Evaluation of the Hospitalized Coronavirus Disease 2019 Patients in First 3 Months of the Pandemic

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Cite this article as: Alkan S, Akça A, Şener A, et al. Evaluation of the hospitalized coronavirus disease 2019 patients in first 3 months of the pandemic. *Turk Thorac J.* 2022;23(1):52-57.

Abstract

OBJECTIVE: Data about Turkish coronavirus disease 2019 patients are limited. We evaluated hospitalized coronavirus disease 2019 patients who were followed up in the first 3 months of the pandemic.

MATERIAL AND METHODS: This retrospective, single-center, observational study included 415 confirmed hospitalized coronavirus disease 2019 patients. The patients were divided into groups, namely, mild, moderate, and critically ill patients. Symptoms at the time of admission, clinical, laboratory, and imaging findings were examined.

RESULTS: In our study, 6.74% of coronavirus disease 2019 patients had severe disease, 59.5% were male, and the mortality rate was 11.3%. Diabetes mellitus and chronic obstructive pulmonary disease were more frequently seen in critically ill patient groups and hypertension in moderate patient groups. Anemia and aspartate aminotransferase levels were higher in non-survivors among mild coronavirus disease 2019 patients. In the moderate patients' group, aspartate aminotransferase, lactate dehydrogenase, international normalized ratio, ferritin, and D-dimer levels were higher and lymphocyte, hemoglobin levels were lower; in the critically ill patients' group, platelets were lower and uric acid levels were higher in non-survivor patients.

CONCLUSION: In mild patients, anemia, lymphopenia, and increased aspartate aminotransferase levels; in moderate patients, leukopenia, anemia, and increased aspartate aminotransferase, lactate dehydrogenase, international normalized ratio, ferritin, and D-dimer levels; in the critically ill patient group, lower platelet and increased uric acid levels should be followed closely as they are mortality predictors.

KEYWORDS: COVID 19, disease severity, mortality, symptomsReceived: May 4, 2021Accepted: August 31, 2021

INTRODUCTION

The first coronavirus disease 2019 (COVID-19) case in our country was detected on March 11, 2020, and the increase in the number of cases continues. With the increasing number of COVID-19 infected cases, literature knowledge is expanding. It has been reported that the clinical findings of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in hospitalized patients range from asymptomatic disease and mild conditions such as mild upper respiratory tract infection to severe viral pneumonia accompanied by respiratory failure or even death. There are still unknowns about the disease, from the symptoms to the radiological, clinical, and laboratory findings. Also, the knowledge of the international literature has been acquired so far that the disease is generally detected in individuals with advanced age or comorbidities such as hypertension, diabetes, cardiovascular disease, cancer, and chronic lung diseases.¹⁻³ However, data about Turkish patients are limited.

In our study, we evaluated hospitalized COVID-19 patients who were followed up in the first 3 months of the pandemic. Symptoms at the time of admission; clinical, laboratory, and imaging findings were examined. The patients were divided into groups according to the severity of the disease. Underlying diseases, symptoms, laboratory findings, radiological involvement, and mortality rates were compared according to disease severity. Thus, we aimed to contribute to the scientific literature by revealing the similarities/differences of the data obtained with the general literature.

MATERIAL AND METHODS

Study Design

This retrospective, observational study was conducted in a pandemic hospital in Çanakkale province, Turkey. The study population was 415 confirmed COVID-19 patients who were hospitalized between March 23, 2020, and June 1, 2020.

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Patient Selection

Inclusion Criteria

The sample of the study consisted of patients over 18 years of age who were hospitalized in pandemic wards with the diagnosis of COVID-19. Patients diagnosed with COVID-19 according to the World Health Organization (WHO) provisional guidelines with positive SARS-CoV-2 RNA detection or possible cases according to WHO definition. A positive result of the SARS-CoV-2 "real-time" reverse transcriptase-polymerase chain reaction (RT-PCR) test in upper respiratory tract specimens of the patients as a definite case, although the SARS-CoV-2 RT-PCR test of the patient was negative, finding an appearance compatible with viral pneumonia in thorax computed tomography (CT) together with appropriate clinical findings was defined as a possible COVID-19 patient.⁴

Exclusion Criteria

The exclusion criteria include;

- patients under 18 years of age,
- patients who are pregnant,
- patients who did not perform thorax CT,
- non-hospitalized patients, and
- missing data.

