



Correlation of CT Chest Findings with RT-PCR in Suspected Cases of Covid-19 Pneumonia

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ABSTRACT

The outbreak of an unknown viral pneumonia in December 2019 in Wuhan City, Hubei Province, China, led to the identification of a novel coronavirus, later named SARS-CoV-2 by the World Health Organization (WHO) on March 13, 2020. This virus rapidly spread worldwide, causing the COVID-19 pandemic. By the time the pandemic was declared, over 2 million infections and 100,000 deaths had been reported globally, with numbers escalating, particularly in the United States and Europe. As of October 1, 2021, India alone reported over 33.7 million cases and 447,062 deaths, underscoring the virus's widespread impact. The rapid transmission of SARS-CoV-2, with an average doubling time of 3-4 days, placed immense pressure on healthcare systems. Early detection and isolation of infected individuals became crucial in controlling the spread of COVID-19. The reference standard for diagnosing COVID-19 is the RT-PCR test, which detects viral nucleic acid in respiratory specimens. The Centers for Disease Control and Prevention (CDC) developed two key tests: the CDC 2019-Novel Coronavirus Real-Time RT-PCR Diagnostic Panel for COVID-19, introduced in February 2020 and the CDC Influenza SARS-CoV-2 Multiplex Assay, which simultaneously diagnoses COVID-19, influenza A and influenza B. Despite being the gold standard, RT-PCR has limitations, with sensitivity ranging from 50-62% due to various factors such as viral load, specimen source and timing. False negatives are a significant concern, particularly in patients with strong clinical suspicion and typical chest CT findings. This has led to ongoing transmission and increased strain on healthcare facilities. Chest CT scans have been proposed as a complementary diagnostic tool due to their ability to detect pneumonia with typical viral infection patterns, including ground-glass opacities (GGO), patchy consolidations and crazy-paving patterns. Some studies report sensitivity rates for CT imaging as high as 98%, making it a valuable tool in diagnosing COVID-19, especially when RT-PCR results are inconclusive. This study aimed to analyze the correlation between RT-PCR results and chest CT findings in patients with COVID-19 pneumonia. After obtaining ethical approval, patients suspected of having COVID-19 who were referred for chest CT between April 2020 and April 2022 were included. Exclusion criteria included incomplete clinical or laboratory information, excessive motion artifacts in imaging and age below 18 years. RT-PCR tests were performed on respiratory specimens, with patients classified as COVID-19 positive or negative based on these results. Chest CT scans were conducted without contrast and images were evaluated by experienced radiologists for typical COVID-19 findings. Among 362 patients with suspected COVID-19 pneumonia, 174 tested positive on the initial RT-PCR test and 92 were positive on retesting. There were 229 males and 135 females, with ages ranging from 18 to 87 years (mean age 49.28 ± 16.15 years). Common symptoms included fever (47.52%), cough (45.32%), and shortness of breath (17.58%). CT findings were categorized by lobe involvement and included GGO (76.3%), consolidation (24.8%) and crazy paving (7.9%). Bilateral lung involvement was observed in 73.3% of patients. CO-RADS classification was used to assess the severity of findings, with most patients falling into CO-RADS categories 6 and 1. Despite RT-PCR being positive, 33.1% of patients showed no abnormalities on chest CT.

INTRODUCTION

Since December 2019, a number of cases of unknown viral pneumonia related to a local seafood market were reported in Wuhan City, Hubei Province, China^[1]. On March 13, 2020 World health organisation officially named the new coronavirus and resulting illness as SARS COV2^[2]. World health organisation announced the new coronavirus disease as a pandemic. To date over 23,263,662 approx COVID 19 cases and 4,762,089 deaths have been reported by WHO^[2]. By the time of announcement as pandemic, severe acute respiratory syndrome corona virus 2 (SAR COV-2) had caused >2,000,000 infections and 1,00,000 deaths worldwide with rapidly increasing numbers in US and Europe^[3]. It has an average doubling time of 3-4 days that overburdened hospitals. Infections spread rapidly across China and other countries around the world. Till 1 Oct 2021, there were 3,37,39,980 cases in india and 4,47,062 deaths reported with 23529 new cases registered^[2]. In order to contain the disease, early identification of COVID 19 infection and isolation of patients is necessary.

