RESEARCH ARTICLE / *Araştırma Makalesi*

Clinical Characteristics and Prognostic Factors of Patients with COVID-19

COVID-19 Hastalarının Klinik Özellikleri ve Prognostik Faktörler

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Abstract

Objective	We aimed to determine the main demographic features of COVID-19, reveal the clinical differences to patients in other countries, evaluate severe adverse effects in terms of number and types of comorbidities and provide information about prognosis possibilities.
Materials and Methods	Patients' records, followed at Sakarya University Hospital between late March 2020 and late April 2020 with a diagnosis of COVID-19, were evaluated for this study. Demographic features were noted retrospectively with records, and data were recorded in the MS Excel program for analysis with SPSS. Statistical significance was set at $p < 0.05$.
Results	The records of 1443 cases, 704 (48.8%) women and 739 (51.2%) men, a mean age of 44.98 ± 18.72, were examined retrospectively. Among them, 9.9% were medical staff, 1.8% had a history of travel abroad, and 1.1% were pregnant. Radiological findings of 59.4% of our polymerase chain reaction (PCR) positive patients were compatible with COVID. The mean length of hospital stay was 4.5 days. Frequent comorbidities were hypertension, diabetes (DM), and ischemic heart disease. Eighty (5.5%) patients treated in intensive care (ICU) died.
Conclusion	Based on the data of 1443 patients, the mean length of hospitalization of COVID-19 patients was 4.5 days, or followed up in intensive care, having DM and a long period of hospitalization, which increased mortality risk. None of the outpatients died.

Keywords COVID-19; Mortality; Prognosis

Öz

Amaç	*COVID-19 için başlıca demografik özelliklerin belirlenmesini, diğer ülkelerdeki hastalara göre klinik farkları ortaya koymayı, ciddi yan etki riskini komorbidite sayısı ve tipine göre değerlendirmeyi ve olası prognozla ilgili bilgileri ortaya çıkarmayı amaçladık.*
Gereç ve Yöntemler	*Bu araştırma Sakarya Üniversitesi hastanesinde 27 Mart 2020- 27 Nisan 2020 tarihleri arasında COVID-19 enfeksiyonu tanısıyla izlenen hastaların kayıtlarından elde edilmiştir. Hastalara ait demografik özellikler hasta kayıtlarından retrospektif olarak elde edilmiş, elde edilen veriler MS Excell programına kayıt edilmiştir. Elde edilen veriler SPSS programıyla analiz edilerek karşılaştırılmış ve p<0,05 istatistiki olarak anlamlı bulunmuştur.*
Bulgular	*Hastaların yaş ortalaması 44,98±18,72 olan 704 (%48,8) kadın ve 739 (%51,2) erkek olmak üzere toplam 1443 olgunun retrospektif kayıtları incelenmiştir. Hastaların %9,9'u sağlık personeli olup, %1,8'inde yurt dışı öyküsü varken, %1,1'i gebeydi. PCR pozitif olan hastalarımızın %59,4'ünde COVID ile uyumlu radyolojik görünüm vardı. Hastalarımızın ortalama yatış süresi 4,5 gündü. Hastalarımıza en sık eşlik eden komorbid durumlar hipertansiyon, diyabet ve iskemik kalp hastalığı idi. Yoğun bakım tedavisi alan hastaların 80'i (%5,5) öldü.*
Sonuç	*1443 hastanın verisine göre; COVID-19 hastalarının ortalama yatış süresi 4,5 gün olup, yoğun bakımda izlenmek, diyabeti olmak ve uzun süre yatırılıyor olmak ölüm açısından riskliydi. Ayaktan izlenen hastaların hiçbirinde ölüm gözlenmedi.*

Anahtar Kelimeler *COVID-19, Mortalite, Prognoz*

INTRODUCTION

Coronaviruses (CoVs) are zoonotic viruses common in nature, while orthocoronavirinae are positively-polarized, enveloped RNA viruses without segments that cause viral respiratory infections, especially in winter. Yet, a new type of coronavirus, emerging at the end of 2019 and later called SARS-COV-2, infected millions of patients and caused thousands of deaths in a worldwide pandemic.[1] In Turkey, the first case was detected in mid-March 2020. There were 200,000 cases in Turkey, with the number of deaths exceeding 500 in June 2020.[2]

