

ORIGINAL ARTICLE

Determining the Diagnostic Accuracy of Non-Contrast High-Resolution Computed Tomography Chest Study in COVID-19 Pneumonia Keeping PCR Assay as Gold Standard

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ABSTRACT

Objective: To determine the diagnostic accuracy of high-resolution computed tomography (HRCT) chest in determination of corona virus disease (COVID-19) taking polymerase chain reaction (PCR) as gold standard.

Methods: This diagnostic cross-sectional study was conducted at Shifa International Hospital Islamabad (SIH) from February 2020 to April 2020. All patients suspected for COVID 19 pneumonia were consecutively enrolled. Diagnosis was done via both HRCT chest and PCR assay. Patient's demographic characteristics and PCR results were retrieved from hospital database. Diagnostic accuracy was explored by calculating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall diagnostic accuracy.

Results: Of 250 patients, the mean age was 58.5 years \pm 14.7 years. HRCT findings in positive scans showed that of 181 patients, majority of the patients presented with multifocal peripheral rounded ground glass opacities (GGOs) with crazy paving observed in 77 (42.5%), multifocal peripheral rounded in GGOs 51 (28.1%), and multifocal peripheral rounded GGOs with crazy paving and consolidations 45 (24.8%). Furthermore, bilateral lungs and multifocal multilobar involvement of lungs was observed in 179 (98.8%) each. While peripheral lung involvement was observed in 176 (97.2%) patients. The sensitivity, specificity, PPV, NPV, and overall diagnostic accuracy of HRCT chest in diagnosing COVID-19 pneumonia was 93.4%, 53.5%, 71.2%, 86.9%, and 75.6% respectively.

Conclusion: HRCT chest has a higher sensitivity and comparable diagnostic accuracy to PCR testing in diagnosing COVID 19 pneumonia and thus in the epidemic areas, it can be used as an important adjunct to PCR testing.

Key words: Diagnostic accuracy, HRCT chest, PCR, sensitivity, specificity.

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INTRODUCTION

Corona Virus Disease (COVID-19) was pneumonia initially reported as epidemic in Wuhan, China due to novel Corona virus outbreak in late 2019. It has now assumed the status of pandemic with global infection spread.¹⁻³ This infection has diversified clinical presentations ranging from milder symptoms like flu to severe symptoms as seen with severe respiratory distress syndromes (SARS) and middle east respiratory syndrome (MERS) having mortality rates of 10% and 37% respectively.^{1,4,5} Considering high contiguity of virus, early differentiation between infected and non-infected patients is of extreme importance to prevent transmission of infection to non-infected population and health care providers.⁶

Polymerase chain reaction (PCR) assay is the standard reference diagnostic modality for detection of infection caused by Corona virus. PCR may produce compromised results in the terms of sensitivity, for

example, lesser viral load in the initial phases of COVID-19 infection may be undetectable. Also due to technical limitations; including inappropriate sampling technique or errors in sample handling may produce false negative PCR results.⁷ Further, PCR test result may take up to 24 hours or more depending upon regional circumstances.⁸ Also the probability of getting false negative PCR assay results described in literature is also not rare.⁹ The number of PCR laboratory test kits is also limited, hence mass screening in an epidemic area becomes logistically difficult.¹⁰⁻¹¹

HRCT chest being non-invasive and readily available modality for detection of COVID 19 infection is suggested in recent literature for diagnosing COVID-19 infection in pneumonia suspected cases. Studies have shown significant number of cases having abnormal findings on HRCT chest where PCR had false negative results.⁹⁻¹¹

Characteristic findings on HRCT chest includes multifocal, multi-lobar ground glass opacities (GGOs)

having bilateral peripheral predominance with concomitant crazy paving pattern and consolidations.^{3,10-15} Radiology society of North America (RSNA) consensus statement for reporting of COVID-19 pneumonia has classified these imaging features as typical, indeterminate, atypical and negative for COVID 19 findings.¹⁶ The purpose of this study was to establish the diagnostic accuracy of HRCT chest in detecting COVID 19 pneumonia in our local population using PCR testing as gold standard.

