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Research Article

HRCT: A Tool to Curtail the Spread Rate of SARS-CoV-2 for Early and Authentic Triaging of COVID-19 Patients

Ayma Aftab[1], Samia Afzal[1]*, Muhammad Idrees[1], Aftab Ahmad[2], Tabasum Naz[2], Vivek Sharma[3] and Liaqat Ali[2]*

[1]Division of Molecular Virology and Infectious Diseases, Centre of Excellence in Molecular Biology (CEMB), University of the Punjab, Lahore, Pakistan

[2]Department of Microbiology and Immunology, National University of Medical Sciences, Rawalpindi, Pakistan

[3]Department of Environmental Sciences, University of Freiburg, Freiburg, Germany

***Corresponding Author:** Samia Afzal, Division of Molecular Virology and Infectious Diseases, Centre of Excellence in Molecular Biology (CEMB), University of the Punjab, Lahore, Pakistan and Liaqat Ali, Department of Microbiology and Immunology, National University of Medical Sciences, Rawalpindi, Pakistan.

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Abstract

To explain the characteristics of chest high resolution computed tomography (HRCT) among COVID-19 suspected cases. To reveal the consistency of HRCT chest findings with real-time polymerase chain reaction diagnosis in order to analyze the sensitivity and reliability of these two methods for the detection of omicron. This will help in early triaging of positive patients from negative patients and will eventually reduce the spread rates. A comparative study conducted on Pakistani COVID-19 suspected patients during June, 2021 to December, 2021. 2494 suspected COVID-19 patients were included in the study who were tested using both RT-PCR and chest HRCT. Based on HRCT analysis, patients were categorized as "Confirmed COVID positive", "Likely COVID positive" or "COVID negative" by radiologists. RT-PCR was selected as standard of reference to evaluate chest HRCT sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). 1114 patients were RT-PCR positive and 1380 were RT-PCR negative. 1164 (46.6%) were included in "Confirmed COVID positive", 1277 (51.2%) in "COVID negative" and 53 (2.1%) in "Likely COVID positive" on the basis of HRCT. 87.70% sensitivity, 97.46% specificity, 96.54% PPV and 90.76% NPV were obtained by comparing "Confirmed COVID positive" with RT-PCR. Depending upon the obtained sensitivity, CT scan can be used as a reliable time efficient tool to diagnose COVID-19 suspected patients instead of only relying upon RT-PCR that is time intensive along with certain limitations. Moreover, some RT-PCR negative patients also showed remarkable changes in lungs physiology that confirms the coronavirus disease.

Keywords: *False Negative; COVID-19; Real Time Polymerase Chain Reaction (RT-PCR); High Resolution Computed Tomography (HRCT)*

Abbreviations

HRCT: High Resolution Computed Tomography; CoVs: Coronaviruses; RT-PCR: Real Time Polymerase Chain Reaction

Introduction

SARS-CoV-2 is an infectious agent with a relatively high mortality rate. The information and research on this fatal agent have grown over the last couple of years. Coronaviruses (CoVs) are the largest family of positive-sense RNA viruses. They are known to infect a wide range of natural hosts. The evolution of Coronaviruses has proved a global threat to mankind. Genomic and proteomic studies of SARS-CoV-2

have identified the origin and source of its spread. The severity of the disease is intensified in patients with comorbidities that may lead to death. An aberrant immune response due to CoV-2 infection plays an important role in its pathogenesis.

Surging cases of the coronavirus have burdened the health care system of many countries [1]. Alterations in its genome have led to the emergence of pathogenic variants. Omicron emerged immediately after the fourth wave of COVID-19. It has now infected the people of at least 77 countries in 2021 [2] and has a very high infection rate. This urges us to address the disease as early as possible. Now a days, WHO has declared Omicron as its variant of concern [2]. Pakistan is a third world country and COVID-19 breakouts have shaken its health infrastructure [3]. During this wide spread of coronavirus anyone with a respiratory ailment is advised for the diagnosis of coronavirus. So, categorizing the patients into COVID positive and negative has become an urgent need of time to quarantine and treat the positive patients as early as possible to avoid the spread of this deadly virus. RT-PCR is known as the gold standard for the diagnosis of coronavirus [4]. Though RT-PCR is a commonly used molecular technique to detect the presence of RNA virus, its inconsistent sensitivity [5], scarcity of diagnostic kits [6], erroneous sample collection and sampling variability due to variable viral load [7] has urged the researchers to find other quick methods of diagnosis. Therefore, a prompt and reliable diagnostic test is mandatory to isolate the COVID -19 patients from the COVID-19 negative patients as soon as possible so as to protect the community and health care workers. Radiological analysis can be used as the first and foremost way of early detection of CoV-2 infection [8]. High false negative rates of RT-PCR are due to insufficient incubation period of the virus [9] *in vivo* and also due to high mutation rate [10]. These factors add to the burden of health care facilities and hamper the timely management of COVID-19 confirmed cases.

