Nat. Volatiles & Essent. Oils, 2021; 8(4): 12685-12700

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Natural Volatiles & Essential Oils

The Study Of The Correlation Between Clinical Characteristics And Chest CT Findings In Symptomatic And Asymptomatic Patients Affected With Covid-19

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Abstract

Background: COVID-19 can be symptomaticand asymptomatic in patients. The evaluation and treatment of asymptomatic patients is a critical component in halting or slowing the spread of the disease.

Objectives: To investigate the correlation between clinical characteristics and chest CT findings in symptomatic and asymptomatic Covid-19 patients.

Methods: A total of 458 COVID-19 patients, positive chest CT and RT-PCR were included retrospectively. Demographic, signs, and symptoms as well as CT imaging characteristics were recorded and compared between symptomatic and asymptomatic patients who had no comorbidities.

Results: Of the 458 SARS-CoV-2 cases, 383 (83.6%) were symptomatic and 75 (16.4%) were asymptomatic cases. There was no significant gender difference between the two groups. Compared to the symptomatic group, the asymptomatic patients were younger (P = 0.000). The most common symptoms among the symptomatic patients

were fever 306 (66.8%) and cough 242 (52.8%). CT imaging revealed Ground-Glass Opacities (GGO) was the most common pattern inboth asymptomatic and symptomatic patients(69.3% and 62.7%, respectively)and it was present alone or with consolidation. Symptomatic patients showed considerably higher peripheral and central distribution, compared to asymptomatic patients, 200 (52.2%) vs 20 (26.7%). While, the peripheral distribution was significantly higher in asymptomatic patients, 53 (70.7%) vs 177 (46.2%).

Conclusions: Asymptomatic COVID-19 infections may be silent with significant clinical risk due to possible delayed symptoms and a high proportion of positive chest CT imaging findings. A combination of RT-PCR testing and chest CT can be used for the optimum identification of infected asymptomatic patients.

Summary: A combination of RT-PCR and chest CT scan distinguished the presence of chest findings in symptomatic and asymptomatic covid-19 patients who had no comorbidities.

Keywords: Chest CT, COVID-19, SARS-CoV-2, symptomatic patients, asymptomatic patients.

Highlights

- Fever and cough are the most frequent symptoms in SARS-CoV-2 symptomatic patients.
- Younger patients had significantly higher asymptomatic infections than elderly patients.
- Bilateral GGO is often peripherally located in asymptomatic patients.
- Bilateral GGO was shown as a mixed peripheral and central distribution in symptomatic patients.
- Reversed halo signs and crazy paving were observed significantly in symptomatic patients.

Abbreviations

COVID-19(Coronavirus Disease 2019),CT (Computed Tomography), GGO (Ground-Glass Opacities),RT-PCR(Reverse Transcription Polymerase Chain Reaction), SARS-Cov-2 (Severe Acute Respiratory Syndrome Coronavirus 2).

Introduction

The novel coronavirus disease (COVID-19 or SARS-CoV-2 infection) pandemic is currently a major global issue (1). SARS-CoV-2, which causes a severe acute respiratory syndrome, is evolving and expanding rapidly and its full spectrum of effects is becoming evident, from mild respiratory tract illness to acute respiratory distress syndrome (ARDS), leading to multiple organ failure and death (2). Typical COVID-19 symptoms involve fever, cough, muscle soreness, chest pain, andsputum. However, asymptomatic