SARS-CoV-2 infection progresses with various clinical findings. About 30-40% of cases are asymptomatic.[3] The most common symptoms of COVID-19 are cough, fever, and weakness. It does not have a specific feature that can distinguish it from other viral respiratory infections. The most common initial symptoms are fever (98%), cough (76%), myalgia or fatigue (44%), with atypical symptoms being sputum (28%), headache (8%), hemoptysis (5%), and diarrhea (3%). Approximately half the patients had shortness of breath. The World Health Organization (WHO) reported common symptoms as fever, fatigue, and dry cough.[4]

According to recent information, COVID-19's clinical findings are heterogeneous. Of the 44,000 confirmed cases, 81% showed mild (absent or non-severe pneumonia), 14% showed moderate, and 5% showed severe (respiratory failure, septic shock, and multiple organ failure).5 It was reported that 20-51% had one similar comorbidity: diabetes (DM) (10-20%), hypertension (10-15%) and cardiovascular and cerebrovascular diseases (7-40%).[6]

Our goal was to determine the main demographic characteristics of COVID-19 cases in our country, given a large cohort of patients, to highlight clinical differences compared to patients in other countries, evaluate the risk of serious side effects based on the number and type of comorbidities, and to demonstrate possible prognostic information.

MATERIALS and METHODS

Center

This study was performed in a single center, i.e., a tertiary teaching hospital with 1200 inpatient beds, including 138 intensive care unit (ICU) beds.

Ethics approval

This was received from the Ethics Committee of the SAU Medical Faculty. (Approval number: E.5586, Date: June 26, 2020)

Patients

Data were retrospectively obtained from patient files, i.e., those hospitalized/followed at Sakarya University Training and Research Hospital between late March and late April 2020.

Case definition

The Turkish Ministry of Health defines COVID-19 as an individual having at least one symptom, including fever, cough, and shortness of breath, a history of travel abroad alone, or with an individual in close contact with a COVID-19 patient, 14 days before the onset of symptoms. Patients with severe respiratory infections requiring hospitalization, as well as sudden-onset fever, cough, and shortness of breath without runny nose, but inexplicable for other reasons, were also considered as COVID-19 cases.

Treatment

Our first choice was hydroxychloroquine (HDC) for five days, according to the Turkish Coronavirus Guide. If a patient had pneumonia, oral azithromycin (once a day) was added to HDC. Favipiravir was used for patients who did not respond to other options for 5 days.

Intensive care follow-up

Patients with a severe course were followed in the ICU. The

patient was considered to have severe disease in the presence of any of the following:

- Respiratory failure requiring mechanical ventilation;
- Respiratory distress and / or a slow respiratory rate for more than 30 minutes;
- Oxygen saturation < 93%;
- Resting and partial arterial oxygen pressure (PaO2) / inspiratory oxygen fraction (FiO 2) ratio ≤ 300 mmHg;
- Shock;
- Other organ failures requiring ICU treatment.

Data acquisition

Patient data were obtained retrospectively via the hospital registry, recorded in MS Excel and statistically analyzed. Patient records were secured from files and electronic records.

Data analysis

Data were completed by transferring them to IBM SPSS Statistics v. 23 (Armonk, NY, USA). Frequency distribution (number, percentage) and descriptive statistics (mean, standard deviation) were given for categorical and numerical variables, respectively. Any significant difference between the two groups was evaluated with an independent sample t-test and with more than two groups, one-way analysis of variance (one-way ANOVA) was used. The Levene test was used for variance homogeneity for results of ANOVA, and to assess from which group(s) the difference originated, with a "multiple comparison test" (Bonferroni or Tamhane's T2): these tests evaluated differences between groups in terms of variables which provided variance homogeneity, respectively. The Chi-square test and logistic regression analyses determined the relationship between the categoric variables and OR (odds ratio) values, respectively. The statistical significance level was set at $p < 0.05$.

RESULTS

The records showed a total of 1443 patients, 704 females (48.8%) and 739 (51.2%) males, with a mean age of 44.98 ± 18.72 years, and were retrospectively evaluated. Results included general demographic data, with patient complaints presented in Table 1.

