SYSTEMATIC REVIEW

Better Diagnostic Modality for COVID-19: CT Chest or RT – PCR? – A Systematic Review

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ABSTRACT

Background and Objective: A set of new studies is offering perspective and guidance on the differences between using Real Time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) and chest Computerized tomography (CT) in terms of sensitivity and specificity. This review paper addresses the comparative diagnostic potential of CT chest and RT-PCR for COVID-19.

Method: An online literature search was carried out from Jan. 2020 to Apr. 2020 from Google -Scholar, Web of Science, Science Direct and PubMed using the MeSH key words. Twenty-five articles were retrieved. Articles with incomplete information and covering other factors like ethnicity were excluded and only the articles with comparison between two clinical diagnostic methods were included. Avoiding the duplication of issues, 5 articles were finally selected for review.

Result: This review observed 98% pooled sensitivity of CT-chest being much higher than that of RT-PCR (75%).

Conclusion: Patients with suspicion of COVID-19 should be screened using CT scan chest as a more sensitive technique.

KEYWORDS: COVID-19, SARS-CoV-2, CT Chest, RT-PCR.

INTRODUCTION

"December 2019" made a mark on global history due to the occurrence of a pneumonia like illness, of unknown origin in Wuhan, China; which was later diagnosed a COVID-19 (Corona virus disease 2019), caused by Corona virus. It is perceived to be caused by ingestion of wild animals, most probably Rhinolophus bats.[1] Till February 24, 2020; 77658 confirmed cases, out of which 9126 were severe cases and 2663 deaths were recorded in China.[2]Majority of the cases had travelled to the affected area.[3] Increased number of cases would lead to increased burden medical system.[4]However, since within two months, it has become a pandemic disease enrolling many countries worldwide - Italy, Spain, Iran, England and USA being affected the most. Early diagnosis of the disease is crucial to put a stop to this deadly virus. The diagnosis can be made by RT-PCR (Reverse Real Time - Transcriptase Polymerase Chain Reaction) and CT (Computed Tomography) Chest. RT-PCR may report to be false negative due to number of

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reasons like lack of resources, transportation issues and lack of kits. Furthermore, CT scan is the routine diagnostic tool for pneumonia.[2] Chest CT could be done in patients with RT-PCR being negative.[3] Early arrival of vaccine and anti-viral therapy is the need of hour. But before that, best diagnostic tool for screening of patients' needs to be identified.[4]

The purpose of the study is to get convincing results by systematic evaluation of research data in detailfor concluding a better diagnostic tool for screening of patients with COVID-19.

