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Original Article

Relationship between RT-PCR & HRCT of chest in COVID-19 patients

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Abstract

Introduction: COVID-19 pandemic is affecting Bangladesh like other countries and its early detection, management became major public health concern of the government as well as private sector. So, this present study was conducted to systematically analyze RT-PCR, HRCT of chest in COVID-19 subjects and to detect diagnostic accuracy of HRCT of chest comparing RT-PCR as gold standard. **Materials and Methods:** This observational study was carried out enrolling 266 study subjects at Department of Medicine in TMSS Medical College and Rafatullah Community Hospital, Bogura. Suspected subjects of novel coronavirus infection who underwent both chest CT imaging and laboratory virus nucleic acid test (RT-PCR assay with throat swab samples) were included in this study. Demographic characteristics, co-morbidities and symptoms were recorded. **Results**: Sensitivity, Specificity, PPV, NPV of RT PCR for detection of COVID-19 infection was 89.4%, 76.6%, 95% and 7% respectively. Considering RT-PCT as gold standard test, Sensitivity, Specificity, PPV, NPV of HRCT chest for Detection of presence of COVID -19 infection were 94.8%, 85.7%, 99.1% and 48% respectively. **Conclusion:** HRCT of chest was a comparable tool for detection of presence of COVID -19 infection.

Key words: COVID-19, RT-PCR, Chest HRCT.

Introduction

Since December 2019, a number of cases of "unknown viral pneumonia" related to a local Seafood Wholesale Market were reported in Wuhan City, Hubei Province, China.[1] A novel coronavirus (SARS-CoV-2) was suspected to be the etiology with Phinolophus bat as the alleged origin. The coronavirus pandemic has infected more than 9.6 million people and killed more than 16,665,702 worldwide since late January, when it was first reported.[2-4] The outbreak spread from the Chinese city of Wuhan to more than 180 countries and territories—affecting every continent except Antarctica.[5] In absence of specific therapeutic drugs or vaccines for 2019 novel coronavirus disease (COVID-19), it is essential to detect the diseases at an early stage, and immediately isolate the infected person from the healthy population. According to the latest guideline of Diagnosis and Treatment of Pneumonitis Caused by 2019-nCoV (trial sixth version) published by the China government, the diagnosis of COVID-19 must be confirmed by the reverse transcription polymerase chain reaction (RT-PCR) or gene sequencing for respiratory or blood specimens, as the key indicator for hospitalization.[6-9] However, with limitations of sample collection and transportation, and kit performance, the total positive rate of RT-PCR for throat swab samples was reported to be about 30% to 60% at initial presentation.[9] In the current emergency, the low sensitivity of RT-PCR implies that many COVID-19 patients may not be identified and may not receive appropriate treatment in time; such patients constitute a risk for infecting a larger population given the highly contagious nature of the

virus. Chest CT, as a routine imaging tool for pneumonia diagnosis, is relatively easy to perform and can produce fast diagnosis. In this context, chest CT may provide benefit for diagnosis of COVID-19. As recently reported, chest CT demonstrates typical radiographic features in almost all COVID-19 patients; including ground-glass opacities, multifocal patchy consolidation, and/or interstitial changes with a peripheral distribution.[10] Those typical features were also observed in patients with negative RT-PCR results but clinical symptoms. It has been noted in small-scale studies that the current RT-PCR testing has limited sensitivity, while chest CT may reveal pulmonary abnormalities consistent with COVID-19 in patients with initial negative RT-PCR results.[11-13] A real-time reverse transcription–polymerase chain reaction (RT-PCR) test is the gold standard for COVID-19 infection diagnosis.[14-15] However, sample quality hinders the accuracy of the test. In addition, the RT-PCR test requires a relatively long time. Several studies have compared the consistency between RT-PCR and CT findings.[1-5] This present study was conducted to systematically analyze RT-PCR, HRCT of chest in COVID-19 subjects and to determine whether chest CT was superior in rapid diagnosis in terms of sensitivity, specificity, positive predictive value, negative predictive value and to take prompt management of this disease compared with RT-PCR.

