Research Article — **Open Access**

Presenting Characteristics and ICU Admission among Patients Hospitalized with COVID-19

Aral Surmeli[1]*, Öykü Beyaz[2], Elif Sitre Koç[2], Yasemin Gündoğdu[2] , Çağlar Çuhadaroğlu[3] and Sesin Kocagöz[4]

[1]Medical Rescue Association of Turkey, Istanbul, Turkey
[2]Department of Internal Medicine, School of Medicine, Acıbadem Mehmet Ali Aydınlar University, Istanbul, Turkey
[3]Department of Chest Diseases, School of Medicine, Acıbadem Mehmet Ali Aydınlar University, Istanbul, Turkey
[4]Department of Clinical Microbiology and Infectious Diseases, School of Medicine, Acıbadem Mehmet Ali Aydınlar University, Istanbul, Turkey

Abstract

Introduction: Information describing the presenting baseline and clinical characteristics and outcomes of coronavirus disease 2019 (COVID-19) patients in Turkey is currently limited. Our aim is to describe clinical characteristics and outcomes of patients hospitalized with COVID-19 and compare patients who required Intensive Care Unit (ICU) admission with those who did not require.

Methods: This retrospective cross-sectional study was conducted in a large tertiary care hospital Istanbul. A total of 215 consecutive patients hospitalized with suspect and confirmed COVID-19 between 9 March 2020 and 30 April 2020 were included. Demographic, clinical, laboratory and radiological data on admission and outcomes were collected and analysed. Main outcome measures included COVID-19 ward or ICU hospitalization, requirement of invasive mechanical ventilation, discharge or death. Presenting characteristics were compared between patients who required ICU admission with those who did not require.

Results: Among 215 patients, 64% were male, and median age was 53. Most prevalent comorbidity was hypertension followed by diabetes mellitus and coronary artery disease. Prevalence of comorbidities and median age was higher in patients admitted to intensive care unit. Most common symptom of presentation was fever (72%). Almostall patients had increase in their inflammatory laboratory parameters and majority of patients stayed less than 10 days in hospital. C-reactive protein, lactate dehydrogenase, neutrophil and lymphocyte count, ferritin and d-dimer levels were significantly different between ICU and non-ICU patients. However, in the final logistic model, among presenting symptoms, initial radiography and laboratory tests; having dyspnea, C-reactive protein, lactate dehydrogenase were significantly associated with intensive care unit admission.

Conclusion: Of 215 hospitalized patients with confirmed and suspect COVID-19 infection, 17% of patients required ICU admission and mortality rate was 4.4%. Older age, having coronary artery disease, high levels of C-reactive protein, lactate dehydrogenase, and presenting with dyspnea was significantly associated with ICU admission.

Keywords: Coronavirus infections; Pneumonia; Intensive Care Unit; Coronavirus Disease 2019; Clinical characteristics; Infectious diseases

Introduction

The novel coronavirus (SARS-CoV-2) started in December 2019 in China, has infected over 4.2 million people worldwide, resulting with a death toll of 290,000 as of May 13, 2020 [1]. It causes a multi-systemic infection named as Coronavirus Disease 2019 (COVID-19) [2]. The symptoms reported are non-specific and usually comprise of fever, cough, dyspnea and fatigue [3]. The virus predominantly attacks the respiratory system, rendering some of the patients with respiratory distress [4]. To this day, even though some treatment guidelines exist and many randomized controlled trials are being conducted, no consensus on effective treatment modalities exist [5].

Turkey, with a population of nearly 85 million people, is 17th most populated country in the World. Ministry of Health has been working to control the disease since the first confirmed case was declared in the country on March 11, 2020 [6,7]. A preliminary national COVID-19 guideline was released on January 24, and it has been updated regularly according to emerging evidence [8]. As of May 5, Turkey ranks the 9th among the countries in the world in terms of total cases [9].

Istanbul, with its 15 million inhabitants, emerged as an epicenter for COVID-19 pandemic [10]. Over 60% of the COVID-19 cases in Turkey were situated in İstanbul [11]. The risk of disease transmission is high, being the most populated city in Europe and hosting nearly 200,000 domestic and international passengers daily [12].

New local outbreaks are expected in the course of this pandemic, and thus, COVID-19 will continue to be a threat to the healthcare system. Matching with the clinical evidence, the bottleneck of management of this disease is the Intensive Care Units (ICU) capacity. One of the major determining factors on mortality for critically ill patients is the availability of the ICUs [13]. Therefore, a strategic approach is necessary to help identify patients on their first admission, who will most likely require being in an ICU.

