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Ct scan of Chest in Covid 19 Infection-A Comprehensive Study

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ABSTRACT: Background-It all began in Wuhan city of China in December 2019 when the coronavirus induced severe acute respiratory syndrome was first detected. Since then the disease has spread like wildfire causing devastating effects on the human race physically, mentally, emotionally, socially and economically.
Aims-This retrospective study was conducted to understand the role of CT (computed tomography) scan of chest in COVID 19 infections by correlating CT findings with pathophysiology of the disease, usefulness of CT scan in triage of COVID patients and significance of CORADS and CT severity scoring in COVID patients.
Methods and Material-A total of 258 adult patients referred to the department for CT scan of the chest for varied symptomatology were reviewed to assess the role of CT in COVID 19. Both adult male and female patients of different age groups were included in the study.
Results-Of the 258 patients reviewed 86 patients fell in the CORADS 1 and 2 category thus establishing no or extremely low suspicion of COVID 19 infection in these patients. Rest of the 172 patients fell in CORADS 3 to 6 categories with male preponderance in all age groups. Majority of the patients (85 patients) assessed fell in category 5.
Conclusions-CT study plays an important role in COVID 19 patients for decision making in triage of patients especially in emergency situations as it is faster and less time consuming. CORADS scoring has become a uniform and standardized means of communication between the radiologists and treating physicians in understanding the degree of suspicion. CT severity score is a good method to prognosticate the course the disease.
KEYWORDS: COVID-19, CT scan of chest, CORADS, Ground glassing

I. INTRODUCTION

In December 2019, a lower respiratory tract febrile illness of unknown origin was reported in a cluster of patients in Wuhan City, Hubei Province, China. Their bronchoalveolar lavage revealed a novel strain of Corona virus. [1],[2] The pulmonary syndrome was later named coronavirus disease 2019 (COVID-19) by the World Health Organization.

Despite the imposition of strict quarantine rules and travel restrictions, the virus transmitted rapidly out of China with a number of confirmed cases reported in different / practically all parts of the world. The pandemic has affected the human race physically, mentally, emotionally, socially and economically in a devastating manner.
The official name of the illness is COVID-19 (a shortening of Corona VIrus Disease-19) and it is caused by the "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) [3],[4] The names of both the disease and the virus should be fully capitalized, except for the letter 'o' in the viral name, which is in lowercase [3],[5]

II. AIMS AND OBJECTIVES

The study was conducted with the following aims and objectives.

a) To understand the pathophysiology of COVID 19 infection and to correlate it with the CT findings.
b) To assess the role of CT scan of chest in the triage of fever patients.
c) To analyse the CT findings by CORADS for degree of suspicion.
d) To assess the severity of the findings using CT severity score.

III. MATERIALS AND METHODS

A retrospective study was done wherein all patients referred to the radiology department for CT study of the chest from 01/05/2020 to 30/09/2020 were analysed. The study included both male and female adult patients who were referred for CT scan of chest for varied symptomatology. All the patients had undergone CT scan on a 64 slice CT scanner-SOMATOM Sensation 64 using standard parameters. All precautions and protocols in accordance to the care required in COVID pandemic were uniformly followed and adhered to

in each and every patient. There were a total of 258 patients during the period from 01/05/2020 to 30/09/2020.
The CT findings were analysed and reported by two consultant radiologists of the hospital with description of findings and the CORADS score. CT severity score was mentioned as and where applicable.

Ethics
Permission from the ethical committee was waived off in view of retrospective nature of the study

IV. RESULTS

The following observations were made after analysing patients in CORADS categories 3-6

Age Groups

Age group	Male	Female
21-30 years	5	0
31-40 years	25	10
41-50 years	33	10
51-60 years	29	15
61-70 years	20	11
71-80 years	12	3
81-90 years	2	1

The majority of patients fell in the age group of 41-50 and 51-60 years (43 and 44 respectively) with predominantly male preponderance in all groups. There were only 5 male patients in the age group of 21-30 years with no female patients in this age group.

