

Analysis of Predictive Factors of Post-Covid-19 Associated Pulmonary Fibrosis: A Longitudinal Study

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ABSTRACT

Aim: To assess the predictive factors related to the development and progression of pulmonary fibrosis in the patients who are COVID-19 infected.

Study design: A cross-sectional study

Place and Duration: This study was conducted at Ghulam Muhammad Mahar Medical College hospital Sukkur SMBBMU Larkana Pakistan from March 2021 to March 2022

Methodology: This study included patients admitted due to COVID-19 infection. The Presence of SARS-CoV-2 was confirmed by RT-PCR on the samples collected via nasopharyngeal swabs from suspected patients. CT severity score (CSS) was recorded for all the patients admitted, and their chest CT scans were conducted initially. Chest CT scans were performed during 3 and 6 months follow-up to assess the progression of fibrotic abnormalities.

Results: It was observed that out of 173 patients, male patients were 32.9% and 53.62 years was the mean age of patients. After the first CT follow up i.e., 3 months, pulmonary fibrosis was present in 52% of patients. Out of them, 62 patients had undergone a second CT scan, among which 66.1% patients had exhibited no significant signs of fibrotic findings whereas 33.9% patients had exhibited diminished lung fibrosis.

Conclusion: In half of the COVID-19 patients, lung fibrosis was present and patients having severe pneumonia were more prone to developing pulmonary fibrosis.

Keywords: Pulmonary fibrosis, COVID-19 infection, CT scan

INTRODUCTION

One of the deadly epidemics, the world has encountered is the spread of coronavirus disease 2019 (COVID-19). It is respiratory tract syndrome whose causative agent is severe acute respiratory tract syndrome coronavirus 2 (SARS-CoV-2).¹ The first case was discovered in China in December 2019 which later on spread across the world putting the entire world on pause. It was reported that by 2021 June, there were 180 million active cases and 4 million deaths across the globe.² There were different respiratory symptoms manifested by the patients of COVID-19, severe pneumonia and acute respiratory distress syndrome are the most adverse symptoms.³ It was also observed that in certain cases, tests from the laboratory were negative once the patients have recovered from the disease, however, the symptoms i.e., mild to severe respiratory distress because of the presence of residual sequelae i.e., the presence of pulmonary fibrosis.⁴ Chest computed tomography (CT) scan is an important diagnostic tool for pulmonary fibrosis. It has been observed by CT scans that there is a mild to the severe chance of lung getting involved in the infected individuals.⁵ Different fibrotic consequences are also involved in some patients as in one of a study it was reported that among COVID-19 survivors almost one-third of patients had exhibited different types of fibrotic abnormalities in the CT scans taken during their follow-up of 6 months.⁶

It is important to identify certain risk factors which can cause lung fibrosis in the patients infected by COVID-19 which would help manage pulmonary fibrosis post-COVID-19 by minimizing risk factors and suggesting anti-fibrotic medicines to the patients who are at high risk. The current study includes the prospective assessment of lung fibrotic-like changes along with the exploration of its predictive factors.

METHODOLOGY

The current study, cross-sectional in nature, included patients who were successfully treated for moderate or severe pneumonia caused by COVID-19. Permission was taken from the ethical review committee of the institute. Presence of SARS-CoV-2 was

confirmed by RT-PCR on the samples collected via nasopharyngeal swabs from suspected patients. Chest CT scans were also performed. Pneumonia associated with COVID-19 was classified as moderate when oxygen saturation was more than or equal to 94% but had a lower respiratory disease, whereas severe when it was less than 94%, more than 30 respiratory rate, more than 50% lung infiltration, and the ratio between arterial partial oxygen pressure and inspired oxygen fraction less than 300 as defined by World Health Organization. From the patients' records, their age, gender, and their comorbidities were extracted. The exclusion criteria included individuals whose information regarding their results of RT-PCR, and comorbidities were incomplete or were not willing to take part in the study. CT scans were performed twice during the follow-up of six months. For CT scans, non-enhanced 16 detector-row CT scans were performed. No additional image reconstructions were required. The features of CT imaging included honeycombing, interlobar septal thickening, traction bronchiectasis, and parenchymal bands which were considered fibrotic changes, in which, the presence of interlobar septal thickening, and parenchymal bands were considered as moderate fibrosis, and honeycombing and traction bronchiectasis were considered as severe fibrosis. At the time of admission, the CT severity score (CSS) was calculated for all the patients according to the lung zone involvement. If no zone is involved 0, less than 5% zones are involved 1, on 5-25% involvement 2, 26-50% involvement 3, 51-75% involvement 4, and more than 75% involvement the score is given as 5. Total CSS was calculated by adding all the scores i.e., ranging from 0-25. For statistical analysis SPSS version 22 was used, and a P-value less than 0.05 was considered significant.