RT PCR is the reference standard to make definite diagnosis of COVID 19 infection^[4]. Viral nucleic acid test by RTPCR is the first line screening method of choice^[4]. CDC developed two lab tests that able to detect SARS-CoV-2, the virus that causes COVID-19 infection. The first one is used for COVID-19 diagnosis and it came into market in February 2020. This test is called the CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel. The second test, more newly developed, can be used for SARS-CoV-2, influenza A and influenza B viruses 3 diseases diagnosed simultaneously. This test is called the CDC Influenza SARS-CoV-2 (Flu SC2) Multiplex Assay^[4]. The CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel is a molecular in vitro diagnostic test that aids in the detection and diagnosis of SARS-CoV-2 infection and is based on widely used nucleic acid amplification technology. The product contains oligonucleotide primers and dual-labeled hydrolysis probes (TaqMan) and control material used in rRT-PCR for the invitro qualitative detection of 2019-nCoV RNA in respiratory specimens^[4,5]. But sensitivity of RT PCR is insufficient ranging from 50-62% based on large scale reports^[6,7]. RTPCR testing accuracy may be affected by number of factors including viral load in the respiratory tract, specimen source sampling procedure, timing, quality control of the test and inherent performance of testing kits. Some patients who are highly suspected based on the established close contact with confirmed cases with typical clinical symptoms and CT chest findings, still may test false negative by initial RT PCR test, increasing the train of transmission in the community and burden on already overburdened Hospitals. High false negative rate and lack of RTPCR kits limited the

prompt diagnosis of infected patients in the initial days.

Chest CT may be a noninvasive imaging diagnostic, tool to diagnose pneumonia and is comparatively easy to perform and may make quick diagnosis. CT scans showed typical features of viral infection^[8]. Studies also showed CT imaging findings of COVID 19 had typical appearance of virus infection with sensitivity of 60% and 98%^[9,10]. Some literatures reported the standard imaging features including ground glass opacities (GGO's), patchy consolidations and crazy paving pattern. However, few literatures reported the time difference in RT PCR results and CT abnormality^[11]. So as to understand the diagnostic value of chest CT and course of the disease we decide to analyse correlation between RTPCR Results and CT changes in patients with COVID-19 Pneumonia. Some recent literature suggested that the primary test is negative during a number of cases and it has been observed in some studies that positivity develops within the second, third, or even later tests. Some studies showed that multiple negative RT-PCR test results from nasopharyngeal samples that are positive in tests using broncho alveolar lavage (BAL) samples. The target receptor of the virus is angiotensin-converting enzyme 2 (ACE2). This receptor isn't expressed at the nasal and oral levels but substantially in type 1 and type 2 alveolar epithelial cells, making the BAL method more effective^[12]. Some recent literature reported benefits of CT chest imaging in COVID19 complications like spontaneous pneumomediastinum, spontaneous pneumothorax unrelated to barotrauma which is seen commonly in moderate to severe hospitalised COVID19 patients^[13].

MATERIALS AND METHODS

After approval from ethics committee all patients clinically suspected of novel corona virus infection referred to our department for CT Chest between April 2020 and April 2022 were enrolled in our study. The correlation between RT PCR results and CT imaging will be analyzed. Exclusion criteria will be incomplete clinical or lab information and images with excessive motion artifacts. RTPCR of respiratory secretion specimen from nasopharyngeal swab, oropharyngeal swab was performed using RTPCR kits. Patients with RTPCR positive were termed COVID-19 positive and negative RTPCR termed COVID-19 negative.

Inclusion Criteria:

- Suspected cases of COVID 19 pneumonia in age groups greater than 18 years.

Exclusion Criteria:

- Patients with RTPCR test done within 3 days were excluded

- Incomplete clinical or lab information.
- Images with excessive motion artifacts.
- CORAD 2 suggesting other than COVID 19
- Age groups less than 18 years excluded.

Study Population: Patients presenting with clinical suspicion of COVID-19 pneumonia screening evaluation were included in this study.

CT Image and Data Acquisition: All clinically suspicious patients were underwent CT Chest screening. Chest CT was performed on GE machine with patients in the supine position during end inspiration with scan time 3-4 sec without IV contrast administration with FOV from neck to the upper abdomen . All patients will be evaluated with GE CT scanner at 5mm slice thickness, 120 KV tube voltage and 70-100 MAS tube current, Pitch 0.6x12, Matrix 512x512, with image reconstruction of 1mm.

