

# Incidental chest computed tomography findings in asymptomatic Covid-19 patients. A multicentre Indian perspective

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## Abstract

In December 2019, an unprecedented outbreak of pneumonia of unknown etiology emerged called COVID-19. A vast number of people affected by this disease are asymptomatic and yet contagious with up to 79% of COVID-19 infections reportedly caused by undocumented infections. Surprisingly, these asymptomatic subjects are also known to quietly harbor pneumonia changes on CT scans. RT-PCR, the definitive test for COVID-19, maybe false negative in patients with COVID-19 pneumonia on CT. Incidental findings highly suspicious of COVID-19 pneumonia on CT chest of asymptomatic patients may increase as the community transmission of the virus rises and isolation restrictions are released. It is advisable to be aware of its appearances and the challenges associated with it.

**Key words:** Asymptomatic COVID-19 patients; false positive RT-PCR; incidental COVID-19 pneumonia on CT; RT-PCR COVID-19

## The Covid-19 Pandemic

In December 2019, an unprecedented outbreak of pneumonia of unknown etiology emerged in Wuhan City, Hubei province of China. A novel coronavirus was identified as the causative agent and was subsequently termed SARS CoV-2 and the disease caused by it was called COVID-19 by the World Health Organization (WHO). On January 30, 2020, the WHO declared the Chinese outbreak of COVID-19 to be a Public Health Emergency of International Concern.

At this time (May 27, 2020) COVID-19 has infected 5,591,067 people across the globe and caused 350,458 deaths. India is seeing a rising number of infections (153,230) as well as deaths, though the number of deaths is relatively low (4365, death rate of 2.8% as compared to world 6.2%).

Of the patients who tested positive on RT-PCR for Covid-19, 78% and 88% were asymptomatic in the states of Maharashtra

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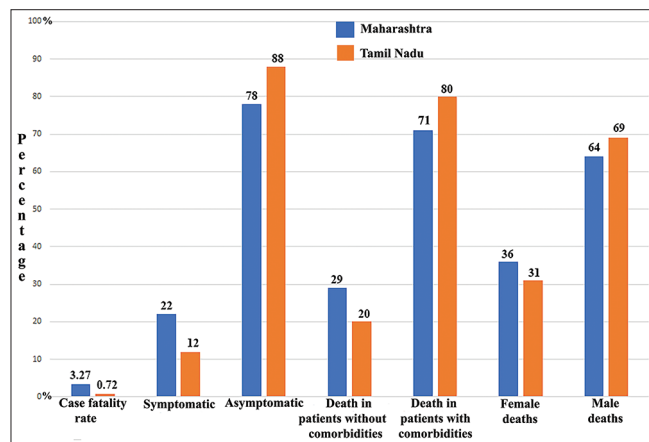
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and Tamil Nadu, India respectively. Figure 1 compares the case fatality rate and the various demographic features of these two of India's most affected states. (Data from Public Health department, Government of Maharashtra and Directorate of Public Health and Preventive Medicine Health and Family Welfare Department, Government of Tamil Nadu <https://stopcorona.tn.gov.in/daily-bulletin/>).

### Asymptomatic COVID-19 Patients as Agents of Transmission

COVID-19 has many similarities with the SARS (Severe Acute Respiratory Syndrome) which was caused by SARS CoV-1 in the year 2003. These include high genetic relatedness, transmission primarily through respiratory droplets, and the frequency of lower respiratory symptoms (fever, cough, and shortness of breath) with both infections developing a median of 5 days after exposure. However, interventions that were used to control SARS-CoV-1, including symptom-based case detection and subsequent testing to guide isolation and quarantine did not work with COVID-19.

This is because there is an important difference between the two illnesses. Covid-19 spreads rapidly by high viral shedding in the upper respiratory tract, even among asymptomatic or presymptomatic subjects unlike SARS-CoV-1, where replication occurs mainly in the lower respiratory tract with peaking of viral loads at symptom onset. Even with influenza, asymptomatic subjects have lower quantitative viral loads in secretions from the upper respiratory tract than from the lower respiratory tract and a shorter duration of viral shedding in asymptomatic than persons with symptoms, which decreases the risk of transmission from pauci-symptomatic persons. Covid-19 is far more contagious and has equal viral loads and shedding in both its asymptomatic and symptomatic population. Its asymptomatic population may become symptomatic or may continue to remain asymptomatic and serve as carriers in the ongoing pandemic.<sup>[1]</sup>



