ISSN: 2309-5288 (Print)
ISSN: 2309-6152 (Online)
CODEN: JCLMC4

Journal of Coastal Life Medicine

Pulmonary Function in COVID-19 Patients After Discharge

Received: 20 October 2022, **Revised:** 24 November 2022, **Accepted:** 26 December 2022

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Keywords:

COVID-19 Pulmonary function test Spirometry

Abstract

Background : The COVID-19 pandemic has affected the whole world. It is now an established fact that the disease affects respiratory system of the victim. In the present study we decided to evaluate pulmonary function of discharged COVID-19 patients (n=335).

Objectives: 1. To carry out Pulmonary function test (Computerised spirometry) in study group and control group. 2. Compare the results between two groups

Methods: Patient's symptoms & associated co-morbidities were noted during history taking. According to the HRCT scores patients were divided into three groups- mild, moderate & severe. Computerized spirometry was carried out in all these patients and controls(n=300). Pulmonary function test(PFT) parameters from both the groups were analysed.

Results: All the PFT parameter values were very significantly low in subject group compared to those of control group ($p < 0.000l$), except FEF.2-1.2, which was reduced in subject group but not to statistically significant level ($p > 0.05$). Out of total 335 patients 57 had restrictive lung disease, 34 obstructive and 65 had mixed disorder whereas 179 had normal FVC & FEV1. Out of 355 patients, 193(57.62 %) had reduction in PEFR and 142 patients (42.38 %) were having normal PEFR.

Conclusion: It was observed that, reduction occurs in lung function for few months after COVID-19 infection to some extent. It is necessary to follow these patients for a longer period of time, to find out the persistence of derangement in lung function after COVID-19 infection.

1. Introduction:

The current worldwide spread of the Corona virus has caused widespread panic. On the eleventh of March in 2020, COVID-2019, a coronavirus illness, was designated a pandemic by the World Health Organisation (WHO). a 6.5 million individuals have been infected, and about 400,000 have died as a result [2]. According to the most up-to-date WHO data (November29, 2020), the COVID-19 pandemic has afflicted over 60 million individuals worldwide, resulting in approximately 1.5 million fatalities [3]. The main system affected is the respiratory system. Patients with asthma or a condition known as acute respiratory distress syndrome are only two of the many possible clinical presentations [4,5,6]. Multiple pathologic lung events have been proposed in recent research on COVID-19. Diffuse alveolar epithelial degradation, hyaline membrane development, capillary injury and bleeding, proliferation of fibrous tissue in the alveoli and consolidation of the lungs are all examples of these [7]. Alveolar epithelium and the endothelial cells sustain severe damage, leading to subsequent

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ISSN: 2309-6152 (Online)
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fibroproliferation [8]. It may cause pulmonary hypertension and fibrosis of the lungs if there is persistent vascular or alveolar remodelling [9]. These results suggest that regular checks on the lung function of recently released patients are warranted. Objective functional respiratory examinations often make use of pulmonary function tests (PFTs) such the use of s diffusion ability, and lung volumes. In addition to a loss of capacity for diffusion and limiting ventilatory deviations, which are both associated with the seriousness of the illness, previous study has shown that patients might have a narrowing of the airway imperfections and tiny airways fail that is permanent yet unrelated to the extent of the illness. The purpose of this study was to correlate disease severity with the extent to those individuals were unable to exhale on their own by using spirometry to measure pulmonary function for a month after admission for COVID-19 at our additional hospital.

2. Methods

335 patients referred from Institutional hospital for spirometry and who could do the PFT satisfactorily were evaluated after noting down their primary information. Primary information was noted down on prepared patient information sheet, that included name, age, sex, anthropometric measurements, HRCT score, any associated co-morbidity etc. Those with history of smoking were excluded. Approval from Institutional Ethical Committee (IEC) was taken prior to commencement of research project. The patients were divided into three groups depending on HRCT score: Mild group (Score between 0-7), Moderate group (Score between 8-17), Severe group (Score ≥ 18) [12]. Those with history of smoking were excluded. Those with poor effort to perform the spirometry were excluded. All preventive measures were taken for protection from spread of infection that included disinfection of PFT laboratory, instruments, use of PPE kit, etc. A control group (300) of age & sex matched apparently healthy individuals and not having suffered from COVID-19 disease was selected from institutional workers. Informed written consent was taken from each person from both the groups. Each person from both the groups was explained in detail about the spirometry procedure before carrying out the test so as to achieve maximum effort from their side. The spirometry was done as per guidelines by American Thoracic Society(ATS) [13]. The instrument used for test was Helios-407(RMS Chandigarh, India). For each manoeuvre three readings were taken and maximum one was chosen as final reading.

