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ORIGINAL ARTICLE

Pulmonary function testing patterns in patients recovering from COVID-19, a prospective observational study.

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ABSTRACT… Objective: To determine the frequency of abnormal pulmonary function tests and their pattern after four weeks in patients recovering from COVID-19. **Study Design:** Survey-based Pospective Observational study. **Setting:** COVID 19 Isolation Ward, Khyber Teaching Hospital, Peshawar. **Period:** June 23, 2021, to December 21, 2021. **Methods:** This study was conducted on 183 patients aged 18 – 70 years of either gender having severe or critical COVID-19 pneumonia necessitating admission to COVID-Unit were enrolled using a non-probability consecutive sampling technique. Discharged patients of COVID-19 were called for follow-up after 4 weeks of discharge, and a pulmonary function test was done to determine the frequency of abnormal pulmonary function tests and their pattern after COVID infection. Results: In our study total of 183 patients were enrolled with a mean age of 36.3±14.6 years. There were 53% male and 47% female patients. The mean height was 155.06 ± 13.3cm, the mean weight was 71.4±11.2 kg, and the mean BMI was 29.7±5.8kg/m2. Abnormal pulmonary function tests were present in 32.8% of patients. Among these patients, 49 (81.6%) had restrictive patterns, while 11(18.3%) patients had an obstructive pattern on spirometry. **Conclusion:** Patients infected with COVID-19 showed deranged lung function, with most patients having a restrictive type pattern 4 weeks after being discharged from the hospital.

Key words: COVID-19, Chronic Lung Diseases, Pandemic, Pulmonary Function Tests, Spirometry.

INTRODUCTION

As the second wave of the COVID-19 pandemic rages through most of the world, healthcare workers must also brace themselves against the sequelae of COVID-19 infections in the future. The novelty of the pathogen, along with its relentless spread across the globe, means that the long-term systemic and pulmonary complications for patients surviving the most severe forms of COVID-19 infection are as yet unknown.[1] Studies have been done worldwide to assess the long-term impact of COVID-19 on lung and respiratory function, and varying results have been reported.

Guler et al. followed 113 patients four months after surviving COVID-19 infection. This study found that the patients with severe pulmonary disease secondary to COVID-19 had significantly reduced Diffusion capacity of the Lung for Carbon monoxide (DLCO) at 73% predicted compared to those with mild to moderate disease.[2] Another study by investigators in China determined the frequency of restrictive lung defects in patients with COVID-19 Pneumonia by performing spirometry a day before or on discharge. Up to 47% of patients had DLCO abnormalities, followed by TLC reduction in 25% and abnormalities in FEV_1 and FVC in 15 % and 10 %, respectively.[3] The strongest evidence so far comes from a study published recently in the journal Chest by investigators in Spain. They followed 125 patients with critical COVID-19 requiring ICU admission three months after hospital discharge. 82% of patients showed a less than 80% diffusion capacity, and 37% showed altered total lung capacity.[4]

At the time of writing, 784,000 people have been affected by COVID-19 in our country alone, with 682,000 recovering from the disease.[5] It bears

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important implications for the future as not much is known about the frequency or prevalence of post-COVID pulmonary sequelae in patients recovering from COVID-19; however, with such large numbers being affected, it is expected to become epidemiologically significant.[6,7] Lung function assessment with spirometry is a cheap and non-invasive method of assessing functional respiratory reserve in patients with pulmonary diseases.[8] Pulmonary Function Testing (PFT) pattern assessment with spirometry can be incorporated into the follow-up of patients who have survived COVID-19 to determine their functional reserve and ascertain if they are likely to have restrictive lung disease. Therefore, the rationale for this study is to determine what percentage of people who have recovered from COVID-19 Pneumonia will have persistent functional deficits in the future. Most primary care physicians and pulmonologists will face these cases long after the pandemic. Knowing the prevalence of this condition would help prepare physicians for the burden of care in the future and their long-term follow-up. The primary objective of this study was to determine the frequency of abnormal pulmonary function tests and their pattern after four weeks in patients recovering from COVID-19.

METHODS

This Prospective Observational study was done at Khyber Teaching Hospital, Peshawar, MTI, COVID Isolation unit from June 23, 2021, till December 22, 2021. The total duration of the study was 6 months, and data were collected after taking ethical approval from the institute on 30th Dec 2020, (No.1033/DME/KMC). Informed consent was taken from all the participants enrolled in our study. The sample size was calculated using the OpenEpi software, and it was calculated to be 183, with a frequency of altered Total Lung Capacity (TLC) taken as 37% from the study by Gonzales et al.[5], confidence interval of 95% and margin error of 7%. We used a non-probability convenience-based sampling technique for our study. All patients aged between 18 – 70 years of either gender admitted with severe or critical COVID-19 pneumonia necessitating admission to COVID-Unit were enrolled in the study. Any patient with a history of interstitial lung disease, chronic obstructive pulmonary disease or other structural lung disease was excluded from the study. We also excluded patients having a history of active malignancy, metastatic disease, debilitating neurological illness or terminal organ failure in the form of decompensated liver disease, end-stage kidney disease or congestive heart failure from our study.

