Frontiers in Life Sciences and Related Technologies 6(1) (2025) 21-27

Contents lists available at Dergipark

Frontiers in Life Sciences and Related Technologies

Journal homepage: http://dergipark.org.tr/en/pub/flsrt

Research article

Possible effect of E-SELECTIN (Ser128Arg), L-SELECTIN (Pro213Ser), P-SELECTIN (Thr715Pro) gene polymorphisms for COVID-19 disease severity

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Abstract

COVID-19 is an inflammatory disease characterized by a severe immune response, the pathogenesis of which is mediated by many cytokines. It was determined that the cytokine storm that occurs during severe infection may trigger coagulopathy by disrupting the interaction between platelets, endothelium, and leukocytes. Selectins (P-SELECTIN, L-SELECTIN, E-SELECTIN) are active in the mammalian immune system, especially in tissues. They are important adhesion molecules that play a part in the formation of the inflammatory response and the healing process. In this study, the probable effects of L-SELECTIN, P-SELECTIN, and E-SELECTIN gene variations on the pathogenesis of COVID-19 (on the severity and course of the disease) were investigated. In this direction, 44 controls and 129 patients (45 mild symptoms, 30 ward patients, and 54 intensive care patients) were included in the study. Genotyping of selectin polymorphisms was performed by the PCR-Restriction Fragment-Length Polymorphism (RFLP) techniques. In E-SELECTIN, CC genotype and C allele frequency were higher in inpatients than in the control group. The allele frequency and AA genotype were higher in the control group (p = 0.0001). No significant relationship was detected with P-SELECTIN and L-SELECTIN polymorphisms. In addition, the binary genotype distribution between the loci studied in our study and the control groups was also examined. Statistically significant differences were detected in P-SELECTIN/E-SELECTIN and E-SELECTIN/L-SELECTIN binary genotypes. Therefore, it was concluded that binary genotypes may affect disease severity or the course of the disease.

Keywords: *COVID-19; E-SELECTIN; L-SELECTIN; P-SELECTIN; polymorphisms; susceptibility*

1. Introduction

COVID-19, which has become a global health problem affecting the whole world and has been accepted as a pandemic by the World Health Organization, has caused many social, psychological, educational, and especially economic problems (Mohanty et al., 2020; Abdelmageed et al., 2025). The most important finding in the diagnosis of COVID-19 disease is high infection, but radiological images and pathological and clinical findings are also necessary for definitive diagnosis (Agrati et al., 2021a). However, clinical findings vary from mild symptoms to severe symptoms and can sometimes be asymptomatic. In cases where severe symptoms are observed, the need for intensive care, respiratory failure, and multiple organ failure occur and result in death (Eketunde et al., 2020). In the early stages of COVID-19, cough, dyspnea, fever, and obstructive sleep apnea are common symptoms in the patient, while in the advanced stages, complaints such as metabolic irregularities,

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https://doi.org/10.51753/flsrt.1580594 Author contributions
Received 07 November 2024; Accepted 21 February 2025
Available online 30 April 2025

thromboembolism, sepsis, kidney damage, and acute respiratory distress syndrome are observed (Attiq et al., 2024; Li et al., 2024). In addition to playing a role in hemostasis, immune response, and angiogenesis, endothelial cells can form different barrier structures and are effective in different physiological functions such as gas exchange, nutrient absorption, and organ protection (Wu et al., 2024). Conditions such as long-term infection, neuronal dysfunction, thromboembolism, and especially endothelial damage are also effective in the multifactorial pathogenesis of post-COVID syndrome (Maltezou, 2025). Studies show that the impairment of vascular endothelial function caused by COVID-19 may be permanent and that this damage is effective in vascular events that develop both during and after COVID-19 infection (Aljadah et al., 2024).

The most well-known cause of death during the COVID-19 epidemic is thromboembolic complications. Interrelated mechanisms such as coagulopathy, endotheliopathy, platelet activation, and enhanced adhesiveness to leukocytes and damaged endothelium have been linked to the hypercoagulability seen in COVID-19 (Watany et al., 2022). The anticoagulant system contributes to the complicated process of coagulopathy in COVID-19. An appropriate balance needs to be struck during this process, particularly concerning fibrinolytic, clotting, and endothelial components (Job et al., 2023; Sayyadi et al., 2023).

