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Positive HRCT Chest Findings and Negative Real-Time Polymerase Chain Reaction Test in Patients with COVID-19 Pneumonia- A Clinical Audit

Hira Waheed✉, **Syed Jahanzeb**

Ziauddin University Hospital, Karachi - Pakistan

Corresponding Author
Hira Waheed
Ziauddin University Hospital, Karachi - Pakistan
E-mail:
hirreed123@gmail.com

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A B S T R A C T

Background: Collection of abnormal amount of fluid in pleura space is referred to as pleural effusion. Etiology of pleural effusion is very wide, varying in different areas suggesting the role of environmental and geographical factors.

Objective: The aim of study was to look in to the different causes of pleural effusions in patients presenting to chest outpatient department in Mardan medical complex.

Methodology: This Descriptive cross sectional study was conducted in Department of Pulmonology and Medicine (medical B unit) of Mardan Medical Complex (MMC) from January 2018 to December 2019. Data was collected by non-probability convenience sampling technique.202 patients were included in study. Diagnosis of effusion was confirmed by chest radiography and where needed with chest ultra-sound. Pleura fluid was aspirated in all cases. Pleural fluid analysis was then followed by the relevant investigations like pleural fluid cytology, culture, pleural biopsy, computer tomoghraphy, echocardiography and connective tissue profile for diagnosis of underlying cause of pleural effusion.

Results: A total of 180 patients, 99 (55%) males, and 81 (45%) females were included. Out of these patients,95.5% (172) patients had positive findings of COVID-19 on HRCT chest scan. 4.44% (08) had negative HRCT chest findings; while 65% (117) had positive and 30.55% (55) had negative first PCR respectively. Among the patients who had an initial negative PCR, a repeat second PCR was performed on 32 patients. On repeated PCR, 65.6% (21) came out negative and 15.87% (10) showed positive PCR results.

Conclusion: Diagnosis of COVID-19 pneumonia can be made on HRCT findings prior to the RT-PCR test result. Moreover, the diagnosis of this rapidly spreading disease should not be excluded on the basis of a negative RT-PCR test.

Key words: RT-PCR; HRCT chest; COVID-19 pneumonia; GGO (ground-glass opacity)

Introduction

Coronavirus disease outbreak came to light for the first time in Wuhan, a city in China, in December 2019. Since then, it demonstrated a massive spread primarily by foreign and subsequently through local transmission, leading to the declaration of COVID-19 pneumonia as a global pandemic affecting almost 213 countries. The most affected countries included America, Italy, Spain, and the UK.[1] Pakistan was ranked in the top '20s of the most affected countries by this disease, the first case being reported in February 2020 in the city of Karachi, Pakistan.[2] The COVID-19 Health Advisory Platform by the Ministry of National Health Pakistan, reported 312, 263 confirmed COVID-19 cases, with 6,479 deaths by 30 September 2020. The peak was observed on 14th June 2020, with 12,073 newly reported cases.[3]

No confirmed prophylactic or curative treatment has been approved by WHO as of yet for this contagious lethal disease. Hence, it has become extremely important to make an early diagnosis of this disease in order to control its spread. Healthcare workers are at a higher risk of contracting the infection ranging from 15-18% and in some cases up to 20% of the entire infected population.[4]

The recommended standard test for the detection of COVID-19 disease is real-time PCR which is taken either through the nasal or oropharyngeal route.[5] Owing to various new mutant strains of SARS-COV-2, the rate of false-positive PCR results are on the rise, resulting in inefficient control of this pandemic secondary to lack of early detection and isolation. Several limitations also contribute to delayed diagnosis, which includes financial burden, sample collection, transportation, and kit performance for third-worldcountries like Pakistan.