High resolution computed tomography (HRCT) is commonly used as a powerful diagnostic tool to monitor the prognosis of COVID-19 [11]. HRCT is 56 - 98% sensitive in the diagnosis of chest pneumonia [12,13]. HRCT has been reported by various researchers as a quick and efficient tool for the early detection of COVID-19 disease [14]. Current study is an effort to reveal the accuracy of HRCT chest in comparison to RT-PCR gold standard.

Materials and Methods

Participants data was handled confidentially via unique identification numbers. The sources were exclusively institutional and required a user ID and password with a user profile. As this was a retrospective study, informed consent forms were not needed. The study was conducted at a Diagnostic Centre, Multan in Pakistan from June 2021 to December, 2021. Patients who were advised for both RT-PCR test and HRCT chest were included in the study.

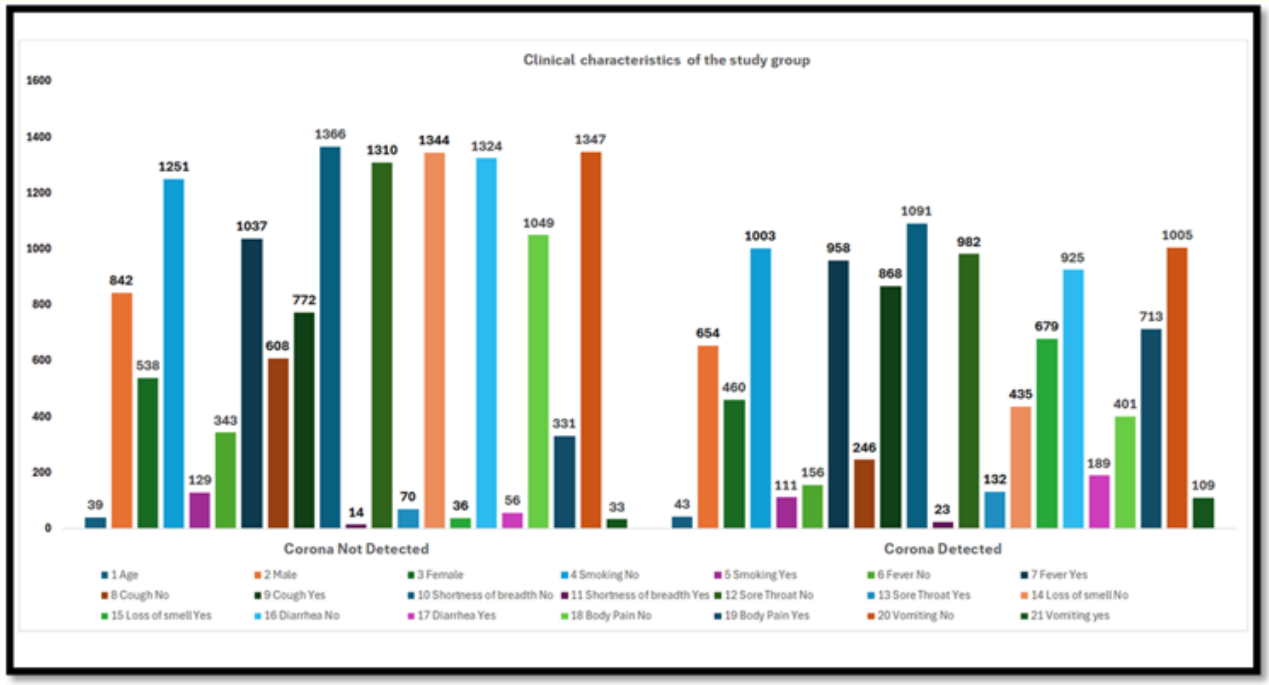
Any patients that were suffering from any other respiratory disease were excluded from the study. Pregnant, lactating women and children of less than 16 years were also excluded from the study. A total 2494 patients were selected for the study. Some patients reported interactions with COVID-19 positive patients. The symptoms usually reported by the patients were fever, body pain, malaise, cough, arthralgia, anosmia, dyspnea, or less than 85% of oxygen saturation. There were 1496 males and 998 females who underwent RT-PCR test and HRCT test. A 64-Slice Toshiba Aquilion CT Scanner was used to scan the patients in the head first supine position. The patients were scanned from the lungs apex to the diaphragm without intravenous contrast agent in the craniocaudal direction. 2 mm slice thickness with 10 mm intersection interval was applied at 120kVp, 300 mAs with 0.5 second rotation time. Automatic reconstruction reduced the intersection interval to 0.5 mm. Coronal, sagittal and axial views of lungs and mediastinum area were analyzed in Vitrea software.

