

Pulmonary Rehabilitation in Post Covid Sequelae in India

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Editorial

An outbreak of pneumonia was reported in Wuhan, Hubei Province, China in December 2019 and quickly spread to all Chinese provinces [1,2]. The coronavirus disease (COVID-19) pandemic spread through 190 countries within 20 weeks from Wuhan, China, affecting 334,000 populations [3]. This caused more than 14,500 deaths by mid-March 2020. The number of infected people has risen to 1,210,956 in the month of April 6, 2020, with 67,594 associated expirations [4].

India recorded its first COVID-19 infection case on January 30, 2020 in a student from China's capital, Wuhan. In 2020, India reported 360 positive COVID-19 cases from 23 states across the country [4]. In India, the number of asymptomatic cases was higher. On April 4, 2019, a novel coronavirus pathogen was proved to be a novel beta coronavirus [2]. Sub-micron sized viruses, narrated as "organisms at the edge of life", are liable for some of the worst human pandemics in history, like influenza (1918), smallpox (1978) and COVID-19, as of September 17, 2020 [2]. The SARS-CoV-2 virus is causative for COVID-19. Nearly 29 million people have been affected by this virus, which caused 936,521 deaths worldwide (WHO, 2020).

Corona viruses are single-stranded positive-strand RNA viruses that are known to contain some of the largest viral genomes, up to around 32 kbp in length. Following an augmentation in the number of coronavirus genome sequences available and following efforts to investigate the diversity in the wild, the family *Corona viridae* now contains four genera. The structure of the coronavirus as given in Figure 1. Those species that belong to the genera Alpha corona virus and Beta corona virus can infect mammalian hosts, while those of Gamma corona virus and the recently defined Delta corona virus mainly infect avian species. The highly pathogenic human coronaviruses, Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV), belong to lineage B (sub-genus Sarbecovirus) and lineage C (sub-genus Merbecovirus) of Betacoronavirus [3].

Symptomatology of Covid-19

The COVID-19 is primarily explained as a disease-causing Severe Acute Respiratory Syndrome (SARS); the systemic manifestations involve other organs, including the Central Nervous System (CNS). The onset of the symptoms occurs on average 5-6 days after exposure, with mild symptoms recovering within 2 weeks. However, in severe cases, the recovery may extend up to 6 weeks [5]. COVID-19 can be transmitted through the respiratory droplets of infected people. Corona viruses seize the lung's alveoli, thereby causing pneumonia [6].

In a few patients, the symptoms may persist for weeks or months following initial recovery. Clinical features in coronavirus disease 2019 are

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given in Table 1. The persistence of the disease after complete recovery is referred to as "long COVID" and it has been observed in many survivors. As COVID-19 patients have shown, about 80% are either asymptomatic or have mild symptoms, while 14% develop severe symptoms, such as pneumonia; 5% develop critical symptoms, such as septic shock, respiratory failure, or multiorgan failure; and 2% of the patients die of the disease. Death rates are much higher among the elderly and those with comorbidities. "Long COVID" is defined as symptoms of fatigue, headache, dyspnea and anosmia. It is more likely to occur in the elderly population, people with a high body mass index and females. The symptoms may persist for 4-12 weeks [7].

Pathophysiology of virus

Origin and route of transmission: Some genomic studies suggest bats are the natural host for Sars var. Others suggest pangolins. With the progression of an outbreak, transmission in humans remains the main mode of spread through coughing or sneezing; aerosol, typically during aerosol production in clinical procedures; and mucosal membrane contact with fomites. Faecal-oral transmission has been hypothesised given the detection of viral RNA in stools and reported ACE2 expression along the GI-tract with gastrointestinal symptoms and no evidence of intrauterine or transplacental transmission has been explained [8].

Respiratory involvement in Covid 19: Common clinical features are fever (99%), fatigue (70%), dry cough (59%), anorexia (40%), myalgia (40%), breathlessness (31%) and sputum production (27%). One study reported only 20% of patients with very low grade fever and other less common symptoms were headache, sore throat and rhinorrhea as per the study [8]. The most frequent and serious manifestation of COVID-19 infection is pneumonia, which is characterised by cough, fever, breathlessness and a chest x-ray showing bilateral infiltrates. 8 Most patients only reported mild symptoms of the disease; some patients experienced rapid progression of their symptoms over the span of a week. A study found that 17% of their patients developed Acute Respiratory Distress Syndrome (ARDS), 65% of whom rapidly aggravated and died from multiple organ failure. In Table 2, the progression of disease is mentioned. It has been seen that ARDS is greatly associated with advanced age (>65 years old) and co-morbidities like diabetes mellitus and hypertension. For many cases, bilateral lower zone consolidation, which has been reported through chest x-ray, peaked at 10-12 days from symptom onset [8].

Cardiovascular involvement of COVID-19: Patients who have existing Cardiovascular Disease (CVD) are at a greater risk of suffering from severe COVID-19 and have a poor prognosis. A meta-analysis study showed 46,248

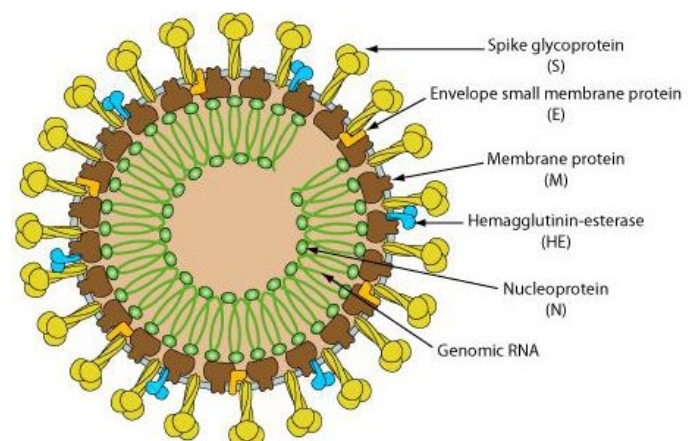


Figure 1. Schematic of a coronavirus.