Methods

An online literature search was carried out from January, 2020 to April, 2020 from reputed search engines like Google Scholar, Web of Science , Science Direct and PubMed using the key term "COVID-19", "SARS-COV-2 infection", "CT Chest", "RT-PCR", "Comparison of CT Chest and RT-PCR" and various synonymous terms from the titles of the articles. This resulted in retrieval of 25 articles initially. After reading the manuscripts, articles with incomplete information and covering other factors like ethnicity and or clinical association studies were excluded and only the articles with Study of Diagnostic Accuracy (STARD) focus between two clinical diagnostic methods were included. Avoiding the duplication of issues, 5 articles were finally selected for review (Fig.1).
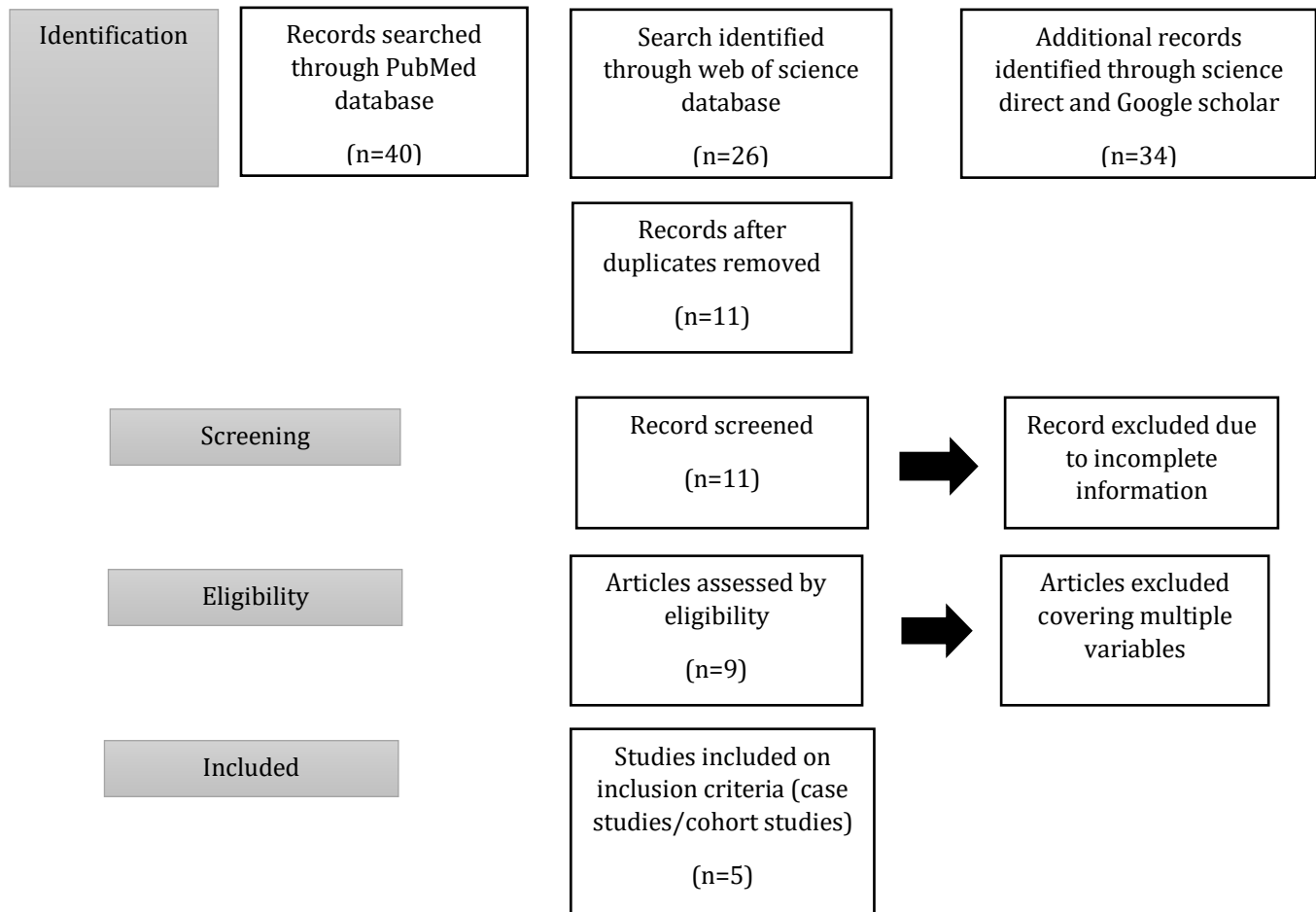
| Identification | Records searched through PubMed database (n=40) | Search identified through web of science database (n=26) | Additional records identified through science direct and Google scholar (n=34) |

| | Records after duplicates removed (n=11) | |

| Screening | Record screened (n=11) | → Record excluded due to incomplete information |

| Eligibility | Articles assessed by eligibility (n=9) | → Articles excluded covering multiple variables |

| Included | Studies included on inclusion criteria (case studies/cohort studies) (n=5) | |

Fig.1: PRISMA 2009 Flow diagram showing study characteristics.

RESULTS

Following is the brief review of comparison between CT Chest and PCR in COVID-19 patients:

a. Fang Y et al.[1] in their retrospective analysis from Jan. 2020 to Feb. 2020 assessed the diagnostic methods. A total of 51 patients

participated in the study. 98% showed abnormal CT Chest findings resembling viral pneumonia. Contrarily, it took about 7 days in all for real time RT-PCR to become positive in the patients (71% sensitive). The study showed that the sensitivity of CT chest being more (98%) as compared to RT-PCR (71%). It was evident that patients with clinical and epidemiological features of COVID-19 should be screened using CT scan chest.

b. Long C et al.[3] in their retrospective study done from Jan. 2020 to Feb. 2020 included 204 suspected COVID-19 initially then 87 went for CT and RT-PCR. Amongst these cases, 36 patients were diagnosed with the COVID-19 pneumonia and 51 without pneumonia were placed in control group. The CT of COVID-19 confirmed patients were assessed for distribution of lesions. It was noted that right lower lobe had 26/36 (72.2%) lesions followed by left lower lobe 24/36 (66.7%), left upper lobe 20/36 (55.6%), right middle lobe 20/36 (55.6%) and right upper lobe 19/36 (52.7%). As far as distribution of pattern was concerned it was maximum at the peripheral 26/36 (72.2%) and central distribution 27.8%. Only 11 patients (30.6%) had single lesion, majority of patients (25/36, 69.4%) had more multiple CT abnormalities. Control group showed peripheral distribution was more in COVID-19 pneumonia group *(P < 00.5)*. The result showed that thirty-five patients had abnormal CT findings at presentation, and only one patient had a normal thoracic CT. Initially 30 cases showed positivity on RT-PCT test and then remaining case showed positive result on subsequent PCR test. Therefore, sensitivity of CT examinations was 97.2% at presentation, whereas first round RT-PCR sensitivity was 84.6%.

