study that blood types did not affect long-term COVID-19 symptoms and clinical conditions. New symptoms after COVID-19 exposure should be investigated, and close screening of such patients is essential, and large randomized controlled trials may provide more definitive evidence.

REFERENCES

1. Nejadghaderi SA, Saghazadeh A, Rezaei N. Health Care Policies and COVID-19 Prevalence: Is There Any Association? 2022 Jan 1 [cited 2022 Aug 11];52(1):9–22. Available from: https://pubmed.ncbi.nlm.nih.gov/33686893/
2. WHO Coronavirus (COVID-19) Dashboard | WHO Coronavirus (COVID-19) Dashboard With Vaccination Data [Internet]. [cited 2021 April 22]. Available from: https://covid19.who.int/
3. Berger SA, Young NA, Edberg SC. Relationship between infectious diseases and human blood type. 1989 Aug [cited 2022 Feb 22];8(8):681–9. Available from: https://link.springer.com/article/10.1007/BF01963752
4. Liu Y, Häussinger L, Steinacker JM, Dinse-Lambracht A. Association between the dynamics of the COVID-19 epidemic and ABO blood type distribution. 2021 [cited 2022 February 22];149. Available from: https://pubmed.ncbi.nlm.nih.gov/33407977/
5. Cheng Y, Cheng G, Chui CH, Lau FY, Chan PKS, Ng MHL, et al. ABO blood group and susceptibility to severe acute respiratory syndrome. JAMA [Internet]. 2005 Mar 23 [cited 2021 Dec 13];293(12):1450–1. Available from: https://pubmed.ncbi.nlm.nih.gov/15784866/
6. Zhao J, Yang Y, Huang H, Li D, Gu D, Lu X, et al. Relationship Between the ABO Blood Group and the Coronavirus Disease 2019 (COVID-19) Susceptibility. Clin Infect Dis [Internet]. 2021 Jul 15 [cited 2021 Dec 13];73(2):328–31. Available from: https://pubmed.ncbi.nlm.nih.gov/32750119/
7. Zietz M, Zucker J, Tatonetti NP. Associations between blood type and COVID-19 infection, intubation, and death. Nat Commun [Internet]. 2020 December 1 [cited 2022 February 22];11(1). Available from: https://pubmed.ncbi.nlm.nih.gov/33188185/
8. Shokri P, Golmohammadi S, Noori M, Nejadghaderi SA, Carson-Chahhoud K, Safiri S. The relationship between blood groups and risk of infection with SARS-CoV-2 or development of severe outcomes: A review. Rev Med Virol [Internet]. 2022 January 1 [cited 2022 August 11];32(1):e2247. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/rmv.2247
9. Gérard C, Maggipinto G, Minon JM. COVID-19 and ABO blood group: another viewpoint. Br J Haematol [Internet]. 2020 Jul 1 [cited 2022 Aug 11];190(2):e93–4. Available from: https://pubmed.ncbi.nlm.nih.gov/32453863/
10. Liu N, Zhang T, Ma L, Zhang H, Wang H, Wei W, et al. The impact of ABO blood group on COVID-19 infection risk and mortality: A systematic review and meta-analysis. 2021 July 1 [cited 2022 August 11];48:100785. Available from: https://pubmed.ncbi.nlm.nih.gov/33309392/
11. Yelin D, Wirtheim E, Vetter P, Kalil AC, Bruchfeld J, Runold M, et al. Long-term consequences of COVID-19: research needs [Internet]. October 1, 2020. Available from: /pmc/articles/PMC7462626/
12. Balachandar V, Mahalaxmi I, Subramaniam M, Kaavya J, Senthil Kumar N, Laldinmawii G, et al. Follow-up studies in COVID-19 recovered patients - is it mandatory? [Internet]. August 10, 2020 p. 139021. Available from: https://pubmed.ncbi.nlm.nih.gov/32360909/
13. Davison GM, Hendrickse HL, Matsha TE. Do Blood Group Antigens and the Red Cell Membrane Influence Human Immunodeficiency Virus Infection? Cells