COVID-19 accounts for approximately 1-73% of all reported cases (3). In asymptomatic individuals, the great majority of infections are still unrecorded. Containment and mismanagement depend, in the meantime, strongly on rigorous isolation that relies on symptoms to diagnose or to self-identify in asymptomatic patients (4). As evidenced by several previous studies, patients with asymptomatic COVID-19 infection are likely to cause infection and have a non-neglective role in the epidemic's spread (5-7).Currently, RT-PCR is considered as a gold standard diagnostic test to diagnose SARS-CoV-2(8). However, the positive rate of COVID-19 nucleic acid testing by RT-PCR is only about 30–50% (9). The high proportion of SARS-CoV-2 false-negative RT-PCR results definitely adds to the challenge of treating the present COVID-19 outbreak, since misdiagnosed patients may miss the best time for adequate treatment, causing disease spread (10). COVID-19 patients frequently have chest CT imaging abnormalities (11). Chest CT is highly suggested in suspected SARS-CoV-2 patients due to the major involvement of the respiratory system for both initial evaluation and follow-up (12). Recent SARS-CoV-2 research reported the RT-PCR sensitivity is as low as 70% (13,14) because of difficulties with sample collection, handling, and performance of the kit (15), while CT sensitivity is 97% (16,17). Additionally, the CT examination is quite significant not only in diagnosing SARS-CoV-2 but also in evaluating therapy efficacy and monitoring the progression of the disease (16). The clinical characteristics and chest CT findings of symptomatic infection of COVID-19 who had no comorbidities have not been fully studied and rarely compared with asymptomatic infection. This study aimed to fill the gap via comparison of clinical characteristics and chest CT findings of symptomatic and asymptomatic SARS-CoV-2 individuals confirmed with RT-PCR with no comorbidities using the single isolation hospital data. By this, our study is the first in our country to analyze the chest CT results of symptomatic and asymptomatic COVID-19 patients. We believe that the findings could provide sufficient evidence for the management of asymptomatic infection with COVID-19.

Materials and methods

1. Patients

In this retrospective cross-sectional study, the written approval of the local ethics committee was obtained, and formal informed consent was waived. There was no potential risk to patients. Patients with SARS-CoV-2 were admitted to our hospital which was designated to isolate and treat COVID-19 patients from 20 November 2020 to 9 March 2021. In this study, a chest CT scan was performed either because of a contact history with patients who had been diagnosed or suspected of having SARS-CoV-2 or because of a high exposure risk due to travel to high prevalence regions. Before CT scanning, all of the

confirmed patients of SARS-CoV-2 were defined as a positive RT-PCR test using pharyngeal swab specimens (18) obtained from the central laboratory of Public Health.

Patients with positive RT-PCR laboratory results and positive chest CT findings were included. Whereas, patients with positive RT-PCR results but negative CT findings, patients with underlying comorbidities, patients with incomplete medical data, or patients with motion CT artifact were excluded.

Definition of Symptoms of COVID-19

A total of 458 patients were included in this study. Patients were divided into symptomatic and asymptomatic groups. COVID-19 patients were categorized as symptomatic if they reported at least one of the disease's typical or atypical symptoms, such as fever, cough, shortness of breathing, loss of appetite, chills, diarrhea, and vomiting (3). Otherwise, patients were classified as an asymptomatic group.

2. Data Collection

The demographic, clinical characteristics, and CT scans of the chest were obtained from patients' files. Clinical symptoms, including fever, cough, shortness of breathing, loss of appetite, chills, diarrhea, and vomiting were extracted. The pattern of the lesions, distribution, and predominance of the lesions in chest CT images was recorded and analyzed.

3. Chest CT Protocols

All of the images were obtained with one of three different CT systems (Revolution, 128 slices [GE Healthcare], Bright speed, 16 slices [GE Healthcare], and Aquilion, 64 slices [Toshiba]). To reduce motion artifacts, patients were positioned in the supine position for a single inspiratory breath-hold. A standard low dose chest CT protocol was applied when possible. The main scanning parameters were as follows: tube voltage = 100 KVp, 60-100 mAs, the field of view = 350 mm× 350 mm, and matrix size = 512 × 512. After that, all of the images were reconstructed using a lung and mediastinum kernel with a slice thickness of 0.625–2 mm and a 70% increment.

