

## ORIGINAL PAPER

## Infectious diseases

# Characteristics of hospitalised COVID-19 patients and parameters associated with severe pneumonia

Onur Turan<sup>1</sup> | Arzu Mirici<sup>2</sup> | Serap Duru Akçali<sup>3</sup> | Pakize Ayşe Turan<sup>4</sup> | Özgür Batum<sup>5</sup> | Aysun Şengül<sup>6</sup> | Zühal Ekici Ünsal<sup>7</sup> | Nalan Işık Kabakoğlu<sup>8</sup> | Nalan Ogan<sup>9</sup> | Şerife Torun<sup>10</sup> | Güntülü Ak<sup>11</sup> | Şule Akçay<sup>12</sup> | Berna Kömürcüoğlu<sup>5</sup> | Nazan Şen<sup>7</sup> | Pınar Mutlu<sup>2</sup> | Ülkü Yılmaz<sup>13</sup>

<sup>1</sup>Chest Diseases Department, İzmir Katip Celebi University Atatürk Research and Training Hospital, İzmir, Turkey

<sup>2</sup>Chest Diseases Department, Canakkale 18 Mart University, Canakkale, Turkey

<sup>3</sup>Chest Diseases Department, Ankara Dışkapı Yıldırım Beyazıt Research and Training Hospital, Ankara, Turkey

<sup>4</sup>Chest Diseases Department, Menemen State Hospital, İzmir, Turkey

<sup>5</sup>Chest Diseases Department, İzmir Dr. Suat Seren Chest Diseases and Surgery Research and Training Hospital, İzmir, Turkey

<sup>6</sup>Chest Diseases Department, Sakarya Üniversitesi University, Sakarya, Turkey

<sup>7</sup>Chest Diseases Department, Başkent University Adana Dr. Turgut Noyan Application and Research Center, Adana, Turkey

<sup>8</sup>Chest Diseases Department, İzmir Bornova Dr. Türkan Özilhan State Hospital, İzmir, Turkey

<sup>9</sup>Chest Diseases Department, Ufuk University, Ankara, Turkey

<sup>10</sup>Chest Diseases Department, Konya Başkent University Application and Research Center, Konya, Turkey

<sup>11</sup>Chest Diseases Department, Eskişehir Osmangazi University, Eskişehir, Turkey

<sup>12</sup>Chest Diseases Department, Başkent University, Ankara, Turkey

<sup>13</sup>Chest Diseases Department, Ankara Atatürk Chest Diseases and Chest Surgery Research and Training Hospital, Ankara, Turkey

## Correspondence

Onur Turan, Chest Diseases Department, İzmir Katip Celebi University Atatürk Research and Training Hospital, İzmir, Turkey.

Email: onurtura@yahoo.com

## Abstract

**Background:** After the first case of coronavirus disease 2019 (COVID-19) was reported in China in December 2019, it caused a global pandemic, including Turkey.

**Objectives:** The aim of this study was to analyse the characteristics of hospitalised COVID-19 patients and assess the parameters related to severe pneumonia.

**Methods:** Included in the study were hospitalised COVID-19 patients with positive naso-oropharyngeal swabs. Patients' demographics, admission symptoms, laboratory and radiological findings were recorded retrospectively.

**Results:** Of 1013 patients, 583 were males (57.6%) and 430 were females (42.4%), with a mean age of  $53.7 \pm 17.9$ . More than half of the patients had at least one comorbidities, the most common of which were hypertension and diabetes mellitus. Cough (59.8%), fatigue (49.5%) and fever (41.2%) were the most common presenting symptoms. Of the hospitalised COVID-19 patients, 84.9% had pneumonia and 83.5% had typical radiological COVID-19 appearances (94.5%: ground-glass areas). The most common laboratory findings were high C-reactive protein (CRP) (73.6%) and lactate dehydrogenase (LDH) (46.2%) levels, as well as lymphopenia (30.1%). Severe pneumonia was present in 28.1% of COVID-19 patients. Multivariate logistic regression

analysis indicated that advanced age, hypotension, anaemia and elevated CRP and LDH serum levels were independent risk factors for the severity of COVID-19 pneumonia ( $P = .011, .006, .017, .003$  and  $.001$ , respectively).

**Conclusion:** This study, as one of the first multicentre studies about characteristics of COVID-19 in Turkey, may guide about disease-related parameters and severity of pneumonia. Age, blood pressure, complete blood count and routine biochemical tests (including CRP and LDH) would appear to be important parameters for the evaluation of the severity of COVID-19 pneumonia.

## 1 | INTRODUCTION

By the end of 2019, a new type of coronavirus—SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2)—was isolated as a factor in cases of pneumonia with an unknown aetiology in China.<sup>1</sup> The disease was first seen in Turkey in March 2020,<sup>2</sup> and since then, more than 380,000 people have been infected, and over 10 000 have died from 'Coronavirus Disease 2019' (COVID-19) in our country.<sup>1</sup>

The clinical diagnoses of COVID-19 are based on clinical manifestations, molecular examinations, thoracic imaging and blood tests.<sup>3</sup> The molecular diagnostic technique, based on a viral genetic real-time polymerase chain reaction (RT-PCR) assay, has been the most common and only direct method of SARS-CoV-2 detection for the diagnosis of COVID-19.<sup>4</sup>