Number of Patients in each CORADS category

3	3	4	4	5	5	6	6
M	F	M	F	M	F	M	F
13	5	24	11	65	20	26	12

Out of the 258 patients analysed 86 patients fell in categories 1 and 2.
Analysis of the rest of the 172 patients revealed only 18 patients in the indeterminate category 3.
Maximum number of patients (85) were in category 5 where the findings were typical of COVID-19 infection.

CT severity scores in different CORADS category

CT SEVERITY SCORE	CORADS 4	CORADS 5	CORADS 6
0-5	3	1	9
6-10	13	11	7
11-15	5	24	10
16-20	5	30	7
21-25	4	15	12

Maximum number of patients (30) were of CORADS 5 with a severity score of 16-20. None of the patients falling in CORADS 6 category had normal or non covid findings on their CT scan with the numbers varying between 7 and 12 in each of the categorised severity scores.

V. DISCUSSION

Coronaviruses are minute viruses containing a single stranded RNA and belong to the Coronaviridae family in the Nidovirales order. They derive their name from the spikes on their outer surface and have alpha, beta, gamma and delta subgroups.[6],[7]

There has been evidence of a rapid increase in the incidence of infection and also transmission by asymptomatic carriers [8,9] thus exhibiting the potential for a pandemic. [6],[10],[11]

Through genetic recombination and variation, coronaviruses can adapt to and infect new hosts. Bats are thought to be a natural reservoir for SARS-CoV-2, but it has been suggested that humans became infected with SARS-CoV-2 via an intermediate host, such as the pangolin [12] ,[13],[14]

COVID-19 usually presents with fever (85%), cough (70%) and shortness of breath (43%), but abdominal and other symptoms are possible and the disease can be asymptomatic.Illness severity can vary from mild to critical with symptoms ranging from mild cough and fever to respiratory failure, shock and multi-organ failure.

Pathophysiology of Covid 19 infection and correlation with CT findings.

The virus gains entry into the cells via the attachment of its virion spike protein (a.k.a. S protein) to the angiotensin-converting enzyme 2 (ACE2) receptor. This receptor is commonly found on alveolar cells of the lung epithelium, underlying the development of respiratory symptoms as the commonest presentation of COVID-19 [15]. The less common cardiovascular manifestations of the disease are also thought to be due to the same ACE2 receptor which are found even in the cardiovascular system cells. [15].

On CT scan, the characteristic pulmonary ground glass opacification can be seen even in asymptomatic patients . The virus tends to enter and destroy the alveolar space epitheilial cells due to high expression of the ACE2 receptor on the apical side of the lung epithelial cells. This matches with the fact that the early lung injury is often seen in the distal airway. [16],[17],[18] .

With progression of the disease there is acceleration of the viral replication resulting in compromise of the epithelial endothelial barrier integrity with added involvement of the pulmonary capillary endothelial cells. This results in accentuated inflammatory response and triggers an influx of monocytes and neutrophils. Autopsy studies have shown diffuse thickening of the alveolar wall with mononuclear cells and macrophages infiltrating airspaces in addition to endothelialitis.[12],[19]

Inflammatory pulmonary intersitial infiltrates and edema develop manifesting as ground-glass opacities on computed tomographic imaging. Subsequent alveolar edema and hyaline membrane formation occurs compatible with early-phase acute respiratory distress syndrome (ARDS) [12],[19] (Images 1a, 1b, 1c). Bradykinin-dependent lung angioedema may contribute to disease.[12],[20] Collectively, endothelial barrier disruption, dysfunctional alveolar-capillary oxygen transmission, and impaired oxygen diffusion capacity are characteristic features of COVID-19 .