Selectins are an essential adhesion molecule in the immune system and inflammatory response, and they are linked to numerous illnesses and biological processes (Selvaraj et al., 2022). The significance of these adhesion molecules in the inflammatory response has been shown by their simultaneous release to the inflamed site (Agrati et al., 2021b).

Platelet cells and endothelial cells are the primary cells that express P-SELECTIN, a 140 kDa single-chain glycoprotein. Immune cells attaching to P-SELECTIN is the initial stage of the inflammatory process (Imhof and Dunon, 1995; Zlibut et al., 2019). P-SELECTIN expression increases depending on a stimulus (thrombin, etc.) and is stored in platelets (in alpha granules) and endothelial cells (in Weibel-Palade bodies) (Longo and Wakefield, 2007). E-SELECTIN, another member of the selectin family, is a 115 kDa adhesion protein that is expressed on the surface of endothelial cells and whose expression rises in response to endothelial cell damage. Shortly after the increase in expression, its levels fall to initial levels (Wong and Dorovini-Zis, 1996; Mantovani and Dejana, 1998). The last member of selectins, L-SELECTIN, is expressed in leukocytes, unlike other members. The main function of L-SELECTINS is to ensure the aggregation and migration of lymphocytes (Hirata, 2016). Research indicates that the degree of COVID-19 and thrombotic disorders is correlated with endothelial, platelet, and neutrophil activity (Petito et al., 2023).

The entry and replication of SARS-CoV-2 into cells, as well as the development of the immune response, are significantly influenced by genetic polymorphisms, which are known to be crucial in determining susceptibility or resistance to other viral diseases. Numerous genes and their combinations are believed to be involved in the pathophysiology of COVID-19 (Debnath et al., 2020; Dieter et al., 2022). As a result, the connection between COVID-19 and single nucleotide polymorphisms has been the subject of numerous investigations (Anastassopoulou et al., 2020; Debnath et al., 2020; Elhabyan et al., 2020; Ozturk et al., 2020; Dieter et al., 2022).

This study aims to explain the role of P, E, and L-SELECTIN gene polymorphisms, which are effective in the inflammatory response and play a role in adhesion interactions in COVID-19 patients, in the susceptibility to this infection, as well as their possible relationship with the severity of the disease.

2. Materials and methods

2.1. Participants

This study included 129 COVID-19 patients with positive RT-PCR test results and 44 healthy controls with negative RT-PCR results, who applied to Tokat State Hospital between 2019-2020. Patients and controls who had previously had COVID-19 were not included in the study. The G*Power version 3.1.9.4 program was used to determine the required sample size and it was determined that at least 30 patients and 30 controls were sufficient for the sample size (Power:0.95, effect size:1.086, margin of error:0.05). This study followed the rules of the Declaration of Helsinki. In addition, necessary permissions were obtained from Tokat Gaziosmanpasa University Non-invasive Clinical Research Ethics Committee (22-KAEK-211). Necessary consent forms were obtained from the participants in the control and patient groups. Volunteers in the study were divided into 3 groups according to the severity of the disease: those with a mild course, those needing intensive care, and inpatients (hospitalized patients).

The intensive care group (collected from patients hospitalized in Tokat Gaziosmanpasa University Intensive Care Unit) included individuals who were >18 years old, vaccinated or unvaccinated, had findings compatible with COVID-19 pneumonia on chest radiography or thoracic tomography and these findings could not be explained by another etiology and other etiologies were excluded, had dyspnea and respiratory distress, tachypnea (respiratory rate >30/min), increased O_2 requirement during follow-up, SpO_2<90%, PaO_2<70mmHg, PaO_2/Fio2:<300 despite >5L/min oxygen support. The mild course group included individuals who were >18 years old, had not been hospitalized due to COVID-19, and were not vaccinated. The inpatient group consisted of individuals who were >18 years old had never been vaccinated and did not need intensive care but needed hospital care. The control group consisted of individuals who were >18 years old, unvaccinated, and had never had COVID-19. Patient and control samples were investigated in terms of E-SELECTIN, P-SELECTIN, and L-SELECTIN polymorphisms. All analyses were first examined among the total patient and control groups, and then subgroup (mild course, intensive care, inpatients, and control) analyses were performed.

