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Correlation of Disease Severity with High-Resolution Computed Tomography (HRCT) Severity Scores in COVID-19 Patients - A Cross-Sectional Study

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ABSTRACT

***Objective*:** To determine the relationship of High-Resolution Computed Tomography Chest Severity Scores with disease severity in COVID-19 patients.

***Study Design*:** Cross-sectional study.

***Place and Duration of Study*:** Pak-Emirates Military Hospital, Rawalpindi Pakistan, from Oct to Dec 2021.

***Methodology*:** The study included 173 symptomatic patients with positive COVID polymerase chain reaction. All patients underwent high-resolution computed tomography chest scans and were given severity scores (from 0 to 40) based on the number of lung segments involved. Disease severity was assessed based on oxygen saturation at room air, C-reactive protein levels, and morality on the 21st day. High-resolution chest computed tomography scores were compared with parameters of disease severity.

***Results*:** Out of a total of 173 patients, 139(80%) were male, and 34(20%) were female, with a mean age of 62.79±13.87 years (17-92 years). Chest computed tomography severity scores were positively correlated with C-reactive protein levels and mortality on the 21st day (p<0.001). Oxygen saturation at room air decreased with increased involvement in chest scans.

***Conclusion*:** Our data suggested that high-resolution computed tomography scores are highly correlated with disease severity and patient outcomes, particularly mortality, in Coronavirus patients.

Keywords: COVID-19, Disease Severity, High resolution computed tomography (HRCT) severity score.

How to Cite This Article: *Dar ARA, Qureshi MZA, Aleem M, khan T. Correlation of Disease Severity with High-Resolution Computed Tomography (HRCT) Severity Scores in COVID-19 Patients - A Cross-Sectional Study. Pak Armed Forces Med J 2024; 74(2): 501-505. DOI: https://doi.org/10.51253/pafmj.v74i2.10193*

INTRODUCTION

SARS-COV-2 induces the production of certain inflammatory mediators, including interleukins and cytokines. These inflammatory markers and tissue and endothelial damage cause a hyper-inflammatory and hypercoagulable state, which causes thromboembolism and tissue injury.[1,2] COVID-19 is also hypothesized to cause lymphopenia in acute stages of infection. Both CD4+ and CD8+ lymphocytes are decreased initially. Lymphopenia, thrombocytopenia and raised IL-6 are thought to be independent markers for increased mortality.[3] The severity of infection ranges from asymptomatic in a few individuals to mild, moderate and severe disease in others. Severe manifestations of the disease include pneumonia leading to acute respiratory distress syndrome, sepsis and multi-organ failure. Some life-threatening complications of the disease include pulmonary embolism, myocardial infarction and stroke.[4,5]

Due to the unpredictable nature of coronavirus infection, doctors and patients need to know the severity of the disease to take the necessary steps to treat it.[6] The most commonly used test was Polymerase Chain Reaction (PCR) of virus particles obtained from nasal swabs, but this test had a sensitivity and specificity of 80% and 98-99%, respectively.[7] Other inflammatory markers like interleukin-6(IL-6), C-reactive protein (CRP) levels and D-dimers were used by several institutions as true markers of disease severity.[8,9] High-resolution chest tomography scans (HRCT) have been reported as a highly sensitive investigation for assessing the severity of coronavirus infection. Ground glass opacities (GGOs) on the HRCT chest were reported to be pathognomonic for COVID-19.[10] This study aimed to assess the relationship of High-Resolution chest CT Severity Score with disease severity and mortality in COVID-19 patients.

METHODOLOGY

The cross-sectional study was conducted at the Pak-Emirates Military Hospital, Rawalpindi Pakistan, from October to December 2021, after approval from the Institutional Ethical Board (Letter number A/28/EC/360.2021). The sample size was calculated

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Received: 06 Apr 2023, revision received: 23 Aug 2023; accepted: 29 Aug 2023

using a WHO sample size calculator, taking the reported COVID-19 point prevalence of 6.5% in Pakistan.[9]

Inclusion Criteria: All symptomatic individuals with confirmed positive real-time Reverse Transcriptase-Polymerase Chain Reaction for COVID-19 were included.

Exclusion Criteria: COVID-PCR-negative patients with similar presenting symptoms and patients who had positive COVID-PCR but were asymptomatic were excluded.