In severe COVID-19, fulminant activation of coagulation and consumption of clotting factors occur.[12],[21],[22] A report from Wuhan, China, indicated that 71% of 183 individuals who died of COVID-19 met criteria for diffuse intravascular coagulation. There may be microthrombi formation due to inflamed lung tissues and pulmonary endothelial cells . This can result in thrombotic complications affecting various systems like deep venous thrombosis, pulmonary embolism, and even arterial complications like limb ischemia, ischemic stroke and myocardial infarction in critically ill patients [23] Multiorgan failure can also be a sequalae following the development of viral sepsis.

The first report of patients with COVID-19 described bilateral lung involvement on initial chest CT in 40 of 41 patients, with patients in ICU revealing a consolidative pattern and the non ICU patients revealing a predominantly ground-glass pattern [1], [24].An investigation of initial chest CT findings in 21 individuals with confirmed COVID-19 reported abnormal findings in 86% of patients, with a majority (16/18) having bilateral lung involvement [1],[25]

Multifocal ground-glass opacities and consolidation were reported in 57% and 29%, respectively, with a peripheral lung predilection. Likewise, the chest imaging in a family cluster of seven people with confirmed COVID-19 showed bilateral patchy ground-glass opacities with greater involvement of the lungs in the older family members. [1]

Occurrence of pleural effusion, cavitation, pulmonary nodules, and lymphadenopathy are not usually seen in patients with COVID-19 . Pneumothorax was reported in 1 of 99 patients with confirmed COVID-19 1, but it was unknown if the pneumothorax was a direct complication of the corona-virus infection.[26]

Role of CT scan chest in the triage of COVID patients.

Early detection and containment of infection caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) has been hindered by the need to develop, mass produce, and widely disseminate the required molecular diagnostic test, a real-time reverse-transcription polymerase chain reaction (RT-PCR) assay.[27]

Although RT-PCR tests have high sensitivity and specificity, they can adversely be affected by a number of variables, including adequacy of specimen, specimen type, specimen handling, and stage of infection when the specimen is acquired (Centers of Disease Control guidelines for in-vitro diagnostics) [27],[28],[29] False-negative RT-PCR tests have been reported in patients with CT findings of COVID-19 who eventually tested positive with serial sampling.[30]

CT screening of 82 asymptomatic individuals with confirmed COVID-19 from the cruise ship “Diamond Princess” showed findings of pneumonia in 54% [31] .Provision of diagnostic imaging services like CT chest in a pandemic setup is very challenging given the need for strict adherence of infection control protocols to minimise risk of transmission and protect the concerned health care professionals and workers.[32] .Droplet transmission followed by contaminated surfaces are believed to be the main modes of spread for SARS-CoV2 in radiology suites; all patients undergoing imaging should be masked and imaged by using dedicated equipment that is cleaned and disinfected after each patient encounter [33]

Fleischner Society outlines suggestions for when chest imaging (mainly CT scan) can beneficially contribute to infection management [27]

- Imaging is not routinely indicated in asymptomatic individuals.
- Imaging is not indicated in patients with mild COVID-19 symptoms unless they are at risk for disease progression.
- Chest imaging is indicated in patients with COVID-19 with worsening respiratory status.
- Patients with moderate-to-severe COVID-19 features are indicated for imaging regardless of their COVID-19 test results.
- In environments with limited personal protection equipment or COVID-19 testing, imaging should be used for medical triage of patients with suspected COVID-19 who have moderate-to-severe symptoms, as well as a high pre-test probability of disease.

In addition, the panel offered these additional suggestions:

- CT is appropriate in patients with functional impairment and/or low blood oxygen after COVID-19 recovery.
- Daily, repeated chest X-rays don't offer any improvements in outcomes for stable, intubated patients over on-demand imaging.
- Reverse-transcription polymerase chain reaction (RT-PCR) testing should be performed on asymptomatic patients who have COVID-19 features on CT scan to potentially limit further transmission.