HRCT scans were evaluated on the basis of size, form and dissemination of opacities linked with Broncho vascular and fibrotic deformations. Patients were classified as “Confirmed COVID positive” cases if symptoms such as ground-glass opacities found bilaterally in the periphery, multiple ground-glass opacities with or without consolidation or evident intralobular lines, reverse halo sign or different signs of developing pneumonia. “Likely COVID positive” cases included those patients who lacked aforementioned typical symptoms. This category of patients may include central, unilateral, multifocal, perihilar ground glass opacities with or without consolidation that is non-specifically distributed, isolated lobar or segmental consolidation without ground-glass opacities, distinct tiny nodules or pulmonary

cavity along with lymphadenopathy or pleural effusion. "COVID negative" cases had normal chest HRCT scan [15]. Statistical analysis was done on GraphPad Prism v8.0 (San Diego, CA).

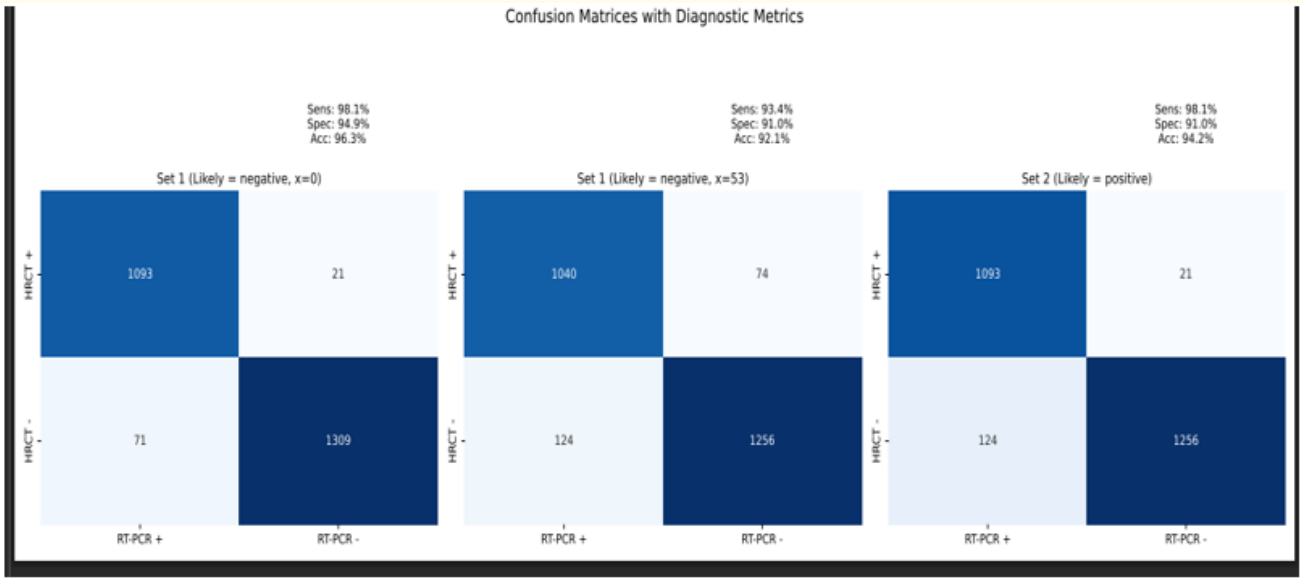
Results

Real-time reverse transcription Polymerase chain reaction (RT-PCR) test detected the presence of corona virus in the nasopharyngeal swab of selected patients. Internal and external positive controls along with negative control to verify the integrity of reaction were used. SARS-Cov-2 Real-TM-Sacace Biotechnologies was used to perform the test. 1114 patients were RT-PCR positive for COVID-19 and 1380 patients were negative for COVID-19. 1164 patients were included in the category of "Confirmed COVID positive", 53 patients were considered as "Likely COVID positive" and 1277 were included in "COVID negative". The selected group of study included 1496 males (59.9%) and 998 (40%) females. The mean age of the study group is 40.3 years (range = 16 to 95 years). 86% of the RT-PCR positive patients reported fever, 77.9% reported cough, 2% reported shortness of breath, 11.9% reported sore throat, 60.95% reported loss of smell or taste, 16.9% reported diarrhea as one of the first symptoms, 9.7% reported vomiting and 64% reported body pain (Graph 1).



