

Frequent clinical and radiological manifestations of the Novel SARS-CoV-2: A review article

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is a highly infectious disease caused by the novel “severe acute respiratory syndrome coronavirus-2” (SARS-CoV-2) and is rapidly spreading worldwide. This review is designed to highlight the most common clinical features and computed tomography (CT) signs of patients with COVID-19 and to elaborate the most significant signs indicative of COVID-19 diagnosis. This review involved five original articles with both clinical and radiological features of COVID-19 published during Jan and Mar 2020. In this review, the most frequent symptoms of COVID-19 were fever and cough. Myalgia, fatigue, sore throat, headache, diarrhea, and dyspnea were less common manifestations. Nausea and vomiting were rare. Ground-glass opacity (GGO) was the most common radiological finding on CT, and mixed GGO with consolidation was reported in some cases. In addition, elevated C-reactive protein and lymphopenia are the pertinent laboratory findings of COVID-19. CT is an effective and important imaging tool for both diagnosis and follow-up COVID-19 patients with varied features, duration, and course of the disease. Bilateral GGOs, especially in the periphery of the lungs with or without consolidation, are the hallmark of COVID-19.

Keywords: Clinical manifestations, COVID-19, CT features, fever, ground-glass opacity

Introduction and Background

Coronavirus disease 2019 (COVID-19) is a highly infectious disease that is rapidly spreading worldwide. It first emerged in Wuhan City, China in December 2019 as an outbreak of a new phenotype of pneumonia caused by the novel “severe acute respiratory syndrome coronavirus-2” (SARS-CoV-2). It is a single-stranded ribonucleic acid (RNA) virus and classified as

a member of the *Coronaviridae* family.^[1,2] The virus transmits through air droplets generated during coughing or sneezing by symptomatic or asymptomatic infected individuals and through respiratory fomites.^[3-5] The incubation period of the virus varies from 2 to 14 days, and the clinical features vary from asymptomatic infection, fever, dry cough, sore throat, headache, diarrhea, vomiting, myalgia, fatigue, shortness of breath, to acute respiratory distress syndrome. It can progress to pneumonia, respiratory failure, acute kidney injury, multiorgan dysfunction, and even death, especially in patients with comorbidities such as diabetes mellitus, hypertension, and heart disease.^[3,5] The seventh edition of guidelines for the diagnosis and treatment of COVID-19 by the Chinese National health commission (NHC) divided the patients with COVID-19 into four clinical types:

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(1) Mild, patients with no or mild symptoms and no pneumonia on medical imaging, (2) Moderate, patients with symptoms and fever with pneumonia on clinical and medical imaging, (3) Severe, patients with respiratory distress (respiration rate >30 cycle/min) or oxygen saturation at a resting state <93% or lesion progress more than 50% of the lungs within 48 h on medical imaging, or PaO₂/FiO₂<300 mmHg, and (4) Critical, patients with respiratory failure or shock or other multiorgan failure and need intensive care.^[6] According to the sixth edition of the official “guidelines for the diagnosis and treatment of COVID-19” declared by the NHC of China, computed tomography (CT) is an effective and important screening tool to diagnose, monitor progression, and evaluate treatment effectiveness. Bilateral ground-glass opacities (GGOs) in the peripheral regions of the lungs with or without consolidation are the hallmark of COVID-19. Diverse CT features like crazy-paving pattern, reverse-halo sign, and airway changes and pleural changes can be present.^[7] Features of COVID-19 start to appear on CT in 4–7 days from the onset of the initial clinical manifestations and subsequently appear in all stages of the disease.^[8] Significant correlations are found between the severity of clinical manifestations and the severity of lung involvement on CT.^[9] The American College of Radiology and the European society of radiology (ESR) recommended against the use of chest CT as a widespread screening tool for patients with COVID-19, including patients with no or mild symptoms. The “Real-time reverse transcription polymerase chain reaction” (RT-PCR) is considered as a standard diagnostic test for patients with COVID-19.^[10]