Table 1. The demographic and clinical characteristics of patients

		n	%
Gender	Female	704	48.8
	Male	739	51.2
Age	Mean SD	44.98±18.72	
Healthcare professional	Yes	144	10.0
	No	1291	89.4
	Unknown	8	0.6
History of travel abroad	Yes	26	1.8
	No	1380	95.6
	Not inquired	37	2.6
History of contact	Yes	210	14.6
	No	68	4.7
	Not inquired	1165	80.7
Pregnancy	Yes	16	1.1
	No	688	98.9
Thorax CT findings	Compatible with Covid	857	59.4
	Minimally compatible with Covid	17	1.2
	Incompatible with Covid	434	30.1
	Not obtained	135	9.4
PA Lung x-ray	Yes	113	7.8
	No	1330	92.2
Mean duration of hospitalization	Mean SD	4.55±6.23	
Survivor/Non-survivor	Non-survivor	80	5.5
	Survivor	1363	94.5
Place of follow-up and treatment	ICU	122	8.5
	Ward	828	57.4
	Outpatient	493	34.2
Intubation	Intubated	72	5.0
	Not intubated	877	60.8
	Outpatient	493	34.2
Presenting complaint/ finding	Cough	629	60.5
	Dyspnea	254	24.4
	Fatigue	216	20.8

	Fever	158	15.2
	Sore throat	133	12.8
	Difficulty in tasting	104	10
	Joint / Muscle Pain	70	6.7
	Headache	54	5.2
	Diarrhea	54	5.2
	Nausea/vomiting	41	3.9
	Chills	29	2.8
	Anorexia	27	2.6
	Chest pain	18	1.7
	Runny nose	16	1.5
	Abdominal pain	10	1
	Mouth/throat dryness	9	0.9
	Stuffed nose	9	0.9
	GIS	5	0.5
	Sweating	4	0.4
	Palpitation	2	0.2
	Sneezing	2	0.2
	Hypertension	2	0.2
	Constipation	1	0.1
Comorbidities	Hypertension	263	38.3
	Diabetes	169	24.6
	Ischemic heart disease	63	9.2
	COPD	35	5.1
	Acute/chronic renal failure	19	2.8
	Asthma	16	2.3
	Cancer	13	1.9
	Thyroid disease	11	1.6
	Heart Failure	9	1.3
	CVE	8	1.2
	Psychiatric Disorders	8	1.2
	Alzheimer	7	1.0
	Bronchitis	7	1.0
	Hyperlipidemia	5	0.7
	Cardiac valvular diseases	5	0.7
	Circulatory Disorder	5	0.7
	Pulmonary Artery Diseases	4	0.6
	Single kidney	4	0.6
	Renal tx	4	0.6
	Epilepsy	3	0.4
	Mental Retardation	3	0.4
	Down Syndrome	2	0.3
	Immune deficiency	2	0.3
	Psoriasis	2	0.3

The most common complaints were cough (60%), shortness of breath (24%), weakness (21%), fever (15%) and sore throat (13%). In one-way analysis, the mortality rate of those with shortness of breath and anorexia was significantly higher, as the death rate of those with sore throat was significantly lower ($p < 0.05$). The presence of hypertension, COPD, DM, cancer, ARF / CRF, Alzheimer's, CVE, ischemic heart disease, and pulmonary artery disease was significantly higher in patients who died ($p <0.05$) (Table 2).

Table 2. One-way analysis of the relationship between presenting complaints, underlying diseases, and the distribution of survivors/non-survivors

Symptoms / Findings	Non-survivor	Survivor	p*
	n (%)	n (%)	
Fever	17 (22.4)	141(14.6)	0,071
Cough	38 (50.0)	591 (61.4)	0,051
Change in taste	4 (5.3)	100 (10.4)	0,152
Fatigue	12 (15.8)	204 (21.2)	0,265
Headache	1(1.3)	53 (5.5)	0,173
Stuffed nose	1(1.3)	8 (0.8)	0,497
Palpitation	0 (0)	2 (0.2)	1
Chills	0(0)	29 (3.0)	0,263
Joint/muscle pain	2(2.6)	68 (7.1)	0,138
Chest pain	2(2.6)	16 (1.7))	0,384
Runny nose	0(0)	16 (1.7)	0,623
Nausea / vomiting	4(5.3)	37 (1.7)	0,534

