ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA MAKALESİ

Novel Coronavirus (SARS-CoV-2) Infection Disease (COVID-19) Pandemic: A Single-Center Experience

Yeni Tip Koronavirus (SARS-CoV-2) Enfeksiyonu Hastalığı (COVID-19) Pandemisi: Tek Merkez Deneyimi Tanzer Korkmaz¹[©], Selin Özdemir²[©], Elife Özkan³[©], Emine Sevcan Ata⁴[©], Çağlar Alptekin⁵[©]

ABSTRACT

Aim: COVID-19 was declared a pandemic disease by the World Health Organization as a rapidly spreading viral disease. It can cause serious health problems such as pneumonia, necrotizing encephalopathy, systemic and pulmonary thromboembolism, acute respiratory distress syndrome, systemic inflammatory response, and sepsis. The study aims to provide an overview of the rapidly expanding global coronavirus disease epidemic within the framework of a district hospital.

Material and Methods: The clinical-laboratory-imaging data, comorbid conditions, disease course, and the medical treatments of probable or definite COVID-19 adult cases admitted to the COVID-19 outpatient clinic and emergency service between March/2020-May/2020 were collected retrospectively.

Results: Of the 650 admitted patients, 471 patients with a probable/definite diagnosis of COVID-19 were included in the study. Seventy-three patients were hospitalized, and eight of the hospitalized patients (1.7%) died. The majority of our patients were male (n = 260, 55.2%) and the median age was 42±17.2 years (IQR:24, range 18-99 years). It was determined that hypertension, diabetes, and chronic obstructive pulmonary disease were the three most common comorbidities. Patients with mortality had at least one additional disease. On tomography, the most common lung involvement is <5% and 5-25% of the lung.

Conclusion: The data of our study, which was conducted in a small area and a short period of time, contains similarities with the literature data of that day. As a result of our study, within the age data of the disease, unlike the information in the first days of the pandemic, it was seen that most of the patients were under 65 years old.

Keywords: SARS-CoV-2, COVID-19, pneumonia, tomography

ÖZ

Amaç: COVID-19 hızla yayılan bir viral hastalık olarak Dünya Sağlık Örgütü tarafından pandemik bir hastalık olarak ilan edildi. Özellikle pnömoni, nekrotizan ensefalopati, sistemik ve pulmoner tromboembolizm, akut solunum sıkıntısı sendromu, sistemik inflamatuar yanıt ve sepsis gibi ciddi sağlık sorunlarına neden olabilmektedir. Çalışmanın amacı, kısa sürede küresel olarak hızla genişleyen koronavirüs hastalığı salgınına bir ilçe hastanesi çerçevesinde genel bir bakış sunmaktadır.

Gereç ve Yöntemler: Mart/2020-Mayıs/2020 tarihleri arasında, COVID-19 polikliniğine ve acil servise başvuran olası veya kesin COVID-19 erişkin vakalarının, klinik-laboratuvar-görüntüleme verileri, komorbid durumları, hastalık seyri ve medikal tedavileri retrospektif olarak toplandı.

Bulgular: Başvuran 650 hastadan olası/kesin COVİD-19 tanısı olan 471 hasta çalışmaya alındı. Yetmiş üç hasta yatırılarak takip edildi ve yatırılan hastaların sekizi (%1,7) mortal seyretti. Hastalarımızın çoğunluğunun erkek (n=260, %55,2) ve yaş ortancasının da 42 (95%CI: 42.7-45.8) (aralık 18-99 yaş) olarak tespit edildi. Hipertansiyon, diyabet ve kronik obstrüktif akciğer hastalığı en sık üç komorbidite olduğu ve mortal seyreden hastaların en az bir ek hastalığı olduğu görüldü. Tomografide en sık akciğerin <%5'inin ve %5-25'inin tutulumu olduğu görülmektedir.

Sonuç: Küçük bir bölgede ve kısa bir süreçte yapılan çalışmamızın verileri o günün literatür verileriyle benzerlikler içermektedir. Çalışmamızın sonucu olarak hastalığın yaş verileri dahilinde, pandeminin ilk günlerindeki bilgilerden farklı olarak, hastaların çoğunun 65 yaş altı olduğu görülmüştür.

