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Clinical Outcomes and Risk Factors of Post-Covid Pulmonary Fibrosis in Hospitalized Patients

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ABSTRACT

Background: Post-COVID pulmonary fibrosis is an important long-term respiratory complication among patients recovering from moderate-to-severe COVID-19, particularly those requiring hospitalization. Persistent fibrotic changes may lead to chronic dyspnea, impaired pulmonary function, oxygen dependency, and reduced quality of life. Identification of high-risk patients is essential for timely follow-up and intervention.

Objective: To evaluate the clinical outcomes and risk factors associated with post-COVID pulmonary fibrosis among hospitalized patients.

Methodology: This retrospective observational study was conducted at the Department of Medicine, Liaquat University of Medical & Health Sciences, Jamshoro, from August 2024 to July 2025. A total of 212 adult patients previously hospitalized with RT-PCR-confirmed COVID-19 infection were included through consecutive non-probability sampling. Patients with follow-up high-resolution computed tomography chest performed at least 12 weeks after recovery were included. Data were analyzed using SPSS version 26.0.

Results: Post-COVID pulmonary fibrosis was identified in 49 patients, giving a prevalence of 23.1%. Patients with fibrosis were significantly older than those without fibrosis (59.8 ± 12.6 vs 50.7 ± 13.2 years, p=0.0003). Multivariable regression identified advanced age, smoking history, ICU admission, and mechanical ventilation as independent predictors.Conclusion: Post-COVID pulmonary fibrosis affected nearly one-quarter of hospitalized COVID-19 survivors and was associated with severe acute illness and poorer respiratory outcomes.

Keywords: COVID-19; Pulmonary Fibrosis; Post-COVID Syndrome; HRCT Chest; Risk Factors

Introduction

Coronavirus disease 2019 (COVID-19) pandemic has put an unprecedented strain on health systems throughout the world, creating a substantial population of survivors with persistent respiratory sequelae.[1] Most patients make an entirely normal recovery, but a substantial number of hospitalized patients have long term pulmonary complications such as persistent radiologic abnormalities, decreased lung function and pulmonary fibrosis. Pulmonary fibrosis is a serious complication following COVD-19, known as Post-COVID pulmonary fibrosis (PCPF), which is a fibrotic remodeling of lung parenchyma that may lead to chronic respiratory disability and reduced quality of life. Recent research indicates that fibrotic lung damage can occur months after acute infection and is more common in those who were hospitalized or on an intensive care unit for severe disease.[2,3]

Pulmonary fibrosis after COVID-19 is thought to be due to an overactive inflammatory response, diffuse alveolar damage, cytokine storm, endothelial dysfunction, and abnormal wound healing mechanisms that occur during acute severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection.[4] In some patients, excessiveness of fibroblasts activation and ECM deposition can result in permanent structural injury and dysfunction of gas exchange, similar to fibrotic interstitial lung diseases. Those with severe pneumonia, long duration of mechanical ventilation (MV) and acute respiratory distress syndrome (ARDS) seem to be at risk of fibrotic complications.[5,6]

Patients hospitalized with COVID-19 are a high-risk subpopulation as they have higher levels of inflammation, longer oxygen use, and higher levels of disease severity. Some studies performed in the post COVID world have found that advanced age, male gender, smoking history, obesity, diabetes mellitus, hypertension, high inflammatory biomarkers, intensive care admission and hospitalisation were potential risk factors for fibrosis.[7] Other high resolution computed tomography (HRCT) features associated with poor pulmonary outcome are ground glass opacities, reticulations, traction / bronchiectasis, and parenchymal bands. Incidence and determinants of post-COVID pulmonary fibrosis, however, are strikingly different between populations, perhaps reflecting differences in study designs and follow-up duration and patient characteristics.[8]

Post-COVID pulmonary fibrosis can have significant clinical manifestations, including exertional dyspnea, chronic cough, and persistent hypoxia and decreased pulmonary function.[9] These complications can have a negative impact on physical functioning, mental health and health service utilization. Despite increasing recognition of the condition, substantial uncertainty remains regarding its natural course, predictors, and long-term clinical outcomes, particularly in low- and middle-income countries where local epidemiological data remain scarce. It is therefore essential to know the burden and determinants of pulmonary fibrosis after hospitalisation for COVID-19 survivors so that they can be risk-stratified, followed-up and treated in time.

