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Relationship between chest computed tomography findings and clinical conditions of coronavirus disease (COVID-19): A multicentre experience

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Abstract

Aims: This study aimed to investigate the clinical and chest computed tomography (CT) features associated with clinical parameters for coronavirus disease (COVID-19) in the capital of Turkey, Ankara.

Materials and methods: Epidemiological, clinical features, laboratory findings and radiological characteristics of 1563 hospitalised patients with COVID-19 in Ankara were collected, reviewed and analysed in this study. The risk factors associated with disease severity were investigated.

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Results: Non-severe (1214; 77.7%) and severe cases (349; 22.3%) were enrolled in the study. Compared with the non-severe group, the severe group were significantly older and had more comorbidities (ie, hypertension, diabetes mellitus, cardiovascular disease and chronic kidney disease). Smoking was more common in the severe group. Severe patients had higher respiratory rates and higher incidences of cough and dyspnoea compared with non-severe patients. Compared with the non-severe patients, the severe patients had increased C-reactive protein (CRP), procalcitonin, neutrophil to lymphocyte ratio (NLR) and CRP/albumin ratio and decreased albumin. The occurrence rates of consolidation, subpleural sparing, crazy-paving pattern, cavity, halo sign, reversed halo sign, air bronchogram, pleural thickening, micronodule, subpleural curvilinear line and multilobar and bilateral involvement in the CT finding of the severe patients were significantly higher than those of the non-severe patients. **Conclusions:** Many factors are related to the severity of COVID-19, which can help clinicians judge the severity of the patient and evaluate the prognosis. This cohort study revealed that male sex, age (≥55 years), patients with any comorbidities, especially those with cardiovascular disease, dyspnoea, increased CRP, D-dimer and NLR, and decreased lymphocyte count and CT findings of consolidation and multilobar involvement were predictors of severe COVID-19.

1 | INTRODUCTION

The outbreak of a novel coronavirus (SARS-CoV-2) in China in December 2019 led to an ongoing pandemic that has profoundly challenged healthcare systems worldwide. As of 2 February 2021, almost 103 million cases of coronavirus disease (COVID-19) have been reported worldwide, and 2.5 million cases have been reported in Turkey.[1] The course of COVID-19 is long, and it is highly contagious even during the incubation period. Presentations of COVID-19 range from asymptomatic/mild symptoms to severe illness and mortality.[2] Wu and McGoogan reported that among 72 314 COVID-19 cases reported to the Chinese Center for Disease Control and Prevention, 81% were mild (absent or mild pneumonia), 14% were severe (hypoxia, dyspnoea and >50% lung involvement within 24-48 hours), 5% were critical (shock, respiratory failure and multiorgan dysfunction) and 2.3% were fatal.[3] Since COVID-19 can cause higher mortality due to respiratory failure or multiple organ failure and there is no cure, it is very important to find related factors of disease severity in clinical practice.[4] Risk factors for severe COVID-19, regardless of age are chronic kidney disease, smokers with structural lung disease, chronic obstructive pulmonary disease (COPD), an immunocompromised state due to solid organ transplant, heart disease, sickle cell disease and type 1 and type 2 diabetes mellitus.[3-6]

There are some cost-effective biomarkers available for assessing the severity of COVID-19. One is the neutrophil to lymphocyte ratio (NLR), which is easily calculated from a routine blood test by dividing the absolute neutrophil count by the absolute lymphocyte count and NLR is indicative of systemic inflammation and the prognostic role has been documented in multiple cancers.[7] C-reactive protein (CRP) is an acute phase sensitive, non-specific inflammatory marker and elevated CRP levels increase modestly and independent of confounding factors risk for both vascular and non-vascular mortality.[8] The other biomarkers are albumin, high D-dimer levels, lymphopenia and high ferritin levels, which appear to be the most promising biomarkers for COVID-19.[4,8]

What's known

- COVID-19 presents an unprecedented challenge to healthcare professionals.
- Clinical findings, RT-PCR tests and radiological findings are complementary for the diagnosis of the disease; however, the clinical severity of COVID-19 infection is variable, presenting as a mild or severe disease.

What's new

- The CRP to albumin ratio(CAR) can be used as a cost-effective biomarker for assessing severity of COVID-19. CAR was higher in severe COVID-19 patients.
- Male sex, age (≥55 years), patients with any comorbidities, especially those with cardiovascular disease, dyspnoea, increased CRP, D-dimer and neutrophil to lymphocyte ratio, and decreased lymphocyte count and CT findings of consolidation and multilobar involvement were predictors of severe COVID-19 cases in Turkey.