HRCT chest plays a vital role in establishing a diagnosis of COVID-19 pneumonia. The classical imaging features on an HRCT include bilateral, peripherally located, subpleural, ground-glass attenuation in a posterior basal distribution.[6,7] This may further develop consolidation or crazy paving appearance resulting in complete involvement of pulmonary parenchyma.[8,9]

Xie described a case series stating that the above-mentionedcharacteristic HRCT findings with initial negative RT- PCR test results have warranted the need for using HRCT along with PCR in the diagnosis of COVID-19 pneumonia.[10] The positive rates of RT-PCR assay and chest CT imaging were described as 59% (601/1014), and 88% (888/1014) for the diagnosis of suspected patients with COVID-19, respectively.[11] Taking RT-PCR as a reference, the sensitivity of HRCT imaging for COVID-19 was reported to be 97% (580/601).[11]

As COVID-19 continues to infect communities and societies globally, bringing life to a halt, the hunt for a diagnostic test that is rapid and close to accurate prevails. Therefore the need for Pakistani data on comparison of RT-PCR and HRCT-Chest in the diagnosis of corona virus disease is inevitable.

Methodology

The present study was conducted at department of Noninvasive Cardiology and Radiology, Tabba Heart Institute, Karachi, from 1st April to 30th September 2020. Patients aged 18 to 80 years, who presented in the emergency department with clinical symptoms (fever, cough, and shortness of breath), highly suspicious of COVID-19 were included. These patients underwent their chest HRCT scans from the Radiology Department and RT-PCR was performed at the hospital's clinical laboratory. The data were retrieved from the electronic system of HOPE. Results were grouped as positive and negative findings for COVID-19 pneumonia.

This study included all patients referred from the Emergency room for HRCT chest examination to the Radiology CT scan department, from April 1 – September 30, 2020, with clinically suspected COVID-19 pneumonia, e.g., fever, shortness of breath (SOB), decreased O2 saturation, and cough. There was also exclusion criteria for this study as patients younger than 17 years or older than 75 years and patients referred from outpatient departments or clinics were not included in this study.

Having applied the inclusion and exclusion criteria, a total of 180 patients (99 men and 81 women; age range 42-53, mean age 48, median age 51) who underwent a chest CT were included in the study. Twenty-seven patients, out of which 23 were referred from outpatient clinics and 4 were young patients (<18 years of age), were excluded from the sample size.

All patients went through a chest HRCT scan on the same day their initial RT-PCR testing was performed. HOPE system database was used to review patients' clinical findings, RT-PCR results, and imaging findings of HRCT chest examinations.

All patients were scanned using the defined protocol for unenhanced high-resolution CT (HRCT) examination. All images were performed on a CT scanner (Toshiba Aquilion prime 80 slices) with patients in a supine position. Technical parameters for HRCT is 120 kV, auto-modulated mA, 0.5 slice thickness, 256 x 256 matrix.

All Images were reviewed by two consultant radiologists with 4 and 3 years of experience respectively. These were blinded to the RT-PCR results. The chest CT images were evaluated on an individual basis by each radiologist on a Radiant DICOM viewer.

Individual radiologists' results were gathered and were reviewed for any discrepancies to achieve a consensus decision regarding lesion features.

Chest HRCT images were evaluated on both mediastinal and lung window settings. Positive HRCT chest findings for COVID-19 were described as multifocal, multilobar, bilateral ground-glass opacities with or without subsegmental consolidations or crazy paving patterns in a peripheral distribution.[11,12]

These cases were further categorized as positive and negative for COVID-19 on the basis of clinical symptoms/signs, RT-PCR results, and mutual consensus. This characterization was in reference to the Radiological Society of North America Expert Consensus Statement on CT Chest Reporting Findings Related to COVID-19.[13]

Two radiologists described lung parenchymal lesions according to their location, margins, and density.

The location of the lung lesions was recorded according to their lobar distribution (central or peripheral). The densities of the lesions were classified as GGO, consolidation, or mixed. The margins were defined as regular or irregular.