Anahtar Kelimeler: SARS-CoV-2, COVID-19, pnömoni, tomografi

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Introduction

The newly emerged novel coronavirus (SARS-CoV-2), as the causing agent of COVID-19 disease, is the seventh member of enveloped RNA coronavirus that is believed to originate from infected bats (1). As a rapidly spreading viral disease, COVID-19 was announced by WHO as a global pandemic on March 11, 2020. It can cause serious health problems, especially necrotizing encephalopathy, systemic and pulmonary thromboembolism, acute respiratory distress syndrome (ARDS) and sepsis (2-4). The mortality rate of COVID-19 that is rapidly spreading across the world cannot be accurately estimated yet. However, elderly patients with comorbidity appear to have a higher mortality level as compared to seasonal flu (5). The reverse transcriptionpolymerase chain reaction (RT-PCR) test was accepted as the gold standard for the diagnosis of COVID-19. However, chest x-ray and computed tomography (CT) have an essential role since in the early phases of the infection or the presence of disease with a low viral load, the RT-PCR test has a high falsenegative rate and limited availability during the outbreak (6-8). The most common laboratory findings are lymphocytopenia and thrombocytopenia. Elevated D-dimer, serum ferritin, troponin I were identified as "poor prognostic factors" associated with severe disease and mortality (9,10). Although chest x-ray is the primary radiological diagnostic method for COVID-19, thorax CT is more commonly used for diagnosis since it can be difficult to see low densities such as ground-glass opacities (GGO) in chest x-ray (11). It is essential to report thorax CT to rapidly finalize the diagnosis and initiate the treatment. Therefore, different categories in thorax CT have been identified for the diagnosis of COVID-19 to create a common language (8,12,13).

PCR is used as the gold standard for diagnosis, but one or more negative results do not exclude the possibility of COVID-19 virus infection completely. For this reason, repeated tests are performed (14). Diagnosis and treatment protocol determined by the Ministry of Health is applied to patients defined as definitive cases (14).

This study aims to provide a general overview of the coronavirus outbreak that has spread globally within a short period, within a district hospital. We suggest that the resulting data will provide an insight into the response mechanism directed by health systems against the disease-causing such a global outbreak. The results of our study will contribute to the literature for more comprehensive studies. The data on prophylaxis and progression of the infectious disease caused by COVID-19 will be guiding and constitute a source for future studies.

The data obtained will contribute to preventing both health and economic damages suffered by society during the COVID-19 pandemics.

Material and Methods

This retrospective descriptive study included adult patients with suspected or confirmed COVID-19 who were admitted to the COVID-19 department and emergency service in Tire State Hospital between March 2020 and May 2020. Since pediatric patients are subjected to different follow-up and treatment protocols, they were excluded from the study. The data on cases who were registered into the hospital information system with ICD U07.3 code was used. In the period when the study was conducted, the treatment and follow-up protocol was not based on PCR results yet. Patients whose follow-up, clinical and CT findings were compatible with Covid-19 were considered as Covid-19 cases and treated accordingly. Therefore, PCR test results were not included in the study. In our study, the diagnosis and treatment data were collected using the guideline prepared by the Directorate of Public Health, Ministry of Health. The probable case/confirmed case definitions, follow-ups, and treatment methods for the patients admitted to our hospital with suspected Covid-19 infection were agreed based on the current national Covid-19 (SARS-COV-2 infection) Guideline (14). The age, sex, and occupation data of the patients were recorded. Their comorbidities, laboratory data [WBC, lymphocyte, platelet, urea, creatinin, CRP, ferritin, troponin, d-dimer] and thorax CT reports were recorded. The radiological evaluation categories were determined based on the visual qualitative evaluation in the "Consensus Statement on Reporting Chest CT Findings Related to COVID-19" (8,15). In the cases with typical findings, the prevalence of the disease was scored according to the number of involved lobes and the extent of the infiltration area. The percentage of involvement in both lobes, as well as the overall lung "total severity score" (TSS), were recorded. Each of the five lung lobes was assessed for percentage of the lobar involvement and classified as none (0%), minimal (1-25%), mild (26-50%), moderate (51-75%), or severe (76-100%), with the corresponded score as 0, 1, 2, 3, or 4. The TSS was reached by summing the five lobe scores (range from 0 to 20).

The treatments to the patients in the follow-up process were recorded. Hydroxychloroquine (HC) (2x100 mgx5 days if uncomplicated, 2x400 mg loading and 2x200 mgx5 days if complicated plus a 10-day treatment in cases with severe clinical symptoms and progressive pneumonia), Oseltamivir (2x75 mgx5 days-if indicated), antibacterial drugs (if indicated), Favipiravir (2x1600 mg loading and 2x600 mg x5 days in complicated and severe probable/definite cases), Corticosteroid (methylprednisolone1-2mg/kg/day in cases on ventilator and ARDS cases), Immune plasma (cases with COVID-19 positive symptom, typical thorax CT finding and ARDS), Tocilizumab (8mg/kg- maximum 800mg), Cytokine storm (in cases with macrophage activation syndrome), anticoagulant (Enoxaparin sodium 1 mg/kg) and vitamin C treatments were recorded.

