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Clinical characteristics of adult patients hospitalized with laboratory-confirmed COVID-19 pneumonia

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1. Introduction

Coronavirus disease 2019 (COVID-19) was first identified in Wuhan, China, on December 31, 2019. COVID-19 is a respiratory illness caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Unfortunately, SARS-CoV-2 had quickly spread to the other countries and resulted in a pandemic. The number of infected patients continues to rise dramatically. Globally, as of June 17, 2020, there have been 8,061,550 confirmed cases of COVID-19, including 440,290 deaths, reported to WHO [1–4].

In Turkey, the first case of COVID-19 was reported by the Ministry of Health of the Republic of Turkey on March 10, 2020. Although this was somewhat later than in European countries, as of June 17, 2020, the total number of COVID-19 cases and deaths reached 181,298 and 4842 respectively on. Our country has managed to slow the spread of the virus as a result of the very strict measures we have followed during the last two months [4].

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The clinical spectrum of COVID-19 has a great variation from asymptomatic infection to acute respiratory distress syndrome and eventually death. The mortality rates vary across the countries probably due to the heterogeneity in study characteristics and patient cohorts as well as treatment strategies. As there is not currently approved drug to treat COVID-19, there were great variations in the mortality of COVID-19 globally even in the same city [3,5–7]. Therefore, we aimed to summarize the clinical characteristics and outcomes of 722 adult patients hospitalized with laboratory-confirmed COVID-19 pneumonia in Istanbul, Turkey.

2. Methods

2.1. Study design and participants

This single-center retrospective study was approved by the Ethics Committee of Istanbul Gaziosmanpasa Training and Research Hospital, and the requirement for written informed consent was waived by our ethics committee. Our hospital has served as a pandemic hospital during the outbreak in Istanbul, Turkey.

A total of 1153 adult patients (≥18 years old) with suspected or laboratory-confirmed COVID-19 pneumonia were hospitalized between March 15 and May 1, 2020. All patients had a fever or other respiratory symptoms with manifestations of pneumonia. Of these patients, 722 (62.6%) had a positive nasopharyngeal real-time polymerase chain reaction (RT-PCR) result for COVID-19 with chest computed tomography (CT) findings compatible with COVID-19 pneumonia were included in this retrospective study. All patients were followed up to death or discharge or the end of the study (May 20, 2020).

2.2. Data collection

Demographic, clinical findings, laboratory results, radiological features, treatments (antiviral, antibacterial, systemic corticosteroid, tocilizumab, and respiratory support), and outcomes were obtained from electronic medical records of patients. We divided patients into two groups according to age, as an elderly group (≥65 years old) and non-elderly group (<65 years old). All raw data were initially evaluated by trained physicians. The outcomes were discharge, ICU admission, mortality, and risk factors for mortality.

2.3. CT technique and image interpretation

Among the 722 patients, CT scans of 65 patients were performed in another hospital. Thus we were able to evaluate CT scans of 657 patients. The chest CT scans were obtained using the standard dose protocol of our hospital with a 128-slice multi-detector CT scanner (Optima; General Electric Healthcare, Wisconsin, USA). All CT scans were performed during a single breath-hold without contrast administration. All CT images were reviewed by a radiologist with 9 years of experience in interpreting chest CT imaging (FC), on a PACS imaging workstation (Infinitt PACS; Infinitt Healthcare, Seoul, Korea).

The CT features that were evaluated included: ground-glass opacities (GGO), consolidation, crazy paving pattern, tree-in-bud sign, air bronchogram, subpleural linear opacity, halo and reversed halo signs. The terms were defined in accordance with the Fleischner Society guidelines [8]. The location of the lesion was classified as predominantly central or predominantly peripheral, depending on whether it was found in the inner or outer half of the lung field, respectively. The affected lung and lobes pleural and pericardial effusion, the presence of mediastinal lymphadenopathy (short axis>1 cm) and bronchiectasis were also noted.

