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RESEARCH

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The Effect of Prognostic Factors and Potential Treatment Regimens on Fatality Covid-19 Patients

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Abstract

The ongoing outbreak of the coronavirus disease 2019 (COVID-19), as named by the World Health Organization, has millions of confirmed cases worldwide and has claimed hundreds of thousands of lives. The virus was named SARS-CoV-2 in February by the International Committee on Taxonomy of Viruses. COVID-19 presents as fever, dry cough, dyspnea, headache, and pneumonia. In a small subset of severe cases, the disease quickly progresses to respiratory failure and even death. This study aimed to know the effects of clinical and laboratory features on investigated death. The diagnosis was based on typical findings in thoracic computed tomography (CT) and positive results of the Real-Time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) SARS-CoV-2. The demographic characteristics of COVID-19 patients treated, accompanying comorbid conditions and laboratory criteria (blood lymphocyte counts, C Reactive Protein (CRP), D-dimer, Interleukin 6 (IL-6), blood neutrophil count/lymphocyte counts) were collected retrospectively. The results show that 121 cases, 66 (54.54%) were male, 55 (45.46%) were female, and the mean age was \pm Std (Min-Max), 59.63 ± 17.4 (22-91). Neutrophil percentage ($p = 0.027$), neutrophil / lymphocyte ratio (NE / LE) ($p = 0.028$), CRP ($p = <0.001$), PCT ($p = 0.004$), D dimer ($p = 0.021$) and IL 6 ($p = 0.047$) in patients with a fatal course, higher values were found than those recovered. Blood lymphocyte count ($p = 0.001$) and percent ($p <0.001$) were lower. Number of blood white spheres ($p = 0.010$), blood neutrophil counts ($p = 0.001$) and percentage ($p <0.001$), NE / LE ($p <0.001$), CRP ($p <0.001$), PCT ($p = 0.003$) and IL -6 ($p <0.001$) levels were higher in patients with severe clinical findings than in mild cases. The case death rate was observed as 9%. Covid-19 patients should consider blood neutrophil percentage, blood lymphocyte count, blood lymphocyte percentage, NE / LE, CRP, D dimer, and IL 6 values as an early warning in terms of prognosis. More experience was needed to assess the benefits of immune plasma, tocilizumab, IVIG treatments, and remdesivir therapy recently introduced to the treatment protocol.

Keywords: Prognostic Factors, Covid-19, Fatality, Neutrophil Lymphocyte Ratio

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1. INTRODUCTION

In December 2019, unknown pneumonia cases were detected in Wuhan city of the Hubei State in China. It was later determined that these cases were a new type of coronavirus (SARS-CoV-2) that caused the severe acute respiratory failure (WHO, 2020). It was observed that the virus, which was called by the World Health Organization as the *novel coronavirus disease 19* (COVID-19), could appear in various clinical pictures ranging from asymptomatic form to respiratory failure, sepsis, septic shock and multiple organ dysfunction (MODS) that require mechanical ventilation support in the intensive care unit (ICU).

It was reported that patients had symptoms such as fever, fatigue, dry cough, shortness of breath, and they had areas of atypical pneumonia on Thoracic CT (Huang, C., 2019). Many factors affect fatality in the disease, where there is still no definitive active treatment and vaccine (Casella, M., 2020; Ji, Y., 2020).

This study aimed to investigate the clinical features, treatment results, and factors affecting the fatal course in patients admitted to our center. The study will be guiding because it is the first clinical study since the onset of the pandemic in our region, the effectiveness of the treatment regimen, the determination of mortality status, and the examination of markers that aid diagnosis.

2. RESEARCH METHOD

The study included patients over 18 years of age, who were followed up at the inpatient or outpatient treatment due to suspected/confirmed COVID-19 case diagnoses in the pandemic clinics and intensive care unit of Ordu State Hospital that was listed among the pandemic hospitals by Ministry of the Health Republic of Turkey, during the COVID-19 pandemics. The data were obtained from the hospital registration system and the health ministry information system. SARS-Cov-2 RT-PCR test was performed from the swab samples taken from both the oropharynx and nasopharynx from all patients included in the study and from the tracheal aspirate sample of intubated cases in the intensive care unit. Low-dose non-contrast Thoracic CT was taken from all cases, and rapid radiological evaluation was performed. Patients with positive SARS-CoV-2 RT-PCR tests and cases with typical findings in Thoracic CT were admitted as COVID-19 patients and included in the study (Fang, Y., 2020; Ai, T., 2020; WHO, 2020).

Patients who were not performed thorax CT did not have typical findings in the thorax CT or had negative results in SARS CoV-2 RT-PCR were excluded from the study. Before the study, a case information form was created. The demographic characteristics, comorbid diseases, complaints, and contact stories of the patients were recorded in the information system of our hospital. Also, laboratory test results, thorax CT reports, SARS CoV-2 RT-PCR results, treatment regimens, department and period of hospitalization or intensive care unit, complications and fatality conditions of all patients were scanned and recorded. Laboratory parameters of patients with outpatient follow-up and follow-up only in the clinic were compared to those with severe clinical findings (ICU).

