Correlating CT Chest with RT-PCR in Diagnosing COVID-19: Experience at a Tertiary Health Care Hospital in Pakistan

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Abstract

Objective: To establish the accuracy of computed tomography(CT) chest in the diagnosis of COVID-19 pneumonia by taking reverse transcriptase-polymerase chain reaction(RT-PCR) as a reference standard and to analyze discordant CT chest and RT-PCR results.

Materials and Methods: A retrospective cross-sectional study of patients presented to a tertiary health care hospital in Punjab, Pakistan for CT examination with suspicion of COVID-19 from April 1, to June 30, 2020. Each CT chest was categorized as positive/negative for COVID-19 pneumonia and the results were compared with the RT-PCR test. Discordant CT chest and PCR results were also investigated.

Results: The study population had a mean age of 48 years ± 6.6 years with 54.5% males and 45.4% females. Sensitivity(Sn), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of CT in diagnosing COVID-19 pneumonia taking RT- PCR as gold standard was 92.5%, 46.6%%, 82.2%, 70% and 80% respectively.

Conclusion: CT chest has high sensitivity but modest specificity in diagnosis of COVID-19 pneumonia. It can be employed as an adjunctive screening and diagnostic test for early diagnosis of disease in places where disease prevalence is high.

Keywords: COVID-19, CT chest, RT-PCR, ground-glass opacities, diagnostic accuracy.

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1. Introduction

In the city of Wuhan (China), numerous cases of viral pneumonia appeared in the month of December 2019. A new virus of the Coronaviradae group of viruses was found the causative agent and was labelled as SARS CoV-2(severe acute respiratory syndrome coronavirus 2).[1] The new coronavirus is the seventh member of the Coronaviradae family which previously included six RNA viruses. Four viruses of this family cause only mild disease. However, two coronaviruses i.e. SARS and MERS caused previous epidemics in 2002 and 2012 respectively had high mortality rates.[2] This new human infecting coronavirus causes coronavirus disease 19 (COVID-19) with lesser mortality rates than SARS and MERS, however, it is highly infectious. At present, the diagnostic test for COVID-19 is the RT-PCR test (Reverse transcriptase-polymerase chain reaction).[3] However; there are certain limitations of this test. It is time-consuming and test results become available after 24 hours. Moreover, it has a low sensitivity of 60-71%.[4,5,6] This low sensitivity is mainly attributed to sampling issues and low viral load in the early stages of the disease.[7] Repeat RT-PCR testing is often needed due to high false-negative test results. This often is challenging due to issues related to infrastructure and availability of test kits.

CT scanning of the chest is useful in the detection and screening of patients having COVID-19 pneumonia. Moreover; the results of CT scans are readily available.[8,9] The predominant radiological features of COVID-19 pneumonia on CT chest include ground-glass opacities (GGOs), consolidation with bilateral multilobe involvement having predominant peripheral distribution.[10,11] Recent studies have found that early changes of COVID-19 pneumonia are detected on CT chest even with initial negative results on RT-PCR and in asymptomatic patients.[12,13] Conversely, in some studies, it is also found that patients with positive results on RT-PCR may have no abnormal finding on CT chest.[13] As a result of these diverse presentations, the evolution of COVID-19 pneumonia on CT is not well understood. CT is preferred over chest radiography for diagnosing COVID-19 pneumonia because the prime imaging finding found in early disease is ground-glass haze/opacification, which is

often difficult to perceive on chest radiography. This is in contrast to the previous SARS epidemic where chest X-rays had a major role in diagnosis because both GGOs and consolidation were found in the early stages of the disease.[14,15] CT chest has a high sensitivity but moderate specificity in the diagnosis of COVID-19 pneumonia. This can particularly be attributed to false-negative PCR tests and similar imaging findings seen in other respiratory viruses.

Since early distinction of patients with COVID-19 pneumonia is crucial for immediate patient isolation, a CT scan can prove to be a fast screening tool and may help to overcome suboptimal early false-negative results on RT-PCR. More research is required for improved patient selection for CT chest examination and to ascertain the usefulness of CT scanning in the screening and diagnosis of disease.

Objective:

To establish the accuracy of CT chest in the diagnosis of COVID-19 pneumonia in patients presenting to Radiology Department of tertiary health care hospital in Punjab, Pakistan having suspicion of COVID-19 taking RT-PCR (repeated) testing as a reference standard. Since RT-PCR is reported to have high initial false-negative results, we will also analyze discordant CT chest and RT-PCR test results.