Table 1. Clinical manifestations in COVID-19.

System	Symptoms
General	Fever
	Headache
	Fatigue
Respiratory	Dry cough
	Difficulty to breathe
	Congestion of nose
	Runny nose
	Sore throat
CNS and sensory organs	Acute psychosis
	Loss of sense of smell
	Loss of sense of taste
	Loss of speech
	Dizziness
	Impaired consciousness
	Stroke
	Ataxia
	Seizure
	Impaired vision
	Pink eye
Cardiac	Hearing loss
	Otagia
	Vertigo
Cardiac	tinnitus
	Acute chest pain / pressure
	Arrhythmia
Digestive	Heart failure
	Nausea and vomiting
	Anorexia
Digestive	Diarrhea
	Abdominal pain
Renal	Cloudy urine with frequent urge
Musculoskeletal	Myalgia
Skin	Hair and nail Rash
	Discoloration of fingers or toes Hair fall and baldness
	Red half-moon nail sign

Table 2. Progression of disease.

Mild Illness	Shows upper respiratory tract infection. May have symptoms such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion, or headache. Rarely, patients may also present with diarrhea, nausea and vomiting
Pneumonia	Pneumonia present but no requirements for supplemental oxygen
Severe Pneumonia	Fever or suspected respiratory infection, with one of the following problem: respiratory rate >30 breaths/min; severe respiratory distress or SpO ₂ 93% on room air
Acute Respiratory Distress Syndrome (ARDS)	Within a week worsening of respiratory symptoms. Chest radiographs express bilateral opacities which is not volume overload, lobar or lung collapse, or nodules. Cardiac failure and fluid overload must be ruled out.
Sepsis	Organ dysfunction caused by dysregulated host response to suspected infection. Signs of organ dysfunction include: difficult or fast breathing, low oxygen saturation, altered mental status, reduced urine output, fast heart rate, low pulse, cold extremities or low blood pressure and laboratory study shows thrombocytopenia, high lactate, cogulopathy, acidosis and hyperbilirubinemia.
Septic Shock	Persistent of hypotension despite fluid resuscitation, requires vasopressors to maintain Mean Arterial Pressure (MAP). MAP 65 mm Hg and serum lactate level >2 mmol/L

patients who died with confirmed COVID-19 found that the most common co-morbidities were hypertension (17%), diabetes (8%) and CVD (5%). The

precise mechanism of cardiovascular involvement in COVID-19 is unknown; however, elevated cardiac biomarker levels are commonly observed. One study showed that in COVID, 19 patients have either elevated troponin levels or new electrocardiography or echocardiography abnormalities which cause cardiac injury [8].

Excessive extracellular calcium level lead to myocyte apoptosis which are mechanisms of damage which cause by Cytokine storm from systemic inflammation and the hypoxic state from ARDS.8 rush in cytokine levels due to hyperinflammatory response and secondary hemophagocytic lymphohistiocytosis increases myocardial demand in the setting of acute infection which can result to atherosclerotic plaque instability and myocardial injury, increasing the risk of acute myocardial infarction.8 Blood pressure abnormalities seen in response to illness, namely the effects of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers on COVID-19 susceptibility and prognosis, but which are still unknown. Some evidence suggests that increasing ACE2 expression facilitates COVID-19 infection, but other studies suggest potential beneficial effects of reducing lung injury [8].

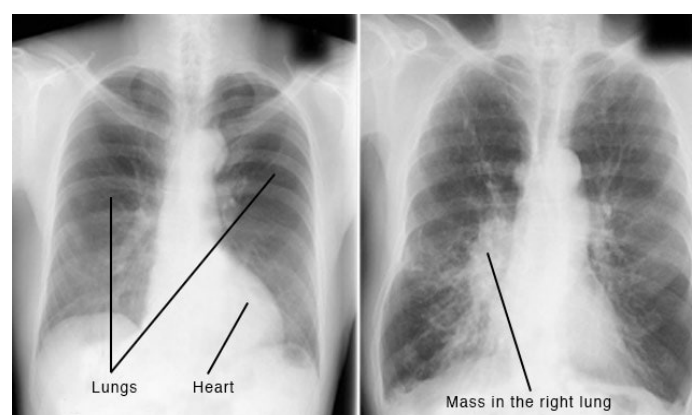
Renal involvement of COVID-19: Acute Kidney Injury (AKI) is the sudden loss of kidney function that develops within 7 days. It is found that AKI in COVID-19 accompanies sepsis, multiorgan failure and shock, which progresses to acute tubular necrosis. A study based on single-cell transcriptome analysis proved ACE2 receptor expression in kidney cells, suggesting the plausibility of direct renal cellular damage from SARS-CoV.

Gastrointestinal involvement of COVID-19: A notable number of patients reported GI symptoms such as diarrhea, nausea, vomiting and abdominal pain. Detection of SARS-CoV-2 RNA in stool samples of infected patients suggests that ACE2 receptors are highly expressed in the GI tract. Either mild and transient liver injury or severe liver damage can occur in COVID-19. Wong, et al. expressed that in his study; 14.8-53.1% of COVID-19 patients had abnormal levels of alanine aminotransferase, aspartate aminotransferase and bilirubin during the time of the disease, with bilirubin showing very mild elevation. Gammaglutamyl transferase was elevated in 54% of patients in 1 cohort study that included 56 COVID-19 patients [8].

Chest x-ray and CT scan findings in Covid 19

Detection of COVID-19 lung disease, a chest X-ray is a less sensitive modality compared to a CT scan. Chest x-ray and CT scan findings of COVID-19 show lung consolidation and ground glass opacities. 10 Chest radiographs showed in individuals with SARS focal or multifocal, unilateral, ill-defined air-space opacities in the middle and lower peripheral lung zones, with progressive multifocal consolidation over a course of 6 to 12 days involving one or both lungs. Figures 2-5 show various chest radiographs for a better understanding of chest x-ray in COVID 19. A CT scan of the chest reveals areas of ground-glass opacity and consolidation in the involved segments [9,10].