Graph 1: *Clinical characteristics of the study group.*

HRCT of 1164 (46%) patients showed typical COVID-19 symptoms, 1277 (51%) patients showed no change in lungs physiology whereas 53 (2.2%) patients showed atypical pulmonary modifications. The patients were classified into 2 sets on the basis of HRCT characteristics and RT-PCR result. Set 1 consists of type 1 ("Confirmed COVID") patients and type 2 ("COVID negative" and "Likely COVID positive") patients. Set 2 comprises of type 1 ("COVID positive" and "Likely COVID positive") and type 2 ("COVID NEGATIVE") patients. Diagnostic sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and overall accuracy of the HRCT test was calculated by comparing set 1 with set 2. The values for each set are shown in the graph 2.



Graph 2: *Confusion matrix and diagnostic metrics of HRCT in comparison with Rt-PCR (Sens.=Sensitivity, Spec.=Specificity, Acc.=Accuracy).*

When "Confirmed COVID" cases were mixed with the "Likely COVID positive" cases the results were altogether changed. The number of true positive cases decreased, the number of true negative (specificity = 91.0%) cases also decreased and overall classification (accuracy = 94.9%) also changed.

SARS-CoV2 is continuously mutating its genome to evade the human immune system [16]. The virus has modulated itself into different variants as selective forces drive molecular evolution. The variants of concerns were alpha, beta, gamma and delta [17].

Sets	TP	FN	FP	TN	Sensitivity (%)	Specificity (%)	Accuracy (%)
Set 1 (x=0, Likely=negative)	1093	21	71	1309	98.1	94.9	96.4
Set 2 (x=53, Likely=negative)	1040	74	124	1256	93.3	91.0	92.1
Set 2 (Likely=positive)	1093	21	124	1256	98.1	91.0	94.9

Table 1: *Confusion matrix and diagnostic metrices of HRCT compared with Rt-PCR.*

Discussion

When the coronavirus invaded Pakistan, the conditions were alarming and precarious [18]. The whole world knew about the lack of medical facilities, low literacy rate and the delayed realization of the seriousness of disease in Pakistan. Therefore, a high death toll was anticipated. In an underdeveloped country like Pakistan, quick diagnosis plays a vital role. Wearing a mask and social distancing were successfully adopted, yet the need for early diagnosis and its importance could not be ignored to save the most number of people. By the end of 2021, once again, the whole country is endangered by the mutant coronavirus, omicron. The fast-spreading omicron has threatened the whole world. The best shield against the fast, piercing attack of omicron to use the time efficient, faster diagnostic tool of HRCT. This will positively help deaccelerate the infectious rate. On November 26, 2021, WHO declared omicron (B.1.1.529 variant) as the variant of concern (VOC) [19]. The authorities are concerned and seek to control the propagation of this disease among the population.

