

Ancillary findings on high resolution CT chest associated with typical features of COVID-19 pneumonia (Observational descriptive study at a tertiary care hospital)

Saerah Iffat Zafar,¹ Aliya Halim,² Hina Nasir,³ Abdur Rahim Palwa,⁴ Nadeem Zafar,⁵ Shamaila Burney⁶

Abstract

Objective: To determine the frequency of ancillary pulmonary signs and their relation to the severity of disease seen on high-resolution computed tomography of chest in patients of coronavirus disease-2019 pneumonia.

Methods: The observational descriptive study was conducted at the Armed Forces Institute of Radiology and Imaging, Rawalpindi, Pakistan, from March to July 2020, and included in place of comprised all coronavirus disease-2019 patients who were found positive on reverse transcription-polymerase chain reaction-and were referred to have high-resolution computed tomography of chest. Ancillary pulmonary findings in addition to typical features of coronavirus disease-2019 pneumonia were recorded. These included vacuole sign, halo sign, reverse halo sign, subpleural white line, subpleural translucent line, microvascular dilatation, fibrotic streaks and bronchiectasis. Relative frequency of these signs were determined for mild versus and severe disease, as determined by the computed tomography severity score. Data was analysed using SPSS 26.

Results: Of the 1645 patients, 1286(78.2%) were males and 359(21.8%) were females. The overall mean age was 47.5±15.7 years (range: 1-92). High-resolution computed tomography was normal in 418(25.4%) patients, typical findings for coronavirus disease-2019 were seen in 1110(67.5%), indeterminate in 113(16.9%) and atypical in 4(0.2%). Vacuole sign, subpleural white line, subpleural translucent sign, microvascular dilatation and fibrotic streaks were more commonly seen in severe disease ($p<0.001$), while discrete pulmonary nodule was identified more in the milder form ($p<0.05$). Halo and reverse halo signs as well as bronchiectatic changes demonstrated no significant propensity to the degree of disease severity ($p>0.05$).

Conclusion: Coronavirus disease-2019 pneumonia demonstrated various ancillary pulmonary features on high-resolution computed tomography of the chest in addition to typical findings more commonly described; radiologists should be aware of these signs and their relation to disease severity.

Keywords: Ancillary, COVID, Pneumonia. (JPMA 72: 1983; 2022)

DOI: <https://doi.org/10.47391/JPMA.3901>

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has affected millions of people worldwide, with devastating impact on the world in general and the medical science in particular. To date it continues to baffle human minds as well as science and medical authorities as it spreads across the globe unabated. Continuous work on this disease is required to understand the nature and course of this disease, its long-term effects on the lungs and health in general.

High-resolution computer tomography (HRCT) of the chest remains a very effective imaging tool for confirmation of lung involvement in coronavirus disease-2019 (COVID-19), detecting its progression and predicting

.....
^{1,2}Department of Radiology, Armed Forces Institute of Radiology and Imaging, Rawalpindi, ³Department of Radiology, Islamabad Diagnostic Centre, Rawalpindi, ⁴Department of Radiology, Combined Military Hospital, Peshawar, ⁵Department of Histopathology, Armed Forces Institute of Pathology, Rawalpindi, ⁶Islamic International Medical College, Rawalpindi, Pakistan.

Correspondence: Saerah Iffat Zafar. Email: saerah_syk07@yahoo.com

the nature and outcome for individual patients. Due to the heavy burden of patients worldwide with laboratory testing under strain, it is replacing the reverse transcription-polymerase chain reaction (RT-PCR) test in the initial diagnosis to its easy availability and early results. It is imperative to be familiar with all types of imaging features that can be seen on HRCT chest in COVID-19 pneumonia. Initial findings described in the literature were ground glass opacities (GGOs) following a subpleural, peripheral and basal distribution.¹ Progression of disease was seen with the confluence of these GGOs resulting in the formation of consolidations. In the early days of the disease around the beginning of 2019, most radiological findings were limited to GGOs, consolidation, nodules and pleural effusion.² However, with the passage of time owing to evolution of the disease process and after larger studies, multiple signs are seen as part of the imaging spectrum on HRCT of the lungs. These include vacuole sign, halo sign, reverse halo sign, subpleural white line, subpleural translucent line, microvascular dilatation, fibrotic streaks, bronchial changes and mediastinal changes.