METHODS

The diagnostic cross-sectional study was conducted at Shifa International Hospital (SIH), Islamabad, Pakistan from February 2020, to April 2020. Approval from the institutional review board and ethics committee of SIH was obtained prior to conducting the study (IRB#: 144-964-2020). All COVID 19 suspected patients (having fever > 38°C with symptoms of lower respiratory tract illness like a cough or shortness of breath and history of traveling from abroad or contact with a RT-PCR positive COVID-19 patient within 14 days of onset of symptoms or with fever >38°C with a severe acute respiratory illness like pneumonia or acute respiratory distress syndrome requiring hospitalization along with confirmed cases (RT-PCR positive) presenting to the emergency department of SIH were consecutively enrolled. While those suspected cases whose HRCT chest or PCR were not conducted upon presentation or patients with underlying lung diseases (COPD, Interstitial lung diseases, tuberculosis) and known cardiac failure were excluded. Patient's demographic data and PCR results were retrieved from hospital database using Radiology information system (RIS). Imaging HRCT chest studies were retrieved from Picture Archive and Communication System (PACS).

CT technique and image interpretation: Non contrast High resolution computed tomography (HRCT) chest scans were performed on CT scanner Somatom Definition Edge Siemens (128 slice CT scanner) and 320 slice CT scanner Toshiba Aquilion one. Following were the detailed image acquisition parameters: tube current and voltage= 20 mAs and 100 kVp respectively; slice thickness and reconstruction interval each of 1 mm and scan time, 3.32 seconds. The CT scan was performed in all patients, position being supine and in full inspiration. No contrast medium was used in acquisition of CT images. Kernel Bf37 for mediastinum and kernel BI57 for lungs were used with SAFIRE strength 2 for both.

The acquired HRCT chest images were reviewed by two independent consultant radiologists at SIH (having radiological experience of more than 5 years). The reviewers were blinded to results of PCR assay. These HRCT chest scans were classified according to RSNA consensus statement for COVID 19 disease as typical for COVID 19 pneumonia, indeterminate, atypical, or negative for pneumonia on the basis of certain CT characteristic manifestations. These included presence or absence of ground glass opacities, consolidations, pleural effusions, and other features along with the predominant pattern of lung involvement i.e., multifocal, bilateral, central, and peripheral location of the lesions. All the CT scans having RSNA typical or indeterminate category were labelled as positives while RSNA atypical and negative categories were labelled as negative for COVID 19 pneumonia.

Data were analyzed using SPSS version 21.0. The continuous variables were presented as mean with standard deviation. The categorical variables were displayed as counts and frequency percentages. A 2 x 2 contingency table constituted and specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV) along with diagnostic accuracy of HRCT chest were determined using PCR results as gold standard.

RESULTS

Of 250 patients, the mean age of the patients was 58.5 years \pm 14.7 years. Majority 169 (67.6%) were males and 81 (32.4%) were females. The predominant symptom upon presentation was shortness of breath 225 (90%) followed by fever and cough 202 (80.8%) patients. Generalized muscle pain and weakness was present in 189 (75.6%) patients. Out of 250, 3 (1.2%) patients presented with loss of sense of smell and taste only, while 22 (8.8%) patients had no symptoms at all. There were 138 (55.2%) COVID-19 positive on PCR while 112 (44.8%) were found to be COVID-19 negative on PCR. Positive CT chest was seen in 181 (72.4%) and negative CT chest was seen in 69 (27.6%) patients. There were 129 (51.6%) true positive (TP) whereas 52 (20.8%) were false positive (FP). There were 60 (24%) True negative (TN) and 09 (3.6%) false negative (FN). (Figure 1) The sensitivity, specificity, PPV, NPV and overall diagnostic accuracy was found to be 93.4%, 53.5%, 71.2%, 86.9% and 75.6% respectively. (Table 1) Stratification was done to see the effect of age and gender on the diagnostic accuracy. Results are shown in detailed in table 2. HRCT findings in positive scans showed that of 181