The clinical spectrum of COVID-19 is wide, ranging from asymptomatic patients with mild forms of the disease to severe pneumonia requiring admission to the intensive care unit (ICU).<sup>5</sup> The common initial symptoms include fever, cough and shortness of breath, although symptoms such as weakness, fatigue, myalgia and loss of taste and/or smell have also been reported.<sup>6</sup>

Radiological examinations play an important role in the early detection and diagnosis of COVID-19 pneumonia. Chest radiography is not sufficiently sensitive as a radiological approach in the early stage of infection, so thorax computed tomography (CT) is generally applied to assist in the diagnosis of COVID-19 pneumonia.<sup>7</sup>

Laboratory parameters have been used both for diagnostic purposes and for the prediction of prognosis in COVID-19. The routine tests requested for COVID-19 patients include complete blood count (CBC), coagulation cascade (including PT, aPTT and D-dimers) parameters, and inflammation-related parameters such as CRP, ferritin and procalcitonin.<sup>8</sup> Since COVID-19 may also impair such organs as the heart, liver and kidneys,<sup>9</sup> the use of biochemical factors to assess the functional activity of these vital organs is important for clinicians.

The aim of this study was to determine the epidemiologic and the clinical, radiological and laboratory features of hospitalised COVID-19 patients and to assess the parameters related to severe pneumonia.

### What's known

- COVID-19 may be a serious and fatal disease, especially when it is accompanied by pneumonia.

### What's new

- Age, blood pressure, complete blood count and routine biochemical tests (including CRP and LDH) would appear to be important parameters for the evaluation of the severity of COVID-19 pneumonia.

## 2 | PARTICIPANTS AND METHODS

This multicentre, retrospective nationwide cohort study of COVID-19 patients admitted to Turkish hospitals included patients with positive naso-oropharyngeal swabs taken using real-time PCR (RT-PCR) assay kits in 10 different centres between March and September 2020. Ethics committee approval for the study was obtained from the Ethics Committee of the İzmir Katip Çelebi University Atatürk Training and Research Hospital, and permission for the study was obtained also from the Ministry of Health of the Republic of Turkey. The requirement for informed consent was waived due to the retrospective design of the study.

All of the enrolled patients were over the age of 18 years, and were confirmed as SARS-CoV-2 RNA positive based on oronasopharyngeal swab specimens obtained using real-time reverse-transcriptase polymerase chain reaction (RT-PCR) assays.

The patients' demographics, risk factors for COVID-19, comorbid diseases, vital signs and symptoms at admission, as well as their laboratory and radiological findings, were accessed from the digital medical records of the hospitals participating in the study.

COVID-19 pneumonia was considered to be present in cases with an official thorax CT report confirming the diagnosis. The radiological findings of pneumonia in a thorax CT were evaluated according to the COVID-19 pneumonia imaging classification laid out in the Radiological Society of North America Expert Consensus Statement.<sup>10</sup> The patients were subsequently divided into four

**TABLE 1** Demographic and epidemiologic characteristics of COVID-19 patients

Demographics	COVID group (n = 1013)
Age (year)	53.7 ± 17.9
Gender	
Male (n, %)	583, 57.6%
Female (n, %)	430, 43.3%
Time from first symptom onset to hospital admission (days)	4.36 ± 3.34
Smoking history	
Yes (n, %)	405, 40%
No (n, %)	608, 60%
Exposure history for disease transmission	
Yes (n, %)	458, 45.2%
No (n, %)	555, 54.8%
Comorbidities	
Present (n, %)	524, 52.1%
Not present (n, %)	489, 47.9%

Abbreviation: COVID-19, coronavirus disease 2019.

categories as negative for pneumonia, typical appearance, indeterminate appearance and atypical appearance.

The laboratory data in this study include routine blood tests, such as complete blood count, biochemistry tests, blood clotting tests and a number of infection-related parameters that were assessed at the time of admission. The initial values of these laboratory indexes were collected for analysis in this study.

The COVID-19 patients were divided into two main groups, being those with severe or non-severe (mild) pneumonia. Severe pneumonia was defined as 'the presence of dyspnoea, respiratory frequency  $\geq 30$ /min and/or blood oxygen saturation  $\leq 90\%$  (PaO<sub>2</sub>/FiO<sub>2</sub> ratio  $\leq 300$  mm Hg)', based on the National Guidelines for COVID-19 issued by the Scientific Advisory Board on Coronavirus affiliated with the Turkish Ministry of Health.<sup>2</sup>

## 2.1 | Definitions

Tachycardia is defined as  $\geq 100$  beats/min, tachypnoea as  $>20$  breaths/min at presentation, hypotension as a decrease in systolic blood pressure to less than 90 mm Hg or diastolic blood pressure to less than 40 mm Hg. Neutropenia is defined as an absolute neutrophil count below  $2 \times 10^9$ /L, and lymphopenia as blood lymphocytes lower than  $1 \times 10^9$ /L. Thrombocytopenia is defined as a platelet count below  $150 \times 10^9$ /L. The normal haemoglobin (Hb) level for males is 14-18, and 12-16 g/dL for females. The lower Hb level is considered anaemia.

An elevated transaminase level is considered to be a high serum level of alanine transaminase (ALT) ( $>55$  U/L) or aspartate transaminase (AST) ( $>35$  U/L).