The Duch Radiological Society provided COVID-19 Reporting and Data system (CO-RADS) as a categorical CT assessment scheme for the level of suspicion of lung involvement in patients with moderate to severe symptoms of COVID-19 on a scale ranges from 0 to 6 as follows: (1) CO-RADS 1: no suspicion on normal CT, (2) CO-RADS 2: low suspicion when CT abnormalities are consistent with other infections, (3) CO-RADS 3: intermediate suspicion when CT abnormalities

are compatible but unsure of COVID-19, (4) CO-RADS 4: high suspicion when CT abnormalities suspicious for COVID-19, (5) CO-RADS 5: very high suspicion when CT abnormalities are typical of COVID-19, (6) CO-RADS 6: proven by RT-PCR positive for COVID-19. If CT is technically insufficient for assigning the score, this is categorized as CO-RADS 0.^[11]

This article was designed to summarize and highlight the most common clinical features and radiological signs seen on the CT of patients with COVID-19 and to elaborate the most significant clinical and radiological signs indicative of COVID-19 diagnosis. This review involved five original articles published between January and March 2020. Inclusion criteria involved the original articles interested in both the clinical and radiological features of COVID-19. We excluded review articles, case reports, articles interested only with clinical or radiological manifestations or with other ideas, articles focused only on a specific point, and articles available in other languages. Overall, five articles that met the inclusion criteria involved in this review.^[12-16] The diagnosis of patients with COVID-19 was confirmed with RT-PCR in all cases of the involved studies. This article elaborates the most frequent features of COVID-19 for primary care physicians and family care doctors to be alert for detecting the disease as early as possible and to avoid bad complications resulting from delayed diagnosis during the pandemic.

Review

Clinical manifestation

In this review, the most common symptoms of COVID-19 were fever then cough [Table 1].

Fever was reported as the presenting symptom in 82%, 98%, 98.5%, 86.7%, and 83% and cough was reported in 61%, 76%, 59.4%, 78.3%, and 82% of patients in similar previous studies.^[17-21] However, the less common clinical features of COVID-19 were fatigue, myalgia, sore throat, headache, diarrhea,

Table 1: Common Clinical manifestations of COVID-19

Author	Han et al., 2020 ^[12]	Zhao et al., 2020 ^[13]	Xu et al., 2020 ^[14]	Xu et al., 2020 ^[15]	Lomoro et al., 2020 ^[16]
Study date	From Jan 4-Feb 3, 2020	NA	From Jan-Feb 2020	From Jan 23-Feb 4, 2020	From Feb 15-Mar 15, 2020
Patients (n)	108	101	50	90	58
Age (range) (Mean)	21-90	17-75 (44.44)	3-85 (43.9±16.8)	18-86 (50)	18-98 (66.3±16.6)
Gender (m)	38 (35.2)	56 (55.4)	29 (58%)	39 (43)	36
Fever	94 (87)	79 (78.2)	43 (86)	70 (78)	58 (100)
Cough	65 (60)	63 (62.4)	20 (40)	57 (63)	33 (57)
Sore throat	14 (13)	12 (11.9)	4 (8)	23 (26)	NA
Headache	14 (13)	NA	5 (10)	4 (4)	NA
Dyspnea	NA	1 (1)	4 (8)		24 (41)
Myalgia	12 (11)	0 (0.0)	8 (16)	25 (28)	0 (0.0)
Fatigue	42 (39)	0 (0.0)	8 (16)	19 (21)	18 (31)
Myalgia or fatigue	0 (0.0)	17 (16.8)	0 (0.0)	0 (0.0)	0 (0.0)
Diarrhea	15 (14)	3 (3)	NA	5 (6)	NA
Nausea/vomiting	NA	2 (2)	NA	7 (8)	NA
↓ lymphocyte	65 (60)	NA	14 (28)		48 (83)
↑ CRP	NA	NA	26 (52)	38 (42)	56 (96.5)