The purpose of this study is to assess the clinical outcomes and to identify risk factors among the hospitalized COVID patients for development of post-COVID pulmonary fibrosis to provide local evidence for timely recognition and management of this emerging post-COVID complication.

Objective

To evaluate the clinical outcomes and risk factors associated with post-COVID pulmonary fibrosis among hospitalized patients.

Materials And Methods

This is a retrospective observational study carried out in the Department of Medicine, Liaquat University of Medical & Health Sciences from August 2024 to July 2025. This study was designed to assess the clinical outcomes and identify risk factors of hospital-based PF in COVID-19 patients with confirmed disease. Ethical approval was given by the institutional ethical review committee before the study commencement.

A minimum sample size of 212 patients was calculated using the WHO sample size calculator from an expected prevalence of 18% for post-COVID pulmonary fibrosis, based on recent published literature,[10] a 95% confidence level and a margin of error of 5.2%. Thus, 212 hospitalized post-COVID patients who met the inclusion criteria were selected for this study using consecutive non-probability sampling.

The study included patients with documented history of hospitalization as a result of RT-PCR confirmed COVID-19 infection with available follow-up records, including chest HRCT imaging at least 12 weeks after recovery. To minimize confounding, patients with existing interstitial lung disease, pulmonary fibrosis before COVID-19 infection, active pulmonary tuberculosis, connective tissue disorders with lung fibrosis, chronic occupational lung diseases, lung malignancy, or incomplete medical records were excluded.

Data were retrieved from hospital medical records, radiological archives, and outpatient follow-up files using a structured proforma. Demographic factors such as gender, age, body mass index, smoking habits and comorbidities including diabetes mellitus, hypertension, ischemic heart disease, chronic obstructive pulmonary disease and chronic kidney disease were documented. Other clinical data such as length of hospitalisation, admission to intensive care unit, need for oxygen

supplementation or mechanical ventilation, inflammatory markers, and severity of acute COVID-19 disease were also recorded. Persistent fibrotic changes on HRCT chest scan performed by consultant radiologists and pulmonologists were the criteria used to diagnose post-COVID pulmonary fibrosis, which included reticulations, traction bronchiectasis, architectural distortion, parenchymal bands and fibrotic opacities. During follow-up, the clinical outcomes of persistent dyspnea, cough, oxygen dependency, rehospitalization, and pulmonary function abnormalities were evaluated.

The Statistical Package for Social Sciences (SPSS) version 26.0 was used to enter and analyze the data. Data for quantitative variables were reported as mean + SD and data for qualitative variables as frequencies and percentages. Independent t-test and chi-square test were used for the comparison of variables between pulmonary fibrosis and nonpulmonary fibrosis patients. A binary logistic regression analysis was conducted to determine independent risk factors associated with Post-COVID pulmonary fibrosis. The p value<0.05 was deemed as statistically significant.

Results

A total of 212 hospitalized post-COVID patients fulfilling the inclusion criteria were included in the final analysis. The mean age of the study population was 52.8 ± 13.7 years, with a predominance of males (126, 59.4%) over females (86, 40.6%). Post-COVID pulmonary fibrosis was identified in 49 patients (23.1%), while 163 patients (76.9%) showed no evidence of fibrosis on follow-up HRCT chest. Patients who developed pulmonary fibrosis were significantly older than those without fibrosis (59.8 ± 12.6 vs 50.7 ± 13.2 years, p=0.0003). Male gender, smoking history, obesity, and presence of diabetes mellitus were observed more frequently among patients with pulmonary fibrosis Table 1.

Patients with post-COVID pulmonary fibrosis experienced significantly more severe acute illness during hospitalization. The fibrosis group had longer hospital stays (12.9 ± 4.8 vs 7.2 ± 3.5 days, p=0.0001), greater intensive care unit (ICU) admission rates (42.9% vs 14.1%, p=0.0002), and a higher requirement for mechanical ventilation (26.5% vs 6.7%, p=0.0004). Inflammatory biomarkers, including C-reactive protein (CRP) and serum ferritin, were significantly elevated in the fibrosis group compared with non-fibrosis patients Table 2.