2.2. Genotyping

Blood samples from both COVID-19 patients and controls were isolated using the PureLink™ Genomic DNA Mini Kit (USA). Polymerase Chain Reaction and Restriction Fragment Length Polymorphism (PCR-RFLP) techniques were utilized to establish the genotypes of L-SELECTIN Pro213Ser (rs2229569), P-SELECTIN Thr715Pro (rs6136) and E-SELECTIN Ser128Arg (rs7799039) polymorphisms. The PCR program, primers, restriction enzymes, and restriction products used in the determination of polymorphisms are shown in Table 1. The PCR and restriction products obtained were visualized using agarose gel electrophoresis. For doubtful results, we performed a second PCR-RFLP.

Table 1
Primer sequences, restriction enzymes, PCR program, PCR lengths, and restriction lengths for selectin polymorphisms.

Polymorphism	Primer sequence	PCR Product Lengths	PCR programme			Restriction enzyme	Restriction product size
E-SELECTIN Ser128Arg	5′AGAAAGAGGCAAGAACCAGACT-3′ 5′AAAGGCACTCAGTATAAGCACA-3′	193 bp	95°C 94°C 58°C 72°C 72°C	5 min 20 sec 30 sec 45 sec 7 min	40 cycle	PstI	109+84 bp 193 bp
P-SELECTIN Thr715Pro	5′ATTGTACCTTGGCAGGTTGG-3′ 5′TTTCTGCAGCTGTGAAATGC-3′	198 bp	94°C 94°C 60°C 72°C 72°C	5 min 30 sec 30 sec 30 sec 7 min	38 cycle	Eco91I (BsteII)	163+35 bp 198 bp
L-SELECTIN Pro213Ser	5′TGATTCAGTGTGAGCCTTTG-3′ 5′CTTGACAGGTTGGTTCTG-3′	186 bp	94°C 94°C 55°C 72°C 72°C	5 min 20 sec 30 sec 30 sec 7 min	40 cycle	HphI	141+45 bp 186 bp

2.3. Statistical analysis

SPSS 16.0 and OpenEpi statistical software were used to analyze allele and genotype frequencies. Genotype and allele frequencies in the patient and control groups were determined using the $\chi 2$ test. $p<0.05$ values were considered statistically significant. $\chi 2$ or Fischer's exact test was used to determine the combined genotypes of polymorphisms. Allele and genotype distributions were determined by Hardy-Weinberg equilibrium. 95% odds ratios (ORs) and confidence intervals (CIs) were used to assess risk factors. *p* values were interpreted as significant when they were less than 0.05, and all *p* values were two-tailed.

3. Results

The study included 129 patients (78 men and 51 women) infected with COVID-19 and 44 controls. The average age of the 129 patients with COVID-19 was 49.27±19.26 years and the average age of the 44 controls was 39.20±11.55 years.

When the genotype and allele distributions in COVID-19 patient and control groups were analyzed, no statistically significant association was determined between COVID-19 and E-SELECTIN gene in terms of genotype and haplotype distributions (p=0.28 and p=0.13, respectively). When AA and AC+CC or AA+AC and CC were evaluated, no statistically significant relationship was detected between COVID-19 patients and controls in AA and AC+CC, but borderline significance was detected in AA+AC and CC (p= 0.34 and p=0.049, respectively) (Table 2).

L-SELECTIN polymorphism was examined in terms of genotype and allele distributions in COVID-19 patient and control groups, but no statistically significant result was obtained (p=0.36 and p=0.94, respectively). When CC and TC+TT or CC+TC and TT were evaluated, no statistically significant difference was found between COVID-19 patients and controls (p=0.62 and p=0.24, respectively).

In terms of P-SELECTIN polymorphism genotype distribution in the COVID-19 patient and control groups, it was seen that 92.43% of the patients had the AA genotype, 7.56% had the AC genotype, and no patient with the CC genotype was encountered. In the control group, 95.12% AA genotype and 4.87% AC genotype were detected, while no CC genotype was found. When P-SELECTIN polymorphism was analyzed in terms of allele distributions in COVID-19 patients and control groups, no statistically significant result was found (p=0.61). When AA vs AC+CC was appraised, no statistically significant difference was detected between COVID-19 patients and controls (p=0.6). When AA+AC vs CC was evaluated, statistical analysis could not be performed because there were no patients or controls with the CC genotype.