The normal serum creatinine level is considered to be 0.7-1.3 mg/dL in males and 0.6-1.1 mg/dL in females. High serum levels of Troponin I ( $>0.08$  ng/mL) or CK-MB ( $>5$   $\mu$ g/L) are considered as elevated cardiac

enzyme levels. Other biochemical parameters and their normal ranges are as follows: albumin 35-50 g/L, calcium (adjusted) 8.5-10.5 mg/dL, bilirubin (total) 0.2-1.2 mg/dL, sodium 135-145 mmol/L, potassium 3.5-5.5 mmol/L, lactate dehydrogenase (LDH) 220 U/L and fibrinogen 200-400 mg/dL. In this study, patients were grouped also according to their serum ferritin levels, with a cut-off of 500 ng/mL and a D-dimer cut-off of  $>1000$   $\mu$ g/L, which are stated as poor prognostic criteria in the National Guidelines for COVID-19.<sup>2</sup>

## 2.2 | Statistical analyses

Statistical analyses were performed using the SPSS Version 16.0 (Chicago, SPSS Inc) software package. Baseline characteristics, including demographic data, the presence of symptoms and radiological and laboratory findings were summarised using descriptive statistics. The continuity correction  $\chi^2$  test and a Fisher's exact test were used for the comparison of the frequency rates of the categorical variables of the severe and non-severe COVID-19 patients. The Pearson correlation was used to assess the strength of the linear relationship between two variables. The demographics and initial symptoms, and radiological and laboratory findings with significant differences between the two groups were assessed with a multivariate logistic regression analysis (using a stepwise backward LR method) to explore the risk factors associated with the disease severity of COVID-19. A paired sample *t*-test was used to compare the means of the groups. A *P*-value  $<.05$  was considered as statistically significant.

## 3 | RESULTS

Of the 1013 patients included in the study, 583 were males (57.6%) and 430 were females (42.4%), with the mean age of  $53.7 \pm 17.9$ .

A history of suspected contact with COVID-19 cases was present in 45.2% of patients. The most likely routes of transmission were as follows: family contact (30.5%), hospital (14%), prison (12.8%), nursing home (10.3%) and travel history (4.6%).

The demographics and general information of the COVID-19 patients are presented in Table 1.

### 3.1 | Comorbidities

More than half (52.4%-51.7%) of the patients had at least one comorbidity, the most prevalent of which were 54.2% hypertension (HT), 24.4% chronic heart disease (54.7% coronary artery disease, 31.3% congestive heart failure, 10.9% arrhythmia, 3.1% valve disease), 21.2% chronic lung disease (54% Chronic obstructive pulmonary disease, 42.3% asthma, 3.7% bronchiectasis), 11.5% diabetes, 6.5% neurologic disorders, 4.6% thyroid disorders, 4.4% malignancy, 4% kidney disease, 3.2% psychiatric disorders, 4.4% hematologic disorders, 3.2% stroke and 2.7% rheumatic diseases. The incidences of comorbidities are presented in Figure 1.

### 3.2 | Molecular diagnostic technologies

Of the total, 788 patients (77.8%) recorded a positive RT-PCR nasopharyngeal swab in the first specimen. The COVID-19 diagnoses of the remaining 225 patients were confirmed by second or third swab tests.

### 3.3 | Presenting symptoms

The median duration of symptoms at admission was 4.4 days. Upon admission, most patients had experienced cough (59.8%). Fatigue (49.5%) and fever (41.2%) were the other most common presenting symptoms, with less frequent symptoms being myalgia (34%), dyspnoea (28%), sore throat (7.9%), anosmia (7.3%) and headache (4.5%). Gastrointestinal symptoms such as nausea (3.1%) and diarrhoea (2%) were present in 15.9% of patients. Of the total, 12% of the COVID-19 patients had experienced no symptoms until the time of diagnosis. Figure 2 details the presenting symptoms at the time of hospital admission of the COVID-19 patients.

### 3.4 | Radiological findings

Pulmonary infiltrates accepted as COVID-19 pneumonia were identified from a thorax CT in 84.9% of the hospitalised COVID-19 patients. Among the 860 patients with pulmonary infiltration, 85.1% were evaluated as typical (peripheral ground-glass opacities), 12.8% as indeterminate and 2.1% as atypical pattern of COVID-19 based on chest CT findings. The predominant pattern of abnormality was ground-glass opacity (GGO), with 94.5% among patients with COVID-19

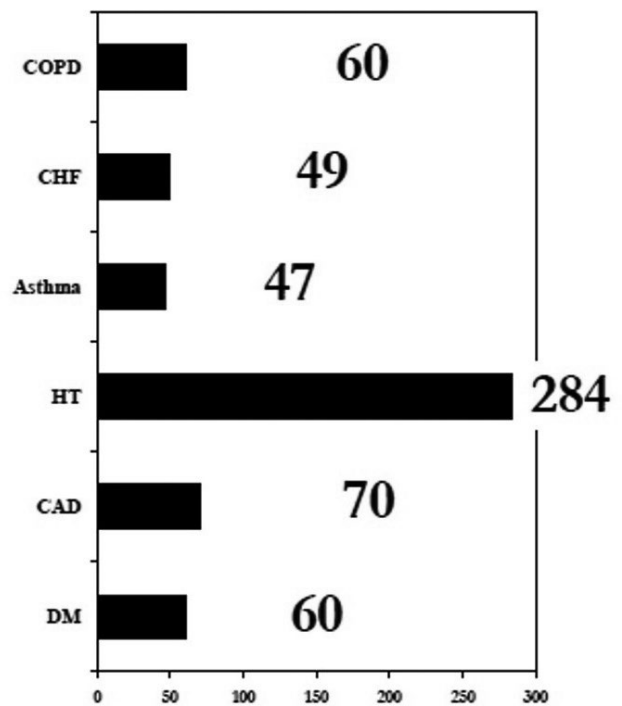


FIGURE 1 The incidence of comorbid diseases in patients diagnosed with coronavirus disease 2019 (COVID-19). CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HT, hypertension

pneumonia. The incidence of consolidation was 29.5%, crazy paving was 7.8% and the other radiological findings (such as tree-in-bud sign, cavitate) was 3.6%. The locations of the lesions were peripheral in 61.7%, bilateral in 83.9% and multifocal in 81.5% of the patients. The disease affected the lower lobes in 29.8%, the upper lobes in 18.9% and both the upper and lower lobes in 51.3% of the patients.

