Correlation between chest CT and RT-PCR testing in India’s second COVID-19 wave: a retrospective cohort study

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Abstract

Objectives To assess the diagnostic accuracy of chest CT in clinically suspected patients with COVID-19 using reverse transcriptase PCR (RT-PCR) as the reference standard and establish the correlation between CT Severity Score (CTSS) and RT-PCR results.


Participants We enrolled 112 clinically suspected patients with COVID-19 between 1 April 2021 and 31 May 2021. Chest CT and RT-PCR tests were performed for all patients at a time interval of no longer than 7 days between the two tests. Patients with prior chronic respiratory illnesses were excluded. The diagnostic performance of chest CT was evaluated using RT-PCR as the reference standard. The CTSS was calculated for all patients with positive chest CT findings, and it was correlated with results of the RT-PCR assay.

Main outcome measures The primary outcome measures were determination of the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of chest CT using RT-PCR as the standard of reference. The correlation between CTSS and RT-PCR was the secondary outcome.

Results 85/112 (76%) patients tested positive on the RT-PCR whereas 91/112 (81%) had chest CT findings typical of SARS-CoV-2 infection. Chest CT had a sensitivity of 90.6% (95% CI 82.3% to 95.8%), a specificity of 48.1% (95% CI 28.7% to 68.0%), a PPV of 84.6% (95% CI 79.2% to 88.8%), an NPV of 61.9% (95% CI 43.0% to 77.8%) and an accuracy of 80.4% (95% CI 71.8% to 87.3%). There was a significant correlation between the CTSS and RT-PCR positivity (p value=0.003).

Conclusion In our experience, chest CT has a good sensitivity and provides a reliable diagnostic tool for moderate-to-severe COVID-19 cases in resource limited settings.

Introduction

In December 2019, a novel coronavirus, that would later be designated as SARS-CoV-2, was found to be responsible for a cluster of pneumonia cases originating in Wuhan City, Hubei province, China. The clinical disease caused by it came to be known as COVID-19 and spread rapidly all over the world, being responsible for more than 190 million infections as of 16 July 2021. In symptomatic patients, cough (50%), fever (43%), myalgia (36%) and headache (34%) are the most commonly reported symptoms. Other presenting features include dyspnoea, sore throat, diarrhoea, nausea/vomiting and loss of smell or taste. Symptomatic infection can range from mild to severe and patients initially presenting with non-severe symptoms may later progress to severe disease.

Complications frequently described in COVID-19 include respiratory failure due to acute respiratory distress syndrome, cardiovascular complications (arrhythmias, myocardial injury and infarction, heart failure and shock), thromboembolic phenomena, neurological complications (stroke, encephalopathy and Guillain-Barré syndrome), secondary infections and septicemia.

Tests in use for diagnosing COVID-19 infection in India include molecular-based tests—reverse transcriptase PCR (RT-PCR), TrueNat and CBNAAAT, Rapid Antigen Detection Tests and Antibody Rapid Tests. The current reference standard is the RT-PCR test which detects viral RNA in respiratory samples such as nasopharyngeal or
oropharyngeal swabs and bronchial aspirates. The RT-PCR test has been found to have varying sensitivities ranging from 28% to 85%.7–12 This test is time consuming and false negative results are common within the first 7 days of infection and if the sample is not collected in the time period of viral replication or if the viral genome is missed.13

As COVID-19 primarily targets the lungs, and due to inability of the RT-PCR to successfully diagnose all cases of COVID-19, it would appear that chest CT would play a crucial role in the diagnosis, evaluation and management of the disease. However, evidence available regarding its clinical utility in COVID-19 is conflicting.9–14 Islam et al in their review included 51 studies and found the chest CT to have a pooled sensitivity of 87.9% and a pooled specificity of 80.0%.15 A meta-analysis including 60 articles, found the sensitivity and specificity of initial chest CT to be 87% and 43%, respectively. It is reported that among dead patients with positive chest CT findings but negative RT-PCR, 87% are COVID-19 positive. Hence, it is recommended that patients with positive chest CT and negative RT-PCR, be tested with repeat PCR up to three times.16 Xu et al reported the chest CT scan to have high sensitivities in endemic areas but low specificity.17

