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ORIGINAL ARTICLE

Pattern of pulmonary function tests in subjects recovered from COVID 19 infection

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Abstract

Introduction and Aim: The pulmonary sequelae of COVID-19 have not been extensively studied in the Indian population. This study was taken up with the aim to assess the pulmonary function tests (PFT) in subjects recovered from COVID-19. **Material and Methods:** In this observational cross-sectional study PFT was assessed in 50 adults in the age group of 18-60years. Rapid Antigen Testing was performed to rule out active COVID-19 infection. Subjects with acute or chronic respiratory illnesses that could affect lung functions were excluded. **Results:** We performed PFT on 50 subjects, with a mean age and BMI of 36.09 years and 25.17 kg/m^2. Fatigue and/or breathlessness were the most common complaints present post-recovery. A normal PFT was found in 22 participants and 28 showed a restrictive pattern. Based on the severity of the disease they had experienced the study population was classified into three groups mild, moderate or severe COVID. The three groups were found to be comparable in their demographic parameters, the PFT parameters were significantly different between the groups with significantly lower values seen in subjects who recovered from severe COVID. **Conclusions:** Restrictive pattern on PFT was the common abnormality found in patients recovered from COVID-19. This finding emphasises the need for long-term follow-up and establishment of a plan of assessment and management in patients recovered from COVID-19.

Keywords: SARS CoV 2, coronavirus, lung function test, lung disease

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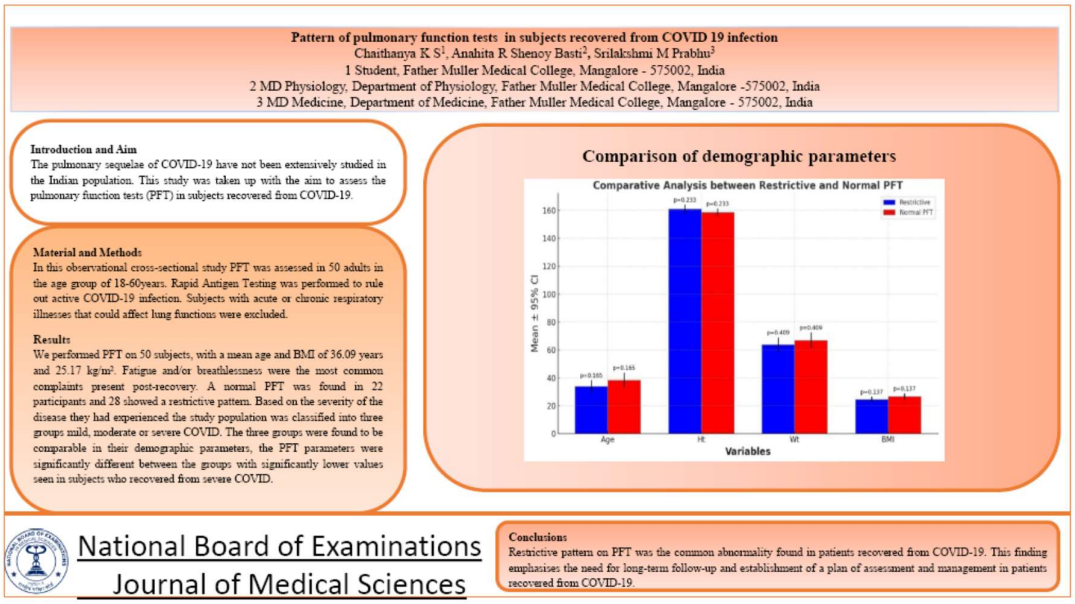
Graphical Abstract



Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) is the coronavirus that has led to the coronavirus disease 2019 (COVID-19) pandemic. 6,931,000 confirmed cases comprising 400,857 deaths globally were reported by 8th June 2020 [1]. With the onset of the second wave, an accumulative global surge of up to 141 million confirmed cases and 3.01 million global deaths as of April 2021 have been reported [2].

The most common symptoms include fever, fatigue, cough and expectoration accompanied by frequent muscle soreness, anorexia, chest tightness, dyspnoea, nausea, vomiting, diarrhoea and headache. The patients developing COVID-19 pneumonia had bilateral lung lesions and respiratory failure or acute respiratory distress syndrome (ARDS) [1,3].