Also, cases with and without typical findings in thorax CT were compared among themselves; and cases with positive and negative results in the SARS CoV-2 RT-PCR were compared among themselves according to laboratory parameters and fatality. The fatality rate was calculated according to age groups and comorbidity status. The proportion of patient groups receiving single or multiple antiviral treatments was determined. In our cases, the treatment plan was administered based on the COVID-19

(SARS-CoV-2) Infection Guideline published by the Ministry of Health, General Directorate of Public Health, for the first time on February 21st, 2020 and recently on April 14th, 2020 (Nebraskan Medicine, 2020). In line with the guideline recommendations, hydroxychloroquine-/+azithromycin treatment was added in patients with mild clinic pictures; favipiravir and tocilizumab treatment were added in certain patients with the severe clinical picture, particularly those in the ICU. The presence of bacterial infection was decided based on the clinical findings, laboratory, and procalcitonin (PCT) values (>0.5).

Statistical analysis was performed using the SPSS (Statistical Package for Social Science) software (version 20.0; SPSS Inc. Chicago IL, USA). Pearson Chi-square test was used to compare the distribution of groups for categorical variables. Continuous variables were tested for compatibility with a normal distribution (Kolmogorov-Smirnov or Shapiro-Wilk). Those that were compatible with the normal distribution were compared by the Test of Significance for Difference Between Two Means. Those that were not compatible were compared using the Mann Whitney U Test. The study was approved by the Ordu University Clinical Research Ethics Committee.

3. RESULTS AND DISCUSSION

A total of 121 patients were included in the study. Of the patients, 66 (54.54%) were male, and 55 (45.46%) were female. Of all cases, the average age (years) was average±SD (Min-Max), 59.63±17.4 (22-91). Patients applied to our center, the most frequent complaint of cough (74%). Also, there were 47% dyspnea complaints, 33% fever complaints, 27% fatigue complaints, 12% nausea complaints, 11% vomiting complaints, and less frequently, there were complaints about the blurring of consciousness, myalgia, loss of taste and smell, and redness of the eyes. HT was the most common (53%) comorbidity, while there were other comorbidities of CVD (43%), respiratory disease (40%), diabetes mellitus (DM) (26%), chronic kidney disease (CKD) (9%) and malignancy (TM) (6%). Thirty-seven patients (30.5%) did not have any comorbidities. Looking at the history of the patients taken during the examination, there were 6 (4.9%) patients with international travel experience and 12 (9.8%) patients with a history of contact with the confirmed or suspected case within the last 14 days before the application. One (0.8%) patient was a healthcare professional. When the thorax CT reports of the patients were examined, it was observed that there were typical findings in 102 (83.6%) cases.

Table 1. Demographic Characteristics, Clinical Picture, Comorbid Diseases and Characteristics of the Contacts.

Demographic Characteristics	Values	
Age (Years) Avg±Std (Min-Max)	59.63±17.4 (22-91)	
Female/Male	55/66	
Comorbidity	n	%
DM	26	(21.3%)
HT	53	(43.4%)
CVD	43	(35.2%)
CKD	9	(7.4%)
Respiratory	40	(32.8%)
TM	6	(4.9%)

Immunosuppression	1 (0.8%)
Pregnancy	1 (0.8%)
Liver Diseases	1 (0.8%)
Without risk factor	37 (30.5%)
Complaint	n %
Fever	33 (27.0%)
Cough	74 (60.7%)
Fatigue	27 (22.1%)
Sore throat	4 (3.3%)
Headache	1 (0.8%)
Dyspnea	47 (38.5%)
Diarrhea	1 (0.8%)
Abdominal pain	1 (0.8%)
Nausea	12 (9.8%)
Vomiting	11 (9.0%)
Myalgia	5 (4.1%)
Smell and taste disorder	1 (0.8%)
Redness in the eyes	1 (0.8%)
The blurring of consciousness	7 (5.7%)
History of Contact	n %
Abroad	6 (4.9%)
Possible confirmed contact	12 (9.8%)
Healthcare professional	1 (0.8%)
Tests	n %
Typical findings in the thorax CT	102 (83.6%)
SARS-CoV-2 PCR 1	38 (31.1%)
SARS-CoV-2 PCR 2	11 (9.0%)
SARS-CoV-2 PCR 3	2 (1.6%)
SARS-CoV-2 PCR 4	1 (0.8%)