4. Image Analysis

Tow radiologists with 17 and 12 years of experience in interpreting chest CT images, reviewed all chest CT images on a picture-archiving and communication system (PACS) with multiplanar reconstruction tools. The reviewers were blinded to the symptoms of Statius. The described parameters evaluated

include the main CT pattern (GGO, consolidation, and GGO with consolidation). The predominance of the infected lung was categorized as right lung, left lung, as well as right and left lungs..Transverse lesion distribution patterns were visually characterized as peripheral predominant (involving mainly the peripheral one-third of the lung), central, or both peripheral and central distribution (8). The distribution of pulmonary defects was also described as bilateral and unilateral distribution. The presence or absence of reversed halo sign, crazy paving, interlobular septal thickening, pleural effusion, thoracic lymphadenopathy (as defined by lymph node with a size of ≥ 10 mm in short axis dimension) (8), and Pulmonary nodules were also described.

Statistical Analysis

The quantitative variables were presented in terms of mean ± standard deviation (range), categorical variables were presented in terms of frequency and percentage of the total, and the differences between symptomatic and asymptomatic groups were compared by chi-square or Fisher exact test between groups. Statistical significance was defined as a two-sided $p < 0.05$. All statistical analyses were performed with SPSS software (version 24.0, IBM).

Results

1. Clinical Findings

The study population comprised 458 COVID-19 infected patients (259 (56.6%) male, mean age, 43.78 years ±14.89, range:15-88 years; 199 (43.4%) female, mean age, 41.82 years ±14.10, range: 14-80 years. Of these patients, 383 (83. 6%) were symptomatic and 75 (16.4%) were asymptomatic. The most common symptoms when admitted were fever in 306 (66.8%) patients and cough in 242 (52.8%) patients. Table 1 provides a summary of the demographic and clinical features of the study groups.

There was no statistically significant difference in gender affected by COVID-19. As shown in Table 2, asymptomatic infections were significantly more common in younger patients (10-29) than in elderly patients (>30). While symptomatic infections were predominance in patients more than 30 years old.

2. Chest CT Findings

CT patterns were compared between symptomatic and asymptomatic COVID-19 individuals. Table 3 summarizes the results. Of 383 (83.6%) symptomatic COVID-19 patients, 240 (62.7%) patients had GGO, 41 (10.7%) consolidation, and 102 (26.6%) GGO with consolidation. Of 75 (16.4%) asymptomatic COVID-19 patients, 52 (69.3%) patients had GGO, 11 (14.7%) consolidation, and 12 (16.0%) GGO with

consolidation (Fig. 1). In terms of the prevalence of lung parenchymal results, asymptomatic patients showed significantly higher GGO predominance over symptomatic than asymptomatic patients, 52 (69.3%) vs 240 (62.7%).

In terms of the transverse distribution, more than 50% of the symptomatic patients were more likely to show peripheral and central distribution, compared to asymptomatic patients, 200 (52.2%) vs 20 (26.7%). The peripheral distribution was significantly higher in asymptomatic than symptomatic patients, 53 (70.7%) vs 177 (46.2%), While the Central Distribution did not show any significant differences (6 (1.6%) and 2 (2.7%) for symptomatic and asymptomatic patients, respectively). On the other hand, mixed left and right lobes involvement were present without significant difference in 306 (79.9%) of symptomatic patients and 59 (78.7%) of asymptomatic patients. In addition, for both clinical groups, bilateral lung distribution of the lesion was shown in more than 372 (81.2%), while unilateral lung distribution was shown in 86 (18.8%) (Fig. 2).

CT scans also indicated interlobular septal thickening in approximately 12 (3.1%) of the symptomatic vs 1 (1.3%) in the asymptomatic patients. For reversed “halo sings” and crazy paving, there was statistically a significant difference between both groups (33 (7.2%) vs. 0 (0%) and 47 (10.3%) vs. 0 (0%), respectively).Plural effusion was observed in 7 (1.8%) of symptomatic patients and not recorded in asymptomatic patients.Thoracic lymphadenopathy was not observed in the study.Pulmonary nodules were less common imaging findings in the symptomatic patients 13 (3.4%) and were not observed in the asymptomatic cases (Fig 3).