Imaging plays an important role in the diagnosis and management of COVID-19 pneumonia. As computed tomography (CT) is commonly available, it is considered the first-line imaging modality for highly suspected COVID-19. CT is also helpful for monitoring clinical changes during treatment. Therefore, CT has been identified as an efficient clinical diagnostic tool for people with suspected COVID-19.[9] It has the potential to identify people with negative reverse transcription–polymerase chain reaction (RT-PCR) assays in whom COVID-19 is highly suspected.[10,11] COVID-19 pneumonia is the most common clinical presentation of COVID-19, and the findings of CT images may reflect the severity of the disease. However, previous studies have presented imaging features from small sample sizes.[12-14] Therefore, in this study, we compared epidemiology, clinical features, laboratory findings and radiological characteristics of 1214 non-severe and 349 severe, hospitalised patients with COVID-19 in Ankara.

2 | MATERIALS AND METHODS

2.1 | Patients and data collection

Thirty-three researchers from five research and training hospitals registered the data of their patients with clinically and/or radiologically confirmed COVID-19 in a database, which was prepared and shared between April and June 2020, during the pandemic. A total of 1871 patients older than 18 years and diagnosed with COVID-19 were registered in the database. Due to insufficient data, 308 patients were excluded from the study. Thus, 1563 patients were finally included in the study.

Severe patients met any of the following conditions: (1) respiratory rate of 30 breaths per minute or greater, (2) finger oxygen saturation of 93% or less in a resting state, (3) arterial oxygen tension/inspiratory oxygen fraction of 300 mm Hg or less and (4) respiratory failure having occurred and mechanical ventilation required.[15] A positive RT-PCR was not required due to the high percentage (15%) of false negatives in our cohort and reported in the literature. [16] Demographic data, smoking history, comorbidities, clinical symptoms and signs, laboratory parameters and radiologic findings were collected within the first 24 hours after hospital admission. All laboratory blood parameters, including complete blood count, blood chemical analysis (including renal and liver function, total protein and albumin), acute phase reactants, CRP and procalcitonin (PCT), were measured on admission.

This study was approved by the Turkish Ministry of Health and the Ethical Committee of Gazi University (Project identification code 363).

2.2 | CT examinations and imaging evaluation

Patients underwent CT scanning on the same day as an initial nasopharyngeal swab test. In each centre, two experienced radiologists evaluated radiological findings related to COVID-19 pneumonia from chest X-rays (CXR) and thoracic CT scans. The initial chest CT images were evaluated for the following characteristics based on Fleischner Society nomenclature recommendations and similar studies: ground-glass opacity (GGO), subpleural sparing, consolidation, vascular enlargement, crazy-paving pattern, air bronchogram, bronchial wall thickening, halo sign, reversed halo sign, air bubble sign, subpleural curvilinear line, nodule, pleural effusion, pleural thickening, cavity, tree-in-bud appearance, lymph node enlargement, interlobular septal thickening and pericardial effusion.[17,18] Also, the frequency of lobe and peripheric or central involvement was recorded.

2.3 | Statistical analysis

All the statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), Version 21.0 (SPSS, Chicago, IL, USA). Categorical variables were described as frequency rates and percentages, and quantitative variables were described using mean (SD) or median (interquartile range) values. The χ^2 test and Fisher's exact test were used for the categorical variables. Quantitative variables were tested for normality using Kolmogorov–Smirnov tests. Normally distributed data were analysed by independent sample t-tests; otherwise, the Mann–Whitney *U* test was used. For logistic regression analysis, quantitative variables were transformed into categorical variables according to their reference ranges. A multivariate logistic regression analysis was then performed to identify the clinical and CT features associated with cases of severe COVID-19. Statistical significance was indicated by a *P*-value $< .05$.

3 | RESULTS

The demographic and baseline characteristics of the study patients are presented in Table 1. A total of 1563 patients were included in the study: 77.7% of them were non-severe cases and 22.3% of them were severe cases. Although 59.2% of all the patients and 62.8% of the severe patients were male, no difference was observed in the proportion of men and women between the two groups. The patient age ranged between 18 and 98 years, and the mean age (±SD) was 51.2 ± 15 years. Compared with the non-severe group, the severe patients were significantly older (mean age, 60.9 years [SD, 17.3] vs 48.4 years [SD, 19.2]; $P < .001$) and had more comorbidities (63.8% vs 36.2%): hypertension, diabetes mellitus, cardiovascular disease, any immunosuppression (glucocorticoids and/or other immunosuppressive treatments) and chronic kidney disease ($P = .000$). Smoking was more common in the severe group (37% vs 27.9%, $P = .003$). The most common symptoms were cough, fever and dyspnoea. Compared with the non-severe group, the severe group had higher respiratory rates and higher incidences of cough and dyspnoea (Table 1). No significant differences in heart rate and arterial pressure were found between the two groups.