Definitions

The patients were divided into groups according to the severity of the disease and according to the diagnosis and treatment protocol as defined in Turkey's Ministry of Health guidelines for diagnosis and treatment COVID-19:

- a. **Group 1 (patients with mild disease):** Defined as mild clinical symptoms and no sign of pneumonia on imaging or oxygen saturation of 93% or more at rest or more than 50% lesions in thoracic CT.
- b. **Group 2** (patients with moderate disease): Defined as fever and respiratory symptoms with radiological findings of pneumonia but without the severe or critical features.
- c. Group 3 (critically ill patients): Defined as respiratory distress (≥30 breaths/min), oxygen saturation of 93% or less at rest, ratio of arterial partial pressure of oxygen to the fractional concentration of oxygen in inspired air of 40 kPa or less, or more than 50% lesion progression over 24-48 hours in thorax CT.

Procedures

All the medical records such as demographic, clinical, laboratory tests, and radiological imaginations were done at admission day and outcomes (discharge or exitus) of confirmed COVID-19 cases were reviewed retrospectively. The information about the patients was obtained from the hospital automation system. Symptoms at the time of admission; clinical, laboratory, and imaging findings were examined. Comorbidities, symptoms, laboratory findings, radiological involvement, and mortality rates were compared according to disease severity. The levels of white blood cell count (WBC), neutrophil count, lymphocyte count, monocyte count, platelet count, hemoglobin (Hgb), hematocrit (Hct), alanine aminotransferase (ALT), aspartate aminotransferase (AST), uric acid, lactate dehydrogenase (LDH), international normalized ratio (INR), D-dimer, and ferritin in COVID-19 patients were evaluated at the time of admission according to disease severity.

Statistical Analysis

The data were analyzed with Statistical Package for the Statistical Package for Social Sciences version 20.0 software (IBM Corp.; Armonk, NY, USA). Number, percentage, mean, standard deviation, median, minimum, and maximum were used in the presentation of descriptive data. Chi-square test was used to compare categorical data. The compliance of the data to normal distribution was evaluated by Kolmogorov-Smirnov test and Shapiro-Wilk test. Student's t-test and one-way analysis of variance test were used for comparing variables conforming to a normal distribution, Mann-Whitney U test and Kruskal-Wallis test were used for comparison of non-compliant variables. Tamhane's T2 correction was applied for binary comparison of variables that were found to be statistically significant in the normal distribution, and Dunn-Bonferroni correction was applied for binary comparison of variables that did not fit. For statistical significance, P < .05 was accepted.

RESULTS

This study included 415 with proven/probable hospitalized COVID-19 patients. There were 222 (53.5%) patients in the mild patient group, 165 (39.8%) patients in the medium patient group, and 28 (6.7%) patients in the critically ill patient group.

A statistically significant difference was found between the groups in terms of age (P = .0001). The median age of mild patients was statistically significantly lower than the median age of moderate and severe patients. As the disease severity increased, the mean age increased. There was no significant difference between the groups in terms of gender (P > .05).

As comorbidities, diabetes mellitus (DM) was found in 60 (14.4%), hypertension (HT) in 105 (25.3%), and chronic obstructive pulmonary disease (COPD) in 31 (7.5%) patients. There was a significant difference between the groups in terms of DM, HT, and COPD (P = .0001, .0001,and .0001). Diabetes mellitus and COPD were detected more frequently in the critically ill patient group and HT was detected in the moderate patient group.

Although there was a significant difference between the groups in terms of fever, dyspnea, sore throat, and nasal discharge (P = .029, .0001, and .0001), there was no significant difference in terms of dry cough, loss of taste odor, and diarrhea (P > .05).

Fever, sore throat, and runny or stuffy nose symptoms are mild; shortness of breath was found to be statistically significantly higher in patients with severe disease (Table 1).

Hemoglobin and Hct levels of non-survivors were lower and AST levels were statistically significantly higher in non-survivors among mild COVID-19 patients' groups (P = .029, .025, and .018) (Table 2).

