Original Article

CT Characteristics of Coronavirus Disease 2019 Pneumonia and Its Association with C-Reactive Protein, Erythrocyte Sedimentation Rate and Gender

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Abstract

Background: This research intended to investigate the characteristics of COVID-19, accurately evaluate radiological findings, and compare it with laboratory evidence of coronavirus. **Materials and Methods:** A retrospective study of 120 consecutive cases with a mean age of 55.9 ± 15.82 years and laboratory-confirmed COVID-19 pneumonia was performed. On admission, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels were tested. Computed tomography (CT) findings and scored pulmonary involvement were evaluated. **Results:** An elevated level of CRP and mildly raised ESR was seen in all patients. ESR showed a meaningful difference between both genders ($P < 0.05$). Ninety-four (78.3%) patients showed peripheral pulmonary lesions and 119 patients had ground-glass opacity (99.2%), 110 (92.4%) had consolidation, and 9 patients (7.5%) had linear opacities. Of 120 cases, 25 (20%) had bronchial changes, 25 (20%) had air bronchogram, 11 (9.2%) had bronchial distortion, and 2 had mediastinal lymphadenopathy. The CT scores in males and females were 17.41 ± 4.86 and 14.65 ± 4.96, respectively with a significant difference between both genders ($P = 0.001$). CT score difference was significant between both genders ($P = 0.01$). The largest lung lesion diameter in both sexes (male: 46.0725.75 and female: 57.9131.14) showed a meaningful difference. CRP ($r = 0.10$; $P < 0.05$) and ESR ($r = 0.15$; $P < 0.05$) were correlated with the CT scores. **Conclusion:** the results indicated that the infection involved lung parenchyma and interstitium. CRP and ESR levels were correlated with lung lesions and showed positive performance in predicting severity and disease monitoring.

Keywords: *Chest computed tomography scan, COVID-19, C-reactive protein*

Introduction

In December 2019, a cluster of pneumonia cases of unexplained sources happened in Wuhan, Hubei Region, China.[1] Because of the high-throughput sequencing technology, the pathogen that led to this series of pneumonia was quickly recognized.[2,3] This novel betacoronavirus is now identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[4] The disease is also named 2019 novel coronavirus disease (COVID-19).[4] Like other coronaviruses, human-to-human transmission of COVID-19 pneumonia has been confirmed in several reports.[1] Therefore, the World Health Organization has recently declared the COVID-2019 a public health emergency of international concern.[5] Although SARS-CoV-2 is a member of the coronavirus group of viruses, it is more outmost from SARS-CoV and Middle East respiratory syndrome coronavirus.[2] It is considered being a novel sort of betacoronavirus that infects individuals and, based on the present pandemic, is more contagious than SARS-CoV.[6] Evidence indicates that the elderly with comorbidities were susceptible to develop acute respiratory distress syndrome.[7,8] COVID-19 pneumonia is a health necessity because of its high infectiousness and serious case mortality in seriously ill patients.[7] Clinical monitoring and proper management programs were essential to ameliorate case fatality.[9] Computed tomography (CT) played an essential role in determining the disease.[6,10] Although most patients show mild symptoms, COVID-19 causes mass casualty and poses major challenges to the global health-care system.[11] Early diagnosis

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of severe illness is pivotal to initial classification and improvement of patients' prognosis. The early identification of cases who will develop ill could aid the allocation of the limited medical resources to patients in need of aggressive treatment. Accordingly, better investigation is required on immediate diagnosis and prognosis. Differences in the number of lymphocytes, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) have been described in COVID-19 patients, but investigation about their relation with disease severity needs more validation.[8,11] CRP levels can be utilized in the initial recognition of pneumonia, and patients with severe pneumonia had high CRP levels.[12] Hence, it is essential to distinguish the clinical laboratory biomarkers that will provide primary and differential diagnosis of SARS-CoV-2 infection and anticipate the intensity of the inflammation. We evaluated the correlation between CRP and ESR levels and lung lesions to evaluate useful indicators for predicting disease severity and better clinical management.