Table 2
Genotype distributions and allele frequencies of E-SELECTIN polymorphism.

Gene (Polymorphism)	Patients n=129 (%)	Controls (n=44)	*p*	OR (95% Cl)
E-SELECTIN Ser128Arg				
Genotypes				
AA	90 (%70)	34 (%77.2)		
AC	26 (%20)	9 (%20.5)	p=0.2844	
CC	13 (%10)	1(%2.3)		
AA:AC+CC	90 (%70): 39 (%30)	34 (%77.2): 10 (% 22.8)	p=0.3499	0.9029 (0.7419- 1.099)
AA+AC:CC	116 (%90): 13 (%10)	43 (%97.7): 1 (%2.3)	**p=0.049**	0.9201 (0.8551- 0.9901)
Allel				
A	206 (%80)	77 (%)	p=0.131	
C	52 (%20)	11 (%9.8)		

In the analysis of subgroups as patients (mild course, intensive care unit, hospitalized patients) and controls, no statistically significant difference was detected in terms of allele frequencies and genotype distribution in E-SELECTIN polymorphism in both mild course and intensive care patients. However, the genotype distributions and allele frequencies of E-SELECTIN polymorphism in inpatients were statistically significant (p=0.0001 and p=0.000000794, respectively). When AA vs AC+CC and AA+AC vs CC were evaluated, a statistically significant difference was determined among these groups (p=0.0002 and p=0.0003, respectively) (Table 3).

Genotype distributions and allele frequencies of P and L-SELECTIN polymorphisms were not statistically significant in all three groups (mild, intensive care, inpatient) compared to the control group. When examined for all groups AA vs AC+CC and AA+AC vs CC in the P-SELECTIN polymorphism, no statistically meaningful difference was identified among the two

groups. Similarly, when CC vs TC+TT and CC+TC vs TT were examined for all groups in L-SELECTIN polymorphism, no statistically significant difference was determined between the two groups.

Table 3
Genotype distributions and allele frequencies of E-SELECTIN polymorphism at inpatients.

Gene (Polymorphism)	Patients (inpatients) n=30 (%)	Controls (n=44)	*P*	OR (95% Cl)
E-SELECTIN Ser128Arg				
Genotypes				
AA	10 (%33.33)	34 (%77.2)		
AC	10 (%33.33)	9 (%20.45)	**0.0001**	
CC	10 (%33.33)	1 (%2.27)		
AA:AC+CC	10 (%33.33): 20 (%66.66)	34 (%77.2): 10 (22.72)	**0.0002**	1.15 (0.05-0.42)
AA+AC:CC	20 (%66.66): 10 (%33.33)	43 (%97.72): 1 (%2.27)	**0.0003**	0.04 (0.002-0.31)
Allele				
A	30 (%50)	77 (%87.5)	**0.0000**	0.14 (0.06-0.32)
C	30 (%50)	11 (%12.5)		

COVID-19 groups and control groups were also compared in terms of binary genotype for E-SELECTIN and P-SELECTIN, P-SELECTIN and L-SELECTIN, and E-SELECTIN and L-SELECTIN regions. Results for the E-SELECTIN and P-SELECTIN binary study were obtained from 118 COVID-19 patients and 41 control samples. 1 out of 9 binary genotypes (AA/CC) was statistically different between the groups (p=0.0457) (Table 4). Results for the E-SELECTIN and L-SELECTIN binary study were obtained from 115 COVID-19 patients and 41 control samples. No statistically significant difference was detected between COVID-19 patient and control groups in terms of E-SELECTIN and L-SELECTIN binary genotypes. Likewise, results for the P SELECTIN and L SELECTIN binary study were obtained from 110 COVID-19 patients and 41 control samples. No statistically significant difference was detected between the COVID-19 patient and control groups in terms of P-SELECTIN and L-SELECTIN binary genotypes.

