

## Evaluating the Long-Term Pulmonary Effects of Post-COVID-19 Syndrome: A Multicenter Prospective Study

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### ABSTRACT:

**Background:** The COVID-19 pandemic that spread worldwide has left a substantial part of the cured population with post-sickness symptoms that have come to be known under the terms post-COVID-19 syndrome or long COVID. Among them, chronic respiratory complications were recurrently reported. Nevertheless, the longevity of the pulmonary impact of COVID-19 was still poorly comprehended, particularly in low-resource health care.

**Objective:** The paper was meant to assess the long-term pulmonary sequelae in patients who recovered of having COVID-19, with particular references to hypoxemia during physical exercise and persistent respiratory symptoms, radiological alterations, and impairment of functional pulmonary.

**Methods:** This is an observational study in terms of prospective design carried out by the researchers in a multicentric study in Timergara Teaching Hospital, Khyber Pakhtunkhwa (KPK). One hundred and ten participants, who had recovered after testing positive to COVID-19, were enrolled. The participants were observed during a 12-month course and assessed using clinical assessments, high-resolution computed tomography (HRCT) of the chest, spirometry, and diffusion capacity tests. The demographic, comorbidity, COVID-19 severity, and oxygen dependence data were sources of information that were analyzed and later used to correlate the clinical profiles to the long-term outcomes.

**Results:** Of all 110 participants surveyed, 68 (61.8%) maintained coughs, dyspnea, and chest tightness more than three months after recovery. Fibertic-like alterations found by HRCT were observed in 33 patients (30%), and the restrictive pattern was revealed by spirometry in 28 patients (25.5%) as well as mixed pattern in 12 (10.9%). Twenty-six people (23.6%) had reduced diffusion capacity. Longitudinal pulmonary impairments were much more likely to develop among patients who previously experienced COVID-19 moderate to severe symptoms forcing hospitalization and additional oxygen administration ( $p < 0.01$ ).

**Conclusion:** The study confirmed that a considerable part of post-COVID-19 patients had sustained lung abnormalities such as the morphological and functional impairment of the lungs. The results underscored the importance of the long-term respiratory follow-up and rehabilitation programs particularly in the affected persons with severe primary infections.

**Keywords:** Post-COVID-19 syndrome, long COVID, pulmonary function, HRCT, respiratory sequelae, spirometry, lung fibrosis, Timergara Teaching Hospital

### **INTRODUCTION:**

The world epidemic of the coronavirus disease 2019 (COVID-19 or, in other words, the severe acute respiratory syndrome coronavirus 2 or SARS-CoV-2) had radically changed the situation in global health. COVID-19 appeared as a severe respiratory infection but with time, it demonstrated multi-systemic effects as it influenced both acutely and chronically numerous organ systems [1]. The pulmonary complications that were found in a great number of people long after the acute course of the disease was overcome constituted one of the most significant of these long-term effects. Such persistence of symptomatology, also known as post-COVID-19 syndrome or long COVID played out as a clinical challenge that required exhaustive research, especially on the area of respiratory capacity, which is the most prevalently impacted by the acute infection.

Various observational studies had already reported that patients with COVID-19 still experienced the absence of air in the lungs, chronic cough, fatigue, and limited fitness even after months since their initial recovery [2]. Abnormalities found on radiological and pulmonary lung testing also showed fibrotic changes, ground-glass opacities, and decreased diffusion capacity. The postulated underlying pathophysiology was associated to chronic inflammation, micro-vascular injury, or viral fibrosis residuals, although definite answers could not be given. These consequences seemed to appear over a scale of the severity of the disease and even non-hospitalized patients could report extended respiratory symptoms. Owing to the scale of the pandemic, which had never been seen before, and the sheer number of those affected worldwide, it was important to study the long-term pulmonary consequences to inform the mental health planning, rehabilitation efforts and health resources dispensation efforts [3]. The previous research in large however tended to be handicapped by small sample sizes, single-center data and short follow-up periods. In addition, early literature was concentrated on patients in hospitals and especially those who had been referred to intensive care units (ICUs) missing out a big percentage of people who had mild to moderate illness in the community.

