

Pulmonary Fibrosis on High resolution Computed Tomography (HRCT) in Post Covid Patients

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Covid Patients

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ABSTRACT

Objective: To detect people who may develop lung fibrosis early, allowing for the early administration of anti-fibrotic medications, which will not only benefit the infected patients with timely effective disease management, but will also ensure appropriate use of medical resources for this purpose.

Study Design: Descriptive case series study

Place and Duration of Study: This study was conducted at the Department of Radiology, Sharif Medical City Hospital, Lahore for one year from September 2020 to August 2021.

Materials and Methods: This study was conducted after the approval of the ethical review board. Cases of Covid-19 were included as per inclusion criteria using non-probability, consecutive sampling.

Results: Among the patients included in the study, 171 (45.6%) were male and 204 (54.4%) were females. Majority of the patients were of age group more than 50 years. The frequency of pulmonary fibrosis in our study population was 27.5% (103) with degree of pulmonary involvement: mild in 21 (20%), moderate in 39 patients (37.9%) and severe involvement in 43 of 103 patients (41.7%). Data was stratified for various effect modifiers including age ($p=0.19$), gender ($p=0.01$), socioeconomic status ($p=0.002$), BMI ($p=0.11$), history of chronic illness ($p<0.00001$), degree of pulmonary involvement ($p=0.01$) and history of steroid use ($p<0.00001$).

Conclusion: The aim of this study was to detect people who may develop lung fibrosis early, allowing for the early administration of anti-fibrotic medications. Along with determination of disease severity using HRCT severity scoring, which will not only benefit the infected patients with timely effective disease management, but will also ensure appropriate use of medical resources for this purpose. Side by side our study will guide the medical and government authorities to take suitable steps for the local population depending upon the lethality of disease in the second wave. This study will also able to identify the population at risk of developing fibrosis.

Key Words: Covid-19, HRCT, Pulmonary fibrosis

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INTRODUCTION

Covid-19 has been labeled a worldwide medical emergency, impacting practically the whole world, including Pakistan. In March 2020, WHO declared it a pandemic.¹

Although Covid-19 can affect any of the body organs, pulmonary involvement has been identified as a main cause of morbidity and mortality in effected individuals.² HRCT Chest CT plays a key role in the diagnosis of pulmonary disease in infected patients and also helps in determining the disease severity based on

the proportion of pulmonary involvement.³ Radiological Society of North America Consensus statement has described ground-glass opacities with or without consolidation in a peripheral, posterior, and diffuse or lower lung zone distribution as typical CT finding of Covid-19 Pneumonia.⁴

COVID-19 pulmonary pneumonia can result in progressive fibrotic lung disease. The long-term lung alterations caused by post COVID-19 infection are yet unknown and should be investigated further.

The goal of this study was to detect people who may develop lung fibrosis early, allowing for the early administration of anti-fibrotic medications. Along with determination of disease severity using HRCT severity scoring, which will not only benefit the infected patients with timely effective disease management, but will also ensure appropriate use of medical resources for this purpose. Side by side our study will guide the medical and government authorities to take suitable steps for the local population depending upon the lethality of disease in the second wave.

MATERIALS AND METHODS

This study conducted at the Department of Radiology, Sharif Medical City Hospital, Lahore during September

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2020 to August 2021 after the approval from ethical review board. Sampling was done using non-probability, consecutive sampling. Primary Objective of the study was to determine the frequency of pulmonary fibrosis among the patients with history of COVID-19. Secondary objective was to determine the degree of pulmonary involvement in suspected and diagnosed cases of COVID-19 patients during the second wave of pandemic by using HRCT.

All patients, regardless of gender or age group, who had positive CT chest findings of COVID-19 verified by PCR test were enrolled in the research and were monitored for 4 weeks following discharge. Following the negative PCR result, a follow-up HRCT chest was performed to examine the degree of healing and remaining fibrotic changes. All pregnant women, patients with significant respiratory motion abnormalities on CT images, and patients with a history of chronic interstitial lung disease were excluded from the research.

Sample size of 375 was calculated using WHO sample size calculator, and taking expected pulmonary fibrosis among the patients with history of COVID-19: $P = 31.2\%$ with confidence level of 95% and absolute precision of 5%.

HRCT – High resolution CT scan of the chest was done to determine the presence of disease and its complications like pulmonary fibrosis. HRCT is a sampling tool that combines 1 to 2mm thin slices with high spatial frequency algorithm to generate exquisite lung details. Severity of the pulmonary involvement was accessed using the 25-point CT severity scoring for COVID 19 using HRCT. (Table no. 1)

After approval from Institutional Review Board, all the patients fulfilling the inclusion criteria who presented to the Radiology department of Sharif Medical City Hospital for HRCT Chest were selected.