Following 8 additional findings were also recorded. These included bronchial wall thickening, sub pleuralreticulations/bands, linear opacity, interlobular and intralobularseptal thickening, crazy paving pattern, pleural effusion, mediastinal lymph nodes, and air bronchogram.

The majority of the identified lesions were patchy, with irregular, and ill-defined margins. There fore, the size of the lesion was not assessed.

All study cases had undergone nasopharyngeal swab tests for RT-PCR, X-ray, neutrophils, lymphocytes, Creactiveprotein (CRP), and D-dimer testing.

Results

A total of 180 patients were included as being referred from the Emergency department with clinical suspicion of COVID-19 pneumonia. Out of the 99 (55%) were males and 81 (45%) were females.

95% (171) patients showed positive HRCT chest findings of COVID-19 and only 4.44% (08) demonstrated negative HRCT chest findings. Only one patient had a negative HRCT but a positive PCR test result.

65% (117) patients had positive first PCR test results and 30.55% (55) had negative first PCR test results.

Among the patients who had an initial negative PCR, a repeat second PCR was performed on 32 patients within 3 days of the initial PCR test. 23 patients did not get a repeated PCR test. On repeated PCR, 65.6% (21) came out negative and 15.87% (10) showed positive PCR results.

Among all patients demonstrating positive COVID-19 pneumonia features on HRCT scan, 121 patients showed multifocal ground-glass opacities. 51 showed mixed ground-glass opacities with patches of consolidation. The spread of lesions was also characteristic of COVID-

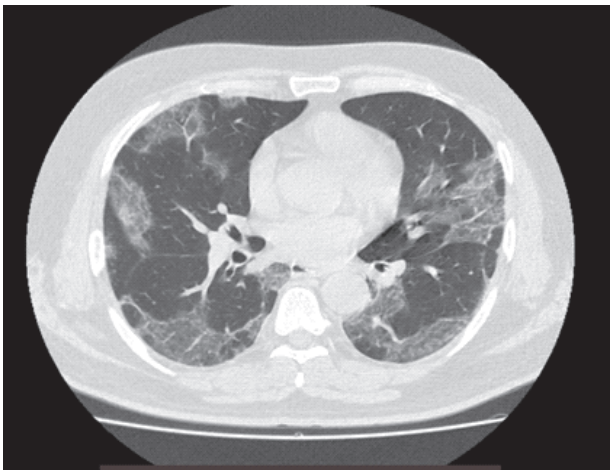

Fig A. 50-year-old man with a history of cough and fever. PCR for COVID-19 pneumonia was negative. HRCT Chest axial section reveals multifocal central and peripherally distributed ground-glass opacities in both lungs. Findings represent severe COVID-19 pneumonia.

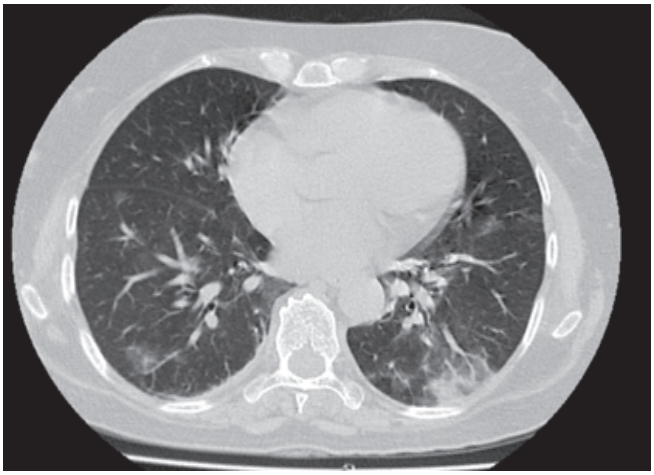

Fig B. 48-year-old woman with a history of fever and cough. Her initial PCR was positive for COVID-19 pneumonia. Her HRCT chest axial section shows peripherally distributed ground-glass opacities in bilateral upper and lower lobes. Findings represent moderate COVID-19 pneumonia. Her PCR for COVID 19 at the time of HRCT was reported negative.