Discussion

Early studies on the pandemic reported the presence of asymptomatic SARS-CoV-2 cases (19,20) and numerous studies on COVID-19 patients reported that 1-73% of COVID-19 patients were asymptomatic (8,16,18).In addition, the SARS-CoV-2 epidemic has overloaded hospitals worldwide, placing an unprecedented burden on the ambulatory setting with significant numbers of generally healthy COVID-19 patients. This emphasizes the importance of determining the relevance of chest CT imaging in this patient population, especially when the capability of resources is critically constrained. Herein, we report our findings in 458 symptomatic and asymptomatic patients with COVID-19 admitted to our hospital.

Interestingly, the male gender was associated with symptomatic and asymptomatic infection groups. However, there was no significant difference in the gender ratio. Previous studies had been described younger patients with COVID-19 tend to be mild or even asymptomatic presentations (5,6,21) and the

older ages are more vulnerable to the development of acute respiratory distress and death (22,23). This study reported that asymptomatic cases were significantly younger in comparison to the symptomatic patients (P = .000), and this may result in increased transmission of infection. In this study, the signs and symptoms characteristics of 383 (83.6%) symptomatic COVID-19 patients were in general consistent with the previous studies (19,24-26). Fever (306, 66.8%) and cough (242, 52.8%) were the most typical symptoms at the infection onset in symptomatic patients. Other prevalent symptoms include shortness of breath (71, 15.5%), loss of appetite (65, 12.2%), chills (43, 9.4%), diarrhea (45, 9.8%), and vomiting (25,5.5%). Our results appear to be similar to those of patients in previous studies (26,27).

GGO appears to be an early parenchymal finding since the virus is predominantly invading the interstitium and causing thickening and edema in the interlobular, intralobular, and peribronchovascular interstitium. The consolidation progressive later and shows the parenchyma infected by the virus (15). GGO with or without consolidation or consolidation only were the common characteristic CT patterns detected in different studies (10,23,25). In general, GGO was the most common for each group of symptoms and it was present alone or with consolidation. However, no significant differences were observed between the two groups. Predominate over peripheral and central transverse distribution was clear in symptomatic patients, whereas the peripheral transverse distribution was observed in the majority of asymptomatic patients. Therefore, a significant difference in the transverse distribution between the symptomatic and asymptomatic groups may indicate that lung damage from COVID-19 was different between the two groups. Infected lung involvement frequency was very similar, and no significant differences were identified between the two groups. A difference was reported between right and left lung involvement rates for both groups. Lesions were mainly located in the right lung. These findings could be attributed to the innate anatomical features of the right inferior lobar bronchus. The bronchial bronchus of the right lung lower lobe is steeper and straighter than the bronchial branches of the left lung lower lobe, and the angle between the right lower lobe and the long axis of the trachea is smaller. Thus, in the early phase of SARS-CoV-2, the virus is more likely to invade and infect the branches of the right inferior lobar bronchus (3).

Previous investigations of chest CT on SARS-CoV-2 lesions found that the typical pattern in the early stages of infection is unilateral and multifocal GGO. These lesions progress to bilateral distribution and diffuse GGO before being replaced by consolidation and mixed lesions (28-30). In this study, the rate of bilateral involvement was determined at 81.7% for symptomatic patients that were slightly higher than asymptomatic patients (78.7%). CT images also showed a definite interlobular septal thickening in about 12 (3.1%) of symptomatic patients and one asymptomatic patient (1.3%). A focal rounded GGO encircled

by a more or less full ring-like consolidation is defined as a reversed halo-sign, also known as an (atoll sign). This sign was recently observed in multiple SARS-CoV-2 cases, which could be due to disease progression causing consolidation around the GGO or lesion absorption, leaving a lower intensity in the center (17). Reversed halo sign was reported in merely 8.6% of symptomatic patients, while it was not shown in asymptomatic patients. In 12.0 % of symptomatic and 1.3 % of asymptomatic individuals, crazy paving pattern (thicker interlobular septal, intralobular lines with GGO superimposed and related irregular paving stones) were found. Significant differences in reverse halo signs and crazy paving patterns were shown between symptomatic and asymptomatic groups ($p = .003$).

