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Original Article

Physiology Section

Assessment of Pulmonary Function in COVID-19 Recovered Health Science Students: A Descriptive Cross-sectional Study

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ABSTRACT

Introduction: Coronavirus Disease-2019 (COVID-19) impacts multiple organs like the kidneys, heart, and liver, but primarily affects the respiratory system, leading to symptoms such as cough with sputum production, fever, and in severe cases, respiratory failure. Research on Severe Acute Respiratory Syndrome (SARS)-Coronavirus-2 (CoV-2) has revealed impairments in lung function during the early recovery phase following COVID-19 infection. The aim is to understand the virus's impact and identify any obstructive, restrictive, or mixed pulmonary alterations in medical professionals six weeks after recovery.

Aim: To assess Pulmonary Function Tests (PFTs) six weeks after COVID-19 recovery in health science students at a medical college in North Karnataka.

Materials and Methods: A descriptive cross-sectional study was conducted in the Department of Physiology at Jawaharlal Nehru Medical College in North Karnataka, India, from January 2021 to December 2021. A total of 155 COVID-19-recovered health science students were included, and their anthropometry, physiological parameters, and pulmonary parameters were recorded. The "Spirometer Helios 401" was used to estimate an individual's PFT. Data were analysed using independent sample t-tests, with a p-value <0.05 considered statistically significant.

Results: The mean age of the participants was 21.73±3.04 years. The Mean±Standard Devaiation (SD) of Forced Vital Capacity (FVC) (L), Forced Expiratory Volume (FEV) at the end of one second (L), Peak Expiratory Flow Rate (L), forced mid expiratory flow 25-75 (L/s), forced mid expiratory flow 25% (L/s), forced mid expiratory flow 50% (L/s), forced mid expiratory flow 75% (L/s), Inspiratory Reserve Volume (IRV) (L), Expiratory Reserve Volume (ERV) (L), Inspiratory Capacity (IC) (L), and Maximum Voluntary Ventilation (MVV) (L)±SD of post-COVID-19 subjects were less compared to their corresponding predicted values. The Mean±SD of FEV1/FVC (%) and tidal volume (L) of COVID-19 recovered subjects were higher than their corresponding expected value. The FEV, Forced Expiratory Flow (FEF), and FEV1 values were significantly less in females compared to males.

Conclusion: Coronavirus Disease-19-recovered subjects showed altered respiratory functions even after six weeks, with the majority having restrictive disease, followed by a mixed pattern and obstructive diseases, while the remaining showed no changes in lung function. Altered pulmonary functions in COVID-19 patients may be due to alveolar destruction or pulmonary interstitial fibrosis.

Keywords: Coronavirus disease-2019, Expiratory volume, Inspiratory reserve volume, Tidal volume

INTRODUCTION

Coronavirus Disease-2019 (COVID-19), was first discovered in Wuhan, China, in December 2019 [1]. COVID-19 causes severe acute respiratory syndrome and affects multiple organs like the heart, kidneys, liver, and lungs. A study has shown that COVID-19 seems to have the most significant effects on the lungs, displaying various pathophysiological symptoms such as the destruction of the alveolar epithelium diffusely, formation of a hyaline membrane, destruction of the capillaries followed by bleeding, alveolar septal fibrous proliferation, and pulmonary consolidation [2]. Case-to-case variations were observed among COVID-19 patients, although the most common symptoms include fever, persistent dry cough, and fatigue [2]. It has been declared as a highly contagious disease, with coughing, sneezing, and inspiration of droplets and micro-droplets loaded with viruses from infected people described as the most common transmission methods [3].

It is believed that patients positive for COVID-19 take an average of 2-6 weeks to recover from the infection, but the symptoms may persist for weeks or even months, even after discharge from the hospital. Worldwide, the assessment of discharged patients' lung injuries has been followed-up. According to early research, the majority of COVID-19 patients experienced changes in their lung function [4,5]. Lung function defects after COVID-19 infection have recently been identified in the early recovery phase among studies on SARS-CoV-2. In a single-centre study, 45 individuals exhibited restrictive and obstructive ventilatory issues six weeks after hospital discharge [6].

Pulmonary Function Tests (PFTs) provide an assessment of an individual's respiratory function. PFTs are an age-old but time-tested parameter for assessing a person's respiratory health [7-9]. Various PFTs offer a quantitative and objective assessment of respiratory function [10,11]. Post-infection incidences of interstitial lung disease have also been frequently reported [12]. This can have a long-term impact on affected individuals' diffusing capacity and total lung capacity. Circulating factors associated with acute neutrophil activation, fibrosis signaling, and alveolar epithelial repair remain elevated in COVID-19 infection survivors and are strongly associated with impaired pulmonary function. In such instances, pharmacological intervention is only partially efficacious. Consequently, it is crucial to monitor patients with PFT even after the infectious period has passed [13].

