THE POSSIBLE FACTORS THAT AFFECT THE CLINICAL SEVERITY AND MORTALITY OF COVID PNEUMONIA

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ABSTRACT

Introduction: In 2019, an estimated 11.8 million people worldwide have been affected by coronavirus disease (COVID-19), with around 215.000 reported cases of COVID-19 infection in Turkey. At the time of this manuscript, there have been almost 571.000 COVID-19 associated deaths globally. The aim of this study was to investigate and present data regarding the clinical characteristics and outcomes of patients infected with COVID-19 virus in our hospital.

Materials and methods: This was a retrospective, descriptive, observational clinical study using cross-sectional data collected from confirmed COVID-19 patients in our institution. Patients were categorized into three groups based on the severity of the illness. Patients' demographic andclinical characteristics, mortality rates, and the factors associated with mortality were analyzed.

Results: The study included 132 positive cases confirmed by the real-time PCR (RT-PCR). The mean age was 41±16 years. The disease was mild in 78.8 % of the cases and severe in 18.9%, with 2.3% being identified as critically ill. In-hospital mortality rate was 2.3 %. Age, WBC, lymphocytes, CURB-65, Sequential Organ Failure Assessment SOFAand quick SOFA scores, and C-reactive protein (CRP) were identified as factors associated with mortality.

Conclusion: Factors affecting mortality and clinical severity in covid-19 patients should be determined, this patient group should be followed up and treated carefully.Certain therapeutic interventions may lead to reduced mortality due to infection caused by the novel coronavirus.

Keywords: COVID-19, severity, mortality, treatment.

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Introduction

Severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2) is a global, rapidly emerging coronavirus disease[1]. Current public health strategies to mitigate transmission include rapid identification of cases, isolation, contact tracing, and self-quarantine of exposed individuals. Once exposure occurs, the standard care consists of observation and quarantine during a 14-day incubation period. Several studies have reported associations between higher mortality and advanced age and higher SOFA scores[2,3]. Also, in the current study we have identified several factors associated with increased mortality, including elevated CURB-65, SOFA, and rapid SOFA scores, increased CRP and WBC, as well as lymphopenia.

Methods

Study design and patient population

This was a retrospective, descriptive and observational clinical study using cross-sectional data obtained from confirmed COVID-19cases, who were monitored and treated in emergency rooms (ERs), outpatient and inpatient clinics as well as in intensive care units (ICUs) in our province. The Project was carried out by volunteers in theour hospital des-

ignated as 'COVID-19. Only cases that were confirmed by molecular methods were included in the study.

Patients were assigned into three groups as mild, severe, and critically ill, according to the clinical presentation based on the"COVID-19 Diagnosis and Treatment Guidelines" endorsed by the Turkish Ministry of Health.

Accordingly, mild illness consisted of features such as fever, muscle/joint pain, cough, sore throat, and nasal congestion, with or without mild pneumonia,along with a respiratory rate <30/min and an O2 saturation> 90% while breathing room air.Severe illnesswas defined on the basis on the strong suspicion of pneumonia in chest radiography or computed tomography (CT). Critical illness was defined as the requirement for ICU[4].

Epidemiological data including risk factors as well as clinical, radiological, and laboratory findings were recorded. Also, data were collected on the treatment modality utilized, length of hospital stay, disease course, and mortality.

Statistical analysis

Data analysis was carried out by IBM SPSS V23 software and normal distribution of the data was checked using Shapiro-Wilk test. Data without normal distribution were compared according to the severity of illness based on the Kruskal-Wallis test. Mann-Whitney U test with Bonferroni correction was used to determinethe severity group responsible for the statistical significance of differences, as calculated by the Kruskal-Wallis test. All categorical data were tested with chi-square test. Prognostic significance of parameters was compared using the Mann-Whitney U test. The threshold for significance was set at p<0.05.

Ethics committee approval

Ethics committee approval was received from the Ethics Committee of Karadeniz TechnicalUniversityMedical faculty (Ethics Committee No: 46362034-108.99-E.3470).

Results

A total of 132 patients with confirmed COVID-19 based on nucleic acid methods and receiving either ambulatory care or inpatient care in isolated ward or intensive care unit (ICU) between 1st April 2020 and 15th May 2020 were included in this study. While 53% of our patients (n=70) reported close contact with individuals with similar symptoms, 47% (n=62) reported no such contact. Healthcare workers comprised 5.3% of our study population.

The most common symptoms at admission were cough in 86.4 % (n=114), fever in 62.9% (n=83), and fatigue in 51.5% (n=68)(Table 1).

A total of 9.8% (n = 13) of the study population consisted of patients have diabetes mellitus, 5 coronary artery disease and diabetes mellitus, 3 chronic obstructive pulmonary diseases, and 2 chronic renal failure.

