International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

Original Research Article.

Spirometric Analysis in Post-COVID Patients

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ABSTRACT

Background: The spread of COVID-19 has taken on pandemic proportions, affecting almost 50 million people and causing more than 1 million deaths worldwide. The COVID-19 pandemic has gained global attention owing to its rapid transmission despite extensive measures to contain it. The majority of patients developing COVID-19 pneumonia have bilateral lung involvement leading to respiratory failure or acute respiratory distress syndrome. As a new infectious disease-carrying risk of severe course and ICU admissions, it is particularly important to explore its sequelae. There has been extensive research on the acute course of disease but enough studies are not available about the long term fibrotic sequelae and its effect on quality of life. Hence the present study.

Aims and Objectives: 1. To study pulmonary function impairment in post covid patients. 2. To correlate spirometry changes with the severity of SARS-COV2 infection.

Methods: A prospective study was conducted in the Medicine department at Rajindra Hospital/ Govt Medical College Patiala involving patients recovered from COVID-19. The study group included all patients above 18 yrs of age who were diagnosed as COVID-positive. So 100 post-COVID patients admitted at Rajindra hospital/Govt Medical College Patiala were followed up after discharge to study the spirometric changes and risk of development of chronic lung disease. It was a prospective study where patients were analysed spirometrically at regular intervals.

Results: Abnormal spirometry was present in 16% patients after 6 months of COVID infection, thus necessitating longer follow-up in all post covid patients. Among the patients with abnormal spirometry, the majority of patients were had severe COVID-19.

Keywords: Spirometry, COVID-19, SARS-COV2 infection.

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Article History:

Received: 23-01-2023, **Revised:** 19-02-2023, **Accepted:** 12-03-2023

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2023.9.2.004	

INTRODUCTION

The spread of COVID-19 has taken on pandemic proportions, affecting almost 50 million people and causing more than 1 million deaths worldwide.[1] In December 2019, China reported an outbreak of pneumonia of unknown cause in Wuhan, the capital city of Hubei province.[2] Based on phylogeny and taxonomy on February 11, 2020, the *Coronaviridae* study group of the International Committee on Taxonomy of Viruses named the virus SARS–CoV2.[3] The World Health Organization (WHO) named the resultant disease Coronavirus disease (COVID-19).[4]

The entry route of SARS-CoV-2 into human cells is mainly facilitated by the angiotensin-converting enzyme 2 (ACE2) receptors, which seem to be expressed by type 2 pneumocytes.[5] The binding of SARS-CoV-2 to the ACE2 receptors could arise in acute systemic inflammatory responses and cytokine storm, consequentially leading to lung-resident dendritic cells (rDCs) activation, and to T lymphocytes production and release of antiviral cytokines into the alveolar septa and interstitial compartments.[5] Physicians across the globe are encountering a vast number of patients who have recovered from their acute COVID-19 pneumonia only to be left with severe residual lung fibrosis leading to limitation of their activity and long-term oxygen dependence.[6] Not much data is available yet on residual lung damage and its effect on lung function. In this prospective study, we aim to assess lung fibrosis and lung damage by spirometry and correlate it with the severity of the infection.

MATERIALS AND METHODS

Ous was a prospective study conducted in Rajindra Hospital, Patiala, Punjab involving patients who recovered from COVID-19. The patients were followed up for 6 months for persisting symptoms and changes in pulmonary function. All the patients included in the study were lab confirmed cases of COVID-19 infection (RTPCR or CBNAAT or TRUNAAT or RAT). Patients <18 years of age and pregnant females were excluded from the study population. Patients were categorized as mild, moderate and severe at the time of admission as per ICMR guidelines.[7]

Mild COVID-19 was defined as patients with uncomplicated upper respiratory tract infection, may have mild symptoms such as fever, cough, sore throat, nasal congestion, malaise, and headache without evidence of breathlessness or hypoxia (normal saturation). Moderate COVID-19 was defined as moderate pneumonia with no signs of severe disease with the presence of clinical features of dyspnea and or hypoxia, fever, cough, including SpO2 <94% on room air (90-94%), RR more or equal to 24 breaths/min.

Severe COVID-19 was defined as patient with clinical signs of pneumonia plus one of the following: respiratory rate >30 breaths/min, severe respiratory distress, SpO2 <90% on room air.