A study conducted by Ducray et al [34] reported excellent diagnostic performances of chest CT (accuracy, sensitivity, specificity, PPV and NPV at 88.9%, 90.2%, 88%, 84.1% and 92.7% respectively) compared to RT-PCR as method of reference and a significant shorter delay necessary for a diagnosis of COVID-19 (187 +/- 148 minutes for CT report versus 573 +/- 327 minutes for RT-PCR report, p<0.0001).These findings demonstrated that chest CT is a rapid and sufficiently accurate tool to refer patients requiring hospitalization to the "COVID +" or "COVID -" hospital units, when response times for virological tests are too long, in order to decrease congestion in the emergency departments.

CORADS

The CO-RADS classification is a standardized reporting system for patients with suspected COVID-19 infection developed for a moderate to high prevalence setting. This is a proposed classification system for radiologists in the Netherlands.

CORADS stands for COVID 19 reporting and data system.Although the seventh edition of the Chinese Novel Coronavirus Pneumonia Diagnosis and Treatment Plan incorporates CT imaging into the criteria that clinically define COVID-19 [35] the American College of Radiology, among others, discouraged the use of CT in the initial work-up of patients [35],[36],[37], only advocating its use for problem solving. The Fleischner Society, however, sees a role for imaging in various scenarios, with imaging, in particular CT scanning, as a major tool to use if symptoms worsen or in an environment that is resource-constrained for RT-PCR [38].

In early March 2020, the Dutch Radiological Society (NederlandseVerenigingvoorRadiologie) initiated a COVID-19 network to develop a standardised reporting system to assess the pulmonary involvement in COVID19 infection by studying the disease pattern and thereby comment upon the degree of suspicion of lung involvement by COVID 19 infection. The authors developed it to compare data across institutions and populations and thus, provide a basis for gathering scientific evidence and improved communication with referring physicians. The term CORADS was coined owing to its similarity to other methods of standardization in reporting like Lung Imaging Reporting and Data System (LI-RADS), Prostate Imaging Reporting and Data System (PI-RADS), or Breast Imaging Reporting and Data System (BIRADS).[39]

The system was iteratively refined through feedback from members and input from clinical partners. This type of system has been shown to work well in clinical practice and to allow for selection of optimal cutoff points for various clinical decisions depending on the tasks at hand.

CO-RADS gives the level of suspicion of pulmonary involvement in COVID 19 infection in moderate and severe cases and ranges from very low (CO-RADS category 1) to very high (CO-RADS category 5) on unenhanced CT sections of the chest. There are two additional categories namely CO-RADS category 0 encoding a

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technically inadequate study and CO-RADS category 6 wherein the patient is RT-PCR positive at the time of examination.

COARDS is a CT-based system that is used to assess the suspicion of pulmonary involvement in COVID-19. It needs to be supplemented by laboratory test results, clinical findings, and type and duration of symptoms for actual interpretation.. At present, the reference standard for diagnosing COVID-19 remains positive RT-PCR results as the gold standard. Rapid antigen testing has also acquired importance.

CO-RADS Category 0

Category 0 is chosen when the study is technically inadequate in terms of incomplete study or of insufficient quality to assign any one of the five categories (CORADS 1 to CORADS 5).

CO-RADS Category 1

CO-RADS category 1 suggests a very low level of suspicion based on either normal CT findings or findings consistent with a non infectious origin. Conditions like emphysema, lung neoplasms, fibrosis etc fall in this group. This category is equivalent to the negative for pneumonia category of the RSNA consensus statement [40]

CO-RADS Category 2

CO-RADS category 2 implies a low level of suspicion for pulmonary involvement by COVID-19 where the CT findings are consistent with an infectious origin but not compatible with COVID 19 infection. Findings include tree in bud appearance, consolidation which is lobar or segmental, cavitation and centrilobular nodules. Conditions like bronchitis, infectious bronchiolitis, lobar pneumonia, abscesses etc fall into this group. This category also includes cases of typical interstitial pulmonary edema where there is smooth interlobular interstitial thickening and pleural effusion. Findings of associated ground glassing is categorised as CORADS 3 in view of ground glassing commonly seen in pulmonary involvement in COVID 19. These findings are similar to the atpical appearance category of the RSNA consensus statement. [40]

