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Original Article

Role of High Resolution Computed Tomography (HRCT) In Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR) Test Negative Symptomatic Patients for Covid-19 Pneumonia

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Abstract

Background: For the diagnosis of SARS-CoV-2 infection RT-PCR test has become a standard. Because of insufficient specimen or laboratory error RT-PCR testing results may be falsely negative. HRCT has a higher rate of detection of patients with disease in incubation period, particularly with initial negative RT-PCR results. Thus, CT is helpful for early diagnosis, timely isolation, and treatment of COVID-19 pneumonia.
Aim: The aim of the study is to know the role of High-resolution computed tomography (HRCT) in those with negative initial RT-PCR results with highly suspected SARS CoV-2 infection.
Materials and Methods: For a duration of 6 months from May 2020 to October 2020 , A cross sectional study was conducted with a total of 100 patients after obtaining the informed consent at Department of Radio diagnosis , KR Hospital attached to Mysore Medical College and Research Institute, Mysore**.**
High resolution Computed tomography (HRCT) of thorax was performed with 128 slice single source dual energy Multi-detector Computed tomography machine.
Results: In our study Ground glass opacity and consolidation are two main HRCT features of COVID-19 lesions in RTPCR negative symptomatic patients and is seen among 70 and 32 patients respectively, while combination of ground glassing and consolidation was seen in 42 patients. The lesions were predominantly peripheral or subpleural in 44 patients (48%), both subpleural and centroparenchymal in 45 patients (50%) and only 1 patient (1.1%) in centroparenchymal location.
Conclusion: HRCT chest scan plays an important role in detecting COVID-19 in those symptomatic patients in whom RT-PCT test results are negative. In the context of the current pandemic and multiple genetic mutations of the virus, in patients with clinical symptoms or a history of exposure, positive HRCT should be regarded as strongly suspicious for COVID-19 pneumonia, despite negative RT-PCR test results.
Keywords: Ground glass opacity, Consolidation, Crazy paving**.**

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Introduction

On December 31, 2019, the World Health Organization (WHO) was alerted to several cases of a respiratory illness of unknown causation emerging from Wuhan, China. Corona virus was found to be the culprit in bronchoalveolar lavage fluid analysis and electron microscopy.[1]

SARS-CoV-2 virus primarily affects the respiratory system, although other organ systems are also involved. Respiratory tract infection related symptoms including fever, dry cough and dyspnea. However, it is now widely recognized that COVID-19 respiratory symptoms are extremely heterogeneous and dangerous as it can cause ARDS.[2,3]

Currently for the diagnosis of SARS-COV-2, Reverse transcription–polymerase chain reaction (RT -PCR) test detects the virus in most of the patients. Because of insufficient specimen or laboratory error RT-PCR testing results may be falsely negative. Nowadays, genetic mutations of SARS-CoV-2 virus is one of the most important cause for RT-PCR negativity[4]

Computed Tomography (CT) had a higher detection rate in patients with disease in the incubation period, particularly for those with negative initial RT-PCR results.[1]

For those with negative RT-PCR screening and high suspicion of COVID-19 infection, Computed Tomography (CT) imaging can be used as a tool to diagnose the disease[4]

Knowledge of the common CT patterns encountered in RTPCR negative patients helps us in early diagnosis enabling patients to be isolated and treated early, thus avoiding the spread of disease, improving prognosis, and reducing mortality.

Thus, the study aims to Enumerate the chest Computed Tomography (CT) features in patients with negative RTPCR results with highly suspected COVID-19 pneumonia.

Material and Methods

Study population: For a duration of 6 months from May 2020 to October 2020, A cross sectional study was conducted with a total of 100 patients after obtaining the informed consent at Department of Radiodiagnosis , KR Hospital attached to Mysore Medical College and Research Institute, Mysore

Inclusion criteria: Patients who had symptoms of cough, breathlessness, fever of > 38^{0}C with strong COVID-19 pneumonia suspicion, But RT-PCR tests are negative.

Exclusion criteria: Paediatric age group less than 18 years, Pregnant women.

Ethics Committee's approval was obtained (EC REG: ECR/134/Inst/KA/2013/RR-19).