Pleural effusion is a common sign of a pleural lesion and can indicate a more serious condition (27). In symptomatic and asymptomatic patients, pleural effusion and pulmonary nodules were fewer common features on CT (1.5% and 2.8%, respectively). Lymphadenopathy was not observed in the study. Of all CT imaging characteristics, only peripheral and central distribution (52.2% vs. 26.7%), reversed halo sign (8.6% vs. 0.0%), and crazy paving pattern (12.0% vs. 1.3%) were significantly higher in symptomatic than asymptomatic patients.

This study could explain the pathophysiology of the disease process as it organizes and could also explain the chest CT hallmarks of SARS-CoV-2 infection by increasing the frequency of GGO, bilateral diseases, the crazy-paving pattern of lesions, and the appearance of an Interlobular septal thickening, as well as reversed halo sign lesion. Chest CT imaging results can be correlated with the severity of the infection.

Limitations

Several limitations exist in our study. Mainly, it was a single-center retrospective study. Second, we excluded all patients with positive CT findings but negative RT-PCR results. This study missed a lot of mild or asymptomatic cases that did not consult the hospital during the study reference period.

Conclusion

In this viral enigma of a pandemic, CT provides a noninvasive and repeatable informational window into lung disease dynamics. Our study analyzed comprehensively demographic, signs and symptoms, and imaging characteristics of 458 symptomatic and asymptomatic COVID-19 patients. The signs and symptoms for SARS-CoV-2 patients that were symptomatic were essentially consistent with prior studies. According to the findings, the most common symptoms at disease onset in symptomatic patients are fever and cough with other typical symptoms including shortness of breath, loss of appetite,

chills, diarrhea, and vomiting. Asymptomatic infections were significantly more frequent in younger patients, compared to elderly patients.

The present study showed that common CT imaging features of SARS-CoV-2 included frequent involvement of GGO, bilateral lesion distribution, as well as mixed right and left lung involvement for both symptomatic and asymptomatic patients. Peripheral and central distribution, interlobular septal thickening, and crazy paving patterns were more common in symptomatic patients. Lymphadenopathy was absent in this study. Reversed halo sign, pleural effusion, and pulmonary nodules have not been detected in asymptomatic patients. In conclusion, Asymptomatic COVID-19 infections may be silent in patients with significant clinical risk due to possible delayed symptoms and a high proportion of positive chest CT imaging findings. A combination of RT-PCR testing and chest CT can be used for the optimum identification of infected asymptomatic patients. More emphasis should be placed on identifying and quarantining asymptomatic patients to prevent the spread of SARS-CoV-2.

Conflicts of Interest

The authors have no potential interest conflicts to declare.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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The Tables

Table1: Characteristics of the Patients

Parameter	All patients n = 458(%)
Male	259(56.6%)
Female	199(43.4%)
Age (y)*	42.93 ±14.57 (14–88)
Symptoms on admission	
Fever	306 (66.8%)
Cough	242 (52.8%)
Shortness of breathing	71 (15.5%)
Loss of appetite	65(12.2%)
Chills	43(9.4%)
Diarrhea	45(9.8%)
Vomiting	25(5.5%)

Note. —Data is the number of patients. Percentage within Parentheses is in comparison with all patients.

* Data are means ± standard deviation, with the range within parentheses.