Statistical analysis: The data collected was summarized by computing mean and standard deviation (S.D.) of each study variable. Analysis was done by applying paired 't' test and one way ANOVA by using Instat 3 software. The difference was said to be significant if $p < 0.05$.

3. Results

The mean age of patient group was 46.7 ± 6.97 and that of control was 49.28 ± 14.62. Table 1 shows the findings of other anthropometric parameters among these two groups.

Table 1: Anthropometric measurements

Parameter	**Control(n=300)** **Mean ± SD**	**Subjects (n=335)** **Mean ± SD**	**p value**
Age	46.7 ± 6.97	49.28± 14.62	0.22 ns
Height(cm)	164.55 ±7.36	162.04 ± 9.9	0.08 ns
Weight(kg)	61.65 ± 45.82	68.87 ± 45.82	0.29 ns

ns: Statistically not significant

There was no any significant difference in height and weight of the two groups ($p>0.05$). The symptoms noted in these patients (Table 2) at time of PFT were-generalized weakness in 67(20%), breathlessness on exertion in 35 (10.4%), dry cough in 22 (6.5%), chest pain in 10 (2.9%),leg pain in 9 (2.6%), fever in 8 (2.3%), common cold in 7 (2.08%), sore throat in 4(1.1%), headache in 3(0.8%) and GI upset in 3(0.8%).

Table 2: Symptoms and comorbidities in COVID-19 patients after discharge

Symptom	**Number of patients**	**%**
Weakness	67	20

ISSN: 2309-5288 (Print)
ISSN: 2309-6152 (Online)
CODEN: JCLMC4
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Breathlessness	35	10.4
Dry cough	22	6.5
Chest pain	10	2.9
Leg pain	09	2.6
Fever	08	2.3
Common cold	07	2.08
Sore throat	04	1.1
Headache	03	08
GI upset	03	0.8
Co-morbid condition	**Number of patients**	**%**
Hypertension	91	27.1
Diabetes mellitus	67	20
Bronchial Asthma	02	0.5
Hypothyroidism	02	0.5

The associated co-morbidities present in these patients were (Table 2) hypertension in 91 (27.1%), diabetes mellitus in 67 (20%), bronchial asthma in 3 (0.5%) and hypothyroidism in 3 (0.5%).

In table 3 values of different PFT parameters of two groups are shown.

Table 3: PFT Parameters in control & subject group

PFT parameter	Control (n=300) Mean ± SD	Subjects (n=335) Mean ± SD	P value
FVC (L)	3.07 ± 0.3	2.41 ± 0.7	<0.0001
FEV1(L)	2.79 ± 0.36	2.06 ± 0.62	<0.0001
FEV1/FVC (%)	91.25 ± 5.55	85.63 ± 7.5	<0.0001
FEF25-75(L/S)	3.68 ± 0.85	2.43 ± 0.97	<0.0001
FEF.2-1.2(L/s)	5.87 ± 1.56	4.33 ± 10.71	<0.3112
PEFR(L/s)	6.78 ± 1.61	4.93 ± 1.91	<0.0001
MVV(L/min)	119.22 ±± 26.68	82.02 ± 26.23	<0.0001

All the PFT parameter values were very significantly low in subject group compared to those of control group (p <0.000l), except FEF.2-1.2 whose value was reduced in subject group but not to significant level (p>0.05). Table 4 shows the values of different PFT parameters in control & mild groups.

In comparison to the control category, all PFT metrics were considerably lower in the group with mild illness (p0.0001). The amounts of the various PFT parameters in both the control and strong groups are shown in Table 4. When comparing the group with moderate activity to the control group, all PFT values were considerably lower in the moderate group (p0.001). The amounts of the various PFT parameters in both the control and severe group are shown in Table 4. When comparing the group with severe illness to the control group, all PFT metrics were considerably lower in the serious group (p0.0001). Variables of the PFT are compared among the three groups of subjects in Table 5.

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Table 4: PFT Parameters in control & mild, moderate and severe groups.