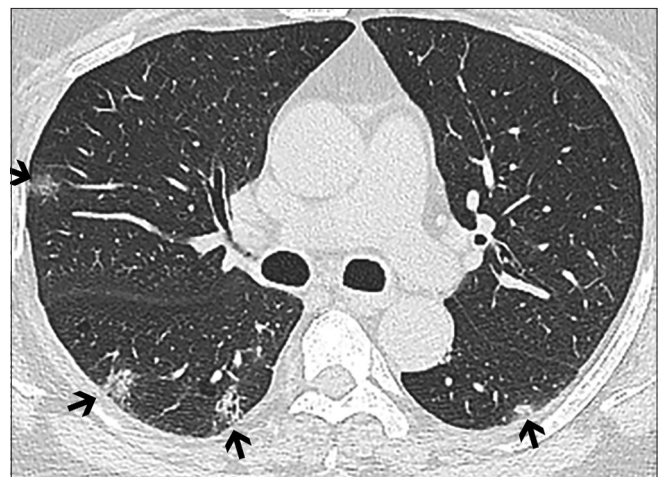
**Figure 1:** Comparison of various demographic features of Maharashtra and Tamil Nadu, two of India's most affected states by COVID-19

Upto 79% of COVID-19 infections have been reportedly caused by undocumented infections<sup>[2]</sup> made up of the asymptomatic and pauci-symptomatic population. These asymptomatic COVID-19– positive patients, therefore assume a place of special importance in this pandemic.

Asymptomatic carriers of COVID-19 have been estimated to comprise 17.9%<sup>[3]</sup> to 30.8%<sup>[4]</sup> of all infected cases. In addition, in a pandemic setting, patients may refute symptoms for fear of being quarantined and add to the numbers of undetected cases as we see in India.

Surprisingly, these asymptomatic subjects are also known to quietly harbor pneumonia changes on CT scans. Shi *et al.*, in their cohort of 81 patients with COVID-19 pneumonia, found 18.5% asymptomatic patients.<sup>[5]</sup> In the cruise ship "Diamond Princess" 54% of the asymptomatic Covid-19 positive patients had changes of pneumonia on chest CT, 83% of which were ground glass opacities (GGO) [Figure 2].<sup>[6]</sup>

Further compounding this is a peculiar presentation of COVID-19 called *asymptomatic hypoxia* in some patients with a remarkable discrepancy between relatively well-preserved lung compliance and a severely compromised pulmonary gas exchange, leading to grave hypoxemia without proportional signs of respiratory distress. This is postulated by some to be due to extreme hypocapnia as a result of disproportional pulmonary exchange of CO<sub>2</sub> and O<sub>2</sub> in these patients. These patients with extreme hypoxemia show little distress; rather they tend to be impassive, cooperative, and hemodynamically stable. However, sudden and rapid respiratory decompensation may occur. This particular clinical presentation in COVID-19 patients contrasts with critically ill patients in respiratory failure, in which patients with decompensated heart failure, sepsis, or massive pulmonary embolism tend to present with



**Figure 2:** A 58-year-old man with hypertension and no symptoms of COVID-19 was found RT-PCR positive on contact tracing. His chest CT shows multiple, bilateral, peripheral, small, and round areas of GGO (arrows)

air hunger, dyspnea, distress, arterial hypotension, and isocapnic or hypercapnic hypoxia [Figure 3].<sup>[7]</sup>

Others postulate that asymptomatic hypoxia may be caused by the neuroinvasive potential of the virus involving not only the brain stem but also the cortex.<sup>[8]</sup>

Hence, incidental CT findings in asymptomatic COVID-19 patients cannot be ignored.

### Incidental Covid-19 Pneumonia on CT

Due to many asymptomatic subjects in the population, as the pandemic progresses, it is anticipated that patients will have incidental lung findings on CT obtained for unrelated reasons that could be attributable to COVID-19.<sup>[9]</sup> [Figure 4A and B] Reports of such occult Covid-19 infections are now beginning to appear in literature. Albano *et al.* report that as high as 9% of their patients that underwent PET/CT for various malignancies showed unexpected signs of interstitial pneumonia on CT and elevated regional FDG-avidity with subsequent proof of COVID-19 by RT-PCR.<sup>[10]</sup> A similar case was seen in Kochi, Kerala, India at a large multispecialty hospital [Figure 4C and D].

A report of a patient undergoing spine CT for trauma who was incidentally found to have lung abnormalities later confirmed to be COVID-19<sup>[11]</sup> matches that of a patient from a large municipal hospital at Mumbai, Maharashtra, India [Figure 5].