Chest scans and x-rays of healthy people and pneumonia infected patients show the difference is based on the presence of white hazy patches known



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Figure 2. Normal lungs.



Figure 3. Bacterial pneumonia.



Figure 4. Viral pneumonia.

as "ground-glass opacity" in infected patients, which is not present in healthy people [11,12]. Many studies have explained that the use of chest x-rays and CT scans along with DL models helps to achieve result automated detection of COVID-19 pneumonia and other types of pneumonia such as non-COVID-19 viral pneumonia and bacterial pneumonia [13,14]. Many studies have demonstrated the utility of TL models, which are deep networks pretrained for differentiate pneumonia from healthy CT scans [15]. Chowdhury MEH, et al. utilised the approach of TL in DL to differentiate between COVID-19 and viral pneumonia based on a data acquired from a public database. Chowdhury MEH, et al. showed in his study The TL & DL models were trained using 423 COVID-19, 1458 viral pneumonia and 1579 normal chest X-ray images based on augmentation and with no augmentation [16]. In order to show the difference between COVID-19 and Community-acquired Pneumonia (CAP), Li L, et al. used in their study a three-dimensional DL framework known as the COVID-19 detection neural network (COVNet). He used 4352 CT scans (1292 of COVID-19, 1735 of CAP and 1325 normal CT scans) to prove his study. Li L, et al. achieved 90% sensitivity and 96% specificity for COVID-19 detection and 87% sensitivity and 92% specificity for CAP detection in their study [17].

Higher performance achieved for the classification of COVID-19

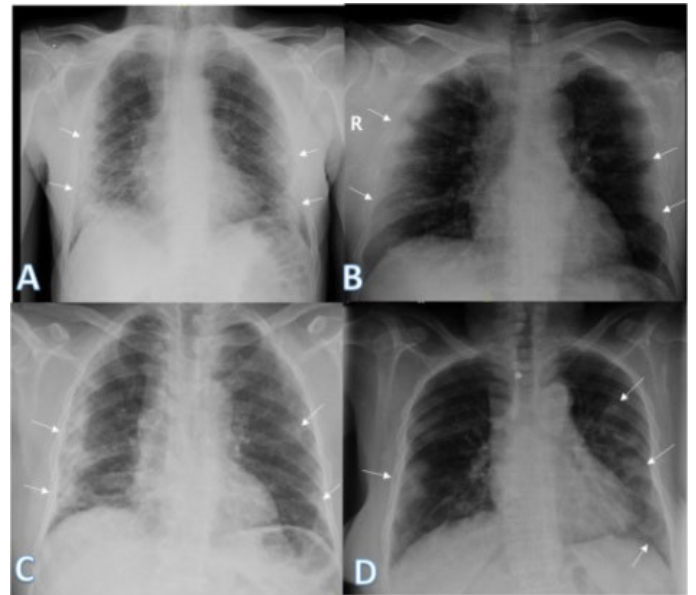


Figure 5. COVID19.

pneumonia and non-COVID-19 viral pneumonia and COVID-19 pneumonia with healthy chest x-ray has shown that the computer detection approach can be used as an alternative and a confirmatory approach to the RT-PCR method, which has been shown to be less sensitive and time-consuming [18].

Physiotherapy evaluation and management of Covid 19 worldwide

Chest physiotherapy has been used in many different respiratory conditions. It improves gas exchange, reverses pathological progression and reduces or avoids the need for artificial ventilation when it is provided very early [19].

Respiratory physiotherapists are healthcare professionals involved in the management and care of patients. They play a role in non-invasive support management, postural changes, mobilization, as well as during the weaning from invasive mechanical ventilator support. According to the Italian Association of Respiratory Physiotherapists, acute hypoxemic patients may experience breathlessness that may persist after the administration of oxygen flows of >10-15 L/min with a reservoir mask. In these cases, High-Flow Nasal Oxygen (HFNO), the application of Continuous Positive Airway Pressure (CPAP), or Non-Invasive Ventilation (NIV) may be useful. A potential exacerbation of hypoxemia with the need for intubation and invasive mechanical ventilation has to be taken into account in patients with SARS-Cov-2. Considering the risk of NIV failure, it is important to manage these patients with immediate endotracheal intubation. Physical therapists have to be careful when treating them because it is proven that NIV may increase the risk of aerial spread of the virus. If any patient shows prognostic factors suggesting the need for invasive ventilation, it is preferable to use elective intubation rather than emergency intubation in critical conditions which will allow us to minimise complications of intubation for patients as well as reduce the risk of contamination [18].

Recommendations for patients in Invasive mechanical ventilation:

To reduce droplet dispersion during the treatment of patients in invasive mechanical ventilation, it is recommended to verify the pressure in the endotracheal cuff (25-30 cm H₂O) and to avoid using a pneumatic jet nebulizer. It is always better to use dry inhalers or ultrasonic nebulizers connected to the mechanical ventilator in a closed circuit and the antimicrobial filter should not be removed from the expiratory branch of the circuit [18].

Bronchial hygiene techniques: As airway clearing causes massive droplet dispersion, so bronchial hygiene techniques should be administered only when strictly needed for the improvement of the patient. On the basis of the study done by Lazzeri M, et al. airway clearance is not frequently required in COVID-19 patients [18].

Endotracheal suction: Through their study, Lazzeri M, et al. believe disconnections from the ventilator are necessary to avoid loss of Positive End Expiratory Pressure (PEEP) and atelectasis worsening. Therefore, it is advised to use a close suction circuit. Close circuit suctioning also decreases the risk of droplets spreading. Bronchoscopic suctioning should only be done when absolutely necessary [18].