The study included all patients of either gender or age group who had positive CT chest findings of COVID-19 verified by a PCR test. The COVID severity score was generated using a 25-point CT grading system, and patients were classified as having mild, moderate or severe illness. Patients were monitored for four weeks following discharge. Following a negative PCR result, a follow-up HRCT chest was performed to examine the degree of healing and remaining pulmonary fibrosis. HRCT was performed using Toshiba Aquilion 16 slicer CT with the patient in prone position. HRCT images were collected and assessed by two experienced radiologist for the presence or absence of pulmonary fibrosis.

Collected data was analyzed by using SPSS 24.0. Data was stratified in age groups, gender and socioeconomic status. Mean and standard deviation was calculated for age. Frequency and percentage was calculated for gender, history of chronic illness, CT severity score category i.e. mild, moderate and severe, and presence of

pulmonary fibrosis on follow-up. Chi square test was used to compare the CT severity score with age, gender, socioeconomic status and presence or absence of chronic illness in patients. Student T- test was used to compare CT severity score among the different age groups and gender. $P < 0.05$ to be statistically significant.

RESULTS

In this study the primary objective was to determine the frequency of pulmonary fibrosis among the patients with history of COVID-19. Secondary objective was to determine the degree of pulmonary involvement in suspected and diagnosed cases of COVID-19 patients.

Among the patients included in the study, 171 (45.6%) were male and 204 (54.4%) were females. Majority of the patients were of age group > 50 years. Details of the patients in various age groups are shown in the table 2. Other demographic details of the patients including socioeconomic status, BMI and history of various chronic co-morbidities are also shown in the table 2. The frequency of pulmonary fibrosis among the COVID 19 affected patients in our study population was 27.5% (103) with degree of pulmonary involvement: mild in 21 (20%), moderate in 39 patients (37.9%) and severe involvement in 43 of 103 patients (41.7%).

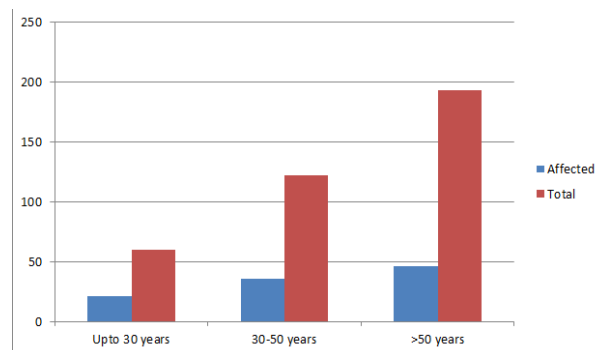
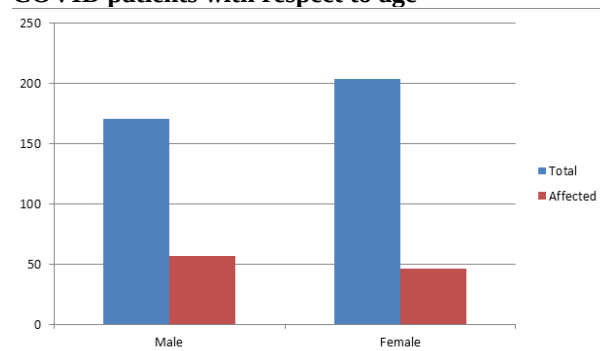
Data was stratified for various effect modifiers including age, gender, socioeconomic status, BMI, history of chronic illness, degree of pulmonary involvement and history of steroid use. The difference of incidence of pulmonary fibrosis was significant for gender, socioeconomic status, history of chronic illness and history of steroid use. Post stratification chi square p-value was significant. (Table no. 2)

Table No.1: Table showing 25-Point CT severity scoring for COVID 19 using HRCT

25-Point CT severity Score:	
Objective visual assessment by two observers of each lung lobe for the degree of involvement and classified as:	
0 or $<5\%$ involvement-score of 0	0
5–25%	1
26–50%	2
51–75%	3
$>76\%$ score	4
Total severity score will be then calculated by summing scores of all five lobes scores ranging from 0–25	
Total score:	Severity
7 or less	Mild
8-17	Moderate
18 or more	Severe

Table 1: showing the details of various outcome variables of the COVID - 19 patients

Variables		Pulmonary fibrosis		P value
		Yes	No	
Age	Upto 30 yrs	21	39	0.19
	30-50 years	36	86	
	>50 years	46	147	
Gender	Male	57	114	0.01
	Female	46	158	
Socioeconomic status	Poor class	35	67	0.002
	Middle Class	39	75	
	Upper Class	29	130	
BMI	Underweight	19	53	0.11
	Normal weight	22	74	
	Over weight	39	69	
	Obese	23	76	
History of chronic illness	DM	67	184	<0.00001
	HTN	84	160	
	IHD	95	27	
	CLD	88	36	
	CKD	97	30	
Degree of pulmonary involvement	Mild	21	89	0.01
	Moderate	39	107	
	Severe	43	76	
History of steroid use	Yes	24	233	<0.00001
	No	79	39	