**Figure 3:** An 80-year-old man with no symptoms other than mild fatigue was found to have an SPO<sub>2</sub> of 86% suggesting asymptomatic hypoxia. Xray Chest frontal view shows bilateral, peripheral, multilobar, and multiple areas of pneumonia. RT-PCR on the subsequent day was positive for COVID-19

In the Fleischner society multinational consensus statement on the role of chest imaging in patient management during the COVID-19 pandemic, there were two points on which the panel of experts had a 100% agreement. One of these states that COVID-19 testing is warranted in patients incidentally found to have findings suggestive of COVID-19 on a CT scan of the chest. This highlights that asymptomatic COVID-19-positive subjects can have specific CT lung features during a pandemic. RT-PCR testing in this scenario is important to potentially identify an occult infection and limit further transmission both within the community and in healthcare settings.<sup>[12]</sup>

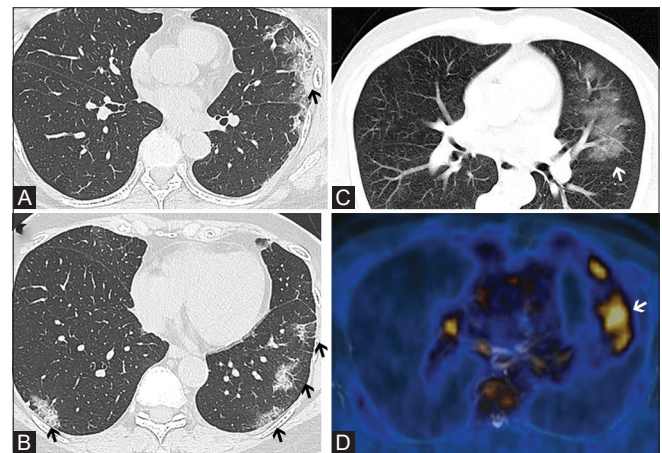
### CT Appearances in Covid-19

CT is an important component of the management pathway for Covid-19.<sup>[13]</sup> The typical CT findings of Covid-19 in the lungs include:

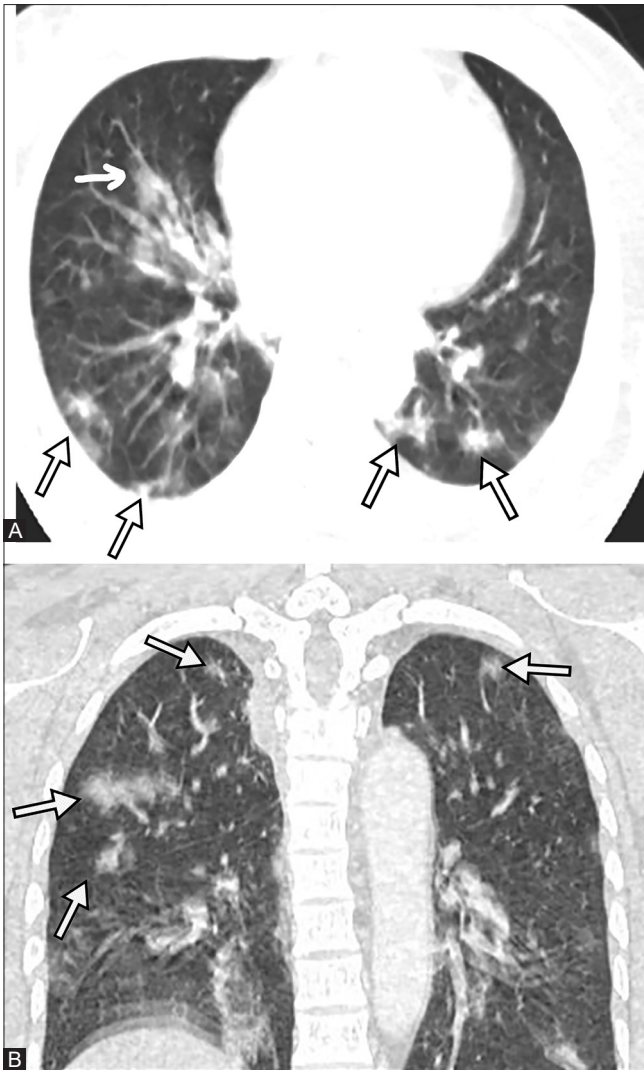
1. GGO (hazy areas of increased attenuation without obscuration of the underlying vasculature) [Figure 6A and B]
2. Consolidation (homogeneous opacification with obscuration of the underlying vasculature), [Figure 6C and D]
3. Mixed pattern (combination of consolidation, ground glass opacity, and reticular opacity in the presence of architectural distortion) [Figure 6E and F]
4. Honeycomb pattern.
5. Subsegmental vascular enlargement within the GGO (>3mm in diameter).