Diarrhea	3 (3.9)	51(5.3)	0,792
Abdominal pain	1(1.3)	9 (0.9)	0,534
Dyspnea	**43 (56.6)**	**211 (21.9)**	**0,001**
Sore throat	**4 (5.3)**	**129 (13.4)**	**0,041**
Anorexia	**5 (6.6)**	**22 (2.3)**	**0,041**
Comorbid Condition			
Hypertension	**49 (71.0)**	**214 (34.7)**	**0,000**
COPD	**8 (11.6)**	**27 (4.4)**	**0,018**
Diabetes	**32(46.4)**	**137 (22.2)**	**0,000**
Cancer	**8 (11.6**	**5 (0.8)**	**0,000**
ARF/CRF	**7 (10.1)**	**12 (1.9)**	**0,001**
Alzheimer	**3 (4.3)**	**4 (0.6)**	**0,025**
CVD	**3 (4.3)**	**5 (0.8)**	**0,038**
Ischemic heart diseases	**14 (20.3)**	**49 (7.9)**	**0,001**
Pulmonary artery disease	**3 (4.3)**	**1 (0.2)**	**0,004**
Single kidney	0(0)	4 (0.6)	1
Asthma	2 (2.9)	14 (2.3)	0,67
Bronchitis	0(0)	7 (1.1)	1
Epilepsy	0(0)	3 (0.5)	1
Thyroid Disease	0(0)	11(1.8)	0,614
Hyperlipidemia	0(0)	5 (0.8)	1
Immune deficiency	0(0)	2 (0.3)	1
Mental Retardation	0(0)	3 (0.5)	1
Cardiac Valvular Disease	0(0)	5 (0.8)	1
Circulatory Diseases	1 (1.4)	4 (0.6)	0,412
Renal Transplantation	0(0)	4 (0.6)	1
Cardiac Failure	2 (2.9)	7 (1.1)	0,227

*:Chi square test (COPD: Chronic Obstructive Pulmonary Disease, ARF: Acute Renal Failure, CRF: Chronic Renal Failure, CVD: Cardiovascular Disease,)

Patients were divided into three groups (outpatient, inpatient, or ICU), according to place of follow-up and treatment. One-way analysis revealed a significant relationship between follow-up venue, gender, age, healthcare status, contact history, tomography results, length of hospitalization, survival, and intubation status. The rate of males in the ICU was higher than those in wards or as outpatients, and the mean age of patients in the ICU was higher than those in wards or as outpatients. Healthcare professionals for outpatients was higher than for those monitored in the ward or ICU. Those with a history of contact were more frequently monitored in the ward, vs. those in ICU or outpatients. Patients with COVID-19-compatible thorax CT were followed in the ICU or ward, vs. as outpatients (Table 3).

A significant correlation was found between thorax CT results and survival status. The mortality rate of those with thorax CT was highly or minimally compatible with COVID-19, and as such, significantly higher (p=0.000). The rate of non-survivors showing compatible thorax CT with COVID-19 was 86.8% (n=59), while the value was 64.4% (n=798) among survivors. The rate of thorax CT incompatible with COVID-19 was 7.4% (n=5) in non-survivors and 34.6% (n=429) in survivors ($p < 0.05$). The rate of hospitalization of 6 days or longer was significantly higher among those with COVID-19-compatible thorax CT results.

There was a significant correlation between place of follow-up and survival rate; the mortality rate of patients in the ICU was significantly higher. Seventy-five (61.5%) of 122 patients followed in the ICU and 5 of 828 patients (0.6%) followed in the ward died. All 493 outpatients survived ($p < 0.001$). We found a relationship between hospitalization time and mortality. Twenty-two (27.5%) of the deceased and 1,033 (75.8%) of the survivors were hospitalized for ≤ 5 days (Table 4). Thirty-six (45%) were deceased and 124 (9.1%) survivors were hospitalized for over 10 days ($p <0.001$)

The rate of comorbid conditions was lower in outpatients. It was observed that all patients with 3 or more comorbid conditions were followed in the ward or ICU. Mortality rate was significantly higher among those with hypertension, COPD, DM, cancer, ARF/CRF, Alzheimer's, CVD, ischemic heart disease, and pulmonary artery disease.