In our study, binary genotyping was performed in the mild course, intensive care, and inpatient subgroups compared to the control group. Comparative analysis of E-SELECTIN and P-SELECTIN combined genotypes in mild course, intensive care, and inpatients revealed statistically significant genotypes in each group. Significant results were obtained for AC/AC (p=0.0579) genotype in patients with a mild course, AC/AA (p=0.001) genotype in the intensive care unit, and AA/AA (p=0.0006) and AA/CC (p=0.00001) genotypes in inpatients (Table 5). In the comparative analysis of P-SELECTIN and L-SELECTIN combined genotypes in mild course, intensive care, and inpatients, no statistically significant data were obtained compared to the control group. When the comparative analysis of E-SELECTIN and L-SELECTIN combined genotypes in patients with the mild course, intensive care, and inpatients were evaluated, statistically significant results were found for AA/TC, CC/TC, and CC/CC genotypes only in inpatients (p=0.0088, p=0.0047 and 0.0305, respectively) (Table 6).

Table 4
Comparative analysis of combined genotypes of E-SELECTIN and P-SELECTIN.

	Patients		Control		*p*
Genotypes E-SELECTIN/P-SELECTIN	n	%	n	%	
AA/AA	81	68.6	31	75.60	0.41
AA/AC	8	6.77	2	4.87	0.71
AA/CC	10	8.47	0	0.000	**0.04**
AC/AA	14	11.86	8	19.51	0.24
AC/AC	4	3.38	0	0.000	0.29
AC/CC	0		0		NA
CC/AA	1	0.84	0	0.000	0.74
CC/AC	0		0		NA
CC/CC	0		0		

4. Discussion

COVID-19 infection is often related to thromboembolic events, particularly venous thrombosis (Srivastava et al., 2022). According to the results of independent studies conducted by many researchers, genetic factors appear to have an important place among the possible risk factors that may lead to COVID-19 susceptibility. However, the effect of genetic polymorphisms on the severity of COVID-19 has not yet been clarified. In this study, the possible role of E, P, and L-SELECTIN gene polymorphisms in disease severity was investigated by comparing 3 groups of COVID-19 patients with mild course, need for hospitalization, and need for intensive care with the control group who were not diagnosed with COVID-19.

Table 5
Comparative analysis of combined genotypes of E-SELECTIN and P-SELECTIN in mild course, intensive care, and inpatient.

Composite	Patients (mild course)	*P* (mild course E-P)	Patients (intensive care)	*P* (intensive care E-P)	Patients (inpatients)	*P* (inpatients E-P)	Control
Genotypes E-SELECTIN/P-SELECTIN	n (%) n=41		n (%) n=51		n (%) n=25		n (%) n=41
AA/AA	33 (%80.48)	0.6072	40 (%78.43)	0.7533	8 (%32)	**0.0006**	31 (%75.60)
AA/AC	0	0.2469	4 (%7.84)	0.6080	3 (%12)	0.3390	2 (%4.87)
AA/CC	0		0		10 (%40)	**0.0000**	0
AC/AA	3 (%7.31)	0.1208	0	**0.001**	4 (%16)	0.7448	8 (%19.51)
AC/AC	4 (%9.75)	**0.0579**	7 (%13.72)		0		0
AC/CC							
CC/AA	1 (%2.43)	0.5	0		0		0
CC/AC							
CC/CC							

Table 6
Comparative analysis of combined genotypes of E-SELECTIN and L-SELECTIN in mild course, intensive care, and inpatients.

Composite	Patients (mild course)	*P* (mild course E-L)	Patients (intensive care)	*P* (intensive care E-L)	Patients (inpatients)	*P* (inpatients E-L)	Control
Genotypes E-SELECTIN/L-SELECTIN	n (%) n=41		n (%) n=43		n (%) n=31		n n=41
AA/TT	2 (%4.87)	0.6204	6 (%13.95)	0.0694	0	0.5694	1 (%2.43)
AA/TC	10 (%24.39)	0.1086	16 (%37.20)	0.6971	4 (%12.90)	**0.0088**	17 (%41.46)
AA/CC	21 (%51.21)	0.1923	17 (%39.53)	0.7866	7 (%22.58)	0.1619	15 (36.58)
AC/TT	0		0		1 (%3.22)	0.4306	0
AC/TC	1 (%2.43)	0.3657	1 (%2.32)	0.3425	4 (%12.90)	0.4614	3 (%7.31)
AC/CC	6 (%12.19)	0.7594	3 (%6.97	0.4471	5 (%16.12)	0,6475	5 (%12.19)
CC/TT	0		0		0		0
CC/TC	0		0		6 (19.35)	**0.0047**	0
CC/CC	1 (2.43)	0.50	0		4 (%12.90)	**0.0305**	0