### 3.5 | Vital signs and laboratory findings

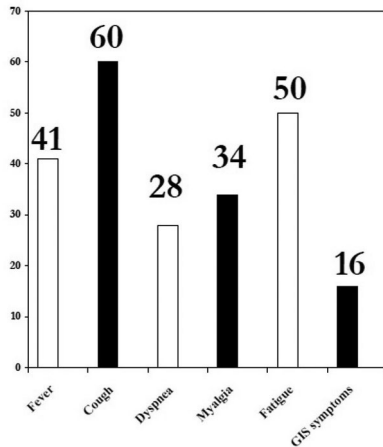
With respect to vital sign abnormalities, tachycardia was determined in 9.6%, hypotension in 4.3% and tachypnoea in 18.6% of the patients.

The mean oxygen saturation at the time of admission was  $92.9 \pm 4.6\%$ . There was hypoxemia in 13.8% of the patients according to the results of both a pulse oximetry and arterial blood gas analysis at the time of hospital admission.

The most common abnormal laboratory findings were high-level CRP (73.6%) and LDH (46.2%), and the presence of lymphopenia (30.1%).

### 3.6 | Pneumonia severity

Severe pneumonia was present in 242 of the 860 (28.1%) patients with COVID-19 pneumonia.



**FIGURE 2** Presenting symptoms of coronavirus disease 2019 (COVID-19) patients upon hospital admission (%). GI, gastrointestinal symptoms

The mean age of the patients with severe COVID-19 pneumonia was significantly higher than that in the non-severe group ( $P < .001$ ). There were more patients with comorbidities (at least one) in the severe COVID-19 group ( $P < .001$ ). The presence of hypotension, tachypnoea and tachycardia on hospital admission were significantly higher in patients with severe COVID-19 pneumonia (all  $P < .001$ ). Table 2 shows the clinical features, symptoms, vital signs and pneumonia severity of the COVID-19 patients.

In patients with severe COVID pneumonia, the mean lymphocyte count, CRP, LDH, procalcitonin levels, CURB-65 and SOFA scores were significantly higher than those in the mild pneumonia patients (LDH and procalcitonin levels:  $P = .010$  and  $.040$ , respectively, other parameters:  $P < .001$ ). Lymphopenia, thrombocytopenia, anaemia, hypoalbuminemia, hyponatremia (all  $P < .001$ ), hyperbilirubinemia ( $P = .008$ ) and hypokalaemia ( $P = .002$ ) were significantly more common in the severe pneumonia group. There were statistically more patients with elevated levels of aminotransferase (ALT/AST), LDH, D-dimer ( $>1000 \mu\text{g/L}$ ), ferritin ( $>500 \text{ ng/mL}$ ), creatinine (all  $P < .001$ ) and cardiac enzymes ( $P = .019$ ) in the severe COVID-19 group.

There were statistically more patients with bilateral, multifocal and peripheral involvement in severe COVID-19 pneumonia group (all  $P < .001$ ). Table 3 presents the numerous differences in the laboratory findings of the severe and non-severe COVID-19 pneumonia cases.

There were statistically more patients with bilateral and multifocal involvement in the group with severe COVID-19 pneumonia (all  $P < .001$ ) and hypoxemia ( $P = .006$  and  $.002$ , respectively). Peripheral involvement in thorax CT was significantly more common in non-severe pneumonia ( $P = .004$ ) and normoxemic patients ( $P < .001$ ). The relationship between severity of pneumonia (including hypoxemia as a separate parameter) and radiological findings is described in Table 4.

A multivariate logistic regression analysis indicated that advanced age, anaemia, hypotension and elevated CRP and LDH levels were independent risk factors for the severity of pneumonia in COVID-19 patients ( $P = .011, .006, .017, .003$  and  $.001$ , respectively) (Table 5).

## 4 | DISCUSSION

This retrospective study has described the clinical, radiological and laboratory characteristics of patients hospitalised with COVID-19 in several centres in Turkey. A total of 1013 COVID-19 patients were included in the study, conducted between March and September 2020, and pneumonia was detected in 860 of 1013 (84.9%) of the hospitalised COVID-19 patients.

Our results suggest that patients with advanced age are more likely to develop severe pneumonia. Consistent with previous reports, advanced age has been found to be one of the most significant predictors of a poor outcome in COVID-19 patients.<sup>11</sup> The greater prevalence of comorbidities in older patients may be a reason for the worsening of the disease into severe pneumonia. The degree of frailty or malnutrition may also facilitate a worse course of COVID-19 in geriatric population.

