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Research Article

Clinical and laboratory factors associated with hospitalization and mortality in the COVID-19 pandemic

COVID-19 pandemisinde hastaneye yatış ve mortalite ile ilişkili klinik ve laboratuvar faktörleri

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Abstract

Introduction: This study aimed to investigate the relationship between MPV and disease prognosis in patients with COVID-19, the chronic diseases that affect the prognosis of COVID-19, and the laboratory data that can help diagnose this disease and provide information about the course of the disease during the treatment process.

Methods: The study was conducted in a cross-sectional format. All participants gave written, informed consent to participate. A questionnaire consisting of two parts, including categorical (socio-demographic) data and laboratory data, was applied to people who had COVID-19 who applied to the internal medicine outpatient clinic of the hospital. The Pearson chi-squared test and Fisher exact test were used for comparing categorical variables. The Mann-Whitney U test, or Kruskal-Wallis test with Bonferroni post hoc comparisons, was used to compare numerical variables between the groups. All analyses were performed using the SPSS 25.0 (SPSS Inc., Chicago, IL, USA) software package.

Results: The participants' mean (±SD) age was 40.8±13.7 years (median: 40, range: 18 – 72). Almost half of the participants (48.0%, n=98) were male, the majority (76.0%, n=155) were married, and 24.0% (n=49) were single. Of the 204 patients, 28 (13.7%) were hospitalized, and five died (2.5%). Of the five patients who died, three had chronic lung disease, one had diabetes and chronic lung disease, and one had no chronic disease.

Conclusion: Older age and the presence of chronic diseases are important factors affecting hospitalization in patients with COVID-19. LDH, CRP, and ferritin levels were high, and the mean platelet volume levels were significantly higher in hospitalized patients.

Keywords: COVID-19, pandemics, prognosis of COVID -19

Öz

Giriş: Bu çalışmada COVID-19 hastalarında MPV ile hastalık prognozu arasındaki ilişkinin araştırılması ve COVID-19'un prognozunu etkileyen kronik hastalıklar ile bu hastalığın teşhisine yardımcı olabilecek ve tedavi sürecinde hastalığın seyri hakkında bilgi sağlayabilecek laboratuvar verilerinin araştırılması amaçlandı.

Yöntem: Çalışma kesitsel bir düzlemde gerçekleştirilmiştir. Tüm katılımcılar yazılı bireysel bilgilendirilmiş onay verdi. Hastanenin dahiliye polikliniğine başvuran COVID-19 tanılı kişilere kategorik (sosyo-demografik) veriler ve laboratuvar verileri olmak üzere iki bölümden oluşan anket uygulandı. Kategorik değişkenlerin karşılaştırılmasında Pearson ki-kare testi ve Fisher Exact testi kullanıldı. Gruplar arasında sayısal değişkenleri karşılaştırmak için Mann-Whitney U testi veya Bonferroni post hoc karşılaştırmalı Kruskal-Wallis testi kullanıldı. Tüm analizler SPSS 25.0 (SPSS Inc., Chicago, IL, ABD) paket programı kullanılarak yapılmıştır.

Bulgular: Katılımcıların ortalama (± SS) yaşı 40,8±13,7 idi (medyan: 40, aralık:18-72). Yaklaşık yarısı (%48,0, n=98) erkek, çoğunluğu (%76,0, n=155) evli ve %24,0' ı (n=49) bekardı. 204 hastanın 28' I (%13,7) hastaneye yatırıldı ve beşi öldü (%2,5). Ölen 5 kişiden 3'ünde kronik akciğer hastalığı, 1'inde diyabet ve kronik akciğer hastalığı saptanırken, 1'inde ise kronik hastalık saptanmadı.

Sonuç: Yaşlılık ve kronik hastalıkların varlığı COVID-19 hastalarında hastaneye yatışı etkileyen önemli faktörlerdir. LDH, CRP, ferritin ve bunlara ek olarak hastaneye yatanlarda ortalama trombosit hacim düzeyleri anlamlı olarak yüksekti.

Anahtar kelimeler: COVID-19, pandemi, COVID-19 prognozu

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Key Points

1. Advanced age and the presence of chronic disease are important factors for the hospitalization of COVID-19 patients.
2. LDH, CRP, and ferritin values are high in patients with COVID-19.
3. Mean platelet volume levels are high in hospitalized COVID-19 patients.