c. Nemati Saeed et al.[4] in their retrospective cohort study, followed patients who were admitted to 12 hospitals across Qazvin province, Iran, during February 20 – March 11 with a primary diagnosis of COVID-19 until March 27, 2020. CT Chest of 998 patients showed evidence of Coronavirus infection. On the other hand, 558 patients resulted in positive RT-PCR test (73·8%). A total of 20.68% was the case fatality rate among test positive

which was higher as compared to 7.5% in test negative.

d. Tao et al.[2] studied 1014 COVID-19 patients from Jan. to Feb. 2020 in China. RT-PCR became positive results after being performed multiple times at regular intervals taking up to 4 days, hence 75% sensitivity. On the other hand, CT Chest showed 97% sensitivity.

e. Xingzhi X et al.[5] in this study described CT imaging features with 5 patients initially showing negative RT-PCR from 167 total patients. A total of 155 (93%) cases showed CT-chest and RT-PCR positive (Fig:2). The five patients were followed when admitted to hospitals and their second laboratory test was done. RT-PCR testing can show false negative results due to laboratory error or insufficient viral material.
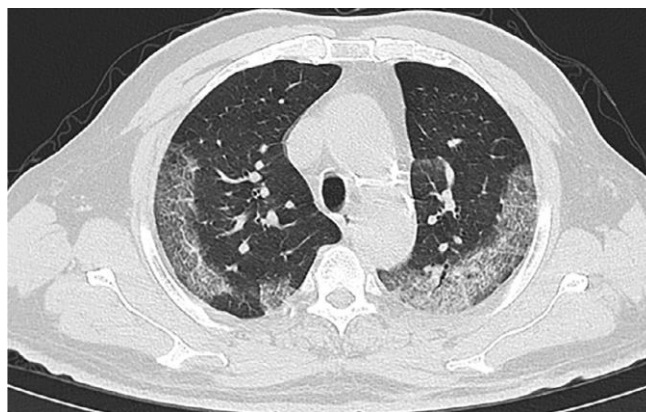

Fig.2: Typical chest CT findings compatible with COVID-19 pneumonia showing bilateral subpleural ground glass opacities (GGO).

DISCUSSION

Coronavirus is a new evolving infectious disease. Since Jan. 30,2020 when WHO declared it "Public Health Emergency", researchers have been working day and night worldwide for its cure and control.[6] Continual research work has targeted various aspects of Coronavirus disease from understanding its spread, pathogenesis and risk factors to diagnosis and treatment. But devising safe, rapid and cost-effective diagnostic modalities can help immensely to contain the disease. Early and prompt diagnosis is most likely the key to success. Up till now CT scan chest and RT-PCR are

at the top of the list for ruling out Coronavirus disease.[7-9]

In this systematic review, the authors have studied latest research publications from January to April 2020 from different regions of the world. It is observed that these two diagnostic tools have their advantages as well as their limitations. It was revealed that CT scan chest surpasses RT-PCR clearly in terms of its sensitivity, less reporting time, non-invasiveness and most importantly less false negative cases.[1,10] Our comparative findings coincide withthe results of Adam et al.[11] in China. They studied 151 patients having similar symptoms of SARS-CoV-2 infection. CT chest done at different intervals showed progressive lung manifestations that could not be detected by RT-PCR in such a way. These results also matched with the observations of Pan F et al.[11] in 21 confirmed COVID-19 patients lung changes progressed with time. Detection in SARS-CoV-2 infected persons with no sign or symptoms have also given positive findings on CT chest (Fig:3).[12] But CT chest is less specific as its ground glass appearance on both lungs along consolidation (Fig:2) may resemble lung diseases like viral pneumonia.[11,13] CT chest also aids non-pulmonary findings in COVID-19 patients.[14,15] Reproducibility is another factor that adds to the credibility of CT chest.[16] But one should keep in mind that trained radiologist and proper machinery are a must for conducting CT chest.