The admission outcomes of the patients were categorized as discharged (uncomplicated cases among those who fit the probable case definition or are diagnosed as a definitive case), hospitalized (complicated cases who fit the probable case definition or are diagnosed as a definitive case), referred and died cases. Of the hospitalized patients, the clinic where they were hospitalized, their treatment outcomes (discharge, referral, death), and hospitalization duration (day) were also recorded.

The study was conducted as per the principles of the Helsinki Declaration with the approval of the Ministry of Health and the approval of the Non-Invasive Clinical Research Ethics Committee in T.C Izmir Bakircay University Ethics Committee (dated 06-19-20 and No. 78).

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Statistical analysis: The statistical analysis was performed using SPSS 22 (SPSS Inc., Chicago, IL) software program. The demographic analyses were evaluated by mean or median values based on their conformity to the normal distribution and the Chi-square test was used in group comparisons. The Mann-Whitney U test was used to analyze the difference in TSS scores between the hospitalized patients and outpatients. The results with p<0.05 were considered statistically significant.

Results

The study included 471 patients with probable/confirmed Covid-19 diagnosis among 650 suspected or confirmed patients who were admitted to the Covid-19 department and emergency service in a secondary care provincial state hospital between March and May 2020. 179 patients were excluded from the study because they had a different diagnosis. The majority of our patients (n=260, 55.2%) were male and their median age was 42±17.2 years (IQR: 24, range 18-97 years). The female median age was 43±17.0 years (IQR:20, range 18-99 years). The majority of them (n=406, 86.2%) were below 65 years old. Patients over the age of 65 constituted 13.8% of all patients. When evaluating the occupational groups, no data could be reached in the records of 86 (18.3%) people. The majority of patients whose data were recorded (n=167, 35.5%) comprised of housewives or retired patients. Seventy-six (17.20%) of them were workers, 57 (12.10%) were healthcare professionals, 21 (4.5%) were students and 60 (12.7%) were in other occupational groups. The majority of the patients had no comorbidity (n=336, 71.3%). It was found that HT, DM, and COPD were the most common three comorbidities and patients with mortality had at least one additional disease (Table 1). The length of stay of the hospitalized patients varied between < 1 day and 43 days (Median: 7.9±7.7 days, IOR: 5).

Comorbidity	Inpatients	Outpatients	Died	Total
	n (%)	n (%)	n (%)	n (%)
None	29 (39.7)	338 (72.1)	1 (12.5)	368 (78.1)
HT	16 (21.9)	56 (12.0)	1 (12.5)	73 (13.4)
DM	13(17.8)	36 (7.7)	3 (37.5)	52 (11.0)
COPD	6 (8.2)	15 (3.2)	-	21 (4.4)
CRF	3 (4.1)	5 (1.1)	1 (12.5)	9 (1.9)
CAD	1 (1.4)	3(0.6)	-	4 (0.8)
CHF	1 (1.4)	2 (0.4)	-	3 (0.6)
Asthma	2 (2.7)	9 (1.9)	1 (12.5)	12 (2.5)
Other	2(2.8)	4 (1.0)	1 (12.5)	7 (1.4)
HT: Hyperten	sion, COPD: Ch	ronic Obstructiv	<i>i</i> e Pulmona	ry Disease, DM:
Dishotos Mo	llitur CDE, Ch	onic Ronal Fail		Coronany Artony

Diabetes Mellitus, CRF: Chronic Renal Failure, CAD: Coronary Artery Disease, CHF: Congestive Heart Failure

Table 1. Table of patient comorbidities

The median values of all laboratory data were given since they did not fit the normal distribution. It is seen that tests were not requested for most of the patients, while D-dimer tests were requested for only 11 (2.3) patients (Table 2). The lymphocyte count was below 0.8×10^3 /uL in 38.4% of the inpatients (n=28), ferritin was above $500\mu g/L$ in 31.5% (n=50), and CRP was above 40mg/dL in 47.9% (n=35), which are critical among the hospitalization criteria. No statistically significant relationship was found between the lymphocyte