Furthermore, GGO can be subcategorized into: Figure 7

1. Pure GGO
2. GGO with smooth interlobular septal thickening



**Figure 4 (A-D):** (A and B) A 61-year-old man referred for CT abdomen for ureteric colic. No symptoms of COVID-19. Following incidental detection of bilateral multiple peripheral GGO (black arrows) RT-PCR was done which was positive. (C and D) A 45-year-old man with a recently detected right renal cell carcinoma and asymptomatic for COVID-19, on a metastatic workup shows a large area of GGO in the left lung (white arrow in C) on CT chest and significant increased uptake in the lesion on PET (white arrow in D). Courtesy Dr K P Sreekumar, Amrita Institute, Kochi



**Figure 5 (A and B):** A 45-year-old man with history of trauma but no chest symptoms or fever shows multiple areas of GGO peripherally as well as centrally marked by arrows. RT-PCR was subsequently positive for COVID-19

3. GGO with interlobular thickening and intralobular lines (crazy-paving pattern)
4. Irregular lines and interfaces with architectural distortion superimposed on GGO

Up to 56% imaged 0 to 2 days after symptom onset (early phase) can have a normal CT scan as opposed to 9% imaged in the intermediate phase and 4% imaged in the late phase.<sup>[14]</sup>

The lesions on CT evolve during the course of the disease showing a pattern of resolution or progression. The predominant pattern soon after symptom onset is the GGO [Figure 6A and B] which progress in extent to peak in the second week. This is followed by the mixed pattern of GGO and consolidation in the second and third weeks [Figure 6C and D]. The GGOs may contain a crazy paving pattern. Beyond this, the consolidations resolve with linear

opacities and architectural distortions and persistent lung changes show predominant GGO again [Figure 6E and F].<sup>[15]</sup>

Reverse halo and halo signs maybe seen rarely in the healing phases [Figure 7]. Pleural effusion, pericardial effusion, lymphadenopathy, cavitation, and pneumothorax are some of the uncommon findings seen with disease progression. In severely ill patients, the most commonly reported CT findings are bilateral and multilobar involvement and subsegmental consolidative opacities. Acute respiratory distress syndrome (ARDS) is the most common indication for transfer to the ICU, with most COVID-19 mortalities occurring among patients with ARDS in the ICU.<sup>[13]</sup> Extensive involvement of both lungs correlated with mortality.<sup>[16]</sup>