TABLE 1 Basic clinical and epidemic characteristics of non-severe and severe group

Parameter	Total (n: 1563)	Non-severe group (n: 1214)	Severe group (n: 349)	*P*
Age, y	51 ± 19.5	48.4 ± 19.2	60.9 ± 17.3	**<.001**
Sex				.138
Female	638 (40.8%)	508 (41.9%)	130 (37.2%)	
Male	925 (59.2%)	706 (58.1%)	219 (62.8%)	
Active smoking	467 (29.9%)	338 (27.9%)	129 (37%)	**.003**
Comorbidity				**.000**
Yes	663 (42.4%)	439 (36.2%)	224 (63.8%)	
No	900 (57.6%)	775 (63.8%)	125 (36.2%)	
Comorbidities				
Hypertension	428 (27.4%)	290 (23.9%)	138 (39.5%)	**.000**
Diabetes mellitus	266 (17%)	165 (13.6%)	101 (28.9%)	**.000**
Cardiovascular disease	215 (13.8%)	124 (10.2%)	91 (26.1%)	**.000**
Chronic kidney disease	60 (3.8%)	37 (3%)	23 (6.6%)	**.004**
Any immunosuppression	57 (3.6%)	32 (2.6%)	25 (7.2%)	**.000**
COPD	15 (1%)	9 (0.7%)	6 (1.7%)	.117
Asthma	11 (0.7%)	8 (0.7%)	3 (0.9%)	.717
Symptoms and signs				**.000**
Yes	1185 (75.8%)	878 (72.3%)	307 (88%)	
No	378 (24.2%)	336 (27.7%)	42 (12%)	
Symptoms				
Cough	683 (43.7%)	506 (41.7%)	177 (50.7%)	**.003**
Dyspnea	475 (30.4%)	301 (24.8%)	174 (49.9%)	**.000**
Fever	634 (40.6%)	485 (40%)	149 (42.7%)	.387
Fatigue	346 (22.4%)	267 (22.3%)	79 (22.8%)	.827
Myalgia	218 (14.1%)	180 (15.1%)	38 (11%)	.065
Abdominal pain/ diarrhoea	138 (8.9%)	104 (8.7%)	34 (9.8%)	.522
Signs				
Respiratory rate	17 (11-48)	15 (11-36)	24 (11-48)	**.004**
Median arterial pressure, mm Hg	90.7 (43-159.3)	90.6 (±11.4)	90.3 (±14)	.304
Heart rate, beats per minute	87.5 (43-143)	86 (±14)	90 (±17.5)	.427

Abbreviation: COPD, chronic obstructive pulmonary disease.
P-value < .05 are indicated in bold.

3.1 | Laboratory parameters

RT-PCR was positive in 66.9% (1046/1563) of all cases, and 269 (25.7%) of these cases had no CT findings of viral pneumonia. Initially, 517 (33.1%) of the patients had a negative RT-PCR. Of these, 11 (2.1%) had no CT findings of viral pneumonia, but their clinical symptoms were compatible and the later second or third PCR test was positive. The rest of the negative cases had positive chest CT patterns consistent with viral pneumonia. Compared with the non-severe patients, the severe patients had increased CRP, PCT, NLR and CRP/albumin ratio (CAR) with decreased albumin (Table 2). Lymphocyte counts were numerically decreased in the severe group; however, this difference did not reach statistical significance. The oxyhaemoglobin saturation of the severe patients was significantly lower than that of the non-severe patients ($P = .002$).

3.2 | Chest CT findings

Chest CT findings were normal in 269 (27.4%) patients, and 1134 (72.6%) patients had CT findings of viral pneumonia. The most

common chest CT features for both groups included consolidation (83.6%), subpleural sparing (76.2%), crazy-paving pattern (34.1%) and cavity (19.7%) (Table 3).

The occurrence rates of consolidation, subpleural sparing, crazy-paving pattern, cavity, reversed halo sign, air bronchogram, halo sign, pleural thickening, micronodule and subpleural curvilinear line in the severe patients were significantly higher than those of the non-severe patients. However, GGO was common in the non-severe group ($P = .000$) (Figures 1 and 2).

Lesions present on the CT images of patients were more likely to have a peripheral distribution (84.6%), bilateral involvement (52.3%) and multilobar involvement (56.2%). Bilateral lung disease and multilobar lung disease were common in the severe group ($P = .000$). Transverse distributions were not significantly different between the two groups ($P = .493$).

3.3 | Factors associated with severe COVID-19

Table 4 shows the results of the multivariate logistic regression analyses of the relationships with severe COVID-19. The clinical factors of male sex, age (≥55 years), patients with any comorbidities, especially those with cardiovascular disease, dyspnoea, increased CRP, D-dimer and NLR, and decreased lymphocyte count were risk factors for severe COVID-19. CT findings of consolidation and multilobar involvement were imaging features of severe COVID-19.