CO-RADS Category 3 (Images 2a, 2b, 2c)

Category 3 suggests equivocal findings for pulmonary involvement of COVID-19 based on CT features that can also be found in other viral pneumonias or non-infectious causes. This category includes findings like extensive ground glassing , perihilar ground glassing , picture of pulmonary edema revealing ground glassing with or without pleural effusion or a picture of organizing pneumonia in the absence of typical findings of COVID 19. The category also includes ground glass opacities that are not subpleural or centrilobular in location. This category partially overlaps with the indeterminate appearance category of the RSNA consensus statement but includes those cases with lower likelihood for COVID-19.[40]

CO-RADS Category 4 (Images 3a, 3b)

CO-RADS category 4 suggests a high level of suspicion for pulmonary involvement by COVID-19 based on CT findings that are typical for COVID-19 but also show some overlap with other (viral) pneumonias. Findings are similar to those for CO-RADS category 5; however, they are not in a subpleural location or are located strictly unilaterally in a predominant peribronchovascular distribution or are superimposed on severe diffuse pre-existing pulmonary abnormalities. CO-RADS category 4 consists of the features of the indeterminate appearance category of the RSNA consensus statement that are associated with a higher likelihood of COVID-19. [40]

CO-RADS Category 5 (Images 4a, 4b,4c, 4d, 4e,4f)

CO-RADS category 5 suggests a remarkably high level of suspicion for pulmonary involvement by COVID-19 based on typical CT findings . The mandatory findings include mutifocal and bilateral areas of sunbpleural consolidation.CO-RADS category 5 requires the presence of at least one confirmatory pattern that aligns with the temporal evolution of the disease .

The areas of ground glassing attenuation may be (half) rounded and unsharply demarcated and multiple in early the early stages but can also be sharply demarcated cconforming to the shape of the secondary pulmonary lobules. A crazy paving pattern may appear later in the course of the disease.

Areas of consolidation start occurring within the ground glassing as the disease progresses. Findings of organising pneumonia like atoll sign or ground glassing with extensive subpleural consolidation with air bronchograms may also be seen. Subpleural curvilinear lines or bands of subpleural ground glassing or consolidation in a teethered arching pattern are also considered typical findings. Thickened vessels within lung abnormalities are typical and are frequently found in all other confirmatory patterns. CO-RADS category 5 is largely identical to the typical appearance of the RSNA consensus statement .[40]

CO-RADS Category 6
CO-RADS category 6 includes patients with RTPCR positive status.

Typical Features for Pulmonary Involvement of COVID-19
Obligatory Features
These include subpleural areas of ground glassing with or without consolidation and multifocal bilateral distribution

Confirmatory Patterns

Ground-glass regions which may or may not be sharply demarcated. The unsharply demarcated areas may reveal a half rounded shape and the sharply demarcated may conform to the shpe of the secondar pulmonary lobules.

Crazy paving pattern , patterns compatible with organising pneumonia ,subpleural lines or bands of ground glassing or consolidation in a teethered arch pattern and thickened vessles within the involved lung.

The coronavirus disease 2019 (COVID-19) Reporting and Data System (CO-RADS), developed by the Dutch Radiological Society, provides a framework that builds on other reporting schemes for COVID-19 but expands the concept in a way similar to systems like LI-RADS. Categories 1–5 provide increasing suspicion for pulmonary involvement of COVID-19 at unenhanced chest CT, thus allowing for task-specific cut-off points for clinical decision making. It provides very good performance in predicting COVID-19 in patients with moderate to severe symptoms and has substantial interobserver agreement, especially for CO-RADS categories 1 and 5. The system fulfils the need for a structured and fast reporting system that decreases ambiguity in communications with referring physicians and facilitates collection of CT performance data for further research of this worldwide health care problem.