Materials and Methods

The observational comparative was performed at Department of Medicine in TMSS Medical College and Rafatullah Community Hospital, Bogura to determine diagnostic accuracy of HRCT of chest as well as RT-PCT in COVID-19 patients. Suspected patients of novel coronavirus infection who underwent both HRCT of chest imaging and laboratory virus nucleic acid test (RT-PCR assay with nasal swab samples) would be enrolled in this study. When time-interval between chest CT and the RT-PCR assay would be longer than 7 days, patients would be excluded. The RT-PCR assays was performed by using TaqMan One-Step RT-PCR Kits from Shanghai Huirui Biotechnology Co., Ltd or Shanghai BioGerm Medical Biotechnology Co., Ltd, both of which were being approved use by the China Food and Drug Administration (CFDA). For patients with multiple RT-PCR assays, the repeated testing conducted up to and including 3 days after the initial test would be adopted for confirmation of diagnosis. Repeated testing more than 3 days after the initial RT PCR Test would be used to analyze conversion of RT-PCR results, in correlation with the HRCT chest CT scan images. For patients with multiple RT-PCR assays the diagnosis of COVID-19 would be confirmed when any one of the nucleic acid test results would be positive. If a patient had multiple chest CT scans, shortest interval (less than or equal to 7 days) scan would be included to compare with the RT-PCR assay for the analysis of diagnostic performance; any other chest CT scans in the same patient would be used to assess the temporal change of the disease. Two experienced radiologists (At least 3 years of experience in interpreting chest CT imaging, respectively), who were blinded to RT-PCR results, reviewed all chest CT images and decided on positive or negative CT findings by consensus. The epidemiological history and clinical symptoms would be available for both readers. The radiologists classified the chest CT as positive or negative for COVID-19. This study would be conducted from April, 2020 to September, 2020. Statistically 97 subjects were calculated. But at the end of study total, 266 subjects included in this study. In this study, keeping compliance with Helsinki Declaration for Medical Research Involving Human Subjects 1964, the nature and purpose of the study was informed in detail to all participants. Voluntary participations were encouraged. There was no physical, psychological and social risk to the subjects. Informed and understood written consent was taken from every patient before enrollment. Privacy, anonymity and confidentiality of data information identifying any patient were maintained strictly. Before starting this study ethical clearance was taken from Institutional Review Board (IRB). Data taken from the participants were coded and regarded as confidential and kept locked under investigator for purposeful use only. No experimental new drug was administered and no placebo will be

used here. The statistical analysis was performed using SPSS version 23.0 (SPSS Inc. Chicago, IL). Continuous variables were displayed as mean ± standard deviation and categorical variables as counts and percentages. Using RT-PCR results as reference, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of chest CT imaging were calculated.

Results

Table-I: Demographic characteristics, Co-morbidities and symptoms of study subjects (n=266)

Characteristics	Number (n)	Percentage (%)
Age (years): 52.99 ±14.99, range of 19-105 years.		
20 and below	03	01.1
21-30	15	05.6
31-40	35	13.2
41-50	59	22.2
51-60	78	29.3
60 and above	76	28.6
Sex		
Male	185	69.5
Female	81	30.5
Smoking history		
Non-smoker	138	51.9
Smoker	70	26.3
Ex-smoker	33	12.4
Co morbidities		
DM	138	51.9
HTN	133	50.0
Heart disease	23	08.6
CKD	22	08.3
Bronchial asthma	36	13.5
COPD	08	03.0
Symptoms		
Fever	242	91.0%
Cough	227	85.3%
Shortness of breath	147	55.3%
Sore throat	75	28.2%
Diarrhea	47	17.7%
Headache	63	23.7%
Fatigue	76	28.6%
Mayalgia	57	21.4%

It was observed that, majority (29.3%) of the subjects were from 51-60 years age groups. Rest 28.6% from above 60 years, 22.2% from 41-50 years age group and about 1.1% subjects were from below 20yeras age group. Most of the subjects were male [185 (69.5%)] and remaining were female [81 (30.5 %)]. DM (51.9%), HTN (50%), Asthma (13.5%), Heart disease (8.6%), CKD (8.3%) and COPD (3%) were mostly prevailed Co-morbidities. Majority of the subjects had fever (91%), followed by cough (85.3%), shortness of breast (55.3%), sore throat (28.2%), diarrhoea (17.7%), headache (23.7%), Fatigue (28.6%) and myalgia (21.4%).