[Internet]. 2020 March 31 [cited 2022 February 24];9(4). Available from: https://pubmed.ncbi.nlm.nih.gov/32244465/

14. Tyrrell DAJ, Sparrow P, Beare AS. Relation between Blood Groups and Resistance to Infection with Influenza and some Picornaviruses. Nat 1968 2205169 [Internet]. 1968 [cited 2022 Feb 24];220(5169):819–20. Available from: https://www.nature.com/articles/220819a0
15. Hashan MR, Ghozy S, El-Qushayri AE, Pial RH, Hossain MA, Al Kibria GM. Association of dengue disease severity and blood group: A systematic review and meta-analysis. 2021 January 1 [cited 2022 September 2];31(1):1–9. Available from: https://pubmed.ncbi.nlm.nih.gov/32776660/
16. Noori M, Shokri P, Nejadghaderi SA, Golmohammadi S, Carson-Chahhoud K, Bragazzi NL, et al. ABO blood groups and risk of human immunodeficiency virus infection: A systematic review and meta-analysis. 2022 May 1 [cited 2022 September 2];32(3):e2298. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/rmv.2298
17. Rios M, Bianco C. The role of blood group antigens in infectious diseases. 2000 Apr 1 [cited 2022 Feb 24];37(2):177–85. Available from: https://pubmed.ncbi.nlm.nih.gov/10791886/
18. Ray JG, Schull MJ, Vermeulen MJ, Park AL. Association Between ABO and Rh Blood Groups and SARS-CoV-2 Infection or Severe COVID-19 Illness : A Population-Based Cohort Study. Ann Intern Med [Internet]. 2021 Mar 1 [cited 2022 Feb 24];174(3):308–15. Available from: https://pubmed.ncbi.nlm.nih.gov/33226859/
19. Pourali F, Afshari M, Alizadeh-Navaei R, Javidnia J, Moosazadeh M, Hessami A. Relationship between blood group and risk of infection and death in COVID-19: a live meta-analysis. New microbes new Infect [Internet]. 2020 September 1 [cited 2022 September 2];37. Available from: https://pubmed.ncbi.nlm.nih.gov/32837730/
20. Mendy A, Keller JL, Apewokin S, Morrow AL. Is Blood Type Associated with COVID-19 Severity? medRxiv [Internet]. 2020 August 14 [cited 2022 February 24];2020.08.11.20172676. Available from: https://www.medrxiv.org/content/10.1101/2020.08.11.20172676v1
21. Rathmann W, Kuss O, Kostev K. Incidence of newly diagnosed diabetes after Covid-19. Diabetologia [Internet]. 2022 [cited 2022 May 9];65(6):949–54. Available from: https://pubmed.ncbi.nlm.nih.gov/35292829/
22. Noori M, Nejadghaderi SA, Sullman MJM, Carson-Chahhoud K, Ardalan M, Kolahi AA, et al. A Review on the Possible Pathophysiology of Potassium Abnormalities in COVID-19. Iran J Kidney Dis. 2021 November 1;15(6):397–407.
23. Dixit NM, Churchill A, Nsair A, Hsu JJ. Post-Acute COVID-19 Syndrome and the cardiovascular system: What is known? 2021 May 1 [cited 2022 May 9];5:100025. Available from: https://pubmed.ncbi.nlm.nih.gov/34192289/
24. Akpek M. Does COVID-19 Cause Hypertension? Angiology [Internet]. 2022 August 1 [cited 2023 January 27];73(7):682. Available from: /pmc/articles/PMC9260192/
25. Wu Y, Feng Z, Li P, Yu Q. Relationship between ABO blood group distribution and clinical characteristics in patients with COVID-19. 2020 October 1 [cited 2021 December 13];509. Available from: https://pubmed.ncbi.nlm.nih.gov/32562665/
26. Cirulli ET, Schiabor KM, 1 B, Riffle S, Bolze A, Neveux I, et al. Long-term COVID-19 symptoms in a large unselected population. medRxiv [Internet]. 2020 December 1 [cited 2023 January 27];2020.10.07.20208702. Available from: https://www.medrxiv.org/content/10.1101/2020.10.07.20208702v3
27. Gallo Marin B, Aghagoli G, Lavine K, Yang L, Siff EJ, Chiang SS, et al. Predictors of COVID-19 severity: A literature review. Rev Med Virol [Internet]. 2021 January 1 [cited 2022 September 2];31(1). Available from: /pmc/articles/PMC7855377/
28. Malik P, Patel U, Mehta D, Patel N, Kelkar R, Akrmah M, et al. Biomarkers and outcomes of COVID-19 hospitalizations: systematic review and meta-analysis. 2021 Jun 1 [cited 2022 Sep 2];26(3):107–8. Available from: https://ebm.bmj.com/content/26/3/107
29. Kiss S, Gede N, Hegyi PJ, Németh D, Földi M, Dembrovszky F, et al. Early changes in laboratory parameters are predictors of mortality and ICU admission in patients with COVID-19: a systematic review and meta-analysis. Med Microbiol Immunol [Internet]. 2021 Feb 1 [cited