Scanning protocol: High resolution Computed tomography (HRCT) of thorax was performed with 128 slice single source dual energy Multidetector Computed tomography machine.

Region from both apices to adrenals were included. Patient position was supine with arms above head and following parameters were used: 20 mA, 100 kV, slice thickness 0.6mm, scan orientation: craniocaudal. The images were reconstructed to obtain 0.6mm section in sagittal and coronal planes.

Computed tomography Image Evaluation: All the unenhanced CT images were evaluated in preset standard pulmonary (width, 1500–2000 HU; level, −450 to 600 HU) and mediastinal (width, 400 HU; level, 60 HU) windows.

The radiological features in our study are described in various headings as follows: (a) Involvement of unilateral or bilateral lungs; (b) Location of the lesion (s) are studied, if they are present in lower, upper, or both lobes; (c) Number lesion (s) - single lesion, if there is only one lesion; multiple lesions, if there are 2 –4 lesions in every lung, and diffuse lesion, if lesions involved the entire lobe bilaterally; (d) Distribution of lesion (s) - defined as central, peripheral or both central and peripheral; (e) Ground glass opacities (f) Consolidation (g) Presence or absence of reticular opacities (h) Presence or absence of nodules (i) Presence or absence of vascular thickening, septal thickening, bronchial wall thickening; (j) Presence or absence of air bronchogram. (m) Cavity; (n) Cyst (o) Crazy-paving (p) Halo sign; (q) Reverse halo sign; (r) Pleural effusion (s) Pleural thickening; and (t) Lymphadenopathy, described as a lymph node with size than greater than 1 cm in short axis.

Statistical analysis: Microsoft excel was used to tabulate and evaluate descriptively the results of the study.

Results

Our study included 100 patients. It comprised of 60 males and 40 females. Among these patients, 90 patients show CT features related to covid-19; 10 patients didn't show any CT features even though they were symptomatic.

Most affected age group in our study was 4th decade, youngest patient to show CT changes aged 24yrs, whereas the oldest one aged 84 years and the mean age was 42.5 years. [Table-1].

Table-1 Age Distribution among COVID-19 infection patients.

Age	Frequency	Percentage
21-30 yrs	10	10%
31-40 yrs	30	30%
41-50 yrs	22	22%
51-60 yrs	18	18%
61-70 yrs	14	14%
71-80 yrs	4	4%
>81yrs	2	2%
Total	**100**	**100.0**

In our study showed that disease affected all five lobes in 55 patients, right upper lobe in 70 patients, right middle lobe in 63 patients, right lower lobe in 67patients, left upper lobe in 64patients, left lower lobe in 61 patients. 59 patients in our study showed the bilateral involvement.84 patients showed multiple lesions, i.e > 3 lesions Table- 2.

Ground glass opacity (GGO) and consolidation were the two main HRCT features of COVID-19 lesions on CT images. Ground glass opacity is seen among 70 patients; among them 40 patients (66%) had predominant peripheral distribution. Ground glass opacities with consolidation, seen among 42 patients (46.6%). And consolidation was seen in 32 patients Table-2.

Table -2 : Distribution of lesions

Lobes of lung	No of patients n (%)
Right upper lobe	70(77.7%)
Right middle lobe	63(70.0%)
Right lower lobe	67(74.4%)
Left upper lobe	64(71.1%)
Left lower lobe	61(67.7%)
All Five lobes involved	55(61.1%)
Unilateral lung involvement	31(34.4%)
Bilateral lung involvement	59(65.5%)
Multiple (>3) lesions	84(93.3%)

Additional patterns of COVID-19 lesions which were noted in our study are listed in Table-3.

Table-3: Distribution of HRCT characteristics.

HRCT characteristics	Distribution n (%)
Ground glass opacities	70(77.7%)
GGO with consolidation	42(46.6%)
Consolidation	32(35.5%)
Linear opacities	18(20.0%)
Crazy paving	20(22.2%)
Reticular opacities	21(23.3%)
Halo sign	5(5.5%)
Reversed halo sign	1(1.1%)
Nodules	0
Airbronchogram	9(10%)
Cavitation	4(4.4%)
Pleural effusion	4(4.4%)
Pericardial effusion	3(3.3%)
Lymphadenopathy	9(10%)

Predominantly peripheral or subpleural lesions seen in 44 patients (48%), both subpleural and centroparenchymal in 45 patients (50%) and only 1 patient (1.1%) in centroparenchymal location Table-4.