The study was conducted on patients admitted to the department of Medicine, Govt Medical College, Patiala, Rajindra Hospital Patiala. All lab-confirmed patients >18 years of age who gave informed consent to participation were included in the study.

All subjects were called for a follow-up visit at 1 month, 3 months, and 6 months after discharge at a post-COVID outpatient clinic at Rajindra Hospital, Patiala. Each subject answered a health-related questionnaire about persisting symptoms (if any) and underwent spirometry. A fully integrated PC-driven Easy on-PC spirometer with TrueFlow technology was used. The following parameters were measured: Forced vital capacity (FVC), Forced expiratory capacity at the first second of exhalation (FEV1) and FEV1/FVC ratio. The procedure was performed following ATS/ERS guidelines.[8] The height of the patients was also recorded. The results were compared with predicted values of FEV1, FVC & FEV1/FVC for their age and height which were calculated by NHANES spirometric reference standards as recommended by the latest ATS-ERS guidelines.[9,10] Spirometry was considered 'abnormal' if it met either of the obstructive or restrictive criteria.

Obstructive spirometric 'abnormality' was defined as the ratio of the forced expiratory volume in one second to the forced vital capacity (FEV_1/FVC) below the lower limit of normal for the reference standard. Restrictive spirometric 'abnormality' was defined as the FEV_1/FVC ratio greater than or equal to the lower limit of normal and FVC below the lower limit of normal for the reference standard. The lower limit of normal for FEV_1, FVC, and FEV_1/FVC ratio was directly obtained from the literature for the NHANES III reference standard.[9] Each subject had done three accepted manoeuvres and then the highest values were recorded and used in the subsequent analyses.

Data Collection and Analysis

The information collected was filled in a Microsoft Excel sheet. All the statistical calculations were done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

Data was described in terms of range; mean ± standard deviation (±SD), median, frequencies (number of cases), and relative frequencies (percentages) as appropriate. A comparison of quantitative variables between the study groups was done using paired T-test for non-parametric data. For comparing categorical data, the Chi-square ($\chi 2$) test was performed, and an exact test was used when the expected frequency is less than five. A probability value (*p-value*) less than 0.05 was considered statistically significant.

Table 1: Epidemiological and clinical parameters of study population

Mean Age (years)	51.32 ± 15.56
Males	31%
Females	69%
Hypertension	25%
Diabetes	19%
Cardiovascular disease	12%
Chronic respiratory disease	9%
Length-hospital stay (in days)	12.84
Length – oxygen therapy (in days)	8.93
Mild COVID	18%
Moderate COVID	27%
Severe COVID	55%

Table 2: Spirometric parameters after 1 month, 3 months and 6 months

	PREDICTED (Litres)	LLN(Litres)	AFTER 1 MONTH(Litres)	AFTER 3 MONTHS(Litres)	AFTER 6 MONTHS
FVC	4.19	3.38	3.61	3.72	3.80
FEV1	3.28	2.60	2.70	2.76	2.82
FEV1/FVC	0.78	0.68	0.75	0.74	0.74

Table 3: Spirometric patterns at the end of 1 month, 3months and 6 months

	At First Month		At Third Month		At Sixth Month	
PATTERN	**No. of patients**	**%**	**No. of patients**	**%**	**No. of patients**	**%**
NORMAL	70	70.0%	77	77.0%	84	84.0%
OBSTRUCTIVE	9	9.0%	8	8.0%	8	8.0%
RESTRICTIVE	21	21.0%	15	15.0%	8	8.0%
Total	100	100.0%	100	100.0%	100	100.0%

Table 4: Relation Of Age With Severity Of COVID-19

		Severity of COVID						Total	Chi-square value	p-value
		Mild		Moderate		Severe				
AGE GROUP	**< 40**	12	66.7%	8	29.6%	9	16.4%	29	25.712	0.001
(in years)	**41-50**	1	5.6%	7	25.9%	8	14.5%	16		
	51-60	1	5.6%	6	22.2%	21	38.2%	28		
	61-70	1	5.6%	4	14.8%	14	25.5%	19		
	> 70	3	16.7%	2	7.4%	3	5.5%	8		
Total		18	100.0%	27	100.0%	55	100.0%	100		