Table-II: Relation between HRCT of chest with RT-PCR reports (n=266)

HRCT of chest reports and RT-PCR reports					
			RT-PCR reports		
			negative	positive	Total
HRCT of chest report	Positive	Count	39	202	241
		% within RT -PCR report?	79.6%	93.1%	90.6%
	Negative	Count	10	15	25
		% within RT -PCR report?	20.4%	6.9%	9.4%
Total		Count	49	217	266
		% within RT -PCR report?	100.0%	100.0%	100.0%

Total 241 cases were positive at HRCT of chest among which 202 were positive at RT-PCR. Among 25 HRCT negative cases, 15 were negative at RT-PCR. So, considering this, Sensitivity, Specificity, PPV, NPV of RT PCR were 89.4%, 76.6%, 95% and 7% respectively. Considering RT-PCT as gold standard test, Sensitivity, Specificity, PPV, NPV of HRCT chest were 94.8%, 85.7%, 99.1% and 48% respectively.

Discussion

Nearly 526485 cases being confirmed in Bangladesh till, 15th January, 2021 and death reached 7862. Bangladesh is the eighth-most populated country in the world with almost 2.2% of the world's population. Bangladesh has one of the highest population densities in the world. Based on United Nations Data 2020 figures for population (164,689,383) and land area (130,170 km^2), Bangladesh has the highest population density among large countries, 1265 persons per square kilometre, and 10th overall, when small countries and city-states are included. In this huge gathering, Detection of COVID-19 infection is really challenging. RT-PCR remains the gold standard, but sample collection, timely delivery of report to huge number of population is almost impossible as well as this hinders the affected population to take timely proper treatment. At Government level, RT-PCR is free of cost, takes sometimes one week to get result and sometimes gives false negative result. At Government, private levels RT-PCR costs almost same compared to HRCT of chest and results of HRCT of chest yields quickly. The chest computed tomography (CT) scan plays a central role on the disease staging and checking the treatment efficacy, while the reverse transcription-polymerase chain reaction (RT-PCR) remains the mainstay of COVID-19 diagnosis[4,5], though limited to identify the virus, which poses important restrictions[6]. Recent studies claim that initial chest CT may enable the detection of the disease with higher sensitivity in comparison to RT-PCR[7]. Chan et al[11] (2020) suggested that the keys to control COVID-19 were early discovery, early isolation, and early treatment. Real-time reverse transcription polymerase chain reaction (RT-PCR) assay remains the standard of reference, but it was reported that false-negative RT-PCR was not rare and, in these patients, initial chest CT might present abnormal findings indicating COVID-19. Moreover, shortage of laboratory test kits limited the use of RT-PCR with the spread of the epidemic, especially in regions severely affected by the epidemic. Therefore, some experts suggested that chest CT could be regarded as a diagnosis standard of COVID-19. The guideline of Diagnosis and Treatment of Pneumonitis Caused by 2019-nCoV (trial sixth version) published by the China government recommended chest CT as an effective method to screen suspicious cases.[8] The addition of chest CT for diagnosis of COVID-19 resulted in tens of thousands of clinically diagnosed cases in worldwide which played an important role in controlling epidemic situation.[4,5,8,9] Therefore, comprehensive and timely evaluation of the effectiveness of chest CT for COVID-19 diagnosis remains urgent and mandatory. In the present study, we validated the effectiveness of chest CT for COVID-19 diagnosis comparing with RT-PCR.