COVID-19=Corona virus disease 2019, CRP=C-reactive protein (normal range=0-10 mg/liter), ↓ =decrease, ↑ =elevated, NA=Not available

and dyspnea. Many previous studies reported these symptoms less common than fever and cough.^[17,18,22] Furthermore, nausea, vomiting, and other gastrointestinal symptoms were relatively rare clinical features of COVID-19. Previous studies reported these as rare manifestations of COVID-19.^[23,24]

In this review, elevated C-reactive protein ((↑) CRP) is a laboratory marker of inflammation and decreased lymphocytes (lymphopenia) were the pertinent laboratory findings of COVID-19. These findings were reported in many previous studies.^[25-27]

Radiological manifestations

In this review, GGO [Figure 1] was the most common radiological finding on CT [Table 2].

Previous studies reported GGO as the radiological sign in 97.6%, 100%, 91%, and 77% of the cases.^[20,27-29] Table 2 shows that mixed GGO with consolidation [Figure 2] was the second most common radiological feature, which was reported as 59% and 50% in previous studies.^[29,30]

Here, the CT findings were peripheral in 67.5% of the cases and reported as 89%, 86%, 75%, and 76% in previous studies.^[27,29-31]

In addition, a crazy-paving pattern [Figure 3] was the third most common radiological feature in this review; however, previous studies reported crazy paving in 36%, 29%, and 19.5% of the patients.^[20,28,32]

Furthermore, here pleural effusion was reported in 6.5% of cases, and it was reported as a rare finding (3%) in previous studies.^[27,33] Lymphadenopathy was reported in 2.4% in this review. However, lymphadenopathy was reported as a common finding (58%) in a previous study in Italy,^[27] and a rare finding in multiple previous studies.^[28,33]

El Homsy *et al.* reported that CT findings change with stages of COVID-19: (1) Early stage (the first two days), 56% of patients have negative CT; however, GGO was found in 44% and consolidation in the remaining 17%; (2) Intermediate stage (3–5 days), GGO was found in 88% and

consolidation in 55%; bilaterally in 76% and peripherally in 64%; (3) Late-phase (6–12 days), GGO was found in 88% and consolidation in 60% of the cases; bilateral in 88% and peripheral

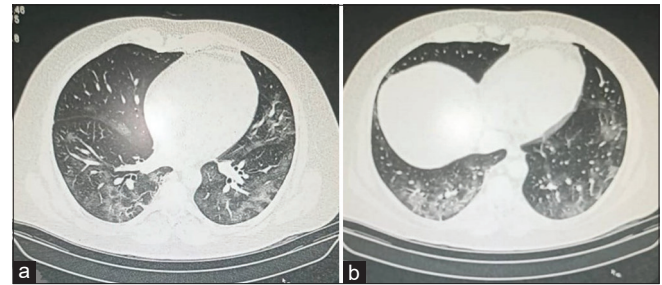


Figure 1 : Selected computed tomography images of a 37-year-old male patient with COVID-19 on day 3 after symptoms show scattered ground-glass opacities predominantly in the peripheral aspect of both lower lobes

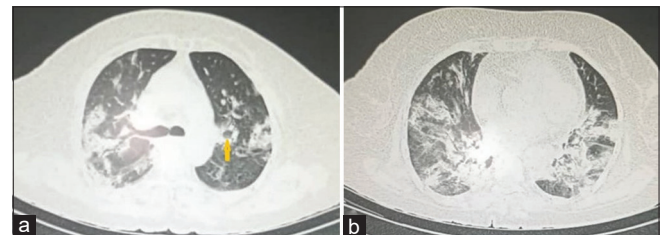


Figure 2: Selected computed tomography images of a 60-year-old female patient with COVID-19 on day 10 after symptoms show mixed ground-glass and consolidative opacities predominantly in the peripheral zones. Reverse halo sign is also noted (arrow)