2. Materials & Methods

Study design, duration, and setting:

This is a retrospective cross-sectional study of patients who presented to the Radiology department of a tertiary health care hospital in Punjab, Pakistan for CT examination with suspicion of COVID-19 from April 1, to June 30, 2020.

Inclusion criteria:

During this period, all adult patients with a CT chest scan and an RT-PCR test on arrival were included in the study. If the initial result of RT-PCR was negative, then repeat PCR tests done within a time period of 3 days were taken into account.

Exclusion criteria:

Patients were excluded if the time period between the RT-PCR test and CT scan was greater than 7 days.

Chest CT protocol and Image analysis:

Ethical approval from the institution's ethical review board was obtained. Since it is a retrospective analysis of patient records and no personal identifiers were used, therefore patient consent was not required. Chest CT

scans were performed with a multi-detector (16 slice) TOSHIBA Aquilion CT scanner. The study was done in a supine position with tube voltage and current set at 120 kvp and 350 mA respectively. Each scan was performed in the craniocaudal direction in a single breath-hold with a slice thickness of 1mm. No intravenous contrast was used. Reporting of scans was done on the workstation by two experienced radiologists in consensus (having a minimum of 5 years of post-graduation experience) who were blinded to PCR test results. Each study was evaluated for the presence of GGOs, consolidation, distribution (central, peripheral, or mixed pattern), crazy paving, reverse halo sign, pleural effusion, nodules, cavitations, and other findings. Each study was categorized as positive/negative for COVID-19 pneumonia.

Statistical Analysis:

Typical as well as atypical imaging features of COVD-19 pneumonia were evaluated for each patient. IBM SPSS Statistics for Windows, version 21.0. Armonk, NY was used to perform the statistical analysis. Quantitative variables were expressed as mean ± standard deviation and qualitative variables as counts (n) and frequency (%). The sensitivity (Sn), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), and accuracy of CT chest in the diagnosis of COVID-19 pneumonia taking RT-PCR as reference was determined using a 2 X 2 table(Table 1). In patients with discordant results of CT chest and PCR, repeat PCR was done in all these patients; however, a repeat CT scan was not done and the results were analyzed.

Table 1: A 2 x 2 table

Ct chest		RT-PCR	
		Positive	Negative
	Positive	True Positive (a)	False Positive (b)
	Negative	False Negative (c)	True negative (d)

Sensitivity(Sn):a / a + c x 100
Specificity(Sp): d / b + d x 100
Positive predictive value(PPV): a / a + b x 100
Negative predictive value(NPV): d / c + d x 100
Diagnostic accuracy(DA): a + d / a + b + c + d x 100

3. Results

Patient Demographics:

Overall 135 patients suspicious of COVID-19 pneumonia undertook CT chest and RT-PCR tests during the study period. In 25 patients duration of CT

examination and RT-PCR testing was more than 7 days, resulting in exclusion from the study (Figure 1). The age range of the study population was 20-80 years with a mean of 48 years ± 6.6 years. Out of the 110 study patients fulfilling the inclusion criteria, there were 60 (54.5%) males and 40(45.4%) females. The median time period between PCR and CT chest was one day. Ground glass opacity (GGO) was the commonest finding seen in 88.8% of patients followed by consolidations in 55.5% and crazy paving in 32.2% (Figure 2, 3). While 45.5% of patients showed both ground-glass haze and consolidations (Figure 4). The majority of the patients showed bilateral, multilobe involvement with predominant peripheral distribution (Table 2).