CT severity score in COVID 19 infection

CT severity score has a potential role in predicting the outcome of SARS-CoV-2 patients. CT score commensurates well with laboratory findings and disease severity and is useful in road mapping the diagnostic workflow in symptomatic cases. [41]

Ran Yang et al [42] developed a chest CT severity score (CT-SS) for assessing COVID-19 burden on the initial scan obtained at admission. This score uses lung opacification as a measure of parenchymal involvement and the extension of the disease in the lungs. In this method the 18 segments of both lungs were divided into 20 regions in which the posterior apical segment of the left upper lobe was subdivided into apical and posterior segmental regions and the anteromedial basal segment of the left lower lobe was subdivided into anterior and basal segmental regions.

All the 20 regions were evaluated for lung opacification and assigned a score of 0,1 or 2 based on 0%, less than 50% or more than 50% of parenchymal opacification of each of the 20 regions. The total severity score was then calculated by adding all the scores with a minimum score of 0 and a maximum possible score of 40. The individual scores of in each lung, as well as the total CT-SS were higher in severe COVID-19 when compared with mild cases ($P<0.05$). The optimal CT-SS threshold for identifying severe COVID-19 was 19.5 (area under curve, 0.892), with 83.3% sensitivity and 94% specificity.

This retrospective study however had several limitations. First it was based on the assumption that lung opacification is a measure for COVID 19 burden with no histological conformation of the findings. Second the first CT chest obtained on admission was analysed not taking into account the number of days since the start of symptoms and third the study was only investigated within a small group (n = 2) of relatively experienced radiologists.

Pan et al [41],[43] proposed a semi-quantitative CT severity scoring by dividing both lungs into 5 lobes (both upper and lower lobes and right middle lobe) . Each lobe was assigned a score between 0 and 5 which was based on the extent of anatomic involvement, as follows: 0, no involvement; 1, < 5% involvement; 2, 5–25% involvement; 3, 26–50% involvement; 4, 51–75% involvement; and 5, > 75% involvement . The total score which was the sum of the scores of all the 5 lobes thus ranged between 0 and 25 Other related features like fibrosis, pleural effusion, subpleural lines etc were also described.

CT score was compared with clinical categories and significant difference was observed when all categories were compared together ($p < 0.0001$). When multiple comparisons were made, CT score was significantly higher in the critical category (mean value ± SD: 20.3 ± 3; range 15–24) than in the mild category (8.7 ± 4; range 0–19) ($p < 0.0001$). CT score was also significantly higher in the severe category (17.4 ± 3.1; range 11–24) versus the mild category (8.7 ± 4; range 0–19) ($p < 0.0001$). No statistical significance was observed between severe and critical categories (p = 0.7921) .

Marco et al [42] demonstrated that a cut-off value of 18 is highly predictive of short-term mortality. Similar observations were recently reported by Colombi et al [44], who found a positive correlation between the extent of CT lung involvement and intensive care unit admission or death, in a cohort of 236 patients.

Marco et al [42] also compared CT scoring with most important independent risk factors associated with ARDS and fatal outcome, which were reported to be age, dyspnea at admission, and the presence of pre-existing comorbidities like coronary arteries and cerebrovascular diseases [45],[46]. Their mortality data confirmed the prominent prognostic importance of age: all-cause mortality was significantly higher in patients older than 75 years (n = 12/36; 33.3%). Age-dependent mortality was also demonstrated in their univariate analysis, showing an increasing risk of death of 1.069 times per year-increase.

CT severity scoring method proposed by Pan et al and followed by Marco et al was used in reporting and predicting the severity score in our patients.