CT Image Evaluation: Two experienced radiologists (with experience of 8-18yrs) were review the CT images independently at our PACS workstation. The CT Images were be evaluated for ground glass opacities, consolidations, reticulations, mediastinal nodes, pleural effusion, interlobular septal thickening. Findings will separated lobe wise using CORADS grading and CT severity index given to patients .In case of any discrepancy those findings were discarded and given after mutual consensus. RTPCR positive and negative were recorded in the patient data.

Statistical Analysis: Continuous variables are represented as mean and standard deviation where data follows normal distribution, otherwise as median with range. Categorical variables are represented as frequencies and percentages. The statistical significance in the difference in the outcome variables between the groups will be determined by Fisher exact test, chi square test, t test if normal, otherwise Mann Whitney u test. Data was analyzed using R studio.

RESULTS AND DISCUSSIONS

A total of 362 patients with symptoms suspicious of COVID 19 Pneumonia were included in this study. Of these 174 patients had a positive RT PCR report on the initial test which 92 were positive on are-test. 98 patients tested negative on the RT PCR test. There were 229 males and 135 females in this study with ages ranging from 18-87 (mean+/-STD deviation 49.28+/-16.15).

The symptoms observed were fever-173 (47.52%), SOB-64 (17.58%), cough-165 (45.32%), loose stools-9 (2.47%) and loss of smell-5 (1.37%).

The CT findings observed were categorized with lobar involvement, ground glass opacities, consolidations,

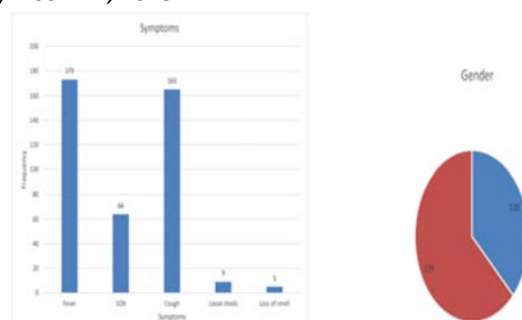


Fig. 1: Diagrammatic presentation

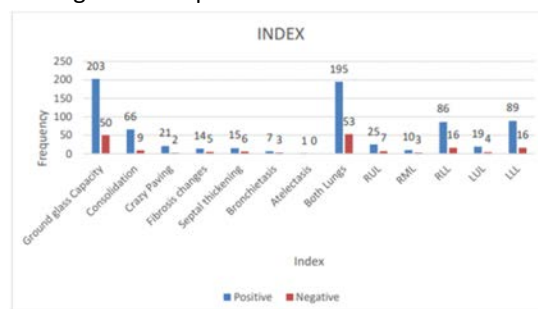


Fig. 2: Diagrammatic presentation

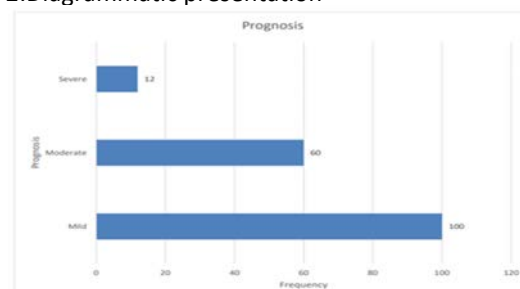


Fig. 3: Diagrammatic presentation

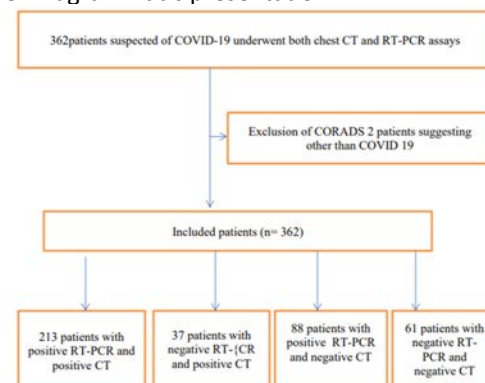


Fig. 4: Flowchart

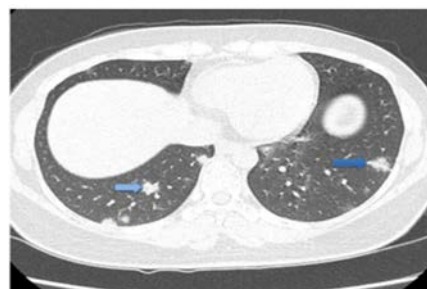


Fig. 5: A case of female patients age 46 presented with fever showing only multifocal patchy opacities (block arrows) in bilateral lung-consolidation