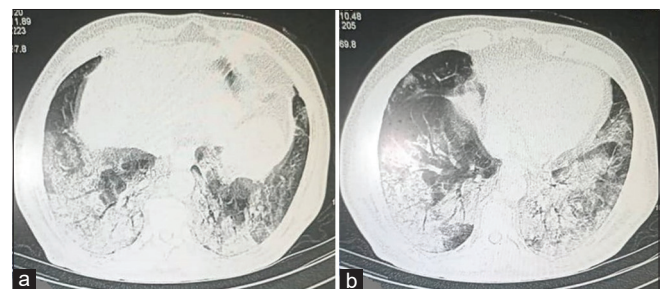


Figure 3: Selected computed tomography images of a 60-year-old male patient with COVID-19 on day 14 after symptoms show consolidations predominantly in the peripheral lower lobes, with ground-glass and crazy-paving patterns

Table 2: Common Radiological signs of the involved patients (Pattern and distribution)

Author	Han <i>et al.</i> , 2020 ^[12]	Zhao <i>et al.</i> , 2020 ^[13]	Xu <i>et al.</i> , 2020 ^[14]	Xu <i>et al.</i> , 2020 ^[15]	Lomoro <i>et al.</i> , 2020 ^[16]
Patients with CT (n)	108	93	41	90	42
GGO	65 (60)	87 (86.1)	30 (73.17)	65 (72)	15 (35.7)
Mixed GGO	44 (41)	65 (64.4)	25 (60.97)	NA	25 (59.5)
Consolidation	6 (5.55)	44 (43.6)	15 (36.58)	12 (13)	0 (0.0)
Crazy-paving	43 (40)	NA	NA	11 (12)	24 (57.1)
Pleural effusion	0 (0.0)	14 (13.9)	4 (9.75)	4 (4)	3 (7.1)
Lymphadenopathy	0 (0.0)	1 (1)	1 (2.43)	1 (1)	6 (14.3)
Peripheral	97 (90)	88 (87.1)	NA	46 (51)	27 (64.3)
Central	2 (2)	1 (1)	NA	NA	1 (2.4)
Mixed	9 (8)	NA	NA	NA	12 (28.6)

in 72%; (4) Absorption stage (more than 14 days), GGO was found in 65% and consolidation in 75%; bilateral in 88% and peripheral in 72%.^[10]

Zheng *et al.* reported that CT features differ at various stages of COVID-19—early stage, progression stage, and absorption stage.^[33] Bhandari *et al.* reported that CT features of COVID-19 vary with the duration and course of the disease. GGO is high in the early stages and low in the late stages.^[34] Bernheim *et al.* reported that lung involvement was bilateral in 28%, 76%, and 88% in the early, intermediate, and late stages, respectively.^[35]

Ultimately, CT is crucial and provides an effective diagnosis of COVID-19. In patients with clinical features of COVID-19, low-dose CT can provide a diagnosis with comparable sensitivity to PT-PCR and high specificity to distinguish it from other similar clinical diseases.^[36] CT sensitivity for the diagnosis of COVID-19 increases after the fifth day of symptoms.^[37] CT is a fast, adequate, and reliable diagnostic modality to refer patients with COVID-19 for hospitalization when the response of PT-PCR is late.^[38]

Conclusions

Fever and cough are the most common clinical features of COVID-19. Fatigue, myalgia, sore throat, headache, diarrhea, and dyspnea are less common clinical manifestations. Nausea, vomiting, and other gastrointestinal symptoms are relatively rare. Elevated C-reactive protein and lymphopenia are the pertinent laboratory findings of COVID-19. CT is an effective and important imaging tool for the diagnosis and follow-up of COVID-19 with varied features, duration, and course of the disease. Bilateral GGOs, especially in the peripheral lungs, with or without consolidation, are the hallmark of COVID-19.

Key messages

1. Fever and cough are the frequent clinical features for diagnosis of COVID-19.
2. Bilateral GGOs, especially in the peripheral lungs, with or without consolidation, are the hallmark of COVID-19.

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Conflicts of interest

There are no conflicts of interest.

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