Controlling the spread rate is the key factor that can drastically reduce the dissemination of the disease. Social distancing has played an important role in this scenario. During this crucial time the medical facilities are overloaded with patients and there exist a high risk of contracting COVID-19 disease from corona positive patients to suspected patients. So, there is a dire need for early diagnosis of the definitely positive patients that will help in early isolation of patients which in turn will curtail the spread rate. A computational study showed that omicron more readily binds to human angiotensin converting enzyme 2 (ACE2) compared to other variants of coronavirus. This change in affinity is due to mutations in its receptor binding domain (RBD). The genetic modifications that enhance the viral spread rate are Q493R, N501Y, S371L, S373P, S375F, Q498R, and T478K. Omicron spike protein and the RBD undergo disorder-order transition at 468 to 473 [20]. This increases the dissemination rate among people. In order to curtail the onrush of omicron HRCT investigation method is the foremost need of medical sciences. RT-PCR has been recognized as the gold standard for the detection of SARS-CoV-2 virus but some of its discrepancies (false negative results, scarcity of diagnostic kits and considerable time of test) has urged the scientists to consider an alternate reliable diagnostic test. HRCT has been reported as an important tool in diagnosis and prognosis of COVID-19 [21]. The purpose of this study is to find the accuracy, sensitivity and specificity of HRCT of chest in comparison to RT-PCR test. The study included only those patients for whom both RT-PCR test and HRCT chest were advised by their physicians. Exclusion criteria comprise of pregnant, lactating women, children of less than 16 years and those suffering from any other respiratory disease. 2494. patients fulfilled the inclusion criteria. The data of these patients was categorized into 2 sets. The first set showed the comparison of "Confirmed COVID positive" on HRCT with RT-PCR. The evaluation of this comparison showed 94.9% accuracy of HRCT as a diagnostic test for COVID-19 detection with specificity of 91.0% and sensitivity of 98.1% (Table 1). Earlier studies reported the sensitivity to be as high as 60% to 98% and specificity to be 25% to 80% [22,23]. The current study shows 95% probability of classifying the suspected COVID-19 patients as confirm COVID-19 positive by HRCT. This may affirm the utility of HRCT as an alternate reliable diagnostic test for the diagnosis of COVID-19 [24]. The sensitivity of HRCT is 97% that shows true positive rate. The positive predictive value (PPV) is 89.8% for HRCT showing that high proportion of positively diagnosed COVID-19 patients are true positive for COVID-19. The negative predictive value is 98.3% that unravel HRCT reliability for reporting true negative results. Rt-PCR clinical sensitivity reported previously is 60 - 80% [27,28]. Comparing to that HRCT sensitivity is 98.1% means HRCT is more sensitive than RT-PCR.

Most of the studies have shown higher specificity than sensitivity for HRCT when compared with RT-PCR because of similar features of COVID-19 and other viral pneumonia [25]. However, the current study shows that when "Likely" cases were treated as negative then diagnostic metrics of HRCT were specificity 94.9%, sensitivity 98.1%, positive predictive value (PPV) 94.0%, negative predictive value (NPV) 98.4% and accuracy 96.4% (Table 1). The reason may be that the study group inclusion criteria excluded those patients who were suffering from any other respiratory disease. This constraint may have crucial effect on this evaluation as it increases predictive positive value (94.0%). The raised PPV reflects the integrity of HRCT in COVID-19 detection as probability of true positive diagnosis is higher than RT-PCR. Similarly, these selection criteria also influenced NPV (98.4%) that is higher than PPV (94%) because the patients in the study group were with severe pulmonary symptoms [15]. In set 2 when "Likely" cases were grouped with conformed HRCT positives then with the same sensitivity (98.1%) specificity reduced to 91.0%, PPV reduced to 89.8%, NPV was 98.3% and overall accuracy was 94.9%. Depending upon various studies conducted on the chest CT reliability, HRCT can be used to detect COVID-19. The National Health Commission of the People's Republic of China also added to the importance of chest CT as a diagnostic tool for COVID-19 [26]. The present study unravels the importance of HRCT as a reliable and time efficient diagnostic test while considering RT-PCR as the gold standard. HRCT is inherently a wonderful test because it maximizes spatial resolution of lungs.

Analytical specificity of RT-PCR is ~98 to 100% [29,30] whereas the current study shows outperformance of HRCT as compared to RT-PCR but still RT-PCR has an edge due to very high specificity. Raised PPV and NPV are attributable to the inclusion criteria of excluding respiratory disease. Above all the turnaround time of HRCT is another contributing factor in the diagnosis of any virus mediated respiratory disorder.

Conclusion

RT-PCR limitations can be mitigated by using a HRCT test. HRCT is a time effective diagnosis that proved helpful in segregation of COVID-19 positive and negative patients. Pakistan is a third world country, so most people do not have access or the resources to perform repeated diagnostic tests. Repeated testing could further add to the research to determine sensitivity, specificity, PPV, NPV and accuracy during different stages of disease. All the drawn results confirm that HRCT is more Reliable, accurate, and time efficient.

Author Contributions

Ayma Aftab: Writing - original draft, Formal analysis. Samia Afzal: Conceptualization, Project administration. Liaqat Ali: Conceptualization, Writing - review and editing, Visualization. Muhammad Idrees: Writing - review and editing. Aftab Ahmad: Formatting and editing. Tabassum Naz: Provided critical input and feedback.

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Conflicts of Interest

We declare that we have no conflict of interest.

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