Our study has revealed a greater prevalence of chronic diseases in COVID-19 patients with severe pneumonia. Comorbidities such as HT, diabetes and chronic cardiovascular disease have been identified as poor prognostic factors in COVID-19.<sup>12</sup> There was a high prevalence of HT in patients with severe COVID-19 pneumonia according to our results, which was similar to the study by Lippi et al., which indicated that patients with HT may be at greater risk of developing severe COVID-19.<sup>13</sup> The expression of angiotensin-converting enzyme 2 (ACE2) in HT may decrease, which may cause severe infections such as pneumonia and Acute respiratory distress syndrome (ARDS) due to increased levels of angiotensin II.<sup>14</sup>

Similar to other recent studies, the most common symptoms at the onset of illness were dry cough, fatigue and fever in our COVID-19 patients.<sup>15,16</sup> Typical pneumonia, which develops secondary to bacterial microorganisms, usually manifests with a sudden onset of fever and a productive cough.<sup>17</sup> As sputum production is rarely seen in COVID-19 ( $<1\%$ ), it may be helpful in differentiating between bacterial and COVID-19-related pneumonia.

Gastrointestinal (GI) symptoms such as nausea and diarrhoea were present in 16% of the patients in this study. GI symptoms have been described in 4%-11% of cases in previous studies,<sup>18</sup> and the findings of this study confirm the importance of GI symptoms among COVID-19 patients as early signs of the disease.

Most patients had multifocal lung involvement located in the peripheral area, and mostly the lower lobes were affected, with a predominant GGO pattern, in our study. Our results also showed bilateral involvement to be more common, especially in patients with severe COVID-19 pneumonia. The typical imaging features

Demographics	Severe COVID-19 pneumonia (n = 242) (n, %)	Non-severe COVID-19 pneumonia (n = 618) (n, %)	P-value
<b>Gender</b>			
Male	145 (60%)	355 (57.4%)	.280
Female	97 (40%)	263 (42.6%)	
Age, years	60.3 ± 16.7	53.1 ± 16.6	<.001*
<b>Comorbidities</b>			
Present	165 (68.2%)	307 (49.7%)	<.001*
Not present	77 (31.8%)	311 (50.3%)	
Time from symptom onset to hospital admission <days>	5.16 ± 4.00	4.17 ± 3.04	.006*
<b>Symptoms (admission)</b>			
<b>Fever</b>			
Present	118 (49%)	258 (41.7%)	.081
Not present	124 (51%)	360 (58.3%)	
<b>Cough</b>			
Present	139 (57.3%)	386 (62.5%)	.205
Not present	103 (42.7%)	232 (37.5%)	
<b>Fatigue</b>			
Present	130 (53.8%)	306 (49.6%)	.179
Not present	112 (46.2%)	312 (50.4%)	
<b>Myalgia</b>			
Present	73 (30.3%)	222 (36%)	.153
Not present	169 (69.7%)	396 (64%)	
<b>Gastrointestinal symptoms</b>			
Present	39 (16.2%)	101 (16.4%)	.934
Not present	203 (83.8%)	517 (83.6%)	
<b>Vital signs (admission)</b>			
<b>Tachypnoea</b>			
Present	171 (70.7%)	10 (1.6%)	<.001*
Not present	71 (29.3%)	608 (98.4%)	
<b>Hypotension</b>			
Present	220 (90.9%)	18 (2.9%)	<.001*
Not present	22 (9.1%)	600 (97.1%)	
<b>Tachycardia</b>			
Present	40 (16.5%)	49 (8%)	<.001*
Not present	202 (83.5%)	600 (92%)	

Abbreviation: COVID-19, coronavirus disease 2019.

\*Statistically significant.

**TABLE 2** Clinical features, symptoms and vital signs according to the severity of pneumonia in COVID-19 patients

of COVID-19 pneumonia include peripherally distributed ground-glass areas in both lungs, particularly in the lower lobes.<sup>19</sup> Bilateral lung involvement seems to be more common in the early stages of COVID-19 pneumonia, unlike with MERS and SARS, and this may cause the disease to be more severe.<sup>20</sup>

COVID-19 pneumonia may result in cardiovascular manifestations leading to worse clinical outcomes. Low blood pressure is

to be an important vital parameter that may indicate severe sepsis and septic shock in bacterial infections, including COVID-19 pneumonia. Hypotension on admission was found to be an independent risk factor predicting the critical status of COVID-19 infection.<sup>21</sup> In this study, a significant relationship was identified between the presence of hypotension at the time of hospital admission and the development of severe COVID-19 pneumonia, which indicates the

TABLE 3 Laboratory findings according to the severity of pneumonia in COVID-19 patients