### Specific Patterns of Asymptomatic and Incidentally Detected Covid-19 Pneumonia on CT

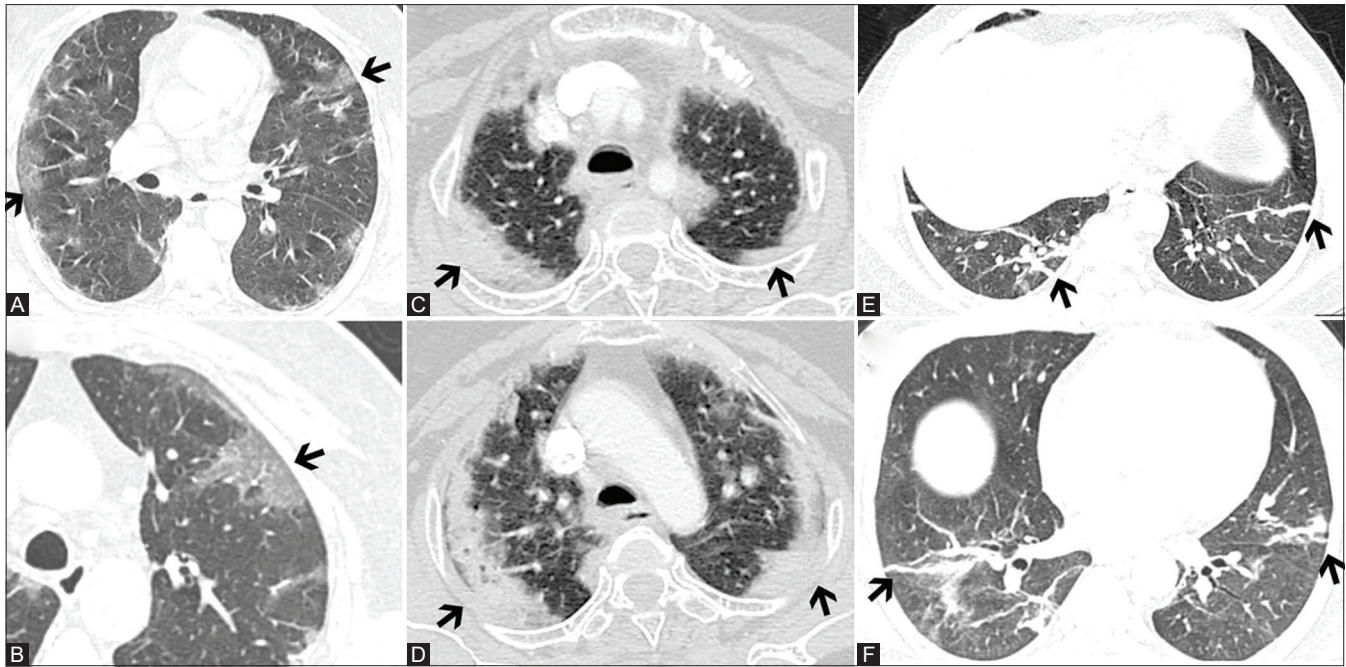
Meng *et al.* found that 95% of their asymptomatic patients presented with GGOs and 5% with consolidation. There was a predominant and subpleural distribution (76%), mostly involving one or two lung lobes (65.5%), mostly lower lobar, with right more than left lung involvement.<sup>[17]</sup> In another study of the asymptomatic subjects, more than 90% showed GGO and the remaining showed consolidations which were mild with involvement of less than 5 lung segments.<sup>[5]</sup>

GGO have been described during the first or second weeks of the exposure when the patient is contagious. They may also represent a healing phase of the disease in the fourth week when the patient is not contagious. In an asymptomatic subject, it is impossible to conclude the temporal phase of the infection. Our experience shows bilateral lung involvement with multiple opacities. Though central distribution of GGO is reported rare in asymptomatic subjects,<sup>[18]</sup> we find both peripheral and central involvement in India. Multiple segment involvement is also common. The upper lobes are also seen to be involved in many of these patients. A crazy paving pattern is also seen within the GGO in some patients. Several of our asymptomatic patients with small lesions reveal a shrinking contour [Figure 8]. The CT lesions undergo similar temporal changes as in the symptomatic population. And the patient may continue to remain asymptomatic on follow up during the transition [Figure 9].

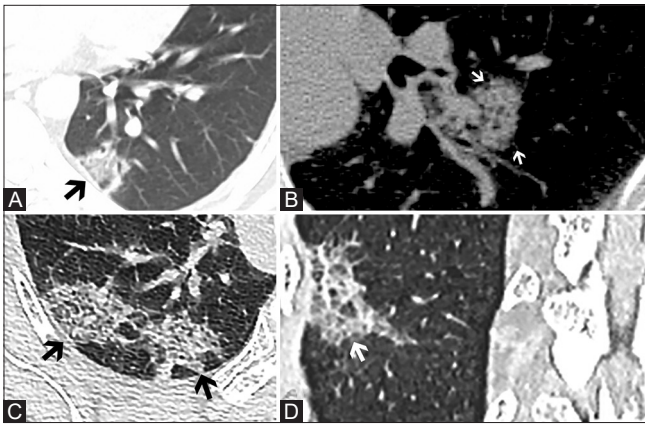
### CT Differential Diagnosis of Covid-19 Asymptomatic Pneumonia

In the clinical setting of absence of symptoms specific of Covid-19, the possibility that a given CT finding may be due to another etiology needs to be ruled out even during a pandemic [Figure 10].

Cryptogenic organizing pneumonitis (COP) and other viral pneumonia are very difficult to differentiate from Covid-19 on CT. However, these are rarely asymptomatic.



**Figure 6 (A-F):** (A and B) Early phase of COVID-19 GGO in a 65-year-old man with dyspnea for less than a week. The RT-PCR test at this time was negative and subsequently turned positive a week later. (C and D) The intermediate phase with predominant consolidations with a few GGO in a 55-year-old woman with dyspnea for more than a week. The RT-PCR was positive. (E and F) show the late phase of COVID-19 in a 42-year-old man with linear opacities and architectural distortion representing resolving consolidations. At this time, the RT-PCR which was initially positive had turned negative



**Figure 7 (A-D):** (A) A reverse halo or an atoll sign in an asymptomatic 36-year-old health care worker with central clearing of a small area of consolidation. (B) Crazy paving pattern within a central GGO in a 49-year-old male health care worker. (C and D) Crazy paving pattern in different patients who were asymptomatic

Respiratory syncytial virus differs from COVID-19 and has more of a tree in bud appearance.