During follow-up, patients with pulmonary fibrosis demonstrated significantly poorer clinical outcomes compared to those without fibrosis. Persistent dyspnea (71.4% vs 24.5%, p=0.0001), chronic cough (44.9% vs 17.2%, p=0.0003), oxygen dependency (26.5% vs 4.9%, p=0.0002), and pulmonary function abnormalities (63.3% vs 19.0%, p=0.0001) were markedly more common among fibrotic patients. Rehospitalization within six months was also significantly higher in the fibrosis group (18.4% vs 6.1%, p=0.011) Table 3.

Binary logistic regression analysis identified advanced age (OR=1.08, 95% CI: 1.03–1.12, p=0.001), smoking history (OR=2.41, 95% CI: 1.18–4.89, p=0.015), ICU admission (OR=3.16, 95% CI: 1.52–6.57, p=0.002), and mechanical ventilation (OR=2.87, 95% CI: 1.19–6.93, p=0.019) as independent predictors of post-COVID pulmonary fibrosis Table 4.

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants According to Presence of Post-COVID Pulmonary Fibrosis (n=212)

Variable	Fibrosis (n=49)	No Fibrosis (n=163)	p-value
Age (years), Mean ± SD	59.8 ± 12.6	50.7 ± 13.2	0.0003
Male Gender, n (%)	34 (69.4)	92 (56.4)	0.041
Smoking History, n (%)	21 (42.9)	37 (22.7)	0.007
BMI ≥30 kg/m², n (%)	18 (36.7)	34 (20.9)	0.028
Diabetes Mellitus, n (%)	27 (55.1)	58 (35.6)	0.015
Hypertension, n (%)	24 (49.0)	63 (38.7)	0.189
COPD, n (%)	8 (16.3)	14 (8.6)	0.118
Ischemic Heart Disease, n (%)	9 (18.4)	20 (12.3)	0.279

Table 2. Acute COVID-19 Clinical Severity and Hospitalization Characteristics

Variable	Fibrosis (n=49)	No Fibrosis (n=163)	p-value
Hospital Stay (days), Mean ± SD	12.9 ± 4.8	7.2 ± 3.5	0.0001
ICU Admission, n (%)	21 (42.9)	23 (14.1)	0.0002
Mechanical Ventilation, n (%)	13 (26.5)	11 (6.7)	0.0004
Severe/Critical COVID-19, n (%)	33 (67.3)	49 (30.1)	0.0001
Oxygen Requirement, n (%)	39 (79.6)	78 (47.9)	0.0002
CRP (mg/L), Mean ± SD	74.5 ± 28.2	46.1 ± 22.8	0.0001
Ferritin (ng/mL), Mean ± SD	628.4 ± 196.3	394.7 ± 171.5	0.0001

Discussion

The burden of post-COVID pulmonary fibrosis in the present study was found to be high with 23.1% of hospitalized patients having pulmonary fibrosis after COVID-19 infection. This is similar to recent literature reporting ongoing fibrotic abnormalities in hospitalized COVID-19 survivors with moderate to severe disease [11]. The relatively low prevalence seen in this study could be attributed to variations in severity, ethnicity, time of radiological assessment, vaccination and inclusion criteria. Importantly, fibrosis assessment in our study was performed at least 12 weeks after recovery and thus the possibility of transient inflammatory infiltrates being misclassified as fibrosis was minimised.

In our study, advanced age was identified as a significant risk factor for pulmonary fibrosis, with mean age being significantly higher in patients with pulmonary fibrosis compared to those without pulmonary fibrosis. The correlation between age and persistent fibrotic changes following COVID-19 infection was also reported by Abdelrafie et al.[12] The older age may be due to the decrease in regenerative capacity of the alveoli, immunosenescence, and hyperactive inflammatory response of elderly patients that lead to fibrotic remodeling and fibrosis. Further, older patients are more likely to present with co-morbid conditions and more likely to become severely ill and require long hospital stays, thus increasing the risk of irreversible damage to the lungs.[13]

In our study, smoking history also was an independent risk factor for fibrosis. The observation is consistent with recent literature indicating that smokers are also at higher risk for more severe lung damage following COVID-19, which may be caused by chronic tobacco exposure leading to oxidative stress, epithelial injury, endothelial dysfunction and dysregulated immune responses that make the lung tissue more susceptible to COVID-19 fibrogenesis.[14] Multiple studies, however have shown less correlation, perhaps due to variations in smoking habits, frequency of pre-existing lung disease and regional population factors.[15,16]

