International Journal of Physiotherapy and Research,
Int J Physiother Res 2020, Vol 8(6):3706-14. ISSN 2321-1822
DOI: https://dx.doi.org/10.16965/ijpr.2020.180

Case Series

REVIEW OF PHYSIOLOGICAL RATIONALE OF PHYSIOTHERAPY IN COVID-19 PATIENTS: A CASE SERIES

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ABSTRACT

Physiotherapy interventions have been evidenced to assist early liberation from ICU in COVID-19 patients. This case series of three COVID patients admitted to the COVID ICU, explains the physiologic rationale of physiotherapy intervention in acute care of COVID patients. Early mobilization is seen to help early recovery.

KEYWORDS: Physiologic rationale, COVID, physiotherapy, crocodile breathing.

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Access this Article online	Journal Information	
Quick Response code	**International Journal of Physiotherapy and Research** ISSN (E) 2321-1822 | ISSN (P) 2321-8975 **https://www.ijmhr.org/ijpr.html** **DOI-Prefix:** https://dx.doi.org/10.16965/ijpr	(cc) BY-NC-SA
	Article Information	
DOI: 10.16965/ijpr.2020.180	Received: 25 Oct 2020 Peer Review: 26 Oct 2020 Revised: None	Accepted: 30 Nov 2020 Published (O): 11 Dec 2020 Published (P): 11 Dec 2020

INTRODUCTION

The Novel Coronavirus disease 2019 (COVID-19), is a lower respiratory tract infection caused by a newly emergent beta coronavirus, the SARS-CoV-2, that predominantly affects the airway epithelial cells [1]. A highly communicable disease, the common symptoms exhibited are fever, dry cough, fatigue with other symptoms like expectoration, dyspnoea, headache, hemoptysis and diarrhoea [1]. The rapid occurrence of atypical Acute Respiratory Distress Syndrome (ARDS) is the main cause for admissions to intensive units and mortality [2]. The need for supplemental oxygen arises mainly due to hypoxia, caused by shunting and ventilation-perfusion mismatch. The viral replication elicits an inflammatory response leading to a "cytokine storm" with elevated levels of inflammatory markers like Procalcitonin (PCT), serum ferritin, C-reactive protein (CRP), Interleukin-6 (IL-6), associated with an increase in severity [3]. The spectrum of this disease ranges from symptomatic infection to severe viral pneumonia with respiratory failure and/or death [4].

Initially, pneumonia in COVID-19 largely presents as a "Type L" phenotype (Fig 1). The alveolar cells and type 2 pneumocytes are the main sites for virion mediated alveolar cell apoptosis [5]. Subsequently, the inflammation triggers a modest local interstitial oedema, focused in the lower zones of the lung, where the stresses are more, manifesting as ground glass opacities on the High-Resolution

Computed Tomography (HRCT) [5]. As opposed to healthy individuals, the resultant ventilation-perfusion (V/Q) mismatch does not elicit hypoxic ischemic vasoconstriction, hypothesized to be the work of endogenous prostaglandins and bradykinin[6].

This altered response, along with preserved lung compliance is the main cause of arterial hypoxemia without dyspnoea, termed as "Happy Hypoxemia" [6]. With time, patients may progress to a more classic H-phenotype.

Physiotherapy, an internationally established profession, plays an integral part in critical care and rehabilitation of the COVID-19 patient[7]. The success of rehabilitation depends upon acute care physiotherapy received by the patient in the Intensive Care Unit (ICU). As an essential member of the critical care team, planning and executing an individually tailored rehabilitation program, comes under the purview of a physiotherapist. In addition to providing airway clearance in ventilated patients, physiotherapy provides strategies to optimise oxygenation. Given that the medical management in ICU includes prolonged protective lung ventilation, sedation and use of neuromuscular blocking agents, COVID-19 patients are at high risk of developing ICU acquired weakness (ICU-AW) [8], thus high morbidity and mortality. It is hence essential to initiate early rehabilitation in order to limit the severity of ICU-AW and promote rapid functional recovery. Acute care in ICUs and a general rehabilitation program for the hospitalized, undoubtedly, prevents readmissions and halts the onset of multiple complications.