The Radiological Society of North America (RSNA) proposed a classification based on HRCT findings, categorising them as negative (normal lungs), typical (specific pattern of bilateral, peripheral well-defined GGOs / consolidations), indeterminate (if the findings were typical but unilateral), and atypical (if no commonly reported findings of COVID-19 were found).³ To have a quantitative assessment of the lung involvement, CT severity score (CTSS) was devised which helps in providing a baseline for patient's follow-up and also assists in providing prognosis of the disease. The CTSS is determined by dividing both lungs into 10 segments (considering apical and posterior segments of the left upper, and anterior and medial segments of the left lower lobes as separate segments). If the diseased part of the segment is <50% it is assigned a score of 1, and >50% is scored 2; making a maximum of 20 points on each side, or 40 for both lungs.⁴

It is vital for the radiologists to identify different radiological signs in patients of COVID-19 pneumonia, and to be aware of their correlation with the disease duration and severity to help predict the disease progression and prognosis. The current study was planned to determine the frequency of ancillary pulmonary signs and their relation to the severity of the disease seen on HRCT chest in patients of COVID-2019 pneumonia.

Patients and Methods

The observational descriptive study was conducted at the Armed Forces Institute of Radiology and Imaging (AFIRI), Rawalpindi, Pakistan, from March to July 2020 after approval from the Institutional Ethical Review Board. The sample size was calculated with confidence interval (CI)

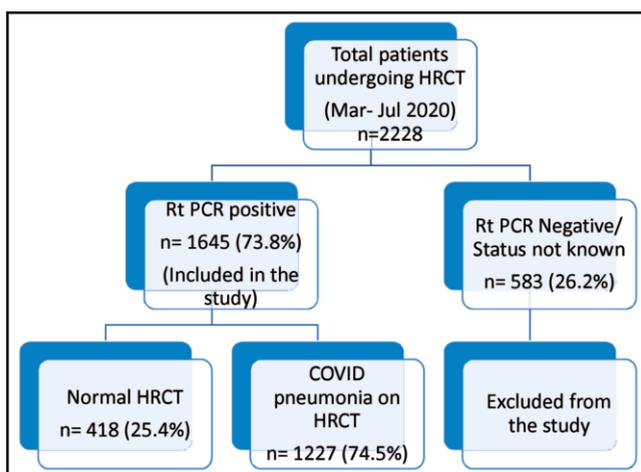


Figure-1: Flow chart depicting the number of patients undergoing high-resolution computed tomography (HRCT) for coronavirus disease-2019 (COVID-19) pneumonia/ screening, with exclusion and inclusion criteria.

99.9% and standard deviation (SD) 0.5, keeping the COVID-19-positive population as per the official figures of Pakistan government⁵, utilizing stratified random sampling technique. All COVID -2019 patients who were found positive on RT-PCR and were referred to have HRCT of chest were included (informed consent not required), while suspected patients with negative RT-PCR were excluded (Figure-1).

All the patients underwent 16-slice HRCT chest (Toshiba Alexion CT scanner). Type of predominant lung abnormality was classified into GGOs, consolidation, interlobular septal thickening or mixed type. Ancillary signs were defined as features other than typical findings of GGOs / consolidation which could be seen in patients of COVID-19 pneumonia. These included vacuole sign, halo sign, reverse halo sign, subpleural white line, subpleural translucent line, microvascular dilatation, fibrotic streaks, discrete pulmonary nodule and bronchial changes. Mediastinal findings, like pleural effusion, pneumomediastinum and mediastinal lymphadenopathy, were not considered.

HRCT findings were categorised using RSNA classification.³ Disease severity of lungs was assessed according to the CTSS,⁴ and the frequency of occurrence of the ancillary signs was calculated and its relation to disease severity was determined.

Data was analysed using SPSS 26. Qualitative data was expressed as frequencies and percentages, while quantitative data was expressed as mean \pm SD. Odds ratio (OR) with 95% CI was also calculated. Chi-square test was applied to determine the preponderance of the signs in mild versus severe COVID disease. $P < 0.05$ was considered statistically significant.

Results

Of the 1645 patients, 1286(78.2%) were males and 359(21.8%) were females. The overall mean age was

Table-1: Ancillary pulmonary findings in coronavirus disease-2019 (COVID-19) pneumonia on high-resolution computed tomography (HRCT).