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Tests	Mean±SD	Minimum	Maximum	IQR	n (%)
Leukocyte	8.1±6.1	2.8	58.9	3.6	150 (31.8)
(x10³/L)					
Lymphocyte	1.8±1.6	0.4	13.8	1.3	150 (31.8)
(x103/L)					
Platelet	253±105.1	59	732	109	150 (31.8)
(x103/L)					
Urea (mg/dL)	27.0±18.2	11	104	17	151 (32.1)
Creatinine	0. 67±0.3	0.03	2.05	0.2	136 (28.9)
(mg/dL)					
Troponin	70.0±28.7	1	187	29	136 (28.9)
(ng/mL)					
Ferritin	65.0±131.5	5	872	82	123 (26.1)
(ml/ng)					
D-dimer	308.0±467.2	57	1299	854	11 (2.3)
(ng/mL)					
CRP (mg/L)	5.0±50.3	0	211	35	193 (41.00)
CRP: C-Reactive	Protein				

Table 2. Distribution of Patients' Biochemical Parameters

count and ferritin level and discharge or hospitalization of the patients (p=0.09, p=0.12, respectively).

Seventy-three patients (15.5%) were hospitalized, and eight (1.7%) of these patients died. Five of the patients who died were male. Two of the male patients were referred to an advanced healthcare center (Table 3). The mortality rate among the geriatric patients (older than 65 years) was found to be 16.7%.

Patients		Outpatients	Service	ICU	Service and ICU	Total	
Male	n	221	35	2	2	260	
	%	85	13.5	0.8	0.8	100	
Female	n	177	31	2	1	211	
	%	83.9	14.7	0.9	0.5	100	
Total	n	398	66	4	3	471	
	%	84.5	14.0	0.9	0.6	100	

ICU: Intensive care patients

Table 3. Distribution of the patients by sex

Radiological evaluation; the Thorax CT scans of most patients showed no evidence of pneumonia, while the Thorax CT scans of 37 (7,9%) of the 323 (%68.6) cases were typical for the covid disease. The second most frequent CT scan finding of the hospitalized patients were typical for the covid disease following the normal appearance (Figure 1).

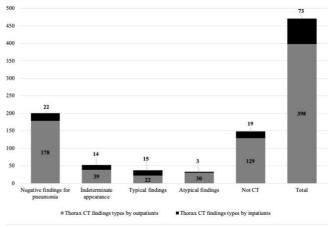


Figure 1. The distribution of Covid -19 Thorax CT finding types by the followed outpatients or inpatients

Of the outpatients who had typical Covid pneumonia, 15 (68.2%) had bilateral involvement, six (27.3%) had involvement in the right lobe, one (4.5%) had involvement in the left lobe. 15 (100%) of the inpatients had bilateral involvement. Most involvement was observed in the left lower lobe (LLL) and the right middle lobe (RML) (Figure 2). The right lower lobe showed more involvement in the

severe-serious score (>75%) (Figure 2). In the CT visual quantitative evaluation, the TSS medians were 6.5 (December 2-19, 95% CI:4.47-8.80) in the outpatients and 9.0 (December 2-19, 95% CI:7.74-13.59) in the inpatients. A statistically significant relationship was found between them (M-W U=94.0, p=0.02). The TSS scores of the inpatients were higher than that of the outpatients.

At the time of the study, the treatment protocol for the outpatients involved the combination of HC, Oseltamivir, and Azitromisin in the 1st line. Favipiravir was used at very low rates (n=6, 1.3%). HC, oseltamivir, and C-vit, as well as anticoagulant and steroid, were administered to most of the inpatients (Table 4). Plasma was administered to only one of the inpatients (1.36%) (n=73), and IL- Blocker was administered to two of them (2.73%).

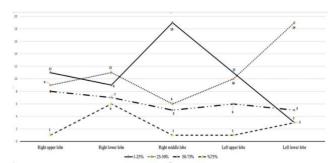


Figure 2. The distribution by the number of lobes involved in thorax CT and the extent of the infiltration area

		HC	HC OS	FA	AZ	CVit		AC	ST	
								L	н	
Outpatients	n	62	49	-	31	5	-	1	-	
	%	15.6	12.3	-	7.8	1.3	-	0.3	-	
Service	n	53	52	3	33	28	17	26	14	
	%	81.5	80	4.6	50.8	43.1	26.2	40	21.5	
ICU	n	3	2	2	3	1	2	3	4	
	%	75	50	50	75	25	50	75	10	
Service and ICU	n	3	3	1	2	2	1	1	3	
	%	100	100	33.3	66.7	66.7	33.3	33.3	10	
Referral	n	-	-	-	-	-	-	-	-	
	%	-	-	-	-	-	-	-	-	
Total	n	350	106	6	69	36	20	31	21	
	%	74.3	22.5	1.3	14.6	7.6	4.2	6.6	4.5	