In this observational study, our objective was to describe demographic and clinical characteristics and outcomes of patients hospitalized with COVID-19 in a tertiary hospital in Istanbul. We compared patients who required ICU admission with those who did not

require, with an intention to ultimately inform clinicians and hospitals about the need for ICU admission among hospitalized patients.

Methods

Study design

We performed a retrospective cross-sectional study at a large tertiary hospital in İstanbul. The hospital is located in Istanbul and is designated as a pandemic center throughout Covid-19 outbreak, accepting all patients and serving free-of-charge as per regulations of Turkish Ministry of Health using national COVID-19 treatment algorithm. The study was approved by the Institutional Review Board of Acıbadem Mehmet Ali Aydınlar University School of Medicine (ATADEK) with decree number 2020-9/11.

The hospital capacity and COVID-19 adjustments

The hospital serves around 20,000 patients per month with 50 ICU and 200 inpatient beds. Following the first confirmed Covid-19 case in Turkey on March 11, 2020, all attending staff was alerted and a 24-bed isolation ward was prepared for suspected and confirmed COVID-19 cases with 25 beds in ICU with droplet and contact isolations. Another 24 beds were made available for isolation ward afterwards. In case of full ICU bed occupancy, 9 beds in cardiac intensive care unit were also prepared. At the peak point of the COVID-19 outbreak, a total of 48 beds in the wards and 25 beds in ICU were fully occupied. The hospital has not reached 100% occupancy throughout the pandemic period and all patients requiring any level of care was taken care of.

Participants

We enrolled all consecutive adult patients admitted to our hospital between March 9, 2020 and April 30, 2020 that fulfilled the criteria of confirmed or suspect cases of COVID-19 according to the Ministry of Health Guideline.

Data collection

Data were collected from the electronic health record system of the hospital and national COVID-19 surveillance system. During COVID-19 outbreak, national system was used in real time for daily data collection of suspected or confirmed cases and contact tracing by Ministry of Health.

Data included patients' sex, age, current smoking status, Body Mass Index (BMI), comorbidities, presenting clinical signs and symptoms, initial laboratory tests, assessments of chest Computed Tomography (CT), final outcome (length of stay, discharge, mortality), prognoses on day 5, 10, 14, 21, and test result of real time Reverse Transcription (RT)-polymerase chain reaction (PCR) from nasopharyngeal specimens.

Presenting clinical and laboratory parameters included temperature, respiratory rate, oxygen saturation and heart rate; comorbidities included hypertension, diabetes mellitus, cardiovascular disease, Chronic Obstructive Pulmonary Disease (COPD) and asthma. Initial laboratory tests comprised complete blood count, C-reactive protein (CRP), ferritin, Lactate Dehydrogenase (LDH), d-dimer, interleukin-6 and CD4/8. Chest CT scan was defined as positive if any sign of COVID-19 was marked by radiologist on the basis of the existence of features consistent with pneumonia such as ground glass opacities, consolidation, interlobular septal thickening. PCR test was regarded as positive if the patient had at least one positive result on consecutive tests.

Main outcome measures were the following: COVID-19 ward or ICU hospitalization, requirement of invasive mechanical ventilation, discharge or death. Mortality data was very low (4.4%), therefore not used as an endpoint in the analysis, but presented separately. A numeric scale ranging from 1 to 4 was developed to assess prognosis as follows: Discharged, COVID-19 ward stay, ICU admission, ICU admission plus intubation.

The clinical outcome was evaluated on day 5, 10, 14 and 21 of the hospitalization. The selection of these dates was based on the 5-day and 10-day regimens of treatment protocols and 14- and 21-days follow-up days recommended by Turkey Ministry of Health COVID-19 treatment guideline. As of April 30, 2020, 26 patients were still hospitalized (12% of the cases).

Statistical analysis

Data were collected and aggregated on Microsoft Excel and statistical analysis was performed on Stata. Continuous variables are presented as median (IQR), categorical variables are expressed as percentages (%). For continuous variables, difference in two groups (ICU and non-ICU patients) was analyzed with t-test if distribution was normal and Mann-Whitney test for non-normal distribution. Variables with small sample sizes were disregarded. In the analyses, p value less than 0.05 is used as the cut off for significance for univariate analysis. For multivariable analysis logistic models with clinically and statistically significant variables (from univariate analysis) were used and known confounders were added. An iterative logistic modelling was used to produce the final model.