CT finding	Relative frequency (n=1645)
Discrete pulmonary nodule	151 (9.2%)
Fibrotic streaks	568 (34.5%)
Subpleural line	588 (35.7%)
Subpleural translucent line	300 (18.2%)
Microvascular dilatation	103 (6.3%)
Bronchiectasis	36 (2.2%)
Vacuole sign	146 (8.9%)
Halo sign	47 (2.9%)
Reverse halo sign	74 (4.5%)

Table-2: Pulmonary ancillary signs in mild versus severe coronavirus disease-2019 (COVID-19) disease.

CT Finding		CTSS Grade		Chi Squared Statistic	p Value	OR (95% CI)
		Mild	Severe			
Discrete Pulmonary Nodules	Present	133 (10.7%)	18 (4.4%)	14.68	< 0.001	0.384 (0.232, 0.637)
	Absent	1105 (89.3%)	389 (95.6%)			
Fibrotic Streaks	Present	353 (28.5%)	215 (52.8%)	80.09	< 0.001	2.807 (2.230, 3.535)
	Absent	885 (71.5%)	192 (47.2%)			
Sub-pleural White Line	Present	339 (27.4%)	249 (61.2%)	152.33	< 0.001	4.179 (3.303, 5.288)
	Absent	899 (72.6%)	158 (38.8%)			
Sub-pleural Translucent Line	Present	147 (11.9%)	153 (37.6%)	135.87	< 0.001	4.471 (3.432, 5.823)
	Absent	1091 (88.1%)	254 (62.4%)			
Microvascular Dilatation	Present	54 (4.4%)	49 (12.0%)	30.76	< 0.001	3.001 (2.003, 4.497)
	Absent	1184 (95.6%)	358 (88.0%)			
Bronchiectasis	Present	22 (1.8%)	14 (3.4%)	3.96	0.047	1.969 (0.998, 3.885)
	Absent	1216 (98.2%)	402 (96.6%)			

CTSS: Computed tomography severity score OR: Odds ratio, CI: Confidence interval.

47.5±15.7 years (range: 1-92). HRCT was normal in 418(25.4%) patients, typical findings for COVID-19 were seen in 1110 (67.5%), indeterminate in 113(16.9%) and atypical in 4 (0.2%). Out of the patients demonstrating pneumonia on HRCT (n=1227), bilateral lung involvement was seen in 1105 (90%) while only 122 (10%) showed unilateral disease. Predominant pattern seen on HRCT chest was that of GGOs 847(51.5%). The commonest detected sign was subpleural lines 588 (35.7%), followed by fibrotic streaks 568(34.5%) (Table-1).

Vacuole sign, subpleural white line, subpleural translucent sign, microvascular dilatation and fibrotic streaks were more commonly seen in severe disease ($p<0.001$), while discrete pulmonary nodule was identified more in the milder form ($p<0.05$). Halo and reverse halo signs as well as bronchiectatic changes demonstrated no significant propensity to the degree of disease severity ($p>0.05$) (Table-2).

Though mediastinal findings were not considered in the study, lymphadenopathy was identified in 193(11.7%) patients, pleural findings, including effusion, were seen in 52(3.2%), pleural retraction in 23(1.4%), pneumothorax <7(0.4%) patients.

Discussion

The current study included RT-PCR-positive patients of COVID-19 for HRCT chest. None of the patients was vaccinated as data was collected in the pre-vaccination era of COVID-19 pneumonia.

Vacuole sign is described as a small lucency (<5mm) within an air space opacification likely representing partially-filled alveolar space within a lesion⁶ (Figure-2). This sign was earlier described in the 1990s in peripheral tumours of the lung, in particular the adenocarcinomas, differentiating it

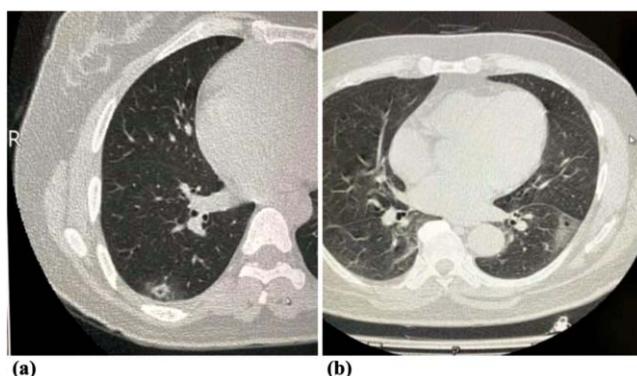


Figure-2: Axial high-resolution computed tomography (HRCT) of a patient with coronavirus disease-2019 (COVID-19) pneumonia showing: (a) Vacuole seen as a small lucency within a focus of consolidation in posterobasal segment of the right lower lobe (b) vacuole within a ground glass opacity (GGO) in the apical segment of the left lower lobe.

