

ROLE OF HIGH-RESOLUTION COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF REVERSE TRANSCRIPTASE POLYMERASE CHAIN REACTION NEGATIVE COVID-19 INFECTION CASES

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ABSTRACT

Objective: During the early phases of COVID-19 infection the diagnosis of the disease is made difficult by the negative result of RT-PCR test. RT-PCR shows variable sensitivity to detect COVID-19 infection and has a lengthy turnaround time. These two limitations of RT-PCR test results in delayed detection of COVID-19 infection, delayed isolation of these suspected cases and undermines efforts at the containment of infection. In this study we investigated the role of High-Resolution Computed Tomography (HRCT) in the diagnosis of COVID-19 infections in patients who tested negative for COVID-19 infections on RT-PCR. We studied 41 patients suspected of COVID-19 who presented with fever, dry cough, tiredness, sore throat, headache, breathlessness and diarrhea. Out of 41 patients, 30 patients were males and 11 were females. Initial RT-PCR for COVID-19 was negative. HRCT was done which showed pulmonary involvement in 35 out of 41 patients. Findings on HRCT were ground glass haze, multilobular involvement, consolidation and vascular enlargement. This study has shown that HRCT has a role in early detection of RT-PCR negative COVID-19 infection cases.

Material and Methods: This study was carried out between April 2020 and June 2020 in the department of Radiology Fauji Foundation hospital Rawalpindi. We studied 41 suspected patients of COVID-19 infection, 30 were males and 11 were females. Male to Female ratio was 3:1. Age range was 30-65 years. All these patients were suspected of COVID-19 infection. They presented with fever, dry cough, tiredness, sore throat, headache, breathlessness and diarrhea. RT-PCR test was performed at National Institute of Health (NIH) Islamabad for COVID-19 infection which was initially negative in all these cases. All these cases underwent HRCT examination.

Results: Out of 41 patients, 35 patients showed pulmonary involvement. Findings on HRCT were bilateral involvement of lungs (80% cases), peripheral distribution (74.8% case), posterior involvement (80% cases), Multi lobular involvement (89.3% cases), ground glass haze (86.6% cases), consolidation (33% cases) and vascular enlargement (60% cases). RT-PCR was repeated after one-week interval which was positive in 21 patients and negative in 20 patients.

Conclusion: In this study 41 suspected patients of COVID-19 were enrolled who presented with signs and symptoms of COVID-19 infections; however, RT-PCR testing was negative in all cases. Initially on HRCT scan pulmonary involvement was seen in 35 out of 41 patients. Findings of HRCT were ground glass haze, multilobular involvement, consolidation and vascular enlargement. This study has shown that HRCT has a role in early detection of COVID-19 infection cases in which RT-PCR is negative.

Key Words: COVID-19 infection, Pulmonary involvement on HRCT, RT-PCR diagnostic test.

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INTRODUCTION

Corona viruses are RNA viruses and known to cause common cold but in late 2019 infection with a novel beta corona virus Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) subsequently named COVID-19 can cause severe pneumonia, respiratory failure and death. SARS-CoV-2 primarily spreads from person to person through

respiratory droplets [8]. SARS-CoV-2 enters human cells by binding to angiotensin-converting-enzyme 2 (ACE2) receptor [2,5]. The most important initial symptoms of mild to moderate COVID-19 infection are cough, fever, malaise, anorexia, myalgia and diarrhea [15]. Dyspnea is the most important symptom of severe disease followed by rapid progression of respiratory failure soon after the onset of dyspnea and hypoxemia [3]. Patients with severe COVID-19 may progress and develop acute respiratory distress syndrome (ARDS) which is defined as the acute onset of bilateral infiltrates, dropping oxygen saturation and develop pulmonary

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edema not fully explained by fluid overload and heart failure [4].

The diagnosis of COVID -19 can be established on the basis of a suggestive clinical history and the detection of SARS-CoV-2 RNA in respiratory secretions using (RT-PCR). RT-PCR is highly specific test and a gold standard for diagnosis of COVID-19 infection. However, it has two major shortcomings; RT-PCR shows variable sensitivity to detect COVID-19 infection and it has lengthy turnaround time. Delayed turnaround time can mean that infected person may not remain isolated and spread the virus to others [13]. Early pulmonary involvement was detected on HRCT examination even in cases in which RT-PCR was negative for COVID-19 infection [10,11]. We performed HRCT in RT-PCR negative cases and evaluated the role of HRCT examination in the early detection of RT-PCR negative COVID-19 cases.

