Section: Physiology

Original Research Article

FORCED MID-EXPIRATORY FLOW ($FEF_{25-75\%}$) IN SUBJECTS RECOVERED FROM MODERATE AND SEVERE COVID-19

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Abstract

Background: Novel coronavirus disease 2019 (COVID-19) has infected more than 80 million people worldwide. This study was done to assess any impact of COVID-19, six months after initial infection, on pulmonary function in subjects recovered from moderate and severe COVID-19, in first wave (March 2020-August 2020).**Materials and Methods:** This was a cross-sectional observational study conducted in Department of Physiology, Gandhi Medical College and Hospital, Hyderabad- nodal centre of Telangana for COVID-19 after approval from institutional ethical committee. It was done in 30 subjects recovered from COVID-19, after six months of initial infection (study group) and compared with 30 normal subjects (control group). Subjects were explained about the procedure and informed consent was taken. Test was done using Digital Spirometer supplied by Schiller Health Care. Percentage predicted values of FVC, FEV1, FEV1/FVC, $FEF_{25-75\%}$ was noted. **Results:** The mean age of study and control group was comparable. The mean FVC (99.74 ± 14.44 %), FEV1 (117 ± 26.32 %), and FEV1/FVC (112.25 ± 17.17 %) in study group were lesser in comparison with control group, but were statistically not significant ($p > 0.05$). FEF25-75% in study group was 180.56 ± 56 %, lesser compared to control group (212.19±62.38) and was statistically significant ($p < 0.05$).**Conclusion:** Reduced $FEF_{25-75\%}$ in study group compared to control group indicates likely early onset of small airway obstruction.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has affected >367 million individuals and resulted in >5 million deaths worldwide.[1] In India it has affected >4 million people and caused>5 lakhs deaths.COVID-19 involves multiple organs primarily affecting lungs. Person-to-person transmission of SARSCoV-2 gained global attention and extensive measures were undertaken to effectively control its outbreak and for its treatment. Researchers across the globe have joined hands to investigate SARS-CoV-2 in terms of pathogenicity and transmissibility to deduce therapeutics in order to control this infection. However, the knowledgea bout the sequelae of SARS-CoV-2 infection remains limited. Follow up studies on lung function impairment up to six months.[2,3] have been done to show restrictive ventilatory dysfunction. Persistent impairment of pulmonary function and exercise capacity have been known to last for months or even years.[4] in there covered survivors from other coronavirus pneumonia severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Physiological and radiological abnormalities were still found in a considerable proportion of COVID-19survivors without critical cases 3 months after discharge.[5] In consideration to the widely documented l ung injuries related to COVID-19.[6], concerns have been raised regarding the assessment of the long-term impact of the infection on survivors. So present study was undertaken to describe the characteristics of pulmonary function inCOVID-19 survivors, six months after recovery.

Objectives

1. To compare the FEF25-75% of subjects recovered from moderate and severe COVID-19 with normal healthy subjects.
2. To assess small airway dysfunction (if any).

MATERIALS AND METHODS

Place of study: The present study was conducted at the Department of Physiology, Gandhi Medical College and Hospital.
Duration of study: October 2020 - June 2021

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Source of data: Study was done in 30 subjects after six months of initial infection, who got admitted in Gandhi Hospital during first wave, with moderate and severe disease (study group) and compared with 30 normal subjects (control group).
Sample size: 60
Study design: Cross-sectional observational study

Inclusion Criteria

1. Age group 20-60 years
2. Subjects recovered from moderate and severe COVID-19.

Moderate disease - clinical signs of pneumonia (fever, cough, dyspnoea, tachypnoea), SpO2 ≥ 90% on room air.
Severe disease - clinical signs of pneumonia (fever, cough, dyspnoea) plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO2 < 90% on room air.

Exclusion Criteria

1. Smokers
2. Individuals with history of lung diseases like tuberculosis, bronchial asthma,

COPD, interstitial lung diseases etc.
Equipment used: Digital spirometer supplied by the Schiller Health care India Pvt Ltd.