The Society of Thoracic Radiology and the American Society of Emergency Radiology do not recommend routine CT chest for screening patients under investigation for COVID-19 and recommend its use in evaluating complications.18 The American College of Radiology does not recommend chest CT for screening or diagnosis of COVID-19, reserving its use for hospitalised and symptomatic patients with clinical indications.14 A consensus statement from the Fleischner Society suggests chest CT scanning for patients with moderate to severe symptoms, regardless of COVID-19 test results.19 According to WHO recommendations, chest CT should be a part of the diagnostic work-up in a suspected patient with COVID-19 when RT-PCR testing is unavailable, results are delayed or in case of a negative test but with high clinical suspicion. They also advise chest CT to decide on hospitalisation, intensive care unit admission and therapeutic management under specific circumstances.20 In the Indian scenario, Garg et al recommend the use of chest CT in suspected cases of COVID-19 with moderate- to-severe respiratory symptoms and a high index of suspicion for COVID-19 but who test negative on RT-PCR and have a normal/indeterminate chest X-ray.21

India experienced a sharp rise in COVID-19 cases beginning from mid-March 2021, a crisis which overwhelmed the healthcare system leading to a shortage in oxygen supplies and hospital beds all over the country. This may have resulted from the spread of a new variant of the virus, now known as B.1.617, believed to have more transmission ability, and a disregard of ‘COVID-19 Appropriate Behaviour’ by a vast majority of the population.22–24 The second wave has also seen an increase in the number of negative RT-PCR tests in patients with COVID-19 symptoms,21 raising questions about the quality of testing and the ability of the mutant virus to evade detection. The value of chest CT in diagnosing COVID-19 in areas with a high incidence and prevalence has been suggested by Falaschi et al.24 A study from China has reported a 97% sensitivity of chest CT in diagnosing COVID-19 in a group of 1014 patients.25

Our study aims to determine the accuracy of chest CT in diagnosing COVID-19 infection using the RT-PCR as the reference standard. Furthermore, we seek to determine the correlation between CT Severity Scores (CTSSs) (an adaptation of the method used in the SARS epidemic, 2005)25 and RT-PCR results.

Materials and methods

Patient population and study design

We enrolled a series of 112 patients admitted to our emergency department from 1 April 2021 to 31 May 2021. Inclusion criteria for patients were:

1. Patients aged 18 years and above.
2. Clinically suspected COVID-19 as defined by the Ministry of Health and Family Welfare, Government of India.26
3. Having undergone a chest CT and at least 1 RT-PCR assay within 7 days of admission.

Exclusion criteria were:

1. Time interval between chest CT and RT-PCR >7 days.
2. Unknown RT-PCR report.
3. Pre-existing chronic respiratory illness like pulmonary tuberculosis, chronic obstructive pulmonary disease (COPD) and interstitial lung disease.

A flowchart of the study is shown in figure 1.

For patients with multiple RT-PCR assays, the diagnosis of COVID-19 was made when any one of the test results was positive. Patients with a time interval between chest CT and RT-PCR assay longer than 7 days were excluded from the study group.

Patient details

Details such as age, sex, date of RT-PCR and chest CT scans were obtained for each patient.

Each patient was assigned a progressive identification number. This was done to guarantee anonymity and non-disclosure of sensitive information.

Chest CT protocol and image analysis

All images were obtained on a 16 slice CT scanner (Philips MX16Evo, Philips Healthcare, Netherlands). The scanning parameters were as follows: tube voltage 120 kVp, tube current modulation 250 mAs, pitch 0.99–1.22 mm, matrix 512x512. All images were reconstructed with a slice thickness of 1.5 mm.