Accuracy of CT Chest in Diagnosing COVID-19 Pneumonia

Out of the 110 patients fulfilling the inclusion criteria, 72.7% (80/110) patients were positive on RT-PCR while 27.3% (30/110) patients were negative on RT-PCR testing giving a positive rate of 72.7%. In patients having PCR positive results, radiological features indicative of COVID-19 were seen in 92.5% (74/80) cases (true positive) while 7.5% (6/80) patients did not show any abnormal findings on Chest CT (false negative). In patients having PCR negative results, radiological features indicative of COVID-19 were seen in 53.3% (16/30)cases (false positive) while 46.7% (14/30) cases did not show any abnormal finding (true negative) (Figure 1). The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of CT in diagnosing COVID-19 pneumonia by taking RT- PCR testing as the gold standard was 92.5%,46.6%%, 82.2%, 70%, and 80% respectively (Table 3).
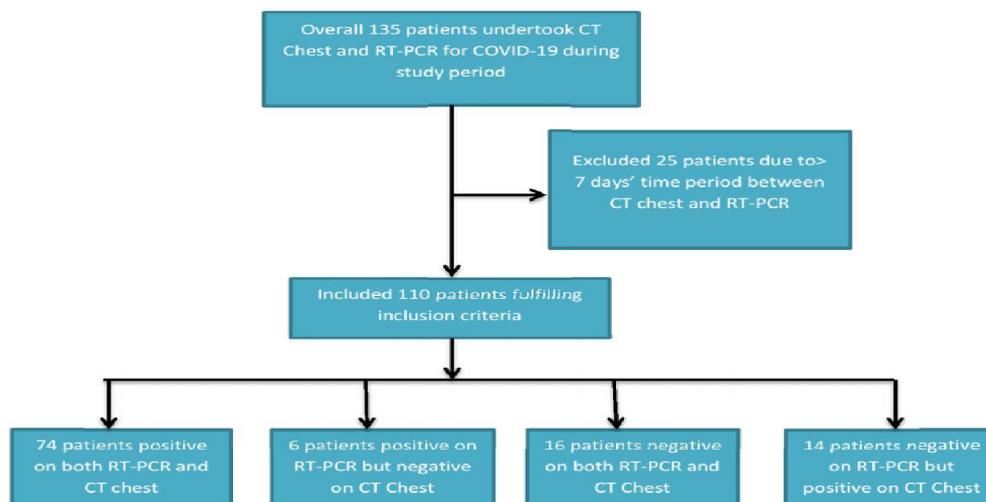

Figure 1: Flowchart showing study patients

Figure 2: Female patient with cough and difficulty in breathing. RT-PCR test was negative. CT shows multifocal ground-glass opacities with septal thickening (crazy paving) in bilateral lung fields predominantly in peripheral and basal distribution. Note the vascular dilatation in pulmonary parenchyma affected by ground-glass haze.

Figure 3: Initially RT-PCR positive patient turned negative after 12 days. Initial CT shows a few areas of ground-glass haze with crazy paving.

Figure 4: PCR-positive patient with worsening breathlessness and dropping oxygen saturation. CT shows severe disease with widespread patches of consolidation and ground-glass haze in peripheral as well as the central distribution

Table 2: Radiological features of COVID-19 on CT chest

Radiological Features	Frequency (% of Total)
Ground glass opacity (GGO)	80 (88.8%)
Consolidation	50(55.5%)
GGO + Consolidation	41 (45.5%)
Crazy Paving	29 (32.2%)
Reverse halo Sign	0 (0%)
Nodules	0(0%)
Pleural effusion	2 (2.2%)
Bronchiectasis and vascular dilatation	10(11%)
Distribution	
Unilateral (U/L)	25(27.7%)
Bilateral (B/L)	65(72.2%)
Central	26(28.8%)
Peripheral	71 (78.8%)
Central + Peripheral	24(26.6%)
Total	90

Table 3: Accuracy of HRCT chest in diagnosing COVID-19

CT Chest		RT-PCR	
		Positive	Negative
	Positive	74	16
	Negative	6	14

Sn-92.5%, Sp-46.6%, PPV-82.2%, NPV-70%, DA-80%

Discordant CT Chest and RT-PCR Results:

In 7.5% (6/80) patients with positive RT-PCR tests, no abnormal findings were seen on chest CT. Repeat PCR was done in all of these patients; however, a repeat CT scan was not done. All of these 6 patients turned negative on repeat PCRs after a medial time period of 10 days (7-14 days); 4 patients on the 3rd PCR and 2 on the 4th PCR. All of these patients were either asymptomatic or paucisymptomatic but had a positive history of contact.

In 53.3% (16/30) patients with initial negative PCR results, findings suspicious for COVID-19 were seen on the CT chest. CT features in these patients included GGOs seen in 7, consolidations in 5, and mixed GGOs with consolidations in 4 cases. Based on CT findings; 7

out of these 16 patients were considered highly suspicious, 6 with moderate suspicion, and 3 with intermediate suspicion of COVID-19 pneumonia. All patients (13) having high and moderate suspicion of COVID-19 pneumonia on CT chest turned positive on repeat PCR in the median time period of 5 days (4-8 days). While 3 patients having intermediate suspicion on CT chest remained negative on repeat PCRs. In 2 out of these 3 patients, an alternate diagnosis of bacterial infection was made at the time of discharge while in 1 patient possibility of COVID-19 pneumonia could not be excluded.