Study Protocol

The ethical committee clearance was obtained from the Ethical Committee of Gandhi
Medical College and Hospital. The study was performed after procuring informed
written consent from all the participants involved. Subjects were explained about the procedure. Test was done using Digital Computerized Spirometer supplied by Schiller Health Care (India).Percentage predicted values of Forced vital capacity (FVC),Forced expiratory volume in the first second of forced expiration (FEV1), Forced expiratory volume in the first second expressed as a percentage of FVC
(FEV1/FVC) Forced mid-expiratory flow (FEF25%-75%) were noted.

Data Analysis

The data was enteredand analysed using Microsoft Excel.

Statistical Analysis

For comparisons between two groups, Student's unpaired t-test was used for all
quantitative parameters and a p-value < 0.05 was considered to be statistically
significant.

RESULTS

Table 1: Shows The Anthropometric Data of the Subjects

	Control Group (Mean ± SD)	Study Group (Mean ± SD)
Age	35.4 ± 8.96	36.87 ± 10.35
Height (cm)	164.67 ± 8.91	165.93 ± 8.31
Weight (kg)	62 ± 11.28	67.66 ± 12.14
BMI (kg/m^2)	22.8 ± 3.5	24.6 ± 4.2

Table 2: Shows the Pulmonary Function Test Parametersin Control and Study Groups

Test Variables	Control Group (Mean ± SD)	Study Group (Mean ± SD)	p Value
FVC	104.16 ± 3.12	99.74 ± 14.44	> 0.05
FEV_1	121.93 ± 17.59	117 ± 26.32	> 0.05
FEV_1/FVC	113.65 ± 9.62	112.25 ± 17.17	> 0.05
$FEF_{25-75\%}$	212.19 ± 62.38	180.56 ± 56	< 0.05

Table 2 shows the mean FVC of study group and control group were 99.76 ± 15.06 and 104.16 ± 13.12 respectively. There was a decrease in the mean value of FVC in the study group compared to the control group, but the value was not statistically significant (p > 0.05). The mean FEV1 of the study group was 117.72 ± 26.32 and of the control group was 121.93 ± 17.60. There was a reduction in mean FEV1 of the study group compared to control group, but it was not statistically significant (p > 0.05).The mean FEV1/FVC of the study group was 112.25 ± 17.17 and of the control group was 113.64 ± 9.62. There was a decrease in the mean FEV1/FVC of study group compared to control group, but it was not statistically significant (p > 0.05).The mean FEF25-75% of the study group was 179.87 ± 55.25 and of the control group was 212.18 ± 62.38. There was a reduction in the mean FEF25-75% of study group compared to control group and it was statistically significant (p < 0.05).The same is depicted in the figure 1.