One hundred seventy-three symptomatic patients with COVID interstitial pneumonia were included in the study with positive polymerase chain reaction ((PCR) and admitted to the COVID ward. All patients underwent high-resolution chest computed tomography scans in a supine position on the Toshiba Alexian 16-slice computed tomography (CT) scan machine. Consultant radiologists viewed all HRCT chests on a console. Both lungs were divided into 20 regions. Each region was given a score of 0,1 and 2 points depending on the degree of opacification. The CT severity score was 0-40 based on the total score in all 20 lung segments. Disease was categorized as mild (<10), moderate (10-20), severe (20-30) and very severe disease (30-40) based on total CT severity score.

Data was analyzed using Statistical Package for Social Sciences (SPSS) software version 25.0. Quantitative variables were expressed as mean±SD and qualitative variables were expressed as frequency and percentages. Frequencies of CT severity scores were calculated and compared with demographic, laboratory and mortality variables with the help of the Pearson correlation coefficient. At the same time, a *p*-value of ≤0.05 was taken as statistically significant.

RESULTS

Of 173 patients who participated in the study, 139(80%) were male, while 34(20%) were female. Mean age was 63±13 years (interquartile range 17-92 years). The mean day of illness of having coronavirus infection was 8±4 days. 63(37%) patients had hypertension and diabetes mellitus, while 43(25%) had ischemic heart disease. Mean oxygen saturation at room air for males and females were 86±11% and 86±10.4 %, respectively. The mean CT severity score was 25/40.

According to the CT Severity Scoring Index, approximately 60(35%) patients had mild, 53(31%) moderate, 36(21%) severe, and 22(13%) very severe disease (Table). A negative correlation means the longer the illness duration, the lower the oxygen saturation, hence, the more severe the disease (r=-0.145, p<0.001). An inverse correlation between age and oxygen saturation was also found, depicting severe disease in patients in the higher age group (r =−0.131, p<0.001). An inverse correlation was found between CRP levels and oxygen saturation, indicating that patients with lower room air oxygen saturation had higher CRP levels (r=-0.571, p<0.001). Similarly, a negative correlation existed between CTSS and oxygen saturation, indicating higher CT scores resulted in lower oxygen saturation levels and higher mortality (r= -0.551, p<0.001). CRP levels and mortality on the 21st day showed a positive correlation with CT severity scores (r=0.433, p<0.001) as depicted in Figure.

Table: Comparison of HRCT Chest Lung involvement with Parameters of Disease Severity (n=173)

Disease Categories	Lung Involvement on HRCT Scan (%)	Number of Cases n(%)	Oxygen Saturation Levels at Room air (%) Mean±SD	Mean CRP Levels (mg/dL) Mean±SD
Mild	<25%	60(35%)	92.62±5.83	49.29±44.20
Moderate	25-50%	53(31%)	87.28±9.56	91.06±65.93
Severe	50-75%	36(21%)	81.22±11.12	125.07±76.99
Very Severe	>75%	22(13%)	73.41±12.51	154.40±74.26

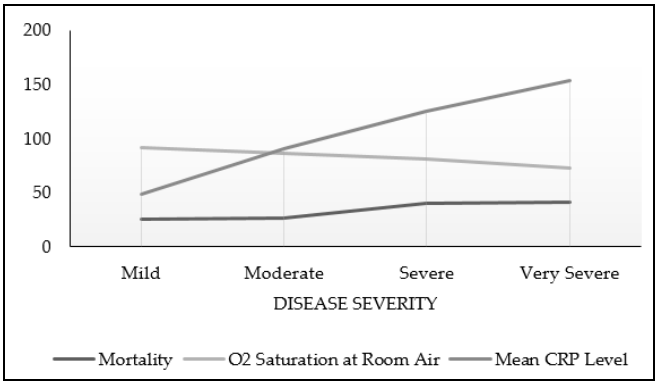

Figure: Comparison of Disease Severity with Oxygen Saturation (%), Mean CRP Levels (mg/dL) and Mortality (%)

DISCUSSION

Our study suggests that High-Resolution Computed Tomography scores significantly correlate

with disease severity. High CT severity scores are correlated with increasing age, raised C-reactive protein levels, lower oxygen saturations and increased mortality in COVID-19 patients. Qi *et al*. [9] found that extensive bilateral ground glass opacities on high-resolution CT scan chests, mostly in the lower lung segments, were the hallmarks of severe COVID-19 pneumonia, as found in our study. This ground glass opacity may be found in other diseases like interstitial lung diseases or viral types of pneumonia. CT severity scoring has emerged as one of the most useful tools for ascertaining disease severity in COVID patients, specifically based on the number of lung segments and their area of involvement. Li *et al*. [10] found its usefulness in its ability to early recognition of severe COVID pneumonia even before the clinical signs or rise in levels of inflammatory markers.