The following case series is based on patients admitted to a COVID centre of a tertiary care hospital in Mumbai. It attempts to explain the physiologic rationale underlying the physiotherapy protocols suggested in the rehabilitation of COVID patients. Additionally, it traces the course of rehabilitation in ICU and the efficacy of combining certain treatment strategies in patients on Non-Invasive ventilation (NIV), High Flow Nasal Cannula (HFNC), with co-morbidities and pre-existing pulmonary diseases.

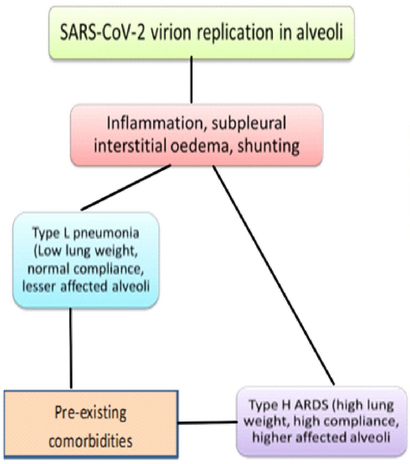


Fig. 1: Pathophysiology and phenotypes in COVID-19

Fig. 2: Physiological Rationale of physiotherapy interventions

CASE SERIES

Case Study 1: A 54-year old diabetic and hypertensive male was admitted on the 2nd day after the onset of acute febrile illness, with complaints of breathlessness. As his SpO2 was at 87%, he was given 15L of O2 by Bag Mask Ventilation (BMV), shifted to the ICU after his Rapid Antigen Test (RAT) came positive. Chest x-ray showed patchy infiltrates bilaterally in lower zones. HRCT revealed multifocal patchy areas of ground glass opacities, coarse reticulations and traction bronchiectasis in both lung fields with lower lobe predominance. Lung involvement was 30-40%, indicating atypical pneumonia and late stage fibrosis. Being isolated, he was extremely reluctant, hence there was a need to alleviate anxiety. He was counselled at length, regarding his condition, the ill effects of restricted mobility, and therapeutic opportunities to help him recover faster. Breathing exercises to improve ventilation and oxygenation, upper and lower limb mobility exercises were initiated. At each step, he was assured of the safety of exercise by showing him the change in saturation (Table 1). Exercises to improve lower limb strength were given at the edge of the bed, then progressed to ambulation. Prone position and crocodile breathing were given initially for 10 minutes, later increased as per the patient's comfort and repeated multiple times during the day. Single breath count test was done every day, where the count increased by 24. The patient was ambulated with O2, then progressed to walking without oxygen support, while maintaining saturation. He was transferred thereafter.

Table 1: Physiotherapy management, daily parameters in Case study 1.

Session no.		1	2	3	4	5	6	7	8	9	10
O_2 (in liters)		15	35	35	14	6	3	3	1	1	Off O_2
Mode of delivery		BMV	HFNC	HFNC	BMV	NP	NP	NP	NP	NP	-
Vitals											
Heart rate	Pre	82	82	82	80	85	96	98	90	79	80
	Post	79	89	90	84	88	98	98	94	82	85
SpO_2 (%)	Pre	99	99	99	98	98	98	94	94	99	99
	Post	99	99	97	99	99	99	99	98	99	99
SBC				6	10	12	20	25	25	30	30
BHT							11	12	12	12	12
Treatment components											
Breathing exes, TEE		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Mobility exercises			✓	✓	✓	✓	✓	✓	✓	✓	✓
Standing/ Spot march					✓	✓	✓	✓	✓	✓	✓
Positioning	Prone		✓	✓	✓	✓	✓	✓	✓	✓	✓
Ambulation	Distance					Bedside	10m	20m	40m	60m	60m

Case study 2: A 57-year old retired male, with no known co-morbidities, was admitted 3 days after onset of diarrhea and breathlessness. As he was breathless at rest withSpO2 below 85%, he was put on BMV (12 litres). As saturation worsened, he was shifted to ICU and put on NIV with the fraction of inspired O2 (FiO2) at 60%. Chest x-ray showed heterogeneous opacities in bilateral lower zones and right middle lobe. CRP levels were at 30mg/l, indicating inflammation along with respiratory alkalosis on ABG. Physiotherapy sessions were initiated on the 3rd day, with goals emphasizing on facilitating ventilation and breath control. Anterior basal lift in supine, breathing exercises, intercostal stretches were given, first in the incomplete prone position with a pillow under the right shoulder, coupled with mild vibrations and then in prone, for posterior basal segments. Prone, under observation, was given for an hour during the session and later repeated 6-7 times in the day. Once the breathing pattern improved, mobility exercises, with the NIV, alternating with sets of breathing exercises were given (Table 2). Bedside walking with NIV was accomplished on the 5th day, where he walked 16-20 steps, with pacing techniques. At every stage, the saturation was closely monitored and a drop more than 4 % from baseline value was an indication to pause. As the sessions progressed, the FiO2 was reduced gradually till he was weaned off NIV onto BMV. On the 7th session, he walked 20 meters, maintaining saturation at 92%. The distance and laps walked with oxygen were gradually increased. After the 10th session, the patient was shifted to the ward while comfortable on 2 litres O2 by face mask. Having normal ABG reports, he was discharged soon after.