Evidentiary studies have shown lungs to be the most common organ that is affected. Pulmonary injury following COVID-19 pneumonia occurs as a result of pathophysiological events like diffused alveolar epithelium destruction, hyalinisation of the membranes, capillary damage and bleeding, alveolar septal fibrous proliferation and pulmonary consolidation leading to pulmonary fibrosis and hypertension [4,5].

Although the pathophysiology of the disease has been determined to some extent, the long-term consequences and its effect on pulmonary function tests have not been studied in detail.

Evaluation of pulmonary function in recovered patients is important in assessing and understanding the prognostic attributes of the virus [6].

A wide spectrum of tools can be used to objectively assess functional respiratory parameters and the most commonly used tools are the pulmonary function tests such as spirometry, diffusion capacity and lung volumes, and evaluation of airway resistance or respiratory muscles. Epidemiological study report implicates that the above tools help in analysis of abnormalities which can lead to pulmonary fibrosis [4,7,8].

Reports have shown that short-term radiological and abnormal pulmonary functions are most likely to be evaluated in recovered patients' post-acute phase of infection. Little light has been thrown on long-term changes in the PFT which aids in understanding the recovery post-infection [1].

Thus, it is of utmost importance to determine pulmonary functions in the follow-up of patients recovered from COVID-19. This study was taken up with the objective of analysing pulmonary function tests (PFT) in subjects who have recovered from COVID-19 infection.

Methodology

This observational descriptive study recruited 50 adults in the age group of 18-60 years who survived mild, moderate or severe infection with COVID-19 virus.

Subjects who were previously diagnosed with COVID-19 by positive PCR on nasopharyngeal swab and/or presence of bilateral lung infiltrates on chest X-ray were included in the study. Baseline information regarding symptoms at initial presentation and severity of the disease was retrieved from medical records. Subjects underwent clinical examination and any persisting symptoms were noted. Rapid Antigen testing (RAT) was performed to exclude active COVID infection. Negative RAT was followed by performance of Pulmonary function test by a trained technician.

Subjects with acute or chronic respiratory illnesses that could affect lung functions were excluded.

PFT was conducted and interpreted using easy one connect software. The parameters assessed were Forced vital capacity (FVC), forced expiratory volume 1 second (FEV1), FEV1/FVC ratio, Forced expiratory flow (FEF) 25-75%, Peak expiratory flow (PEF).

Descriptive statistics were reported as mean ± standard deviation [SD]. Differences between the groups were analysed for statistical significance by chi-square or Fisher's exact test for categorical variables and by t-test or Wilcoxon rank sum test for continuous variables as applicable.

Results

In this study, we performed PFT on 50 participants majority of whom had complaints fatigue and/or breathlessness. Their mean age and BMI were found to be 36.09 years and 25.17 kg/m^2. Their demographic data is represented in Table 1. A normal PFT was found in 22 participants and 28 showed a restrictive pattern.

Table 1. Shows the demographic characteristics of the study population

n=50		Count (%)
Sex	F	39(78.0%)
	M	11(22.0%)
Presence of comorbidities	No	32(64%)
	Yes	18(36%)
Severity of COVID	Mild	32(64.0%)
	Moderate	15(30.0%)
	Severe	3(6.0%)
PFT	Restrictive pattern	28(56.0%)
	Normal pattern	22(44.0%)

A comparison of demographic parameters between subjects with restrictive pattern PFT and normal PFT has been depicted in Figure 1. The two groups were found to be comparable.

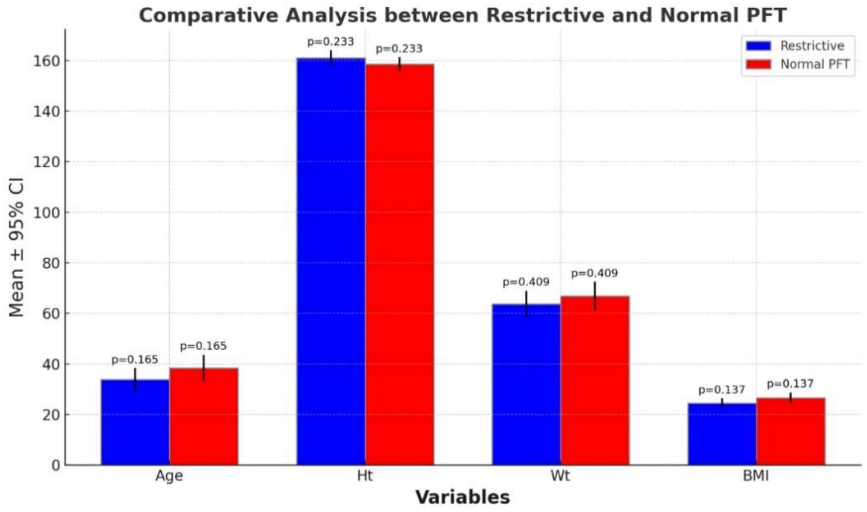


Figure 1. Comparison of demographic parameters between subjects with restrictive pattern PFT and normal PFT