Introduction

In December 2019, a pneumonia epidemic emerged from a new coronavirus (severe acute respiratory syndrome coronavirus 2, SARS-CoV-2, COVID-19) in Wuhan, Hubei province of the People's Republic of China. It could not be brought under control and soon spread to other states and then to the whole world, especially Europe and the North American continent, causing a pandemic. A bat is thought to be the primary source of the COVID-19 disease [1]. While the origin of COVID-19 is still being investigated, available evidence suggests that it was transmitted to humans from wild animals illegally sold at the Huanan Seafood Wholesale Market [1]. Symptoms of COVID-19 include fever, nonproductive coughing, dyspnea, myalgia, fatigue, normal or decreased leukocyte counts, and radiographic evidence of pneumonia. In severe cases, organ dysfunction (e.g., shock, acute respiratory distress syndrome (ARDS), acute heart injury, and acute kidney injury) and death may occur [1,2].
In Turkey, the first case of COVID-19 was detected on March 11, 2020. As of May 12, 2020, the total number of tests applied in Turkey was 1.440.671, while the total number of cases from COVID-19 on the same date was reported as141.475 and the total number of deaths as 3.894 [2]. It is accepted that the virus enters the cell through angiotensin-converting enzyme (ACE-2) receptors in the mucosal epithelium of the upper and lower respiratory tract, and replication continues with the transmission of the disease by droplet and direct contact [3]. The incubation period of the disease is 2-14 days. The virus can cause clinical pictures ranging from a mild upper respiratory tract infection to fever, cough, shortness of breath, sore throat, loss of taste and smell, muscle pain, and diarrhea symptoms, as well as pneumonia, multi-organ failure, and thromboembolic complications [1].

Among the risk factors that increase the development of infection and mortality in the COVID-19 epidemic, chronic diseases are among the leading causes of death worldwide [1]. Risk factors affecting the prognosis of the disease are advanced age, hypertension (HT), cardiovascular disease (CVD), diabetes mellitus (DM), chronic lung disease, malignancies (especially hematological cancers), immunosuppressive therapy or disease, organ transplantation, chronic kidney failure, obesity, and smoking [1]. Both severe disease and mortality are higher in males and patients over 60 years of age [1,4]. Laboratory parameters that adversely affect the prognosis have been reported as a decrease in the number of lymphocytes and an increase in serum IL-6, ferritin, lactic dehydrogenase, and C-reactive protein (CRP) levels [4]. Additionally, a 3-4 fold increase in D-dimer levels indicates high mortality. Studies have shown that patients with high D-dimer, prolonged prothrombin time (PZ), and thrombocytopenia have higher ICU admission and mortality [1].

To the best of our knowledge, the relationship between mean platelet volume (MPV) and the prognosis of COVID-19 disease has not been extensively studied in published articles. A review by Lippi G. stated that MPV values can be a distinguishing feature in various thrombotic disorders, including acute coronary syndrome, stroke, venous thromboembolism, abdominal vein thrombosis, and even preeclampsia [5]. The same study stated that MPV values may reflect hyperactivity and hyperreactivity of platelets in the bloodstream and trigger vascular thrombosis, and MPV is a simple and relatively inexpensive laboratory parameter that reliably reflects platelet size [5].

Objectives

Laboratory tests such as C-reactive protein (CRP), creatine phosphokinase (CPK), ferritin, D-Dimer, troponin, and lactate dehydrogenase (LDH) that indicate a serious disease course bring a lot of financial burdens and are not always possible to be ordered at in primary health care institutions [4]. However, a hemogram is a very easy examination regarding cost and test duration. In addition, with a hemogram, information can be obtained about the lymphocyte count and mean platelet volumes. In our study, the mean platelet volume is essential regarding the prognosis of the disease in patients with a suspected diagnosis of COVID-19. This study aimed to investigate the relationship between MPV and disease prognosis in patients with COVID-19, and to investigate the chronic diseases that affect the prognosis of COVID-19 and the laboratory data that can help diagnose this disease and provide information about the course of the disease during the treatment process.

Methods

Study design

The study was conducted in a cross-sectional plane. Study reporting was done following the STROBE guidelines [6]. All participants gave written individual informed consent to participate. Ethics committee approval dated 24.03.2021 and numbered 2021/03-35 was obtained from the Health Sciences University Izmir Tepecik Education and Research Hospital. Additionally, permission was taken from the study-site health institution (dated 08.09.2021). The study was conducted between 08.09.2021 and 20.03.2022 in the Private Izmir Karsiyaka Metropol Health Center. The health center contains an internal medicine outpatient clinic without inpatient services. Approximately 80 outpatients are served daily.