In present study it was seen that observed that, majority (29.3%) of the subjects were from 51-60 years age groups. Most of the subjects were male (69.5%) and remaining were female (30.5%). This might be due to low socio-economic condition of our country lead male to go outside for family income and became more affected. On the other hand, female were less affected. Possible causes were they were at home in lockdown. But one thing to remember that, those male who were admitted in hospital were attended by their female partner or female attended and they had no clinical manifestation of disease. Possibly hormonal cause and inherent immunity of female gender helped women to give natural immunity against this disease. Reports from China, Italy, and the United States indicate that men appear to suffer more severe cases and die of the disease at greater rates than women, with deaths possibly up to 20 percent higher.[12,13] Researchers suggested Women have a more robust immune response to disease-causing viruses and bacteria. This could be because X chromosomes improve the expression of key immune functions, and

women have two X chromosomes rather than a single X as found in men. Another possibility is that the female sex hormones estrogen and progesterone can, respectively, help promote immune response and reduce inflammation.[13,14]

DM (51.9%), HTN (50%), Asthma (13.5%), Heart disease (8.6%), CKD (8.3%) and COPD (3%) were mostly prevailed Co-morbidities among the study subjects. In present research, 26.3% were smoker. Previous studies[14-17] revealed that multiple comorbidities are associated with the severity of COVID-19 disease progression. Many of the poorer outcomes for COVID-19 have been related to cardiovascular comorbid conditions. Patients with type 2 diabetes were also more likely to have increased severity of COVID-19. In a cohort study of 7337 patients with COVID-19 with and without type 2 diabetes, it was shown that those with type 2 diabetes required increased interventions for their hospital stay versus those that were nondiabetic. Among other comorbidities, chronic obstructive pulmonary disease (COPD) has also been associated with poor disease progression. A meta-analysis of multiple studies in China found that there was a four-fold increase in mortality in patients with preexisting COPD that were diagnosed with COVID-19. In this analysis, the smoking status of patients and severity of COVID-19 were also studied.

CDC[17] reported that People with COVID-19 had a wide range of symptoms elicited – ranging from mild symptoms to severe illness. Symptoms might appear 2-14 days after exposure to the virus. People with these symptoms might have COVID-19 Fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, diarrhea. In present study majority of the subjects had fever (91%), followed by cough (85.3%), shortness of breast (55.3%), sore throat (28.2%), diarrhoea (17.7%), headache (23.7%), Fatigue (28.6%) and myalgia (21.4%). According to Chowdhury et al[14], though COVID-19 patients in Bangladesh commonly presented with fever, cough, fatigue, shortness of breath, and sore throat, but symptoms like myalgia, diarrhea, skin rash, headache, Abdominal pain/cramp, nausea, vomiting, restlessness, and a higher temperature of >100^{0}F have a greater presentation rate and more frequent than other published studies.

Unenhanced chest CT may be considered for early diagnosis of viral disease, although viral nucleic acid detection with real-time polymerase chain reaction (RT-PCR) remains the standard of reference.[18-20] Present study showed that, considering this, Sensitivity, Specificity, PPV, NPV of RT PCR were 89.4%, 76.6%, 95% and 7% respectively. Considering RT-PCT as gold standard test, Sensitivity, Specificity, PPV, NPV of HRCT chest were 94.8%, 85.7%, 99.1% and 48% respectively. Mahmoud et al, reported that sensitivity of computed tomography in diagnosing COVID-19 is 98% while RT-PCR sensitivity is 71%.[19] Kovács[20] revealed that High sensitivity (67–100%) and relatively low specificity (25–80%) was reported for the CT scans. However, the sensitivity of RT-PCR was reported to be modest (53–88%), hence cannot serve as an appropriate ground truth. The "reverse calculation approach" showed that CT could have a higher specificity (83–100%) if we consider the modest sensitivity of the RT-PCR. Researchers[21-23] found that, sensitivity, specificity, positive predictive value, and negative predictive value of chest CT scan compared to RT-PCR were 87% (95% CI 85–90%), 46% (95% CI 29–63%), 69% (95% CI 56–72%), and 89% (95% CI 82–96%), respectively. It is important to rely on the repeated RT-PCR three times to give 99% accuracy, especially in negative samples. Regarding the overall diagnostic sensitivity of 87% for chest CT, the RT-PCR testing is essential and should be repeated to escape misdiagnosis.[24]

Conclusion

Considering current situation of COVID-19 infection in Bangladesh, HRCT was almost comparable with Gold standard RT-PCR considering parameters of diagnostic accuracy. HRCT of Chest can never replace RT-PCR, but considering its Cost-benefit ratio, time saving for early diagnosis as well as staging of COVID-19 infection, HRCT of chest can be applied to diagnose COVID-19 infection at present scenario of Bangladesh.

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