Logistic regression analysis showed a statistically signifi-

Table 3. Comparison of demographic characteristics of groups (ICU, Ward, Outpatient)

		Place of Admission						
		ICU		Ward		Outpatient		
		N	%	N	%	N	%	
Gender	Female	46	37,7	420	50,7	238	48,3	*0,026**
	Male	76	62,3	408	49,3	255	51,7	
Age (mean SD)		68,83±13,37		47,62±18,71		34,67±11,65		*0,000***
Healthcare professional	Yes	3	2,5	61	7,4	80	16,4	*0,000**
	No	119	97,5	764	92,6	408	83,6	
History of travel abroad	Yes	2	1,7	18	2,2	6	1,2	0,444*
	No	116	98,3	789	97,8	475	98,8	
Pregnancy	Yes	0	0	13	1,6	3	0,6	0,135*
	No	122	100	804	98,4	473	99,4	
Thorax CT findings	Minimally compatible with Covid	4	3,3	9	1,1	4	0,8	**0,000***
	Compatible with Covid	89	73	646	78	122	24,7	
	Incompatible with Covid	10	8,2	107	12,9	317	64,3	
	Not obtained	19	15,6	66	8	50	10,1	
Lung x-ray	Yes	22	18	69	8,3	22	4,5	**0,000***
	No	100	82	759	91,7	470	95,5	
Duration of Hospitalization (Mean±sd)		15,3±11,04		5,68±4,38		-		**0,000*****
Survival status	Ex	75	61,5	5	0,6	0	0	**0,000***
	Survivor	47	38,5	823	99,4	493	100	
Intubation	Yes	71	58,2	1	0,1	0	0	**0,000***
	No	51	41,8	826	99,9	0	0	
	Outpatient	0	0	0	0	493	100	

*:Chi square test, **:One-way ANOVA test, ***:Independent sample t-test (ICU: Intensive Care Unit)

Table 4. The relationship between the ward of the patient and duration of hospitalization with respect to mortality

		NON-SURVIVOR		SURVIVOR		**p***
		n	%	n	%	
Place of monitorization	ICU	75	61,5	47	38.5	**0.000**
	Service	5	0.6	823	99.4	
	Outpatient	0	0	493	100	
Duration of hospitalization	≤5 days	22	27.5	1033	75.8	**0.000**
	6-10 days	22	27.5	206	15.1	
	11-15 days	12	15.0	70	5.1	
	≥16 days	24	30.0	54	4.0	

***:Chi square test, (ICU: Intensive Care Unit)**

Table 5. Multiple-way analysis of effects on mortality

	B	S.E.	Sig.	Exp(B)	95% C.I.for EXP(B)	
					Lower	Upper
Place of hospitalization	-5,503	0,599	0,000	245,534	75,891	794,393
Age	1,101	0,459	0,016	3,007	1,223	7,393
Duration of hospitalization	-1,015	0,474	0,032	2,760	1,089	6,992
Diabetes	-1,060	0,421	0,012	2,886	1,265	6,585
Constant	7,516	1,722	0,000	1837,925		
Cox & Snell R Square=0,327 Nagelkerke R Square=0,682						

cant effect of the hospitalized ward, age, duration of hospitalization, and a diagnosis of DM, in terms of mortality (Table 5). The mortality risk of those receiving ICU treatment was 245.53 times higher for those 60 or more, but over that, it was 3.007 times higher (for those hospitalized for 10 days or longer, it was 2,760 times higher, and for those diagnosed with DM, it was 2,886 times higher).