Participants

A questionnaire consisting of two parts, including categorical (socio-demographic) data and laboratory data, was applied to people who had COVID-19 who applied to the internal medicine outpatient clinic of the hospital. A total of 2250 people applied to the polyclinic during the research. Of these, 230 were PCR positive by PCR test (RT-PCR test kits, BioGerm, China). Six of the patients did not accept to participate in the study. Laboratory data of 20 patients who agreed to participate in the study could not be obtained and were excluded from the study.

Variables

Scopus, MEDLINE (via Pub Med interface), and Web of Science were searched using the keywords "mean platelet volume or MPV, "coronavirus disease" and "coronavirus disease prognostic markers". The title, abstract, and full text of 56 articles that could be retrieved according to the search criteria of (until March 21, 2022) were examined in all fields without language or date restrictions. A standardized questionnaire was developed by combining general medical information and information obtained from the literature review. The questionnaire included the following information: age, sex, socio-demographic data, chronic diseases (diabetes mellitus, chronic lung disease, atherosclerotic heart disease, chronic kidney disease, chronic liver disease), and laboratory data that are thought to be effective on disease prognosis (CPK, troponin, LDH, CRP, ferritin, D-Dimer, white blood cell value, lymphocyte value, hemoglobin value, platelet value, mean platelet volume value, and lung CT findings). Patients who accepted to participate received a face-to-face interview questionnaire lasting 5-7 minutes for each patient. Laboratory examinations of the

patients during their illness were obtained retrospectively from the hospitals electronic patient record system. The laboratory tests examined were routinely performed in the health institutions to which the patients applied during COVID-19 pandemic, and no non-routine tests were performed during the study period. In addition to routine laboratory examinations, lung tomography, hospitalization, and mortality status of the patients were also recorded.

Study Size

The sample size calculation was based on the main outcome variable, "hospitalization status." Of the persons infected with SARS-CoV-2, approximately 14% require hospitalization [7]. Therefore, to estimate the hospitalization proportion with a 95% confidence interval in an infinite population with a 0.05 margin of error and a 0.14 expected proportion, 185 participants are needed [8].

Ethical approval

The study was carried out with the permission of Tepecik Training and Research Hospital, Non-invasive Clinical Ethics Committee (Date: 24.03.2021,Decision No: 2021/03-35).

Statistical Analysis

Descriptive statistics were presented as frequencies, percentages, median, and interquartile ranges. Pearson Chi-squared test and Fisher exact test were used for comparing categorical variables. The Kolmogorov-Smirnov test was used to assess the assumptions of normality of the numerical variables. The Mann-Whitney U test or Kruskal-Wallis test with Bonferroni post hoc comparisons was used to compare numerical variables between the groups. Binary logistic regression analysis was performed to check the effects of the individual variables on hospitalization. (Back LR method). All analyses were performed using the SPSS 25.0 (SPSS Inc., Chicago, IL, USA) software package.

Results

Data of 204 participants were analyzed. The participants' mean (±SD) age was 40.8±13.7 years (median: 40, range: 18 – 72). Almost half of the participants (48.0%, n=98) were male, the majority (76.0%, n=155) were married, and 24.0% (n=49) were single. Of the participants, 153 (75.0%) were secondary school graduates, 42 (20.6%) were high school graduates, and 9 (4.4%) had a university degree.

A quarter of the participants had chronic diseases, atherosclerotic heart disease and diabetes being the most common ones. In addition, approximately one-third were smokers (Table 1).

Table 1. Distribution of chronic diseases and smoking status of the patients

		n	%
Chronic Diseases	Absent	153	75.0
	Present	51	25.0
Diabetes Mellitus	Absent	180	88.2
	Present	24	11.8
Atherosclerotic Heart Disease	Absent	178	87.3
	Present	26	12.7
Lung Disease	Absent	185	90.7
	Present	19	9.3
Liver Disease	Absent	203	99.5
	Present	1	0.5
Smoking	No	141	69.1
	Yes	63	30.9

Of the 204 patients, 28 (13.7%) were hospitalized, and five died (2.5%). Of the five patients who died, three had chronic lung disease, one had diabetes and chronic lung disease, and one had no chronic disease. All five deceased patients were smokers.