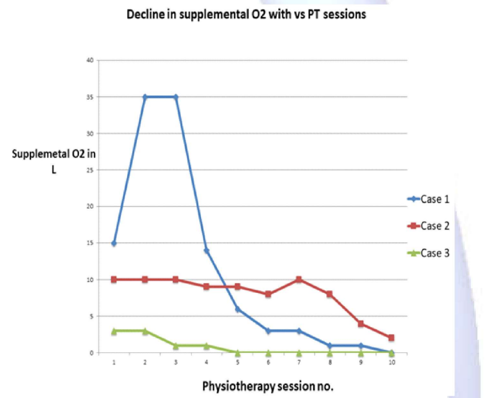
Table 2: Physiotherapy management and daily parameters in Case study 2.

Session no.		1	2	3	4	5	6	7	8	9	10
NIV/FM		NIV	NIV	NIV	NIV	NIV	NIV	BMV	FM	FM	FM
FiO_2(%)/ O_2(liters)		60%	60%	60%	55%	55%	50%	10 L	8L	4L	2L
Vitals											
Heart Rate	Pre	71	82	91	91	87	85	80	91	92	94
	Post	65	75	81	98	98	98	94	94	94	95
SpO_2 (%)	Pre	98	99	98	92	81	81	78	88	88	90
	Post	98	100	100	100	99	98	98	96	98	99
Treatment Components											
Positioning	Incomplete Prone	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Prone	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Chest PNF		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Breathing exes, TEE		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Mobility exercises				✓	✓	✓	✓	✓	✓	✓	✓
Standing, spot march					✓	✓	✓	✓	✓	✓	✓
Bedside Walking						✓	✓	✓	✓	✓	✓

Case study 3: A 62-year-old male, hypertensive and asthmatic for 20 years, was hospitalized 5 days after the onset of breathlessness and cough. He had a history of pulmonary tuberculosis 2 years back with a completed AKT course. As the SpO2 was at 86%, oxygen support of 15 L was given by BMV. He was shifted to the ICU after his swab tested positive, then transferred to the ward. D dimer levels were raised (>0.8), suggestive of thrombosis. HRCT showed late stage atypical pneumonia (COVID Reporting and Data System- CORADS score 6) with 30-40% lung involvement. Fibro-cavitatory changes, seen in left lower lobe and apical segment of right upper lobe, were indicative of post Koch's sequelae. The patient's vitals were assessed with the help of monitors and pulse oximeter, considering the co-morbidities. The session started only if the parameters were within normal ranges and the patient had no discomfort. Inspiratory breathing exercises, thoracic mobility exercises in sitting, mobility exercises in bed were initiated (Table 3). Subsequently, upper and lower limb mobility exercises at the edge of the bed were introduced according to the physiologic response to the previous exercise. He was then made to stand and march in place, then progressed to ambulation. Ambulation was done with supplemental O2 from the 2nd session. Prone position was given for at least 30 minutes with crocodile breathing. Single breath count, performed daily, improved by 6 counts. Prior to discharge, the six-minute walk test was performed to set the goals for further rehabilitation in which, Six-minute walk distance (6MWD) was 120 meters without pauses, oxygen was titrated up to 2 L to complete the test and SpO2 on recovery was 97%.

Table 3: Physiotherapy management and daily parameters in Case study 3.