Materials and Methods

In this retrospective study, measurements were performed by searching for CT images of the lungs and biochemical blood tests including CRP and ESR in the Hospital Information System and Picture Archiving and Communication System at Razi Educating Hospital, Ahvaz, Iran. Razi Medical Center is the pointed hospital that treats COVID-19 for adults in Ahvaz. All patients with COVID-19 engaged in this research were diagnosed based on the WHO for provisional instruction.[13] The survey was approved by the IRCCS Bioethics Committee (protocol number: IR.AJUMS.REC. approval date July 12, 2020) and patient consent form was waived.

In the Razi Educating Hospital, a total of 120 patients were retrospectively enrolled between 5 August and 10 September 2020, who were identified as subjects infected with SARS-COV-2.

All cases with COVID-19 recruited in this research were diagnosed corresponding to World Health Organization's interim guidance.[14] Laboratory results: C-reactive protein, ESR, leucocytes, neutrophils, and lymphocytes at admission were collected. Exclusion criteria were as follows: cases with chest CT images that did not show pneumonia at admission, when the time between chest CT scan and the RT-PCR test was longer than 7 days, and those patients with insufficient data.[15] The radiographic scores for COVID-19 patients were blindly assessed by two expert radiologists. We performed CT protocol and chest CT scores based on previous researches.[16,17] In specific, 5 scores were determined corresponding to visual assessment of the involvement of each of the five lung lobes separately: 0 point, no involvement; 1 point, <5% involvement; 2 points, 25% involvement; 3 points, 26%–49% involvement; 4 points, 50%–75% involvement; and 5 points, over 75% involvement.[18]

SPSS version 24.0.0 statistically analyzed attained data (SPSS Inc., Chicago, IL, USA). Pearson's Chi-square test was used to analyze categorical variables as appropriate and was reported by frequencies and percentages. Continuous variables were represented as means and standard deviations or medians and interquartile ranges based on variable distributions. Continuous variables were interpreted by Student's *t*-test as appropriate. The receiver operating characteristic curves were created to assess the sensitivity and specificity for the prediction of COVID-19 severity. $P < 0.05$ was considered statistically significant.

Results

One hundred-twenty affected patients by SARS-CoV-2 as of September 12, 2020, with a mean age of 55.9 ± 15.82 years (range: 22–83 years, 55 females and 65 males) were retrospectively enrolled in the present survey. The duration from inception of symptoms to hospital admission was 4–5 days. The first routine laboratory blood tests of all admitted patients were performed. An elevated level of CRP (female: 50.89 ± 7.36 and male: 49.0923 ± 3.69) (mg/L) and mildly raised ESR (female: 58.94 ± 4.19 and male: 47.1077 ± 3.16) (mm/h) was seen in all patients, respectively. ESR level showed meaningful difference between both genders ($P = 0.03$) [Table 1].

Chest computed tomography findings

As shown in Table 2, the CT presentations of COVID-19 pneumonia comprised lung changes, ground-glass opacity (GGO), consolidation, GGO plus a reticular pattern, bronchial alterations (air bronchogram and bronchus distortion), and pleural changes. Degree of involvement of each lung lobe in addition to overall extent of lung involvement was measured by means of a total severity score. The distribution of pulmonary lesions in COVID-19 pneumonia patients was peripheral in 94 (78.3%) patients. In terms of lung changes, chest CT showed that 119 patients had GGO (99.2%), 110 (92.4%)

Table 1: In this table, we utilized a nonparametric test, and using Mann-Whitney test, the variables of C-reactive protein, erythrocyte sedimentation rate, diameter of the largest lung lesion, and computed tomography score were measured in both genders

Variable	Mean±SD		*P*
	Female	Male	
CRP (mg/L)	50.89±54.62	49.09±29.81	0.38
ESR (mm/h)	58.94±30.8	47.1±25.51	0.03
Diameter of the largest lung lesion	46.07±25.75	57.91±31.14	0.02
CT score	14.65±4.96	17.41±4.86	0.001