Laboratory findings	Severe COVID-19 pneumonia (n = 242) (n, %)	Non-severe COVID-19 pneumonia (n = 618) (n, %)	P-value
Neutropenia			
Present	6 (2.5%)	37 (6%)	.052
Not present	236 (97.5%)	581 (94%)	
Neutrophil count, $\times 10^9/L$	4.20 $\pm$ 1.31	3.15 $\pm$ 0.93	.114
Lymphopenia			
Present	116 (48%)	172 (27.8%)	<.001*
Not present	126 (52%)	446 (72.2%)	
Lymphocyte count, $\times 10^9/L$	1.17 $\pm$ 0.64	1.52 $\pm$ 0.64	<.001*
Thrombocytopenia			
Present	34 (14%)	40 (6.5%)	.001*
Not present	208 (86%)	578 (93.5%)	
Anaemia			
Present	55 (22.7%)	74 (12%)	<.001*
Not present	187 (77.3%)	544 (88%)	
Elevated aminotransferase levels			
Present	67 (27.7%)	75 (12.1%)	.001*
Not present	175 (72.3%)	543 (87.9%)	
High serum creatinine level			
Present	68 (28%)	77 (12.4%)	<.001*
Not present	174 (72%)	541 (87.6%)	
Hypoalbuminemia			
Present	81 (46%)	101 (21.2%)	<.001*
Not present	95 (54%)	376 (78.8%)	
Hypocalcaemia			
Present	23 (27.7%)	53 (21.8%)	.270
Not present	63 (72.3%)	131 (78.2%)	
Hyperbilirubinaemia			
Present	14 (8%)	17 (3.9%)	.008*
Not present	160 (92%)	422 (96.1%)	
Hyponatraemia			
Present	68 (28.2%)	110 (17.9%)	<.001*
Not present	174 (71.8%)	508 (82.1%)	
Hypokalaemia			
Present	22 (9%)	22 (3.5%)	.002*
Not present	220 (91%)	596 (96.5%)	
High serum LDH level			
Present	158 (65.4%)	279 (45.1%)	<.001*
Not present	84 (34.6%)	339 (54.9%)	
LDH level	360.4 $\pm$ 85.3	246.8 $\pm$ 31.3	.010*
CRP level	96 $\pm$ 25.9	38.8 $\pm$ 8.3	<.001*
Procalcitonin level	1.34 $\pm$ 0.59	0.47 $\pm$ 0.11	.040*
CURB-65 score	1.27 $\pm$ 0.35	0.45 $\pm$ 0.13	<.001*
SOFA score	1.85 $\pm$ 1.32	0.32 $\pm$ 0.08	<.001*

(Continues)



TABLE 3 (Continued)

Laboratory findings	Severe COVID-19 pneumonia (n = 242) (n, %)	Non-severe COVID-19 pneumonia (n = 618) (n, %)	P-value
Elevated cardiac enzymes (troponin/CK-MB)			
Present	63 (33.5%)	118 (24.5%)	.019*
Not present	125 (66.5%)	363 (75.5%)	
Serum ferritin level (>500 ng/mL)			
Present	54 (24.8%)	57 (10.1%)	<.001*
Not present	164 (75.2%)	507 (89.9%)	
Serum D-dimer level (>1000 µg/L)			
Present	64 (28.4%)	75 (12.8%)	<.001*
Not present	161 (71.6%)	512 (87.2%)	
High serum fibrinogen level			
Present	56 (50.9%)	154 (48.3%)	.634
Not present	54 (49.1%)	165 (51.7%)	

Abbreviations: COVID-19, coronavirus disease 2019; CRP, C-reactive protein; LDH, lactate dehydrogenase.

\*Statistically significant.

importance of monitoring vital signs and making the necessary interventions, especially in those with hypotension, in COVID-19 patients.

Our results revealed anaemia as an independent risk factor for severe COVID-19 pneumonia. While anaemia is not a common laboratory finding in COVID-19 patients, cases with severe pneumonia have been identified with severely decreased Hb levels.<sup>22</sup> Low concentrations of Hb in circulation may decrease the transport of oxygen to several organs, leading to hypoxia, multiple organ dysfunction and potentially severe outcomes in cases with COVID-19 infections. This mechanism may explain the high rate of severe COVID-19 cases with anaemia.

Several biochemical factors have been found to predict COVID-19 severity.<sup>8</sup> A multivariate logistic regression analysis in this study revealed elevated levels of LDH to be an independent predictor of severe COVID-19 pneumonia. LDH is considered to be an inflammatory marker, reflecting acute or chronic tissue damage. Huang et al suggested that high levels of LDH could be used to discriminate severe and non-severe COVID-19 patients.<sup>23</sup> Since LDH is also present in lung tissue, patients with severe COVID-19 infections can be expected to release greater amounts of LDH into circulation,<sup>24</sup> which may cause elevated levels of LDH in severe COVID-19 patients.

Plasma CRP levels were found to be positively associated with the COVID-19 pneumonia severity in the results of this study. CRP is known to be a good parameter, reflecting the effects of inflammatory cytokines, which can damage the lung tissue when the system hyperactivates, leading possibly to lung damage and a worsening prognosis.<sup>25</sup> In addition, high CRP values are frequently seen in secondary bacterial infections, which have been reported in severe COVID-19 cases.<sup>26</sup> Several studies of COVID-19 patients have reported that higher concentrations of inflammatory markers such as CRP may indicate a more severe disease.<sup>27,28</sup> Accordingly, CRP may be considered useful as an early indicator of severe illness and nosocomial infections in COVID-19 patients. Physicians

can thus take such precautions as prioritising patients for intensive care unit transfer, or the administration of empirical antibiotic treatment.

There are different definitions of severe pneumonia of COVID-19 in different guidelines. Severe COVID-19 pneumonia was defined as the PCR-positive patient who had oxygen saturation <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen ( $\text{PaO}_2/\text{FiO}_2$ ) < 300 mm Hg, respiratory frequency >30 breaths/min or lung infiltrates >50% by the National Institutes of Health.<sup>29</sup> We accepted the definition of severe pneumonia, which was mentioned in 'National Guideline for COVID-19' issued by the Turkish Ministry of Health in our study. This definition includes the criteria of the presence of dyspnoea, tachypnoea and/or hypoxemia; however, there was no radiological criteria included.<sup>2</sup> There were statistically more patients with bilateral and multifocal involvements in severe COVID-19 pneumonia group in our study, which revealed that presence of severe pneumonia may also be correlated with radiological findings.