Table 1. Comparison of Demographic Characteristics, Comorbidities, and Symptoms According to the Severity of COVID-19

	Mild (n = 222)		Moderate (n = 165)		Severe (n = 28)		
	$Mean \pm SD$	Mean (Min-Max)	$Mean \pm SD$	Mean (Min-Max)	$Mean \pm SD$	Mean (Min-Max)	Р
Age	49.2 ± 17.4	46.0 (19.0-94.0)	62.7 ± 15.9	63.0 (21.0-93.0)	72.0 ± 12.1	70.5 (46.0-93.0)	.0001
	n (%)		n (%)		n (%)		
Male	13	1 (59.0)	95	5 (57.6)	2	1 (75.0)	.216*
DM	1	4 (6.3)	39	9 (23.6)	7	(25.0)	.0001*
HT	34 (15.3)		62 (37.6)		9 (32.1)		.0001*
COPD	5 (2.3)		21 (12.7)		5 (17.9)		.0001*
Fever	82 (36.9)		40 (24.2)		9 (32.1)		.029*
Dry cough	118 (53.2)		80 (48.5)		10 (35.7)		.190*
Shortness of breath	42 (18.9)		75 (45.5)		16 (57.1)		.0001*
Loss of smell or taste	6 (2.7)		3 (1.8)		0 (0.0)		.861*
Diarrhea	Q	9 (4.1)	I	5 (3.0)	(0.0)	.508*
Myalgia	(5 (2.7)	3	3 (1.8)	(0.0)	.861*
Sore throat, runny or stuffy nose	109 (49.1)		56 (33.9)		5 (17.9)		.0001*
Bilateral involvement in thorax CT	21	6 (97.3)	16	2 (98.2)	28	(100.0)	.861*

SD, standard deviation; %, column percentage; P, Kruskal-Wallis test; COPD, chronic obstructive pulmonary disease; CT, computed tomography; HT, hypertension; DM, diabetes mellitus.

*Chi-square test.

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Bold values are statistical significance.

Table 2. Comparison of the Laboratory Values of Survivors with Non-survivors Among Mild COVID-19 Patients' Group						
	Surviv	vors (n = 215)	Non-survivors (n = 7)			
Laboratory Parameters	Mean \pm SD	Mean (Min-Max)	Mean \pm SD	Mean (Min-Max)	Р	
White blood cell count, 10º cells/L	7293.9 ± 3105.6	6400.0 (2700.0-19 900.0)	7657.1 ± 3799.5	5800.0 (4300.0-13 100.0)	.913	
Neutrophil count, 10 ⁹ cells/L	4538.9 ± 2734.5	3600.0 (1000.0-17 700.0)	6057.1 ± 3369.4	4500.0 (2700.0-10 900.0)	.139	
Lymphocyte count, 10 ⁹ cells/L	1856.3 ± 904.9	1700.0 (100.0-5100.0)	4228.6 ± 8819.8	800.0 (400.0-24 200.0)	.061	
Monocyte count, 10 ⁹ cells/L	643.2 ± 283.2	600.0 (100.0-1900.0)	657.1 ± 528.7	500.0 (100.0-1700.0)	.570	
Platelet count, 10º cells/L	220 896.7 ± 80 493.9	213 954.9 (87 000.0-693 000.0)	210 714.3 ± 45 613.3	217 000.0 (133 000.0-276 000.0)	.971	
Hemoglobin, g/dL	13.7 ± 1.7	14.0 (8.0-17.0)	12.1 ± 1.8	12.0 (10.0-15.0)	.029	
Hematocrit, g/dL	39.7 ± 4.7	39.8 (24.5-50.7)	35.9 ± 4.0	34.6 (32.7-42.8)	.025	
ALT, U/L	27.7 ± 42.9	18.9 (4.3-473.5)	23.8 ± 10.9	20.0 (12.8-38.6)	.555	
AST, U/L	28.6 ± 39.0	21.0 (9.3-425.0)	45.2 ± 28.8	33.2 (17.1-93.5)	.018	
Uric acid, mg/dL	5.1 ± 2.7	4.6 (1.9-26.8)	8.9 ± 4.7	8.9 (5.5-12.2)	.094	
Lactate dehydrogenase, units/L	245.5 ± 100.2	218.0 (93.0-831.0)	329.9 ± 186.0	306.0 (150.0-724.0)	.101	
INR	1.0 ± 0.1	1.0 (0.8-1.5)	1.1 ± 0.1	1.1 (0.9-1.2)	.074	

COVID-19, coronavirus disease 2019; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; SD, standard deviation; P, Mann-Whitney U test.

Bold values are statistical significance.

In the moderate patients' group, AST, LDH, INR, ferritin, and D-dimer levels were statistically significantly higher and lymphocyte and Hgb levels were lower in non-survivor patients, respectively (P = .023, .029, .024, .001, .0001, .004, and .016). However, no significant difference was found in terms of WBC, neutrophil, monocyte, thrombocyte, Hct, ALT, and uric acid levels (P > .05) (Table 3).