The present study also showed significant association between disease severity parameters such as ICU admission, length of hospitalisation, requirement of oxygen and mechanical ventilation with post-COVID

Table 3. Clinical Outcomes During Follow-up

Variable	Fibrosis (n=49)	No Fibrosis (n=163)	p-value
Persistent Dyspnea, n (%)	35 (71.4)	40 (24.5)	0.0001
Chronic Cough, n (%)	22 (44.9)	28 (17.2)	0.0003
Oxygen Dependency, n (%)	13 (26.5)	8 (4.9)	0.0002
Pulmonary Function Abnormality, n (%)	31 (63.3)	31 (19.0)	0.0001
Rehospitalization, n (%)	9 (18.4)	10 (6.1)	0.011

Table 4. Multivariable Logistic Regression Analysis for Risk Factors Associated with Post-COVID Pulmonary Fibrosis

Variable	Adjusted OR	95% CI	p-value
Age	1.08	1.03–1.12	0.001
Smoking History	2.41	1.18–4.89	0.015
Diabetes Mellitus	1.63	0.82–3.22	0.161
ICU Admission	3.16	1.52–6.57	0.002
Mechanical Ventilation	2.87	1.19–6.93	0.019
Severe/Critical COVID-19	1.94	0.97–3.89	0.061

fibrosis. Diffuse alveolar damage, cytokine storm, and ventilator-associated lung injury are common complications in severe acute disease, which is also known to significantly contribute to higher likelihood of long-term pulmonary complications, as reported previously.[17,18] Mechanical ventilation, especially in those with acute respiratory distress syndrome (ARDS), can worsen structural lung damage from barotrauma and volutrauma.

In our study CRP and ferritin were significantly higher in fibrotic patients and suggest a role for persistent systemic inflammation in the development of pulmonary fibrosis. This is similar to recent studies that show that inflammatory biomarkers are associated with ongoing radiological abnormalities and decreased pulmonary function, which can lead to permanent architectural distortion of the pulmonary parenchyma.[19,20]

As far as clinical results were concerned, patients with PF had significantly worse respiratory recovery, such as continued dyspnea, chronic cough, need for oxygen, pulmonary function abnormalities, and re-hospitalisation rates. These findings are similar to the longitudinal studies showing that chronic respiratory symptoms remain in a significant number of post-COVID fibrosis survivors, and indicating the need for long-term follow-up and pulmonary rehabilitation plans.[21,22]

In general, the results of this study support the accumulating evidence that severe acute disease, mechanical ventilation, intensive care unit (ICU) admission, and advanced age are significantly associated with post-COVID pulmonary fibrosis, as are smoking and increased inflammatory burden. The results were generally similar to those found in the international literature, but the differences could be due to patient demographics, the healthcare system, disease severity and/or the timing of radiological assessment. Importantly, this study provides valuable local evidence from Pakistan where there is limited data on pulmonary fibrosis after COVID infection and highlights the importance of early risk stratification and structured follow-up of the respiratory function after COVID infection.

The present study has certain limitations that should be acknowledged. The results of this single center retrospective study performed in a tertiary care hospital might not be generalizable to other health care centers and other populations. Selection bias and information bias from the relatively small sample size and reliance on medical records may have resulted in some clinical variables being inadequately documented. Furthermore, serial follow-up imaging and pulmonary function testing beyond the conclusion of the study were not performed in all patients and were not available for assessing the progression and/or reversibility of fibrotic changes over time. The present study, despite its limitations, offers local evidence on burden and predictors of post-COVID pulmonary fibrosis among hospitalized patients in Pakistan.

Conclusion

Post-COVID pulmonary fibrosis was seen in nearly 25% of hospitalized COVID-19 survivors, and it was strongly associated with increased inflammatory burden, severe illness, mechanical ventilation, ICU admission, advanced age, and smoking history. Patients with fibrosis had worse respiratory function, such as chronic cough, persistent dyspnea, oxygen dependency, and abnormalities in pulmonary function. Initiated prompt intervention and structured post-COVID respiratory follow-up may help identify high-risk patients early and help ensure optimal long-term clinical outcomes.

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