On the other hand, real time RT-PCR is based on viral load in COVID-19 patients.[17] Although its sensitivity is low but it has been widely used as diagnostic tool. Li Y et al.[18] studied 610 hospitalized patients, repeated their RT-PCR at intervals and found significant false negative results. They emphasized on the use of CT scan chest for diagnosis as well as screening of SARS-CoV-2 infection. Hence coinciding with our findings. Probable causes of false negative results include manufacturing defects in the detection kits, expired reagent and human errors, depicting those pre-analytical errors cannot be overlooked. Too early screening in terms of development of sign and symptoms might also be one of the reasons of false negative results (Fig:4).[19] Unavailability of sufficient kits according to the population of that area is a harsh fact faced by different countries.[18]
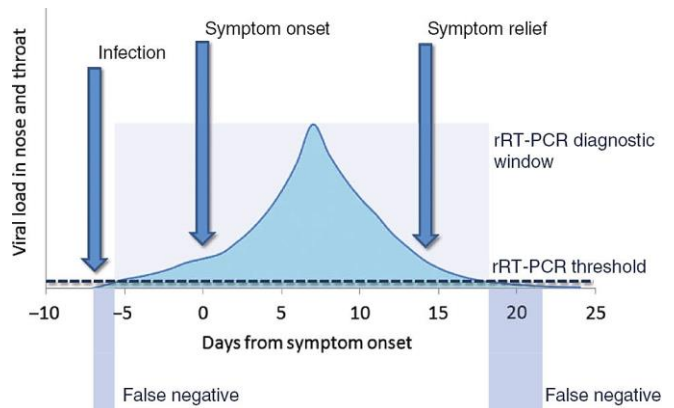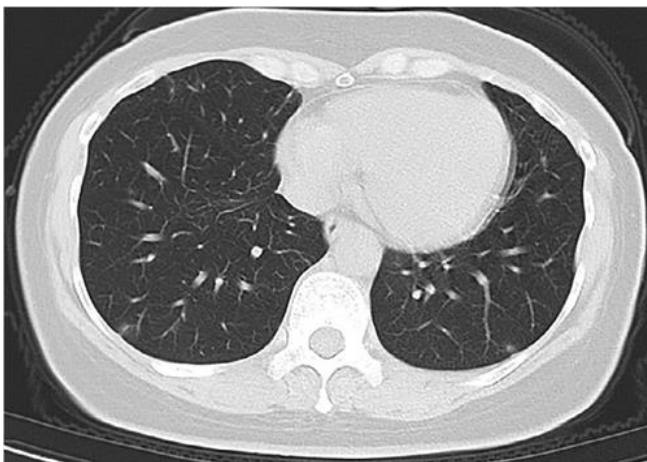

Fig. 4: Real time RT-PCR diagnostic window.

Observations of our systematic review have also been supported by a meta-analysis done Kim Het al.[10] including studies of eight countries (from Jan. 1 to Apr. 3, 2020) where pooled sensitivity of CT chest turned out to be 94% and that of RT-PCR was 89%. Thus, justifying CT chest as a screening tool.[10]

Rodriguez-Morales et al.[20] did meta-analysis and an elaborate review study from Jan. 1 to Feb. 23, 2020. They assessed broad spectrum of Coronavirus disease with regard to its multidimensional manifestations – clinical, laboratory and radiological outcomes. But they compared neither CT chest nor RT-PCR.[20]

Another systematic review by Yang et al.[81] studied only CT chest imaging in Coronavirus patients available till Feb. 19, 2020. They also observed significance of CT chest inthe course of

Fig.3: Atypical chest CT findings compatible with COVID-19 pneumonia showing bilateral subpleural ground glass opacities (GGO).

disease as well as a screening tool. But they did not compare RT-PCR as well.

In Pakistan, observational studies regarding demographics and mental health of COVID-19 patients have been done. But such comparative study of diagnostic accuracy has not been done yet.

CONCLUSION

CT chest has better diagnostic potential than real time RT-PCR for COVID-19 patients even at earlier stages of clinical presentation. Therefore, CT Chest may be usedas a primary modality for diagnosis as well as screening of COVID-19 where professional expertise and equipment facilities are available.

LIMITATIONS OF STUDY

The present systematic review has some limitations. Only a few studies have been included yet majority belongs to China. Demographic information, profession, life style, socioeconomic status and vaccination history was not taken as a study variable. Future papers will be addressing these issues at length.

CONFLICT OF INTEREST

None to declare.

FINANCIAL DISCLOSURE

None to disclose.

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Author's Contribution

ST: Conception and design of study, Acquisition of data.

AF: Acquisition of data.

SS: Analysis of data, Drafting of manuscript.

SA: Critical review and intellectual input, Final approval of the version to be published