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Respiratory manifestations of long COVID syndrome and pulmonary function abnormalities at 3-months after COVID-19 infection: A single center experience from Sri Lanka

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Abstract

Background: Long COVID syndrome (LCS) is a recognized sequel of SARS-CoV-2 infection. The aim of this study was to identify the respiratory symptoms of LCS and pulmonary function abnormalities in asymptomatic patients and those with mild to moderate disease, following their recovery from SARS-CoV-2 infection.

Methods: An observational study was conducted by recruiting COVID-19 patients presenting for follow-up at 3-months after discharge from intermediate care centre, Gampaha. Patients who had asymptomatic or mild-moderate COVID-19 were recruited by convenient sampling. Symptoms were assessed by an interviewer-administered questionnaire. Lung function was assessed by spirometry.

Results: There were 88 patients with a median age of 40 (28-51) years with female predominance (n=85, 96.6%). COVID-19 severity assessment revealed asymptomatic infection in 24 (27%), mild disease in 38 (40.9%) and moderate disease in 26 (31.8%) patients. Symptoms of LCS were present in 13 (54.2%) individuals who were asymptomatic and in 51 (79.7%) patients who had mild-moderate disease at the time of diagnosis. At least one respiratory symptom of LCS was seen in 64 (73%) patients at 3-months and the commonest was shortness of breath (SOB) (n=59, 67%). Majority of patients had mMRC grade 1 (n=39, 66.1%) or grade 2 (n=17, 28.8%) shortness of breath. Presence of LCS was significantly associated with the disease severity (p=0.013) and presence of a comorbidity (p=0.016). Abnormal spirometry was noted in 67% and majority had a restrictive pattern (n=56, 64%). Abnormal spirometry findings were identified in 17 (71%) asymptomatic patients and 50 (78%) with mild-moderate disease.

Conclusions: Presence of respiratory symptoms of LCS is common following SARS-CoV-2 infection. SOB was the commonest manifestation and the frequency of respiratory symptoms was significantly higher in the presence of a comorbidity and increased disease severity. Abnormal spirometry were seen in a majority at 3 months following COVID-19.

Key words: SARS-CoV-2, COVID-19, long COVID, respiratory symptoms, dyspnea, spirometry

Introduction

Long COVID syndrome (LCS) is a recognized sequel of COVID-19 infection. It is defined as a wide range of new, returning or ongoing health problems that people can experience, four or more weeks following infection with the SARS-CoV-2 virus.[1] Long term clinical sequalae have been found in COVID-19 survivors irrespective of age or comorbidities and therefore pose a significant burden for people of all age groups including adults with multiple comorbidities, as well as healthy younger population.[2]

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Most studies done up to now regarding long term sequelae of the infection have focused on patients with moderate-severe disease as they are the ones who are usually admitted to healthcare institutions for management.[3] Therefore, asymptomatic and mildly symptomatic patients have not been widely evaluated for the presence of such sequelae and they may present later with long term complications of the disease. At the time of writing, there are 237 million confirmed cases of SARS-CoV-2 infection worldwide.[4] In Sri Lanka, there are over 550,000 reported cases[5] with approximately 500,000 discharges from hospitals. A proportion of these patients are likely to develop LCS.

At present, there are no published data on the post-infection sequelae in Sri Lanka. Thus, it is important to investigate for possible long-term effects and associated factors predisposing to such consequences and thereby incorporate measures for early recognition and intervention. The aim of this study was to determine the respiratory symptoms of LCS and pulmonary function abnormalities at 3-months, following recovery from asymptomatic or mild-moderate COVID-19 disease.

Methods

An observational study was conducted at the respiratory clinic, District General Hospital, Gampaha for a period of 6 months commencing from December 2020. The study participants were individuals above 18 years, presenting for follow up at 3-months after recovery from asymptomatic or mild-moderate COVID-19 infection. These were patients managed at a designated intermediate care centre during the period of acute infection. Disease category was defined according to the WHO COVID-19 disease classification.[6] Asymptomatic infection was defined as individuals with a positive test for SARS-CoV- 2 with absent symptoms; mild disease was defined as symptomatic patients meeting the case definition for COVID-19 but without evidence of pneumonia or hypoxia and moderate disease was defined as patients with clinical signs of pneumonia but no signs of severe pneumonia such as SpO2 ≤ 90% on room air. The disease severity was determined by the details on the diagnosis card given at the time of discharge.