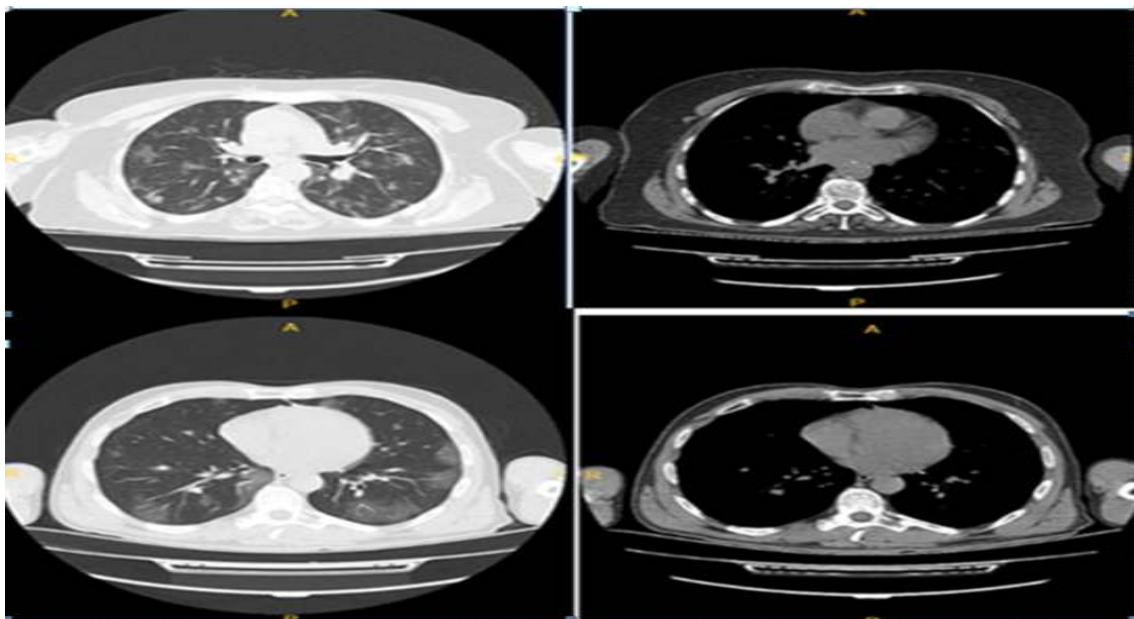


Figure 1. Typical Thorax CT Findings of Cases

In 43 of the cases (35.5%), RT PCR was confirmed, while 64.5% of the cases were diagnosed with thorax CT findings. When the results of the SARS CoV-2 RT-PCR that was performed for diagnosis were scanned, it was observed that the 1st sample was positive in 38 (31.1%) cases, the 2nd sample was positive in 11 (9%) cases, the 3rd sample was positive in 2 (1.6%) cases, and the 4th sample was positive in 1 (0.8%) case (Table 1). When the comorbidities of the patients were examined, it was observed that there were 31 (30.3%) cases with a single comorbid disease, 26 (21.3%) cases with two comorbid diseases, 14 (11.5%) cases with three comorbid diseases, 12 (9.8%) cases with four comorbid diseases. There was a 1 (0.8%) case with five comorbid diseases.

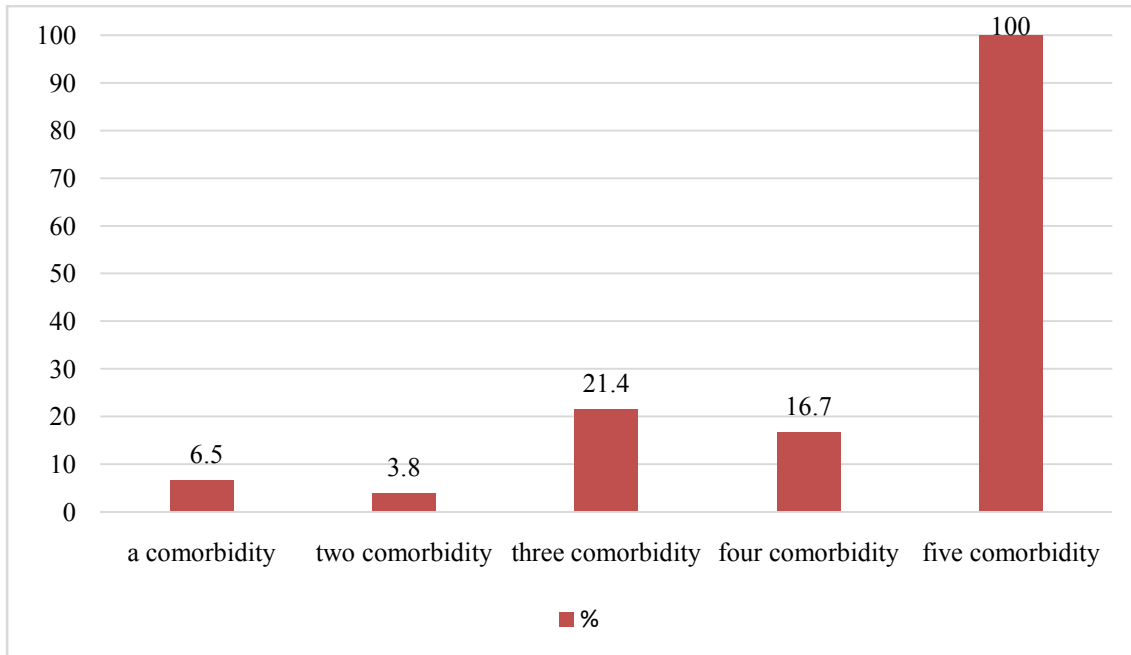
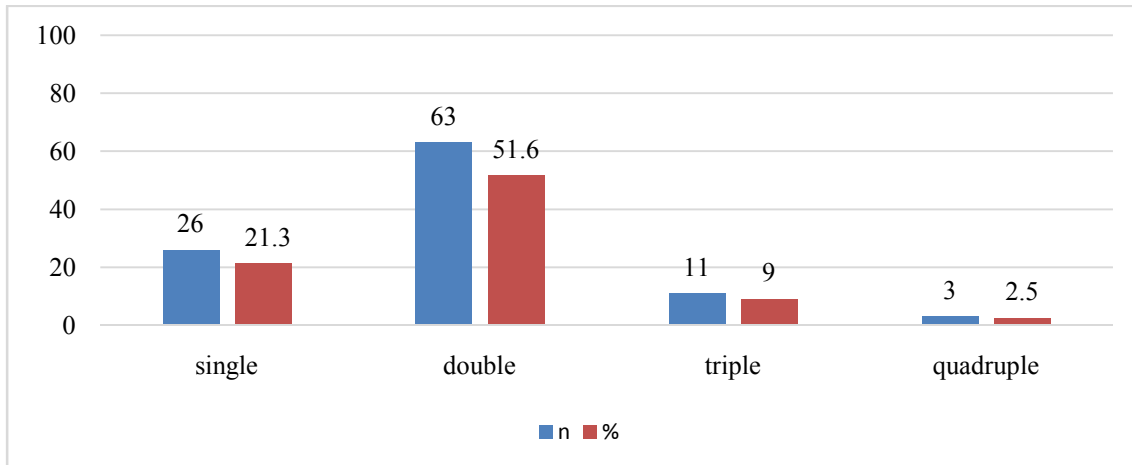


Figure 2. Fatality Rate by Comorbidity Groups

The fatality rate was observed to be 6.5% in the cases with a single comorbid disease, 3.8% in the cases with two comorbid diseases, 21.4% in the cases with three comorbid diseases, and 16.7% in the cases with four comorbid diseases. It was observed that the only case with five comorbid conditions resulted in exitus. There were no comorbidities in the 2 cases with the fatal course.