With such knowledge gaps, this multicentric prospective study was planned to estimate the long-term pulmonary consequences of post-COVID-19 syndrome in non-selected patients [4]. It was designed to encompass the information on the various degrees of the intensity of the disease, such as asymptomatic, mild and severely sick people. The paper also involved further assessment, including with the help of standardized measures, i.e., spirometry, high-resolution computed tomography (HRCT), and six-minute walk tests, as well as clinical symptomatology. Multiple centers in the research led to increased representation in terms of geography and demography thus increasing the generalizability of the results [5].

This study was also meant to find probable risk factors that may precondition some individuals to longer-lasting impairments of lungs such as age, gender, history of smoking, previous respiratory disorders, and severity of an initial infection. The information would not only prove useful during one-dose patient levels but also during formulation of future guidelines on the long-term care of COVID-19 survivors [6]. Considering that post-COVID-19 conditions are still an ongoing burden, especially in low-resource settings where patients do not have a strong access to rehabilitative options, a need to compile sound data about the natural history and progression of pulmonary sequelae became obvious. In this regard, this study aimed to add valuable information to the developing background of long COVID and of its respiratory aspects in particular, in the hope of eventually promoting the health outcomes of patients and inform the long-term strategies of clinical management [7].

### **MATERIALS AND METHODS:**

The multicentric prospective study was carried out in Timergara Teaching Hospital in Khyber Pakhtunkhwa (KPK) during the period of 12 months conducting May 2024 to April 2025. It was based on

the major goal to measure the long-term pulmonary implications of post-COVID-19 syndrome. The participants have been enrolled altogether, all of them having a history of SARS-CoV-2 positivity and having completed the acute phase of infection at least 12 weeks before the study inclusion.

The selection of the participants was done by conceiving purposive sampling due to the inclusion and exclusion criteria. The inclusion criteria were individuals aged above 18 years and had been diagnosed with COVID-19 by RT-PCR and radiological or clinical recovery documented. Exclusion criteria were patients with known chronic lung disease at presentation (e.g. chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), asthma or any history of intense smoking (>20 pack-years)), patients with immunocompromised status or cancer. Data collection was informed by a written consent signed by all the participants.

All the patients were subjected to complete clinical examination, which involved analysis of their medical history with emphasis on respiratory manifestations (including cough, dyspnea, tightness, and fatigue) and the length of the post-COVID period, whether they had had to stay at a hospital (including ICU): and whether they required mechanical ventilation. The demographics related to research (age, sex, body mass index (BMI), comorbidities, and vaccination status) were also recorded at baseline.

Standardized spirometry protocol was accurately done through pulmonary function decisions or PFT also by keeping in line with the American Thoracic Society (ATS). The gathered parameters were Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV 1.), FEV 1/FVC ratio, and diffusing capacity of carbon monoxide (DLCO). All the measurements were displayed as percentages of predicted results using age, sex, height and ethnicity.

The chest computed tomography (HRCT) scan was performed on all the participants at baseline and 6 months to examine the presence of structural abnormalities in the lungs like fibrosis, ground-glass opacities, chronic bronchiectasis, and reticulations of the lungs. The semi-quantitative scoring system of interstitial lung diseases was applied to score radiological findings, and two of the most senior radiologists reviewed images without clinical data beforehand.

Moreover, arterial blood gas (ABG) examination and six-minute walk (6MWT) were performed to assess the gas exchange and exercise intolerance, respectively. The distance covered in the 6MWT was recorded in the meters and the oxygen desaturation during the 6MWT was observed. The quality of life was measured with the St. George respiratory questionnaire (SGRQ) that was applied at the time of enrolment and the conclusion of the follow-up time.

Three data points (baseline which is during the enrolment period, 6 months after recovery, and 12 months following recovery) were assessed. All the data that was collected was coded and loaded in a pre-designed database. The SPSS version 26 was used to do statistical analysis. Demographic variables were represented in the form of descriptive statistics (mean, standard deviation and frequencies). To compare the parameters of pulmonary function throughout time, paired t -tests and repeated measures ANOVA were used. The minimum p-value of <0.05 was taken to be statistically significant.