Ameer *et al*. studied disease severity in COVID patients based on symptoms, comorbidities, physical examination, laboratory and imaging workup.[11] It was found that patients who had fever and shortness of breath as their initial symptom developed severe disease later on. Liu *et al*. defined severe disease as patients with oxygen saturations below 90% at room air who required supplemental oxygen, had respiratory distress with a respiratory rate of >30 breaths per minute, signs of shock and raised inflammatory markers.[12] Chen *et al*. described unpredictable disease symptomatology ranging from asymptomatic patients to severe shortness of breath with high-grade fever. However, there was a lack of an authentic prognostic marker to predict disease severity and its possible outcomes precisely.[13] This study found that CT severity scoring was very useful in precisely predicting the disease severity in COVID patients. Moreover, this study also proved that higher scores were associated with prolonged hospital stay and increased mortality. Similar findings were reported by Colombi *et al*., who found a positive relationship between CT severity scores and intensive care unit admissions and death in a cohort of 236 patients.[14] Inoue *et al*. also found a positive correlation between CT severity scores and short-term poor prognosis in COVID patients.[15]

Alshanbari *et al*. showed a positive correlation between age and CT severity scores and the need for supplementary oxygen therapy.[16] Our study also confirmed age as an independent risk factor for all-cause mortality, showing a direct correlation between higher CT severity scores in patients of higher age groups. Several studies have examined the relationship of inflammatory markers with disease severity and mortality in COVID-19 patients. Ali *et al*. proposed a model for disease severity in COVID-19 based on clinical and biochemical markers[17] They found that raised inflammatory makers were highly accurate in predicting disease severity. Our study found similar facts: CT severity scores positively correlated with raised inflammatory markers, leading to increased hospital stay and mortality. Zhang *et al*. looked into different markers of severity and found age, raised ESR, D dimers, IL-6, and reduced leukocyte counts to be directly related to severe disease.[18] They found CRP levels to be the most powerful predictor of severe disease. Similar findings were presented in our study, where CRP levels were determined to be a powerful predictor of disease severity and increased mortality.

Xue *et al*. studied novel biomarkers in predicting disease severity in COVID-19 patients. They found high levels of CRP, raised neutrophil-lymphocyte ratio, and higher derived neutrophil-lymphocyte ratios associated with severe disease.[19] These findings were consistent with the findings of our study, where raised CRP levels were associated with higher CT severity scores and increased hospital stay. Higher CRP values were also positively correlated with higher CT severity scores, increasing age and increased short-term mortality risk. However, CRP levels are a marker of inflammation rather than infection, and they are very useful in predicting disease severity and clinical outcomes in COVID-19 patients with severe disease. The rise in CRP values lagged behind the changes in chest CT scans, making high-resolution CT chests early and reliable predictors of severe COVID disease. Agarwal *et al*. reported the lowest oxygen saturations in patients with severe disease and the highest CT severity score. They also reported increased duration of the non-rebreather mask, non-invasive ventilation, and high-flow nasal cannula in patients with higher scores on high-resolution CT scans (p<0.001).[20] Our study also found the lowest oxygen saturations among patients with greater lung involvement. Hence, it is assumed that the risk of death increases with increasing age, high scores on chest CT scans, high levels of C-reactive protein and lower oxygen saturations at room air, leading to more dependency on supplementary oxygen.

LIMITATIONS OF STUDY

CT scan assessment of the disease severity can be arbitrary. We did not consider variables like lifestyle habits that can affect the results. It is also important to consider the comorbidities that patients self-report. The study did not record the COVID-19 treatment delivered, which may impact mortality and length of hospital stay.

ACKNOWLEDGEMENT

We acknowledge the contributions made by our colleagues Dr Ali Akhtar and Dr Roshan Tahir and our mentor, Prof. Dr Farhan Majeed.

CONCLUSION

Our study suggests that High-Resolution Computed Tomography scores significantly correlate with disease severity. High CT severity scores are correlated with increasing age, raised C-reactive protein levels, lower oxygen saturations and increased mortality in COVID-19 patients. Therefore, high-resolution computed tomography chest scoring can be pivotal in predicting disease severity and possible outcomes in coronavirus-infected patients. CT severity scores can help physicians in the management plan of such patients. However, more studies are required to ascertain the prognostic value of high-resolution chest computed tomography in coronavirus patients.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

ARAD & MZAQ: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

MA & TK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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