

Spectrum of ground-glass opacities in chest CT of COVID-19 patients in Karbala

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Objective To describe the ground-glass opacities (GGO) seen in chest CT scans of COVID-19 patients and to estimate the association between these opacities and the time of clinical presentation.

Methods A cross-sectional study involving 81 COVID-19 confirmed patients in Imam Al-Hussein Medical city in Karbala-Iraq during the period from March 1 to April 20, 2020. Chest CT scan findings were evaluated by two radiologists and categorized accordingly. Chi-square test was used for statistical analysis and a p-value of less than 0.05 was considered statistically significant.

Results The mean age \pm standard deviation of patients was 53.5 ± 17.1 years, with male predominance as 63 (77.8%) of cases were males. Nearly half of the patients were presented within the second week of starting the sign and symptoms. GGO was present in 79 scans (97.5%), followed by consolidation opacity in 29 patients (35.8%). Four types of GGO were described. Bilateral multiple subpleural GGO was the most prevalent type. There was a significant association between late time of patient presentation and more extensive GGO type.

Conclusion Chest CT scan is valuable in diagnosis and management of COVID-19 cases. The presence of GGO in CT scan of a patient that previously had no chest illness is highly suggestive of COVID-19 disease, different types of GGO were seen. Bilateral confluent type of GGO is associated with more serious and delayed status and warns the need for intensive care unit admission.

Keywords COVID-19, Chest CT, Corona COVID-19, Ground-glass opacity, RT-PCR, Consolidation.

Introduction

Novel coronavirus disease 2019 (COVID-19) is a serious contagious disease result from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), initially diagnosed in Wuhan, Hubei, China in December 2019, then a rapid epidemic of coronavirus 2019 infection occurs. On March 11, 2020, The World Health Organization (WHO) declared it a pandemic. It's almost the most serious pandemic in recent history. Whereas *far as writing this article, it affects more than 4 million people all over the world with more than 250,000 deaths.*¹⁻³

The RT-PCR test is the reference standard for the definitive diagnosis of COVID-19 infection. Despite the indicators of its lower sensitivity and specificity at levels 30-60%.^{4,5} Further, the RT-PCR test is not easily available and need a relatively time consuming for processing. Meanwhile, the early diagnosis of COVID-19 infection is a cornerstone in the management, by which the complications and the numbers of contacts can be reduced. The CT scan suitable alternative where it is available and can be done in a relatively short time as it was in previous SARS epidemics accordingly.^{6,7} However, the CT can be normal especially in the early period of the disease as reported.⁸⁻¹⁰

Most COVID-19 patients are presented with signs and symptoms of upper and/or lower respiratory tract infection. Severe respiratory distress may occur, fever reportedly being the most common presentation. The reference standard for its diagnosis was the real-time reverse transcription-polymerase chain reaction (RT-PCR). Chest computed tomography (CT) reported having higher sensitivity than PCR as high as 98% in the early detection of COVID-19 patients.^{10,11} Main CT findings were peripheral ground-glass opacities (GGOs), consolidation opacities, and crazy paving appearance,^{9,12} gradually CT became an important part of the official diagnostic criterion of COVID-19, CT provides information about early

diagnosis, differential diagnosis, clinical classification, and can assess disease progression. Furthermore, it detects pulmonary complication and follows up after discharge, the most important findings were:

- The GGO: which is an area of increased attenuation in the lung parenchyma, with the preservation of bronchial and vascular margins.
- Consolidation: which is an area of increased attenuation in the lung parenchyma, which obscures the pulmonary vessels and bronchiolar walls. And
- Crazy-paving alternating areas of GGO with thickened interlobular septa and intralobular lines in between.^{10,13,14}

In Iraq, the first confirmed case was reported in Al-Najaf city on February 24, 2020, and by April 30, more than 2000 cases were confirmed including more than 90 deaths.^{11,15} The first case of COVID-19 reported in Karbala was on March 3. And Karbala is well-known as a religious city that is located in the middle of Iraq with a population of nearly 1.5 million peoples. The holy city is attended by tens of million visitors each year, and several big mass gathering visits including the Arbaeen visit, which represents the biggest annual mass gathering in the world occur in Karbala.¹⁶

This study aims to describe CT scans' findings of COVID-19 patients, particularly GGOs, and to estimate the association between these opacities and the time of clinical presentation.

