LONG COVID: ITS CLASSIFICATION, PATHOPHYSIOLOGY, RISK FACTORS, CLINICAL MANIFESTATIONS, AND MANAGEMENT GUIDELINES

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***Abstract*: Post-COVID syndrome or long COVID is defined as COVID-19 associated illness that extends for more than three weeks from the onset of symptoms and chronic COVID-19 is an illness that extends beyond 12 weeks from the onset of symptoms. Two main symptom clusters of long COVID include those characterized solely by fatigue, headache, and upper respiratory symptoms; and those with multi-system complaints including ongoing fever and gastroenterological symptoms. The pathogenesis of post-COVID syndrome remains largely unknown and evidence states that prolonged inflammation has a key role in the pathogenesis of most post-COVID manifestations. The presence of more than five symptoms during the acute stage of the disease is linked to a higher likelihood of protracted COVID. Most commonly associated symptoms with long COVID include fatigue, headache, dyspnea, hoarse voice, and myalgia. Thus, the patients with COVID-19 require long-term monitoring and management of their post-COVID symptoms, even after they have recovered.**

***Keywords*: Long COVID-19, Inflammation, Pathogenesis, Fatigue syndrome, Management, Follow-up**

INTRODUCTION

More than 462 million infections and 6 million deaths as of March 16, 2022, were affected due to the global COVID-19 pandemic that began in late 2019. Disability-adjusted life years are increasing and the survivors experience long-lasting psychological, medical, and economical consequences. The health consequences of COVID-19 remain urgent even despite vaccination efforts. The long-term effects of COVID-19 in individuals with a variety of clinical presentations and degrees of severity are urgently needed to be understood.[1] Approximately 10%– 15% develop severe illness and 5% become critically ill whereas the majority of people with COVID-19 experience mild-to-moderate illness.[2] Based on symptom severity the average recovery time from COVID-19 is 2-3 weeks.[3–5] Regardless of the severity of their acute infection, 1 in 5 may exhibit symptoms for 5 weeks or more, whereas 1 in 10 may have symptoms lasting 12 weeks and more.[6] Thus, the patient-coined term 'long COVID' was proposed.[7] Classic cases of acute COVID-19 are characterized by respiratory symptoms, fever, and gastrointestinal problems (Larsen et al., 2020). [8] However, a wide range of other symptoms can also be presented, including neurological issues suggesting central nervous system (CNS) involvement (Harapan and Yoo, 2021). [9] Acute COVID-19 cases range in length and severity. Many are asymptomatic, while others require hospitalization and ventilation (Cunningham et al., 2021).[10] Lingering or protracted illness that patients of COVID-19 continue to experience even in their post-recovery phase is termed as 'Long-COVID-19'. It is also called as 'post-acute COVID-19′, 'ongoing symptomatic COVID-19′, 'chronic COVID-19′, 'post COVID-19 syndrome', and 'long-haul COVID-19′. [11]

LONG COVID: Definition and Classification:

COVID-19 is defined as a case with laboratory-confirmed SARS-CoV-2 infection through real-time positive RT-PCR (Reverse Transcriptase- Polymerase Chain Reaction) in a patient with or without symptoms. Post-COVID syndrome or long COVID is defined as COVID-19 associated illness that extends for more than three weeks from the onset of symptoms and chronic COVID-19 is an illness that extends beyond 12 weeks from the onset of symptoms.[19] 'Long-COVID-19′ is a term first used by a patient Elisa Perego from Italy, as a hashtag on Twitter in May 2020 while describing her own experience with persisting symptoms of COVID-19 even after recovery. [11] Recent joint guidelines proposed by the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), and the Royal College of General Practitioners (RCGP) have divided COVID-19 infection into 3 phases – 'Acute COVID-19′ with signs and symptoms of COVID-19 infection up to 4 weeks, 'ongoing symptomatic COVID-19′ from 4 weeks up to 12 weeks, and 'post-COVID-19 syndrome' when signs and symptoms continue beyond 12 weeks.[12] The term 'Long COVID-19′ is given to the signs and symptoms that continue or develop after the 'acute COVID-19′ phase and include both 'ongoing symptomatic COVID-19′ and 'post COVID-19 syndrome'. The chronic or long-haul COVID are the other names used to describe the sequel of COVID 19. [13,14,15] Persistent medical problems reported after acute COVID-19 can include a wide range of symptoms and are linked to residual inflammation during the convalescent phase,