Results

A total of 215 patients were included in the study. Among these, 186 had an outcome (death or discharge) at the end of the study period. For remaining 29 patients, their current place of hospitalization (ICU with or without intubation or COVID-19 ward) was used. Of the 186 patients that had an outcome, 8 patients died (4.4%), 32 patients (17%) required ICU admission. Among ICU patients 26 (15% of total population) were intubated. Twenty-nine people were still hospitalized at the time of analysis. Mortality was not used for outcome analysis due to low number of events.

Median age was 53 (IQR: 41-64). Sixty-three per cent of the patients were male. Most prevalent comorbidity was hypertension (29.38%) followed by coronary artery disease (16.43%). Most common symptom was fever, with more than two out of three patients presenting with the symptom (Table 1).

	All patients (n=215)	ICU (n=38)	No ICU (n=177)	p-value[1]
ICU admission (%)	82.33			
Age	53 (41-64)	61 (49-73)	51 (40-62)	0.0014
Sex (male sex, %)	64	66	63	0.7280
Smoker (%)[2]	9.18	8.72	11.43	0.682
Hypertension (%)[3]	29.38	48.65	25.29	0.0042*
Diabetes mellitus (%)[4]	16.43	27.03	14.20	0.0541
CAD (%)[5]	16.43	40.54	11.36	0.0001*
COPD/Asthma (%)[6]	9.91	21.62	7.43	0.0081*
Obese or overweight[7] (%)	65.73	70.37	64.90	0.5197
BMI	26.64(24.34-31.30)	27.47(24.69-33.03)	26.60 (24.24-30.08)	0.20
Most common symptom	Fever	Fever	Fever	
Fever (%)	72.1	68.4	72.9	0.5757

Dyspnea (%)	28.4	60.5	21.5	0.0001*
Cough (%)	60.9	63.3	50	0.1373
Pulse	81.5(78-90)	84(78-90)	81(78-88)	0.507
Oxygen Saturation[8]	97(96-98)	95(92-97)	97.5(97-98)	0.0001*
Fever[9] (%)	55.35	76.32	50.85	0.0043

[1]P values below 0.05 with 0.20 power calculation are marked with *.
[2]Active smokers in the time of admission.
[3]A clinical diagnosis of hypertension before the time of admission.
[4]A clinical diagnosis of diabetes mellitus Type 2 before the time of admission.
[5]A clinical diagnosis of coronary artery disease before the time of admission.
[6]A clinical diagnosis of COPD or asthma before the time of admission.
[7]Defined as BMI over 25.0
[8]Out of %100 saturation levels.
[9]This is objective fever measured from axillary area and counted as positive if higher than 37.0 Celcius

Table 1: Demographic and baseline characteristics of patients.

Majority of patients had an outcome in 10 days of their stay (68%). Median day for ICU admission was 2.5 days (IQR=2-5 days, mean=3.4). Median day for intubation was 4 (IQR=3-7 days, mean=5.1) (Table 2).

Length of stay	No of patients	Percentage	Cumulative percentage
5 days	58	27%	27%
10 days	87	41%	68%
14 days	37	17%	86%
21 days	12	6%	92%
+21 days	18	8%	100%

Table 2: Length of hospitalization.

Comparison baseline characteristics and symptoms of ICU and non-ICU patients

Patients who did not require ICU admission had a median age of 51 (IQR: 40-62) while patients who required ICU admission had a median age of 61 (IQR: 49-73) with a statistically significant difference. Proportion of men was 66% and 63% in ICU patients and non-ICU patients respectively, however no significant difference was found.

All parameters except a fever higher than 37.0 Celsius were higher in ICU admitted patients and having a coronary artery disease, hypertension, COPD or asthma were statistically significant. Diabetes mellitus was marginally insignificant (p-value of 0.0541). In terms of presenting symptoms, ICU patients were significantly more likely to have dyspnea as compared to non-ICU patients (Table 1).

Laboratory variables and radiology

CComputed tomography was the main modality of radiography with 94% of all admissions receiving at least once. Eighty-five per cent of all patients had some sort of sign in their CT, as evaluated by at least one radiologist. No further analysis in difference in signs (e.g. number of lobes involved) was done. There were more patients with a CT suggestive of COVID-19 or viral pneumonia among patients who were admitted in ICU than non-ICU patients, with proportions with CT signs 92% and 82% respectively, however, no statistically significant difference was found.