Patients and Methods

A cross-sectional study conducted during the period March 1 to April 20, 2020, at the diagnostic imaging department in Al-Imam Al-Hussein medical city in Karbala\Iraq, which is the biggest hospital in the governorate with more than 500 beds and represent the referral site for other hospitals and the one that receives all COVID-19 cases.

Patients with positive CT scan findings and positive RT-PCR were included in the study. Those patients were referred from the respiratory clinic, for suspicion with COVID-19 infection. They had signs and symptoms of upper and/or lower respiratory tract infection. An unenhanced CT scan was done for all patients routinely following the guidelines of Karbala Health Directorate for management of COVID-19. Where every suspected case or symptomatic person who had contact with COVID-19 patient or travel to an endemic area should manage by complete blood count lab test, RT-PCR, and CT scan. So, 81 patients with a positive CT scan and a positive PCR test were included out of total 86 diagnosed cases including 6 deaths, 5 patients were excluded, 2 with heart failure, 2 with pulmonary tuberculosis, and 1 was a known case of Churg-Strauss syndrome.

Chest CT examinations were performed by using a multidetector-row scanner (SOMATOM Definition Edge Siemens Medical System, Germany). The examination was carried out without a patient preparation, in supine, hands up position, from the upper neck to the upper renal poles depending on the scanogram, in a single breath-hold cluster, with 5-mm collimation, reconstruction at 1 mm interval and energy level of 120 Kv and 200–250 mA. The CT scan results were evaluated by two independent radiologists to decrease interobserver bias.

Ethical approval was obtained from the research ethics committee in Karbala Health Directorate. Further, the patient's names and personal information were kept confidential.

Demographic information of patients and CT findings were entered and analyzed using Statistical Package for Social Sciences (SPSS, Version 21). Data were expressed as frequencies and percentages while age was expressed as mean and standard deviation (SD). Chi-square test was used for statistical analysis and a probability (p) value of less than 0.05 was considered statistically significant.

Results

A total of 81 COVID-19 confirmed patients with positive CT scans were included in the study. Their age ranged from 12 to 83 years with a mean \pm SD of 53.5 ± 17.1 years. The male to female ratio was 3.9:1 where 63 (77.8%) of the patients were men. All patients had symptoms at the onset of the disease, including fever, cough, and shortness of breath.

Complete blood count tests were performed for all patients. 23 (28.4%) patients had leukopenia, 66 (81.5%) had lymphocytopenia, while C-reactive protein (CRP) was elevated in 56 (69.1%) patients. Nearly half of patients, 41 (50.6%), were presented within the first week of symptoms' appearance and half of them 40 (49.4%) were presented late in the second week as shown in Fig. 1.

GGOs were present in 79 scans (97.5%). According to the distribution and severity of GGO, four configurations were described as shown in Figs 2,3 and 4 as follows:

Type 1: Unilateral single GGO in 17(21.52%) patients.

Type 2: Bilateral multiple discrete GGO in 21(26.58%) patients.

Type3: Bilateral multiple predominantly subpleural GGO in 25(31.65%) patients, and

Type 4: Bilateral diffuse confluent patches of GGO in 16(20.25%) patients.

There was a significant association (p -value <0.001) between the type of GGO and the time of clinical presentation,

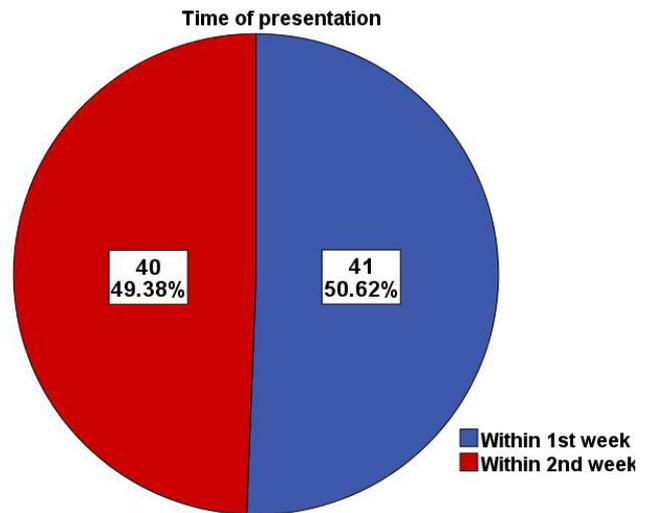


Fig. 1 Pie chart of patient's presentation time within first and second weeks.

most patients with unilateral single GGO (Type 1) and bilateral subpleural GGO (Type 3) presented in the first week. While patients presented in second week exhibiting bilateral multiple discrete GGO (Type 2) and bilateral confluent GGO (Type 4), as shown in Table 1.