When the treatments received by the patients at the outpatient clinic or during hospitalization in the clinic or ICU were examined, it was observed that 103 (85.12%) cases were administered multiple antiviral treatments. Among these patients, 26 (21.3%) were administered only Hydroxychloroquine treatment, 63 (51.6%) were administered Hydroxychloroquine + Azithromycin treatment, 11 (9%) were administered Hydroxychloroquine + Azithromycin + Favipiravir treatment, and 3 (2.5%) were administered Hydroxychloroquine + Azithromycin + Favipiravir + Tocilizumab treatment. No antiviral treatment was applied to 18 (14.8%) of the cases with normal clinical findings and generally under 50 years of age at the time of admission. The clinical observation was made only for 14 days. Anticoagulant treatment was administered to 29 (23.9%) of the cases (low-molecular-weight heparin, enoxaparin). Also, 3 cases received steroid treatment, and 1 case received immune plasma treatment. When the fatality rates were analyzed according to treatment groups, it was observed that the fatality rate was 3.8% in those who received only

Hydroxychloroquine treatment, it was 4.8% in those who received Hydroxychloroquine + Azithromycin treatment, 18.2% in those who received Hydroxychloroquine + Azithromycin + Favipiravir treatment and it was 33.3% in those who received the quadruple treatment of Hydroxychloroquine + Azithromycin + Favipiravir + Tocilizumab (Figure 3).



Single: Hydroxychloroquine,
 Double: Hydroxychloroquine + Azithromycin,
 Triple: Hydroxychloroquine + Azithromycin + Favipiravir
 Quadruple: Hydroxychloroquine + Azithromycin + Favipiravir + Tocilizumab

Figure 3. Treatment Regimens (%)

When the morbidity rates were examined, hypoxemia (19.7%), sepsis (12.3%), acute kidney failure (10.7%), septic shock (9.8%), bacterial infection (9.8%), arrhythmia (5.7%) and, more rarely, Acute Respiratory Distress Syndrome (ARDS) (0.8%) were observed in decreasing percentages. The fatality rate for total cases was found to be (9%) (Figure 4).

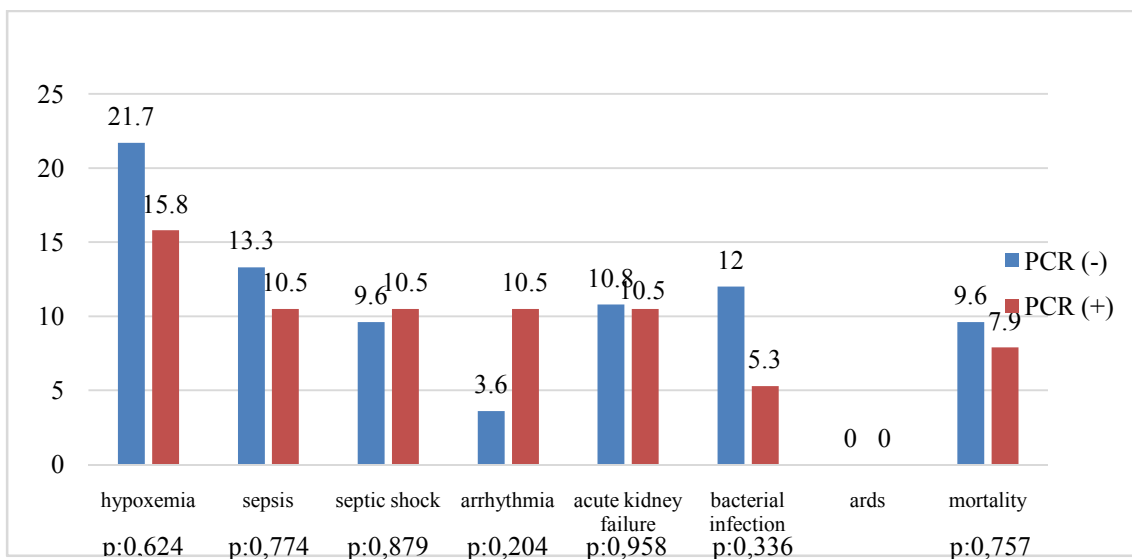


Figure 4. Comparison of Morbidity and Fatality According to the Results of SARS CoV-2 RT-PCR (%)

It was observed that the rate of fatality was 41% in patients with bacterial infection during follow-up, 60% in patients with sepsis, 70% in patients with septic shock, and 46% in patients with acute kidney failure while 11 (9.09%) of the patients were followed-up as outpatients, 81 (67%) were followed up in the clinic, 17 (14%) were in the ICU, and 12 (9.91%) were in both the clinic and the ICU. Hospitalization periods in the clinic and ICU were Mean±SD (Min-Max) 5.1±3.4 (1-25) and 10.5±9.0 (1-39). Out of the 29 cases who were directly hospitalized in ICU or transferred to the ICU from the clinic, 15 (51.7%) were intubated due to the requirement for mechanical ventilation. It was observed that 9 (60%) of the intubated cases had fatal courses.