CT images were evaluated by two radiologists with 8 and 12 years’ experience, respectively. History and clinical features were available to both the interpreters, but they were blinded to RT-PCR results. The CT scans were defined as positive or negative based on CT findings compatible with SARS-CoV-2 infection as defined by the RSNA consensus statement.27 The radiologists also described the main CT features (ground-glass opacity, consolidation, thickened interlobular septa, crazy paving) and site of lesion (left, right or bilateral). CT scans with ‘typical’ and ‘indeterminate’ findings were considered positive and those with ‘atypical’ or ‘negative’ findings were considered as negative (figures 2 and 3).

Severity of lung involvement on the chest CT was assessed using the severity score developed by Chang et al.25 and is shown in tables 1 and 2.

RT-PCR testing

Laboratory confirmation of SARS-CoV-2 infection was done using the RT-PCR assay. The test was based on detection of the E gene (envelope protein), and RdRP (RNA-dependent RNA-polymerase) of the SARS-CoV-2 using nucleic acid amplification by RT-PCR. This test is currently considered the reference standard for diagnosis of COVID-19 and was the test used to assess the diagnostic accuracy of chest CT. RT-PCR reporting was performed by microbiologists blinded to results of the chest CT.
The statistical analysis was performed using the SPSS V.26.0 (IBM Corp). Continuous variables were reported as median (IQR) and categorical variables as counts and percentages. Using the RT-PCR as the standard of reference, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and

Figure 1  Flowchart of the study. RT-PCR, reverse transcriptase PCR.

Figure 2  Chest CT images of a 78-year-old man with symptoms of fever and shortness of breath for 6 days, showing bilateral ground-glass opacities and bronchiectatic changes. The CT Severity Score was 10/25 suggestive of moderate COVID-19 pneumonia.
diagnostic accuracy of chest CT was calculated. Diagnostic accuracy was calculated using the formula (TP+TN)/(TP+FP+TN+FN) where TP=true positives, TN=true negatives, FP=false positives and FN=false negatives. A 95% CI was provided by the Wilson score method. \( \chi^2 \) test was used for comparing the performance of chest CT in different predefined age groups (<60 years and ≥60 years) and between males and females. An age cut-off of 60 years was taken based on findings of Ai et al, who reported a higher PPV and diagnostic accuracy of the chest CT in ≥60 years age group.9 The Standards for Reporting Diagnostic Accuracy (STARD) guidelines have been followed in reporting all observations.

The CTSS was correlated with RT-PCR positivity using the Spearman correlation coefficient. A p value <0.05 was considered as significant in all cases.

Patient and public involvement

Patient details were collected from hospital records after approval from the Institutional Ethics Committee from 1 April 2021 to 31 May 2021. Informed consent was waived, and all patient details were kept anonymous by using unique identification numbers. Patients/public were not directly involved in the development of the research question or in the implementation of the study as this was a retrospective study.

Results

Patient details

As shown in figure 1, a total of 326 patients with clinically suspected COVID-19 were admitted in our emergency department from 1 April 2021 to 31 May 2021. Out of these 187 patients were excluded as a test other than RT-PCR was used for diagnosis (eg, TrueNat, Rapid Antigen Detection Test) and 27 patients were excluded as the time interval between RT-PCR and chest CT was longer than 7 days. After the exclusion of these patients, a total of 112 patients (median age 48 (IQR 24), 69% (77/112) male) were included in the analysis.

Seventy-six per cent (85/112) (95% CI 61% to 94%) patients had a positive RT-PCR result and 24% (27/112) (95% CI 16% to 35%) had a negative RT-PCR test. Out of the patients that tested positive, 4 required ≥1 RT-PCR assay (2, 2, 3 and 2, respectively) for diagnosis. The median time interval between chest CT and RT-PCR assay was 2 days (range 0–7 days). Positive chest CT findings were seen in 81% (91/112) (95% CI 65% to 99%) patients, while 19% (21/112) (95% CI 12% to 29%) patients had negative chest CT scans. Baseline characteristics are shown in table 3.