The second most common finding was consolidation opacities (as seen in Fig 5a,b) were seen in 29 (35.8%) patients. The crazy-paving appearance was seen only in two CT scans represent 2.4%, also there was a significant association between the presence of consolidation and time of presentation (p -value < 0.001) as shown in Table 1.

Pleural effusion was seen only in two (2.4%) very ill patients, who sooner died.

Discussion

Chest CT is a mainstay in the diagnosis and management protocol of COVID-19 cases in Iraq. As the RT-PCR is limited to certain centers and with a limited number of tests per day. Especially in the beginning of the spread of disease in Iraq, where CT is highly sensitive and almost all cases with positive

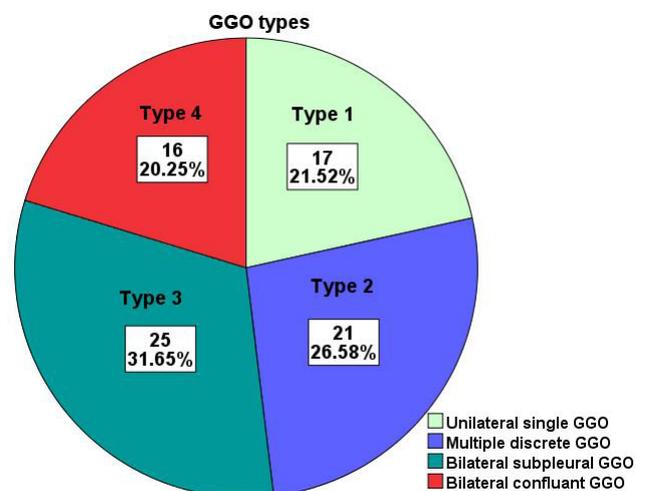


Fig. 2 Categories of GGO finding among 79 patients.