When the laboratory test results of the cases with fatal course and recovered cases were compared, it was observed that the percentage of blood neutrophils ($p=0,027$), neutrophil/lymphocyte ratio (NE/LE) ($p=0,028$), CRP ($p=<0.001$), PCT ($p=0,001$), urea ($p=0,004$), creatinine ($p=0,003$), troponin ($p=0.006$), D dimer ($p= 0.021$), and IL 6 ($p = 0.047$) values were higher in cases with fatal course at a statistically significant level; blood lymphocyte count ($p=0,008$) and the percentage of blood lymphocytes ($p=0,032$) were found to be higher in recovered cases at a statistically significant level. No statistically significant difference ($p>0.05$) was found between the other values (Table 2).

Table 2. Laboratory Parameters in Cases with Fatal Course and Recovered Cases

Parameters	Recovered			Fatal course			P-value
	n	(mean ±std)	Min-Max	n	(mean ±std)	Min-Max	
WBC x10 ³ U/L	106	8.6±6.0	2.4-47.0	10	9.7±5.0	2.2-18.3	0.316
Neutrophil x10 ³ U/L	106	6.1±5.3	1.1-41.1	10	8.1±5.1	1.3-16.6	0.158
Neutrophil %	106	66.9±14.4	30.0-94.2	10	78.0±15.9	47.2-96.1	0.027
Lymphocyte x10 ³ U/L	106	1.6±0.9	0.1-4.2	10	0.9±0.7	0.2-2.8	0.008
Lymphocyte %	106	22.4±12.2	2.4-55.9	10	14.1±13	3.2-37.7	0.032
NE/LE	106	5.1±5.3	0.5-38.7	10	12.4±10.8	1.2-29.5	0.028
CRP, mg/dL	106	4.5±6.4	0-39.6	10	19.2±13.5	7.5-41.2	<0.001
PCT, ng/ml	60	0.7±3.7	0.01-28.3	7	1.9±4.3	0.1-11.9	0.001
Urea, mg/dL	100	48.3±40	9.5-253.4	9	73.3±44.9	33.3-170.9	0.004
Creatinine, mg/dL	100	1.1±1.1	0.4-9.4	9	1.5±0.7	0.7-2.6	0.003
AST, U/L	105	26.5±17.5	7.1-157.4	10	291.7±809.9	8.0-2595	0.469
ALT, U/L	106	20.2±12.9	3.3-72.5	10	282.7-771.5	3.3-2473	0.894
LDH, U/L	100	271.8±194.9	20.0-1812.0	7	1954.1±3262.8	199.0-8754	0.135
CK-MB, ng/ml	28	3.8±7.2	0.2-39.1	4	32.5±51.	1.1-	0.190

					3	108.9	
Troponin, ng/ml	46	0.6±25.2	0.1-13.4	5	4.5±9.5	0.1-21.7	0.006
Fibrinogen mg/dL	14	535.0±169.4	203.0-790.0	4	521.5±316.4	82.0-779.0	0.832
D Dimer, ng/ml	50	1198.9±2174.6	0-8852.0	5	3031.8±2202.8	621.0-5176	0.021
Ferritin, ng/ml	23	247.8±379.3	6.5-1853	-	-	-	-
IL 6, pg/ml	30	125.8±263.7	1.5-1275	4	183.5±76.3	121.9-287.9	0.047

When fatality rates of the cases were examined in terms of the age groups, it was found that the fatality rate was higher in the age group of 60 and over. The fatality rate was observed to be 0.81% in the 20-30 and 50-60 age groups, 1.62% in the 60-70 age group, 3.24% in the 70-80 age group, 1.62% in the 80-90 age group and 0.81% in the 90-100 age group. There were no fatal cases between the ages of thirty and fifty (Figure 5). When the cases aged fifty, over and below were compared, it was observed that the fatality rate was higher in patients over 50 years old at a statistically significant level ($p=0.285$). There was no significant difference between male and female genders in terms of fatality ($p=0.745$).

The laboratory parameters of cases with the mild clinical picture were compared to the laboratory parameters of cases in ICU and cases with the severe clinical picture. In cases with severe clinical picture, blood white blood cell counts ($p=0.010$), blood neutrophil counts ($p=0,001$) and percentages ($p <0,001$), NE/LE ratio ($p0,001$), CRP ($p0,001$), PCT ($p=0.003$), Troponin I ($p=0.008$) and IL-6 ($p0,001$) were significantly higher in cases with mild clinical picture; blood lymphocyte counts ($p=0,001$) and percentages ($p0,001$) were lower.