Table 2: Demographic data according to the gender and age group for symptomatic and asymptomatic COVID-19 patients

Parameter	All patients (n = 458)	Symptomatic patients 383(83.6%)	Asymptomatic patients 75(16.4%)	P-Value
Gender				.163
Male	259 (56.6%)	211(55.1%)	48 (64.0%)	
Female	199 (43.4%)	172 (44.9%)	27 (36.0%)	
Age Group				.000

10-19	14 (3.1%)	5 (1.3%)	9 (12.0%)
20-29	77 (16.8%)	54 (14.1%)	23 (30.7%)
30-39	102 (22.3%)	86 (22.5%)	16 (21.3%)
40-49	118 (25.8%)	103 (26.9%)	15 (20.0%)
50-59	86 (18.8%)	79 (20.6%)	7 (9.3%)
60-69	35 (7.6%)	31 (8.1%)	4 (5.3%)
70-79	18 (3.9%)	17 (4.4%)	1 (1.3%)
>80	8 (1.7%)	8 (2.1%)	0 (0.0%)

Table 3: Chest CT finding for symptomatic and asymptomatic COVID-19 patients

Parameter	**All patients (n = 458)**	**Symptomatic patients 383 (83.6%)**	**Asymptomatic patients 75(16.4%)**	**P Value**
Pattern				.125
GGO	292 (63.8%)	240 (62.7%)	52 (69.3%)	
Consolidation	52 (11.4%)	41 (10.7%)	11 (14.7%)	
GGO & Consolidation	114 (24.9%)	102 (26.6%)	12 (16.0%)	
Transverse Distribution				.000
Peripheral Distribution	230 (50.2%)	177 (46.2%)	53 (70.7%)	
Central Distribution	8 (1.7%)	6 (1.6%)	2 (2.7%)	
Peripheral and Central Distribution	220 (48.0%)	200 (52.2%)	20 (26.7%)	
Infected Lung				.685
RT Lung	66 (14.4%)	56 (14.6%)	10 (13.3%)	
LT Lung	27 (5.9%)	21 (5.5%)	6 (8.0%)	
RT & LT Lung	365 (79.7%)	306 (79.9%)	59 (78.7%)	
Distribution of the Lesion				.521
Unilateral	86 (18.8%)	70 (18.3%)	16 (21.3%)	
Bilateral	372 (81.2%)	313 (81.7%)	59 (78.7%)	
Interlobular Septal Thickening	13 (2.8%)	12 (3.1%)	1 (1.3%)	.704

Reversed Halo Sing	33 (7.2%)	33 (8.6%)	0	.003
Crazy Paving	47 (10.3%)	46 (12.0%)	1 (1.3%)	.003
Pleural Effusion	7 (1.5%)	7 (1.8%)	0	.605
Lymphadenopathy	0	0	0	-
Pulmonary nodules	13 (2.8%)	13 (3.4%)	0	.140

Legends of the figures

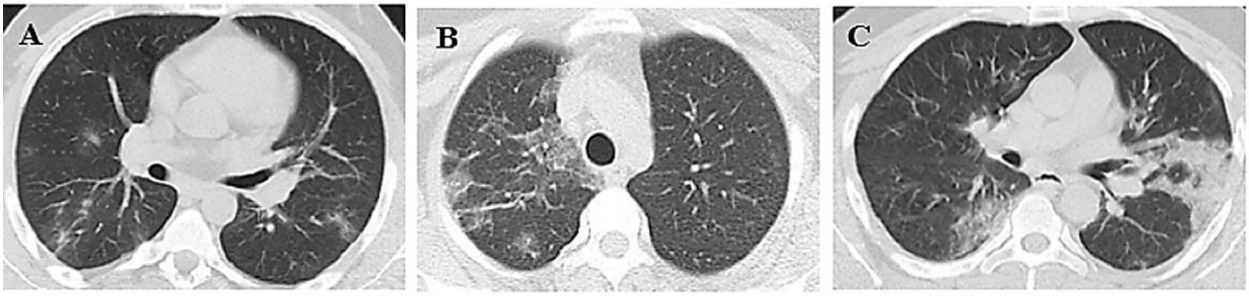

Fig. 1. Main CT pattern for COVID-19 patients. **A.** 35-year-old asymptomatic male. Axial CT image shows GGO demonstrated in both lobes.**B.** 28-year-old symptomatic female presenting with fever. CT image shows the pattern of GGO. **C**. 42-year-old symptomatic male presenting with fever and cough. Chest CT image shows GGO and consolidation in lung lobes.