2.4. Definitions

Disease severity on admission was defined on the basis of COVID-19 Diagnosis and Treatment Guide published by The Ministry of Health of the Republic of Turkey [9]. The patients were categorized into three groups according to their disease severity. The severe illness was defined as the presence of one of the following: (a) respiratory distress with respiratory frequency ≥30/min; (b) pulse oximeter oxygen saturation at rest <93%; and (c) artery partial pressure of oxygen/inspired oxygen fraction, PaO2/ FiO2 ≤300 mm Hg. Critical illness was defined as the requirement of high flow oxygen or non-invasive or invasive mechanical ventilation. The other patients who did not meet the above criteria were classified as having the non-severe illness.

2.5. Treatment

In Turkey, our treatment options for COVID-19 include Hydroxychloroquine (200 mg every 12 h, orally, 5–10 days), Favipiravir (first day 1600 mg, and then 600 mg every 12 h, orally, for 5–7 days) and Lopinavir-ritonavir (500 mg twice daily, orally, for 10–14 days). Most patients have a combination of hydroxychloroquine and azithromycin (500 mg every 24 h, orally, for 5 days). The severe and critically ill patients were received with Favipiravir or Lopinavir-ritonavir based on the COVID-19 Diagnosis and Treatment Guide published by The Ministry of Health of the Republic of Turkey [10]. Oseltamivir (75 mg every 12 h, orally, for 5–10 days) was also added to the current treatment during the influenza season. In addition, methylprednisolone for 3–15 days and Tocilizumab were received in seriously ill patients in a cytokine storm.

2.6. Statistics analysis

The data obtained were analyzed using an IBM SPSS Statistics 25 program and checked for suitability for a normal distribution with the Shapiro-Wilk test. Categorical variables were presented as counts and percentages. Continuous variables were presented as mean and standard deviation (SD), otherwise as the median and interquartile range (IQR). Continuous variables if normally distributed were analyzed by independent sample t-test; otherwise, the Mann-Whitney U test was used. All categorical data were analyzed with the chi-square test. Variables significantly associated with mortality in univariate analysis, analyzed in multivariate logistic regression analysis to determine independent risk factors for mortality. P values <0.05 indicated that the difference was statistically significant.

3. Results

3.1. Characteristics of patients at admission

3.1.1. All patients

A total of 722 laboratory-confirmed patients with COVID-19 pneumonia were included in the study. The mean age was 57.5 ± 15.3 years (range, 18–108 years), and 371 of 722 (51.4%) were male. In total, 183 (25.3%) patients had only one comorbidity, and 215 (29.8%) patients had more than one comorbidities. The most common comorbidities were hypertension (251 [34.8%], diabetes mellitus (198 [27.4%]), and ischemic heart disease (66 [9.1%]) (Table 1). The most common symptoms were cough (512 [70.9%]), followed by fever (226 [31.3%]), and shortness of breath (201 [27.8%]). Less common symptoms included muscle ache, gastrointestinal system (diarrhea, nausea, and vomiting) symptoms, and headache. At triage, 129 patients (17.9%) were febrile (>38 °C), 29

E.S. Altunok, M. Alkan, S. Kamat et al. J Infect Chemother 27 (2021) 306–311
(4.0%) had a respiratory rate greater than 30 breaths/minute, and 150 (20.8%) had oxygen saturation less than 90% (Table 1). The median leucocytes count was 6.2 (x10^3/µL), the neutrophil count was 4.3 (x10^3/µL), lymphocyte count was 1.3 (x10^3/µL), C-reactive protein (CRP) was 37.5 (mg/L), procalcitonin was 0.16 (ng/mL), and ferritin was 171 (ng/mL). Lymphocytopenia was present in 29.7% of the patients, leukopenia in 12.2%, and elevated CRP in 48.8% (see Table 2).

At admission, the CT findings of the patients are shown in Table 3. Of these 657 patients, 87% of patients had involvement of two or more lobes, 87% of lesions were located mainly in the peripheral zone of the lung. When a single lobe was involved, the right lower lobe was most often affected (13/36 [36%]). The most common CT features were patchy or rounded GGO (51%) and GGO with consolidation (39%). Seventy-three (11%) patients had the crazy-paving pattern, 194 (30%) had subpleural linear opacity. The air bronchogram sign was visualized in 216 (33%) patients, the halo sign in 131 (20%), and the reversed halo sign in 60 (9%). The CT findings and other data are presented in Table 3.