from tuberculomas.⁷ It also helped in differentiating atypical adenomatous hyperplasia from adenocarcinoma in situ.⁸ The current study noticed this sign in 146(8.9%) patients. In comparison, this sign was more commonly seen in a study in Egypt (39.5%).⁹ Another earlier study from Wuhan reported the incidence of this sign even higher (54.8%).¹⁰ It was seen in advanced disease more than the earlier stage, as was noted in the current study. The reason behind frequency disparity could be due to the difference in the sample size of the studies. The study in Wuhan categorised features like vacuole sign, subpleural translucency, air bronchogram and pleural changes as secondary findings, while subpleural white line, fibrotic streaks and bronchus distortion were placed in the category of reparative signs.¹⁰

Subpleural lines are defined as linear opacities lying parallel to the pleura, between 2-5cm in length and up to 1mm in thickness. These lines indicate the organisation stage of the

disease as found in one study of 130 patients from different medical centres of China,¹¹ and, hence, is noted in progressive disease as was seen in the current study. In 62 patients of COVID-19 in Wuhan, this sign was detected in 33.9%, more commonly noted in advanced stage of the disease.¹² Interestingly, one of the review papers comparing the frequency of findings in COVID-19 patients found that this was one of the few signs of COVID-19 which was seen more in the older age group.¹³ The current study reflected this finding as these were seen more in age group >40 years (47.3%) compared to those aged <40 years (15.5%).

Subpleural translucent line refers to a thin translucent line adjacent to the deep surface of consolidation or GGOs in subpleural location. This sign was noted in 18.2% of 300 patients, with significant number occurring in severe pneumonia compared to mild disease ($p < 0.001$) as per CTSS. One study had almost similar frequency of its occurrence at 20%.¹⁴

Discrete pulmonary nodule was taken as a focal lesion <3cm in diameter, with solid density and well-defined margins, without associated halo. It was found more in the milder form of COVID-19 pneumonia than in the severe degree. Contrary to the findings, Yang et al. considered a pulmonary nodule an indicator of progressive disease.¹⁵

Microvascular dilatation implies the dilatation of the capillaries coursing through or around the consolidations / GGOs (Figure-3) attributed to inflammatory response of the capillary walls to hyperaemia. In the current study, a

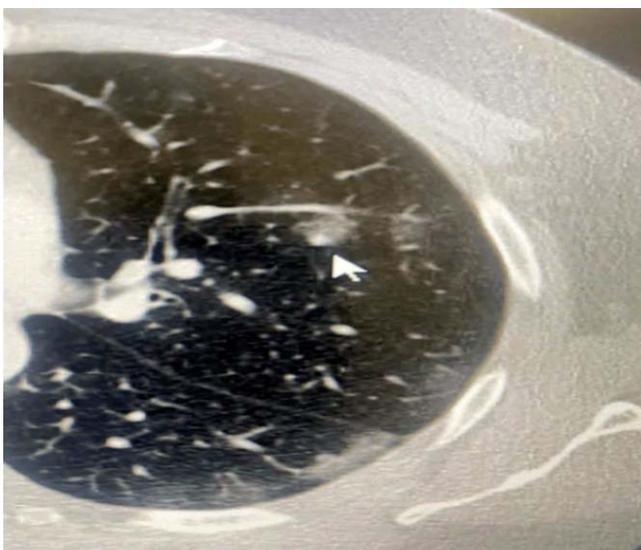


Figure-3: Axial high-resolution computed tomography (HRCT) of a patient with coronavirus disease-2019 (COVID-19) pneumonia showing microvascular dilatation in a small ground glass opacity (GGO) apicoposterior segment of left upper lobe; subpleural lines can be appreciated in apical segment of left lower lobe.

significant number occurred in severe form of the disease, implying capillary damage in progressive disease ($p < 0.001$). One study quoted the presence of this sign in up to 23.8% patients.¹⁶ Fibrotic streaks is another sign noted commonly in the delayed phase of the disease, and represents residue of pneumonic changes.