Community acquired pneumonia (CAP) of bacterial origin is never asymptomatic and is usually characterized by consolidation in one segment or lobe with a sharp limiting pleural surface as compared to the bilateral, peripheral, multiple, and rounded GGOs of Covid-19. Centrilobular nodules, bronchial wall thickening, and mucoid impactions present in CAP are rare in COVID-19.

Pneumocystis pneumonia (PCP) caused by *Pneumocystis jirovecii* presents with diffuse, central, and mid-zone GGO rather than the focal peripheral GGO of Covid-19 and occurs in immunocompromised patients. Pneumatoceles and small cysts may also be seen in PCP.

Several other viral pneumonias are difficult to differentiate from COVID-19 as they may present with bilateral GGO.

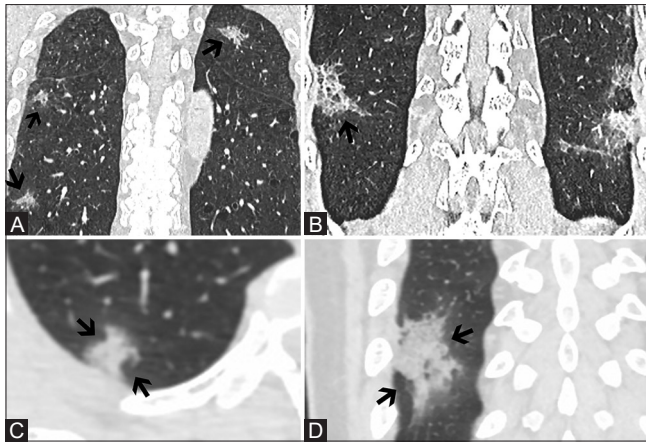
Pulmonary edema causes a central diffuse GGO sparing the periphery unlike COVID-19. It is associated septal lines and pleural effusions aiding differentiation.

Intra-alveolar hemorrhage can present as diffuse GGO again without a peripheral distribution. It is caused by small vessel vasculitis and patients usually present with mild hemoptysis and acute renal failure also associated with Goodpasture syndrome.<sup>[16]</sup>

Drug-induced pneumonitis can cause organizing pneumonia very similar to COVID-19. However, these patients are always symptomatic with history of drug exposure.

Hypersensitivity pneumonitis has a diffuse bilaterally symmetric central type of GGO differentiating it from COVID-19.

Sarcoidosis may present with GGO or small areas of consolidation. However, pulmonary involvement is



**Figure 8 (A-D):** Four different asymptomatic patients show small peripheral areas of GGO and consolidation with a shrinking margin marked by arrows

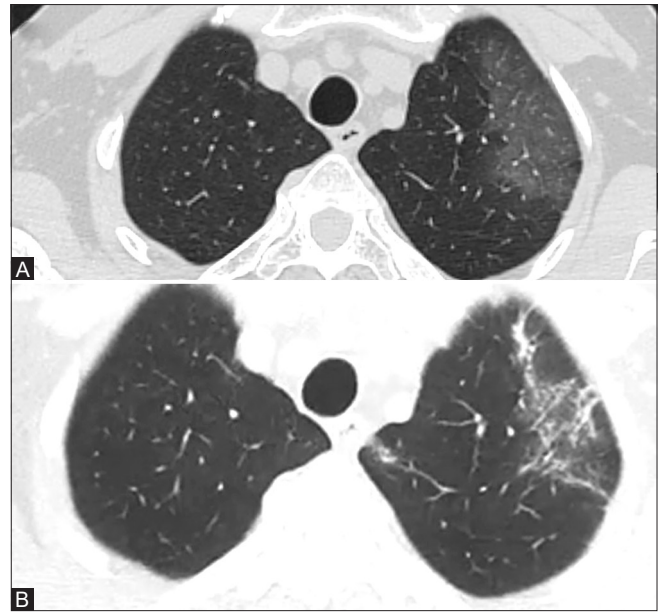
rarely asymptomatic and in majority of cases shows tiny intralobular and septal nodules. Bilateral characteristic hilar nodes are invariably present.