Changes in posture: Prone positioning is recommended at least for 12 to 16 hours per day, preferably within 72 hours of endotracheal intubation. Repeat for at least 4 hours after the supine position until the $\text{PaO}_2/\text{FiO}_2$ ratio (P/F) is 150 mmHg with a PEEP of 10 cm H_2O and a FiO_2 of 0.60. The prone position must be abandoned if oxygenation deteriorates (20% decreases in P/F compared to the supine position) or if serious complications arise. Any treatment should not be applied in the presence of acute respiratory failure; it shows a reduction of lung compliance, which results in increased work of breathing and alteration of blood oxygenation, which causes a rapid and shallow respiratory pattern. Treatments and techniques used by physiotherapists should not cause any labour on the part of the respiratory system and should not increase the risk of respiratory distress for patients. Lazzeri M, et al. used physiotherapy techniques in their study, that is, diaphragmatic breathing, pursed lip breathing, bronchial hygiene/lung re-expansion techniques (PEP Bottle, cough machines), incentive spirometer, manual mobilization/stretching of the ribcage and inspiratory muscle training. But they suggested that it needs to be avoided in the acute phase of COVID-19 disease [18].

The aim of chest physiotherapy in COVID-19 is to reduce breathlessness and relieve anxiety. Long-term goals include improving physical functions and quality of life. Chest physiotherapy treatments recommended for patients with COVID-19 include airway clearance techniques such as active cycle of breathing technique, forced expiratory technique, percussion and vibrations, Positive Expiratory Pressure (PEP) therapy, positioning and gravity assisted postural drainage, high frequency oscillation devices, autogenic drainage, secretion clearance removal (huff and cough), suctioning, assisted or stimulated cough maneuvers, cough assist machine) and early mobilization. The treatment protocol is determined by the individual, the severity of the disease and the grade of the disease. In the acute phase of COVID-19, chest physiotherapy techniques such as diaphragmatic breathing, pursed-lip breathing and bronchial hygiene/lung re-expansion techniques are contraindicated. At this stage, the priority is the use of a mechanical ventilator, especially for those who have severe symptoms. Patients who have exudation and mild to moderate symptoms can be treated with chest physiotherapy. It depends on the patient's condition and the severity of the disease [19].

Physiotherapy used in patients with COVID-19 after discharge

For discharged patients from the hospital, respiratory muscle training is important. Training is given with a hand-held resistance device in which 10 breaths in each set need to be given for three sets. 60% of the individual's MEP with a rest of one min between the 3sets. Coughing training should be intended in which 3 sets of active coughing should be prescribed.

For improving the effectiveness of coughing Diaphragmatic training should be performed by performing 30 maximal voluntary diaphragmatic contractions in the straight lying position by placing a weight cuff 1-3 kg on the anterior abdomen. Corrective posture is important for improving the effectiveness of coughing. The patient should be placed in the straight lying to side lying position with the knees bent to correct the lumbar curve posture. For home programs, patients should be advised to move their arms in flexion, horizontal extension, abduction and external rotation, as well as pursed-lip breathing and coughing training. They should carry out thirty sets per day [19].

In his study, Abdullahi A [19] discussed a case that was referred for respiratory care in the medical ward. The patient was spontaneously breathing and had a past medical history of asthma and chronic obstructive pulmonary disease overlap syndrome. The patient's cough was dry and unproductive, so airway clearance techniques were not indicated. When the author compared his study to other studies, he explained that the requirement for physiotherapy techniques depends on patient to patient. Oxygen desaturation was found

in five patients, which is exertional and positional-related. In his study, he explained that one individual demonstrated persistent postural hypoxaemia. Oxygen saturation decreased by more than 90% during supine to upright sitting and was present more than 4 weeks after ICU discharge. Another case presented with exertional dyspnoea with poor exercise tolerance after discharge from the hospital. The reason was unclear, so it was assumed to be associated with severe ventilation and perfusion mismatch, which is mostly seen in severe COVID-19 [20].

Abdullahi A [19] explained that oxygen desaturation has been previously described in some patients with post-ARDS and survivors of severe acute respiratory syndrome. Various techniques have been followed to improve that manifestation. Physiotherapy sessions have been given with multiple breaks and small interval sessions in between exercise sets. In these conditions, exercise begins with interval training and progresses to continuous aerobic training. Vital signs need to be monitored continuously for all sessions to keep an eye on changes in oxygen saturation. This event has greatly slowed down the progression of rehabilitation, especially during the initial phases. The author has considered while giving therapy: early detection and recognition of this phenomenon of desaturation to avoid any serious alarm, rehabilitation planning according to patient tolerance, A prolonged physiotherapy rehabilitation course for patients who were severely ill as a result of the COVID-19 infection, Prescription of a home exercise programme to improve exercise tolerance and follow-up with the patient regarding telerehabilitation [20]. Narasimman, et al. showed in their study, which was conducted in the Indian population, that physiotherapy evaluation and management vary, which depends on severity of disease, daily activities and functional limitation, investigation and the rehabilitation setting [21]. In the study, they explained rehabilitation based on inpatient care, community-based rehabilitation, center-based rehabilitation and telerehabilitation. According to their study, in-patient care defines the programme provided when the patient is admitted to the hospital after a diagnosis of COVID-19 and physiotherapy rehabilitation given by a physiotherapist to improve the patient's condition.