PFT parameter	**Control(n=300)** **Mean ± SD**	**Mild group (n=255)** **Mean ± SD**	**P value**
FVC (L)	3.07 ± 0.3	2.45 ± 0.70	<0.0001
FEV1(L)	2.79 ± 0.36	2.10 ± 0.62	<0.0001
FEV1/FVC (%)	91.25 ± 5.55	85.74 ± 7.97	<0.0001
FEF25-75(L/s)	3.68 ± 0.85	2.49 ± 0.99	<0.0001
FEF.2-1.2(L/s)	5.87 ± 1.56	3.80 ± 1.76	<0.0001
PEFR(L/s)	6.78 ± 1.61	4.93 ± 1.81	<0.0001
MVV(L/min)	119.22 ±± 26.68	81.81 ± 25.63	<0.0001
PFT parameter	**Control (n=300)** **Mean ± SD**	**Moderate group (n= 72)** **Mean ± SD**	**P value**
FVC (L)	3.07 ± 0.3	2.28 ± 0.68	<0.0001
FEV1(L)	2.79 ± 0.36	1.95 ± 0.63	<0.0001
FEV1/FVC (%)	91.25 ± 5.55	85.22 ± 5.96	<0.0001
FEF25-75(L/s)	3.68 ± 0.85	2.28 ± 0.92	0.0004
FEF.2-1.2(L/s)	5.87 ± 1.56	3.63 ± 2.13	<0.0001
PEFR(L/s)	6.78 ± 1.61	4.92 ± 2.15	0.0038
MVV(L/min)	119.22 ±± 26.68	82.77 ±29.18	<0.0001
PFT parameter	**Control(n=300)** **Mean ± SD**	**Severe group (n=8)** **Mean ± SD**	**P value**
FVC (L)	3.07 ± 0.3	2.12 ± 0.71	<0.0001
FEV1(L)	2.79 ± 0.36	1.83 ± 0.65	<0.0001
FEV1/FVC (%)	91.25 ± 5.55	86.21 ± 4.32	<0.0001
FEF25-75(L/s)	3.68 ± 0.85	2.21 ± 1.00	<0.0001

ISSN: 2309-5288 (Print)
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FEF.2-1.2(L/s)	5.87 ± 1.56	3.69 ± 2.99	<0.0001
PEFR(L/s)	6.78 ± 1.61	5.34 ± 3.55	<0.0001
MVV(L/min)	119.22 ±± 26.68	88.62 ± 24.75	<0.0001

Though the values of all PFT parameters were lowered down as the severity increased from mild to severe, but the difference in them was not statistically significant (p>0.05).

In mild group out of total 255 patients 39 had restrictive lung disease, 24 obstructive and 44 had mixed disorder whereas 148 had normal FVC & FEV1. In moderate group out of total 72 patients 16 had restrictive lung disease, 9 had obstructive and 17 had mixed disorder whereas 30 patients had normal FVC & FEV1.In severe group out of total 8 patients 2 had restrictive lung disease, 1 had obstructive and 4 had mixed disorder whereas 1 patient was having normal FVC and FEV1.Another important striking finding was that out of total 355 patients, 193(57.62 %) had reduction in PEFR and 142 patients (42.38 %) were having normal PEFR.

Table 5: ANNOVA showing comparison between various groups

PFT parameter	**Mild group (n=255)** **Mean ± SD**	**Moderate group (n= 72)** **Mean ± SD**	**Severe group (n=8)** **Mean ± SD**	**p value**
FVC (L)	2.45 ± 0.70	2.28 ± 0.68	2.12 ± 0.71	0.0955 ^{ns}
FEV1(L)	2.10 ± 0.62	1.95 ± 0.63	1.83 ± 0.65	0.1131 ^{ns}
FEV1/FVC(%)	85.74 ± 7.97	85.22 ± 5.96	86.21 ± 4.32	0.8542 ^{ns}
FEF2575(L/s)	2.49 ± 0.99	2.28 ± 0.92	2.21 ± 1.00	0.2192 ^{ns}
FEF.21.2(L/s)	3.80 ± 1.76	3.63 ± 2.13	3.69 ± 2.99	0.7901 ^{ns}
PEFR(L/s)	4.93 ± 1.81	4.92 ± 2.15	5.34 ± 3.55	0.8377 ^{ns}
MVV(L/min)	81.81 ± 25.63	82.77 ±29.18	88.62 ± 24.75	0.7554 ^{ns}