DISCUSSION

This study used the data of 1,443 patients diagnosed with PCR positivity. Moreover, 9.9% of patients were healthcare workers, 1.8% had a history of traveling abroad, and 1.1% were pregnant. Among all, radiological findings of 59.4% of our patients were compatible with COVID-19. The mean length of hospital stay was 4.5 days. Most frequent comorbidities were hypertension, DM, and ischemic heart disease. While mortality was highest among patients in the ICU (61.4%), no mortality was observed among outpatients (0%). The symptomatic spectrum of infection in patients with COVID-19 ranged from mild to critical; most infections were mild.[7] A study with a large sample size reported that 81% of cases had mild (pneumonia or mild pneumonia) disease.[5] Cases with severe disease, such as respiratory failure, shock or multiorgan dysfunction, was 5%. Overall mortality rate was 2.3%, and no mortality was seen in noncritical cases. No mortality was seen in outpatients, while highlighting the mortality of patients in the ICU.

The most common symptoms among our patients included cough (60.5%), shortness of breath (24.4%) and fatigue (20.8%), followed by fever (15.2%). Fever was not among the three most common in our region, as 85% of cases did not have fever. However, one of the most frequent findings to define cases in many publications was fever.[8-10] While fever was present in almost all first cases reported in China, it was not a frequent finding in our cohort. However, in the first published reports, fever was reported in almost all patients. In China, the rate of fever was 89% during hospitalization.[11] In a study with more than 5,000 patients hospitalized for COVID-19 in New York, only 31% had a fever of > 38°C.[12] Based on this, the symptoms in our country were similar to those in the USA, but different from those reported in China. This may be related to racial differences.[13] According to our data, fever is found in very few patients. We would miss many cases if we used fever as an identifying factor. So, each country must define cases according to patient characteristics - or a number of patients could spread the virus without being identified.

As such, fever was an important criterion in guides to define how cases could affect sensitivity in terms of patient identification.

The number of cases in our ICU, ward, plus outpatients, included 122 (8.5%), 828 (57.4%) and 493 (34.2%), respectively. We detected a significant difference in mortality in regards to hospitalization. The mortality among patients in the ICU (61.4%) was different from that of patients in the ward (0.6%) or outpatients (0.0%). The overall risk of mortality among patients in our center was 5.5%. Similar findings were found in various studies. In one with 2,741

patients hospitalized for COVID-19 in the New York healthcare system, with approximately 60% of patients followed in the ICU, it is noted that the rest died.[14] The rate of critical or fatal disease among hospitalized patients was significantly higher, while risky patients were monitored in hospital, but patients with very low risk of worsening were monitored at home.

Thorax CT is not routinely used in many countries (e.g., UK) for the diagnosis of COVID-19. Similarly, in countries with a large number of hospitalized patients (e.g., Italy), CT is not routinely used. Instead, chest radiography (CXR) is used for imaging. Patients with COVID-19 are not routinely monitored with thorax CT, as CXR is a more convenient, reliable, and less expensive test. According to the results of this study, we found CT to be the most utilized imaging modality. While most of our patients could be followed at home, our CXR rate was 7.8%. Routinely obtaining thorax CTs in many centers led to this increase. According to health data, our country is the first in the world with imaging tests per MRI (magnetic resonance imaging) and second with the number of imaging tests per CT (computed tomography). It is the 24th and 34th in MRI and CT imaging, respectively, per one million individuals.[15] Tomography should be reviewed, with less expensive imaging implemented. Postgraduate training and new strategies are required for tomography use in our center.

The rate of fatal infections vary by region. The mortality rate of COVID-19 also varies considerably from country to country. It is reported to be 5.5% in China, 5.5% in the USA, 13.4% in Italy, and 6.9% globally.[16] Many factors determine differences between countries, e.g., more deaths occurred in patients of advanced age or with underlying medical comorbidities.[5] In China, where the young population is high, the mortality rate is low; in Italy, though, the mortality rate is high due to an increased elderly population. In our study, logistic regression revealed that age was an important criterion for determining mortality, especially in patients over 60; the mortality risk increasing more than three times may be associated with more comorbidities in this population. SARS-CoV-2 infection is likely to be symptomatic and severe in adults of middle age or older. Median age ranged from 49 to 56 years in hospitalized patients with COVID-19. In our study, the mortality rate was highest among older individuals, with 80% of deaths occurring ≥ 65 years. For this reason, during the pandemic periods in which limited bed capacity was found, people > 65 years old should be evaluated as priorities to be monitored more closely in the hospital.