Session no.		1	2	3	4	5	6
O_2 status		3 L	3 L	1 L	1 L	Off O2	Off O2
Mode of delivery		Nasal Prongs				Off O2	Off O2
Vitals							
Heart rate	Pre	91	73	85	80	83	86
	Post	89	89	87	86	87	89
SPO_2(%)	Pre	97	99	93	96	95	96
	Post	99	99	92	98	97	99
SBC		10	10	12	10	14	16
Treatment components							
Breathing execs, TEE		✓	✓	✓	✓	✓	✓
Mobility exercises		✓	✓	✓	✓	✓	✓
Standing, spot march		✓	✓	✓	✓	✓	✓
Prone		✓	✓	✓	✓	✓	✓
Ambulation	Distance walked		100m	60m	120m	100m	120m



Graph 1: Decline in supplemental O2 with progress in sessions

DISCUSSION

Early implementation of a concise, customized rehabilitation program is essential in hospitalized COVID-19 patients [9].

The program may vary according to the status of the individual on a daily basis but critical care physiotherapy is a must. The goals are fairly common: To reduce V/Q mismatch, to facilitate breathing control and recruitment of the alveoli, to promote early mobilization, to prevent peripheral deconditioning and alleviate anxiety and depression. The physiological rationale underlying each treatment is given and how this treatment has contributed to achieving the rehabilitation goals is discussed in detail.

Patient Counselling: Moderate to severe anxiety and mild depression is common in patients with COVID-19, with adults and elderly population being the most affected [10]. These symptoms persisted in months post discharge. Patient counselling, an integral part of rehabilitation, not only emphasizes the benefits, but also allows the patient to vent doubts and seek assurance. In COVID-19 patients, loneliness with anxiety is the major setback for patients. Counselling is thus the first step of interaction between the physiotherapist and the patient.

Prone: Positioning in prone was given to reduce V/Q mismatch, improve hypoxemia, facilitate improved oxygenation.

Physiologic Rationale: As per the “Slinky Model” [11], the spring-like lung, deforms under gravity acting on its weight. The weight is largely made of blood and fluid, concentrated in the dependent regions of the lung. Prone position reduces the pleural pressure gradient between dependent and independent lung regions, creating a more uniform lung aeration and strain distribution, recruiting alveoli, thereby reducing V/Q mismatch. Due to oedematous changes, the already distended alveoli, when combined with mechanical ventilation are at risk of trauma. Increased respiratory effort along with PEEP provided by NIV has the potential to damage alveoli[12]. Prone position reduces alveolar trauma thereby eliminating the deterioration to the need for invasive mechanical ventilation. Ventilation in the prone position may not be as effective as in the supine, but the V/Q matching is optimized [13]. The duration of prone position recommended is minimum of 2 hours for the effect to take place[14]. However, in all

3 cases, the duration was initiated from a period that was well tolerated by the patient in terms of saturation and symptoms and slowly progressed to longer periods.

In prone, the Diaphragm shows increased motility in the dorsal regions, freeing the posterior basal segments, enabling expansion [13]. The heart and mediastinum also shift ventrally in prone, reducing the weight on the lungs, recruiting more alveoli [15]. The incomplete prone position (135 degrees) is also a well-tolerated position in NIV patients, having similar effects as prone, but to a lesser extent. As in case study 2, this position can be used as an assistive step to help the patient go further on to prone.

Recent studies on the feasibility of prone position in NIV patients in ICUs, showed that 17% of the patients were uncomfortable in prone [16]. Around half of the patients recruited with NIV showed no significant changes in oxygen saturation with prone [16]. However, in this case study 2, patient tolerated the prone position quite well, showing significant rise in post treatment saturation.

Strategies to facilitate breathing control (PNF): PNF techniques like Intercostal stretch and anterior basal lift were implemented along with breathing exercises at tidal volumes.

Physiologic rationale: Chest PNF techniques reduce the respiratory rate by increasing the gamma neuron mediated stretch reflex, producing a stronger, alpha motor neuron mediated contraction of the Intercostal muscles [17]. Increase in lung volumes immediate post session is attributed to increased chest wall mobility [17]. PNF techniques, when used in conjunction with positioning, as in case 2, showed a significant rise in SpO2 levels from baseline. These same manoeuvres in case study 1 and 3 helped increase chest wall mobility, thus, facilitating ventilation. It helped to recruit the primary muscle of inspiration, maintain adequate diaphragm function and prevent atrophy of the diaphragm without stressing the lung. The patient in case study 2 was on NIV where PNF techniques were given at the patients' tidal volume, as a strong inspiratory effort may damage the over distended alveoli and the diaphragm too[18].

Single breath count (SBC): SBC is the measurement of how far an individual can count in a normal speaking voice after a maximal effort inhalation [19].