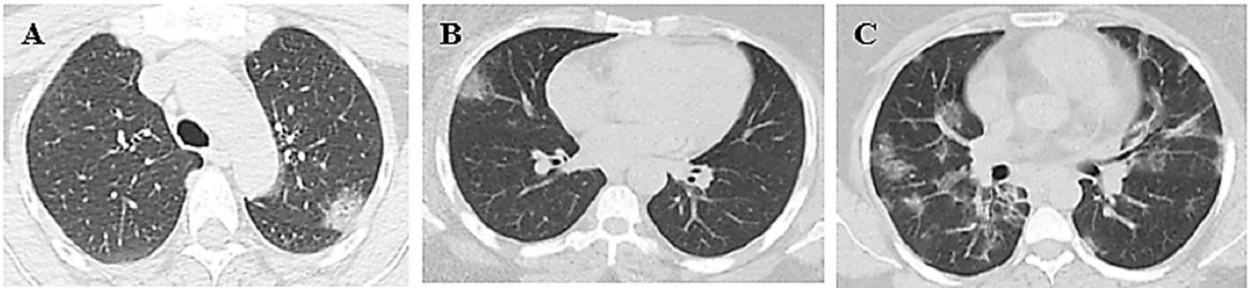

Fig. 2. Patterns distribution of the COVID-19 lesion. **A.** 51-year-old symptomatic female presenting with fever. Axial CT image shows unilateral GGO was demonstrated in the left lobe. **B.** 44-year-old asymptomatic female. CT image shows GGO was demonstrated in the peripheral right upper lobe**. C.** 36-year-old asymptomatic female. Chest CT shows diffuse bilateral GGO with the peripheral distribution.

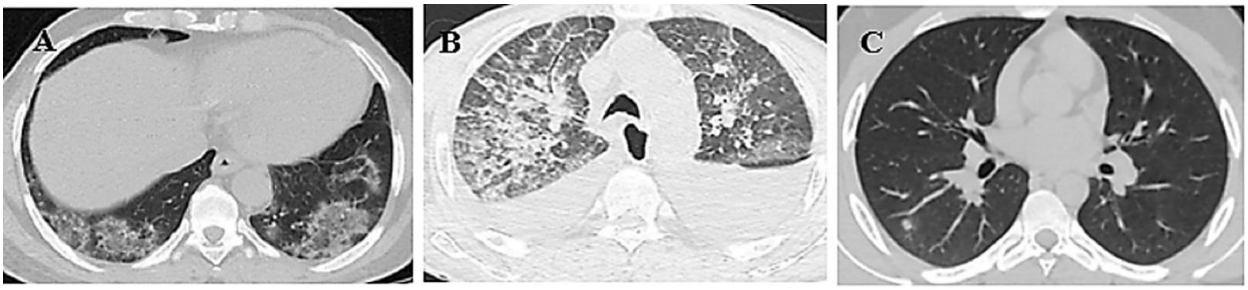

Fig. 3. Different chest CT findings of COVID-19 patients on axial CT images. **A.** 48-year-old symptomatic male presenting with fever, cough, and loss of appetite. CT image shows bilateral GGO, interlobular septal thickening, and a crazy-paving appearance. **B.** 75-year-old symptomatic male presenting with fever, cough, shortness of breath, and loss of appetite. Axial CT image shows bilateral interlobular septal thickening. Pleural effusion is seen in the bilateral lung lobes. **C.** 23-year-old symptomatic male presenting with fever and cough. CT image shows a ground-glass nodule in the right lobe.