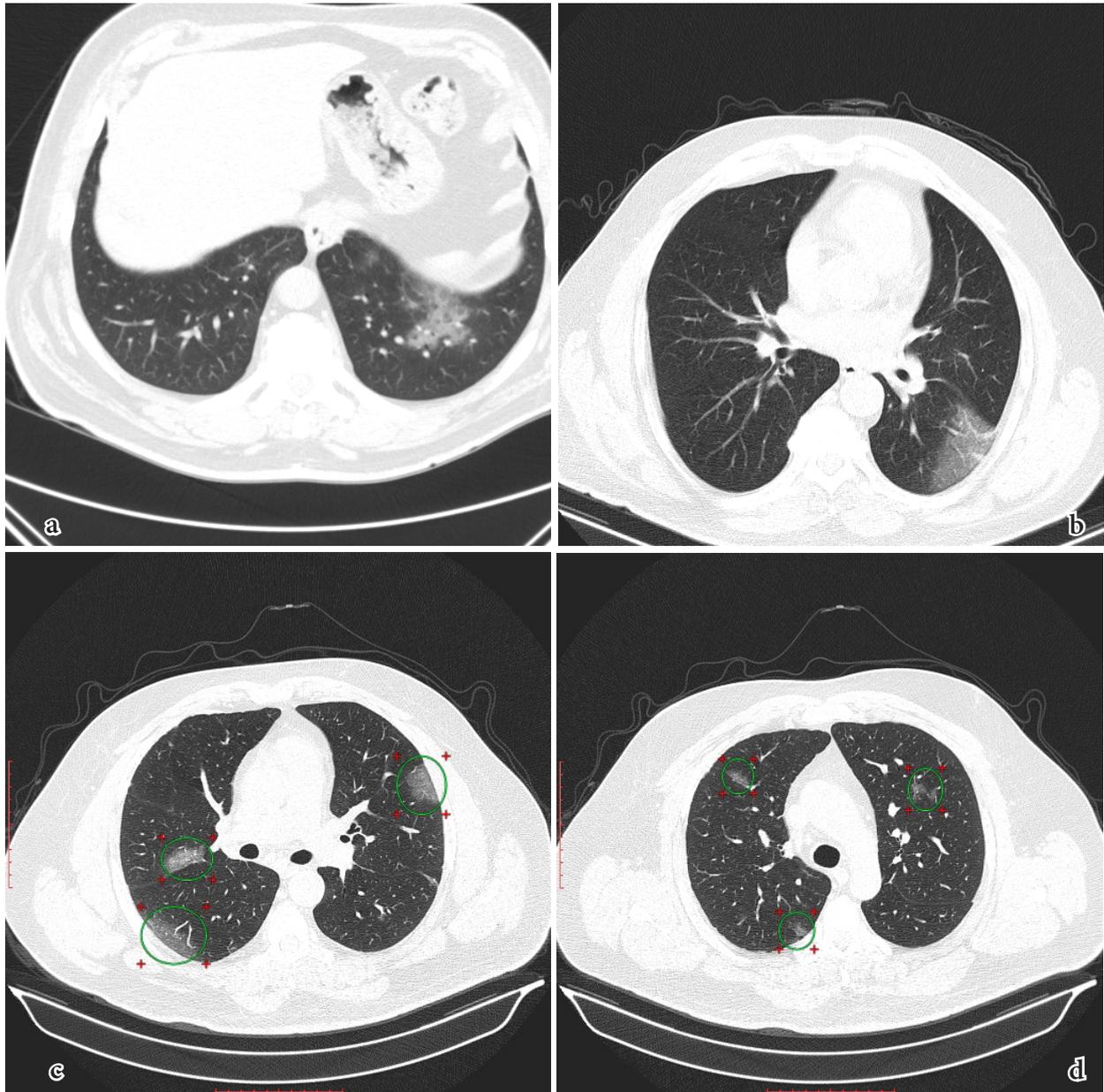


Fig. 3 Axial CT scans lung window showing different types of GGO: (a, b) left lower lobe unilateral ground-glass pulmonary opacity (type 1). (c, d) Shows bilateral discrete foci of ground-glass opacities (Type 2).

RT-PCR had positive findings, and as CT is more sensitive than RT-PCR.^{10,12} Perhaps, some of those with positive CT findings who test negative for PCR might have false-negative RT-PCR. Anyhow, cases with negative RT-PCR were excluded from the study.

The higher male to female ratio of nearly fourfold increase in the current study could be attributed to the social customs in our region, where men can move freely and spend more time outside doors, unlike women. This male predominance is higher than the 60% male involvement reported by a meta-analysis and the 68% reported by Chen et al.^{17, 18} Further, males had shown higher severity and fatality with COVID-19 infection.¹⁹ This was related to social causes including higher cigarette smoking rates among males as well as genetic or hormonal causes.¹⁷⁻¹⁹

Regardless of how the respiratory system is affected, the pathological process involves alveolar edema, proteinaceous

exudate, focal reactive hyperplasia of pneumocytes with patchy inflammatory cellular infiltration, and multinucleated giant cells.^{20,21} These changes are still not sufficient to fill the smallest air space (alveoli). In CT, this process is seen as a mild increase attenuation of lung parenchyma what is called GGO.^{22,23}

According to the severity and distribution of these opacities, four patterns of GGO were identified and highlighted by many researchers.^{10,24-26} The unilateral GGO pattern seen in first week seems to be increased in number and becoming multiple discrete GGO by second week, while the bilateral subpleural patches of GGO seen in first week seems to change to diffuse confluent patches of GGO as most of these seen in second week, this agreed by Han et al.²⁷ The most extensive diffuse confluent patches of GGO which is associated with consolidation representing a late disease, and usually resulting in a bad outcome where six of the cases with Type 4 had been