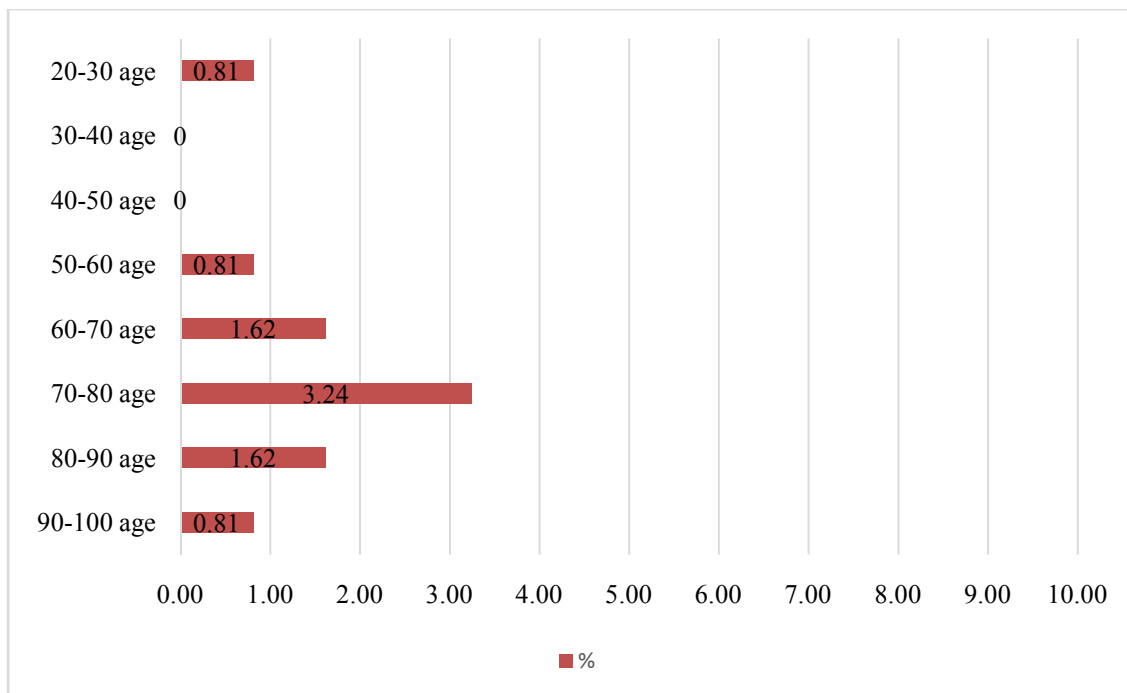


Figure 5. Fatality Rate by Age Groups (%)

When the patients with (-) and (+) results in SARS CoV-2 RT-PCR based on the swab samples taken for diagnostic purposes were compared in terms of thorax CT findings, laboratory values, fatality and morbidity rates, it was observed that the group with (-) results in the SARS-CoV-2 RT PCR had higher WBC ($P<0.001$), neutrophil counts ($p<0,001$), NE/LE ratio ($p=0,019$) and CRP ($p=0,012$) values at the statistically significant level; the group with (+) results in the PCR had higher Lymphocyte % ($p=0,016$) at the statistically significant level. Contrary to what was expected, when the group with (-) results in SARS-CoV-2 RT PCR was compared to the group with (+) results, the percentage of typical findings in thorax CT reports ($p<0,001$) were higher. However, when the fatality and morbidity rates were compared, no statistically significant difference was observed between the two groups.

When the laboratory parameters, fatality and morbidity rates of groups with typical and atypical findings in the radiology reports based on the thorax CT findings were examined, WBC ($p=0,041$), Neutrophil counts ($p=0,022$) CRP values ($p=0.001$) were significantly higher in the group with typical findings in the thorax CT while there was no significant difference in terms of fatality and morbidity.

The first data from China indicated that comorbid conditions and advanced age were important risk factors for COVID-19. In a study where 135 patients with contact history were hospitalized and followed up in Wuhan, 88.9% had a fever, 76.5% had a cough, 32.5% had myalgia and vomiting, 17.7% had a headache; and patients were observed to have dyspnea and diarrhea (13.3%), chest tightness and sputum (8.8%) less frequently. HT 13, DM 12, KVH 7, malignancy 4, chronic liver disease 2, and pulmonary disease were reported as additional diseases in 1 case (Wan, S., 2020).

Another study on 214 patients with confirmed COVID-19 infections and treated in hospital, it was emphasized that 83 (38.8%) of the cases had at least one comorbid disease. HT 51, DM 30, KVH 15, and TM 13 were reported as additional diseases in 13 cases. The most common symptoms at the beginning of the disease were fever (61.7%), dry cough (50%), and anorexia (31.8%). Seventy-eight patients (36.4%) were noted to have symptoms of the nervous system (Mao, L., 2020). On the contrary, fever was identified less frequently, and dyspnea was identified more frequently in our study. Like comorbid conditions, HT and CVD were the most common comorbid conditions, while DM was recorded less frequently.

According to the initial report of WHO on the COVID-19 in the People's Republic of China, the fatality rate was reported to be 3.8% (WHO, 2020). In COVID-19 patients receiving inpatient treatment in ICUs, the fatality rates varied between 16-78% (Huang, C., 2020; Wang, D., 2020; Yang, X., 2020; Arentz, M., 2020; Zhou, F., 2020). Approximately 10% of these patients were intubated due to the need for mechanical ventilation (Wax, R.S., 2020). According to the data of the Republic of Turkey, Ministry of Health, the current fatality rate in our country is approximately 2.7% (The Republic of Turkey Ministry of Health, 2020). In the cases included in our study, the fatality rate was found to be 9%. We believe that the rate that was higher than the country average could be due to the high number of inpatients and intubation rates included in the study. Hence 29 (23.9%) of 121 (100%) cases received inpatient treatment in ICU at the time of application or due to general condition disorder during follow-up in the clinic. Among the 29 (100%) cases admitted to the ICU, 15 (51.7%) were intubated due to the need for mechanical ventilation. This rate does not reflect the average of all cases hospitalized in our center with suspected or confirmed COVID-19. All the patients who died during follow-up were the patients hospitalized in the ICU.

Among 11 exitus cases, two patients developed cardiac arrest immediately after hospitalization in our center; and they did not respond to the intervention. Only 1 of the other 9 cases was taken to the ICU due to clinical deterioration during follow-up in the clinic, while 8 cases had a general disorder when they applied and were directly admitted to the ICU.