Clinical severity assessment of COVID-19 pneumonia was defined in 3 groups. The distribution of clinical severity was 543 (75.2%), 90 (12.5%), and 89 (12.3%) for non-severe, severe, and critical respectively (Table 1).

### 3.1.2. Elderly vs non-elderly patients

There were 235 (32.5%) elderly patients and 487 (67.5%) non-elderly patients. The mean age of elderly patients was 74.5 years (SD, ±7.7; range, 65–108 years), and 109 of 235 (46.4%) elderly patients were male. In elderly patients, 72 (30.6%) patients had only one comorbidity, and 120 (51.1%) patients had more than one comorbidities. The prevalence of more than one comorbidity was significantly higher among elderly patients. The most common comorbidities were hypertension (60.9%), diabetes mellitus (40%), and ischemic heart disease (15.7%). Elderly patients compared to...
Non-elderly patients had higher rates of hypertension, diabetes mellitus, and ischemic heart disease, the difference was statistically significant. The most common symptoms were cough (63.1%), and fever (28.5%). At triage, 30 (13.4%) patients had a respiratory rate greater than 30 breaths/minute, and 71 (30.2%) had oxygen saturation less than 90%. At admission, elderly patients had less fever and low oxygen saturation was more common. The median duration from the onset of hospitalization to ICU admission was 3 days (IQR, 1.7–6) (Table 4).

### 3.2. Treatments and outcomes

#### 3.2.1. All patients

At admission, 712 of 722 patients were admitted to the ward and 10 patients were admitted to the intensive care unit. At ward, oxygen therapy was applied in 108 (15%) patients with the nasal cannula and 32 (4.4%) patients with face mask at admission (Table 1). 79 of 712 patients during the follow up at ward were transferred to ICU. The median duration from the onset of hospitalization to ICU admission was 3 days (IQR, 1.7–6) (Table 4). Overall, 89 (12.3%) patients were admitted to the intensive care unit. In ICU, the number of patients required high flow oxygen support, non-invasive mechanical ventilation, and invasive mechanical ventilation were 19 (2.6%), 10 (1.4%), and 60 (8.3%) respectively (Table 4).

By the end of May 20, 648 (89.7%) patients had been discharged and 60 (8.5%) patients had died; all other patients were still hospitalized. The median hospital duration was 6 [4–10] days. 12 of 14 patients still being hospitalized are followed up at the ward and 2 at the ICU by the end of May 20 (Table 4). Finally, on the multivariable analysis, older age and elevated CRP remained the significant independent risk factors for death (Table 5).

#### 3.2.2. Elderly vs non-elderly patients

At admission, 229 of 235 elderly patients were admitted to the ward and 6 elderly patients were admitted to the intensive care unit. At the ward, oxygen therapy was applied in 51 (21.7%) patients with the nasal cannula and 14 (6%) patients with face mask at admission (Table 1). 40 of 229 elderly patients during the follow up at ward were transferred to ICU. The median duration from the onset of hospitalization to ICU admission was 3 days (IQR, 1.7–6) (Table 4). 12 of 14 (85.7%) patients had died; all other patients were still hospitalized. The median hospital duration was 6 [4–10] days. 12 of 14 patients still being hospitalized are followed up at the ward and 2 at the ICU by the end of May 20 (Table 4). Finally, on the multivariable analysis, older age and elevated CRP remained the significant independent risk factors for death (Table 5).