Community-based care defines a programme given for practise at home post discharge from the hospital, which is done 3 weeks after the detection of COVID-19. Centre-based defines a programme provided to patients at the centre or OPD under physiotherapists' supervision, which is 6 weeks after COVID detection. Telerehabilitation defines programmes provided to patients using social media, such as video calls. Telerehabilitation is the preferred mode to control infection during the pandemic [21]. In their study, they initiated rehabilitation as early as 3 weeks post diagnosis of COVID-19 based on patient needs and functional limitations. An initial physiotherapy assessment in the post-acute phase (3-12 weeks post diagnosis) is a must, which includes COVID-19 history, presentation of COVID-19 symptoms, duration of COVID-19 symptoms, severity of COVID-19 symptoms, type of oxygen support during COVID-19 status Hospitalization and home quarantine number of days after the COVID-19 lab test was negative, limitations in daily living activities at discharge, or time of assessment after COVID-19 Medical management includes respiratory support, co-morbidities, metabolic disorders, past history of respiratory or cardiac disease, past medical history of any neurological disorder and new co-morbidities post COVID-19 disease. By physiotherapist Investigations need to be checked, especially haematological reports CBC, lipid profile, blood sugar level, HBA1C in diabetes, inflammatory markers, chest x-ray, HRCT, last available PFT, abgroutine cardiac investigations. The next evaluation by the physiotherapist that must be done is the vital signs examination: heart rate, blood pressure, oxygen saturation and respiratory rate. A vital examination must be done pre-rehabilitation and post-rehabilitation and throughout the session to find out the differences and check the progression of improvement. It is recommended to evaluate the respiratory system for the presence of airway secretions, breathing pattern, any postural changes and use of accessory muscles during rest and activities of daily living, any oxygen support, Dyspnoea grading and breath holding capacity [21]. Physiotherapy assessment for The neuromusculoskeletal system is important in that evaluation must be done for pain, sensory examination, motor examination, balance and coordination. When they compared their study to other studies, they found most patients got parasthesia after COVID-19 disease. A functional capacity test is important for post-Covid patients. The six-minute walk test was

chosen as a functional capacity test. If the patient fails the 6MWT, then the therapist must try the two-minute walk test to assess the severity of dyspnea and oxygen desaturation during normal activities. They have discussed fatigue examinations in which they used the visual analog scale for fatigue or fatigue severity scale to find out whether there was functional limitation in patients for fatigability or oxygen desaturation. In many studies, it is proven that COVID-19 disease causes neurological as well as psychological impairments. Hence, evaluation of psychological involvement is important. It is recommended for the evaluation of anxiety and depression. They have done nutritional evaluation by measuring loss of weight and BMI as it is noticed patients have reported reduced weight and muscle mass after COVID-19. According to Narasimman, et al. these evaluations are important for post-COVID-19 syndrome patients [21].

Physiotherapy management

The goal of breathing exercises is to improve inspiratory capacity and diaphragm muscle strength. Breathing exercises improve lung compliance and prevent atelectasis. It helps to improve collateral ventilation.

For improving lung compliance and preventing alveoli and lung collapse, the physiotherapy manoeuvre used is inspiratory breath-holds for 3 seconds, which has proved useful in many studies as well as improving collateral ventilation to maintain airway patency and reduce respiratory rate. Breathing control and pursed lip breathing are the best exercises for patients. As we know, COVID-19 patients mostly get breathlessness even in post-COVID-19 syndrome, which can be noticed. Dyspnea-relieving positions are recommended to reduce breathlessness. Airway clearance techniques in most studies which are used for post-COVID-19 syndrome and COVID-19 disease are Active Cycle of Breathing (ACBT) and Autogenic Drainage (AD). Lung volume expansion exercises and chest expansion exercises with proprioceptive feedback with emphasis on thoracic expansion and rib cage mobility, which improve lung volumes, lung capacities and improve ventilation and perfusion match. Incentive spirometry is one device that is mostly used for post COVID-19 syndrome if a patient gets pulmonary fibrosis; it helps to improve respiratory capacity.

Respiratory muscle training is recommended, which helps to reduce work of breathing for patients, as all patients have increased work of breathing after recovering from COVID-19. Inspiratory Muscle Training (IMT) devices such as inspiratory muscle trainers that load the respiratory muscles can be used, 2 sessions of 10 minutes respiratory rehabilitation per week for 6 weeks. Initiation of respiratory muscle training is non-threshold load training for the inspiratory muscles, which should be started from non-load training to a very low load of 3 cm H₂O and slowly increased thereafter, 10 to 15 minutes, 1 time/day. So, depending on the patient category, exercise prescription should be based on frequency, intensity, type and time. Based on various studies, an exercise programme should be a minimum of 6-12 weeks with 2-3 supervised sessions per week of at least 30 minutes duration. During exercise, continuous monitoring of oxygen saturation is recommended for patients who have a risk of desaturation during exercise. The oxygen requirement should be re-evaluated during the follow-up visit. Compared with various studies, it is recommended that the patient should be advised to maintain SpO₂ above 88% at rest and during activity, as well as resting blood pressure, which also needs to be checked for normally acceptable ranges and resting heart rate [21].

Termination of exercises in post covid-19 patients

On the basis of ACSM guidelines Oxygen saturation (SpO₂) drops by 88%, palpitations, sweating, chest tightness and shortness of breath Leg cramps Physical or verbal manifestations of severe fatigue Exercise-induced hypotension Uncontrolled hypertensive response to exercise (SBP>260 mmHg; DBP>115 mmHg), particularly in known hypertensive patients, as well as temperature fluctuation (>37.2 °C), exacerbation and fatigue.

Post covid sequelae

Post Covid Sequelae is a condition in which physical, cognitive and mental health impairments experienced by critical illness survivors of Covid-19. Some COVID-19 survivors experience severe clinical abnormalities lasting more than first 30 days of infection called Post Covid sequelae. It affects the pulmonary

systems, nervous system, neurocognitive disorders, mental health disorders, metabolic disorders, cardiovascular disorders, gastrointestinal disorders and several other clinical manifestations [22].