4 | DISCUSSION

This report, to the best of our knowledge, is the first retrospective large-scale cohort study to describe the epidemiological and clinical characteristics of COVID-19 patients in Turkey.

COVID-19 presents an unprecedented challenge to healthcare professionals; however, within a short time, collaborative efforts and data sharing have led to recommendations for managing patients with COVID-19. Clinical findings, RT-PCR tests and radiological findings are complementary for the diagnosis of the disease; however, the clinical severity of COVID-19 infection is variable, presenting as a mild or severe disease.[2-4]

In this study, we found that the severe patients were older and had more underlying diseases than the non-severe patients. Goyal et al retrospectively evaluated 393 patients with a median age of 62.2 years, of whom 60.6% were male: the most common presenting symptoms were cough (79.4%), fever (77.1%) and dyspnoea (56.5%).[19] In a study by Huang et al, most of the infected patients were men (73%); the median age was 49 years and common symptoms at the onset of illness were fever (98%), cough (76%) and myalgia or fatigue (44%).[12] According to surveillance data reported to the Center for Disease Control and Prevention, as of 30 May, 2020, among COVID-19 cases, the most common symptoms were fever, cough or shortness of breath (70%); muscle aches (36%) and headache (34%).[20] In our study, 59.2% of all patients were men; the mean age was 51 ± 19.5 years and the most common symptoms were cough (43.7%), fever (40.6%) and dyspnoea (30.4%).

TABLE 2 Laboratory findings between non-severe and severe group

Parameter	Total (n: 1563)	Non-severe group (n: 1214)	Severe group (n: 349)	*P*
Results of PCR assay				.402
Positive	1046 (66.9%)	818 (67.4%)	228 (65.3%)	
Negative	517 (33.1%)	396 (32.6%)	121 (34.7%)	
Oxyhaemoglobin saturation, %	94.76 (78-100)	96 (93-100)	89 (78-96)	**.002**
White blood cell count, $\times 10^9$/L	7.31 (0.8-54.3)	7.05 (1.17-30.6)	8.22 (0.9-26.7)	.644
Increased	120 (7.7%)	72 (5.9%)	48 (13.6%)	.524
Decreased	326 (20.9%)	271 (22.3%)	55 (15.6%)	.740
Neutrophil count $\times 10^9$/L	5.19 (1.1-26.7)	7.05 (1.1-23.9)	8.22 (1.4-26.7)	.216
Increased	299 (19.1%)	213 (17.5%)	86 (24.6%)	.233
Lymphocyte count, $\times 10^9$/L	1.51 (0.1-24.9)	1.55 (0.10-24.9)	1.35 (0.10-7.2)	.218
Decreased	700 (44.8%)	511 (42.1%)	189 (54.2%)	.265
NLR	5.11 (±7.19)	4.44 (±6.52)	7.49 (±8.81)	**.000**
C-reactive protein, mg/L	46.9 (0.1-335)	39.5 (0.13-159.9)	72.4 (0.2-444)	**<.001**
Increased	1119 (71.6%)	812 (66.9%)	307 (88%)	**<.001**
Albumin g/dL	3.7 (1.1-7.9)	3.8 (±0.62)	3.4 (±0.57)	**.000**
CAR	15.24 (±25.29)	12.75 (±22.96)	23.71 (±30.94)	**.000**
Procalcitonin, ng/mL	1.03 (0-13.91)	0.768 (0.001-5.5)	1.96 (0.05-9.54)	**<.001**
Increased	269 (17.2%)	127 (10.5%)	142 (40.9%)	**<.001**

Abbreviations: CAR, C-reactive protein to albumin ratio; NLR, neutrophil to lymphocyte ratio.

P-value < .05 are indicated in bold.