Table-4: Location of Ground Glass Opacities

Location of Ground Glass Opacities	Distribution (N=100)
Subpleural	44%
Centroparenchymal	1%
Both (subpleural and centroparenchymal)	45%

Discussion

Our study detects 90 cases who had Chest HRCT features related to covid-19 pneumonia in 100 symptomatic cases.

Thus, HRCT thorax is useful, in patients with a suspicious clinical presentation of COVID-19 and a negative initial SARS-CoV-2 RTPCR.

GGO (Ground glass opacity) and consolidation were the two main HRCT features in RT-PCR negative, symptomatic patients of our study. Presence of bilateral, multiple, sub-pleural ground glass opacities and consolidatory changes are to be considered as covid-19 pneumonia in this current pandemic, even though the RT-PCR results are negative.

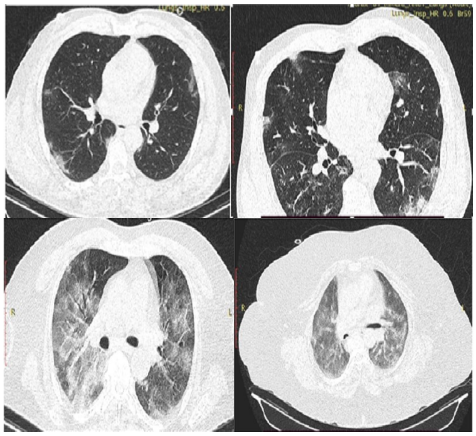
Ground glass opacities (GGO)

Subpleural and peripheral distribution of GGO is common in patients with RT-PCR positive COVID-19 pneumonia.[5] In our study, Ground glass opacities were the major radiological feature with subpleural predominance similar to patients with RT-PCR positive COVID-19 pneumonia. [Table-5 and Figure-1].

Table-5: Comparison table between various studies on COVID-19 pneumonia.

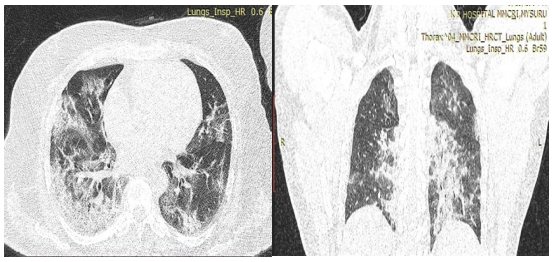
	RT-PCR negative group	**RT-PCR Positive group**	**RT-PCR Positive group**	**RT-PCR Positive group**	**RT-PCR Positive group**
	Our study	Chen, Hui Juan et al	Wu J, Pan J, Teng D, Xu X, Feng J, Chen YC et al	Ali Abbasian Ardakani1 & U. Rajendra Acharya et al	Yan Li, Liming Xia et al
Centroparenchymal	1%	0%	6.1%	10.65%	0%
Subpleural	44%	71%	78.4%	60.25%	96.1%
Both (subpleural and centroparenchymal)	45%	29%	15.5%	29.10%	3.9%
GGO	60%	65%	53.8%	72.54%	35.3%
GGO with consolidation	42%	8%	46.2%	41.39%	54.9%
Bilaterality of lesions	59%	-	89.3%	72.13%	-
Multiple lesions(>3)	84%	76%	86.9%	88.9%	-

Figure-1: Axial HRCT chest images shows ground glass opacities.



Consolidation: Multifocal, patchy, or segmental consolidation, distributed in subpleural areas or along bronchovascular bundles, is seen in patients with RT-PCR positive COVID-19 pneumonia.[5] In our study, consolidation with ground glass opacities was the second most common radiological feature similar to patients with RT-PCR positive COVID-19 pneumonia Figure-2.

Figure-2: Axial and coronal HRCT chest images showing ground glass opacities with adjacent consolidation.