19 infection with a posterior, peripheral, and bilateral predominance.

Discussion

The corona virus disease spectrum is a highly contagious viral disease, which has affected the whole of the world. Its clinical diagnosis depends on the three primary symptoms including fever, shortness of breath, and cough. The RT-PCR test is considered to be a standard test for the diagnosis of COVID-19 despite a few concerns related to its specificity and sensitivity. A few drawbacks associated with this test are increased reporting time and the non-availability of test kits with regard to monitoring the spread of disease. The pulmonary CT features of COVID-19 are being established but, not much has been established on the course and treatment of the disease. Chest X-ray is the primary radiological investigation in diagnosing COVID-19 pneumonia; however, HRCT is superior in disease recognition and follow-up.

The statistical data has revealed that Covid-19 pneumonia has adversely affected the Pakistani population. Therefore, awareness of the available diagnostic tests for clinicians and preventive health experts is compulsory for its early detection.

HRCT chest is a non-invasive, cost-effective, and rapid diagnostic tool. Its comparison with RT-PCR was evaluated in this audit. The results of our audit demonstrated that 95% of the clinically suspicious patients have positive radiological findings for COVID-19 pneumonia on HRCT. Negative HRCT findings were observed in only 4.44% (08) cases. Similar results were observed by N Hanif et al. Their study results showed that 83% of patients had typical HRCT chest findings, 17% had inconclusive HRCT chest findings for COVID-19; while 40.4% had positive and 59.6% had negative first PCR. The cohort with repeat second PCR demonstrated 19.6% negative results, 1.8% positive PCR results; while 78.6% of patients didn't get a repeat PCR. They concluded that the sensitivity of the HRCT chest is more (92%) in comparison to the first RT-PCR (45%).[12]

Ai et al conducted a study on 1,014 patients in Wuhan, China. They reported sensitivity, specificity, NPV, PPV, and diagnostic accuracy of CT chest was 97%, 25%, 68%, 83%, and 65%, respectively. Out of the 413 patients, who were tested negative in the first RT-PCR, 308 (75%) had positive CT chest findings for COVID-19.

A radiological examination like HRCT chest can be performed ahead of the RT-PCR test results and can, therefore, help in initial patient surveillance.

Early identification of the pulmonary manifestation of the disease can assist early supportive treatment as well as help in the prevention of bad outcomes resulting in patients requiring intensive care where the resources are less.

Previous CT studies have indicated that our cohort had typical characteristics of COVID-19 on HRCT including multi focal, peripheral, bilateral lower zones, and posterior pulmonary involvement Among all patients in our study, demonstrating positive COVID-19 pneumonia features, 121 patients showed multi focal ground-glass opacities. 51 showed mixed ground-glass opacities with patchy consolidation.

We observed Crazy paving[16] in several cases as well, pleural effusion was identified in only one case.

Limitations:

A few limitations were observed in relation to this study. These include a retrospective design and a smaller sample size. Another limitation is the lack of financial resources, which has resulted in a decreased number of repeat RT-PCR tests. Out of our 55 patients, only 22 received two RT-PCRtests. Also, a follow-up CT was not performed for every patient.

Conclusion:

Chest HRCT examination plays an important role in diagnosing early COVED lung manifestations prior to the RT-PCT test which may take a longer time to yield results. This is of utmost importance, especially in an emergency setting.

COVID-19 can be diagnosed by HRCT even before the RT-PCR test result, hence RT-PCR test negativity should not exclude the diagnosis of this contagious disease. In view of the ongoing pandemic, patients having a clinical suspicion or a history of exposure, CT features of viral pneumonia should be regarded as strong evidence for COVID-19 pneumonia, in spite of negative RT-PCR test results.

Therefore it is recommended that in such cases, patients should be treated on an appropriate infection control regime with repetition of RT-PCR swab testing.

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