In invariable testing for laboratory parameters, all but thrombocyte count had a significant difference between ICU and non-ICU patients. Interleukin-6 and CD4/8 values had too small sample size for calculation (Table 3).

	Normal value range	All patients (n=215)	ICU (n=38)	No ICU (n=177)	p-value[10]
CRP	<0.5 mg/dL	6.04	10.29	5.12	0.0001*
LDH	85-227 IU/L	230	356.62	229.15	0.0001*
Lymphocyte	1.3-3.76 10³/uL	1.18	1.25	1.36	0.023*
Trombocyte	150-439 × 10³/uL	202	248.87	213.14	0.5
Neutrophile	1.9-7 × 10³/uL	4.01	7.45	4.67	0.0001*
Ferritin	22-322 ng/mL	200	552.5	248.0	0.0002*
D-dimer	0-0.5 mg/L	0.64	1.46	0.56	0.0001*
Interleukin-6[11]	<7 pg/mL	22.5	68.85	18.7	
CD4/8[12]	0.8-3.9	1.91	1.91	2.04	
CT positive (%)		84.16	91.89	82.42	0.1540

[10]P values below 0.05 with 0.20 power calculation are marked with *.
[11]Insufficient sample size for significance calculation.
[12]Insufficient sample size for significance calculation.

Table 3: Laboratory and radiography results.

Multivariate analysis of variables

After adjusting for other values, significant variables were categorized with clinical evidence and previous literature. Having a CRP value of over 10 mg/dL was related with 2.6 times the odds of being admitted to ICU. Similarly, having a LDH value of over 227 IU/L (normal value limit used in our hospital), was associated with 4.3 times the odds of being admitted to ICU. Only dyspnea among presenting symptoms was associated with a significant increase in odds of being admitted to ICU (OR:5.13) (Table 4).

	Odds Ratio	p-value
CRP>10 mg/dL	2.60	0.038*
LDH>227 IU/L	4.18	0.003*
Coronary artery disease	2.09	0.194
Chest CT	3.60	0.081
Fever (subjective)	1.9	0.27
Cough	0.74	0.512
Dyspnea	5.13	0.001*

*P values below 0.05 with 0.20 power calculation are marked with *.

Table 4: Results of multivariate analysis.

PCR results

Serial PCR tests for patient population revealed only three of them stayed PCR(-),0.13% of the sample.

Mortality

Only eight patients have died during the follow-up (4.4%). Median age of patients who died were 72 (IQR: 65-88), six of the patients had hypertension as comorbidity, five were overweight and all were admitted to ICU and intubated during hospitalization.

Discussion

Main objective of this observational study is to describe the baseline and clinical characteristics of hospitalized COVID-19 patients in our hospital. Further, we describe the differences in variables between patients who required ICU admission and those who did not at any time during their hospitalization.

Patients who required ICU admission were significantly more likely to be older, have hypertension, COPD or asthma, and coronary artery disease, as compared to those who did not require. Even though almost two-thirds of our patients were men, the proportion of women and men in two groups were similar. The effects of age and having coronary artery disease remained statistically significant in multivariate analysis. Among the presenting symptoms, dyspnea emerged as significant in both univariate and multivariate analysis.

These findings corroborate with other published evidence from different countries. For example, studies from China and United States [14]. Have shown the effects of older age and comorbidities in deteriorating outcomes in Covid-19 patients. Similar to our findings, independent association of coronary heart disease was found in a study in Wuhan, China, although with a different outcome; mortality.

Laboratory markers on admission also differed between the two groups of patients. Patients who were admitted to ICU had statistically significantly higher levels of CRP, LDH, neutrophil, D-dimer and ferritin, and low levels of lymphocyte. Multivariate analysis showed independent and significant effects of LDH and CRP after adjustment with age and sex. High levels of LDH and CRP on admission may be a useful marker to predict ICU admission. Other studies have reported predictive value of varying factors for disease progression. CRP along with male sex, comorbidity and lymphopenia was shown as predicting severe outcomes in a study from China [15]. In our group, lymphocyte count was significantly lower in the ICU patients. While this relationship did not hold in the multivariate analysis, it is an important parameter used by clinicians in our hospital for decision making and prognostic value.