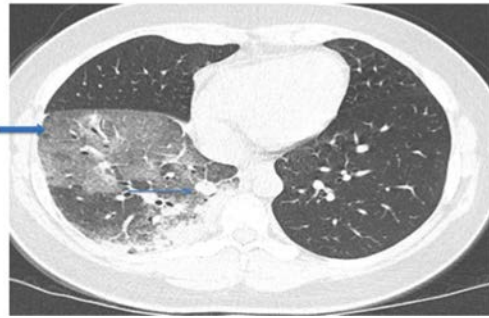


Fig. 6: A case of male patient age 54 showing ground glass opacity (block arrow) and subpleural patchy areas of opacities (straight arrows)-consolidation.

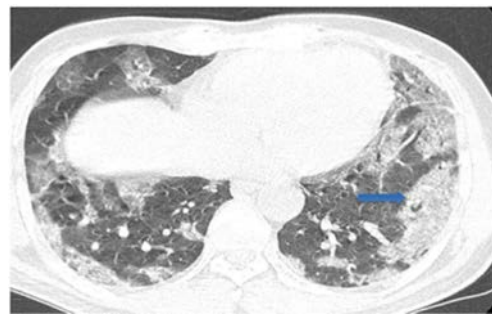


Fig. 10: A male patient of age 70 presented with fever and sob showing extensive crazy paving opacities (block arrow) in bilateral lung parenchyma.

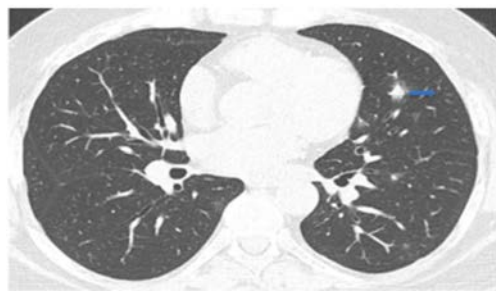


Fig. 7: A female patient of 55y came with complaints of loose stools and epigastric pain showing atypical finding of multifocal nodular ground glass opacities (block arrows) in bilateral lung

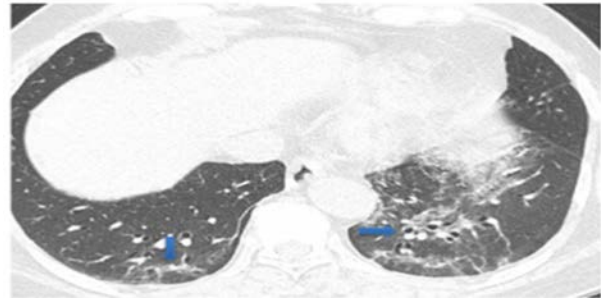


Fig. 11: A male patient of age 85 presented with fever showing bronchiectasis (block arrows) and fibrosis (down arrow) in lower lobes of chest CT

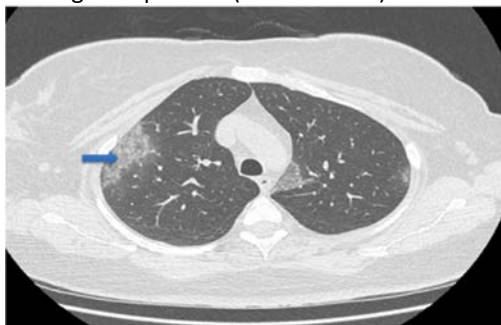


Fig. 8: A male patient of age 53 presented with complaints of fever and sob shows crazy paving opacities in bilateral upper lobes (Block arrow)

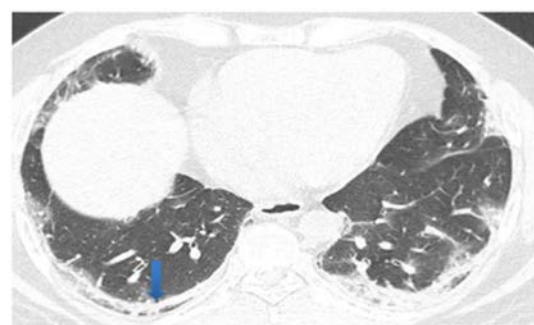


Fig. 12: A male patient of age 55 presented with chief complaints of cough and fever showing predominantly fibrosis (down arrow)