Table 2 Compares the demographic data and PFT values between subjects recovered from mild, moderate and severe COVID-19. Based on the ANOVA p values, no statistically significant differences were found in age, height and weight between the three groups, indicating the groups were comparable in these aspects. However, there were highly significant differences ($p < 0.01$) in FVC, FEV1, FEV6, FEV1/FVC and FIVC values between the groups.

Table 2. Compares the demographic data and PFT values between patients recovered from mild, moderate and severe COVID-19

		n=50	Mean± Std. Deviation	ANOVA p
Age	Mild	32	35.19±11.31	0.497
	Moderate	15	35.67±12.10	
	Severe	3	43.67±16.50	
Ht	Mild	32	158.56±5.67	0.194
	Moderate	15	162.13±9.56	
	Severe	3	163.67±8.39	
Wt	Mild	32	65.44±13.42	0.441
	Moderate	15	62.80±12.99	

	Severe	3	73.33±8.33	
BMI	Mild	32	26.03±5.26	0.249
	Moderate	15	23.73±3.90	
	Severe	3	27.30±0.89	
FVC (% of predicted)	Mild	32	77.88±9.99	<0.001*
	Moderate	15	63.73±14.59	
	Severe	3	55.33±4.73	
FEV1 (% of predicted)	Mild	32	81.44±9.68	<0.001*
	Moderate	15	65.60±16.23	
	Severe	3	47.67±16.04	
FEV1/FVC (% of predicted)	Mild	32	105.63±7.69	0.008*
	Moderate	15	102.93±8.25	
	Severe	3	86.33±29.14	
FEV6 (% of predicted)	Mild	32	78.94±10.22	<0.001*
	Moderate	15	64.73±14.61	
	Severe	3	56.67±4.16	
FEF25-75 (% of predicted)	Mild	32	97.34±22.56	0.007*
	Moderate	15	74.47±33.19	
	Severe	3	56.67±48.69	
PEF (% of predicted)	Mild	32	91.13±12.52	0.004*
	Moderate	15	76.40±16.69	
	Severe	3	69.33±37.82	
FIVC (% of predicted)	Mild	32	75.69±12.03	0.003*
	Moderate	15	63.53±14.74	
	Severe	3	56.33±5.51	

*statistically significant

Table 3 Depicts Post hoc Bonferroni test performed for PFT between patients recovered from mild, moderate and severe COVID. On comparing the PFT values between the groups a significant difference was found in the PFT values between the mild and moderate, mild and severe group, however, no significant difference was found between moderate and severe group except in FEV1/FVC. P value < 0.05 was considered significant for all the parameters.

Table 3. Post hoc Bonferroni test performed for PFT between patients recovered from mild, moderate and severe COVID-19

Post hoc analysis-Bonferroni test			p value
FVC (% of predicted)	Mild	Moderate	0.001*
		Severe	0.006*
	Moderate	Severe	0.751
FEV1 (% of predicted)	Mild	Moderate	<0.001*
		Severe	<0.001*
	Moderate	Severe	0.077
FEV1/FVC (% of predicted)	Mild	Moderate	1.000
		Severe	0.006*
	Moderate	Severe	0.030*
FEV6 (% of predicted)	Mild	Moderate	0.001*
		Severe	0.007*
	Moderate	Severe	0.824
FEF25-75 (% of predicted)	Mild	Moderate	0.033*
		Severe	0.056
	Moderate	Severe	0.942
PEF (% of predicted)	Mild	Moderate	0.013*
		Severe	0.079
	Moderate	Severe	1.000
FIVC (% of predicted)	Mild	Moderate	0.011*
		Severe	0.045*
	Moderate	Severe	1.000

*statistically significant

Discussion

We performed PFT on 50 subjects, with a mean age and BMI of 36.09 years and 25.17 kg/m^2. Generalised weakness and/or breathlessness were the most common complaints present post-recovery. Among the 50 participants, 28 (56%) showed a restrictive pattern while the rest showed a normal PFT.