Physiologic rationale: SBC correlates well with measures of pulmonary function test in adults [20]. COVID-19 pneumonia may result in alterations in pulmonary functions, affecting SBC. Studies have shown that SBC has a strong correlation with forced vital capacity [21]. The numerical count technique has a good correlation with the Slow Vital Capacity (SVC) with great intra-examiner repeatability. A count of 21 reflects SVC below 20 ml/kg [22]. Thus, useful in evaluating lung function in COVID-19 setups with a limitation of equipment for infection control, it is also used as bedside tool for assessment of pulmonary function in addition to being an exercise stimulus. This is seen in case studies 1 and 3.

Early Mobilization: Mobilization was begun in a period of 3 days after admission to ICU and wards. It included mobility exercises and ambulation.

Physiologic Rationale: Mobilization not only has beneficial effects on the physical status of the patient, but also, on the mental status. Short durations of exercise bouts can bring about mood elevation by modulating neurotransmitters. Increased cortisol and lactate levels have excitatory effect on the cortex that alleviates depression and anxiety[23]. This aspect has positive effects on the physical state too. Mechanical ventilation reduces the neural drive, increasing proteolysis leading to sarcomere rupture, contributing significantly to muscle atrophy and injury[24]. The loss of muscle mass in older adults is 3-6 times more than in young adults, putting them at higher risk of injury. Early mobilization (beginning in the first week of admission) has been advocated in ICUs for reduced risk of complications like thrombo-embolism, disuse atrophy, pressure ulcers, bone density reduction and early discharge[14]. Studies have shown upper and lower extremity strength training to provide a strong stimulus to the Diaphragm due to transmission of Intraabdominal pressures. Thus, mobilizing the limbs in upright postures indirectly provides stimulus for Diaphragm strengthening by a non-respiratory manoeuvre [25].

Aerobic activity in critical patients [24] can reduce the severity of ARDS by reducing oxidative stresses and producing Neutrophil Extracellular Traps (NETS), crucial to preventing lung damage. It also produces improvements in markers such as immunoglobulins, T- lymphocytes, and interleukins modulating the immune response against SARS-CoV-2. Lung elasticity has been shown to increase post aerobic activity that can slow the onset of lung fibrosis. Persistently raised CRP levels that can accelerate lung damage are shown to be decreased with aerobic activity, producing short peaks of rise that are effective in damaging the virus cells. This same mechanism may have contributed to arrest of severity in case study 1.

Cough and dyspnea are proven to reduce by autonomic regulation brought about by aerobic activity [24], which was given in the form of 6-minute walking. In asthma, exercise has short duration effects on the smooth muscles of the upper airways that mediates a reduction in obstruction. Thus, short bouts of exercises can bring relief from cough and dyspnoea.

The triad of COVID-19, type 2 diabetes and hypertension produces severe symptoms, likely to cause mortality. Hypertension, a frequent comorbidity seen in severe presentations of COVID-19, is hypothesized to augment the action of SARS-CoV-2 due to the use of ACE in hibitors. Hypertensives have altered immune response that, in conjunction with sympathetic system overactivity, shows infiltration of various tissues by macrophages, causing vascular remodelling[26]. On the other hand, hyperglycaemia is associated with imbalances in the clotting and fibrinolytic mechanisms, often leading to coagulation and high D dimer values[27]. More so, studies have shown the SARS-CoV-2 mediated destruction of beta cells in Islets of Langerhans to cause hyperglycaemia in patients post admission[27]. A single, 1-hour session of exercise can improve glucose transport, enable glucose uptake by skeletal muscles, promoting glucose homeostasis that can persist up to 20 hours[28]. Post mobilization, systolic blood pressure falls due to neurohormonal action, eliciting hypotension that can last up to 24 hours[29]. Studies have already proven the effect of early mobilization in reducing the risk of thrombus formation, thus reducing the risk of thromboembolic events post immobilization. Thus, mobilization not only targets the negative effects of immobilization, but also the altered physiology in pre-existing conditions, preventing their augmentation with effects of SARS-CoV-2, tipping the scales in favour of the patient.

The patients in this case series were mobilized with their supplemental oxygen, which may have produced positive effects. Mobilizing the patient with oxygen supply has been shown to facilitate ventilatory muscles, reduce respiratory rate and reduce the central ventilatory response to hypoxemia[30]. In COVID-19 patients, hypoxic ischemic vasoconstriction responsible for exertional desaturation decreases with oxygen supply, decreasing the patient's perception of dyspnoea, thus improving exercise performance and tolerance.