Table 5: Spirometric parameters in patients with mild disease

	PREDICTED (Litres)	LLN(Litres)	AFTER 1 MONTH(Litres)	AFTER 3 MONTHS(Litres)	AFTER 6 MONTHS
FVC	4.27	3.46	3.93	3.99	4.02
FEV1	3.43	2.75	2.95	3.01	3.05
FEV1/FVC	0.80	0.70	0.75	0.75	0.76

Table 6: Spirometric parameters in patients with moderate disease

	PREDICTED (Litres)	LLN(Litres)	AFTER 1 MONTH(Litres)	AFTER 3 MONTHS(Litres)	AFTER 6 MONTHS
FVC	4.63	3.76	4.05	4.15	4.23
FEV1	3.63	2.90	3.04	3.08	3.14
FEV1/FVC	0.78	0.68	0.75	0.74	0.74

Table 7: Spirometric parameters in patients with severe disease

	PREDICTED (Litres)	LLN(Litres)	AFTER 1 MONTH(Litres)	AFTER 3 MONTHS(Litres)	AFTER 6 MONTHS
FVC	3.95	3.17	3.29	3.43	3.52
FEV1	3.06	2.41	2.44	2.53	2.59
FEV1/FVC	0.77	0.67	0.75	0.74	0.74

RESULTS

The mean age of the study population was 51.32 years with a standard deviation of 15.56 years. In our study, 31% patients were females, and 69% patients were males. Sixty-three percentage of patients were on room air at the time of admission, 29% patients were on an oxygen face mask at the time of admission and 8% patients were on NRM at the time of admission. The mean spO2 was 89.62% with a standard deviation of 8.81%. The mean height of patients was 66.02 inches with a standard deviation of 3.75 inches. Twenty-five percentage of patients had hypertension, 19% patients had Diabetes Mellitus, 12% patients had coronary artery disease, 5% patients had COPD,4% patients had Bronchial Asthma and 3% patients had morbid obesity (BMI>40kg/m^2). In our study,55% patients had severe COVID-19, 27% patients had moderate COVID-19 and 18% patients had mild COVID-19. The mean duration of oxygen therapy was 8.93 days with a standard deviation of 8.02 days. The mean duration of hospital stay was 12.84 days with a standard deviation of 7.07 days.(Table 1)

The mean FVC at the end of 1 month, 3 months and 6 months were 3.61±0.95L, 3.72±0.94L and 3.80±0.93L. Thus, FVC continued to increase in the subsequent follow-ups. Similar findings were seen for FEV1. (Table 2) In the study, at the end of the first month, 21% patients had restrictive spirometric patterns. Out of these, 16% belonged to the severe group. At the end of the third month, 15% of patients had restrictive spirometric patterns out of which 12% had severe disease. Similarly, at the end of the sixth month, only 8% of patients had restrictive lung disease and 7% had severe disease during admission.(Table 3)

Also, 9% of the patients had an obstructive pattern on spirometry after the first month, and 8% had an obstructive pattern after the third month and sixth months as well. This same 9 % of patients were already on treatment for obstructive lung disease.

Among the mild cases of COVID, a maximum number of patients were of <40 years of age (66.7%). Amongst the moderate cases, the maximum number of patients were in the age group of <40 years (29.6%), followed by the age group of 41-50 years (25.9%), Amongst the severe cases, the maximum number of patients were of 51-60 years (38.2%) followed by 61-70 years (25.5%). The relation of age with the severity of COVID-19 is statistically significant with a chi-square value of 25.712 and a p-value of 0.001 (Table 4).

As per the tables 5,6,7; the patients with severe disease had lower FVC values than patients with moderate or mild disease. However, the patients with moderate disease had mean FVC values which were higher than patients with mild disease. Similar results were found with FEV1 values. The relation of FEV1 and FVC with severity was found statistically significant concerning the comparison between the moderate and severe groups. However, regarding the comparison between mild and severe groups or mild and moderate groups, the difference was found statistically insignificant. Also, the relation of FEV1/FVC ratio with severity was not found statistically significant (p-value>0.05).

DISCUSSION

As the COVID pandemic abates, a large number of patients are regularly coming to outpatient clinics with persistent respiratory symptoms. Both the patients as well as the treating physicians are in dilemma that what will be the outcome of the respiratory involvement. Will they recover fully, or they will be left with disabling symptoms? All over the globe, researchers are trying to answer this pertinent question and our current study is also in the same direction.