Analysis of dynamic change of consecutive RT-PCR tests:

The dynamic change was studied in 52 patients who had multiple RT-PCR tests. The dynamic change was defined as the change in the result of consecutive RT-PCR tests after a time period of greater than three days. In 25% (13/52) patients, a change from initial negative RT-PCR result to positive was seen. The median time period of change was 4 days (4-7 days). In 11 out of these 13 patients, positive findings on the initial CT chest were seen either before or analogous to RT-PCR testing while 2 out of these 13 patients did not show any abnormal findings on the CT chest.

A change from positive RT-PCR results to negative was observed in 31% (16/52) patients. The median time period of change was 9 days (7-14 days). In 10 out of these 16 patients, positive findings on the initial CT chest were appreciated either before or analogous to RT-PCR testing while 6 patients did not show any abnormal findings on the CT chest (Table 4).

Table 4: Results of dynamic change of consecutive RT-PCR tests

Dynamic change in RT-PCR ≥4 days	No of patients	Median time period	Positive findings on initial CT	Negative Findings on initial CT
Negative to positive	*13/52*	*4 days (4-7 days)*	*11/13*	*2/13*
(4-7 days)	*16/52*	9 days (7-14 days)	*10/16*	*6/16*
Positive to negative	*15/52*	*-*	*15/12*	*0/15*
Negative to negative	*8/52*	*-*	*2/8*	*6/8*

4. Discussion

Ever since the onset of the COVID-19 outbreak, the affected population is continuously on the rise. Disease presentation ranges from mild symptoms to severe resulting in ARDS (acute respiratory distress syndrome).[16,17,18] In January 2020; World Health Organization (WHO) announced it was a global health emergency and in February 2020 it was declared a pandemic.[19,20] Timely diagnosis is vital for patient management and isolation to contain disease spread.

In this study, the sensitivity of CT chest in the diagnosis of COVID-19 pneumonia was 92.5%, specificity 46.6%, PPV 82.2%, NPV 70%, and accuracy 80%. However, in 20% (22) patients' CT chest and RT-PCR results were not in agreement. All patients having high and moderate suspicion (13) of covid-19 on CT chest turned positive on repeat PCR over a median time duration of 5 days (4-8 days). If we take into account these 13 patients which turned positive on repeated testing; the chest CT sensitivity and specificity increase to 93% and 82%. This highlights the importance of repeated testing and efficient sampling techniques in order to obtain reliable RT-PCR results.

Diagnostic accuracy should be determined cautiously since both CT chest examination and RT-PCR can have false-negative results in the early course of the disease.[5,8,21] In the present study, 92.5% of patients having positive results on RT-PCR showed radiological features indicative of COVID-19 pneumonia on initial CT chest. This is in agreement with studies by Ai T et al. (97%) and Fang Y et al. (98%).[4,5] Another study of 81 RT-PCR positive patients in China reported a sensitivity of 93%.[22] However Zhong et al. and Shohei Inui AF et al. reported a lower sensitivity of 76.4% and 80% respectively.[23,24] Another study in the Netherlands reported CT chest having a sensitivity of 89.2% and specificity of 68.2%.[25]

In this study, dynamic changes in RT-PCR results were also analyzed in patients who underwent multiple RT-PCR tests (n=52). In 25% (13/52) patients, a change from initial negative results on PCR to positive was seen over a median time duration of 4 days. Out of these,84.6% (11/13) patients showed positive findings on initial CT chest either before or analogous to RT-

PCR testing while 15.4% (2/13) patients did not show any abnormal findings on CT chest. A change from positive RT-PCR result to negative was observed in 31% (16/52) of patients over the median time duration of 9 days (7-14 days). Out of these, 62.5% (10/16) patients showed positive findings on initial CT chest either before or analogous to RT-PCR testing. It points out the significance of CT chest for early detection of suspected COVID-19 cases. It is believed that the management of patients having initial false-negative PCR results can be challenging. Thus; a combination of the history of travel or exposure, clinical and CT chest findings should be employed to correctly detect such cases.

There are some limitations to this study. Firstly, since RT-PCR testing is used as a reference standard which has a low positive rate and false-negative results, this can lead to overestimation of sensitivity and underestimation of specificity of CT chest examination for COVID-19. This can have important implications for controlling disease spread. In areas where disease prevalence is high, positive findings on CT chest can be suggestive of COVID-19 pneumonia despite negative PCR results. Secondly, limited clinical and lab data was available due to hospital work overload.

Thirdly, as it is a single-center study, external validity can be limited.

5. Conclusion

It is found that CT chest has high sensitivity but modest specificity in the diagnosis of COVID-19 pneumonia. It can be employed as an adjunctive screening and diagnostic test for early diagnosis of disease in places where disease prevalence is high.

CONFLICTS OF INTEREST- None

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