There is a significant difference between the ESR, diameter of the largest lung lesion, and CT score ($P<0.05$). CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, CT: Computed tomography, SD: Standard deviation had consolidation, 25 (20%) had bronchial changes, 25 (20%) had air bronchogram, 11 (9.2%) had bronchial distortion, and 9 (7.5%) had linear opacities [Table 2]. Only two patients had mediastinal lymphadenopathy on CT images. The CT scores of the bilateral lungs in males and females were 17.41 ± 4.86 and 14.65 ± 4.96, respectively (mean CT score in both sexes was 16.15 ± 0.08), and showed a significant difference between both genders ($P = 0.001$) [Table 1]. The results, as shown in Table 3, indicate the frequency and percentage of CT scores in the present study. Statistical Chi-square test showed a significant difference in CT score between both genders ($P = 0.01$) [Table 4]. From these data, we can observe that 5.5% of females had CT score 0–5 and 10.9% had CT score 20–25, while 1.5% of males had CT score 0–5 and 24% had CT score 20–25 ($P < 0.05$).

Table 2: Chest computed tomography findings of coronavirus disease 2019 pulmonary lesions

CT feature	Number of patients (*n*=120), *n* (%)
GGO	119 (99.2)
Consolidation	110 (92.4)
Bronchial changes	25 (20.8)
Air bronchogram	25 (20.8)
Bronchial distortion	11 (9.2)
Linear opacities	9 (7.5)
Peripheral	94 (78.3)

GGO: Ground-glass opacity, CT: Computed tomography

Table 3: The frequency and percentage of computed tomography scores in coronavirus disease 2019 patients

CT score	Frequency	Percentage	Valid percentage	Cumulative percentage
0-5	4	3.3	3.3	3.3
5-10	6	5.0	5.0	8.3
10-15	44	36.7	36.7	45.0
15-20	41	34.2	34.2	79.2
20-25	25	20.8	20.8	100.0
Total	120	100.0	100.0	

CT: Computed tomography

Table 4: The comparison of computed tomography score between the two sexes

	CT Score					Total
	0-5	5-10	10-15	15-20	20-25	
Sex						
Female						
Count	3	3	28	15	6	55
% within Sex	5.5%	5.5%	50.9%	27.3%	10.9%	100.0%
Male						
Count	1	3	16	26	19	65
% within Sex	1.5%	4.6%	24.6%	40.0%	29.2%	100.0%
Total						
Count	4	6	44	41	25	120
% within Sex	3.3%	5.0%	36.7%	34.2%	20.8%	100.0%

The largest lung lesion diameter was calculated in both sexes (male: 46.07 ± 25.75 and female: 57.91 ± 31.14), and this variable showed a meaningful difference in both genders ($P = 0.02$) [Table 1].

Table 5 shows the correlation between gender and chest CT findings in COVID-19 patients. What is interesting in these data is that there is no significant relationship between gender, consolidation, and GGO, but there is a significant relationship between gender, bronchial distortion ($P = 0.05$), air bronchogram ($P = 0.04$), and bronchial changes ($P = 0.04$). Figure 1 shows CT features and lungs tissue changes caused by SARS-CoV-2 pneumonia in five patients.

Correlation analysis between laboratory biomarkers and computed tomography scores

At present, CT is the principal imaging modality to evaluate disease severity. Correlation analysis revealed that CRP ($r = 0.10$; $P = 0.001$) and ESR ($r = 0.15$; $P = 0.001$) were positively correlated with the CT scores [Figure 2].