Chi-square tests reveal a significant difference between hospitalized and non-hospitalized patients related to their chronic diseases. Diabetes mellitus, atherosclerotic heart disease, lung disease, and smoking were related to hospitalization (Table 2). No comparisons were made in the deceased subgroup due to the low number of cases.

Table 2. Comparison of chronic disease presence and smoking proportions between hospitalized and non-hospitalized groups

		Not Hospitalized		Hospitalized		
		n	%	n	%	p
Chronic Diseases	Absent	145	94.8	8	5.2	<0.001*
	Present	31	60.8	20	39.2	
Diabetes Mellitus	Absent	162	90.0	18	10.0	<0.001*
	Present	14	58.3	10	41.7	
Atherosclerotic Heart Disease	Absent	157	88.2	21	11.8	0.036*
	Present	19	73.1	7	26.9	
Lung Disease	Absent	171	92.4	14	7.6	<0.001
	Present	5	26.3	14	73.7	
Liver Disease	Absent	175	86.2	28	13.8	1.000**
	Present	1	100	0	0	
Smoking	No	129	91.5	12	8.5	0.001*
	Yes	47	74.6	16	25.4	
Lung computed tomography findings	Negative	23	85.2	4	14.8	<0.001*
	Positive	13	40.6	19	59.4	
Sex	Female	87	82.1	19	17.9	0.070*
	Male	89	90.8	9	9.2	

*Chi-square test, **Fisher's exact test

LDH, CRP, ferritin, and mean thrombocyte volume levels were significantly higher in the hospitalized patients, while CPK, troponin, D-Dimer, WBC count, lymphocytes, hemoglobin, hematocrit, and thrombocyte counts were not significantly different between the groups (Table 3).

Table 3. Comparison of median laboratory values regarding hospitalization

	Not Hospitalized			Hospitalized			p
	n	Median	25th-75th percentile	n	Median	25th-75th percentile	
Age	176	38.0	28.0-47.0	28	53	44-62.5	<0.001
CPK	30	76.0	56-117.2	8	92.0	34.5-126	0.886
Troponin	34	3.0	2-5.8	12	5.8	2.6-18.8	0.091
LDH	38	185.5	165-220.7	18	228.5	167.5-288.5	0.055
CRP	76	3.8	1.9-8.8	25	19.5	6.2-54.5	<0.001
Ferritin	62	57.2	18.2-165.2	25	207.0	59.6-642	0.002
D-Dimer	49	0.8	0.1-93.5	25	2.5	0.2-1505	0.080
WBC count	171	7.3	6.1-8.5	28	7.9	6.2-11	0.078
Lymphocyte count	170	2.2	1.7-2.8	28	1.9	1.4-3.4	0.597
Hemoglobin (mg/dl)	171	13.2	12.5-14.3	28	13.0	11.8-13.7	0.330
Hematocrit	171	39.0	36.6-42.5	28	38.3	34.9, 42	0.430
Thrombocyte count	171	235.0	187-290	28	262.0	184-376	0.066
Median thrombocyte vol.	171	8.6	7.6-9.7	28	10.3	8.2-13.2	0.005

*Mann Whitney U Test CPK: Creatine phosphokinase, LDH: Lactate dehydrogenase, CRP: C-reactive protein, WBC: White blood count

Troponin, WBC count, and median platelet volume values were significantly higher in deceased patients; other laboratory values were not significantly different between the survived and deceased groups (Table 4).

Table 4. Comparison of median laboratory values regarding mortality status

	Survived			Died			p
	n	Median	Min.-Max.	n	Median	Min.-Max.	
CPK	35	76.0	8.4-988	3	108.0	96-136	0.151
Troponin	44	3.1	0.1-157	2	16.3	12-20.6	0.059
LDH	52	187.5	72-376	4	276.0	111-368	0.192
CRP	97	4.9	0.02-406	4	39.4	4.3-76	0.070
Ferritin	83	67.8	3.6-1868	4	931.0	10.4-1956	0.292
D-Dimer	71	0.8	0.1-1980	3	1867.0	0.1-1920	0.242
WBC count	194	7.4	3.6-17.4	5	13.6	7.2-14.69	0.005
Lymphocyte count	193	2.2	0.6-44410	5	3.5	1.9-10.6	0.061
Hemoglobin (mg/dl)	194	13.1	8.2-17.3	5	12.8	10.8-13.8	0.279
Hematocrit	194	39.0	15.7-51.4	5	39.6	34.4-42.6	0.813
Thrombocyte count	194	237.0	94-663	5	259.0	211-605	0.100
Mean thrombocyte vol.	194	8.6	5.6-18.6	5	12.8	9.1-16.6	0.007