In a study done during the early convalescence phase found that abnormal pulmonary function tests especially impairment of diffusion capacity and the decline in FEV1/FVC ratio were detected in 43 (75.4%) patients. They also found that total lung capacity was significantly decreased in severe as compared to non-severe cases. However, in their study, only 12.3% of their subjects showed restrictive pattern and 10.5% showed obstructive pattern, as compared to 56% showing restrictive pattern in our study and none of our subjects showed obstructive pattern in PFT [9].

In another study that performed PFT on 100 post-COVID pneumonia subjects, found that restrictive pattern was present in 55% of the patients (N = 55), mixed pattern in 9% of patients (N = 9),

obstructive in 5% of patients (N = 5) with 31% (N = 31) having normal pattern [10].

A possible explanation for the absence of obstructive pattern in our study could be due to the exclusion of smokers and asthmatics who were included in the previous study [9]. Although a high percentage of our study population showed a restrictive pattern, majority (67%) had mild restriction. A higher percentage of restrictive pattern can also be attributed to the fact that the subjects included in our study were symptomatic with complaints of fatigue and breathlessness at the time of PFT recording. Our institution being a tertiary health care centre could also have contributed to a higher percentage of abnormal PFT. A high percentage (36%) of our study population also had comorbidities which could also be attributed to the presence of higher restrictive pattern on PFT.

In another study lung function was assessed in COVID-19 survivors more than 3 months after discharge. They compared patients who had been admitted to the intensive care unit and those who received ward treatments and found pulmonary restriction characterized by reduced vital capacity and/or alveolar volume in 65.4% of all participants. They found that 36.1% of patients had reduced transfer factor (TL_{CO}) but the majority (78.1%) had a preserved/increased transfer coefficient (K_{CO}), indicating an extrapulmonary cause. They attributed this to obesity, fatigue of the respiratory muscles, localized microvascular changes, or hemosiderosis from lung damage. They also concluded that this restrictive pattern was independent of whether or not the patients had received mechanical ventilation or had ward-based respiratory support [11].

A case series where 5 patients who were asymptomatic or had very mild symptoms of COVID-19 infection upon diagnosis and were not hospitalized for the same, were found to have interstitial lung disease four to eight weeks after a COVID-19 diagnosis [12].

In our study, 64% of the participants had recovered from mild COVID yet the percentage of participants showing restrictive pattern was high. As mentioned in the study by James A Stockley et al, other factors of extrapulmonary restriction could have been attributed to the restrictive pattern on PFT and should be considered while evaluating post-COVID sequelae.

We further classified the study population into three groups based on the severity of their disease into mild, moderate or severe COVID. Mild COVID was defined as patients with signs of upper respiratory tract infection without evidence of breathlessness or hypoxia. Moderate COVID was defined as pneumonia with no signs of severe disease, presence of clinical features of dyspnea and or hypoxia, fever, cough, including SpO2. Severe COVID was defined as Severe Pneumonia plus one of the following; respiratory rate >30 breaths/min, severe respiratory distress, SpO2. The three groups were found to be comparable in the demographic data however the PFT parameters were significantly different between the groups with lower values seen in subjects who recovered from severe COVID.

In a study with findings contradictory to ours no difference was found between mechanically ventilated patients for severe COVID pneumonitis and non-ventilated patients 3 months post-recovery [10]. In another cross-sectional follow-up study of 220 COVID-19 patients

performed 10 weeks post-COVID, found restrictive pattern to be prevalent in 38% of the study population. They found the TLC to be below normal in patients recovered from severe COVID [13].

In conclusion, varied abnormalities in pulmonary functions have been reported in different studies, with our study finding a high percentage of the study population having restrictive pattern. Thus, this study underscores the need for a long-term follow-up to understand the consequences of COVID-19 on pulmonary function and to help healthcare professionals and policymakers offer targeted therapies and rehabilitation for the large community of recovered patients.

Limitations

Pre-disease spirometry measurements of the study population were not available for analysis, thus the percentage of restrictive pattern could also be attributed to normal physiological variation, undiagnosed pulmonary or systemic disease.

The PFTs were performed at varied intervals post recovery from COVID, the interval varied from few days up to 14 months post-COVID recovery, this is also a limitation in interpreting the recovery pattern.

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Conflict of interest

The authors declare no conflict of interest

Ethical Approval

The study was initiated after ethical approval and written informed consent from the subjects.

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