Our study has several limitations. The first limitation is its retrospective design. Due to the retrospective nature of the study, there are some missing laboratory parameter results, which may have a negative effect on the strength of the reported findings. Second, the mortality of patients with COVID-19 was not considered, and this would have better reflected the strength of the risk factors than the severity of the disease.

## 5 | CONCLUSION

We present here one of the first multicentre studies detailing the characteristics of COVID-19 in Turkey. The study can serve as a guide for physicians in terms of application complaints, laboratory and radiological features when dealing with COVID-19. Age, blood pressure, complete blood count (for Hb level) and routine biochemical



TABLE 4 Radiological findings according to the severity of pneumonia and hypoxemia in COVID-19 patients

Radiological CT findings	Severe COVID-19 pneumonia (n = 242) (n, %)	Non-severe COVID-19 pneumonia (n = 618) (n, %)	P-value	Patients with hypoxemia (n = 117) (n, %)	Patients without hypoxemia (n = 743) (n, %)	P-value
<b>Bilateral involvement</b>						
Yes	223 (92.2%)	378 (61.2%)	<.001*	110 (93.8%)	604 (81.3%)	.006*
No	19 (7.8%)	240 (38.8%)		7 (6.2%)	139 (18.7%)	
<b>Multifocal involvement</b>						
Yes	227 (93.8%)	515 (83.3%)	<.001*	108 (92.5%)	576 (77.5%)	.002*
No	26 (6.2%)	103 (16.7%)		9 (7.5%)	167 (22.5%)	
<b>Ground-glass opacities</b>						
Yes	226 (93.4%)	592 (95.8%)	.518	105 (90.2%)	701 (94.4%)	.153
No	16 (6.6%)	26 (4.2%)		12 (9.8%)	42 (5.6%)	
<b>Peripheral involvement (only)</b>						
Yes	115 (47.5%)	216 (35%)	.004*	71 (60.5%)	280 (37.6%)	<.001*
No	127 (52.5%)	402 (65%)		46 (39.5%)	463 (62.4%)	
<b>Typical radiological COVID-19 appearance</b>						
Yes	211 (87.2%)	108 (17.5%)	.097	98 (83.7%)	602 (81.1%)	.530
No	31 (12.8%)	510 (82.5%)		19 (16.3%)	141 (18.9%)	

Abbreviations: COVID-19, coronavirus disease 2019; CT, computed tomography.

\*Statistically significant.

**TABLE 5** Multivariate logistic regression analysis of risk factors associated with severe COVID-19 pneumonia

Parameters	Multivariable OR (95% CI)	P-value
Age, years	1.032 (1.007-1.058)	.011*
Comorbidity present (yes vs no)	1.974 (0.883-4.411)	.097
Hypotension (yes vs no)	4.872 (2.202-9.432)	.006*
Anaemia (yes vs no)	2.786 (1.202-6.455)	.017*
CRP, mg/L	1.010 (1.003-1.016)	.003*
Elevated transaminases (yes vs no)	0.427 (0.163-1.121)	.084
LDH level	1.006 (1.003-1.010)	.001*
Procalcitonin level	0.663 (0.516-0.882)	.064

Abbreviations: COVID-19, coronavirus disease 2019; CRP, C-reactive protein; LDH, lactate dehydrogenase.

\*Statistically significant.

tests (including CRP and LDH) would appear to be important parameters in the evaluation of severity COVID-19 pneumonia.

## ACKNOWLEDGEMENTS

All authors (OT, AM, SDA, PAT, ÖB, AŞ, ZEU, NIK, NO, ŞT, GA, ŞA, BK, NŞ, PM and ÜY) have approved this manuscript.

## DISCLOSURES

The authors (OT, AM, SDA, PAT, ÖB, AŞ, ZEU, NIK, NO, ŞT, GA, ŞA, BK, NŞ, PM and ÜY) declare no conflict of interest.

## AUTHOR CONTRIBUTIONS

OT conceptualised and designed the study, and involved in acquisition, analysis and interpretation of data. AM, SDA, PAT, ÖB, AŞ, ZEU, NIK, NO and ŞT involved in acquisition of data. GA, ŞA, BK, NŞ, PM and ÜY conceptualised and designed the study, and analysed the data. All the authors approved the manuscript.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