Those involved in healthcare centers, who form the foundation of health services, are especially susceptible to repeated viral infection exposure [13]. While many studies have been done to date [4,7,9], very few studies have been conducted in this part of India. Therefore, the aim of this study was to assess PFT after six weeks in COVID-19 recovered students. The primary objective was to assess the PFT in the study subjects who have recovered from the COVID-19 disease and to identify any obstructive, restrictive, or mixed pulmonary

alterations. The secondary aim was to compare the PFT between males and females.

MATERIALS AND METHODS

A descriptive cross-sectional study was conducted among COVID-19 recovered health science students in the Department of Physiology at Jawaharlal Nehru Medical College in North Karnataka, India, from January 2021 to December 2021. The study was done after obtaining approval from the Institutional Ethics Committee (Letter No: MDC/DOME/Ethics Comm./2021/dated 04/02/2021). All the subjects diagnosed with COVID-19 during the study period were part of the study. Written informed consent was obtained from every subject.

Inclusion and Exclusion criteria: A total of 155 students diagnosed with mild COVID-19 by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) after six weeks of recovery were included in the study (Republic of Korea's 2020 score under the disease severity categorisation method for COVID-19 <4) [13]. The subjects with asthma, allergic history, tuberculosis, upper respiratory tract infection, re-infection with COVID-19, and a history of smoking were excluded from the study.

Study Procedure

Each subject who met the inclusion criteria had to complete a proforma, which included personal details, history of COVID-19 infection, anthropometry, and pulmonary measurements.

The physiological parameters measured were height in centimeters without footwear. The weight of subjects was measured in kilograms using a standardised machine with minimum clothing, and Body Mass Index (BMI) was calculated in kilograms/meter^2 using the Quetelet Index. A BMI of 18.5 to 24.9 kg/m^2 was considered within the normal range [14].

The respiratory parameters measured included pulmonary functions: Forced Vital Capacity (FVC) (L), Forced Expiratory Volume (FEV), FEV1 (L), Forced Expiratory Flow (FEF) 25-75 (L), Peak Expiratory Flow Rate (PEFR) (L), Forced Expiratory Flow (FEF) 25%, 50%, 75% (L/s), Expiratory Reserve Volume (ERV) (L), Inspiratory Reserve Volume (IRV) (L), Tidal Volume (TV) (L), Inspiratory Capacity (IC) (L), and Maximum Voluntary Ventilation (MVV) (L) were measured [10,11].

The subjects were informed about the process before recording lung function data. Before recording, each subject's permission was obtained. Three readings were taken for each test. Every test was recorded while the subject was sitting at room temperature. The "Spirometer Helios 401" is a spirometer used with a Windows-based computer, manufactured by 'Recorders and Medicare Systems Private Limited' Haryana. It is used to determine lung functions by measuring the FCV, SVC, and MVV. It has a handpiece. This handpiece is connected through a Universal Serial Bus (USB) cable [15]. The handpiece is connected to the mouthpiece, and the patient is asked to respire through the mouthpiece. Once the test was performed, the graphs were recorded on the connected computer and saved. FEV1, FVC, and VC values less than 80% of the expected values were deemed abnormal, while FEV1/FVC values less than 70% of the predicted values were considered abnormal [5].

Forced Vital Capacity (FVC): For the FVC manoeuvre, the subject must first take a deep breath. Then, the subject should place the mouthpiece into the mouth and expires the air with one force. Once all the air has been exhaled, the subject must again breathe in as quickly as possible, with the mouthpiece in the mouth, until the lungs are full.

Slow Vital Capacity (SVC): The SVC is an easy method of finding the vital capacity of the subject. The subject was asked to breathe regularly into the mouthpiece. After 2-3 curves, he/she was asked to take a deep breath, followed by a normal breath, deep expiration, and a few normal breaths at the end.

Maximum Voluntary Ventilation (MVV): The patient was asked to breathe deeply and quickly through the mouthpiece for 15 seconds. Breathing should be as constant as possible, and three readings were taken, out of which the best one was selected.

STATISTICAL ANALYSIS

Descriptive data were presented as mean±SD for continuous variables or number (percentage) for categorical ones. The data obtained were analysed by a statistician using Statistical Package for Social Sciences (SPSS) version 20.0 software. The normality of the data was tested by the Shapiro-wilk test. An unpaired t-test was used for comparison, and a p-value <0.05 was considered statistically significant.

RESULTS

The study was conducted on a total of 155 subjects, out of which 90 (58%) were males and 65 (42%) were females. Out of the 155 students, 50 (32.25%) showed restrictive disease, 20 (12.90%) showed obstructive disease, 15 (9.67%) showed a mixed pattern, and the remaining 70 (45.16%) had no changes in lung function.