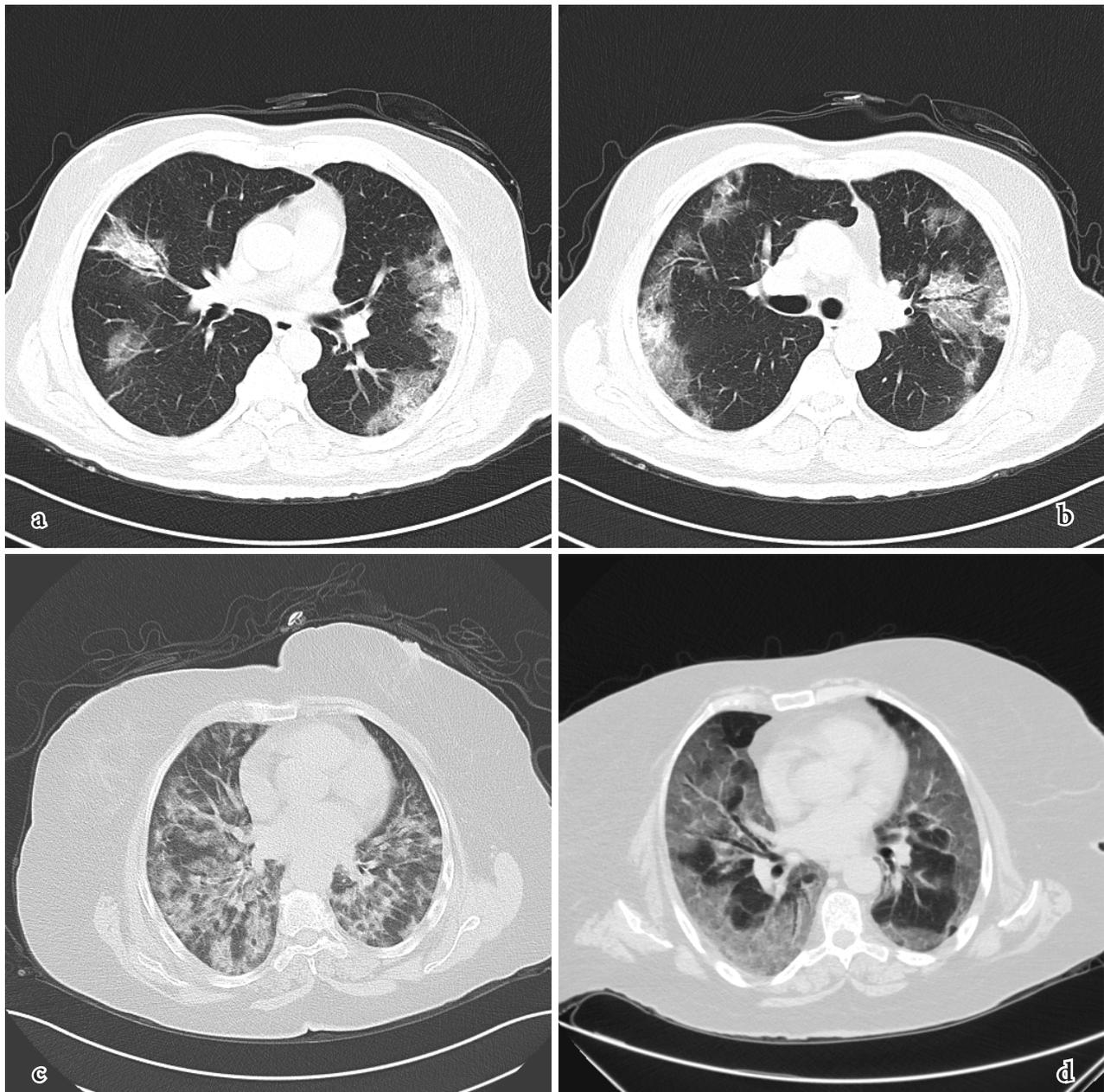


Fig. 4 Axial CT scans lung window showing different types of GGO; (a, b) show bilateral subpleural patchy ground-glass pulmonary opacity (Type 3), (c, d) show bilateral diffuse confluent ground-glass opacities (Type 4).

intubated and then lost. These results are in agreement with what other researchers who had highlighted that the single GGO on the initial CT scan can indicate early-phase of disease while advance-phase disease reflected by CT signs of aggravation perhaps within the second week.²⁸⁻³⁰

So, on the era of COVID-19 pandemic, patients with no previous medical history of chest illness, diagnosed having any type of GGO in chest CT should carry the possibility of COVID-19 until prove otherwise.

The number of cases in Kerbala and Iraq, in general, is probably higher than what was reported. As a significant percentage of the people are afraid of consequences of diagnosis with COVID-19 including being quarantined with their families and relative. As well as, the stigmatization effect of being infected with COVID-19 is present to a certain level. Further,

this could explain why nearly half of patients being diagnosed lately and many being presented at a late stage and denying any history of travel to endemic countries or contact with COVID-19 patients. A related issue noticed that patients presented earlier within first week were more identified to have a phobia of being sick with COVID-19. While others presented late within the second week were complaining from serious respiratory symptoms.