We believe that the rate of clinical deterioration and fatality would be high, particularly in the patient group with advanced age and comorbid conditions as they were in our study since the delayed presentation in the health institution after the symptoms started would delay the treatment. We anticipate that starting treatment as soon as possible would reduce the rate of clinical deterioration, morbidity, and fatality. Clinical studies on this subject would clarify the situation.

In our study, when the fatality rates in the treatment groups were examined, the lowest rate of fatality in hydroxychloroquine areas stemmed from the fact that this group of patients was generally under 50 years of age, did not have comorbid conditions, had a good clinical picture and mostly received outpatient treatment. The higher rate of fatality in multiple treatment groups stemmed from the fact that these patients mostly had a poor clinical picture at the time of admission, they were patients with advanced age and comorbid conditions who were admitted to the ICU. Our study observed that the fatality rate was high in patients with three or more comorbid conditions, particularly in patients over 60 years of age.

While there was a high rate of contact history with suspected or confirmed cases in the studies carried out in China (Wuhan), most of the patients were diagnosed with COVID-19 in our country even though there was no known contact within the last 14 days ([Wan, S., 2020](#)). The majority of the patients do not have a history of contact. This could be explained with the prevalent virus in society and the role that asymptomatic cases played in the infection; therefore, most of the patients do not have the history of contact currently.

Current molecular tests used for the diagnosis of COVID-19 consist of a method based on SARS-CoV-2 RT PCR or genomic techniques that identify the virus through sequencing ([Li, Q., 2020](#); [Lu, R., 2020](#); [Corman, V.M., 2020](#)). In our country, the tests are carried out with one-step reverse transcription (RT) and real-time PCR (qPCR) (RT-qPCR) kit targeting RdRp (RNA-dependent RNA polymerase) gene fragment in the centers authorized by the Ministry of Health, General Directorate of Public Health Microbiology Reference Laboratory ([The Republic of Ministry of Health, General Directorate of Public Health, 2020](#)).

Wang et al. investigated SARS-CoV-2 RNA in 1070 samples from multiple body parts of 205 COVID-19 patients and found the most common positivity in the samples obtained from the lower respiratory tract. The positivity rates of different clinical samples were as follows; BAL 93%, sputum 72%, nasal swabs 63%, pharyngeal swab 32%, stool 29%, and blood 1% ([Wang, W., 2020](#)). Also, studies concluded that CT's sensitivity reached 98% ([Fang, Y., 2020](#); [Ai, T., 2020](#)). In our study, swab samples were taken from the oropharynx and nasopharynx. Although typical findings were observed in thorax CT in approximately 84% of patients, the positivity of SARS CoV-2 RT-PCR remained at 31%. We believe that factors such as the time when the swab sample was obtained, the location and the amount of sample, and the low rate of SARS CoV-2 RT-PCR testing on the tracheal sample in long-term ICU patients affected the positivity rate of SARS CoV-2 RT-PCR. Therefore, the combination of thorax CT + SARS CoV-2 RT-PCR is important in diagnosis.

Mardan Ret all, found included 200 patients diagnosed with COVID-19 through SARS CoV-2 RT-PCR, the accuracy of laboratory parameters were evaluated to predict the cases, and the presence of neutrophil together with leukopenia was interpreted as the predictive value ([Mardani, R., 2020](#)). In the clinical laboratory diagnosis of severe COVID-19 patients in another study, 43 patients, consisting of 28 patients with the mild clinical picture and 15 patients with the severe clinical picture, were included; and, IL - 6, D - dimer, glucose, thrombin time, fibrinogen and CRP values of the two groups were compared. In the early prediction of the clinical course of severe COVID-19 patients, the specificity of IL-6 and D-Dimer values were found to be 93.6%, and their sensitivity was 96.4% ([Gao, Y. et al., 2020](#)).

[Moutchia, J. et al., 2020](#), in another meta-analysis that included 45 studies from six countries, the blood neutrophil, lymphocyte count, and CD4 levels were compared in patients with severe and non-severe COVID-19. High neutrophil count (MMD: 1.23 [95% CI: 0.58-1.88] $\times 10^9$ cell / L), low lymphocyte count and CD4 level (MMD (95%CI) -0.39(-0.47, -0.31) $\times 10^9$ cell/L and -204.9 (-302.6, -107.1) cell/ μ l) were recorded in critical COVID-19 patients. Values of other laboratory parameters were identified as follows: CRP (MMD: 36.97 [95% CI: 27.58, 46.35] mg / L), IL-6 (MMD: 17.37 (95% CI: 4.74,30.00) pg / ml), Troponin I (MMD : 0.01 (0.00, 0.02) ng / ml) and D-dimer (MMD: 0.65 [0.45,0.85] mg / ml) ([Moutchia, J., 2020](#)).

[Yang, A. P., et al., 2020](#) found which 93 COVID-19 patients with confirmed laboratory diagnosis were included, the values of age, NE/LE ratio, lymphocyte/monocyte ratio, platelet/lymphocyte ratio, and CRP were evaluated. It was concluded that the advanced age and NE/LE ratio could be used as independent biomarkers in patients with clinical uncertainty ([Yang, A. P., et al., 2020](#)).