patients, majority of the patients presented with multifocal peripheral rounded GGOs with crazy paving observed in 77 (42.5%), multifocal peripheral rounded GGOs 51 (28.1%), and multifocal peripheral rounded GGOs with crazy paving and consolidations 45 (24.8%). (Table 3, Figure 2) Furthermore, pattern of lung involvement showed that bilateral lungs and multifocal multilobar involvement of lungs was observed in 179 (98.8%) each. While peripheral lung involvement was observed in 176 (97.2%) patients. (Table 4)



Figure 1: Axial non contrast HRCT chest 'Negative' for COVID 19 pneumonia.



Figure 2 (a) and (b): Axial non contrast HRCT chest images showing multifocal multilobar ground glass opacities 'positive' for COVID 19 pneumonia.

Table 1: Diagnostic accuracy of COVID 19 pneumonia keeping PCR assay as gold standard (n=250)

		PCR		Total
		Positive	Negative	
HRCT chest	Positive	129	52	181
	Negative	9	60	69
	Total	138	112	250
Sensitivity		93.4%		
Specificity		53.5%		
PPV		71.2%		
NPV		86.9%		
Overall Diagnostic accuracy		75.6%		

HRCT: High resolution computed tomography, PPV: Positive predicted value, NPV: Negative predicted value, PCR: Polymerase chain reaction

Table 2: Stratification of diagnostic accuracy according to age and gender of the patients

	Age >45 years	Age <45 years	Gender (Male)	Gender (Female)
Sensitivity	95.7%	80.9%	92.3%	96.9%
Specificity	54%	52%	57.8%	47.9%
PPV	73.6%	58.6%	78.2%	56.1%
NPV	90.3%	76.4%	82.2%	95.8%
Diagnostic accuracy	77.9%	65.2%	79.2%	67.9%

NPV: Negative predicted value, PPV: Positive Predicted Value

Imaging appearance	Frequency	Percent (%)
Multifocal peripheral rounded GGOs	51	28.1
Bibasal consolidations without ground glass opacities	5	2.7
Unilateral peripheral GGO	2	1.1
Multifocal peripheral rounded GGOs with crazy paving	77	42.5
Multifocal peripheral rounded GGOs with crazy paving and consolidations	45	24.8
Pleural effusions	1	0.5

HRCT: High resolution computed tomography, GGO; Ground Glass Opacities

Pattern	Frequency	Percentage
Bilateral lungs	179	98.8%
Unilateral lung (right lung in our sample)	02	1.1%
Peripheral lungs	176	97.2%
Non peripheral lungs (central only)	05	2.8%
Multifocal multilobar involvement of lungs	179	98.8%
Solitary focus of GGO	02	1.1%

HRCT: High resolution computed tomography, GGO; Ground Glass Opacities

DISCUSSION

HRCT chest is a substantial adjunct in screening and diagnosing COVID 19 infection, as it is readily available and produces rapid results especially in areas where the disease has emerged as an epidemic. HRCT chest also tends to have high sensitivity values of disease detection and also remains the noninvasive and conventional modality with reproducible results. Studies conducted recently also support the fact that there are certain typical imaging features of COVID 19 disease on CT chest allowing radiologists to diagnose the disease more confidently.¹⁷ Recently published RSNA consensus statement for reporting CT chest in relation to COVID 19 disease, proposed a classification system for classifying CT appearances of COVID 19 disease as typical, indeterminate, atypical and negative.¹⁶ The features Typical for COVID 19 pneumonia include peripheral bilateral ground glass opacities (GGOs) (rounded or non-rounded) with/without consolidations and crazy-paving. Indeterminate features included multifocal, unilateral peripheral, non-rounded, non-peripheral GGOs. Atypical features were isolated lobar consolidations or lung nodules, lung cavitation, smooth septal thickening and pleural effusions. Scan was labelled Negative if

features suggesting pneumonia was present.^{16,17}

In our study with 250 patients, the sensitivity of HRCT chest in diagnosing COVID-19 pneumonia was 93.4 % while specificity was 53.5%. The PPV came out to be 71.2% while NPV was 86.9%.