### 3.3. Initial laboratory test results of adult patients hospitalized with laboratory-confirmed COVID-19 pneumonia

| Parameter | Median (IQR) | p-value |
|-----------|-------------|---------|
| Leucocytes, × 10³/µL (normal range 4.1–11) | 6.2 (4.9–8.1) | 0.001 |
| Leucocytes <4.1 | 88 (12.2) | 0.06 |
| Neutrophils, × 10³/µL (normal range 2–8) | 4.3 (3.1–5.9) | <0.001 |
| Lymphocytes, × 10³/µL (normal range 1–5) | 1.3 (0.9–1.7) | 0.053 |
| Haemoglobin, g/dL (normal range 11.5–15) | 13.4 (12.5–14.4) | <0.001 |
| Platelets, × 10³/µL (normal range 150–400) | 195 (159–241) | 0.47 |
| Aspartate aminotransferase, U/L (normal range 0–35) | 29 (23–41) | 0.76 |
| Alanine aminotransferase, U/L (normal range 0–35) | 23 (17–35) | <0.001 |
| Urea, mg/dL (normal range 17–43) | 32 (24–44) | <0.001 |
| Serum creatinine, mg/dL (normal range 0.5–1.7) | 0.84 (0.67–1.05) | <0.001 |
| Active C-reactive protein, mg/L (normal range 0–5) | 37.5 (33–90.7) | 0.03 |
| C-reactive protein >40 | 330 (48.8) | 0.02 |
| Lactate dehydrogenase, U/L (normal range 0–247) | 271 (217–351) | 0.02 |
| Ferritin, ng/mL (male: 20–250 female: 10–120) | 171 (85–375) | 0.02 |
| Procalcitonin, ng/mL | 0.16 (0.12–0.24) | 0.02 |
| High sensitivity troponin I, ng/L (<11.6) | 4.1 (2.4–9.1) | 0.02 |
| GGO with consolidation | 255 (39%) | 0.001 |
| GGO with consolidation | 255 (39%) | 0.001 |
| Consolidation | 25 (10.6) | 0.01 |
| Crazy paving pattern | 73 (11%) | 0.003 |
| Tree-in-bud sign | 13 (2%) | 0.003 |
| Air bronchogram | 216 (33%) | 0.003 |
| Subpleural linear opacity | 194 (30%) | 0.003 |
| Halo sign | 131 (20%) | 0.003 |
| Reversed halo sign | 60 (9%) | 0.003 |
| Pleural effusion | 32 (5%) | 0.003 |
| Pericardial effusion | 8 (1%) | 0.003 |
| Mediastinal lymphadenopathy | 60 (9%) | 0.003 |

**Abbreviations:** GGO, ground-glass opacities.
In a study conducted in Italy, the mortality rate of elderly patients was significantly higher than that of non-elderly patients. The median hospital duration was 8 days (IQR, 5–12) for all patients, 5 days (IQR, 3–9) for non-elderly patients, and 8 days (IQR, 5–12) for elderly patients. Ventilatory support at ICU was required in 60 (8.3%) of all patients, 30 (6.2%) of non-elderly patients, and 30 (12.8%) of elderly patients. The median hospital duration was 6 days (IQR, 5–10) for all patients, 5 days (IQR, 3–9) for non-elderly patients, and 8 days (IQR, 5–12) for elderly patients. The proportion of patients requiring mechanical ventilation was 13 (5.5%), 3 (1.3%), and 30 (12.8%), respectively (Table 4).

By the end of May 20, 194 (82.6%) patients had been discharged and 34 (14.5%) patients had died; all other patients were still hospitalized. The median hospital duration was 8 days (IQR, 5–12) days. 6 of 7 patients still being hospitalized are followed up at the ward and 1 patient at the ICU by the end of May 20 (Table 4).

### 4. Discussion

A total of 722 adult patients with laboratory-confirmed COVID-19 pneumonia was analyzed in this single-center retrospective study between March 15 and May 1, 2020. We identified major clinical characteristics, laboratory results, radiological features, and outcomes for the disease. We divided patients into two groups according to age, as the elderly group and non-elderly group. We also identified independent risk factors for mortality. Previous reports described different mortality rates for death in adults who were hospitalized with COVID-19 among countries. Mortality rates in studies reported from China vary between 1.4% and 12.8% [10–12]. In the first large case series from the US, mortality rates were reported as 21% [13]. In a study conducted in Italy, the mortality rate in inpatients was reported as 20.6% [14]. According to our study, while our overall mortality rate was 8.5%, this rate was 14.5% in elderly patients, and the difference was significant. Compared to other countries, these mortality rates were significantly lower than the US and Italy and was similar to data reported from China.