In the critically ill patients' group, there was a significant difference in terms of thrombocyte and uric acid between survivors with non-survivor patients (P = .036 and .033). Platelets were lower and uric acid was higher in non-survivors.

But there was no significant difference in terms of WBC, neutrophil, lymphocyte, monocyte, Hgb, Hct, ALT, AST, LDH, INR, ferritin, and D-dimer levels (P > .05) (Table 4).

DISCUSSION

As the number of articles published about COVID-19 increases, many different clinical presentations emerge. In addition, existing studies appear to have very different results. In the meta-analysis study by Zu et al⁵ conducted between January 1, 2020, and February 28, 2020, in which a total of 38 studies including 3062 COVID-19 patients were included, 56.9% of infected patients were male and the mortality rate was 5.5%. Fever (80.4%), fatigue (46%), cough (63.1%), and sputum production (41.8%) were the most common clinical findings. Other common symptoms

included myalgia (33%), loss of appetite (38.8%), chest tightness (35.7%), and shortness of breath (35%). Minor symptoms are nausea and vomiting (10.2%), diarrhea (12.9%), headache (15.4%), sore throat (13.1%), tremors (10.9%), and abdominal pain (4.4%).

In another meta-analysis study in which 6007 articles were examined from January 1, 2020 to April 6, 2020; 281 461 patients and 212 studies from 11 countries/regions were analyzed. In this study, the average age of COVID-19 patients was 46.7 years, 51.8% were men, 22.9% had severe disease, and the mortality rate was 5.6%.⁶ In our study, 6.74% of COVID-19 infected patients had severe disease, 59.5% were male, and the mortality rate was 11.3%.

Zhou et al⁷ suggested that 48% of COVID-19 patients (n = 91) had comorbidities and the most common comorbid diseases was hypertension (30%, n = 58), diabetes (19%, n = 36), and coronary artery disease (8%, n = 15). Hu et al⁸ reported that in their meta-analysis study, among the severe COVID-19 patients: 60% are men, 25% are over 65 years old, 34% are obese, and 55% have comorbidities, and the most common comorbidities were HT (34%), DM (20%), and cardiovascular disease (12%).

Some studies have demonstrated an association of severity, disease progression, and adverse outcome with elderly patients (>60 years) with comorbidities (such as DM, HT, and cardiovascular disease) mainly in males.⁹⁻¹²

 Table 3. Comparison of the Laboratory Values of Survivors with Non-survivors Among Moderate COVID-19 Patients'

 Group

Laboratory	Survi	ivors (n = 146)	Non-survivors (n = 19)		
Parameters	Mean \pm SD	Mean (Min-Max)	Mean \pm SD	Mean (Min-Max)	Р
White blood cell count, 10° cells/L	8538.4 ± 4460.6	7350.0 (2400.0-27 600.0)	10 236.8 ± 6817.4	7700.0 (3400.0-33 700.0)	.256
Neutrophil count, 10º cells/L	6117.8 ± 4211.6	4700.0 (1100.0-24 200.0)	7973.7 ± 6620.7	6300.0 (2500.0-31 800.0)	.124
Lymphocyte count, 10º cells/L	1610.3 ± 1033.5	1400.0 (200.0-8500.0)	1157.9 ± 820.1	900.0 (300.0-3100.0)	.023
Monocyte count, 10º cells/L	717.8 ± 387.7	600.0 (100.0-2400.0)	673.7 ± 375.4	600.0 (200.0-1600.0)	.574
Platelet count, 10º cells/L	240 568.5 ± 100 140.6	223 000.0 (36 000.0-580 000.0)	203 473.7 ± 70 562.3	184 000.0 (78 000.0-361 000.0)	.141
Hemoglobin, g/dL	13.1 ± 2.0	13.0 (8.0-19.0)	11.7 ± 2.9	12.0 (5.0-17.0)	.029
Hematocrit, g/dL	38.8 ± 5.7	38.8 (25.8-52.7)	34.7 ± 8.5	34.6 (13.3-49.4)	$.058^{*}$
ALT, U/L	24.6 ± 28.8	15.9 (4.0-239.2)	30.2 ± 20.4	23.5 (5.0-76.6)	.058
AST, U/L	32.6 ± 30.3	22.8 (9.4-215.9)	45.9 ± 28.0	39.0 (13.3-98.7)	.024
Uric acid, mg/dL	5.4 ± 1.9	5.43 (1.9-12.5)	6.2 ± 3.6	5.2 (0.4-11.6)	.412*
Lactate dehydrogenase, units/L	290.5 ± 118.4	250.0 (127.0-720.0)	444.2 ± 225.2	370.0 (149.0-1122.0)	.001
INR	1.1 ± 0.3	1.0 (0.8-3.8)	1.3 ± 0.5	1.2 (0.9-3.1)	.0001
Ferritin	310.9 ± 355.9	183.0 (10.5-2000.0)	683.5 ± 557.7	364.7 (200.0-1800.0)	.004
D-dimer, µg/mL	444.0 ± 620.6	255.0 (0.7-3298.0)	1337.8 ± 1279.9	890.5 (0.9-3570.0)	.016