Hdroxychloroquine was used in all patients (n=132). Antibiotics that were utilized included azithromycin in 91.7% (n=121), ceftriaxone in 64.4% (n=22), teicoplanin in 19.7% (n=26), meropenem in 16.7% (n=22), piperacilline/tazobactam in 5.3% (n=7), and moxifloxacin in 0.8% (n=1). Antivirals utilized included oseltamivir in 98.5% (n=130), favipravir in 21.2% (n=28), and lopinavir/ritonavir in 3.8% (n=5) (Table 1).

Tocilizumab was administered in 15.1% of the patients (n=20) to prevent the occurrence of macrophage activation syndrome.

During the course of the disease 5.3% (7) patients were ambulatory, 82.6% (109) required inpatient treatment in isolated wards, and 12.1% (16) were treated in the ICU. Independent risk factors affecting the disease course were investigated using multinomial logistic regression analysis, which showed that the likelihood of requiring ICU support increased with age (p<0.001).

As per radiological patterns, the lesions were more likely to be located in the peripheral and lower lobes. The most common radiological findings were bilateral ground glass appearance (59.8%), unilateral ground glass appearance (%7.6), and consolidation (4.5 %) (Table 2).

All patients in our critical and severe patient group had bilateral ground glass in their thorax BT.

Laboratory findings at admission were as follows: mean white blood cell (WBC) count 5.9 (10 3/μL), neutrophil count 4.1 (10 3/μL), lymphocyte count 1.5 (10 3/μL), and C-reactive protein (CRP) 14.8 mg/L. Among these, elevated WBC, lymphopenia, and elevated CRP emerged as laboratory parameters that were associated with increased mortality

Mild cases comprised 78.7% (n=104) of the overall study population, while 2.3% (n=3) had critical disease and 18.9% (n=25) had severe disease (Table 3). Patients with mild disease were significantly younger as compared to those with severe or critical disease (p<0.001).

Mean age ± SD	41 ± 16	
GENDER	N	%
Male	78	59.1
Female	54	40.9
Smoking Habits		
Active smoker	41	31.1
Never smoked	91	68.9
Symptoms		
Cough	114	86.4
Fever (> 37.8℃)	83	62.9
Fatigue	68	51.5
Shortness of breath	27	20.5
Headache	10	7.6
Sputum	6	4.5
Anosmia	8	6.1
Diarrhea	2	1.5
Co-morbidities	13	9.8
Monitoring		
Ambulatory monitoring	7	5.3
Hospital treatment	109	82.6
ICU support	16	12.1
Severity of illness		
Mild	104	78.8
Severe	25	18.9
Critical	3	2.3
Treatment regime		
Hydroxychloroquine	132	100
Teicoplanin	26	19.7
Meropenem	22	16.7
Moxifloxacine	1	0.8
Piperacilline/tazobactam	7	5.3
Azithromycin	121	91.7
Ceftriaxone	85	64.4
Favipravir	28	21.2
Lopinavir/ritonavir	5	3.8
Oseltamivir	130	98.5
Tocilizumab	20	15.1
Discharge status		
Discharged	129	97.7
Death	3	2.3
Health personnel	7	5.3

Table 1: Demographic and clinical characteristics of the patients.

HRCT Findings	N	%
Bilateral ground glass appearance	79	59.8
Unilateral ground glass appearance	10	7.6
Consolidation	6	4.5
Normal tomography of the thorax	40	30.3
Crazy paving	3	2.3
Pleural effusion	1	0.8
Reverse halo	3	2.3
Patchy infiltration	3	2.3
Tree in bud appearance	0	0

Table 2: Distribution of radiological findings.

	Mild (n=104)	Severe (n=25)	Critical (n=3)	P
Age	38 ± 14	52 ± 17	72 ± 11	0.001
WBC	5.8 ± 1.8	5.4 ± 2.3	5.5 ± 2.3	0.8
Neutrophil	3.3 ± 1.5	3.7 ± 2.3	4.22 ± 2.1	0.4
Lymphocyte	1.6 ± 0.6	1.1 ± 0.5	0.6 ± 0.1	0.02
Platelet	232 ± 65	215 ± 72	147 ± 63	0.07
CRP	9.3 ± 17.3	30.6 ± 52.8	34.2 ± 19.8	0.02
CURB 65	0.48 ± 0.40	0.76 ± 0.96	4.0 ± 1.7	0.02
SOFA	0.25 ± 2	1.2 ± 1.6	10.6 ± 1.5	0.001
QUICKSOFA	0.03 ± 0.3	0.6 ± 0.8	2.6 ± 0.5	0.001
DURATION OF HOSPITAL STAY	6.6 ± 2.5	14.5 ± 4.6	7.3 ± 7.5	0.02

Table 3: Comparison of study groups based on disease severity.