### RT-PCR Sensitivity and the Dilemma of RT-PCR-Negative-CT-Positive Asymptomatic Patients

Currently, the definitive diagnosis of COVID-19 relies on real-time RT-PCR on a nasopharyngeal swab or other respiratory specimens. However, RT PCR for COVID-19 has high specificity, whereas its sensitivity varies widely. Its sensitivity depends on several factors, including the quality of the sampling, site of sampling (bronchoalveolar lavage yielding more than nasopharyngeal and sputum specimen), and the viral burden at the time of specimen collection. The false-negative rate for COVID-19 RT-PCR testing is highest within the first 5 days after exposure (up to 67%). Even on day 8 after exposure up to 21% tests can be falsely negative.<sup>[19]</sup> During airport screening at Chennai, Tamil Nadu, India, 53% of the subjects testing positive in the second exit RT-PCR test had an initial negative test. The gap between the two tests was 7 days. (Data from Daily report on Public Health measures taken for COVID-19. State Control Room, Directorate of Public Health and Preventive Medicine Health and Family Welfare Department, Government of Tamil Nadu Media Bulletin 25.05.2020. <https://stopcorona.tn.gov.in/daily-bulletin/>).

The initial false-negative RT-PCR results may turn positive in subsequent tests.<sup>[20]</sup> However, it may take up to 4 days to convert to positive<sup>[9]</sup> In addition, the turnaround times of the test results can also be long.<sup>[16,21]</sup> This means that many infected patients may be missed and contribute to the community spread of the highly contagious virus. Patients may also lose the opportunity of early treatment if the disease progresses.

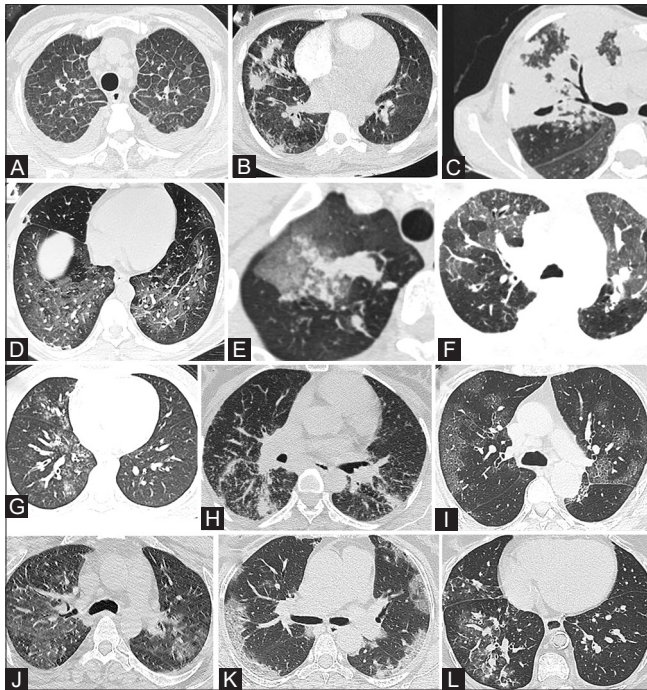
This also presents a special challenge in asymptomatic patients as CT findings precede the RT-PCR test positivity.



**Figure 9 (A and B):** 54-year-old male doctor with well controlled hypertension and no symptoms tested positive on RT-PCR. Subsequent CT showed multiple GGO. (A) shows the left upper lobar GGO at first CT. (B) shows healing phase with reduction in the GGO and appearance of linear opacities within the GGO two weeks later

Ai *et al.* demonstrated discrepant findings between RT-PCR and CT in their study. Of their 1014 patients, 59% had positive RT-PCR results. Of the 41% who had a negative RT-PCR, 75% had positive chest CT findings. In the subgroup where the initial negative RT-PCR turned positive, subsequently, 67% had positive chest CT before the negative RT-PCR results and 93% of these had typical imaging features consistent with COVID-19.<sup>[22]</sup> This means that there would be a significant proportion of patients who would show pneumonia like changes in CT without any symptoms of Covid-19 and a negative RT-PCR test. This could be because they are in the first few days of the infection (contagious phase) and the RT-PCR is yet to turn positive or because they are in the healing phase of the infection (non-contagious phase) where the RT-PCR has turned negative as seen by workers who found persistent CT changes (GGO) at discharge of 94% patients post successful treatment.<sup>[15]</sup>