All patients presenting to the clinic during the study period and fulfilling inclusion criteria were included. Patients with dementia, learning disability, and other cognitive or communication impairment were excluded from the study. Those with preexisting lung disease were not excluded. Informed verbal consent was obtained from all the participants.

An interviewer-administered questionnaire was used to gather sociodemographic data, symptoms during the acute phase of the illness and symptoms present at the follow up visit. Shortness of breath (SOB) was graded using the modified Medical Research Council (mMRC) dyspnoea scale.[7] Pulmonary function was assessed by spirometry performed by an experienced technician. Forced expiratory volume in the 1st second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, forced expiratory flow at 25-75% (FEF 25-75) were measured and these results along with the flow volume loops were interpreted by a respiratory physician.

Ethical approval for the study was obtained from the Ethics Review Committee of the Faculty of Medical Sciences, University of Sri Jayewardenepura. (Ref – COVID 06/21)

Data analysis

Data were entered in MS EXCEL and statistical analysis was performed using IBM SPSS 25.0 software. A p value <0.05 was considered as statistically significant. Categorical variables were expressed as frequencies and compared among groups using the Chi-square test. Continuous variables in a skewed distribution were expressed as median ± interquartile range (IQR) and compared using Mann Whitney-U test.

Results

A total of 88 patients were recruited to the study and 85 (96.6%) were females. The median age was 40 (28-51) years. The comorbidities in the sample included hypertension (n=9, 10.2%), diabetes mellitus (n=8, 9.1%), dyslipidaemia (n=6, 6.9%) and ischemic heart disease (n=1, 1%). Asthma was present among four (4.5%) participants.

Disease severity during their hospital admission revealed asymptomatic disease in 24 (27.3%), mild disease in 36 (40.9%) and moderate disease in 28 (31.8%). Symptoms during hospital admission included body ache (n=25, 28.4%), fever (n=24, 27.3%) and diarrhoea (n=4, 4.5%) in addition to the respiratory symptoms described in Table 1.

Respiratory symptoms of long COVID syndrome

Majority of patients (n=64,72.7%) were found to have at least one respiratory symptom of LCS. Symptoms were present in 13 (54.2%) individuals who were asymptomatic and in 51 (79.7%) patients who had mild-moderate disease at the time of diagnosis.

The commonest symptom was shortness of breath (SOB) followed by headache (Table 1). Frequency of SOB increased from 14% during the acute phase to 67% at 3-months, whereas the frequency of all other symptoms were reduced. SOB was the commonest new-onset symptom at 3-months (n=48, 54.5%).

Severity of SOB in patients revealed mMRC grade 0 in 1 (1.7%), grade 1 in 39 (66.1%), grade 2 in 17 (28.8%) and grade 3 in 2 (3.4%).

Occurrence of any respiratory symptom of LCS was significantly associated with the presence of a comorbidiy (p=0.02) and the severity of COVID-19 infection (p=0.03). Age was not significantly associated with the presence of symptoms (Table 2).

Patients who had mild-moderate disease had higher frequency of SOB at 3-months (n=48,75%) compared to patients with asymptomatic infection (n=11, 45.8%). This difference was statistically significant (p=0.01). The presence of any comorbidity was also significantly associated with SOB at 3-months (χ^2=5.814; p=0.01).

Pulmonary function abnormalities at 3-months

Abnormal spirometry was observed among 67 (76.1%) study participants and restrictive pattern was the commonest abnormality observed (n=56, 63.6%) (Table 3).

Abnormal spirometry at 3 months did not show any association with age, comorbidities (including asthma), presence of shortness of breath and disease severity (Table 4).

Table 1. Presence of respiratory symptoms during hospital admission and at 3-months follow up

Symptom	*During admission n (%)*	*3-months n (%)*	*New-onset symptoms at 3-months n (%)*
Headache	17 (19.3)	9 (10.2)	6 (6.8)
Cough	17 (19.3)	3 (3.4)	3 (3.4)
Sore throat	15 (16.7)	1 (1.1)	0
Shortness of breath	12 (14)	59 (67)	48 (54.5)
Rhinitis	10 (11.4)	1 (1.1)	1 (1.1)
Other*	34 (38.6)	6 (6.8)	4 (4.5)

*Other symptoms included diarrhoea, bodyaches, fever, fatigue

Table 2. Factors associated with the presence of respiratory symptoms at 3-months