Regarding sensitivity of CT chest in diagnosis, study conducted by Wu et al¹⁸ found sensitivity of CT chest to be 69%, which is lower than other similar studies carried out. Other studies including Tao Ai et al¹⁹ reported sensitivity of CT chest up to 97% and another study by Kim et al.²⁰ documented CT chest sensitivity up to 94%. Overall, sensitivity of HRCT chest is higher, particularly within the epidemic areas. HRCT chest remains an important key factor in limiting infection spread; as it aids in prompt diagnosis of disease in suspected patients. Also considering high sensitivity of HRCT chest Pan et al. recommended that apart from diagnosing the disease, accurate reflection of disease evolution and treatment effect monitoring can be done by repeated CT follow up examination.²¹ The sensitivity of CT chest in our study is 93.4% which is higher than that of documented for PCR testing 89%.²⁰

The specificity of CT chest, contrary to high sensitivity was relatively lower about 53.5%. This may be due to the

fact that in initial phases of the disease imaging study could be negative for presence of GGOs. Also an overlap between imaging appearances of many viral pneumonias and COVID 19 disease has also been documented, thus reducing the HRCT chest specificity for COVID 19 disease. In recent studies a wide range of specificity has been documented most of the result are concordant with our result of relatively low specificity. Examples include Tao Ai et al¹⁸ reported specificity of CT chest up to 25%.¹⁹ Meta-analysis by Kim et al.²⁰ reported low specificity of CT chest up to 37% (95% confidence interval 26%-50%). Contrarily the study by Jian long He et al²² in literature states the high specificity 96% (46/48) for chest CT. The overall diagnostic accuracy and sensitivity of HRCT chest in diagnosing COVID 19 pneumonia in our study is comparable to similar local studies performed.²³

Initial PCR false negative results may be seen in patients with COVID 19 disease owing to multiple factors related to inadequate sampling technique or absence of detectable level of viral load in the body. To control the disease transmission, priority is screening the clinically suspected patients and thus identifying the diseased individuals and isolate them timely. It is also mandatory to trace the close contacts of infected patients to prevent disease spread in the population. Keeping in view this, the disease control authorities worldwide recommend measures with high sensitivities while specificity may be sacrificed a bit for vigilant detection of positive cases in the community thus promoting the utility of HRCT chest in the ongoing pandemic. While using ionizing radiations from CT, increased radiation exposure and hence increased risk of developing cancers in future may be of concern. To address the issue, most centers have adapted specific low dose HRCT chest for detection of COVID 19 disease.²⁴ Nonetheless we should remain cautious while performing CT scan in children and infants.

Limitations of our study included small sample size due to initial phases of pandemic and being single center study carried out in a low incidence area. Serial follow ups of patients and temporal change in disease pattern could not be documented due to early phases of pandemic.

CONCLUSION

The overall diagnostic accuracy and sensitivity of HRCT chest in diagnosing COVID 19 pneumonia in our study is comparable to recently performed local and international studies. To conclude, CT chest has higher sensitivity and good diagnostic accuracy comparable to

PCR in quick detection of suspected patients of COVID 19 pneumonia. In appropriate clinical settings, CT chest interpreted by a trained radiologist can lead to reliable and rapid diagnosis of COVID 19 pneumonia. It is crucial to diagnose COVID 19 pneumonia at earliest to control this highly communicable disease.

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ETHICAL APPROVAL: This study was approved by Institutional Review Board & Ethics Committee, Shifa International Hospitals Ltd Islamabad, Pakistan.

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