ns: Statistically not significant

4. Discussion

In present study we assessed pulmonary function of COVID-19 patients (335) by computerized spirometry. All the patients were referred for PFT after 30 days of RTPCR test. It is established fact that COVID-19 patients show some residual lung dysfunction even after few months of discharge from hospital. In our study restrictive pattern was seen in 17.01%, obstructive pattern in 10.15%, mixed pattern in 19.04% whereas 53.43 % patients had normal lung functions. In a systemic review and meta-analysis [14] restrictive pattern was seen in 15% and obstructive pattern in 7% of patients, our study shows almost similar findings. The little difference in findings may be due to time of assessment. When to provide tests to evaluate lung function is a crucial factor. Following discharge, individuals who are suspected to have an interstitial illness should be followed up with a month later, as recommended by the British Thoracic Society (BTS). [15]. In our study 118 patients (35.42%) had reduction in FVC and 94 patients (28.05%) had reduction in FEV1. In

ISSN: 2309-5288 (Print)
ISSN: 2309-6152 (Online)
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a study done at 3 months of follow up noticed 24% and 25% reduction in FVC and FEV1 values respectively [16]. The higher percentage reduction in the values in our study may be due to difference in timing of follow up PFT which was earlier in the present study (30-45days). Another important finding to be noted was, out of total 335 patients, 193 (57.61 %) had reduction in PEFR and 142 patients (42.38 %) were having normal PEFR. This may be due to weakness of respiratory muscles due to which patients were unable to exert greater force required for normal PEFR. 20 % of patients had generalized weakness at the time of evaluation of respiratory function.

Patients having COVID-19 who acquire pneumonia have been reported to have a restrictive lung pattern, which is linked to an elevated risk of potentially fatal concurrent medical conditions in certain research. [17,18]. These patients need to be followed for longer time by screening their pulmonary function so as to monitor and manage clinically relevant sequelae during follow- up [19].

It is now well established that many people infected with COVID-19 go on to develop pulmonary fibrosis. Pulmonary fibrosis has several contributors to its pathophysiology. Following the first phase of lung damage, there is severe inflammation while a repair effort is made [20]. The outcome might be a return to healthy lung architecture or the development of pulmonary fibrosis and permanent lung impairment. Regeneration through resident stem cells as well as tissue deposition fill up damaged regions [21].The phagocytic macrophages that clean up the alveolar debris also play a role in the healing process by producing growth factors and cytokines [22].The healing process includes angiogenesis, fibroblast activation, and collagen deposition. Fibroblastic infiltration of the alveoli, followed by transformation into the cells known as my and finally the deposition of an organising fibroblastic extracellular matrix, or ECM, are hallmarks of the organisational process in the presence of pulmonary exudates [23].Lung fibrosis is characterised by the a great deal of extracellular matrix (ECM). On a chest CT image, you can see that there is traction bronchiectasis and uneven thickening of the interlobular septum [24]. A restricted pattern in pulmonary function tests is seen in patients with pulmonary fibrosis. Weakness in the respiratory muscles might account for the decrease in PEFR seen in 193 (56.62%) participants. Muscle weakness following COVID-19 infection has only been the subject of a small number of research thus far. Long-term mechanical breathing may cause limb weakness, as seen in a research [25] conducted on COVID-19 ICU survivors. This weakness persisted a month after patients were released from the hospital. Few individuals, however, had impairment in their respiratory muscles. These patients will benefit greatly from a large-scale trial with long-term follow-up and chest physiotherapy procedures to improve respiratory function following COVID-19.

The main limitation of this study is that we do not have pulmonary function tests of the patients prior to acquiring COVID-19 infection. This limitation was partially remedied by comparing the values of PFT parameters of the patients with those of control group.

In summary we conclude that there is reduction in lung function for few months after COVID-19 infection to some extent. However it is necessary to follow these patients for a longer period to find how much is residual lung function derangement after COVID-19 infection. Pulmonary function tests is feasible in survivors of COVID-19 disease even in patients having COVID-19 pneumonia, we recommend to include PFT in follow up care of these patients.

Acknowledgements: We are thankful to Dean of the Institution & Head of Physiology department for allowing us to utilize infrastructure and equipment's. We are also grateful to all the patients for their co-operation and giving consent to use the data of investigation for research purpose. We also thank all technical staff in the department for their support in carrying out the PFT.

Conflict of Interest: The authors declare that there is no any conflict of interest (Financial interest or personal relationships that may influence the reported work in this article).

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