The mean age of the participants was 21.73±3.04 years. The mean±SD of age (years), height (centimeters), weight (kilograms), and BMI (kg/m^2) are shown in [Table/Fig-1].

Anthropometric values	Mean±SD (N=155)
Age (years)	21.73±3.04
Height (cm)	160.88±11.62
Weight (kg)	62.42±9.67
BMI (kg/m^2)	24.25±3.88

[Table/Fig-1]: Types of implant used for Internal distrac anthropometric parameters of post-COVID-19 recovered subjects.

The Mean±SD of FVC, PEFR, FEF 25-75%, FEF 25%, 50%, 75%, IRV, IC, and MVV were less than the predicted value and found to be statistically significant. In contrast, the Mean±SD of FEV1/FVC and TV were higher compared to what was predicted and were found to be statistically significant. The FEV1 and ERV were found to be non significant.

The comparison of PFT with predicted values is shown in [Table/Fig-2]. FVC, FEV1, FEF 25-75%, and FEF 25% were lower in females than in males and were found to be statistically significant, as shown in [Table/Fig-3].

PFT parameters	Predicted N=155 Mean±SD	Measured N=155 Mean±SD	p-value
FVC (L)	3.41±0.66	2.7±0.44	0.001*
FEV1 (L)	2.95±1.24	2.7±0.47	0.209
FEV1/FVC (%)	86.5±2.47	91.8±5.88	0.001*
PEFR (L/s)	7.86±1.69	5.0±1.13	0.001*
FEF 25-75 (L/s)	4.16±0.64	3.7±0.75	0.013*
FEF 25% (L/s)	6.76±1.57	4.8±1.07	0.002*
FEF 50% (L/s)	6.47±0.94	3.6±0.95	0.001*
FEF 75% (L/s)	3.64±0.88	2.4±1.79	0.003*
TV (L)	0.05±0.00	1.4±0.45	0.001*
IRV (L)	2.59±0.32	1.0±1.46	0.002*
ERV (L)	1.56±0.26	1.3±0.66	0.095
IC (L)	3.09±0.32	1.6±0.48	0.001*
MVV (L/min)	147.60±29.17	63.7±14.94	0.001*

[Table/Fig-2]: Pulmonary Function Tests (PFT) values of post COVID-19 recovered subjects.
*Independent t-test, indicates level of significance, p<0.05 is significant

PFT parameters	Male n=90		Female n=65		p-value
	Predicted Mean±SD	Measured Mean±SD	Predicted Mean±SD	Mesasured Mean±SD	
FVC (L)	3.31±0.66	2.92±0.70	3.54±1.06	2.44±0.44	0.005*
FEV1 (L)	2.97±1.24	2.92±1.00	2.93±0.52	2.51±0.47	0.003*
FEV1/FVC (%)	86.44±2.47	91.93±5.58	86.51±3.28	91.70±5.88	0.888
PEFR (L/s)	81.21±1.69	5.24±1.25	7.39±1.73	4.81±1.13	0.192
FEF 25-75 (L/s)	4.35±0.64	4.10±0.99	3.92±0.93	3.26±0.75	0.001*
FEF 25% (L/s)	7.13±1.57	5.18±1.12	6.28±1.83	4.49±1.07	0.025*
FEF 50% (L/s)	6.72±0.94	3.73±1.09	6.15±1.44	3.54±0.95	0.514
FEF 75% (L/s)	3.64±0.88	2.40±0.77	3.63±1.11	2.59±1.79	0.599
TV (L)	0.50±0.00	1.43±0.36	0.50±0.00	1.49±0.45	0.572
IRV (L)	2.52±0.32	1.13±0.32	2.69±0.31	1.03±1.46	0.330
ERV (L)	1.58±0.26	1.50±0.70	1.54±0.25	1.26±0.66	0.201
IC (L)	3.02±0.32	1.52±0.69	3.19±0.31	1.75±0.48	0.168
MVV (L/min)	151.03±29.17	68.84±20.61	143.17±33.37	66.29±14.94	0.612

[Table/Fig-3]: Comparison of Mean±SD of pulmonary functions parameters among males and females.
*Independent t-test, indicates level of significance, p<0.05 is significant

DISCUSSION

The present study was undertaken on 155 COVID-19-recovered health science students after six weeks of infection. Out of 155 students, 90 (58%) were males and 65 (42%) were females. The pulmonary functions were assessed by spirometry and lung volumes. Out of 155, 50 (32.25%) students showed restrictive disease, 20 (12.90%) students showed obstructive disease, 15 (9.67%) showed a mixed pattern, and the remaining 70 (45.16%) had no changes in lung functions. The FVC, FEV1, PEFR, FEF 25-75%, FEF 25%, 50%, 75%, IRV, ERV, IC, and MVV were less than the predicted value, whereas the FEV1/FVC and TV were higher compared to predicted and were found to be statistically significant.