Halo and reverse halo signs are also associated with COVID-19 pneumonia. Halo sign is the presence of haze around a focus of consolidation or a nodule. It is described in viral and fungal infections representing alveolar haemorrhage around focal infection, like angioinvasive aspergillosis.¹⁷ The current study did not find it specific to mild or severe degree of pneumonia. In one study, halo sign was seen in larger number of patients (26%), but was considered non-specific as it was seen in 21% of other viral pneumonias.¹⁸ Halo sign was also found to be more common in children, with almost 50% seen in paediatric patients of COVID-19.¹⁹

Reverse halo is the presence of GGO surrounded by consolidation more than 2/3rds of its circumference (Figure-4). This sign was initially described in cryptogenic organising pneumonia, but it is also seen in a variety of other infections, autoimmune diseases and, lately, in COVID-19 pneumonia.²⁰ A study comprising 51 patients considered reverse halo as a sign of progressive disease in COVID-19 pneumonia.²¹ In the current study, this sign along with additional finding of bronchiectasis were not specific to severity of the lung disease. COVID-19 pneumonia is an evolving disease, and the presence of ancillary findings in addition to characteristic features described require documentation and further work-

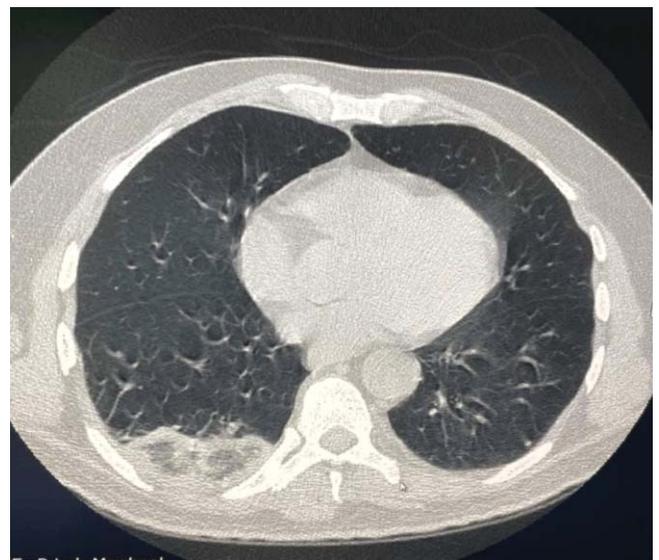


Figure-4: Axial high-resolution computed tomography (HRCT) of a patient with coronavirus disease-2019 (COVID-19) pneumonia demonstrating reverse halo sign: internal ground glass opacity (GGO) surrounded by a thick rim of consolidation in the posterior basal segment of the right lower lobe.

up to identify their significance to determine prognosis and course of the disease.

The current study has the limitation that it did not follow up the patients to determine the contribution of these signs in overall prognosis.

Conclusion

Multiple radiological signs were seen in COVID-19 pneumonia in addition to typical GGOs and consolidations. Radiologists should be aware of different signs, their relation to disease severity and duration, to determine prognosis and disease progression in COVID-19 pneumonia.

Acknowledgement: We are grateful to Dr Muhammad Humza bin Saeed, Associate Professor of Community Medicine, Riphah International University, Rawalpindi, for statistical assistance, and to Dr Zainab Shahzadi and Dr Gul Sanam, second year residents at AFIRI, for assistance in data entering.

Disclaimer: Hina Nasir and Abdur Rahim Palwa were working in AFIRI at the time of Research.

Conflict of Interest: None.

Source of Funding: None.