Graph 1 shows the decline in the supplemental oxygen of all 3 patients with the progress in physiotherapy sessions. The linear graphs show a marked gradual decline in the need for supplemental oxygen in case study 1, while the other two show a steady decline.

Breathing Exercise: Crocodile breathing [31], which is posterior basal breathing exercise in prone position with arms elevated and folded to support the forehead was found beneficial in improving oxygen saturation in patients. It emphasizes on slow diaphragmatic inspiration followed by pursed lip expiration.

Physiologic rationale: Respiration is a constant and powerful modulator of cardiovascular control. The negative intrathoracic pressure through inhalation reduces the pressure on the right atrium, thereby enhancing the venous drainage. During inhalation, the inferior vena cava diameter reduces, the efficiency of this process reaching its zenith in slow and deep respiration. Research has shown that correct physiologic activity of the diaphragm is crucial for venous drainage. Lower limb Mobilization coupled with slow deep breathing involving strong contraction of diaphragm prevents the venous stasis from recumbency[32].

The degree of movement of the diaphragm correlates with the changes in lung volume: the greater the difference in diaphragm movement between inspiration and expiration, the greater the tidal volume. Practicing diaphragmatic breathing technique has also been shown to facilitate slow respiration. Slow breathing reduces the respiratory rate and hence the work of breathing. In crocodile breathing, there is added advantage of prone position as explained above.

The main mediator of controlled breathing exercises on the described health, mental health and cognitive benefits is the Vagus Nerve (VN)[33]. Specific respiration patterns serve as respiratory VN Stimulation (rVNS). The styles of respiration are controlled breathing techniques that slow down and deepen respiration, extending expiration, and probably those that emphasize relatively stronger diaphragmatic breathing providing rVNS[34]. The phrenic nerve blends with the vagus nerve while passing through the opening in diaphragm, further descending into the abdomen. In this manner, the diaphragmatic breath helps in "massaging" the vagus nerve thereby shifting the body in rest and digest mode from fight or flight mode.

CONCLUSION

Thus, in this series, physiotherapeutic interventions, with strong physiological reasoning, may have augmented the medical management and contributed to the improvement of the COVID patient. This case series report may provide insight into the physiological rationale behind each physiotherapeutic exercise component, increasing the efficacy of the rehabilitation program as a whole, thereby helping patients recover better.

ABBREVIATIONS

COVID-19: Coronavirus Disease 19; **ARDS:** Acute Respiratory Distress Syndrome; **PCT:** Procalcitonin; **CRP:** C-Reactive Protein; **IL:** Interleukin; **HRCT:** High Resolution Chest Tomography; **ICU:** Intensive Care Unit; **NIV:** Non Invasive Ventilation; **HFNC:** High Flow Nasal Cannula; **BMV:** Bag Mask Ventilation; **NP:** Nasal Prongs; **RAT:** Rapid Antigen Test; **ABG:** Arterial Blood Gas; **FiO2:** Fraction of Inspired O2; **SBC:** Single Breath Count; **BHT:** Breath Hold Test; **TEE:** Thoracic Expansion exercises; **RPE:** Rate of Perceived Exertion; **PEEP:** Positive End-Expiratory Pressure; **SVC:** Slow Vital Capacity

ACKNOWLEDGEMENTS

The authors acknowledge Dr. Hemant Deshmukh (Dean, Seth GSMC & KEMH), Dr. Milind Nadkar (Academic Dean, Seth GSMC & KEMH), Dr. Saraswati Iyer (Professor and Head, PT School & Center, Seth GSMC & KEMH), Dr. Kaustubh Salagre (Asst. Prof. Dept of Medicine, Seth GSMC & KEMH), Dr. Mariya Jiandani (Associate Prof. PT School & Center, Seth GSMC & KEMH), and all patients from the case series.

Conflicts of interest: None

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How to cite this article:

Mohini N. Kamat, Manali G Sonavane, Jaimala V Shetye, Dipti B. Geete. REVIEW OF PHYSIOLOGICAL RATIONALE OF PHYSIOTHERAPY IN COVID-19 PATIENTS: A CASE SERIES. Int J Physiother Res 2020;8(6):3706-3714. **DOI:** 10.16965/ijpr.2020.180