2022 Sep 2];210(1):33. Available from: /pmc/articles/PMC7679241/

30. Minh LHN, Abozaid AAF, Ha NX, Le Quang L, Gad AG, Tiwari R, et al. Clinical and laboratory factors associated with coronavirus disease 2019 (Covid-19): A systematic review and meta-analysis. Rev Med Virol [Internet]. 2021 November 1 [cited 2022 September 2];31(6). Available from: /pmc/articles/PMC8646520/

31. Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, et al. Attributes and predictors of long COVID. 2021 [cited 2022 Sep 2];27(4):626–31. Available from: https://pubmed.ncbi.nlm.nih.gov/33692530/

32. Latz CA, Decarlo C, Boitano L, Png CYMM, Patell R, Conrad MF, et al. Blood type and outcomes in patients with COVID-19. 2020 September 1 [cited 2021 December 13];99(9). Available from: /pmc/articles/PMC7354354/

33. Kozak R, Armstrong SM, Salvant E, Ritzker C, Feld J, Biondi MJ, et al. Recognition of long-covid-19 patients in a canadian tertiary hospital setting: A retrospective analysis of their clinical and laboratory characteristics. Pathogens [Internet]. 2021 October 1 [cited 2022 September 2];10(10). Available from: /pmc/articles/PMC8537802/

34. Fouladseresht H, Ghamar Talepoor A, Eskandari N, Norouzian M, Ghezelbash B, Beyranvand MR, et al. Potential Immune Indicators for Predicting the Prognosis of COVID-19 and Trauma: Similarities and Disparities. 2022 January 20 [cited 2022 September 2];12:5788. Available from: https://pubmed.ncbi.nlm.nih.gov/35126355/

35. Li J, Wang X, Chen J, Cai Y, Deng A, Yang M. Association between ABO blood groups and risk of SARS-CoV-2 pneumonia. Br J Haematol [Internet]. 2020 Jul 1 [cited 2022 Feb 25];190(1):24–7. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.16797

36. Barnkob MB, Pottegård A, Støvring H, Haunstrup TM, Homburg K, Larsen R, et al. Reduced prevalence of SARS-CoV-2 infection in ABO blood group O. 2020 Oct [cited 2022 February 25];4(20):4990–3. Available from: https://pubmed.ncbi.nlm.nih.gov/33057631/

Ethics

Ethics Committee Approval: The study was approved by Eskişehir Osmangazi University Noninterventional Clinical Research Ethical Committee (Decision no: 26, Date: 22.03.2022).

Informed Consent: The authors declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

Authorship Contributions: A.U. U.B. and Y.B. designed the study and drafted the manuscript. Ş.E.G. and A.U. also made the data analysis and helped to draft the manuscript. And the final version of the manuscript has been reviewed and approved by all co-authors before submission.

Copyright Transfer Form: Copyright Transfer Form was signed by all authors.

Peer-review: Internally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

Acknowledgments

We would like to thank all the devoted health workers who cared for their patients during the pandemic