RESULTS

The study included 173 patients infected by COVID-19 out of which 33.5% patients were male and 66.4% patients were females. The patients were 18-93 years old and recorded mean age was 53.62 years. Among the symptoms, 78.6% patients exhibited fever, 67.6% patients exhibited chills, 63% patients exhibited dry cough, dyspnea, myalgia, sputum, sore throat, and

headache were observed in 57.2%, 56.1%, 37%, 27.2%, and 18.5% of patients, respectively. The most prevalent comorbidity observed was individuals having cardiovascular diseases, observed in 41.6% of cases. When the initial CT scan of the chest was performed, ground-glass opacity was observed in 78.6% of patients, consolidation was observed in 81.5% of patients, and crazy paving was observed in only 17.9% of patients. The results are described in table number 1.

During follow-up CT scans, pulmonary fibrosis was observed in 52% of patients, in which parenchymal bands were present in 33.5% of patients, interlobular septal thickening was present in 43.4%, honeycombing in 2.3%, and bronchiectasis was observed in 6.4% of patients. Differences among comorbidities, gender, and age were not significant. According to the logistic regression analysis, factors which were associated to post COVID-19 lung fibrosis are described in table number 2.

Severe disease was linked with the increased risk of having pulmonary fibrosis at follow-up, similarly, patients having consolidation at the time of the initial CT scan were also at high risk. It was also observed that patients having pulmonary fibrosis had higher CSS than those patients who didn't have it. The median number of CSS was 19. Once the fibrosis was characterized as moderate and severe, it was identified that 13.6% of patients had severe fibrosis. It was observed that after the first follow-up, 68% of patients had undergone a chest CT scan in the second follow-up after 6 months and it was found that the findings remained the same in 66.1% of patients whereas they got severe in 15 patients. Similarly, it was not present in 33.9% of patients. No patient reported progressive signs of fibrotic abnormalities.

Table 1: Initial CT findings and basic demographic features

Variables	Without lung fibrosis	With lung fibrosis	p-value
Mean age in years	52.51	54.66	0.3
Male	27.7%	37.8%	0.15
Cardiovascular diseases	44.6%	38.9%	0.44
Asthma	4.8%	12%	0.083
Severe disease	41%	65.6%	0.001
Diabetes	18.1%	13.3%	0.391
Ground glass	81.9%	75.6%	0.307
Crazy paving	16.9%	18.9%	0.729
Consolidation	72.3%	90%	0.003
Median CT severity score	18 (14-21)	21 (15-23)	0.002

Table 2: Associated factors of COVID-19 lung fibrosis according to logistic regression analysis

Variables	Odds ratio with 95% confidence interval	p-value
Severe disease	2.74	0.001
Moderate disease	1	
Consolidation present	3.45	0.003
Consolidation absent	1	
CT severity score	1.10	0.008

DISCUSSION

The current study investigated the progression of pulmonary fibrosis in COVID-19 patients during their 3 and 6 months follow-ups. Almost 50% of cases exhibited fibrotic changes that progressed towards abnormalities during their 3 months follow-up, among which almost 13.6% of individuals exhibited severe fibrosis. Among 62 patients who had undergone chest CT scans after their 6 months follow-up, 41 patients had their lung fibrosis remain unchanged whereas in 21 of patients it was almost suppressed. In a study conducted by Han et al, 35% of patients had reported fibrotic abnormalities after 6 months.⁷ Another study reported pulmonary fibrosis after 3 months of follow-up in 32% of patients

which was also comparatively less than the ones we identified.⁸ It was also observed that patients having consolidation and higher CSS initially had a high risk of developing COVID-19-associated pulmonary fibrosis. It was also identified that patients having severe COVID-19 pneumonia had an increased risk of lung damage due to fibrosis. A study conducted by Ali et al, reported that cigarette smoking, older age, long-term mechanical ventilation and high CSS had an increased risk of fibrosis. These factors were also similar in Han et al, study as well. However, the actual cause of pulmonary fibrosis after getting infected by COVID-19 is still unclear. There is no definitive study which suggested the use of antifibrotic drugs to prevent lung fibrosis post-COVID-19 infection. Although, there are some drugs which are able to decrease the pulmonary damage in patients who are at high risk. As it is quite evident that developing lung fibrosis is an important adverse outcome in patients who had COVID-19, it is important to make the use of anti-fibrotic drugs common particularly in individuals who are at high risk. It is suggested that studies must be conducted to study the progression of pulmonary fibrosis in longer follow-ups whereas studies with larger sample sizes must also be conducted in future to have a proper understanding.

CONCLUSION

As suggested by the results, almost half patients had reported the pulmonary fibrosis as a post-COVID-19 complication. Patients who were severely infected were more prone to developing pulmonary fibrosis. Along with that, consolidation and a higher CSS in the initial scan had predicted the development of pulmonary fibrosis. Some of the individuals had reported diminished fibrotic abnormalities after their 6 monthly follow-ups. Identification and controlling the predictive factors is important to reduce and prevent lung fibrosis which is an adverse outcome of COVID-19 pneumonia.

Ethical consideration: The study was ethically approved by the institute.

Conflict of interest: None

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