Consolidation was the second most common CT finding, that been seen in nearly third of patients, of those (93.1%) were presented within the second week. So, consolidation might be considered as a sign of severe disease, which probably will be in need to be admitted to intensive care, and this agrees with Das et al.³¹ While pulmonary cavitation, and significant lymphadenopathy that were characteristic of previous SARS

Table 1. Association between time of patient's presentation and both consolidations and the type of GGO.

		Presentation			p value
		In 1st week	In 2nd week	Total	
Consolidation	No consolidation	39 75.0%	13 25.0%	52 100.0%	< 0.001
	Consolidation	2 6.9%	27 93.1%	29 100.0%	
Total		41 (50.6%)	40 (49.4%)	81 100.0%	
	Type of GGO*				< 0.001
Type of GGO*	Unilateral single patch	17 100.0%	0 0.0%	17 100.0%	< 0.001
	Bilateral multiple discrete patches	2 9.5%	19 90.5%	21 100.0%	
	Bilateral multiple subpleural	21 84.0%	4 16.0%	25 100.0%	
Total	Bilateral diffuse confluent patches	1 6.3%	15 93.7%	16 100.0%	
		41 51.9%	38 48.3%	79* 100.0%	

*GGO was present among 79 patients

disease,³² had not been recognized with patients with COVID-19 in Kerbala and this agrees with Bernheim et al.⁸

Conclusion

Chest CT scan is valuable in diagnosis and management of patients with COVID-19 infection. The presence of GGO in CT scan of patient that previously had no chest illness is highly suggestive of COVID-19 disease. Different types of GGO are

seen; bilateral confluent type of GGO is associated with more serious and delayed status and warns the need for intensive care unit management.

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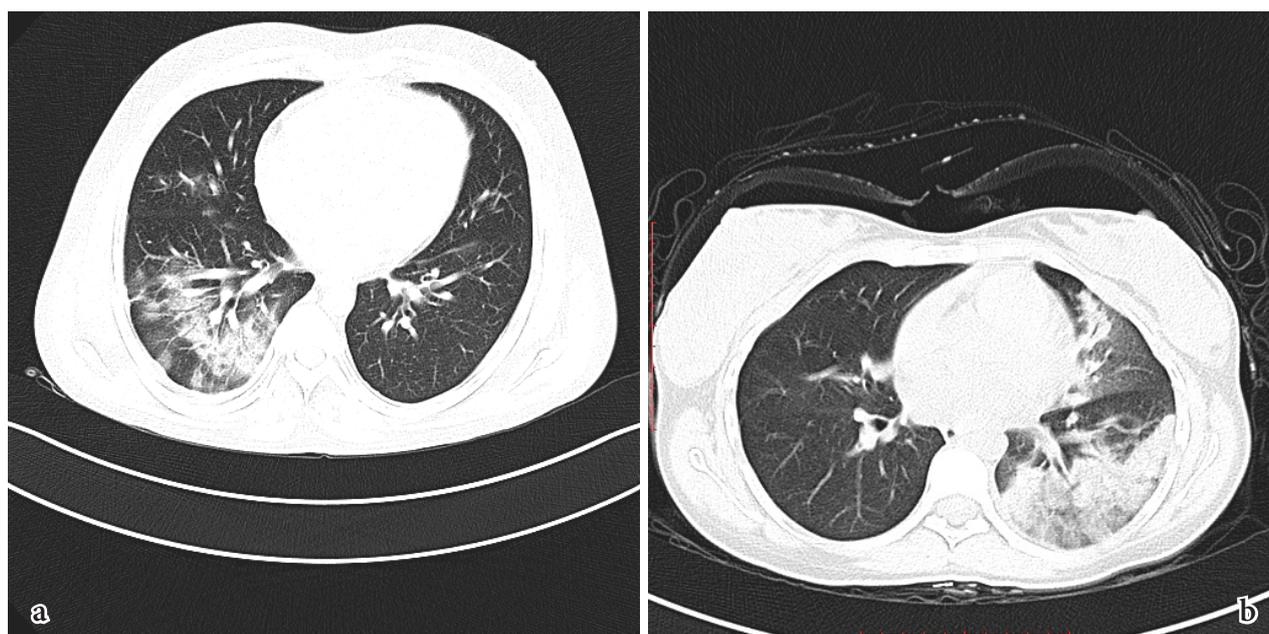


Fig. 5 Axial thin-section unenhanced CT scan images (a) shows right lower lobe consolidation pulmonary opacity. (b) Shows left lower and upper lobes consolidation pulmonary opacities.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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