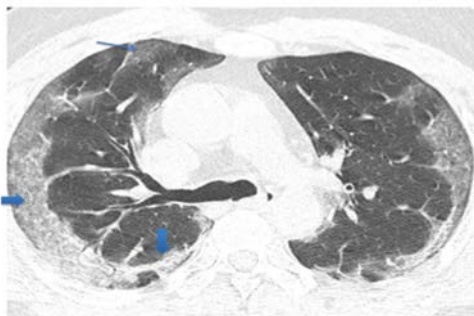


Fig. 9: A male patient of age 57 came with complaints of fever and cough showing crazy paving (block arrow), fibrosis (down arrow) ground glass opacities (thin arrow).

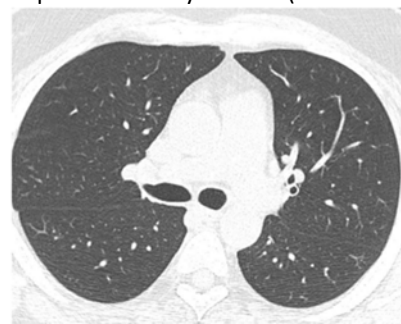


Fig. 13: A RTPCR positive female patient aged 41 came with chief complaints of cough showing no CT chest findings.

Table 1: Descriptive statistics

Variable	Units	Statistics
Gender	Female	135(37.1%)
	Male	229(62.9%)
Age	Mean± std. dev	49.28±16.15 (15-87)
Prognosis	Mild	100(27.5%)
	Moderate	60(16.5%)
	Severe	12(3.3%)

Table 2: Characteristics of common eyelid malignancies including incidence, age of onset and sex predilection.

Complaints	Frequency	Percentage
Fever	173	47.52%
SOB	64	17.58%
Cough	165	45.32%
Loose stools	9	2.47%
Loss of smell	5	1.37%

Table 3: Statistical Inference

Variables	Positive (n=266)	Negative (n=98)	P-Value
Group glass Capacity	203(76.3%)	50(51%)	<0.01
Consolidation	66(24.8%)	9(9.2%)	<0.01
Crazy paving	21(7.9%)	2(2%)	0.04
Fibrosis changes	14(5.3%)	5(5.1%)	0.99
Septal thickening	15(5.6%)	6(6.1%)	0.86
Bronchiectasis	7(2.6%)	3(3.1%)	0.73
Atelectasis	1(0.4%)	0	0.99
Both Lungs	195(73.3%)	53(54.1%)	<0.01
RUL	25(9.4%)	7(7.1%)	0.5
RML	10(3.8%)	3(3.1%)	0.16
RLL	86(32.3%)	16(16.3%)	<0.01
LUL	19(7.1%)	4(4.1%)	0.04
LLL	89(33.5%)	16(16.3%)	0.01

Table 4: Clinical features of different eyelid malignancies, including appearance, common location and metastasis risk.

CO-RADS	Total	Percentage
1	61	61%
3	27	7.4%
4	17	4.6%
5	43	11.87%
6	176	48%

crazy paving pattern, fibrosis and septal thickening. Other findings such as bronchiectasis, pleural effusion and pneumothorax / pneumomediastinum were also observed.

Both lungs were involved in 195 patients (73.3%) with findings seen in the right upper lobe-25 (9.4%), right middle lobe-10(3.8%), right lower lobe-86 (32.3%), left upper lobe- 19(7.1%), left lower lobe-89 (33.5%).

Ground glass opacities (76.3%)-203 with p-value of (<0.01), consolidation-66 (24.8%), p<0.01, crazy paving-21 (7.9%), p-value 0.04, fibrosis-14 (5.3%), septal thickening-15(5.6%) were noted.

CO-RADS distribution is as follows: CO-RADS : 6 were 175 (70.6%), CO-RADS:1-61 (16%), CO-RADS: 3-27 (7.4%), CO-RADS : 4-17 (4.6%), CO-RADS: 5- 43 (11.87%) patients noted.

Prognosis based on CT severity as follows mild-100 (27.5%), moderate-60(16.5%), severe-12 (3.3%).

Patients with RT-PCR positive but no findings on CT chest totalled 88 (33.1%).