According to our data, DM is associated with poor prognosis in COVID-19 disease. In our study, DM posed 3 times greater mortality and prothrombotic risk. Similar findings were shown in different studies. For example, in a large series reported from China, the mortality rate in patients with DM was 7.3%.[5] In a study evaluating fatal cases of COVID-19 in Italy, 35.5% were found to have DM.[17] The mortality of COVID-19 in patients with DM depends on several factors: natural immunity is weaker, there is already an exaggerated cytokine response, along with COVID-19. In this way, COVID-19 further aggravates the clinical status. In patients with DM, interleukin-6 (IL-6), C-reactive protein, and ferritin levels were significantly higher than those without them.[18] The prothrombotic hypercoagulation state in patients with DM can lead to mortality by overactivation of the coagulation cascade in COVID-19.[19] In addition, severe inflammation in patients with COVID-19 increases insulin resistance, so those with DM should therefore be followed more closely.

Critical patients with COVID-19 were older and had other comorbidities, such as hypertension and DM compared to noncritical patients. One of the most important findings in this study was that mortality risk was much higher in patients followed in the ICU. In preliminary reports from Italy and China, 5-12% of all COVID-19 cases and 16% of hospitalized patients showed a need for ICU.[20] In addition, 1,151 (20%) of 5,700 patients hospitalized with COVID-19

in the United States needed mechanical ventilation.[21] In studies dominated by elderly patients, the need for ICU increased.[22] Patients who met these conditions stood out as having a severe course. It should be noted that mortality will be high in patients requiring ICU, with supportive treatments administered as early as possible.

Based on Turkish national guidelines, hydroxychloroquine is a first-line treatment in outpatients. However, patients with COVID-19-related pneumonia were administered hydroxychloroquine and azithromycin in accordance with these guidelines. Patients worsened or were severe from the beginning, despite these treatments being followed in the ICU, while favipravir was administered to severely ill patients in the ICU. Most who received it had already received hydroxychloroquine and azithromycin (separately and together). Patients who did not have pneumonia were expected to receive hydroxychloroquine monotherapy. Hydroxychloroquine and azithromycin were started in patients with slightly more severe disease or positive image findings: their condition improved. Therefore, the combination of hydroxychloroquine and azithromycin was administered most frequently (43.8%) to patients in wards: those treated in the ICU received favipravir 93.3% of the time ($p < 0.005$). The mortality rate of those who received favipiravir was higher, which was expected: in accordance with guidelines, patients whose clinical status worsened or those who were unresponsive to hydroxychloroquine or hydroxychloroquine and azithromycin were given favipravir. The higher mortality rate in this group is not surprising. As such, it would be incorrect to comment on drug effectiveness using these criteria in patient selection.

One important limitation in this study was its retrospective design. However, our data are valuable due to the substantial number of cases. It was not possible to comment on drug efficacy, as its use varied according to patients' severity of disease. There is a need for thoroughly randomized research for drug efficacy.

The mean length of hospital stay was 4.5 days. Being monitored in the ICU, having DM, and being hospitalized for a long period of time were associated with increased mortality risk. As stated, mortality was not observed in any of the outpatients.

Ethics Committee Approval

This was received from the Ethics Committee of the SAU Medical Faculty. (Approval number: E.5586, Date: June 26, 2020)

Conflict of interest statement

The authors declare that there is no conflicts of interest.

Authors' contribution

Concept/Design: OK, AA, AÖ, SY, HD, EG. Analysis/Interpretation: OK, AA, EY, MK, HE. Data Acquisition: OK, SY, HD, EG, HT, MK, FG, ABG, KS, HK, MK, AFE, YA, YY, YT, YG, MHÖ, MAÇ. Writing: OK, AA, SY, HD, EG. Revision and Correction: OK, AA, AÖ, SY, HD, EG, EY, HT, MK, FG, ABG, KS, HK, MK, AFE, HE, YA, YY, YT, YG, MHÖ, MAÇ. Final Approval: OK, AA, AÖ, SY, HD, EG, EY, HT, MK, FG, ABG, KS, HK, MK, AFE, HE, YA, YY, YT, YG, MHÖ, MAÇ

Kaynaklar

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