In a study conducted by Chen, Hui Juan et al on RT PCR negative patients 34 (65%) patients predominant findings was ground-glass opacity in 22 patients, 17 had five lobes of lung involvement, while the 23 (68%) patients had lower lobe involvement.[6]

Similarly In a study conducted by Wu J, Pan J, Teng D, et al on RT PCR Positive patients showed that 89.2% of cases had bilateral disease, 86.9 % of cases had multiple lesions, and Most of lesions are distributed in sub-pleural location.[7] And GGO and consolidation are the most common CT signs of RT-PCR positive COVID-19 pneumonia, mainly with

lobular distribution and subpleural distribution.[7] Similar findings are noted in our study, suggesting that presence of GGO and consolidation in this pandemic can be considered for the diagnosis of SARS -CoV-2 infection.

In a study conducted by Mohammad Karam, et al, reported that CT scanning performs relatively well compared to RT-PCR.[8]

In a retrospective study conducted by Fang et al.[9] reported that the sensitivity of HRCT in detecting COVID-19 pneumonia is higher than RT-PCR. Fang and colleagues retrospectively determined that 50 of the 51 patients (98%) had abnormal findings on baseline CT scans, whereas only 36 of the 51 patients (71%) had positive initial RT-PCR tests.

These studies again reassure that chest CT scan may be a useful adjunct in the initial detection of COVID-19 in the context of a pandemic.

We found that in a study conducted by Yan Li, Liming Xia et al found that chest HRCT had a low rate of missed diagnosis of COVID-19(3.9%, 2/51) and may be useful as a standard method for the rapid diagnosis of SARS-CoV-2 infection to optimize the management of patients.[10]

And the current laboratory tests requires substantial time, and there is a consistent growing need of infected population for test kits which may not be met by RT-PCR testing. RT-PCR testing itself may have inherent laboratory error or insufficient viral sample in the specimen collected.[11]

On further review of literature, in a retrospective study done by Inan Korkmaz, Nursel Dikmen et al which had cases with both positive and negative RT-PCR results with clinical suspicion of COVID-19 showed that ground-glass opacity and combination of ground-glass opacity with patchy consolidation was the most common pattern in both groups with no significant differences in the frequencies and types of lesion patterns among the two groups.[12]

Similarly , In a study conducted by Ulf Teichgraber, Amer Malouhi, Maja Ingwersen et al on 165 patients showed that wherever there is low prevalence of COVID-19, chest CT could be used as a supplement to RT-PCR testing which helps in early COVID-19 exclusion in adults with suspected infection before referral to hospital's general wards.[13]

And Our results are in agreement with results reported by Ali Abbasian Ardakani,U. Rajendra Acharya et al,[4] Yan Li, Liming Xia et al,[10] Chen, Hui Juan et al,[6] and Wu J, Pan J, Teng D et al,[14] which included RT-PCR positive and negative patients and the presence of bilateral, multiple, sub-pleural ground glass opacities and consolidation are common to both and RT-PCR positive and RT-PCR negative symptomatic groups. Findings Summarized in Table-5.

Thus, these findings in the pandemic to be considered as Covid-19 pneumonia even if RT-PCR test is negative.

Thus, use of HRCT chest scan for screening of COVID-19 pneumonia is advised for symptomatic, yet RT-PCR negative patients. And our study further assures the usefulness of chest CT in these settings.

Limitations of the Study

Firstly, Majority of the patients in our study were in middle age group , 20% patients were above 60 years of age. And we have not studied the comorbidities of the patient population in the study, the time of onset of symptoms and their role in various HRCT findings.

Considerable similarity may be found in imaging of SARS CoV-2 pneumonia and other viral pneumonias, however in order to isolate suspicious cases and prevent further spread of disease in community presence of other viral pneumonia may be over looked.

Conclusions

HRCT chest scan plays an important role in detecting COVID-19 in those symptomatic patients in whom RT-PCT test results are negative. In the context of the current pandemic and multiple genetic mutations of the virus, particularly in those symptomatic patients or those with exposure history, positive HRCT should be regarded as strongly suspicious for COVID-19 pneumonia, despite negative RT-PCR test results. Recommendations has to be made that, patients can be managed with appropriate infection control measures and RT-PCR swab testing should be repeated.

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