Patients with positive Polymerase Chain Reaction (PCR), Rapid Antigen Test, or radiologically confirmed COVID-19 Pneumonia were labelled as COVID-19 Pneumonia.[9] Patients with severe or critical diseases were included in the study. Patients with Oxygen Saturation $<94\%$ and/or respiratory rate >25 breaths per minute and Oxygen saturation maintained by nasal cannula or face mask were labelled as severe. Patients with Respiratory compromise severe enough to require Non-invasive ventilation in the form of continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP), High flow nasal cannula or mechanical ventilation were labelled as critical. Age was taken in years, and height was measured in centimeters and converted to meters. Weight was measured in kilograms, and body mass index (BMI) was calculated from the measured height in centimeters converted to meters and the measured weight in kilograms as kg/m2. Pulmonary Function Tests (PFTs) were determined by calculating Forced expiratory volume (FEV_1), Forced vital capacity (FVC) and TLC. Patients having obstructive ($FEV_1/FVC < 80\%$) or restrictive disease patterns ($FEV_1/FVC < 80\%$ with reduced TLC) on spirometry were labelled as having abnormal PFTs.[10,11]

A pre-designed data collection form was used to record information on the admitted patient as it pertains to the study design. These patients were divided according to the severity of the COVID-19 infection according to operational definitions as severe and critical diseases. Other variables included age, gender, and pre-existing comorbidities excluding prior lung disease. These patients were contacted telephonically after 4 weeks of being discharged from the hospital and called for follow-up.

Follow-up comprised of symptom assessment and PFTs using a flow spirometer. Spirometry was done after Explaining the test to the patient while sitting upright. Spirometer was turned on after calibrating the spirometer before testing. The procedure was explained to the patient in detail by a respiratory nurse. Patients were told to take a deep breath and blow into the spirometer as hard and fast as possible. At least 2 tests were done, and the best readings of FVC, FEV_1 and TLC displayed on the spirometer were noted for assessing any abnormality in the pulmonary function test and to determine a restrictive or obstructive pattern.

Data analysis was done via SPSS version 23. Mean ± SD was calculated for all numerical variables such as Age, Height, Weight and BMI. Frequency and percentages were calculated for categorical variables like gender. PFTs were determined, and patients with abnormal PFTs were also calculated as percentages. Abnormal PFTs were further interpreted as obstructive or restrictive. The pulmonary Function Test was stratified by age, gender, height, weight and BMI. Post-stratification Chi-square test was used to assess for any significant difference in different groups. (P value <0.5)

RESULTS

In our study, 183 patients were enrolled with a mean age of 36.3±14.6 years. There were 53% male and 47% female patients. Physical parameters measured in our study population are given in Table-I. Abnormal PFT was present in 60 (32.8%) of patients. Among these patients, 49 (81.6%) had restrictive patterns, while 11(18.3%) patients had an obstructive pattern on spirometry. Abnormal PFTs were stratified among different ages, gender, weight, and height to assess for any significant difference. There was no significant difference in the distribution of abnormal PFTs among different age and gender groups and in patients with different weights.

Data stratification for frequency of abnormal PFT and height group showed a significant difference in distribution, and patients with heights more than 155 cm were affected more than patients with smaller heights. Similarly, there was a significant difference in the distribution of abnormal PFTs in patients with different BMI groups and patients with a BMI of more than 30kg/m2 were more frequently affected. (P-value <0.001). The associations of all study parameters with abnormal PTs are presented in Table-II.

Parameters	Mean ± SD/ frequency (%)
Age (in years)	36.3±14.6
Gender	
Male	53%
Female	47%
Height (cm)	155.06±13.35
Weight (kg)	71.49±11.21
BMI (kg/m2)	29.75±5.82
Abnormal PFT	
Present	60 (32.8%) 32.
Absent	123 (67.2%)

Table-I. Physical parameters of sampled population BMI: Body mass index; PFT: Pulmonary function testing

Parameters	Abnormal Parameters (n)		P-Value
	Present	Absent	
Age categories (in years)			
18-45 years	44%	95%	0.56
46-70 years	16%	28%	
Gender			
Male	30%	67%	0.56
Female	30%	56%	
Height (in cm)			
Equal to or less than 155cm	18%	87%	<0.001
More than 155cm	42%	36%	
Weight (in kgs)			
Equal to or less than 70 kg	30%	63%	0.87
More than 70 kg	30%	60%	
BMI			
More than 30Kg/m2	42%	52%	<0.001
Equal to or less than 30kg/m2	18%	71%	

Table-II. Association between PFT and study parameters

DISCUSSION

Recent evidence suggests that the lungs are the organ most affected by COVID-19, and there is long-term damage to pulmonary function.