COVID-19 test kits are also in short supply in some regions. Given this limited number of RT-PCR kits in some centers, the possibility of false negative results and long turnaround times, some workers have encouraged diagnosis based on clinical and Chest CT findings alone.<sup>[14]</sup> Some in Netherlands have recommended CT to assess the possibility of COVID-19 infection in adults scheduled for surgery in whom an RT-PCR test is negative or missing to prevent a greater risk for adverse post-operative outcomes and prevent infection of hospital workers and other patients.<sup>[23]</sup> A similar concern is also present prior to intensive immunosuppressive therapies in highly prevalent areas.<sup>[12]</sup>



**Figure 10 (A-L):** Various differential diagnosis of COVID-19. (A) Pulmonary edema with central GGO, interlobular septal thickening, and bilateral pleural effusions. (B) COP with peribronchovascular organizing rounded pneumonia. (C) CAP with unilateral lobar consolidation sharply limited by the oblique fissure with air bronchogram. (D) PCP bilateral diffuse central and mid zone GGO. (E) Intra alveolar hemorrhage in a patient with large volume hemoptysis shows central GGO and blood within a linear dilated bronchus. (F) Hypersensitivity pneumonitis shows diffuse bilaterally symmetrical and central GGO. (G) H1N1 influenza GGO in the right lower and middle lobes with centrilobular and peribronchial small nodules. (H) Sarcoidosis showing small bilateral peripheral consolidations with innumerable centrilobular and septal tiny nodules and bilateral hilar adenopathy. (I) COVID-19 pneumonia in an asymptomatic patient with bilateral peripheral and central GGO with crazy paving pattern. (J) Everolimus-induced interstitial pneumonitis with bilateral GGO. (K) COVID -19 showing bilateral peripheral GGO in a patient with cough for a week. (L) *Klebsiella pneumonia* showing right middle and lower lobar centrilobular GGO in an ABO incompatible post renal transplant patient with fever and dyspnea

In India, the cost of RT-PCR test kits and its lack of easy access places a constraint on repeated testing and an initial negative RT-PCR may discourage a second test attributing the CT findings as nonspecific and incidental due to other pathology delaying treatment and spreading infection to vulnerable populations.

### Significance of Incidentally Detected Asymptomatic Covid-19 Pneumonia on CT and Recommendations

COVID-19 has now recognizable appearances on CT. In a pandemic setting, these findings cannot be ignored when the RT-PCR test is negative especially in the absence of an alternative explanation. Radiologically visible COVID-19 pneumonia is potentially contagious. While a small number of these patients can progress to symptoms, a majority can

continue to be asymptomatic and undetected. Meng *et al.* found that 25% of their asymptomatic patients with covid-19 pneumonia on CT presented symptoms while 17% showed evolution of CT findings on the short-term follow-up.<sup>[17]</sup> Therefore, while specific tracks for suspected or known COVID-19 patients have been established, one should keep in mind that asymptomatic or pauci-symptomatic carriers are potentially present in the non-COVID-19 arm of healthcare.<sup>[18]</sup>

Several pathways may be triggered by such patients detected incidentally on CT done for other indications where treatment is being planned.

1. Radiology technicians might be unexpectedly exposed and in a pandemic setting should be provided with adequate protective equipment considering every patient a potential occult COVID-19 carrier in high prevalence areas
2. A screening CT chest may be worthwhile for all patients undergoing a CT procedure as well as those planned for surgery or immunosuppressive therapy
3. Records of Radiology staff attending to every patient should be maintained in the event a significant exposure is detected and a quarantine protocol needs to be initiated
4. Review of screening chest CT is done quickly preferably while the patient is on the CT table to quickly initiate personal protective measures and decontamination measures of the premises post scanning
5. Post scanning, the patient should be directed to the COVID-19 care and treatment arm of the healthcare
6. In the event the RT-PCR is negative and the CT is highly suggestive of COVID-19, the patient should still be treated as strong COVID-19 suspect with close surveillance and appropriate isolation protocols as per the institution. It is prudent to repeat the RT-PCR for COVID-19 a second time in a patient with a strongly suggestive radiological picture.

### Conclusion

Incidental findings highly suspicious of COVID-19 pneumonia on CT chest of asymptomatic patients may increase as community transmission of the virus rises. It is advisable to be aware of its appearances and the challenges associated with it. The COVID-19 pandemic will take some time to run its course and even after if it begins ebbing away, sporadic cases may show up as asymptomatic incidental findings on CT done for other indications. These represent occult community infection and need to be addressed swiftly. Being vigilant and alert to this possibility will help in reducing the returning second waves of the infection.

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**Conflicts of interest**

There are no conflicts of interest.

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