CTSS was calculated for 91 patients with positive chest CT scans (median, 11 (IQR 12)). 17% (16/91) (95% CI 10% to 28%) had a mild CTSS, 42% (38/91) (95% CI 29% to 57%) had a moderate CTSS and 41% (37/91) (95% CI 29% to 56%) had a severe CTSS.

Diagnostic performance of chest CT

Using the RT-PCR as reference (table 4), 77 patients were found to be true positives and 13 patients were true negatives (TN). Fourteen patients tested negative on the RT-PCR but had positive chest CT findings (false positives, FP), whereas eight patients who tested positive on the RT-PCR had negative chest CT findings (false negatives, FN). The sensitivity, specificity, PPV, NPV and diagnostic accuracy of chest CT were 90.6% (95% CI 82.3% to 95.9%), 48.1% (95% CI 28.7% to 68.1%), 84.6% (95% CI 79.2% to 88.8%), 61.9% (95% CI 43.0% to 77.8%) and 80.4% (95% CI 71.8% to 87.3%) respectively.

The performance of the chest CT among different age and sex groups is reported in table 4. There were no statistically significant differences for sensitivity, specificity, PPV, NPV and diagnostic accuracy among different age groups (<60 years and ≥60 years), (p values=0.24, 0.15, 0.17, 0.20 and 0.06, respectively), and in between males and females (p values=0.99, 0.58 0.08, 0.09 and 0.33, respectively). The positivity rate of the RT-PCR was 78.7% in <60-year age group, 74.6% in ≥60-year age group, 68.0% in males and 91.4% in females.

### Table 1

<table>
<thead>
<tr>
<th>Lobar involvement</th>
<th>Score</th>
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<tbody>
<tr>
<td>No involvement</td>
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</tr>
<tr>
<td>5% or less</td>
<td>1</td>
</tr>
<tr>
<td>5%–25%</td>
<td>2</td>
</tr>
<tr>
<td>26%–49%</td>
<td>3</td>
</tr>
<tr>
<td>50%–75%</td>
<td>4</td>
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<tr>
<td>≥75%</td>
<td>5</td>
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### Table 2

<table>
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<tr>
<th>Total score</th>
<th>Severity</th>
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<tr>
<td>7 or less</td>
<td>Mild</td>
</tr>
<tr>
<td>8–17</td>
<td>Moderate</td>
</tr>
<tr>
<td>18 or more</td>
<td>Severe</td>
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In the 91 patients with positive chest CT scans, we correlated the CTSS with RT-PCR results. CTSS was found to have significant correlation with RT-PCR results (p value=0.003) and patients with higher CTSS were more likely to be RT-PCR positive (figures 4 and 5).

### Analysis of FP, FN and TN

14/112 (12.5%) patients had positive chest CT findings but tested RT-PCR negative. All of these patients were isolated and treated according to COVID-19 guidelines based on clinical suspicion, national guidelines and chest CT findings until they were discharged (11/14) or till demise (3/14). 8/14 patients had repeat RT-PCR tests, all of which were negative.

8/112 (11.6%), with positive RT-PCR results, had negative chest CT scans. 7/8 (87.5%) of these patients had clinically mild COVID-19, while 1 patient had moderate symptoms. In 13/112 (11.6%) patients both RT-PCR and chest CT were negative. Out of these, 1/13 (7.7%) patients had a final diagnosis of chronic heart failure, and 3/13 (23.0%) patients had a diagnosis of COPD. In the remaining nine patients, five were treated for community acquired pneumonia with antibiotics and supportive measures, with clinical recovery in three patients and death in two patients. Clinical data were unavailable for four patients, as they opted for treatment at other hospitals or were deferred for home treatment.