In our study, we found that 32.8 per cent of the patient had abnormal Pulmonary function tests 4 weeks after discharge from the hospital. Most of the patients had restrictive-type patterns, while some of the patients had an obstructive-type patterns. This alteration in PFTs can affect patient exercise tolerance and quality of life. A characteristic of COVID-19 is the extensive injury to alveolar epithelial cells and endothelial cells with secondary fibroproliferation, indicating a potential for chronic vascular and alveolar remodelling leading to lung fibrosis and long-term abnormalities in PFTs.[12]

It leads to impairment in diffusion pathways because of abnormalities of the alveolar-capillary membrane due to interstitial alveolitis/fibrosis and reduction in capillary volume due to micro-thrombus formation in the acute stage. COVID-19-infected patients who are discharged from the hospital can have compromised lung function, as shown in our study. These findings generate concerns regarding the assessment and long-term follow-up of discharged patients admitted with COVID-19 infection.[13]

Studies have been done worldwide on the long-term effects of COVID-19 pneumonia on pulmonary function, as the lung is the main organ involved in this infection. The strongest evidence so far comes from a study published recently in the journal Chest by investigators in Spain. They followed 125 patients with critical COVID-19 requiring ICU admission three months after hospital discharge. 82% of patients had a less than 80% diffusion capacity, and 37% showed altered total lung capacity. The 6-Minute Walk test similarly demonstrated significant reductions in this population compared to healthy subjects (Mean -123m, $P < .001$).[4] Guler et al. followed 113 patients four months after surviving COVID-19 infection. This study found that the patients with severe pulmonary disease secondary to COVID-19 had significantly reduced Diffusion capacity of the Lung for Carbon monoxide (DLCO) at 73% predicted compared to those with mild to moderate disease. These patients also exhibited significantly reduced 6 Minute Walk Distance and exercise-induced desaturation.[2] Our results were almost similar to these studies.

Another study by investigators in China determined the frequency of restrictive lung defects in patients with COVID-19 pneumonia by performing spirometry a day before or on discharge. Up to 47% of patients had DLCO abnormalities, followed by TLC reduction in 25% and abnormalities in FEV_1 and FVC in 15 % and 10 %, respectively.[3] Their findings were different as an assessment was performed at the time of discharge from the hospital.

Chaolin Huang et al. conducted an ambi-directional cohort study of 1733 COVID-19 patients six months after discharge. In patients with severe disease, 29 % exhibited reduced 6-Minute Walk tests, and 56% had reduced DLCO.[5] Frija-Massonet al.[14] enrolled 50 patients, PFTs were evaluated after 30 days of onset of symptoms, and 44% of patients had abnormal PFT. Huang et al.[15] enrolled 57 patients, and PFTs were done after 30 days of discharge from the hospital; abnormal PFTs were seen in 52.6% of patients; this high value can be attributed to short follow-up time as compared to our study. In another study conducted in China, investigators recruited 110 patients and evaluated them by PFT after 28 days of onset of the disease; abnormal PFTs were seen in 47.2% of patients, which was higher than our study.[16] Their results were different because the study was conducted in different populations. Zhao et al.[17] enrolled 55 patients and evaluated lung capacity using PFT after 3 months of discharge and found that 27% of patients had abnormal PFT, and their results were almost similar to our findings.

We also found that patients with a height of more than 155 cm had a higher frequency of abnormalities in their PFTs, and tall stature could be a risk factor for long-term impact on PFTs.[18,19] The effect of the patient's height on long-term abnormalities in PFTs is unknown. Different studies have been done to check the association of anthropometric measures with long-term impact on the lungs in a patient with COVID-19 infection, but the results are inconsistent.[13] There was also a significant difference in patients having different BMI groups, and patients with BMI greater than 30kg/m2 were mostly founded to have abnormal PFTs. Various studies have shown that obesity is a risk factor for severe COVID-19.[21] The relationship between obesity and high BMI with worse outcomes in COVID-19 patients concerning severity, gradual recovery and mortality has been established.[22,23] Patients with higher BMI had a higher frequency of abnormal PFTs in our study population, as already proven by studies in other parts of the world.

This study showed that patients infected with COVID-19 have long-term effects on their respiratory reservoirs. Moreover, the effect of anthropometric measures was also checked in different groups. There were a few limitations in our study. Firstly, we could not do the long-term patient follow-up because of time constraints. Secondly, we didn't check DLCO because of non-availability, which could have clarified lung diffusion capacity. Thirdly we didn't have baseline PFTs before the COVID-19 infection, but still, our study proves that a significant number of patients' PFTs were affected on spirometry on follow-up at 4 weeks.

Further studies should be done to assess for long-term effects of COVID-19 infection on respiratory function and its association with anthropometric measures. A cohort study with more patients followed for a longer duration can prove whether changes induced by COVID-19 infection are reversible or permanent.

CONCLUSION
COVID-19 infection causes acute respiratory distress and is associated with chronic lung injury and derangement in PFT even after recovery. All recovered patients should be screened for long-term effects of COVID-19 infection and followed up at regular intervals for at least 1 year after recovering from an acute episode.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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5	Kamaluddin Azam	Data acquisition, data analysis or interpretation, critical manuscript revision, final manuscript approval.	
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