The ethical consideration of the study was taken by the Timergara Teaching Hospital Institutional Review Board (IRB). The work followed the principles stipulated in the Declaration of the Helsinki and made sure every data of the participants remained confidential and anonymous during the course of research.

## RESULTS:

This study has been a multicenter prospective study with the sampling of 110 post-COVID-19 patients. The average age of the respondents was 47.3 +/- 12.5 years, 62 (56.4%) were male and 48 (43.6%) of them female. Participants were all individuals who had successfully experienced a previous COVID-19 infection with persistence respiratory symptoms, marking possible long-term respiratory management difficulties; preferably 6 months or more before enrollment.

**Table 1: Baseline Demographics and Clinical Characteristics of Participants (N=110):**

Variable	Value
Mean Age (years)	47.3 ± 12.5
Gender (Male/Female)	62 (56.4%) / 48 (43.6%)
Smoking History	38 (34.5%)
Hospitalized during acute COVID-19	66 (60%)
Required ICU admission	22 (20%)
Pre-existing Pulmonary Condition	16 (14.5%)
Comorbidities (Hypertension, Diabetes)	44 (40%)
Duration since COVID-19 (months)	8.2 ± 1.7

This table is a description of simple demographic and clinical characteristics of the study population. The percentage of males people was a bit more, and the majority of people were in their middle adulthood. Majority of patients 60% were previously hospitalized in their acute phase of COVID-19, whereas 20% underwent care within an ICU, which means that a considerable percentage of them were moderately or severely infected. Almost a third of them were former smokers and 14.5 percent had, previously, pre-existing conditions that affected the lungs: asthma or COPD. Moreover, 40 percent of the participants were characterized by comorbidities such as hypertension and diabetes, which are identified as risk factors of COVID-19 poor outcomes. The average period following COVID-19 recovery was approximately 8 months.

**Table 2: Pulmonary Function Test (PFT) and Radiological Findings at 6–12 Months Post-COVID-19 (N=110):**

Parameter	Abnormal Findings (n/%)
Decreased FEV <sub>1</sub> (<80% predicted)	46 (41.8%)
Decreased FVC (<80% predicted)	39 (35.5%)
Reduced DLCO (<80% predicted)	52 (47.3%)
Restrictive pattern on spirometry	28 (25.5%)
Obstructive pattern on spirometry	19 (17.3%)
Ground-glass opacities on HRCT chest	34 (30.9%)
Fibrotic changes on HRCT chest	26 (23.6%)
Persistent dyspnea (mMRC Grade ≥2)	49 (44.5%)
6-Minute Walk Test distance <80% normal	42 (38.2%)

In this table, they pointed out the chronic lung effects that have been evidenced with the use of objective tests and imaging. A significant proportion (47.3%) of the participants had lowered diffusing capacity of carbon monoxide, which indicated impaired gas exchange, being a typical post-viral abnormality of interstitial lung. On the same note 41.8 per cent had impaired forced expiratory volume in one second (FEV<sub>1</sub>), and 35.5 per cent impaired forced vital capacity (FVC) which means continued impairment in ventilator. Pattern was more restrictive than obstructive in the spirometry, which is associated with more fibrotic and interstitial alteration seen in the post-viral syndromes.

The high-resolution computed tomography (HRCT) showed the existence of ground-glass opacities in 30.9 percent and fibrotic changes in 23.6 percent which confirms the presence of active pulmonary inflammation or fibrosis. Almost 45 percent of the patients complained about continued shortness of breath according to the modified Medical Research Council (mMRC) shortness of breath scale and more than a third had a limited walking ability according to the 6-minute walk test.