### Discussion

In our study, we analysed 112 patients presenting to our emergency department with clinically suspected SARS-CoV-2 infection to assess the performance of chest CT scan using the RT-PCR as the standard of reference, during the second peak of the COVID-19 pandemic in India. RT-PCR had a positivity rate of 76%, which was comparable to that observed during the first peak. The positivity rate of chest CT was 81%, resulting in a sensitivity of 90.6% and a specificity of 48.1%. Unlike previous studies, there was no significant difference in the performance of chest CT between different age groups (<60 years and ≥60 years) and between males and females. Patients with more severe CT scan findings were more likely to test RT-PCR positive (p value=0.003).

The sensitivity of the chest CT in our study was higher than that reported in previous systematic reviews. In a disease where diagnosing every case is crucial to limit the spread and prevent the associated morbidity and mortality, the requirement of a quick, reliable diagnostic tool is essential.
RT-PCR has been found to lack sensitivity and requires a long processing time with results sometimes taking up to 7 days in the Indian scenario due to the case burden and inadequate testing facilities. The results are also influenced by factors like the timing and adequacy of sampling site, sample collection and reliability of the diagnostic kits. Wang et al found bronchoalveolar lavage fluid to have the maximum RT-PCR positivity rate (93%), followed by sputum (72%), nasal swabs (63%), fiberbronchoscope brush biopsy (46%), pharyngeal swabs (32%), faeces (29%) and blood (1%).

Nasopharyngeal samples have been found to have maximum positivity rates around the onset of symptoms, gradually declining by 2–3 weeks. Nucleic acid targets detected by RT-PCR kits also influence the sensitivity of the assay, with certain combinations of nucleic acid targets showing higher sensitivities. Furthermore, genetic mutations in the SARS-CoV-2 viral genome can affect annealing in the PCR assay. For these reasons, it is safe to say that the RT-PCR is an imperfect reference standard. In a setting where RT-PCR may be unreliable or not available, chest CT scanning provides a cheap and non-invasive imaging tool, with a diagnostic accuracy of 80.4%.

In our experience of treating 14 chest CT positive and RT-PCR negative (false positive) patients based on COVID-19 guidelines, 11/14 (78.5%) had a clinical recovery, suggesting that they might indeed have been COVID-19 positive. In the remaining three patients, no alternative clinical/aetiological diagnosis could be established. 7/8 (87.5%) patients who were RT-PCR positive but chest CT negative (false negative), had mild symptoms and median duration of chest CT scan in these patients was 2 days from symptom onset, suggesting that they might have been in the initial phase of the illness and a repeat CT scan may be warranted in such cases.

We believe that chest CT scanning in clinically suspected patients with COVID-19, especially those with moderate to severe symptoms, may be useful and this needs further assessment in the context of the development of clinical practice guidelines.

Our study had various limitations. Due to inadequacy of RT-PCR testing kits and availability of alternative faster diagnostic tests (TrueNat and Rapid Antigen Tests) at our hospital, many patients were subjected to these tests instead of the RT-PCR. Not all patients who tested RT-PCR negative were subjected to repeat RT-PCR tests due to limited resources. The diagnostic accuracy of chest CT is also likely to depend on the site, quality and timing of RT-PCR testing. This could not be assessed in this study due to incomplete clinical data. Patients with pre-existing...
respiratory illnesses were not included in this study. It is conceivable that the number of false positives would be higher in this population subset due to overlapping chest CT findings. Over-reliance on the chest CT in this situation could be detrimental and CT findings should be interpreted with appropriate clinical context. There is a discrepancy between the number of subjects in different age groups (<60 years and ≥60 years) and between males and females. A small sample size may be the reason why we could not reproduce a significant difference in the performance of the chest CT between these groups, seen in previous studies. Due to the small sample size used in this study future studies are required to validate these findings.

Conclusion
Chest CT has a good sensitivity in detecting COVID-19 pneumonia and is useful for moderate-to-severe COVID-19 cases in resource limited settings, where RT-PCR testing is cumbersome due to lack of personnel, time and diagnostic kits.

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Competing interests None declared.

Patient consent for publication Not applicable.

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Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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