Post Covid mechanism: In COVID-19, Systemic Inflammatory Response Syndrome (SIRS) is predominant and long-lasting counterbalancing Compensatory Anti-inflammatory Response Syndrome (CARS) occurs that leads to post infection immune suppression. CARS responses: counter regulation to systemic inflammatory response syndrome to damage the pro-inflammatory state, prevent maladaptive multiple-organ dysfunction and govern the return to immunologic homeostasis. Excessive inflammatory responses cause viral exposure or inoculum, the state of immune competence and excessive release of inflammatory cytokines such as interleukins and 1, monocyte chemo attractant protein-1 and tissue necrosis factor-collectively known as "cytokine storm." This process results in the development of acute lung injury, ARDS, coagulopathy, hypotension, hypo perfusion, multiple-organ failure and multiple-organ dysfunction syndrome and death. This mechanism is shown in Figure 6. On the other hand, if the inflammatory response is repressed too far in the direction of CARS, then the patient, having managed to "weather" the initial hyper inflammatory cytokine storm and the progression to ARDS, may enter a stage of protracted immunosuppression known as Persistent Inflammation, Immunosuppression and Catabolism Syndrome (PICS) that is seen post-sepsis and which is one of the hypothesised causes of Persistent Post-covid Syndrome (PPCS). Post-septic patients are prone to latent virus reactivation and relapse or reactivation of SARS-CoV-2 in recovered COVID-19 patients. Post-sepsis COVID-19 patients are at risk for the development of secondary bacterial and fungal infections. This causes immune suppression and dysregulation. Patients are prone to the development of pulmonary fibrosis because of immune suppression. This is commonly seen in follow-up imaging of recovered patients and is different than Interstitial Pulmonary Fibrosis (IPF). Transforming growth factor beta is a multifunctional cytokine with profibrogenic, anti-inflammatory and immunosuppressive effects that are elevated during and after sepsis as well as during and after COVID-19 disease [23]. Histologic changes in COVID-19 patients' lungs show fibroblastic proliferations and interstitial fibrosis, indicating TGF-involvement. TGF-signaling, which is mediated by Smad proteins or MAP kinases and Akt, thus represents a potentially attractive target for therapeutic intervention as a potent inducer of fibrosis and immunosuppression.

Clinical features for post covid syndrome

Pulmonary fibrosis and dysfunction: Patients with COVID-19 who were severely affected and developed ARDS progressed to pulmonary fibrosis, characterised by exercise-induced breathlessness and chronic dry cough. Patients with COVID-19 who were severely affected and developed ARDS progressed to pulmonary fibrosis, with prominent symptoms including exercise-induced breathlessness and chronic dry cough. These are the prominent symptoms [24].

Cardiac fibrosis and dysfunction: After Covid-19 disease, myocardial injury is a remodelling process that includes hypertrophy and fibrosis of the left ventricular wall, resulting to reduced contractility and impaired global function. Cardiac abnormalities are mostly reported as myopericarditis, right ventricular dysfunction and ischemia/infarction. Myopericarditis may be suspected clinically based on the presence of one clinical feature that is pericarditic chest pain, heart failure or progression of heart failure symptoms, palpitations, syncope, new onset arrhythmia and one diagnostic criteria that

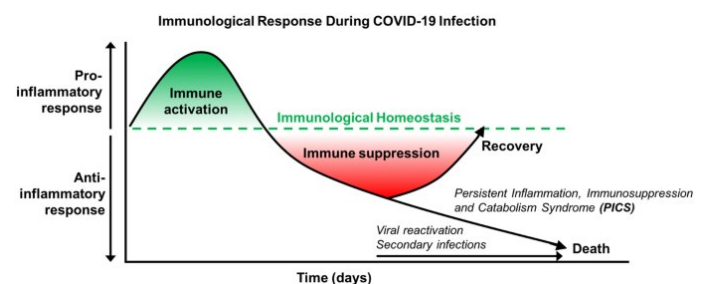


Figure 6. Mechanism of post covid-19 syndrome.

is ECG abnormalities, troponin elevation, or wall motion abnormalities on echocardiogram [24].

Neurological fibrosis and dysfunction: Neurologic and psychiatric sequelae are commonly seen in septic survivors because of COVID-19 disease. Neuropsychiatric symptoms include depression, anxiety and psychosis. Because deregulation of the TGF- signalling pathway has been linked to a variety of neurological disorders, including AIDS dementia complex, Alzheimer's disease, Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis (ALS), multiple sclerosis, anxiety, depression and schizophrenia, this cytokine is a potential therapeutic target for COVID-19-induced neuropsychiatric symptoms [23].

Physiotherapy management for post covid sequelae

ICU-Acquired Weakness (ICUAW), polyneuropathy, or myopathy, is associated with decreased strength and physical function that can persist for years after acute illness. Early rehabilitation within 48 hours of ICU admission is associated with improvement in strength and independent walking in the hospital. Physiotherapy services in the post-acute phase can be provided in the home as well as in the OPD setting. Some standardised assessments of muscle strength and activity of daily living limitations (e.g., exercise capacity and gait speed) in the post-acute setting can be performed both *via* telemedicine and OPD. The 6-min walk test and manual muscle testing score for strength evaluation need to be done. During post-acute period, restorative interventions are of limited efficacy for patients recovering from severe illness. Therefore, physiotherapy rehabilitation in the post-acute setting initially focuses on teaching both patients and patient party compensatory strategies to adapt and improve functioning. Once functioning has been preserved, restorative exercises such as aerobic strength and endurance training recommended to overload can be implemented while assessing cardiorespiratory demand.