COVID-19, coronavirus disease 2019; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; SD, standard deviation; *P*, Mann–Whitney *U* test.

Bold values are statistical significance.

Laboratory	Surviv	rors (n = 7)	Non-survivors (n = 21)		
Parameters	Mean \pm SD	Mean (Min-Max)	Mean \pm SD	Mean (Min-Max)	Р
White blood cell count, 10 ⁹ cells/L	10 814.3 ± 3220.9	11 400.0 (6200.0-15 400.0)	21 342.9 ± 33 494.5	14 600.0 (3100.0-164 000.0)	.228
Neutrophil count, 10º cells/L	9542.9 ± 3038.0	10 000.0 (5400.0-13 500.0)	15 880.9 ± 17 361.9	12 800.0 (2800.0-86 800.0)	.208
Lymphocyte count, 10 ⁹ cells/L	642.9 ± 263.7	700.0 (400.0-1100.0)	2100.0 ± 5331.4	600.0 (200.0-23 900.0)	.796
Monocyte count, 10º cells/L	528.6 ± 197.6	500.0 (300.0-800.0)	3047.6 ± 10 632.6	700.0 (100.0-49 400.0)	.348
Platelet count, 10º cells/L	298 571.4 ± 55 286.7	296 000.0 (206 000.0-370 000.0)	205 619.0 ± 105 097.8	185 000.0 (47 000.0-375 000.0)	.036
Hemoglobin, g/dL	11.9 ± 2.4	12.0 (9.0-15.0)	11.5 ± 2.4	12.0 (8.0-16.0)	.756
Hematocrit, g/dL	34.8 ± 7.1	34.7 (25.2-44.4)	35.1 ± 7.7	35.3 (23.2-49.3)	1.000
ALT, U/L	38.5 ± 32.3	31.2 (7.8-104.7)	70.4 ± 103.4	23.2 (11.0-462.6)	1.000
AST, U/L	40.4 ± 21.9	39.6 (14.7-83.0)	160.1 ± 314.8	37.4 (14.6-1275.0)	.570
Uric acid, mg/dL	3.6 ± 1.6	3.5 (1.9-6.5)	5.7 ± 2.1	6.1 (2.9-10.8)	.033
Lactate dehydrogenase, units/L	422.0 ± 117.4	427.5 (286.0-559.0)	420.1 ± 235.7	292.0 (193.0-921.0)	.541
INR	2.9 ± 4.2	1.1 (1.0-11.5)	1.3 ± 0.4	1.2 (0.9-2.8)	.629
Ferritin	422.3 ± 186.3	416.5 (202.0-642.1)	915.9 ± 751.2	537.4 (54.0-2000.0)	.246
D-dimer, µg/mL	578.3 ± 420.0	500.0 (203.0-1032.0)	1513.9 ± 1167.9	1066.0 (0.5-3695.0)	.291

Table 4. Comparison of the Laboratory Values of Survivors with Non-survivors Among Critically III COVID-19 Patients'Group

COVID-19, coronavirus disease 2019; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; SD, standard deviation; *P*, Mann-Whitney *U* test.

Bold values are statistical significance.