**Figure No.1: incidence of pulmonary fibrosis in COVID patients with respect to age****Figure No.2: Comparing the pulmonary fibrosis among males and females COVID patients**

DISCUSSION

According to a report of WHO, around 80% of COVID-19 patients had mild infection, 14% had severe, while only 6% died. Acute respiratory distress syndrome patients can develop pulmonary fibrosis after few weeks of recovery.⁵

The occurrence of pulmonary fibrosis is determined by the intensity of COVID infection. Many theories have been offered as probable causes of post-COVID pulmonary fibrosis, including cytokine storm, which is caused by an abnormal immune system and contributes to the development of pulmonary fibrosis. The presence of residual pulmonary fibrosis in COVID-19 survivors after discharge is determined by a variety of parameters, including the patient's age, CT severity, consolidation/crazy-paving scores, and ICU stay.⁶

We investigated the progression of lung parenchymal alterations including lung fibrosis in this work. A total of 375 individuals were enrolled and observed for three months after recovering from COVID-19 pneumonia. As previously stated, almost one-fourth of the overall patients displayed indications of fibrotic abnormalities, with 41 percent having severe fibrosis. The current study was to the best of our knowledge, the first report of post-COVID-19 pulmonary fibrosis in our region. Various studies have referenced to COVID-19 symptoms over time; however, only a small number of studies have focused on lung fibrosis as the primary outcome.

In our study, pulmonary fibrosis after COVID-19 was strongly linked to patients aged 50 to 75, with a somewhat greater frequency in the middle age group. Post-pulmonary fibrosis was found to be substantially more common in patients with a history of co-morbid illnesses. According to Wong et al., elderly persons are more likely to acquire pulmonary fibrosis.⁷

A study reported that in the mild group of disease only 7 of 38 patients (18.4%) developed fibrosis whereas in the severe group pulmonary fibrosis was seen in 18 of 42 patients (42.8%), with overall incidence of pulmonary fibrosis of 25 in 80 patients (31.2%) Ali RMM, et al.⁷ Yasin R, et al reported that out of 210 patients enrolled and followed, 101 patients (48.1%) showed pulmonary fibrosis on follow-up CT.⁸ Evidence of pulmonary fibrosis was seen in 90 individuals after a 3-month CT scan (52.0 percent). Consolidation, severe illness, and a higher CT severity score at admission were all linked to a greater probability of fibrotic abnormalities seen on a 3-month CT scan. After a 6-month follow-up, 41 patients (66.1%) exhibited no significant changes in their fibrotic results, whereas the remaining 21 patients (33.9%) showed considerably decreased lung fibrosis.⁹

In the research by Han et al,¹⁰ after 6 months of follow-up, fibrotic abnormalities were found in 35% of the patients, which was lower than our results.

Furthermore, following a 3-month follow-up, Ali et al. observed a rate of 32 percent for pulmonary fibrosis in COVID-19 patients, which was lower than what we discovered in our experiment. Changes in the research population, paraclinical measures and monitoring by technicians and clinicians might all explain the differences.

George PM, et al was of the opinion that there is currently no agreement on the use of anti-fibrotic medications in the prevention and treatment of COVID-19 survivors' lung fibrosis. These medicines, which are already used for interstitial lung disorders, can reduce pulmonary damage in high-risk individuals. Given that lung fibrosis is recognized as a significant adverse event in COVID-19 survivors, it is advised that a consensus be reached on including anti-fibrotic medications into the COVID-19 treatment recommendations, particularly for high-risk patients.

According to Ali et al., older age, cigarette smoking, greater CT severity score, and long-term mechanical ventilation were all connected to an increased risk of lung fibrosis.

Han X, et al reported after six-month follow-up, that 6% patients had dry cough, 10% sputum production 14% slight shortness of breath on exertion. Patients with pulmonary fibrosis more commonly experienced dry cough ($p < 0.05$). In this study, 35% patients of severe COVID-19 pneumonia developed pulmonary fibrosis within 6 months follow-up. Among these 40 of 114 patients with severe COVID-19 pneumonia, fibrosis in the lungs was seen in 55% (22/40) patients within 6 months follow-up.

Early detection of cases of post-COVID-19 pulmonary fibrosis may enable for the prevention or at least reduction of this debilitating complication.¹¹

CONCLUSION

About 1/4 of the survivors had post-COVID-19 pulmonary fibrosis. Patients with severe COVID-19 pneumonia were also at a greater risk of developing pulmonary fibrosis. Furthermore, co-morbid conditions like old age and history of Covid treatment without steroids were linked to an elevated risk of post-COVID pulmonary fibrosis. Further follow-up of the patients should be done.

Author's Contribution:

Concept & Design of Study:	Rafia Irum
Drafting:	Aneesa Qayyum
Data Analysis:	Aisha Asghar
Revisiting Critically:	Rafia Irum, Aneesa Qayyum
Final Approval of version:	Rafia Irum

Conflict of Interest: The study has no conflict of interest to declare by any author.

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