Since the start of the COVID 19 pneumonia pandemic, it has been observed that early diagnosis and isolation are imperative for treatment and containment of the disease. RT PCR is the gold standard for confirming the diagnosis of the same as given in the guidelines issued

by^[4] and^[5]. It plays a crucial role in determining hospital admission and seclusion of the patient. Several studies have shown 60.5% sensitivity and specificity of 99.5% in asymptomatic patients and sensitivity and specificity of 72.1% and 98.7% respectively in symptomatic patients. These low sensitivity rates, along with prolonged test result time, sampling method, timing of sampling and performance of detection kits are all negative factors against RT PCR tests. During the pandemic, the world also reported shortages of these kits initially. CT chest is a non invasive diagnostic test with good accuracy which can be performed in a short duration. Several hospitals resorted to performing CT chest as an accessory tool in diagnosing COVID 19 Pneumonia during the pandemic. Findings on radiographs are delayed and features such as ground glass opacities may not be visible in the early stage of the disease and cannot be relied upon. Though the RT PCR is considered as the standard for diagnosis of COVID 19 pneumonia, false negative results have been identified in the early stage of the disease. Huang *et al.* reported that CT findings confirmed the diagnosis in several patients with an initial false negative report^[33].

In our study as well this was observed with 40% patients testing negative on the initial RT PCR test, but with CORADS grading from 3-5. On a repeat study, the RT PCR was positive, validating the CT findings. Several studies have shown the advantages of performing CT chest as an adjunct diagnostic tool for evaluating patients of COVID 19 pneumonia. Published data also illustrates the various findings seen characteristically in the disease, such as ground glass opacities, consolidations, subpleural bands with characteristic peripheral and subpleural distribution in predominantly the lower lobes. A COVID-19 Reporting and Data System (CO-RADS) was introduced by the Dutch Radiological Society in an effort to standardize the reporting along the lines of Breast Imaging Reporting and Data System. CO-RADS is used to assess the suspicion for pulmonary involvement of COVID-19 on a scale from 1 (very low) to 5 (very high) in patients with moderate to severe symptoms of COVID-19 pneumonia. The findings are attributed as CORADS 1-5 on CT chest with level of suspicion with 5 being the highest on the scale. CORADS 6 is given to patients with positive RT PCR Test at the time of the CT study. The 4 stages of COVID 19 Pneumonia described are (1).early stage (0-5 days after symptom onset), with normal CT chest or predominantly ground glass opacities 2. (2) progressive stage (5-8 days after symptom onset), with increased ground-glass opacities and crazy-paving appearance), (3) peak stage (9-13 days after symptom onset), with progressive consolidations as the main imaging finding and (4) late stage (≥ 14 days after symptom onset), with a gradual

decrease of consolidations and ground-glass opacities, with signs of fibrosis (such as parenchymal bands, architectural distortion, and traction bronchiectasis) seen. In our study a total of 362 patients were evaluated. Of these 266 (73%) had positive RT PCR test report at the time of the completion of the study. 98 (26.79%) Patients with negative RT PCR test report had CT reports CORADS 1 or 3. 26 patients (9.7%) with CORADS 3 grading also tested positive on RT PCR. Only one patient with CORADS 1 grading tested positive. These suggest a good correlation. Several studies have shown the advantages of performing CT chest as an adjunct diagnostic tool for evaluating patients of COVID 19 pneumonia. Published data also illustrates the various findings seen characteristically in the disease, such as ground glass opacities, consolidations, subpleural bands with characteristic peripheral and subpleural distribution in predominantly the lower lobes. A COVID-19 Reporting and Data System (CO-RADS) was introduced by the Dutch Radiological Society in an effort to standardize the reporting along the lines of Breast Imaging Reporting and Data System. CO-RADS is used to assess the suspicion for pulmonary involvement of COVID-19 on a scale from 1 (very low) to 5 (very high) in patients with moderate to severe symptoms of COVID-19 pneumonia. The findings are attributed as CORADS 1-5 on CT chest with level of suspicion with 5 being the highest on the scale. CORADS 6 is given to patients with positive RT PCR Test at the time of the CT study. The 4 stages of COVID 19 Pneumonia described are (1).early stage (0-5 days after symptom onset), with normal CT chest or predominantly ground glass opacities 2. (2) progressive stage (5-8 days after symptom onset), with increased ground-glass opacities and crazy-paving appearance), (3) peak stage (9-13 days after symptom onset), with progressive consolidations as the main imaging finding; and (4) late stage (≥ 14 days after symptom onset), with a gradual decrease of consolidations and ground-glass opacities, with signs of fibrosis (such as parenchymal bands, architectural distortion and traction bronchiectasis) seen. In our study a total of 362 patients were evaluated. Of these 266 (73%) had positive RT PCR test report at the time of the completion of the study. 98 (26.79%) Patients with negative RT PCR test report had CT reports CORADS 1 or 3. 26 patients (9.7%) with CORADS 3 grading also tested positive on RT PCR. Only one patient with CORADS 1 grading tested positive. These suggest a good correlation respectively.^[3] Single lobe involvement was identified only in 16 patients (4.4%). The increased frequency right lower lobe involvement has been attributed to the short and thick right main bronchus making its invasion by the virus easier. However, in our study the left lower lobe had a small increased