## REFERENCES

- World Health Organization. *Director-General's Remarks at the Media Briefing COVID-19*; 2020. <https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-6-november-2020>. Accessed November 6, 2020.
- COVID-19 Guideline: Management of Severe Pneumonia, ARDS, Sepsis and Septic Shock. Ministry of Health, Turkey. <https://covid19bilgi.saglik.gov.tr/>. Accessed November 2, 2020.
- Esakandari H, Nabi-Afjadi M, Fakkari-Afjadi J, Farahmandian N, Miresmaeili SM, Bahreini E. A comprehensive review of COVID-19 characteristics. *Biol Proced Online*. 2020;4(22):19. 10.1186/s12575-020-00128-2
- World Health Organization (WHO). *Laboratory Testing for 2019 novel coronavirus (2019-nCoV) in Suspected Human Cases. Interim Guidance*; 2020. <https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117>. Accessed March 16, 2020.
- Cascella M, Rajnik M, Cuomo A, et al. *Features, Evaluation, and Treatment of Coronavirus*. StatPearls Publishing; 2020. <https://www.ncbi.nlm.nih.gov/books/NBK554776/>
- Lovato A, de Filippis C, Marioni G. Upper airway symptoms in coronavirus disease 2019 (COVID-19). *Am J Otolaryngol*. 2020;41(3):102474. 10.1016/j.amjoto.2020.102474
- Bao C, Liu X, Zhang H, Li Y, Liu J. Coronavirus disease 2019 (COVID-19) CT findings: a systematic review and meta-analysis. *J Am Coll Radiol*. 2020;17(6):701-709. 10.1016/j.jacr.2020.03.006
- Pourbagheri-Sigaroodi A, Bashash D, Fateh F, Abolghasemi H. Laboratory findings in COVID-19 diagnosis and prognosis. *Clin Chim Acta*. 2020;510:475-482. 10.1016/j.cca.2020.08.019
- Wang T, Du Z, Zhu F, et al. Comorbidities and multi-organ injuries in the treatment of COVID-19. *Lancet*. 2020;395(10228):e52. 10.1016/S0140-6736(20)30558-4
- Simpson S, Kay FU, Abbara S, et al. Radiological Society of North America expert consensus statement on reporting chest CT findings related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA—secondary publication. *J Thorac Imaging*. 2020;35(4):219-227. 10.1097/RTI.0000000000000524
- Gupta S, Hayek SS, Wang W, et al. Factors associated with death in critically ill patients with coronavirus disease 2019 in the US. *JAMA Intern Med*. 2020;180(11):1-12. 10.1001/jamainternmed.2020.3596
- Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature*. 2020;584(7821):430-436. 10.1038/s41586-020-2521-4
- Lippi G, Wong J, Henry BM. Hypertension in patients with coronavirus disease 2019 (COVID-19): a pooled analysis. *Pol Arch Intern Med*. 2020;130(4):304-309. 10.20452/pamw.15272
- Tikellis C, Thomas MC. Angiotensin-converting enzyme 2 (ACE2) is a key modulator of the renin angiotensin system in health and disease. *Int J Pept*. 2012;2012:256294. 10.1155/2012/256294
- Elhadad D, Bronstein Y, Yana M, et al. Characteristics and outcomes of patients infected with SARS-CoV-2 in Israel: correlation between laboratory findings on admission to emergency department and subsequent respiratory failure. *Isr Med Assoc J*. 2020;22(10):539-545.
- Itelman E, Wasserstrum Y, Segev A, et al. Clinical characterization of 162 COVID-19 patients in Israel: preliminary report from a Large Tertiary Center. *Isr Med Assoc J*. 2020;22(5):271-274.
- Sattar SBA, Sharma S. *Bacterial Pneumonia*. StatPearls Publishing; 2020.
- Buscarini E, Manfredi G, Brambilla G, et al. GI symptoms as early signs of COVID-19 in hospitalised Italian patients. *Gut*. 2020;69(8):1547-1548. 10.1136/gutjnl-2020-321434
- Ceylan N, Savas R. Radiological findings of COVID-19 pneumonia. *Eurasian J Pulmonol*. 2020;22(1):19-24. 10.4103/ejop.ejop\_41\_20
- Petrosillo N, Viceconte G, Ergonul O, Ippolito G, Petersen E. COVID-19, SARS and MERS: are they closely related? *Clin Microbiol Infect*. 2020;26(6):729-734. 10.1016/j.cmi.2020.03.026
- Chen Q, Xu L, Dai Y, et al. Cardiovascular manifestations in severe and critical patients with COVID-19. *Clin Cardiol*. 2020;43(7):796-802. 10.1002/clc.23384
- Tao Z, Xu J, Chen W, et al. Anemia is associated with severe illness in COVID-19: a retrospective cohort study. *J Med Virol*. 2021;93:1478-1488. 10.1002/jmv.26444
- Huang H, Cai S, Li Y, et al. Prognostic factors for COVID-19 pneumonia progression to severe symptoms based on earlier clinical features: a retrospective analysis. *Front Med*. 2020;5(7):557453. 10.3389/fmed.2020.557453
- Henry BM, Aggarwal G, Wong J, et al. Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and

- mortality: a pooled analysis. *Am J Emerg Med.* 2020;38(9):1722-1726. 10.1016/j.ajem.2020.05.073
25. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. *N Engl J Med.* 1999;340(6):448-454. 10.1056/NEJM199902113400607. Erratum in: *N Engl J Med* 1999 Apr 29;340(17):1376
26. Melbye H, Hvidsten D, Holm A, Nordbø SA, Brox J. The course of C-reactive protein response in untreated upper respiratory tract infection. *Br J Gen Pract.* 2004;54(506):653-658.
27. Chen W, Zheng KI, Liu S, Yan Z, Xu C, Qiao Z. Plasma CRP level is positively associated with the severity of COVID-19. *Ann Clin Microbiol Antimicrob.* 2020;19(1):18. 10.1186/s12941-020-00362-2
28. Ghahramani S, Tabrizi R, Lankarani KB, et al. Laboratory features of severe vs. non-severe COVID-19 patients in Asian populations: a systematic review and meta-analysis. *Eur J Med Res.* 2020;25(1):30. 10.1186/s40001-020-00432-3
29. National Institutes of Health. *NIH Covid-19 Treatment Guidelines. Clinical Spectrum of SARS-CoV-2 Infection*; 2020. <https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum>

**How to cite this article:** Turan O, Mirici A, Duru Akçalı S, et al. Characteristics of hospitalised COVID-19 patients and parameters associated with severe pneumonia. *Int J Clin Pract.* 2021;75:e14786. <https://doi.org/10.1111/ijcp.14786>