Treatment plans from various studies for post-COVID-19 patients. 25 Number of Sessions in Week 1 3 per week. Physiotherapy rehabilitation and exercises that is breathing exercises: Pursed-Lips Breathing (PLB). Diaphragmatic Breathing Thoracic Expansion EDIC stands for Debit Controlled Inspiratory Exercises. Manual mucociliary clearance techniques (in the case of secretions):- active or active-assisted mobilizations Jacobson's autogenic relaxation exercises progressive strengthening exercises. Teaching of energy saving techniques number of sessions in week 2 purse-lips breathing is one of the three breathing exercises. Diaphragmatic breathing or deep breathing with manual resistance, thoracic expansion edic sum breathing along with active mobilizations. Aerobic Exercise which includes treadmill, stationary bike, or elliptical bike at 55-60% of Maximum Heart Rate (MHR) progressive strengthening exercises. Balance exercises number of sessions in week 3 breathing exercises. Aerobic exercise at 60-65% of maximum heart rate (treadmill, stationary bike, or elliptical bike). Progressive strengthening exercises. Balance exercises number of sessions in week 4 3 breathing exercises. Aerobic exercise (treadmill, stationary bike, or elliptical bike) at 70-75% of maximum heart rate progressive strengthening exercises, balance and coordination exercises. Results obtained after the medical reassessment of the patients after completing the 12 sessions of physiotherapy showed a reduction of at least 50% of the post-covid sequelae. In the maximal functional capacity test, few studies showed an improvement of 0.577 METs. There was an increase in the percentage of performance in the 6 MWT of 13% and in the basal oxygen saturation; it was increased by 1.40% at the end of treatment. The results of a few studies showed handgrip strength increased in both the left hand and right hand [25].

Physiotherapy management in post covid sequelae in India: Post-covid pulmonary manifestations present with various manifestations. It includes dyspnea, cough, chest pain, fatigue, palpitation, or exertional breathlessness. The cases with severe COVID and cytokine storm syndrome may later turn into pulmonary fibrosis or hypoxic requiring oxygen support [26]. Pulmonary rehabilitation is an effective strategy in reducing symptoms, improving quality of life and decreasing psychological distress [26]. In Indian studies, post-COVID sequelae patients underwent a 6-min walk test, SpO₂, MMRC scale, Hamilton A and Hamilton D scale, VAFS and numerical rating scale for pain. This helps to find out the patients' problem list.

The goal of pulmonary rehabilitation includes improving both physical and psychological quality of life and enabling the patients to have an optimal return to their family and personal life, reduces breathlessness, improve functional capacity. Breathing retraining, lower limb, upper limb endurance and strengthening exercises must be started on supervision on the basis of frequency, intensity, time and type principle. Patients must be completed 4 weeks of pulmonary rehabilitation training. Many studies proved that pulmonary rehabilitation is an ideal and mandatory intervention that must be done in a post covid-19 syndrome or sequelae patients [26]. In one study, it is discussed how a 33-year-old medical student contracted COVID-19 infection in July 2020, he had a history of seasonal bronchitis and pulmonary tuberculosis. He had complaints of dry cough, hemoptysis and breathlessness during the disease period. Fever started on the 2nd day and persisted for 5 days. His inflammatory markers were high with interleukin-6 of 150 picograms/mL. He was treated with antivirals, steroids, anticoagulants, tocilizumab and other supportive medications. He was admitted to the ICU for 4 days with supplemental oxygenation and started pulmonary rehabilitation Purse lip breathing, diaphragmatic breathing, range of motion exercises, thoracic expansion exercises, upper and lower limb strengthening exercises (shoulder rotation, active straight leg raise, wall pushups, sit-ups, squatting, quadriceps sets and calf muscle stretch) In the same study, the second case explained, a 74-year-old male with a known history of systemic hypertension, coronary artery disease, dyslipidemia, Chronic Obstructive Pulmonary Disease (COPD) and diabetes presented with complaints of low-grade fever, cough and myalgia for 2 weeks. COVID-19 RTPCR was positive in September 2020. He had been initially admitted with COVID-19 pneumonia in the nearby public health facility. Case 2, pulmonary rehabilitation started 4 weeks after COVID. Purse lip breathing, breathing retraining-started with 15 repetitions every 4 h, Diaphragmatic breathing, thoracic expansion exercises, incentive spirometry, positional therapy (leaning forward), upper limb and lower limb endurance training (active straight leg raise, repeated flexion extension of knee and shoulder rotation), calf muscle stretching. In the same study explained regarding the 3rd case, a 48-year-old female staff nurse by profession was diagnosed to have COVID-19 infection. She was asymptomatic during her disease period. There was a history of hypothyroidism and systemic hypertension. Her vitals were normal with a saturation of 98% in room air. Routine blood investigations were within normal limits. She was treated conservatively. After 1 month of her illness, she developed central catchy chest pain which was intermittent.

She had exertional breathlessness with MMRC Grade, for her exercises given flexibility exercises, purse lip breathing, diaphragmatic breathing exercise, Incentive spirometry, thoracic expansion exercise, upper and lower limb strengthening and endurance training (shoulder rotation, active straight leg raise, tread mill walking, wall push-ups, sit-ups, squatting, quadriceps sets and calf muscle stretching). Through this comparative case study, we found pulmonary rehabilitation in post-COVID cases can increase effort tolerance, quality of life and decrease anxiety and dyspnea [26].

SARS-CoV-2 contamination usually influences the breathing system, valuable and peripheral neurological. Several researches advised an affiliation among SARS-CoV-2 contamination and the improvement of GBS or Guillain-Barre Syndrome [27]. One case observes confirmed 27-year-vintage guy advanced fever (of as much as 39 °C) which lasted for five days at the side of cough and dysgeusia with anosmia. At After the resolving of the symptoms, the affected person complained of tingling sensation and numbness in each fingers after round 7 days and additionally in toes after 10 days. Over subsequent 1 week, the affected person advanced weak point strolling impairment related to distal limb weak point and became taken to the emergency branch of tertiary care non-public sanatorium. In that affected person Neurological exam achieved *via* way of means of physiotherapist and exam confirmed MRC rating for muscle power of the extensors muscular tissues of hand and palms 3/5 bilaterally; the dorsi flexors muscular tissues of the foot and the extensors muscular tissues of the feet 2/five at the left aspect and 3/5 at the proper aspect; strolling sample ataxia with huge base astonishing gait with high-stepped gait; faded contact and vibration sensation inside the toes and ankles; decreased tendon reflexes inside the top and the decrease limbs. Quality of life, mobility had been assessed the usage of World Health Organization (WHO) Quality of Life-BREF, medical mobility scale and