The three categories of the selectin family --E-, P-, and L- are calcium-dependent and contribute to immune cells' adherence to the endothelium as well as their admission into lymphoid organs and inflammatory areas. E-SELECTIN is expressed by endothelial cells, L-SELECTIN by leukocytes, and P-SELECTIN by platelets. (Agrati et al., 2021).

Leukocyte adhesion during inflammation is facilitated by the protein E-SELECTIN, which is expressed on the surface of endothelial cells (Zhang et al., 2023). It has been suggested that expression changes of these molecules may affect neutrophil adhesion during the inflammation process observed in COVID-19. It has been noted that increased infiltration by immature and/or inefficient neutrophils might lead to an imbalance in the lungs' immunological response, which exacerbates the condition (Bartolotti et al., 2021). Only a few studies have investigating how soluble (s) E-SELECTIN affects the rise in disease severity or death in COVID-19 patients (Smadja et al., 2020; Bartolotti et al., 2021; Birnhuber et al., 2021; Oliva et al., 2021; Spadaro et al., 2021; Vassiliou et al., 2021; Srivastava et al., 2022). In their study, Smadja et al. and Oliva et al. discovered that patients admitted to critical care had greater levels of sE-SELECTIN. They proposed that sE-SELECTIN expression levels could be employed as a biomarker as they were linked to an increase in the patient's requirement for critical care (Smadja et al., 2020; Oliva et al., 2021). Additionally, Vassiliou et al. (2021) found that sE-SELECTIN levels were higher in patients who passed away in critical care than in those who survived, suggesting that these levels could be used to predict mortality in COVID-19 patients. According to Birnhuber et al. (2021), critically ill COVID-19 patients had much greater levels of sE-SELECTIN than healthy controls.

Leukocyte adhesion to monocytes and neutrophils is facilitated by the membrane protein P-SELECTIN, which is expressed on active platelets and endothelium. It contributes to immunothrombosis by forming leukocyte-platelet and leukocyte-endothelial complexes during the inflammatory response. Elevated circulating P-SELECTIN plasma levels are thought to be a sign of platelet destruction. Studies have demonstrated elevated P-SELECTIN expression on the platelet surface in COVID-19 (Fenyves et al., 2021). P-SELECTIN levels and leukocyte-platelet aggregates on the platelet membrane surface of COVID-19 patients were found to be elevated in the Manne et al. (2020) investigation. Furthermore, the same study discovered that COVID-19 patients had faster platelet aggregation and higher collagen-fibrinogen diffusion. Agrati et al. (2021) discovered that COVID-19 patients had a greater plasma P-SELECTIN level (p=0.0023) than healthy controls. According to a study by Campo et al. (2021), P-SELECTIN levels were higher in patients who died and those who required critical care than in those who survived. Vassiliou et al. (2021) found that sP-SELECTIN and other endothelial markers were higher in critically ill COVID-19 patients admitted to the intensive care unit. Karsli et al. (2021) found that sP-SELECTIN levels were higher in mild-moderate and severe pneumonia groups diagnosed with COVID-19 compared to the control group. Similarly, in the study by Prihatni et al. (2023), it was determined that sP-SELECTIN levels were mostly increased in patients treated in intensive care, while sP-SELECTIN levels were mostly normal in the non-intensive care group. However, unlike the above studies, Spadaro et al. (2021) found that plasma levels of E-SELECTIN and P-SELECTIN did not differ between surviving and non-surviving COVID-19 patients with acute respiratory distress syndrome.