TABLE 3 Radiologic features between non-severe and severe group

Parameter	Total (n: 1563)	Non-severe group (n: 1214)	Severe group (n: 349)	*P*
Chest radiography				**.000**
Normal	277 (61.7%)	218 (83.8%)	59 (31.2%)	
Abnormal	172 (38.3%)	42 (16.2%)	130 (68.8%)	
CT				**.000**
No CT findings of viral pneumonia	269 (27.4%)	248 (23.3%)	21 (6.2%)	
Any CT findings of viral pneumonia	1134 (72.6%)	816 (76.7%)	318 (93.8%)	
Frequency of lobe involvement				
Bilateral lung disease	816 (52.3%)	548 (41.3%)	268 (76.8%)	**.000**
Unilobar lung disease	224 (14.3%)	190 (15.7%)	34 (9.7%)	**.005**
Multilobar lung disease	878 (56.2%)	596 (49.2%)	282 (80.8%)	**.000**
Right upper lobe	1558 (99.7%)	1210 (99.7%)	348 (99.7%)	1.000
Right middle lobe	637 (40.9%)	423 (34.9%)	214 (61.5%)	**.000**
Right lower lobe	885 (56.8%)	605 (50%)	280 (80.5%)	**.000**
Left upper lobe	687 (44.1%)	467 (38.6%)	220 (63.2%)	**.000**
Left lower lobe	819 (52.6%)	561 (46.4%)	258 (74.4%)	**.000**
Transverse distribution				.493
Central	240 (15.4%)	190 (15.7%)	50 (14.3%)	
Peripheral	1323 (84.6%)	1024 (84.3%)	299 (85.7%)	
CT features				
Consolidation	981 (83.6%)	694 (80.5%)	287 (92.3%)	**.000**
Subpleural Sparing	909 (76.2%)	623 (71%)	286 (90.5%)	**.000**
Crazy-paving pattern	400 (34.1%)	265 (30.8%)	135 (43%)	**.000**
Cavity	224 (19.7%)	134 (16.1%)	90 (29.7%)	**.000**
Reversed halo sign	208 (18%)	138 (16.4%)	70 (22.4%)	**.020**
Air bronchogram	201 (17.2%)	132 (15.4%)	69 (22.3%)	**.008**
GGO	179 (15.8%)	154 (18.4%)	25 (8.5%)	**.000**
Halo sign	179 (15.3%)	110 (12.8%)	69 (22%)	**.000**
Pleural thickening	168 (14.7%)	117 (14%)	51 (16.7%)	**.000**
Micronodule	85 (7.5%)	46 (5.5%)	39 (12.9%)	**.000**
Subpleural curvilinear line	22 (1.9%)	10 (1.2%)	12 (3.9%)	**.006**
Architectural distortion	203 (17.9%)	116 (14%)	87 (28.7%)	**.000**
Vascular enlargement	109 (9.6%)	81 (9.7%)	28 (9.3%)	.909
Air bubble sign	75 (6.5%)	61 (7.2%)	14 (4.6%)	.136
Bronchial wall thickening	41 (3.6%)	28 (3.3%)	13 (4.3%)	.473
Pleural effusion	77 (6.7%)	50 (6%)	27 (8.9%)	.108
Tree in bud	67 (5.9%)	35 (4.2%)	32 (10.6%)	.260
Lymph node enlargement	9 (0.8%)	5 (0.6%)	4 (1.3%)	.260

Abbreviations: CT, computed tomography; GGO, ground glass opacity.
P-value < .05 are indicated in bold.

Various publications have found that severe disease is independent of age and predominantly observed in adults with comorbidities, such as cardiovascular disease, diabetes mellitus, hypertension, COPD and malignancies.[21] In a meta-analysis of 3027 patients by Zheng et al, hypertension, diabetes, cardiovascular disease and respiratory disease were significantly higher in critical/mortal patients compared with noncritical patients, with odds ratios of 2.72, 3.68, 5.19 and 5.15, respectively.[22] In our study, at least one comorbidity was present in 663 (42.4%) patients, with the most common comorbidities being hypertension (27.4%), diabetes mellitus (17%) and cardiovascular disease (13.8%). The presence of comorbidities, such as hypertension, diabetes mellitus, cardiovascular disease, chronic kidney disease and any immunosuppression, was significantly higher in the severe disease group.