Characteristic	*Symptoms**		*Total*	*Significance*
	Present n=61	*Absent n=27*	*n=88*	
Age, median (IQR)	43 (28-51.5)	38 (25-46)	40 (28-51)	p=0.09
Presence of a comorbidity, n (%)	18 (90)	2 (10)	20 (22.7)	p=0.02
COVID-19 disease severity, n (%)				
Asymptomatic	12 (50)	12 (50)	24 (27.3)	
Mild	31 (81.6)	07 (18.4)	38 (43.2)	p=0.03
Moderate	18 (69.2)	08 (30.8)	26 (29.5)	

*Headache not included

Table 3. Spirometry results in patients with COVID-19 at 3-months

Spirometry result	*Frequency (%)*
Normal	21 (23.9)
Restrictive	56 (63.6)
Obstructive	3 (3.4)
Mixed (Restrictive + Obstructive)	8 (9.1)

Table 4. Association of patient characteristics and spirometry results at 3-months

	Normal spirometry n=21	*Abnormal spirometry n=67*	*Total n=88*	*Significance*
Age (median, IQR)	30 (26-47)	43 (23-52)	40 (28-51)	p=0.15
Co morbidities, n (%)	06 (30)	14 (70)	20 (22.7)	p=0.46
Asthma*	0 (0)	4 (100)	4 (4.5)	p=0.25
SOB	14 (23.7)	45 (76.3)	59 (67)	p=0.97
Disease severity				
Asymptomatic	7 (29.2)	17 (70)	24 (27.3)	
Mild	7 (18.4)	31 (81.6)	38 (43.2)	p=0.57
Moderate	7 (26.9)	19 (73.1)	26 (29.5)	

* asthma was the only chronic lung disease present amongst the study participants

Discussion

At the time of writing, in Sri Lanka, 511,863 patients have been discharged from COVID-19 treatment centers.[5] Although long term respiratory problems are expected in severe COVID-19 disease as a consequence of lung damage, this may not be expected in patients with asymptomatic, mild and moderate disease. However, it is increasingly recognised that patients who had minimal or no symptoms during the period of infection, subsequently develop symptoms.[8] Studies on clinical sequalae, imaging and functional changes were done at different time periods in the initial stages of the disease outbreak.[2,3,9,10] However, very few studies have followed up patients beyond 3-4 months. No research as of yet has been conducted to study the long term sequalae of the disease in the Sri Lankan setting. Our study is the first study in Sri Lanka to look at the respiratory symptoms and lung function abnormalities following COVID-19 disease.

Findings from our study are comparable to findings from other studies across the world.[11,9] Interestingly, we found that the frequency of SOB is higher at 3-months than during the acute phase of the illness. We also noted that there is new-onset SOB in 48 (54.5%) patients. A similar pattern was noted in a study done in Wuhan, China in patients at 3-months follow up.[10] The Wuhan study included patients who were acutely ill, and the follow up was done on the survivors. The frequency of SOB increased from 5% to 26%. This is comparable to our study, where the frequency of SOB increased from 14% to 67%. The possible casues for new onset shortness of breath in these patients are, reactive airway disease following COVID-19 infection,[12] dysfunctional breathing,[13] muscle weakness,[14] new-onset asthma,[12] pulmonary embolism,[15] and heart failure. This highlights the need for a diagnostic work up to identify the cause for SOB in post COVID patients.

We found lung function abnormalities in 61 (76.1%) of the study participants. Restrictive spirometry was seen in the majority (63.6%) of patients. One reason for this finding could be underlying pulmonary fibrosis. However 12 (13.6) of those with restrictive spirometry were obese (BMI ≥27.5 kg/m^2) and obesity could also result in a restrictive pattern in spirometry.[16] Interestingly in our study, 14 (23.7%) of patients with SOB had normal spirometry.

Further investigations, such as high-resolution CT scan of the chest and diffusion studies are needed to determine the underlying pathology and confirm a restrictive aetiology in these patients. A meta-analyses on lung function abnormalities in post COVID patients, revealed that 39% had abnormal diffusion capacity, 15% had restrictive abnormality and 7% had obstructive abnormalities.[17] Interestingly in our study, the restrictive lung abnormality was much higher (63.3%). They warrant further follow up with imaging and diffusion studies.