MATERIAL AND METHODS

We studied 41 patients, 30 were males and 11 were females. Male to female ratio was 3:1. Age range was 30-65 years. Median age was 49 years. All these patients were suspected cases of SARS-CoV-2 infection and RT-PCR was performed at National Institute of Health (NIH) Islamabad to diagnose SARS-CoV2 infection. They presented with fever, dry cough, tiredness, sore throat, headache, breathlessness and diarrhea. Fever was defined as an axillary temperature of 37.5 degree C or higher. Lymphocytopenia was defined as lymphocyte count of less than 1500 cells per cubic millimeter. Thrombocytopenia was defined as platelet count of less than 150,000 per cubic millimeter. These cases which were suspected suffering from COVID-19 infections but RT-PCR for COVID-19 were negative underwent HRCT examination of chest.

RESULTS

Fever was present in 91.5% of the cases. The second most common symptom was cough (78.7%), anorexia in 27.5% of the cases and diarrhea in 4.5% of the cases. Lymphopenia was detected in 84.5% of the cases and thrombocytopenia in 18% cases. HRCT findings included; bilateral involvement of lungs (80% cases), peripheral distribution (74.8% case), posterior involvement (80% cases), multilobular involvement (89.3% cases), ground glass haze (86.6% cases), consolidation (33% cases) and vascular enlargement (60% cases) as shown in figure.



Figure: Bilateral areas of ground glass haze are seen in both lung field.

DISCUSSION

During the initial phase of COVID-19 infection the diagnosis of the disease is confused by the RT-PCR results for COVID-19 virus detection. False negative RT-PCR results to detect COVID infection adversely affects timely patient management and patient may not be isolated and can infect others. As shown in this study RT-PCR was initially negative in all 41 patients.

As there is no effective vaccine and antiviral treatment available for COVID-19 infections, it is extremely important to detect the disease at stage and immediately quarantine the patient from healthy population and start necessary treatment if required. RT-PCR is a gold standard diagnostic test for COVID-19 infection. However, improper clinical sample collections and transportation, limitation of kit performance, non-availability of properly trained human resource, variation in detection rate from different manufacturer, low patient viral load and shortage of the test kits are major limitations of using RT-PCR for the diagnosis of COVID-19 infections particularly in developing countries.

HRCT may reveal abnormalities in suspected symptomatic cases of COVID-19 infection. These include ground glass haze, consolidation, small peripheral linear opacities, reticulation and thickened interlobular septa [1,7,9]. These typical radiological features were observed in symptomatic patients with negative RT-PCR results [6]. Ai Tao *et al* studied 1014 symptomatic patients with tentative diagnosis of COVID-19 infection. Out of 1014 patients 601 had positive RT-PCR results and 413 patients were negative. All 413 symptomatic patients who were RT-PCR test negative for COVID-19 infections had positive HRCT scans [12]. Fang Y *et al* reported the

sensitivity of HRCT was greater than that of RT-PCR 98% vs 71% respectively) [13]. Other studies also highlighted the concerns about false negative of results of RT-PCR in patients with apparent COVID-19 infection [15]. We studied 41 patients, 30 were males and 11 were females. Age range was 30-65 years. In this study fever was present in 91.5% of the cases. The second most common symptom was cough; 78.7%, anorexia in 27.5% of the cases and diarrhea in 4.5% of the cases. Lymphopenia was detected in 84.5% of the cases and thrombocytopenia in 18% cases.

These cases which were suspected suffering from COVID-19 infection but RT-PCR for COVID-19 was negative underwent HRCT. Clinical features, lymphopenia and thrombocytopenia support the diagnosis of COVID-19 infection but RT-PCR for COVID-19 infection was negative. HRCT findings included bilaterally involvement of lung (80% cases), peripheral distribution (74.8% cases), posterior involvement (80% cases), ground glass haze (86.6% cases), consolidation (33% cases) and vascular enlargement (60% cases). Early diagnosis of COVID-19 infection is extremely important for patient isolation, to control the spread of infection and timely clinical intervention if required.

CONCLUSION

This study concluded that HRCT was able to detect COVID-19 in RT-PCR negative patients. Therefore, HRCT should be used in suspected cases of COVID 19 especially early in the disease when RT-PCR is negative.

RT-PCR is a gold standard diagnostic test to diagnose COVID-19 infection. However, it has two major shortcomings; RT-PCR shows variable sensitivity to detect COVID-19 infection and it has lengthy turnaround time. In developing countries in particular issue is further complicated by non-availability of properly trained human resource, variation in detection rate from different labs and shortage of test kit. This study has shown that HRCT has role in early detection of COVID-19 infection cases in which RT-PCR is negative. Early detection of COVID-19 infection is extremely important for making decision regarding patient isolation and timely medical management.

AUTHORS CONTRIBUTION

Muhammad Harris Ayub: Investigator and writing original draft preparation

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