The mean age was 21.73±3.04 in the present study. A similar study by Mogensen I et al., surveyed 661 young patients with a mean age of 22 years, like the present study [16].

In the current study, it can be noted that FEV1 is normal, FEV1% is increased, and FVC is reduced. FVC is less than 80% of their predicted values [Table/Fig-2]. To determine airway obstruction, the FVC and FEV1% are utilised. A reduced FEV1 compared to FVC implies an obstructive lung illness, whereas a lowered FVC more than FEV1 indicates a restrictive lung disease, such as pulmonary fibrosis, with an increased FEV1/FVC ratio. FEV1/FVC ratios below 70% of the lower limit indicate an obstructive condition, such as asthma. In the present study, the FVC and FEV1 levels are reduced compared to their corresponding predicted values, but FEV1 levels are not statistically significant. A study on the young Indian population found a standard value of FEV1 of 2.60±0.42L/s [17]. Similarly, the FEV1% in the current study was 2.70±0.47, which is comparable to the predicted value. The decreased FVC and increased FEV1% support a restricted lung disease pattern in this cohort, and 32.25% of students showed this pattern. The abnormalities in pulmonary function in these COVID-19 patients are likely caused by coronavirus infection, which is also likely causing damage to alveoli and pulmonary interstitial fibrosis [18]. In contrast to the present study, another study on respiratory function tests in young healthcare workers depicted normal FVC, FEV1, and FEV1% in cases compared to the control. It concluded no change in pulmonary functions after three months of recovery [13].

The other parameters, like FEF 25-75, FEF 25, FEF 50, and FEF 75, were found to be reduced in the present study compared to their corresponding predicted values. The FEF parameter, which measures the highest mid-expiratory flow rate between 25 and 75 percent of FVC, is used to identify small airway obstructions. The reduction in the FEF 25-75% was considered a significant indicator of obstructive disease [19]. A 12.90% of students in the current study were found to have an obstructive pattern. A study by Zhao YM et al., after three months of recovery from COVID-19, also showed reduced small airway functions similar to the present study [1]. Another study also stated a reduction in the FEF 25-75% with normal FVC, FEV1, and FVE1% [13]. A similar prospective cohort study conducted on 87 COVID-19 patients on pulmonary functions again depicted a reduction in FEF 25-75% of less than 65% in eight patients [20]. PEFR in the current study was found to be reduced and was found statistically significant. Large airway obstructions are identified by measuring PEFR. Reduction in PEFR in the recent study supports an obstructive disorder. In contrast to the present study, another study showed average PEFR values [13].

Authors noted a reduction in all the lung volumes except for tidal volume, which was found to be increased. The British Thoracic Society (BTS) guideline recommends evaluating PFTs three months after discharge in patients suspected of having an interstitial illness [21]. Similarly, a review article by Torres-Castro R et al., stated that most investigations were carried out one month after the COVID-19 infection, and as it was not possible to identify whether the limitation was caused by the disease or inflammation, evaluation done early may lead to errors in functional diagnosis [22].

Gender-specific variations were noted with a reduction of FEV1, FVC, FEF 25-75%, and FEF 25% in females compared to males. Females tend to have lower values compared to their male counterparts [23]. A study by Premanand P et al., which found similar results as the present study, stated that lung growth continues for many years after somatic growth has finished in males. Therefore, the value in males tends to be higher than in females [13]. In the north of Karnataka, as far as we know, the present study was the first study on COVID-19 recovery among health sciences students.

Limitation(s)

Including mild cases of COVID-19 and medical professionals from a single private hospital, the non evaluation and comparison of pre-COVID-19 pulmonary functions, and lack of follow-up are some of the study's limitations.

CONCLUSION(S)

The COVID-19-recovered students showed altered respiratory functions. A mixed disease pattern was noted, with a restrictive and obstructive pattern. COVID-19-induced alveolar damage and pulmonary interstitial fibrosis may be the reason for the changes in lung function. FEV1%, FVC, FEF 25%, and FEF 25-75% test values were significantly higher in males than in females of the study group. The generated information has the potential to instill

confidence in younger healthcare professionals, encouraging them to persist with their work schedule without apprehension, while ensuring the implementation of appropriate protective measures. Due to the unpredictability of the disease, it is necessary to evaluate their PFT not only in the short term but also over the long-term. With routine follow-up, the improvement or decline in PFT can be adequately evaluated.

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