L-SELECTIN is a glycoprotein structurally expressed on the surface of certain types of leukocytes. It is responsible for the migration of leukocytes to the lymphoid tissue (from the blood) and communicates with the antigen there. Endothelial cells expressing L-SELECTIN ligands on their surface capture leukocytes with L-SELECTIN and allow them to migrate into the lymphoid tissue (Šmak et al., 2021; Golubeva, 2022). There are limited studies on COVID-19 and L-SELECTIN in the literature. In a study on children with COVID-19, it was reported that neutrophils of children with COVID-19 showed lower L-SELECTIN expression compared to healthy controls (Seery et al., 2021). In a study evaluating P, E, and L-SELECTIN levels as markers of thrombosis in hospitalized COVID-19 patients, a significant difference was found in serum soluble selectins (sL, sP and sE). It has been reported that sP, sL, and sE-SELECTIN levels in COVID-19 patients who developed thrombosis had approximately two times higher expression levels (p<0.001) compared to healthy patients who did not develop thrombosis (Watany et al., 2022).

As seen in the above studies, the possible relationship between the selectin family and COVID-19 is mostly based on determining the expression level. To our knowledge, there is only one study that examined the association of single nucleotide polymorphisms (SNPs) of COVID-19 and the selectin family with COVID-19 susceptibility and disease severity. According to this study, significant differences were found in P-SELECTIN (rs6133) and E-SELECTIN (rs5361) SNPs between COVID-19 patients and healthy controls. In this study, Srivastava et al. (2022) suggested that P-SELECTIN and

E-SELECTIN polymorphisms are significantly associated with COVID-19 disease and that these polymorphisms may be prognostic genetic markers of COVID-19 susceptibility.

As far as we know, our study is the first to examine the relationship between P (rs6136) E (rs7799039), and L (rs2229569) SELECTIN polymorphisms and COVID-19. In our study, while there was no significant relationship in all three polymorphisms when examined as a total patient and control group when the subgroups and control group were examined, E-SELECTIN Ser128Arg polymorphism was statistically significant at both genotypic and allelic levels in the inpatient group (ward patient) (p=0.0001).

This may be attributed to the relatively low and unequal sample size between the total patient and control groups in the study. In addition, in our study, the binary genotype distribution between the studied loci and control groups was also examined. According to the combined genotype results, statistically significant differences were detected in E-SELECTIN/P-SELECTIN and E-SELECTIN/L-SELECTIN binary genotypes.

When E-SELECTIN and P-SELECTIN combined analyses were examined, the AA/AA binary genotype frequency (p=0.006) was found to be higher in controls than in hospitalized patients. In addition, the frequency of the AC/AA (p=0.001) binary genotype was found to be higher in the control group than in the patient group receiving intensive care. It was thought that these dual genotype frequencies may have a protective effect against COVID-19. Furthermore, the AA/CC dual genotype frequency (p=0.00001) and the AC/AC binary genotype frequency (p=0.05) were found to be significantly higher in inpatients and mild course patients, respectively, compared to the control group. It was thought that these dual genotype frequencies may have effects on the susceptibility to COVID-19 and the severity of the disease.

When E-SELECTIN and L-SELECTIN combined genotypes were evaluated in combination, it was determined that the CC/TC (p=0.0047) and CC/CC (p=0.0305) dual genotype frequencies in inpatients were statistically significant compared to the control group. The present study revealed that the AA/TC dual genotype frequency (p=0.0088) was statistically significant in comparison with the inpatients in the control group.

It was hypothesized that the significance of the control group was important in terms of the severity of the disease in the COVID-19 epidemic and could affect the disease being milder. It was commented that CC/TC and CC/CC dual genotypes may have an impact on hospitalizations and increase the severity of the disease.

Data obtained from binary genotypes suggest that the relationship of polymorphisms with different polymorphisms belonging to the same gene family may also have an impact on diseases. As a matter of fact, in our study, while there was no significant relationship when the three loci were evaluated separately, significant relationships were found in dual genotypes, especially between the ward patients and the control group.

5. Conclusions

Although the impact of COVID-19 disease on individuals has now diminished, elucidating the genetic determinants of SARS-CoV-2 infection is important for understanding the pathophysiology of COVID-19 and interindividual variability in its severity; Thus, it can contribute to the development of updated vaccines and new antivirals.

Ethical approval: Blood samples taken from volunteers were used in the study and the Declaration of Helsinki was complied with. Necessary permissions were obtained by Tokat Gaziosmanpasa University Non-invasive Clinical Research Ethics Committee (22-KAEK-211).

Conflict of interest: The authors declare that they have no conflict of interests.

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