surroundings popularity scale. The cranial nerves had been normal. Nasopharyngeal swab check for SARS-CoV-2 with actual time RT-PCR became bad at the same time as the chest X-ray confirmed no symptoms and symptoms of pneumonia. Physiotherapy rehabilitation reference became given to the in-residence physiotherapist and physiotherapy control initiated as quickly as third day of admission. During the section of IPD admission physiotherapy control blanketed limb physiotherapy that is. passive and energetic-assisted actions enables in strain sores prevention and tightness; and breathing physiotherapy such as positioning, respiratory and thoracic enlargement exercises, diaphragmatic respiratory, inspiratory muscle training. After discharge from sanatorium affected person referred for OPD physiotherapy services. They suggested an affected person confirmed development of numbness, tingling sensation and weak point of muscular tissues and frame 7-10 days after the decision of fever, cough, anosmia and dysgeusia. Rehabilitation following covid-19 contamination has tested to have nice outcomes at the fitness consequences of patients as properly as enables in discount of ICU headaches like strain sores, development in recovery, enhance sports of everyday living, facilitation of early discharge, decreased hazard of re-admission etc. General rehabilitation advice within side the post-acute section consist of breathing rehabilitation, useful rehabilitation, early mobilisation, common posture changes, mattress mobilization, take a seat down to face actions, easy energetic mattress exercises, sports of everyday living, electric stimulation, innovative cardio workout, training on strength conservation strategies and conduct change therapies [27]. The domestic-primarily based totally workout interventions had been supplied 3 days according to week *via* video calls. At the start of every consultation, vitals like coronary heart rate, BP, SpO₂ or oxygen saturation of blood and blood glucose had been reviewed and recorded. Exercise packages had been divided in 3 classes primarily based totally on intensity: Light, Moderate or High, the usage of widespread ACSM recommendations for workout checking out and prescription. However, to maximise protection throughout workout, the prescribed workout coronary heart rates had been saved as a minimum 10 beats beneath the 60-80% predicted maximum; Rate Of Perceived Exertion (RPE) became saved < thirteen that's referred to as really tough at the Borg scale and the bottom cost of SpO₂ accredited became 90%. Each workout consultation at the video name lasted 35 mins. Exercise started out with five-10 mins of warm-up the usage of precise calisthenics for the disorder condition (neck and shoulder flexibility workout in most cancers sufferers; lymphatic drainage workout in breast most cancers sufferers; respiratory and chest enlargement in pulmonary and open-coronary heart surgical treatment sufferers; and energetic mobility workout in different cardiac sufferers). Aerobic workout and power training (20-25 mins) had been completed the usage of extraordinary frame actions, frame weight or family items (e.g. water bottles). Patients had been recommended to finish a prescribed quantity of brisk strolling, approximating half-hour according to consultation. All different consults, such as medicinal drug review, weight control training and mental properly-being had been performed through telephonic conversations *via* way of means of the targeted fitness care issuer on a weekly or advert libitum basis [28]. Outcome measures had been recorded at baseline and following the telerehabilitation program. A 6-minute walk test (6MWT) became performed truly on all sufferers within the presence of a care giver at domestic and beneath non-stop tracking *via* way of means of a therapist at the video name. Patients had been instructed "to stroll with no trouble for six mins, preserving their RPE beneath thirteen (Borg scale 6-20), corresponding to "pretty light" to "really tough." A PACER App became used to degree the space walked as it became now no longer possible to have an instantly walkway of ≥ 10 meters for all sufferers. Accordingly, sufferers had been recommended to stroll constantly on an impediment unfastened course inner their domestic. Health Associated Quality of Life (HRQoL) became received through the entirety of questionnaires: Short Form-36 (SF-36) for sufferers with cardiac conditions, Saint George Respiratory Questionnaire (SGRQ) for sufferers with pulmonary diseases. Patients had been dispatched the HRQoL scales and requested to as it should be whole and go back them. This observe suggests Daily step remember gives a with no trouble reachable device to display and set up bodily hobby goals. The HRQoL of our cardiac sufferers (SF-36) stepped forward *via* way of means of 11.6%, HRQoL for pulmonary (SGRQ) and oncology (FACIT) sufferers which discovered statistically great improvements, 29% and 9%,

respectively. Growth in symptoms (SGRQ/rating) in our pulmonary sufferers can be attributed to extra outcomes past workout [29]. we document 3 instances of sufferers with COVID-19 developing Parkinsonism and responding to levodopa. A 72-year-vintage male affected person and not using a beyond comorbidities offered with fever, chills, cough and breathlessness for 4 days. He became recognized with COVID-19 *via* way of means of an actual-time opposite transcription PCR assay and dealt with intravenous dexamethasone, intravenous remdesivir and heparin for 5 days. The affected person advanced Acute Kidney Injury (AKI) and became shifted to our facility. On day five of hospitalisation, his son observed that he became having freezing episodes inside the washroom; it became tough to mobilise him; and he additionally had 3 episodes of falls. On exam, he became discovered to have orthostatic hypotension (supine BP 130/70 mmHg and 3 min status BP 80/60 mmHg), lack of smell, cog-wheel tension, postural instability and bradykinesia. An analysis of Parkinsonism turned into taken into consideration primarily based totally at the scientific features. The postural hypotension turned into controlled with improved fluid and salt consumption and compression stockings and the affected person turned into began out on levodopa a hundred and ten mg, 1/2 of a pill 4 instances a day. The affected person's signs advanced with those measures. He had no falls, the tension subsided and his gait pace improved. On follow-up after 4 months, he pronounced whole decision of signs and done his sports of every day dwelling independently. Pronounced whole decision of signs and done his sports of every day dwelling independently [30].

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