Previous studies have demonstrated impaired pulmonary function in as high as 77.5% post COVID patients 3 months after discharge[11] and a restrictive spirometric pattern in as high as 54% a month after the infection.[12] In a study by Salem at al, he compared 30 controls with 20 post COVID patients and observed restrictive lung impairment in 50% of cases compared to 20% in the control group.(p=0.026).[13] However, some studies reported reduced DLCO as the most common form of pulmonary function impairment.[5,14,15] To date, however, the available data remains heterogeneous, with relatively small sample sizes from single centres and predominantly observational methodology.

In our study, we found a high proportion of patients with altered lung function. After 1 month, 21% patients had a restrictive pattern on spirometry while 9% patients had obstructive pattern. Similiarly, at the end of the third month 15% of patients had restrictive pattern and 8% of patients had an obstructive pattern. After the sixth month, 8% patients had obstructive patterns and 8% patients had restrictive patterns. A total of 16% patients had abnormal pulmonary function testing even 6 months after the infection.

At the end of the first month in our study, 21% of patients had lower FVCs as compared to FVC LLN predicted for their age and height by NHANES spirometric reference standards as recommended by the latest ATS-ERS guidelines.[10] A study by Polese et al[12] who conducted this study after 36 days of discharge reported reduced FVC in 22 (54%) patients. However, reduction in FVC was noted in 27% patients and 7% patients in the studies by Thakur et al[16] and Eksombatchai et al[17] respectively. As per the data available from previous studies, pulmonary functions improved within few weeks with significant improvement during 6 months.[18]

When we compared the severity of COVID -19 infection with spirometric parameters, we found that a higher proportion of patients with altered lung function on spirometry had severe disease in contrast to the patients who had mild disease. In this study, out of the sixteen patients with altered lung function, 12 patients had severe disease during admission and 5 patients had moderate disease. The relation of FEV1 and FVC with severity was found statistically significant concerning the comparison between the moderate and severe groups. However, regarding the comparison between mild and severe groups or mild and moderate groups, the difference was found statistically insignificant. Also, the relation of FEV1/FVC ratio with severity was not found statistically significant (p-value>0.05). In the study by Mo et al, the TLC in severe pneumonia cases was lesser than other patients, suggesting higher impairment of lung volume in severe cases, however there was no significant difference among the discharged survivors with different severity with respect to other ventilatory defects (e.g. FEV1, FVC, FEV1/FVC).[19] A recent Chinese study found in cases of prior severe COVID-19 up to 33% of a restrictive pattern and in 16% small airway dysfunction; however, in that study, there were no significant differences in comparison with prior mild disease.[20] These findings suggest that the severity of disease or CT alterations are not the only factor associated with impairment of respiratory function.

The long-term impact that SARS-CoV-2 infection has on PFT will continue to emerge over the coming years. The studies regarding effect of interventions like systemic steroids on lung function is still lacking.

The limitations of our study include the possible undetected pre-COVID-19 lung function abnormality, the absence of imaging to evaluate myocardial involvement, the lack of study of the diffusion capacity of the lung for carbon monoxide (DLCO)and the inclusion of patients with obesity that might already had restrictive lung impairment.

CONCLUSION

From the study, it appears that pulmonary function impairment is most frequent in those who had a severe acute illness. Impaired pulmonary function testing was noticed in 30% of patients after one month of COVID-19 positivity with the restrictive pattern (21%) being predominant. There was an improvement in FVC in a large majority of patients, however, still, 16% of patients had persistent abnormal spirometry patterns even after 6 months Considering the high number of survivors of COVID-19, it is extremely important to characterize these symptoms, their persistence, and/or future remission to implement therapeutic interventions aimed at their prevention and/or treatment.

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Source of Support: Nil. **Conflict of Interest:** None Declared.

Cite this article as: Jasmeen Kaur Dua, RPS Sibia, Vikas Chander, Harinder Singh Gill. Spirometric Analysis in Post-COVID Patients. Int J Med Res Prof. 2023 Mar; 9(2): 16-20.
DOI:10.21276/ijmrp.2023.9.2.00X