In a case series in which laboratory-diagnosed COVID-19 patients admitted to intensive care in the Lombardy region of Italy were reported, the majority consisted of elderly men, and the intensive care mortality was 26%.¹³ In our study, 75% of the patients hospitalized in the intensive care unit had died. This may be attributed to the higher average age of patients with severe disease in our study. It can also be attributed to the fact that effective antiviral treatments have not yet been used in the first 3 months of the pandemic. In our study, 6.74% of COVID-19 infected patients had severe disease, 59.5% were men, and the most common comorbidity was HT (26%). As the disease severity increased, the mean age increased. In our study, only DM, HT, and COPD were evaluated as comorbidities, but only these 3 comorbidities were evaluated because other comorbidities could not be recorded in the patient file. DM (14.4%), HT (25.3%), and COPD (7.5%) were detected. According to the Chinese study,14 DM and HT were found to be lower. Also, in our study, DM and COPD were detected more frequently in the critically ill patient group and HT moderate patient group.

While there is no consensus on specific biomarkers determining disease severity for COVID-19, acute phase reactants, including C-reactive protein (CRP), ferritin, serum amyloid A (SAA), and procalcitonin, have been used as sensitive markers of acute COVID-19. Increased WBCs; pronounced lymphopenia; decreased CD3, CD4, or CD8 T-lymphocyte counts; high neutrophil count; thrombocytopenia; and significantly higher inflammatory biomarkers are accepted by some investigators as predictors of severe disease.¹⁰ In early years some researchers reported that high neutrophil count (>0.7 \times 10³/µL), lymphopenia (<0.8 \times 10³/µL), high CRP (>47.5 mg/dL; 10 to convert to mg/L), and elevated lactate dehydrogenase (LDH; >593 U/L; to convert to µkat/L, multiply by 0.0167) reported that they were the most important predictors of mortality among SARS infection.14-17 In a study from Turkey comorbidities and COVID-19 pneumonia were evaluated, and shortness of breath, male sex, and hypertension were found to be significant for predicting COVID-19 pneumonia on admission and additionally low level of oxygen saturation, lymphocytopenia, AST/ALT, creatinine, LDH, ferritin, CRP, and D-dimer levels were higher in the pneumonia group but no significant relationship was found in multivariate analysis.¹⁸ Another multicenter study from Turkey included 1500 adults with COVID-19 from 26 centers that reported procalcitonin levels on the 3rd-5th day of admission and were to be the strongest association with mortality.¹⁹ Another study from Turkey by Varol et al²⁰ reported that Charlson Comorbidity Index and lymphocyte ratio were found as prognostic factors for COVID-19-related mortality. Similar to our study, some researchers reported that hematological parameters such as leukocytosis together with the increased neutrophil count, lymphopenia, and thrombocytopenia are findings that show a positive correlation with disease severity in COVID-19 patients.12-17 In our study, Hgb and Hct levels of non-survivors were lower and AST levels were

statistically significantly higher in non-survivors among mild COVID-19 patients. In the moderate patients' group, AST, LDH, INR, ferritin, and D-dimer levels were higher and lymphocyte, Hgb levels were lower among non-survivor patients and in critically ill patients' group, platelets were lower and uric acid was higher in non-survivor patients.

In mild patients, anemia, increased AST level, lymphopenia; in moderate patients, increased AST, LDH, INR, ferritin, and D-dimer levels and leukopenia and anemia; and in the critically ill patient group, lower platelet and increased uric acid levels should be followed closely as they may be mortality predictors.

Limitations of the Study

Our study was retrospective and single-center study. In addition, mortality rates according to underlying diseases were not examined in our study. Despite our study is a single-center study, our university represents the national data of our province as it was the unique pandemic center of our province in the early pandemic.

Ethics Committee Approval: This study was approved by Ethics committee of Çanakkale Onsekiz Mart University, (Approval No: 13/2011-KAEK-27/2020-E.2000064660).

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.Ş., A.A., E.D.; Design – A.Ş., A.A., E.D., B.Y.; Supervision – A.Ş., T.Ş., U.G.; Resources – S.A., A.A., K.Ö., K.K., Ş.Ö.; Materials – S.A., A.A., K.Ö., K.K., Ş.Ö.; Data Collection and/or Processing – S.A., A.A., K.Ö., K.K., Ş.Ö., B.Y.; Analysis and/or Interpretation – B.Y., A.Ş.; Literature Search – S.A., A.A., A.Ş, E.D., U.G., T.Ş., Ş.Ö., B.Y., K.Ö., K.K.; Writing Manuscript – S.A., A.A., E.D., K.Ö., K.K., Ş.Ö.; Critical Review – A.Ş., T.Ş., U.G.

Conflict of Interest: The authors have no conflict of interest to declare.

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

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