This is the first follow up study in asymptomatic and mild-moderate SARS- CoV- 2 infection in Sri Lanka. The use of an interviewer administered questionnaire and the use of spirometry to objectively assess the pulmonary function increased the validity of the study. The main limitations were, small sample size, gender inequality of the study participants and the difficulty in symptom recall after 3-months. Diffusion studies to determine lung parenchymal involvement would have given further information in patients with restrictive spirometry. However, such investigations were not included in our preliminary study. The mMRC dyspnoea scale was used to assess the degree of shortness of breath in the study population and the use of 6-minute walk test would have given added information.

Conclusions

Presence of respiratory symptoms of long COVID syndrome at 3-months was common following asymptomatic, mild-moderate SARS-CoV-2 infection. The commonest respiratory symptom was SOB and this was significantly higher at 3-months than during the acute phase of the illness. Restrictive spirometry was seen in a majority of patients.

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Competing interests

None.

Criteria for authorship

All authors contributed equally. All authors have read and approved the final manuscript.

References

1. Raveendran AV, Jayadevan R, Sashidharan S. Long COVID: An overview. *Diabetes Metab Syndr.* 2021; **15**(3): 869-75. doi: 10.1016/j.dsx.2021.04.007.
2. Xiong Q, Xu M, Li J, et al. Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. *Clin Microbiol Infect.* 2021; **27**(1): 89-95. doi:10.1016/j.cmi.2020.09.023
3. Halpin SJ, McIvor C, Whyatt G, et al. Post discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation. *J Med Virol.* 2021; **93**: 1013-22. doi:10.1002/jmv.26368
4. WHO Coronavirus (COVID-19) Dashboard | WHO Coronavirus (COVID-19) Dashboard With Vaccination Data. Accessed October 12 2021.
5. Health Promotion Bureau | Live updates on New Coronavirus (COVID-19) outbreak. Accessed October 12 2021. https://www.hpb.health.gov.lk/en..
6. OMS. Clinical management Living guidance COVID-19. 2021B. 2021; (January): 16-44.
7. Modified Medical Research Council (mMRC) dyspnea scale. UpToDate. No Title.
8. Mandal S, Barnett J, Brill SE, et al. 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. *Thorax.* 2021; **76**(4): 396 LP -8. doi:10.1136/thoraxjnl-2020-215818
9. Zhao Y miao, Shang Y min, Song W bin, et al. Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. *EClinical Medicine* 2020; **25**: 100463. doi:10.1016/j.eclinm.2020.100463
10. Mo X, Jian W, Su Z, et al. Abnormal pulmonary function in COVID-19 patients at time of hospital discharge. *Eur Respir J.* 2020; **55**(6). doi:10.1183/13993003.01217-2020
11. Xiong Q, Xu M, Li J, et al. Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. *Clin Microbiol Infect.* 2021; **27**(1): 89-95. doi:10.1016/j.cmi.2020.09.023
12. Cho J, Villacreses R, Nagpal P, et al. Small Airways Disease Is a Post-Acute Sequelae of SARS-CoV-2 Infection. medRxiv; 2021. doi:10.1101/2021.05.27.21257944

13. Alhuthail E, Stockley J, Coney A, Cooper B. Measurement of breathing in patients with post-COVID-19 using structured light plethysmography (SLP). *BMJ Open Resp Res.* 2021; **8**: 1070. doi:10.1136/bmjresp-2021-001070

14. Medrinal C, Prieur G, Bonnevie T, et al. Muscle weakness, functional capacities and recovery for COVID-19 ICU survivors. *BMC Anesthesiol.* 2021; **21**(1): 1-5. doi:10.1186/s12871-021-01274-0

15. McGonagle D, O'Donnell JS, Sharif K, Emery P, Bridgewood C. Immune mechanisms of pulmonary intravascular coagulopathy in COVID-19 pneumonia. *Lancet Rheumatol.* 2020; **2**(7): e437-e45. doi:10.1016/S2665-9913(20)30121-1

16. Melo LC, Silva MA, Calles AC. Obesity and lung function: a systematic review. *Einstein (Sao Paulo)* 2014; **12**(1): 120-5. doi: 10.1590/s1679-45082014rw2691.

17. Torres-Castro R, Vasconcello-Castillo L, Alsina-Restoy X, et al. Respiratory function in patients post-infection by COVID-19: a systematic review and meta-analysis. *Pulmonology* 2021; **27**(4): 328-37. doi:10.1016/j.pulmoe.2020.10.013