incidence compared to the right lower lobe with 33.5% involvement compared to 32.3% of the right lower lobe. It has been reported that unilateral involvement is only present in the early and late phases. The most common finding observed on CT was ground glass opacities identified in 76.3% of the patients. 2nd most common finding was consolidation, identified in 24.8% of the patients. The incidence of ground glass opacities were higher in our study when compared to those by Tao Ai who reported an incidence of 46% but lesser than the study done by Damiano C *et al.* and Chen D *et al.* who reported an incidence of 100% and 95% respectively.^[21,3] Cartocci G *et al.* reported that mixed ground glass opacities with consolidations were most frequent in their study.^[23] Crazy paving pattern was identified in 21 patients (7.9%) in our study which is lesser than that reported by Damiano C *et al.*, who reported an incidence of 39%. Interlobular septal thickening was identified in 15 cases (5.6%) which was much less than Chen D *et al.* who reported an incidence of 62%. It has been postulated that ground glass opacities are produced as a result of the serious inflammatory exudates from the pulmonary alveoli with consolidations forming as a result of increased inflammatory exudation.^[3] These can have a prognostic implication as patients with milder forms of disease often presented with on ground glass opacities. While those with consolidations generally had worsened clinical course. This also likely represents the disease course suggesting ggo's as the initial presentation progressing to consolidations in the later stage.^[3] We observed that the CT chest also played a role in triage of the patients, as those patients with a high index of suspicion could be sent to isolation till the report of RT PCR was obtained. This was helpful in our hospital which has only a few beds in the emergency. Also non COVID patients could thus be isolated with a reduced risk of cross infection. Septal thickening and bronchiectasis most likely represent a feature of late progressive or resorptive stage. Pleural effusions were seen in only 2 patients, suggesting an atypical finding. No mediastinal lymphadenopathy was noted in our study. The same was reported Chen^[3]. 2 patients (0.5%) showed pneumo-mediastinum and pneumothorax. These have been reported as spontaneous alveolar air leaks and identified as a rare but definite complication of COVID 19 pneumonia and can occur in the absence of mechanical barotrauma. 88 patients (24.3%) had no findings on CT chest but a positive RT PCR report. Adams *et al.* reported an incidence of 10.6% with normal CT chest findings. Though this could be more commonly identified in the very early stage, a few patients later in the course of the disease were also observed with normal CT chest (39-41). Low viral loads and confinement to the upper

respiratory tract are plausible explanations for false-negative chest CT findings for COVID-19 on a patient level. In addition, there are likely host factors that lead to false-negative chest CT findings. Many patients simply do not elicit the pulmonary inflammatory response needed to produce the chest CT findings of lung injury.

CONCLUSION

It has been concluded that CT chest imaging is better in comparison to RTPCR in diagnosing COVID-19. Due to the high sensitivity and specificity of CT chest and low sensitivity and specificity of RTPCR, CT chest is important in diagnosing suspicious cases fast and quarantine those suspected cases and can be treated in this era of pandemic. CT chest is also useful for monitoring the disease progress by repeating the CT chest imaging at regular intervals. CT chest is also useful in risk stratifying the patients into mild, moderate, severe and treat the patients accordingly. CT chest imaging negativity can be seen earlier than the RTPCR negativity in recovered patients.

Limitations: Limitations in the current observational study is using RT-PCR test with apparently low positive rate as reference and the sensitivity of chest CT for COVID-19 overestimated while the specificity underestimated.

Radiation due to CT scan.

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