References

- Huang Y, Jiang Y, Li W, Ma J, Wang P, et al. Comparison of initial HRCT features of COVID-19 pneumonia and other viral pneumonias. [Online] [Cited 2020 May 21]. Available from: URL: <https://doi.org/10.21203/rs.3.rs-29527/v1>
- L Xiaofan, Zhou H, Zhou Y, Wu X, Zhao Y, Lu Y, et al. Temporal radiographic changes in COVID-19 patients: relationship to disease severity and viral clearance. *Sci Rep.* 2020; 10:10263.
- Jaeger TMH, Krdzalic J, Fasan BACM, Kwee RM. Radiological Society of North America Chest CT Classification System for Reporting COVID-19 Pneumonia: Interobserver Variability and Correlation with Reverse-Transcription Polymerase Chain Reaction. [Online] [Cited 2020 June 11]. Available from: URL: <https://doi.org/10.1148/ryct.2020200213>
- Yang R, Xiang L, Huan L, Zhen Y, Zhang X, Xiong Q, et al. Chest CT Severity Score: An Imaging Tool for Assessing Severe COVID-19. *Cardiothoracic Imaging.* [Online] [Cited 2020 March 30]. Available from: URL: <https://doi.org/10.1148/ryct.2020200047>
- Marina C, Fausto S, Piercarlo SP, Agostini A, Borgheresi A, Minorati D, et al. Chest CT features of coronavirus disease 2019 (COVID-19) pneumonia: key points for radiologists. *Radiol Med.* 2020; 125:636-46.
- Venugopal VK, Mahajan V, Rajan S, Agarwal VK, Rajan R, Syed S, et al. A Systematic Meta-Analysis of CT Features of COVID-19: Lessons from Radiology. [Online] [Cited 2020 December 2]. Available from: URL: <https://europepmc.org/article/PPR/PPR141125>
- Yang XM, Hu MH, Xie YC, Yan HZ, Liu HR, Wang DT, et al. Vacuole sign and nodule sign in early peripheral bronchogenic carcinoma. Diagnostic value and pathologic correlation. *Radiol.* 1990; 30:169-71.
- Pan X, Yang X, Li J, Dong X, He J, Guan Y. Is a 5-mm diameter an appropriate cut-off value for the diagnosis of atypical adenomatous hyperplasia and adenocarcinoma in situ on chest computed tomography and pathological examination? *J Thorac Dis.* 2018; 10(Supply 7):S790-6.
- Sabri YY, Nassef AA, Ibrahim IMH, Abd E, Mageed MR, Khairy MA. CT chest for COVID-19, a multicenter study—experience with 220 Egyptian patients. *Egypt J Radiol Nucl Med.* 2020; 51:43-9.
- Zhou S, Zhu T, Wang Y, Xia L. Imaging features and evolution on CT in 100 COVID-19 pneumonia patients in Wuhan, China. *Eur Radiol.* 2020; 30:5446-54.
- Wu J, Pan J, Teng D, Xu X, Feng J, Chen YC. Interpretation of CT signs of 2019 novel coronavirus (COVID-19) pneumonia. *Eur Radiol.* 2020; 30:5455-62.
- Zhou S, Wang Y, Zhu T, Xia L. CT features of coronavirus disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. *AJR Am J Roentgenol.* 2020; 214:1287-94.
- Ojha V, Mani A, Pandey NN, Sharma S, Kumar S. CT in coronavirus disease 2019 (COVID-19): a systematic review of chest CT findings in 4410 adult patients. *Eur Radiol.* 2020; 30:6129-38.
- LiK, Wu J, Wu F, Guo D, Chen L, Fang Z, et al. The Clinical and Chest CT Features Associated With Severe and Critical COVID-19 Pneumonia. *Invest Radiol.* 2020; 55:327-31.
- Yang Z, Shi J, He Z, Lu Y, Xu Q, Ye C, et al. Predictors for imaging progression on chest CT from coronavirus disease 2019 (COVID-19) patients. *Aging.* 2020; 12:6037-48.
- Lomoro P, Verde F, Zerboni F, Simonetti I, Borghi C, Fachinetti C, et al. COVID-19 pneumonia manifestations at the admission on chest ultrasound, radiographs, and CT: single-center study and comprehensive radiologic literature review. *Eur J Radiol Open.* 2020; 7:100231.
- Alves, GRT, Marchiori E, Irion K, Nin CS, Watte G, Pasqualotto AC, et al. The halo sign: HRCT findings in 85 patients. [Online] [2021 August 26]. Available from: doi:10.1590/S1806-37562015000000029
- Bai HX, Hsieh B, Xiong Z, Halsey K, Choi JW, Tran TML, et al. Performance of Radiologists in Differentiating COVID-19 from Non-COVID-19 Viral Pneumonia at Chest CT. *Radiology.* 2020; 296:E46-54.
- Wei Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: different points from adults. *Pediatr Pulmonol.* 2020; 55:1169-74.
- Shirani F, Shayganfar A, Hajiahmadi S. COVID-19 pneumonia: a pictorial review of CT findings and differential diagnosis. *Egypt J Radiol Nucl Med.* 2021; 52:38.
- Yan Li, Liming Xia. Coronavirus disease 2019 (COVID-19): role of chest CT in diagnosis and management. *Am J Roentgenol.* 2020; 214:1280-6..