	Death	Recovery	P
Age	73.66 ± 9.45	41.02 ± 16.37	0.001
WBC	8.26 ± 2.69	5.71 ± 1.87	0.02
Lymphocyte	0.71 ± 0.10	1.55 ± 0.63	0.02
CRP	48.7 ± 37.5	13.10 ± 28.34	0.03
CURB 65	4.66 ± 0.57	0.17 ± 0.54	0.005
SOFA	16 ± 4.58	0.33 ± 0.99	0.02
QuickSOFA	3 ± 0	0.15 ± 0.49	0.001

Table 4: Factors related to mortality.

Also lymphocyte count was significantly lower among those with critical disease (p<0.001) and CURB, SOFA, and quick SOFA scores were significantly higher in critically ill patients, as compared to the other two study groups (p<0.001).

The overall mortality rate was 2.3% (3/132). In logistic regression analyses age, WBC count, CRP, CURB 65, SOFA score, and quick SOFA scores were found to be significantly associated with mortality. Also, there was a significant association between the risk of mortality and a low lymphocyte count (Table 4).

Discussion

In our study, we evaluated possible factors affecting the mortality and clinical severity of covid-19 positive patients.

The disease was categorized as mild in 78.8% and severe in 18.9% of the cases, and 2.3% of the subjects were critically ill. The percentage of the patients requiring ICU admission was 12.1%. The overall mortality rate was 2.3%. CURB-65, SOFA and quick SOFA scores, CRP, WBC, and lymphopenia were identified as factors associated with mortality. with 9.8% of the patients having one or more co-morbid conditions, 3 of them were diabetes mellitus, 5 were coronary artery disease and diabetes mellitus, 3 were chronic obstructive lung diesas, 2 was chronic renal failure. Co-morbiditesi bulunan tüm hastalarımız hastalığı orta veya ağır geçirdi.

Previous studies have clearly established that most patients infected with COVID-19 have mild disease, while those with moderately severe and severe disease represent a smaller proportion of the overall cases. In one study from China, 81% of the cases had mild disease, while 14% had severe disease, and 5% were critically ill. (5-6). Similarly, 78.8% and 18.9% of our patients had mild and severe disease, with 2.3% having critical illness.

In another large-scale study from China, 81% of the patients had mild symptoms, although the mortality rate was 2.3%. In an Italian study and in a study from New York US, the reported mortality rates were 15% and 21%, respectively (7,8). Compared to our study, all above-mentioned studies have reported significantly higher mortality rates. The mean age in our study was 41 ±16 years. Comparison of our study groups showed significantly lower mean age among those with mild disease than those with severe or critical disease (p < 0.001). Possible reasons for the significantly reduced mortality in our cohort include the younger age, low number of individuals with co-morbid conditions, and the consequent decrease in the proportion of critically ill patients.

Several studies have reported associations between higher mortality and advanced age and higher SOFA scores[2,3]. Also, in the current study we have identified several factors associated with increased mortality, including elevated CURB-65, SOFA, and rapid SOFA scores, increased CRP and WBC, as well as lymphopenia. Furthermore, our critically ill patients had significantly lower lymphocyte counts (p < 0.001). Similarly, critically ill patients had significant elevations in CURB-65, SOFA, and rapid SOFA scores in comparison with mild or severe disease groups (p < 0.001).

The association between gender and COVID-19 infection has been subject to some research[9,10], indicating an elevated risk of COVID-19 infection among men, possibly due to higher rates of ACE2 expression and smoking[11]. Our findings also corroborate these observations, as 59.1% of our study population was men.

In our view several factors may help prevent the disease progression in individuals infected with COVID-19, and these may include early use of hydroxychloroquine even in suspected cases; early use of favipiravir and tocilizumab; and the combined use of high-flow oxygen and noninvasive mechanical ventilation(NIMV)ith the patient in prone position. If possible, invasive mechanical ventilation (IMV) should be avoided, and anticoagulation should not be delayed. For patients with macrophage activation syndrome, immuno-regulatory treatments such as tocilizumab may have a role in reducing the incidence of complications and death in the ICUs, started being utilized in patients with pneumonia who did not require ICU support. As mentioned above, early administration of anticoagulant therapy, continuous high-flow oxygen and NIVM with avoidance from IMV became more pronounced in the next weeks.

In this paper, our aim was to contribute to the existing literature on COVID-19 pandemic by describing our clinical experience and analyzing clinical, radiologic, laboratory, and demographic characteristics of our patient population. The limitation of our study is that it was single centered and did not include sufficient number of cases. New studies with larger numbers are needed for the COVID-19 pandemic.

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