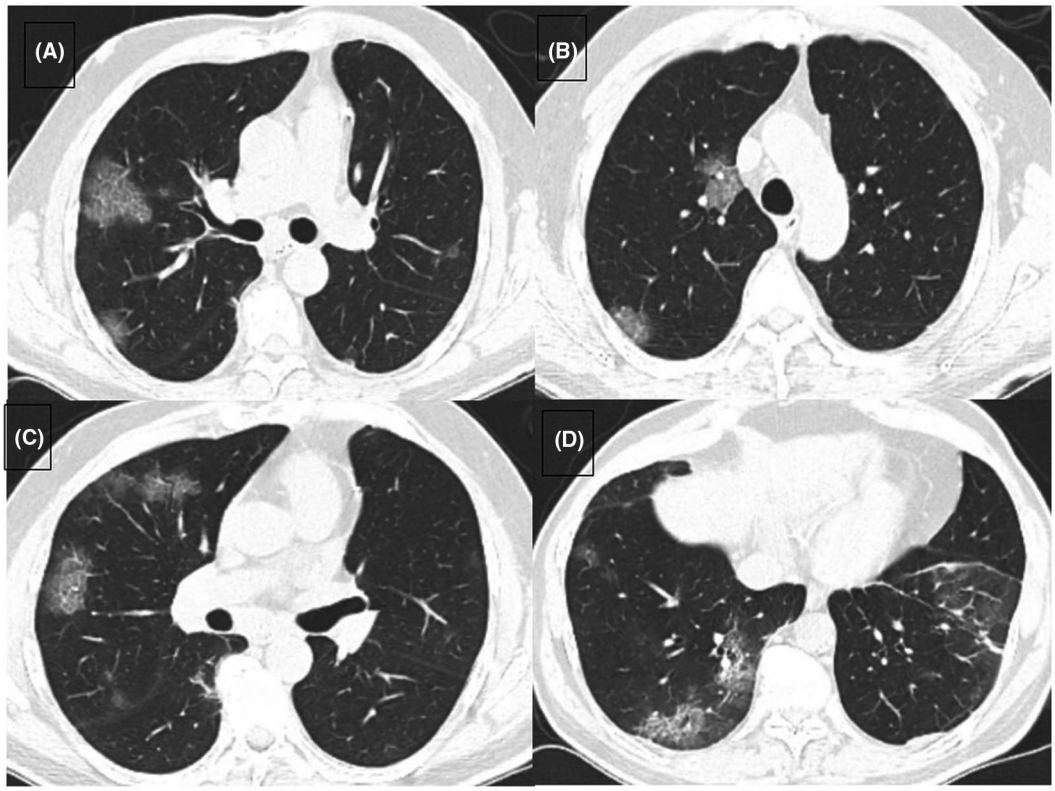

FIGURE 1 Chest CT findings of non-severe COVID-19 pneumonia, a 57-year-old man with dyspnoea and with no comorbid disease. Axial CT images (A-D) showed predominantly peripheral and patchy ground-glass opacities

In our cohort, age ≥55 years was a risk factor for severe disease. Similar to our study, Xie et al evaluated 168 fatal COVID-19 cases and reported that the median age was 70 years, and 95.8% of these patients were older than 50 years.[23]

When assessing a patient with COVID-19, laboratory and radiologic features can be useful to clinicians for management and close monitoring. The average incubation time of COVID-19 was around 6.4 days (0-24 days).[24] This period affects days illness onset and detection of the viral RNA.

A RT-PCR test of a nasopharyngeal or throat swab to detect viral RNA remains the most accurate diagnostic test to determine hospitalisation and isolation for individual patients. However, its lack of sensitivity and relatively long processing were detrimental to the control of the COVID-19 epidemic.[5] Yang et al, investigated the diagnostic accuracy of different respiratory specimens (sputum, nasal- throat swabs, bronchoalveolar lavage fluid) between the mild and severe novel coronavirus pneumonia. Viral RNAs could not be detected in the upper respiratory samples from some severe cases and the positive rate of collected specimens differed according to days after illness onset. They concluded that CT scan could serve as an important make up for the diagnosis of novel coronavirus pneumonia in suspected patients especially those with negative viral RNA.[25] In our study, the positive rate of RT-PCR assay for nasopharyngeal swab samples was 66.9% (95% CI, 56%-62%), which was consistent with same report (30%-60%).[25] Days after illness onset and the exposure history information of patients are missing in our study. This information may have an impact on our negative RT-PCR results.

Laboratory parameters that contribute to the follow-up of COVID-19 patients play an important role in identifying severe and non-severe cases. An increase in neutrophils, a decrease in lymphocytes and a rise in CRP levels are associated with an increase in disease severity in patients with COVID-19.[26] A descriptive study from China reported depleted lymphocyte count levels in the majority of COVID-19 patients.[4] In our study, lymphocyte counts were numerically decreased in nearly half of the patients, but the difference between the non-severe and severe groups did not reach statistical significance. Tan et al, studying the characteristics of severe COVID-19 patients, found that CRP level was significantly increased during the initial stage in severe COVID-19 patients. They concluded that CRP was an early biomarker for predicting the severity of COVID-19 with good performance.[27] The latest research on COVID-19 has suggested that CRP levels differed significantly between a deceased group and a surviving group and may serve as a potential marker for prognosis.[28] In our study, CRP levels were significantly higher in the severe group.