Our study has several limitations. First, it is a descriptive analysis of patients who were hospitalized for COVID-19, and thus, the characteristics of patients who were isolated at home are not included. Second, this study was designed to investigate baseline characteristics and presenting clinical, laboratory and radiological differences of ICU and non-ICU patients. Therefore, analysis of changes in clinical and laboratory parameters during the course of the disease was not carried out. It should however, be noted that although progression of disease can be quite different between patients, severe outcomes are usually seen in those who have poorer clinical presentation on admission [16]. Third, for some of the characteristics that are known to be a risk factor for deterioration of disease such as diabetes mellitus, we were not able to show statistical significance most likely due to sample size limitations.

However, the study has a number of strengths. First, it is among the first case series reported from Istanbul, the epicenter of the COVID-19 pandemic in Turkey. Second, we included all patients admitted with both suspect and confirmed COVID-19 infection to our hospital, decreasing the likelihood of missing cases who may be PCR (-) in the beginning of the infection. Indeed, results of follow up tests among PCR (-) patients revealed that only three of them stayed PCR (-). Third, in terms of important comorbidities such as hypertension and diabetes mellitus, our study sample reflected the high levels seen in Turkey. This may have helped increasing the statistical power of our study despite relatively small sample size. Finally, we used electronic records combining two databases, to ensure completeness and accuracy of the records analyzed.

To our knowledge, this is the first study from Turkey analyzing the baseline and clinical characteristics and outcomes of hospitalized COVID-19 patients. Although our findings are similar to those described in previous studies from other countries, our patient population was younger than seen in other country settings [17]. Reflecting the relatively young age-structure of the country.

Conclusion

COVID-19 pandemic is evolving all around the world while information on the virus, disease and epidemiology of the disease is constantly changing. During global pandemic, predictive values to anticipate the progress of the disease and triage accordingly is important to relieve the burden of the disease. This study presents and compares baseline characteristics of Covid-19 infected patients in ICU and non-ICU settings. In this rapidly evolving crisis, descriptive studies are of value to create more intervention side hypothesis. In our study, we found that having a coronary artery disease in the baseline, presenting with dyspnea, having a high CRP and LDH levels in the first laboratory results upon admission were associated with higher probability of being admitted to ICU due to COVID-19 anytime during the hospital admission.

References

1. World Health Organization. Coronavirus disease (2019) (COVID-19): Situation Report.

2. Zhou F, Yu T, Du R, Fan G, Liu Y (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet 395:1054-62.

3. Wang D, Hu B, Hu C, Zhu F, Liu X (2020) Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA 323:1061-69.

4. Chen N, Zhou M, Dong X, Qu J, Gong F (2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet 395:507-13.

5. Pascarella G, Strumia A, Piliego C, Bruno F, Buono DR (2020) COVID-19 diagnosis and management: A comprehensive review. J Intern Med 288:192-206.

6. Population by Country. Worldometer 2020.

7. McKernan B(2020) Turkey announces its first case of coronavirus.

8. COVID-19 (SARS-CoV-2 enfeksiyonu) rehberi. Ankara: Ministry of Health. TC Saglik Bakanligi.

9. Coronavirus Update (Live): 4,924,383 Cases and 320,816 Deaths from COVID-19 Virus Pandemic. Worldometer.

10. Türkiye İstatistik Kurumu, Adrese Dayalı Nüfus Kayıt Sistemi Sonuçları (2017).

11. Koronavirüs – İstanbul Büyükşehir Belediyesi, Korona Virüs. 2020.

12. Europe Cities by Population 2020.

13. Immovilli P, Morelli N, Antonucci E, Radaelli G, Barbera M, et al. (2020) COVID-19 mortality and ICU admission: the Italian experience. Crit Care 24:228.

14. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW(2020) Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA 323:2052-59.

15. Zhang J, Yu M, Tong S, Liu LY, Tang LV (2020) Predictive factors for disease progression in hospitalized patients with coronavirus disease 2019 in Wuhan, China. J Clin Virol 127:104392.

16. Docherty AB, Harrison EM, Green CA, Hardwick H, Pius R (2020) Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol.

17. Myers LC, Parodi SM, Escobar GJ, Liu VX (2020) Characteristics of Hospitalized Adults With COVID-19 in an Integrated Health Care System in California. JAMA 323:2195-98.