ICU: Intensive care patients; HC: Hydroxychloroquine; OS: Oseltamivir; FA: Favipiravir; AZ: Azithromycin; AC: Anticoagulant, CVit: Vitamin C; ST: Steroid; H: High dosage; L: Low dosage

Table 4. Distribution of the patient treatments

Discussion

The coronavirus (COVID-19) pandemic has created a need to struggle globally against a disease with high mortality and morbidity (15). While different countries apply several treatment protocols, specific anti-COVID-19 treatment has not been clarified so far. However, the urgency of identifying a treatment has arisen potential drugs for good results, especially for critical-serious patients (16). HC medication, which has been abandoned globally today, was also included in our treatment protocol at that time. Favipiravir was being introduced in our protocols more recently at that time. Studies with broader participation combined with treatment protocol changes analyses will light our way in finding the most accurate treatment approach. In an eleven-day analysis, conducted in March 2020 in Italy, which was among the countries most affected by the pandemic, 9-11% of those who were actively infected needed intensive care, and there was a severe shortage in patient care quality and empty hospital beds. They stated that their analysis might help political leaders and health authorities to allocate enough resources, including personnel, beds, and intensive care facilities, to manage the situation in the next few days and weeks (17). Our study may be a precursor study to predict the likelihood of occurrence of similar situations also in small areas. Aggregating data - like our data - can be an information source for health authorities.

Real-time reverse transcription-polymerase chain reaction (RT-PCR) assay is considered, but the high false negative rate, low sensitivity might delay accurate diagnosis.

Therefore, computed tomography (CT) has been reported as an important tool to identify patients with COVID-19 disease at early stage (18). The experiences in China showed that CT is very useful in the diagnosis of COVID-19, and in some cases, the sensitivity of CT is higher than that of RT-PCR, which is the current gold standard (18, 19). It is reported that the result was negative during the first days from the onset of the symptoms, while the ground-glass opacities (GGO) peaked on the 6-13th days of the disease (20, 21). Therefore, a negative CT scan, especially in early disease, may not be sufficient to exclude the possibility of COVID-19. A standardized COVID-19 reporting language will enhance communication within clinicians and facilitate efficient patient management during this pandemic. Many publications have shown that COVID-19 typically appears with a GCO with peripheral, posterior, diffuse, or subzone distribution, and GCO occurs alone or with consolidation (8,20,22).

A study showed that radiologists correctly differentiated COVID-19 from other viral pneumonias with an accuracy of 60-83% based on typical CT imaging features (23). In contrast, Guan et al. found that 20% (n=230/1099) of patients with clinical symptoms and positive RT-PCR findings had normal chest CT findings (24). We considered this information during the study planning stage and based our diagnosis on clinical findings, probable/confirmed case definitions, or positive CT findings for Covid-19 cases (14). With the developing technology, artificial intelligence in

With the developing technology, artificial intelligence in imaging has also developed. A study showed the high

sensitivity and specificity (90%) of artificial intelligence in the COVID-19 diagnosis in patients, if necessary, settings are made for CT images (25).

The covid-19 outbreak, which has been rapidly turned into a global pandemic, challenges both the health system and the global economy. There has been a leap in actions taken and to be taken as well as vaccination studies, but efficient approaches for the treatment and epidemiological control of the disease are still insufficient (26). Another review revealed the need to prevent COVID-19 and invest in expanded health systems, community-led response mechanisms, and global health security (28). This emergency today's world is facing demands from us to develop urgent and effective measures to protect individuals with high infection risk. WHO has accelerated the diagnosis, vaccination, and treatment research for this novel coronavirus (27).

Limitations

The major limitation of our study was that it involved a small rural region and a short period. Another limitation was the insufficiency of RT-PCR examinations and sampling during the data collection period and our inability to provide the test results.

Conclusion

The data of our study, which was conducted in a small area and a short period, contains similarities with the literature data of that day. No country or continent may isolate itself from others during this pandemic period with the technology and civilization developed in this century. In this difficult period, the whole world needs to invest in health systems globally, to develop treatment and disease prevention strategies, and more importantly, to take the necessary measures to prevent such a pandemic again.

Conflict of Interest: The authors declare no conflict of interest regarding this study.

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Authors' Contribution: All authors contrubuted for conception, design of the study, data collection, data analysis, and assembly. The manuscript was written and approved by all authors.

Ethical Statement: Ethical approval for this study was obtained from T.C İzmir Bakırçay University Ethics Committee with the approval number / dated 06-19-20 / 78. All authors declared that they follow the rules of Research and Publication Ethics.

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