Globally, as June 17, 2020, there have been 8,061,550 confirmed cases of COVID-19, including 440,290 deaths, reported to WHO [4]. Although most patients present with mild symptoms that are not life-threatening, the number of deaths is still high owing to the large patients’ population. In the previous studies identified several risk factors for death in adults who were hospitalized with COVID-19. In particular, older age, d-dimer levels greater than 1 μg/mL, elevated levels of blood IL-6, high-sensitivity cardiac troponin I, and lactate dehydrogenase and lymphopenia were more commonly seen in severe COVID-19 illness in-hospital death [15]. Our study confirmed that increased age was associated with death in patients with COVID-19. In addition, those with hypertension and diabetes mellitus were highly prevalent in this case series, but this was not related to the higher rate of comorbidity in elderly patients.

COVID-19 is a viral disease characterized by decreased lymphocyte count. According to our current information, cytokine storm plays an important role in severe COVID-19 cases. SARS-CoV-2 is known to mainly affect lymphocytes, especially T lymphocytes, and virus particles induce a cytokine storm in the body, this results in lymphopenia [3,16]. In our study, the absolute value of lymphocytes in most patients decreased (29.7%). However, lymphopenia was not associated with mortality in the analyzes. Among laboratory abnormalities, only elevated CRP remained the significant independent risk factors for death in our study.

Because of the primary involvement of the respiratory system, chest CT is strongly recommended in suspected COVID-19 cases, for initial evaluation. The characteristic patterns and distribution of initial CT manifestations in COVID-19 cases include bilateral, multilobar ground-glass opacification with a peripheral or posterior distribution (or both), mainly in the lower lobes [17,18]. According to our study, chest CT showed similar characteristics in the majority of patients, such as ground-glass opacification 335 (51%), bilateral involvement 595 (91%), peripheral distribution 569 (87%), and multilobar (more than two lobes) involvement 573 (87%). Pleural effusion, pericardial effusion, cavitation, pneumothorax, and lymphadenopathy are some of the uncommon but possible findings seen with disease progression [19,20]. In our study, halo sign (20%) and air bronchogram (33%) findings were found to be relatively high on admission.

Istanbul is an overpopulated city that can be seen as a reflection of Turkey by having significant citizen diversity as a result of being a migration receiving city. At the same time, this city has been the center of COVID-19 pandemic. During the COVID-19 pandemic, the majority of cases in our country were placed in this city. Therefore it can be said that it is important in terms of the data reflect the turkey.

### 5. Limitations

This study has several limitations. First of all, it shows the results of a single-center in Istanbul, Turkey. Second, Due to the
retrospective nature of the study, the missing data were collected from the patients’ electronic medical records. This precluded the level of detail possible with a manual medical record review. Thirdly, some laboratory tests (for example, D-Dimer, IL-6) were not done in all the patients, and missing data or important tests might lead to bias of clinical characteristics.

6. Conclusions

This case series provides characteristics and outcomes of sequentially adult patients hospitalized with laboratory-confirmed COVID-19 pneumonia in Istanbul, Turkey. In addition, it reveals risk factors associated with mortality.

Contributors

Elif SARGIN ALTUNOK was responsible for the organization and coordination of the trial. Elif SARGIN ALTUNOK was the chief investigator, and responsible for the data analysis with Celal Satici and Mustafa Asim Demirkol. Elif SARGIN ALTUNOK, Celal Satici, Mustafa Asim Demirkol, Mustafa Alkan, Bengul Gursoy and Ferhat Cengel developed the trial design. All authors contributed to the writing of the final manuscript. All authors contributed to the management or administration of the trial.

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Declaration of competing interest

The authors declared that there have no conflicts of interest.

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