Additionally, severe disease can clearly be distinguished by a raised NLR. A retrospective study found a significantly higher NLR in severe COVID-19 patients and concluded that NLR, a well-recognised biomarker, is found to be high in widespread inflammatory conditions and can be used to reflect disease severity.[29] In a cohort study by Liu et al, NLR was significantly associated with an

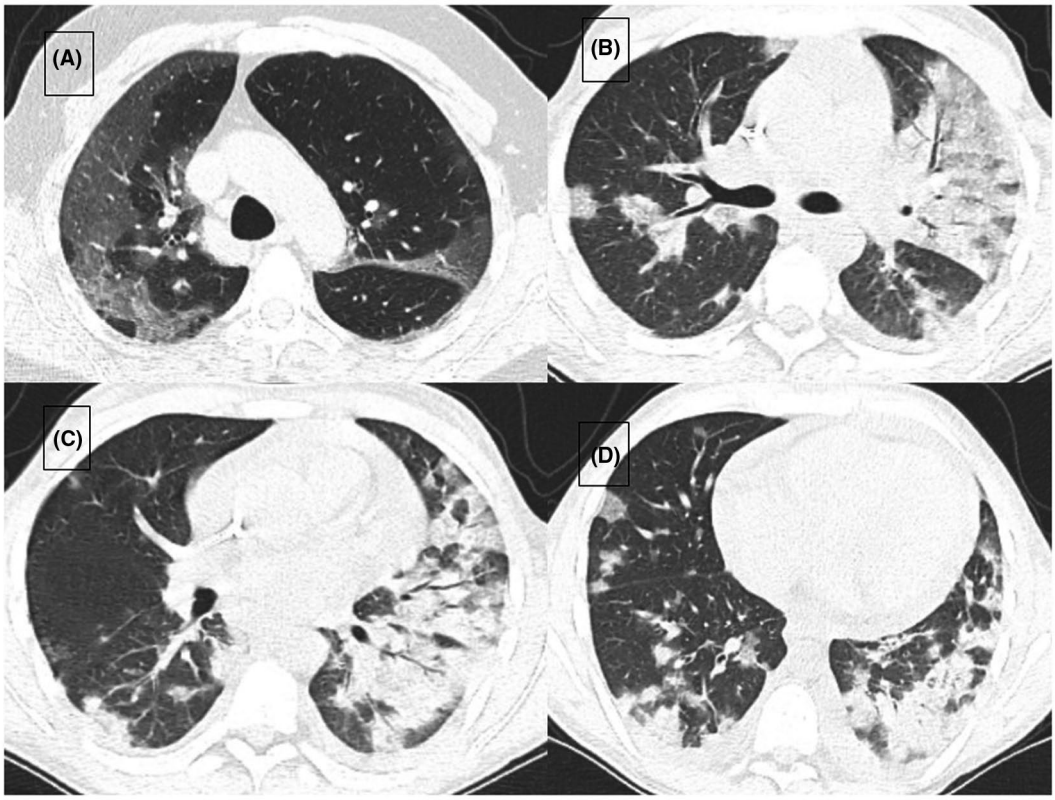

FIGURE 2 Chest CT findings of severe COVID-19 pneumonia, a 21-year-old man with dyspnoea and with chronic renal disease. Axial CT images showed A; ground-glass opacities predominantly at upper lobes and B-D; diffuse extent of consolidation with air-bronchogram predominantly at left

TABLE 4 Multivariate logistic regression analysis of clinical and CT features for severe COVID-19

Variables	Adjusted OR (95% CI)	*P*-value
Male sex	1.50 (1.01-2.13)	.04
Age > 55 y	1.57 (1.01-2.50)	.00
Comorbidity	1.72 (1.02-2.88)	.04
Cardiovascular disease	1.62 (1.07-2.44)	.02
Dyspnea	2.34 (1.63-3.36)	.00
NLR	1.02 (1.00-1.04)	.04
C-reactive protein increased	1.01 (1.00-1.02)	.02
D-Dimer increased	1.00 (1.00-1.00)	.41
Lymphocyte count decreased	1.35 (1.00-1.81)	.05
Consolidation	1.66 (1.02-2.08)	.04
Multilobar involvement	2.75 (1.56-4.56)	.00

Abbreviation: NLR, neutrophil to lymphocyte ratio.

increased risk of all-cause death during hospitalisation in COVID-19 patients.[30] Qin et al reported that severe cases of COVID-19 were likely to have higher neutrophil counts but lower lymphocyte counts compared with non-severe patients (5.5 vs 3.2; $P < .001$), thus the NLR tended to be higher in patients with a severe infection.[29] These findings are consistent with our results. We found a higher NLR in the severe group compared with the non-severe group: 7.49 vs 4.44, respectively.

CAR, as a novel parameter, has been shown to be more accurate than albumin and CRP alone in predicting the overall prognosis of certain clinical conditions, such as infection, malignancy and critical illness, but its clinical importance has not been elucidated as a biomarker for COVID-19.[31-33] In our study, the CAR was 12.75 (±22.96) in the non-severe group and 23.71 (±30.94) in the severe group, and the difference was statistically significant. Nevertheless, we could not compare this finding with data published in the literature since, to the best of our knowledge, no studies have investigated the CAR for disease severity in COVID-19 patients.