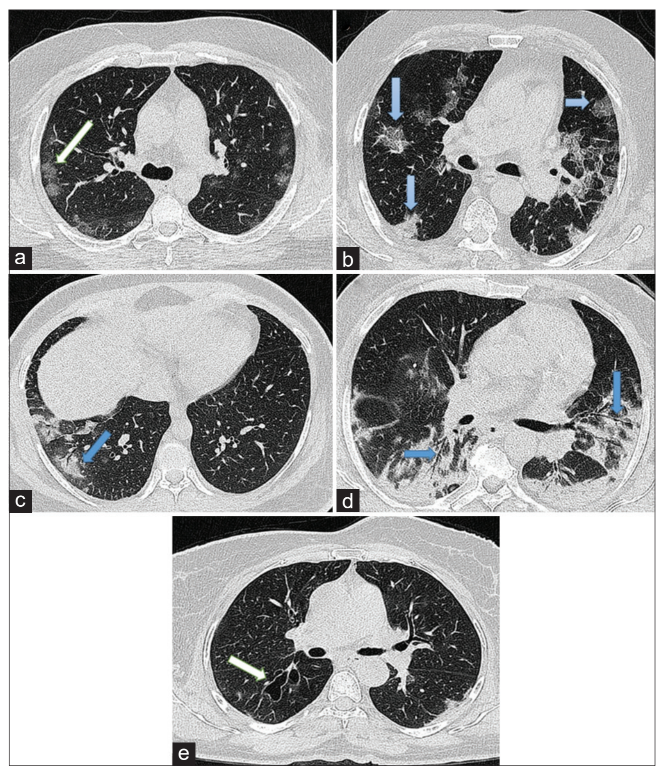

Figure 1: High resolution chest CT features indicating lung changes caused by SARS-CoV-2 pneumonia in five cases. (a) Axial CT image obtained without intravenous contrast injection in a 48-year-old man demonstrates bilateral ground-glass opacities in upper lobes with a rounded morphology (white arrow). (b) Axial CT image obtained in a 67-year-old man shows bilateral ground-glass and consolidative opacities with a peripheral distribution (blue arrows). (c) CT image in a 25 -year-old woman reveals consolidative changes in right lower lobe, while left lung was normal (blue arrow). (d) CT image obtained in a 57 -year-old man 9 days from symptom onset shows airbronchogram with bilateral lung involvement in both lower lobes (blue arrows), subpleural line in right lung is evident. (e) Axial CT image in an 80 -year-old woman exhibits bronchiectasis associated in right lower lobe on day 11 after onset of symptoms (white arrow)

The study results propose that a significant increase in CRP and ESR is a sign of lung deterioration process.

As shown in Table 1, the variables of CRP, ESR, and diameter of the largest lung lesion and CT score were measured in both genders. The results showed that there is a significant difference between the ESR (*P* = 0.03), diameter of the largest lung lesion (*P* = 0.02), and CT score (*P* = 0.001).

In the other analysis, the relationship between age, CRP, ESR, diameter of the largest lung lesion, and CT score was evaluated. The results showed that there is no significant relationship between age and other variables. In another part of the study, the relationship between variables of age, ESR, GGO, CRP, and CT score with CT features was calculated using Mann–Whitney analysis. As shown in Table 6, there is a significant relationship between CRP, ESR, CT score, and consolidation (*P* = 0.001), moreover, bronchial distortion and age revealed a significant correlation (*P* = 0.02).

Table 5: Correlation between gender and computed tomography features

Variable	Frequency, *n* (%)		*P*
	Female	Male	
Bronchial distortion			
Yes	2 (3.6)	9 (13.8)	0.05
No	2 (3.6)	107 (89.1)	
Air bronchogram			
Yes	7 (12.7)	18 (27.7)	0.04
No	48 (87.3)	47 (72.3)	
Bronchial changes			
Yes	7 (12.7)	18 (27.7)	0.04
No	48 (87.3)	47 (72.3)	
Consolidation			
Yes	51 (94.4)	59 (90.8)	0.4
No	3 (5.6)	6 (9.2)	
GGO			
Yes	55 (100)	64 (99)	0.3

Chi-square test showed that there is no significant relationship between gender, GGO, and consolidation, but there is a significant relationship between gender, bronchial distortion, air bronchogram, and bronchial changes. Yes: Existence and no: Nonexistence. GGO: Ground-glass opacity

Discussion

The re-emergence of COVID-19 pandemic in autumn and winter in Iran (third peak), as well as the outbreak of seasonal diseases such as avian flu in this region, led us to more accurately evaluate radiological findings and compare