In this study, the laboratory values examined at the time of admission indicated leukopenia in 12.39% of the cases, neutrophilia in 26.44%, and lymphopenia in 38.84%. In cases with severe clinical picture, Blood white blood cell count (p=0.010) blood neutrophil count (p=0.001) and percentage (p <0.001), NE / LE ratio (p0.001), CRP (p0.001), PCT (p=0.003) Troponin I (p=0.008), CKBM (p=0.0041) and IL-6 (p0.001) levels were significantly higher in cases with mild clinical picture; blood lymphocyte counts (p=0.001) and percentage (p0.001) were lower. Especially in patients with typical findings in thorax CT, the blood neutrophil count was higher at the statistically significant level; the NE/LE ratio and the blood neutrophil counts were statistically significantly higher in patients with negative results in the SARS CoV RT PCR. Our study supported this COVID 19 diagnosis in the number of cases with low laboratory values. The absence of typical COVID-19 findings or the presence of atypical/rare findings in thorax CT, and the presence of leukopenia, neutrophilia, higher than normal ratio of NE/LE in patients with negative results in sars CoV-2 RT-PCR are the laboratory parameters that could help us in case definitions and empirical treatment decisions.

Chloroquine, hydroxychloroquine, azithromycin, favipiravir, tocilizumab, immune plasma, steroid, and recently introduced remdesivir treatments are administered in the empirical treatment of COVID-19 in our country and all over the world. Oseltamivir was also used in addition to these treatments during the *Influenza* season ([The Republic of Turkey, Ministry of Health, General Directorate of Public Health, 2020](#); [Chan, K. S., 2003](#); [WHO, 2020](#); [Nebraska Medicine, 2020](#)). In our country, the treatment plan for outpatients or hospitalized patients is implemented based on the

Republic of Turkey, Ministry of Health, General Directorate of Public Health, COVID-19 (SARS-CoV-2) Infection Guide ([Nebraska Medicine, 2020](#)).

Hydroxychloroquine + azithromycin is administered to cases with mild pneumonia. Other treatment options are evaluated according to the severity of the clinical conditions of the patients. There was a clinical response to the hydroxychloroquine + azithromycin treatment for 5 days cases within mild pneumonia who were hospitalized with the diagnosis of COVID 19. Favipiravir was added on the 3rd or 4th day of hydroxychloroquine + azithromycin treatment in some patients with refractory fever who were followed-up in the clinic, and there was clinical response again. In the patient groups who were in mechanical ventilation at the ICU with the blood lymphocyte count of $<800/\mu\text{l}$ or $\text{CRP} > 40 \text{ mg/l}$ or ferritin $>500 \text{ ng/ml}$ or D-Dimer $>1000 \text{ ng/ml}$ and increased level of IL 6, favipiravir and tocilizumab treatments were tried in addition to hydroxychloroquine and azithromycin; however, the patients remained in the fatal clinical course.

Extending the hydroxychloroquine treatment to 10 days along with favipiravir did not provide any significant benefits to these patients, who were believed to start experiencing cytokine storm. In our study, hydroxychloroquine combined with favipiravir was extended to 10 days in four patients; however, these patients were still unable to be discharged from the ICU. In this context, we anticipate that starting the treatment as early as possible, intubating the patient as late as possible, and controlling morbid conditions would increase the treatment's effectiveness.

Immune plasma treatment was administered to only one patient in our center, and no clinical improvement was observed. There is a need for more experience regarding this treatment in more cases. Another important problem in treatment is the unnecessarily excessive use of antibiotics, and this rate was recorded as 30% in our clinic. One of the main reasons for this was the high CRP value in the majority of patients with COVID-19. Evaluation of bacterial infection with PCT is important for preventing the unnecessary use of antibiotics. It is also important to inform branch physicians other than infectious disease specialists who follow COVID-19 patients. Among the morbid conditions, ARDS was noted only in 1 patient in our study. We believe that this stemmed from the fact that only the reports of thorax CT that was performed at the time of admission were included in the study.

We were found that the patients mostly presented with cough complaints, and most of them did not have a risky contact history. In the follow-up of patients with COVID-19, blood neutrophil percentage, blood lymphocyte count, blood lymphocyte percentage, NE/LE, CRP, D dimer, and IL 6 values should be considered as early stimuli in terms of prognosis. Also, similar to studies in this area, advanced age, and comorbid conditions are important risk factors for fatality thorax CT has an important contribution to the diagnosis of SARS-CoV-2 together with RT-PCR test. In our study, the first RT-PCR test in 38 (31.1%) cases, second RT-PCR test in 11 (9%) cases, third RT-PCR test in 2 (1.6%) cases, and fourth RT-PCR test 1 (% 0.8) was positive in the case. The high rate of fatality is associated with a high number of patients in need of intensive care. More experience is needed to evaluate the benefits of immune plasma, tocilizumab, IVIG treatments, and the remdesivir treatment that was recently introduced to the treatment protocol.

4. CONCLUSION

The conclusion of this research is eighty-one cases (67%) were followed in the clinic, and 12 cases (9.91%) were followed up in the clinic. They were taken to the ICU due to the deterioration in the general situation. Seventeen (14%) cases were hospitalized directly to the ICU. Eleven (9.09%) cases were followed up on an outpatient basis. After swab samples were obtained from outpatients for the SARS CoV-2 RT-PCR test, they were started hydroxychloroquine 2x200 mg tablet empirically. Treatment of cases that were positive as a result of swabs was extended to 5 days, and they were included in the study. Covid-19 patients should consider blood neutrophil percentage, blood lymphocyte count, blood lymphocyte percentage, NE / LE, CRP, D dimer, and IL 6 values as an early warning in terms of prognosis. More experience is needed to assess the benefits of immune plasma, tocilizumab, IVIG treatments, and remdesivir therapy recently introduced to the treatment protocol.

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