*Mann Whitney U Test, CPK: Creatine phosphokinase, LDH: Lactate dehydrogenase, CRP: C-reactive protein, WBC: White blood count

Lung computed tomography (CT) findings were categorized as normal, mild, moderate, or severe. Most of the measured variables significantly increased in parallel with the severity of the CT findings (Table 5). Although the median D-Dimer values in the severe group were significantly higher than the other groups in pairwise comparisons using the Mann-Whitney U test (p=0.035), no difference was observed after the Bonferroni correction.

Table 5. Comparison of the studied variables between the different CT groups

Lung CT		CPK	Troponin	LDH	CRP	Ferritin	D-Dimer
Normal	n	6	6	8	16	15	13
	Median	100.5[a]	2.7[a,b]	212.0[a,b]	2.8[a]	53.8[a]	0.3[a]
	(Min. – Max.)	(9.8-195)	(0.5-6.7)	(126-296)	(0.1-125)	(3.6-980)	(0.1-780)
Mild	n	2	3	3	12	10	11
	Median	49.0[a]	0.3[a]	259.0[a,b]	6.3[a,b]	70.6[a,b]	0.3[a]
	(Min. – Max.)	(22-76)	(0.1-1)	(223-284)	(1.3-36.1)	(10.3-306)	(0.1-68)
Moderate	n	2	5	9	11	11	10
	Median	51.0[a]	4.3[a,b]	217.0[a]	9.5[a,b]	324.0[a,b]	129.8[a]
	(Min. – Max.)	(24-78)	(2-13.4)	(89-277)	(3.1-84)	(49-956)	(0.1-1980)
Severe	n	3	4	6	7	7	7
	Median	96.0[a]	25.1[b]	325.5[b]	64.0[b]	1090.0[b]	1600.0[a]
	(Min. – Max.)	(88-108)	(12-32)	(179-376)	(12-357)	(82-1956)	(0.1-1920)
Kruskal-Wallis H		2.681	12.129	8.832	12.579	14.098	8.597
p-value		0.443	0.007	0.032	0.006	0.003	0.035
Lung CT		**WBC Count**	**Lymphocyte count**	**Hemoglobin (mg/dl)**	**Hematocrit**	**Thrombocyte count**	**MTV**
Normal	n	25	25	25	25	25	25
	Median	7.1[a,b]	1.9[a]	13.6[a]	40.0[a]	255.0[a]	9.1[a]
	(Min. – Max.)	(4.6-10.2)	(0.6-41.4)	(10.8-16.2)	(32-48.4)	(94-393)	(5.6-13.6)
Mild	n	14	14	14	14	14	14
	Median	5.9[a]	1.7[a]	13.4[a]	39.9[a]	252.0[a]	8.6[a]
	(Min. – Max.)	(4-13.1)	(1-2.8)	(11.7-15.4)	(33.6-45.6)	(109-370)	(7.2-11.4)
Moderate	n	11	11	11	11	11	11
	Median	7.6[a,b]	1.6[a]	13.8[a]	39.8[a]	210.0[a]	9.8[a,b]
	(Min. – Max.)	(5.8-11.7)	(0.9-2.8)	(9.2-15.4)	(28-46.5)	(165-459)	(6.7-13.2)
Severe	n	7	7	7	7	7	7
	Median	12.8[b]	3.9[a]	12.7[a]	36.8[a]	392.0[a]	13.8[b]
	(Min. – Max.)	(5.3-14.6)	(1.1-10.6)	(10.8-13.2)	(34.4-42.6)	(167-663)	(6.5-18.6)
Kruskal-Wallis H		9.344	6.115	4.915	1.725	4.090	9.670
p-value		0.025	0.106	0.178	0.631	0.252	0.022

MTV: Median thrombocyte count. CPK: Creatine phosphokinase, LDH: Lactate dehydrogenase, CRP: C-reactive protein, WBC: White blood count. Same superscript letters in the cells indicate no significant difference in pairwise comparisons with Bonferroni correction

Significant variables in the comparisons were entered into a univariate logistic regression analysis. Variables with the highest impact on hospitalization were the presence of chronic diseases, positive CT findings, and smoking.