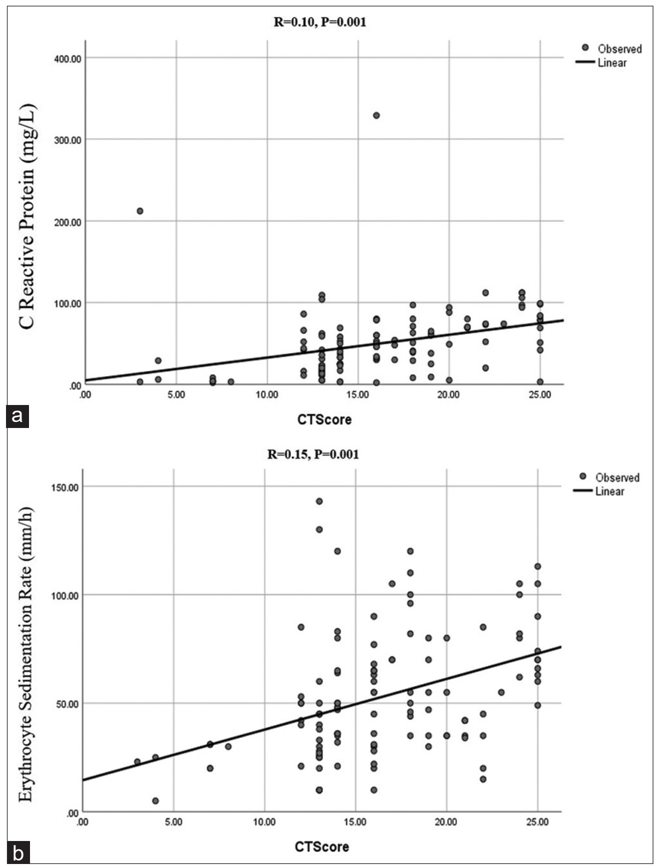

Figure 2: Correlation analysis between CT scores and biomarkers (a and b)

Table 6: The above table compares the mean of C-reactive protein, age, erythrocyte sedimentation rate, and computed tomography score and their effects on computed tomography findings using Mann-Whitney test

Variable	Age	CRP	ESR	CT score	Values
Consolidation	55.9±16.01	50.98±40.88	54.17±28.14	16.7±4.73	Mean
	0.619	0.029	0.003	0.001	*P*
GGO	55.79±15.73	50.08±42.95	52.33±28.61	16.14±5.10	Mean
	0.13	0.68	0.47	0.78	*P*
Bronchial changes	59.92±16.01	48.96±38.88	53.80±33.74	16.4±5.92	Mean
	0.17	0.96	0.97	0.87	*P*
Air bronchogram	59.92±16.01	48.96±38.88	53.80±33.74	16.4±5.92	Mean
	0.17	0.96	0.97	0.87	*P*
Bronchial distortion	64.18±14.02	61.9±40.12	62.81±38.24	17.09±5.88	Mean
	0.02	0.19	0.36	0.75	*P*

As seen, there is a significant relationship between CRP, ESR, CT score, and consolidation, moreover, bronchial distortion and age showed a significant correlation. GGO: Ground-glass opacity, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, CT: Computed tomography it with laboratory evidence of coronavirus. Another aim of this study was to compare its findings with other parts of the world in terms of ethnic medicine. The worldwide incidence of the SARS-CoV-2 pandemic has brought serious burdens to the medical organization. It is essential to distinguish COVID-19 patients who might become severely ill, which would considerably promote the control of the pandemic and the amelioration of the prognosis of patients in finite medical and vaccine resources. Compared with laboratory tests such as RT-PCR, and blood plasma biomarkers, chest CT scan may be a better, valid, effective, and fast technique to recognize and evaluate COVID-19, exclusively in the region influenced by the pandemic. In the present study, we analyzed the chest CT features and scores of patients with COVID-19 and evaluated the correlation between CRP and ESR with CT findings in both sexes in a southwest population of Iran.