VI. CONCLUSIONS

The following conclusions could be made from the study-

CT chest-lung findings correlate well the pathophysiology and progression of the disease process in COVID 19 infection.

If utilised sensibly, logically and according to guidelines CT chest plays an important role in the medical triage of patients.

CT scan plays both complementary and supplementary roles when compared to RT-PCR the gold standard in COVID 19 patients.

CT scan of the chest helps making immediate decisions in COVID 19 infection in medical emergencies.

CORADS used in CT chest has become a good tool in aiding physicians, intensivists in deciding the further line of management in COVID 19 and COVID 19 suspect patients.

CT severity scoring used in COVID 19 infection is a good prognostic indicator of the disease.

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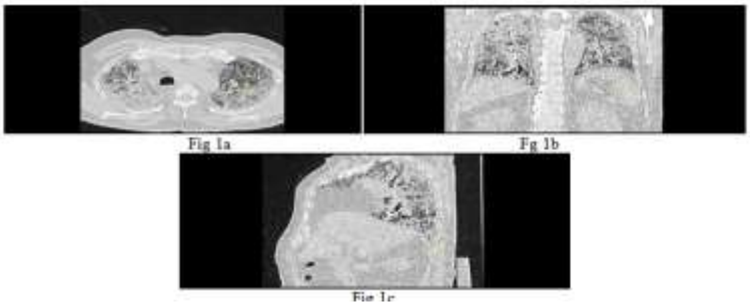
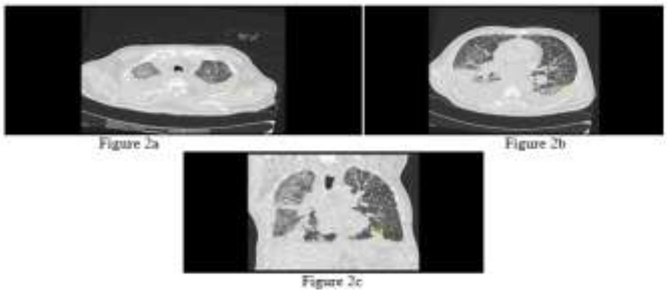


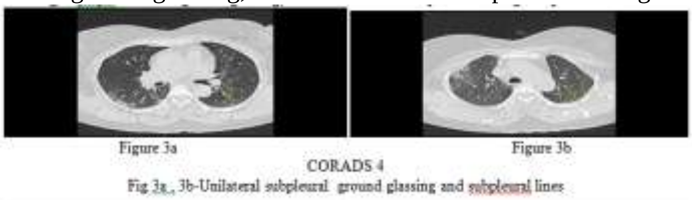
Post COVID sequelae ARDS

Fig 1a ,1b 1c- ARDS like picture with traction bronchiectasis -Post COVID 19 infection sequelae



CORADS 3

Fig 2a,2b,2c- Bilateral ground glassing, smooth interlobular septal thickening and pleural effusion.



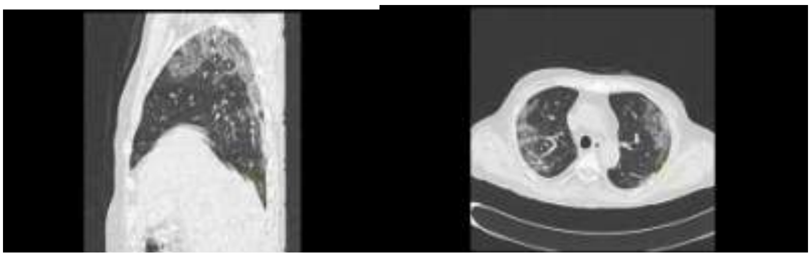


Figure 4c Figure 4d

Figure 4e Figure 4f

CORADS 5

Fig 4a,4b,4c Bilateral multifocal subpleural ground glassing/crazy pavement appearance

Fig 4d, 4e,4f Bilateral multifocal ground glassing with crazy pavement appearance