Table 6. Univariate logistic regression analysis output comparing the effects of the significant variables on hospitalization (ordered according to OR)

					95% CI	
	B	**S.E.**	**p**	**OR**	**Lower**	**Upper**
Chronic diseases (present vs. absent)	2.459	0.463	<0.001	11.694	4.721	28.964
Lung CT findings (present vs. absent)	2.129	0.65	0.001	8.404	2.349	30.068
Smoking (yes vs. no)	1.297	0.418	0.002	3.660	1.612	8.306
Sex (female vs. male)	0.770	0.432	0.075	2.160	0.926	5.034
Mean thrombocyte volume	0.434	0.102	<0.001	1.543	1.264	1.885
WBC count	0.169	0.077	0.027	1.185	1.019	1.377
Age	0.072	0.017	<0.001	1.075	1.041	1.111
LDH	0.010	0.005	0.029	1.011	1.001	1.02
Thrombocyte count	0.007	0.002	0.001	1.007	1.003	1.011
CRP	0.007	0.005	0.106	1.007	0.998	1.016
Troponin	0.004	0.013	0.776	1.004	0.978	1.03
Ferritin	0.003	0.001	0.006	1.003	1.001	1.005
D-Dimer	0.002	0.001	0.005	1.002	1.001	1.004

Dependent variable: Hospitalization. CT: Computed tomography. SE: Standard error, OR: Odds ratio, LDH: Lactate dehydrogenase, CRP: C-reactive protein

Discussion

Old age and the presence of chronic diseases are important factors affecting hospitalization in patients with COVID-19. LDH, CRP, ferritin. Furthermore, mean thrombocyte volume levels were significantly higher in the hospitalized patients, while CPK, troponin, D-Dimer, WBC count, lymphocytes, hemoglobin, hematocrit, and thrombocyte counts were not significantly different between the groups. Among the independent variables affecting hospitalization, presence of chronic disease had the highest odds ratio (OR=11.6), followed by positive lung CT (OR=8.4), smoking (OR=3.6), female sex (OR=2.1), and higher mean thrombocyte volume (OR=1.5). However, the results should be interpreted considering the relatively wide confidence intervals for most variables. Although there were significant changes in some other variables, odds ratios were close to 1; thus, their clinical significance was negligible. Identified risk factors for the severe course of COVID-19 disease are age, gender, comorbidities, and laboratory parameters during the clinical course [1,4].

Studies have shown that advanced age affects hospitalization negatively [9]. In our study, advanced age was statistically significant, supporting the literature. In a study conducted in China, the average age was 47 years, and the proportion of women participating in the study was 41.9% [10]. The mean age of our participants was 40.8±13.7 years, and the majority of the participants were male (52%). This situation, which is not in accordance with the literature, can be attributed to Turkey's relatively young population and that people who apply to hospitals are more exposed to this disease than men working in business life. Jie Xu et al. showed that male gender has a poor prognosis for COVID-19 disease [11]. Contrary to the literature, it was found that gender was not statistically significant in terms of the course of the disease.

Chronic diseases progress slowly, last for three months or more, are caused by more than one risk factor, often have a complex course, and negatively affect the person's quality of life. These diseases, which are risk factors that increase the case mortality rates in the Covid-19 epidemic, are among the leading causes of death worldwide [12]. In a study conducted by Chen N et al. in Wuhan, 51% of the participants had at least one chronic disease history [13]. Supporting the literature, 25% of the people who participated in our study had at least one chronic disease.

COVID-19 affects the cardiovascular system. It has been suggested that there is a relationship between acute myocardial damage caused by COVID-19 and angiotensin-converting enzyme-2 (ACE)-2. ACE-2 is present in heart and lung tissues (13).The COVID-19 disease can damage the heart muscle by recognizing ACE-2 receptors in the heart tissue and triggering inflammatory pathways. Direct damage to myocardial cells infected via ACE-2 receptors can lead to an inflammatory storm or create an oxygen supply-demand imbalance, causing adult respiratory distress syndrome (ARDS) [14]. In a study conducted with 5700 COVID-19 patients hospitalized in New York, the frequency of atherosclerotic heart disease (ASHD) was 11.1% [15].Similarly, in a multicenter cohort study conducted in China, 8% of patients were shown to have ASHD [16]. In a multicenter study including 168 patients who died due to COVID-19 in Wuhan, 18.5% of the patients had ASHD [17]. In our study, the incidence of ASHD was 12.7%, which supports the literature. In a study by Li B. et al., it was determined that the frequency of cardiovascular diseases in those who needed intensive care was higher than in those who did not need intensive care follow-up [18]. In our study, contrary to the literature, it was found that 26.9% of hospitalized patients had a history of ASHD.