In our study, severe patients were more likely to develop an increase in CRP and ESR, which is a sign of lung deterioration process. The present findings are in consistent with previous studies that severe patients have higher rates of CRP, ESR, and CT scores.[13]

In the case of CT scan abnormalities, GGO (100%) and consolidation (92.4%) were the most significant radiologic findings, demonstrating that the virus may invade the terminal respiratory bronchi or alveoli at any stage of illness. The results of the present research are in contrast with Ding *et al*. findings,[16] which could be due to the latest stage of illness in these patients. In the study ahead, 100% of cases confirmed to have COVID-19 with RT-PCR tests exhibited positive chest CT findings, which was higher than that described by Guan *et al*. (86.2%).[19] Evidences of other studies reveal that, for patients with negative RT-PCR tests, over 70% had typical CT manifestations.[20] Because of the overlap of CT imaging presentations between COVID-19 and other viral pneumonia, false-positive patients of COVID-19 can be diagnosed with chest CT scan. CT scoring could indicate the intensity of various stages of this illness. The results of the present research illustrated that males had higher CT score than females, and 29% of males showed CT score 20–25. In supporting this phenomenon, we assumed that female sex hormones such as progesterone and estrogen could reduce the amount of inflammation in the lung tissue in SARS-CoV-2-affected patients. Evidence suggests the effective role of female hormone receptors in the development of innate and adaptive immunity to viral respiratory infections in women.[21,22] Studies in animal models have shown that progesterone treatment reduces pneumonia, improves function, and repairs lung tissue, which leads to faster recovery without affecting the viral load.[23]

About respiratory diseases, chest CT scan can give a reference for defining the type of pathogen with special diagnostic benefits, also can anticipate the prognosis of patients.[24] Based on Nanshan study, the sensitivity of COVID-19 diagnosis with CT scan alone was 76.4%, and the application of CT scan in COVID-19 was appraised as helpful.[25] Disadvantages of CT scan include increasing the radiation absorbed dose of people and imaging center staff, protective equipment, and the transportation of COVID-19 emergency patients. Therefore, a basic index with useful correlation with respiratory pathological alterations is needed.

In another part of the study, CRP and ESR levels were evaluated and compared with age, sex, and chest CT findings. C-reactive protein levels are correlated with the body inflammation condition and can trigger the complement system and increase phagocytosis. The findings of the present study showed that CRP level is not affected by factors such as age and sex, which confirm previous studies.[26] Studies show that CRP levels can be applied for early diagnosis of pneumonia and patients with severe pneumonia have high CRP levels.[13] ESR might serve as a less expensive choice to CRP as an indicator of systemic inflammation in pulmonary disease, and increases in response to rising serum levels of acute-phase proteins, fibrinogen, and immunoglobulins.[27] The result of the present survey revealed that there is a significant correlation between the ESR, diameter of the largest lung lesion, and CT score, while Tan *et al*.[15] reported that CRP changes were more sensitive to the disease status. The present research results support the findings of Matsumoto's report, which showed the value of CRP levels in severe pneumonia.[28] Therefore, in this study, we concluded that significant increase in CRP and ESR can be used as a signal of lung deterioration in areas where imaging equipment is not available. The discrepancy between the CT findings, such as GGO, in the present investigation and previous research may be that patients underwent imaging at different stages of the disease.

The present research is not devoid of limitations. First, only 120 COVID-19 patients were included. Second, some biomarkers such as D-dimer, LDH, and pro-inflammatory cytokines including IL-1 and IL-6 were not enrolled in the survey.

Conclusion

Chest CT findings for patients with SARS-CoV-2 pneumonia indicated that the infection has a varied pattern, with both lung parenchyma and interstitium involved. At any stage of COVID-19, CRP and ESR levels were correlated with lung lesions. We found that the amount of CT score was different between two genders. Importantly, CRP and ESR were correlated with disease progress and lung involvement, and showed positive performance in predicting severity and disease monitoring in COVID-19.

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Conflicts of interest

There are no conflicts of interest.

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