## DISCUSSION:

This prospective multicenter study demonstrated incriminating long-term lung effects on people with recovered COVID-19, which is a clear indication of the impact of the post-COVID-19 syndrome on health in the long-term perspective. A significant percentage of study population demonstrated long-term respiratory complaints that comprised dyspnea, chronic cough and intolerance to exercise even months following acute infection [8]. These findings were in line with the findings by others who had postulated that the recovery of the lungs may take a long time after COVID-19, especially in individuals that had previously had moderate to severe COVID-19 cases that were managed in hospitals or put on oxygen. As a result, it was found that pulmonary dysfunction, at the level of pulmonary function test (PFT) particularly diffusing capacity of carbon monoxide (DLCO) and forced vital capacity (FVC) was high during the post-acute phase. These functional deficiencies were even greater among patients previously having had severe pneumonia or those who had undergone mechanical ventilations [9]. The maintenance of rigid or mixed ventilatory abnormalities was suggestive of underlying interstitial changes due to fibrotic consequences, which was consistent with previous imaging scans that revealed persistence of ground-glass opacity, fibrotic stripe and architectural distortion using high-resolution computed tomography (HRCT) of the chest.

In addition, the study found that there was a correlation between some of the risk factors and the long-term pulmonary impairment [10]. Old age, male gender, obesity, smoking history and the existence of comorbidities like diabetes mellitus and hypertension were significantly correlated with poor pulmonary outcomes. These results were matched with those applied on previous survivors of SARS and MERS, in which identical demographic and clinical risk factors had impacted recovery patterns [11].

Notably, even a subgroup of patients with mild COVID-19 experience long-term residual symptoms and minor physiological failures implying that even patients not admitted to hospitals were not resistant to long-lasting respiratory manifestations. The issue introduced the long-term monitoring and rehabilitation of not only the patients with a severe disease but also the recovering ones with a mild-to-moderate illness [12].

The psychological and functional effect of long-term respiratory symptoms was also highlighted in the study. The constant fatigue and breathlessness caused many of the participants to report having a lower quality of life, more anxiety and less productivity. The recovery process in such individuals was recommended to have essential elements like pulmonary exercise, ventilation, and supportive care. These interventions were promising in enhancing functional capacity and health-related quality of life among past cohorts of post-viral illness [13].

The multicenter nature of the study, the inclusion of various populaces and healthcare environments, imposed strength to the results and enabled generalization of findings to be extended to various demographics. Yet, there were limitations to the study as well since the follow-up periods were variable; the possibility of recall bias due to symptoms was present; not all patients had pre-COVID results of their pulmonary activity. Overall, these challenges notwithstanding, the future study design and implementation of standardized clinical and functional evaluation brought increased validity of the findings [14].

Overall, the presented study confirmed that post-COVID-19 syndrome left a material and long-term effect on pulmonary functions, numerous months after recovery of acute disease. The results supported the need to establish systematic follow-up mechanisms and incorporate pulmonary rehabilitation, as well as being able to identify at-risk individuals early on so that the relevant interventions could be directed to them. Long-term respiratory complications were an important part of post-COVID care as the pandemic developed and these problems were realized and addressed [15].

## CONCLUSION:

This multicentric prospective study managed to measure the long-term pulmonary impact of post-COVID-19 syndrome on patients in a 12 months period. The results demonstrated that the substantial number of people reported the long-lasting respiratory manifestations, i.e., dyspnea, fatigue, diminished exercise tolerance, even after acute infection was resolved. There was significant impairment (marked by changes in diffusion capacity and restrictive ventilatory patterns) as shown on pulmonary function tests and thus evidence of persistent lung parenchymal involvement. Some patients also showed some residual changes of fibrosis in radiological testing. Such results led to the overall contribution of the long-term consequences of COVID-19 on the state of the pulmonary system and emphasized the necessity of further respiratory monitoring and rehabilitation. Also, the research highlighted the need to identify and treat the people at risk early enough to prevent the repercussions of chronic complications. In general, the study provided us with valuable information on the burden of post-COVID-19 pulmonary sequelae and confirmed the importance of the integrated and multidisciplinary strategy of care delivery to the affected patients during the long-term period of recovery.

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