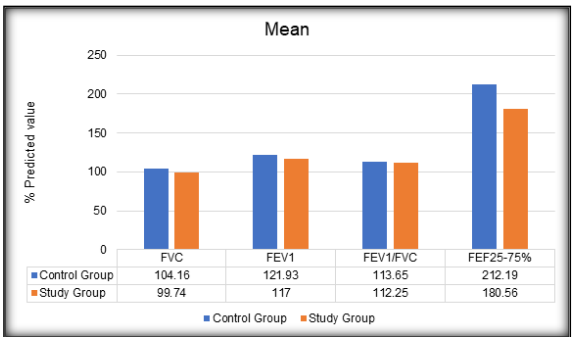

Figure 1: Pulmonary Function Test Parameters in Control and Study Groups

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DISCUSSION

The results from the present study had shown that, six months after the patients recovered from COVID-19, the average values of pulmonary functions were within the normal range, though reduced in the study group compared to the control group. The mean percentage predicted values of FVC, FEV1 and FEV1/FVC were within the normal range although reduced in the study group compared to the control group as seen in table 2 and figure 1. This reduction was not statistically significant ($p > 0.05$). Probable reason could be that these parameters had improved over the time of six months since the subjects recovered from COVID-19. This finding was consistent with a few previous studies. A prospective cohort study by Dararat Eksombatchai et al.[7] on pulmonary function and six-minutewalk test in patients after recovery from COVID-19 showed the mean percentage predicted values of FVC, FEV1, FEV1/FVC to be within the normal range. In a study on pulmonary function in patients surviving to COVID-19 pneumonia Alessia Fumagalli et al.[8] observed an improvement in pulmonary function after 6 weeks, though FVC was still lower than normal suggesting that some degree of restrictive alteration still persisted. In another study on a cohort of SARS survivors D S Hui, G M Joynt et al.[9]found that mean percentage predicted values of FVC and FEV1 were within the normal limits both at 3 months and 6 months. Among 110 subjects, only 6 (5.5%) subjects had FVC < 80% of the predicted value and 3 (2.7%) subjects had FEV1 < 80% of the predicted value at the end of 3 months after recovery from SARS. At the end of 6 months, 4 (3.6%) subjects had FVC < 80% of predicted value and 4 (3.6%) subjects had FEV1< 80% of the predicted value. Another probable reason for the improvement of FVC, FEV1 and FEV1/FVC could be due to pulmonary rehabilitation followed consistently by the subjects even after the recovery. A randomized controlled study was done by Kai Liu et al (10) on respiratory rehabilitation in elderly patients with COVID-19 to investigate the effects of 6-week respiratory rehabilitation training on respiratory function. They recruited 72 participants, of which 36 patients underwent respiratory rehabilitation and the rest without any rehabilitation intervention. After 6 weeks of respiratory rehabilitation in the intervention group, they found significant differences in FEV1(L), FVC(L) and FEV1/FVC%. Thus, they concluded that six-week respiratory rehabilitation can improve respiratory function.

The mean percentage predicted value of FEF25-75% was within the normal limit but reduced in the study group compared to the control group as seen in table 2 and figure1. This reduction was statistically significant ($p < 0.05$) and it may be probably due tolikely early onset of small airway dysfunction, functioning of small airways is yet to be recovered, as in normal healthy subjectsor any occult airway disease. It was well correlated with observation in previous studies.[11,12] In a study done by Rachna Parashar, Ankur Joshi et al.[13]they found that the mean percentage predicted value of FEF25-75% was within the normal limits in the overall study group (n=255) as well as in mild (n=42), moderate (n=82) and severe (n=131) groups of COVID-19 survivors, greater than or equal to 2 weeks after discharge from the hospital. There were no significant changes in the mean percentage predicted value of FEF25-75% among the severity groups (p-value > 0.05).A prospective study on lung ventilation function characteristics of survivors from severe COVID-19 was conducted by Xianyong Li et al.[14] They observed that the abnormal rate of lung ventilation function was high near discharge, with small airway dysfunction accounting for 50% of all patients. Autopsies of three deceased COVID-19 patients showed necrotizing bronchiolitis, alveolar inflammatory cell infiltration partial alveolar hyaline membrane formation and alveolar structure destruction in a study done by Yao X H et al.[15] which could explain the small airway dysfunction. Another study by Z. Xu, L. Shi, Y. Wang et al.[4] showed the pathophysiological changes after COVID-19 infection mainly were double diffuse lung tissue damage associated with cellular fibre mucous exudate, leading to a wide range of interstitial inflammatory change, whose manifestations after the invasion of the coronavirus in the airway were bronchial epithelial basement membrane thickening, alveolar walls transparent sample, the structure of lung tissue damage, extracellular matrix accumulation in great quantities, interstitial fibrosis caused by the inflammation injury of lung tissue, desquamation of type II alveolar pneumocytes resulting in lack of surface active substance, which leads to the closed small airways, and these pathological changes result in the decrease of lung compliance and abnormal small airway function, thereby seriously affecting pulmonary gas exchange. The final manifestations were restricted ventilation dysfunction, small airway dysfunction, and diffuse dysfunction. So, it was not only restrictive ventilation dysfunction but also obstructive pattern or mixed pattern and small airway dysfunction were observed as long-term sequelae of COVID-19.[13]

Limitations of the study

Limitations of the present study were that, it was a cross-sectional study with a small sample size and a simple spirometric approach. There was also a lack of baseline value of pulmonary function tests before COVID-19 infection. Another concern was that COVID-19 pneumonia during the study period was mostly caused by alpha variants, which have different clinical manifestations to other variants of more recent concern in India

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CONCLUSION

Significant reduction of FEF25-75% is suggestive of, likely early onset of small airway dysfunction, which calls for further follow up and recommendation of pulmonary rehabilitation intervention, to prevent the post COVID-19 sequalae.