The Fleischner Society for thoracic radiology stated that chest radiography can be insensitive in mild or early COVID-19 infection.[34] A retrospective case series of 64 patients hospitalised with COVID-19 infection in Hong Kong found that 31% had normal chest radiographs on admission.[35] In our study, 28.7% of the patients had CXR on admission, and 61.7% of them were normal.

Radiological imaging, particularly chest CT, plays an important role in the diagnosis of COVID-19 pneumonia, and characteristic imaging findings are helpful for diagnosis and guidance in the differentiation of alternative diagnoses. Chest CT is more sensitive with higher accuracy and accessibility than chest radiography and RT-PCR assay in the detection of COVID-19 pneumonia and may be preferred in certain clinical settings.[35]

The most common CT findings of COVID-19 pneumonia include multifocal and bilateral GGO and/or consolidation in the peripheral, posterior and lower lobes of the lungs. Halo or reverse halo sign, vascular enlargement, crazy-paving pattern, pleural thickenings, pleural effusion and subpleural lines are less common CT findings.[34-38] In most cases, the disease and CT findings are mild and moderate and heal completely, but severe cases may develop acute respiratory distress syndrome or pulmonary fibrosis and lung volume loss.[36-38] Yu et al observed that more severe disease had more lung segment involvement, more extensive opacities and frequent findings of interlobular septal thickening, air bronchograms and even pleural effusions.[39] In a study by Zhao et al, the typical imaging features were GGO (86.1%), mixed GGO and consolidation (64.4%), reticulation (48.5%) and vascular enlargement (71.3%) that might have been caused by an acute inflammatory response.[9]

In this study, we found that the most common CT findings were consolidation, subpleural sparing, crazy-paving pattern and cavity formation, and GGO was common in the non-severe group. The occurrence rates of consolidation, subpleural sparing, crazy-paving pattern, cavity, reverse halo sign, air bronchogram, halo sign, pleural thickening, micronodule and subpleural curvilinear line in the severe patients were significantly higher than those in the non-severe patients. Bilateral lung disease and multilobar lung disease were common in the severe group.

Some chronic illnesses may contribute to COVID-19 severity. Immune response to viral infections is impaired in diabetes patients, and diabetes and hypertension damage vascular structures.[40,41] Heart failure patients express significantly higher levels of angiotensin-converting enzyme-2(ACE2) at both mRNA and protein levels, which partially explains the severe presentation of COVID-19 in these patients.[42] The prevalence of asthma and COPD in reported cases of COVID-19 is conflicting. While asthma is a negative factor in some studies, in others it is not.[43,44] This is also the case with COPD.[45-47] In a meta-analysis, Zheng et al showed that males aged over 65 who were smokers with comorbidities, such as hypertension, diabetes, cardiovascular disease or respiratory diseases, and laboratory examinations such as WBC, aspartate aminotransferase, creatinine, hypersensitive cardiac troponin, PCT, lactatedehydrogenase and D-dimer could affect the prognosis of COVID-19.[22] In another meta-analysis, Figliozzi et al found that increased age (≥50 years), male sex, comorbidities (ie, hypertension, diabetes, COPD and a history of cardiovascular disease), acute organ injury, lymphocytopenia and raised D-dimer levels were risk factors for mortality.[48]

In our study, male sex, age (≥55 years), patients with any comorbidities, especially those with cardiovascular disease, dyspnoea, increased CRP, D-dimer and NLR, and decreased lymphocyte count were risk factors for severe COVID-19. However, asthma and COPD were the least common comorbid diseases and not associated with severe disease. This may have been due to the low number of patients with asthma and COPD.

This study has some limitations. First, it was a retrospective study, the data of the two groups were not balanced, and the sample size of the severe group was relatively small. A second limitation is that clinical and laboratory data were limited during this urgent period and within the first 24 hours after hospital admission which is a bit short, and indicators such as mortality need further observation.

However, this study has provided the best available evidence to date that shows the usefulness of the CAR for clinical assessment of COVID-19 severity and the study's sample size was sufficient to provide information about patients with COVID-19 in Turkey.

5 | CONCLUSIONS

In conclusion, this large cohort study of COVID-19 cases in Turkey revealed epidemiological, clinical and radiological characteristics. The clinical factors of male sex, age (≥55 years), patients with any comorbidities, especially those with cardiovascular disease, dyspnoea, increased CRP, D-dimer and NLR, and decreased lymphocyte count were risk factors for severe COVID-19. CT findings of consolidation and multilobar involvement were imaging features of severe COVID-19 in Turkey.

DISCLOSURE

There are no conflicts of interest of the authors regarding this manuscript.

DATA AVAILABILITY STATEMENT

Data is transparent and available upon request.

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