One of the chronic diseases affecting the course and mortality of COVID-19 disease is type 2 diabetes mellitus (type 2 DM). Diabetes causes physio pathological disorders in patients and increases the tendency to infectious diseases. Any infection in diabetic patients also causes a rise in blood sugar levels. Both type 1 and type 2 diabetes increase susceptibility to infections and complications. The deterioration of the natural immune response in the background of chronic diabetes causes proinflammatory hypercoagulability, the formation of infections, and their more severe course via endothelial dysfunction and impaired barrier structure [19]. In the study performed by Singh AK et al., the frequency of type 2 DM in patients with COVID-19 was 5% [20]. In our study, this rate was 11.8%. Yan et al., in their study with 193 diabetic patients diagnosed with COVID-19, found that hospitalization in the intensive care unit, mechanical ventilation, and mortality was higher [21]. In our study, contrary to the literature, it was found that the hospitalization rate of patients with diabetes mellitus diagnosed with COVID-19 was lower.

Although it is known that viral respiratory tract infections play a role in exacerbating chronic lung disease, there has been no increase in the frequency of hospital admissions of people with chronic lung disease with COVID-19 compared to the general population in the literature [22].In a review examining the clinical features of patients infected with COVID-19 in China, chronic lung disease rates were between 0.0% and 17.0% (median 2%) [23]. In our study, contrary to the literature, the frequency of hospitalization with COVID-19 in people with chronic lung disease was quite high (73.7%). In the study of Zhao Q. et al., it was determined that the risk was approximately doubled in COVID-19 patients who were active smokers [24]. Contrary to the literature, active smoking was low in hospitalized patients in our study.

In a study by Ozer et al. with 166 patients, lung computed tomography involvement was found in 60.8% of COVID-19 patients hospitalized in the pandemic ward [25]. In this study, lung computed tomography involvement was detected in 59.4% of the patients followed up with the diagnosis of COVID-19 in the pandemic service, supporting the literature. Routine biochemical, hematological and immunochemical laboratory tests play an important role in evaluating the severity of the disease, selecting appropriate treatment options, and monitoring the treatment response. The relationship between disease severity and laboratory abnormalities is gaining more importance [26].

The main routine tests requested for COVID-19 patients include complete blood count, tests for coagulation and fibrinolysis cascades (PT, aPTT, and D-dimer), and inflammation-related parameters (erythrocyte sedimentation rate, CRP, ferritin, and procalcitonin). The SARS-CoV-2 virus can severely disrupt many vital organs such as the heart, liver, and kidneys. Therefore, the analysis of biochemical parameters will be appropriate to evaluate the functional activities of these organs [27]. Ferrari et al. stated that simple hematological tests can be used to diagnose COVID-19 in developing countries where RT-PCR testing is limited [28]. On the other hand, Li et al. reported that the hemoglobin level was similar to the control group [29]. Our study determined that there was no statistically significant difference between the hemoglobin values of hospitalized patients and those of non-hospitalized patients.

Lymphopenia has been reported as a common anomaly in COVID-19 patients [29,30]. As a result of its apoptosis, lymphopenia was detected in patients with a poor clinical picture in Middle East Respiratory Syndrome-Coronavirus (MERS) infection [31]. In a study by Qin et al., it was reported that lymphocytes decreased by almost half in COVID-19 patients, and it was stated that coronaviruses had an effect, especially by reducing the number of T-lymphocytes [30]. In our study, contrary to the literature, the mean value of lymphocyte count was 2.2 in non-hospitalized patients and 1.9 in hospitalized patients. However, it was found that there was no statistically significant difference between them. In the study of Li et al. in which they examined 989 patients, significant leukopenia was found in COVID-19 patients [29]. In our study, contrary to the literature, leukopenia/leukocytosis was not found in patients with or without hospitalization, and no significant difference was found between the two groups. Thrombocytopenia is an important parameter that indicates the severity of COVID-19 disease. It is believed that thrombocytopenia develops due to consumptive coagulopathy. Thrombocytopenia was described in 57.7% of patients with severe infection and 31.6% of patients with less pronounced COVID-19 symptoms [32]. In our study, contrary to the literature, thrombocytopenia was not found in hospitalized and non-hospitalized patients. There was no significant difference between the two groups.