Conflict of Interest – Nil
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REFERENCES

1. WHO Coronavirus (COVID-19) Dashboard. (2022). Accessed: 26.01.2022: https://covid19.who.in.
2. Sonnweber T, Sahanic S, Pizzini A, et al. Cardiopulmonary recovery after COVID-19—an observational prospective multi-center trial. Eur Respir J. 2020. https:// doi. org/ 10. 1183/ 13993 003. 03481- 2020.
3. Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. The Lancet. 2021. https:// doi. org/ 10. 1016/ S0140-6736(20) 32656-8.
4. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020 Apr;8(4):420-422.
5. Park WB, Jun KI, Kim G, Choi JP, Rhee JY, Cheon S et al. Correlation betweenPneumonia Severity and Pulmonary Complications in Middle East Respiratory Syndrome. J Korean Med Sci. 2018 May 10;33(24): e169.
6. Yu-miaoZhaoa, Yao-min Shangc, Wen-bin Songd, Qing-quan Lie, Hua Xiee, Qin-fu Xuf et al. Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. EClinicalMedicine. Aug 2020; 25:100463.
7. DararatEksombatchai, Wongsinin T, Phongnarudech T, Thammavaranucupt K, Amornputtisathaporn N and Sungkanuparph S. Pulmonary function and six-minute-walk test in patients after recovery from COVID-19: A prospective cohort study. PLoS One. 2021 Sep 2;16(9): e0257040.
8. Alessia Fumagalli, Misuraca C, Bianchi A, Borsa N, Limonta S, Maggiolini S et al. Pulmonary function in patients surviving to COVID-19 pneumonia. Infection. 2021 Feb;49(1):153-157.21.
9. Hui DS, Joynt GM, Wong KT, Gomersall CD, Li TS, Antonio G et al. Impact of severe acute respiratory syndrome (SARS) on pulmonary function, functional capacity and quality of life in a cohort of survivors. Thorax. 2005 May;60(5):401-9.
10. Liu K, Zhang W, Yang Y, Zhang J, Li Y and Chen Y. Respiratory rehabilitation in elderly patients with COVID-19: a randomized controlled study. Complement Ther Clin Pract. 2020;39(101166):1.
11. Ayad Mohammed Salem, Al Khathlan N, Alharbi AF, Alghamdi T, AlDuilej S, Alghamdi M et al. The Long-Term Impact of COVID-19 Pneumonia on the Pulmonary Function of Survivors. Int J Gen Med. 2021 Jul 9; 14:3271-3280.
12. Darcis G, Bouquegneau A, Maes N, Thys M, Henket M, Labye F et al. Long-term clinical follow-up of patients suffering from moderate-to-severe COVID-19 infection: a monocentric prospective observational cohort study. Int J Infect Dis. 2021 Aug; 109:209-21.
13. Rachna Parashar, Joshi A, Raghuwanshi P, Joshi R, Hulke S and Sharma JP. Patterns and Trajectories of Pulmonary Function in Coronavirus Disease 2019 Survivors: An Exploratory Study Conducted in Central India. Cureus. 2022 Jul 17;14(7): e26955.
14. Xianyong Li, C. Wang, S. Kou, P. Luo, M. Zhao and K. Yu. Lung ventilationfunction characteristics of survivors from severe COVID-19: a prospective study. Critical Care 2020; vol. 24, no. 1, p. 300.
15. Yao XH, Li TY, He ZC, Ping YF, Liu HW, Yu SC, et al. A pathological report of three COVID-19 cases by minimally invasive autopsies. Zhonghua Bing Li Xue Za Zhi. 2020; 49(5): 411–417. pmid:32172546.

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