Mean platelet volume (MPV) indicates platelet size and activity. Several studies have shown that MPV changes may be associated with mortality and morbidity in diabetes, sepsis, myocardial infarction, and chronic inflammatory diseases [33]. In a study by Sertbas et al., MPV was high in patients followed up in the hospital with COVID-19 disease. In the same study, MPV was higher in those who lost their lives [34].In a study by Ouyang et al., MPV was higher in deceased individuals than survivors [35]. In our study, MPV was high in both hospitalized and deceased patients. There was a significant difference between hospitalized and non-hospitalized patients and between survivors and those who died. Patients with high cardiac troponin values were more likely to be admitted to the intensive care unit and die in the hospital [36].

Myocardial damage has been identified in some COVID-19 patients, resulting in cardiac dysfunction and arrhythmias [36]. A study investigating the effect of cardiovascular diseases in COVID-19 patients concluded that troponin elevation was observed more frequently in patients with underlying CVD, and complications such as malignant arrhythmia and acute kidney injury were more common in patients with high troponin levels [37]. In our study, contrary to the literature, it was found that troponin levels were not high in hospitalized and non-hospitalized patients, and there was no statistically significant difference between them. Therefore, it was determined that the elevation of troponin did not affect the patients' prognosis.

Other predictors of poor prognosis include serum lactate dehydrogenase (LDH) [1]. No relationship was found between LDH levels and hospitalization or survival in our study. On the other hand, CRP levels are increased in COVID-19 patients, and they correlate with disease severity and prognosis. The median CRP values of the survivors were approximately 40 mg/L, while the deceaseds' median CRP values were approximately 125 mg/L [38]. Contrary to the literature, in our study, the survivors' median CRP values were 4.9 mg/L, while it was 39.4 mg/L for those who died. There was no significant difference between the two groups.

Elevated D-dimer coagulation parameter has been associated with multiple thrombo-embolic events in patients with COVID-19, including disease prognosis, pulmonary micro-thrombosis, deep vein thrombosis, and disseminated intravascular coagulation (DIC) [26]. Although D-dimer was high in the deceased in our study, there was no significant difference between the low D-dimer levels measured in the survivors. This finding, which contradicts the literature, can be attributed to the low number of deaths.

Ferritin measurement has diagnostic value and can be used for diagnostic purposes in COVID-19 [26]. Ferritin levels due to secondary hemophagocytic lymphohistiocytosis and cytokine storm syndrome seen in severe COVID-19 patients are much higher and indicate a poor prognosis [1]. In the study conducted by Sahin et al., it was determined that there was no statistically significant difference in ferritin levels between hospitalized and non-hospitalized patients [39]. Contrary to the literature, the ferritin level was high in hospitalized patients in our study. In a study conducted by Saygideger et al., ferritin levels were high in deceased individuals [40]. In our study, ferritin levels were high in patients who died. However, there was no significant difference between the measured ferritin value of the surviving patients and the ferritin value of the deceased patients. This was attributed to the low death toll.

Conclusion

Advanced age and the presence of chronic diseases are important factors affecting hospitalization in patients with COVID-19. While CPK, troponin, D-Dimer, WBC count, lymphocytes, hemoglobin, hematocrit, and thrombocyte counts were not significantly different in hospitalized and non-hospitalized groups, LDH, CRP, ferritin, and mean thrombocyte volume levels were significantly higher in the hospitalized patients. Therefore, advanced age, chronic disease, and laboratory parameters should be considered important prognostic factors for the success of treatment in patients with COVID-19. Mean platelet volume is an easy and cost-effective laboratory test. Besides being important in the triage of patients with COVID-19, it is also an important marker in managing the disease prognosis. Nevertheless, there is a need for further studies with larger sample sizes.

Conflict of interest: None

Author Contributions		Author Initials
SCD	Study Conception and Design	DA, VB
AD	Acquisition of Data	DA, VB
AID	Analysis and Interpretation of Data	DA, VB
DM	Drafting of Manuscript	DA, VB
CR	Critical Revision	DA, VB

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