organ damage, non-specific effects from prolonged ventilation such as post-intensive care syndrome, prolonged hospitalization, social isolation, or impact on underlying medical conditions.[8, 26] Two main symptom clusters of long COVID include

i. those characterized solely by fatigue, headache, and upper respiratory symptoms; and
ii. those with multi-system complaints including ongoing fever and gastroenterological symptoms.[16]

Based on the proposed criteria of the University of Cincinnati Medical Center for COVID-19 sequelae, there are five categories of long COVID-19 syndrome, based on initial symptoms, duration of symptoms, time of onset, and period of quiescence. Type 1 includes patients with different duration of recovery which directly relates to the severity of the acute infection, complications of organ, and various other medical conditions; Type 2 is characterized by symptoms persisting six weeks from the onset of illness; Type 3 includes a quiescence period or nearly full recovery which is followed by a recurrence of symptoms persisting for at least three months known as Type 3A or at least six months as Type 3B; Type 4 includes patients who are initially asymptomatic and is SARS-CoV-2 positive but become symptomatic one to three months is the Type 4A, or at least three months later is the Type 4B, and Type 5 includes patients who are asymptomatic at the time of diagnosis and die within the next 12 months.[4] Lastly, Fernandez-de-Las Penas et al. considered also undiagnosed cases and proposed a time-based classification as follows: potentially infection-related symptoms lasting up to 4–5 weeks, acute post-COVID symptoms lasting from week 5 to week 12, long post-COVID symptoms lasting from week 12 to week 24, and persistent 3 of 12 post-COVID symptoms lasting more than 24 weeks. Intrinsic and extrinsic predisposing factors are also considered. [17,22,33]

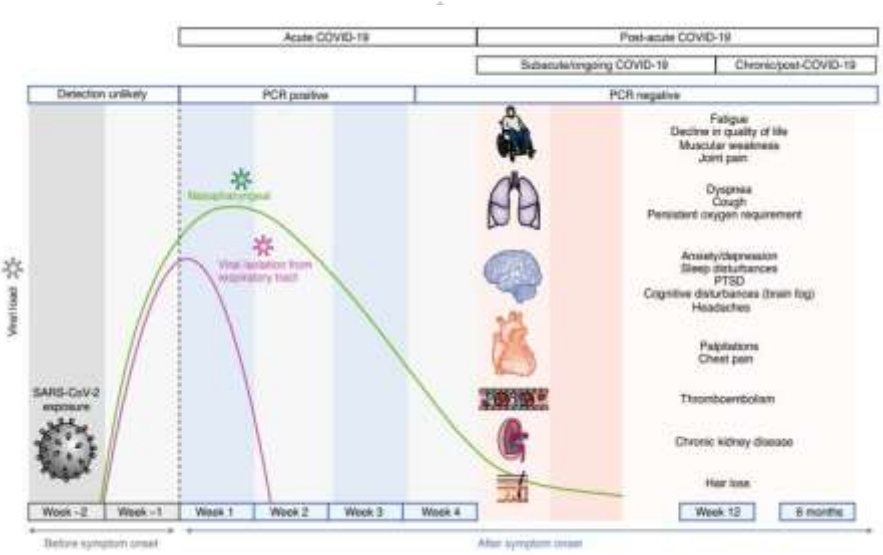

Fig.1: Timeline of post-acute COVID-19 with common symptoms observed in post-acute COVID-19 are summarized.[18]

PATHOPHYSIOLOGY:

The pathophysiologic mechanisms of acute COVID19 include direct viral toxicity, endothelial damage, and microvascular injury; immune system dysregulation and stimulation of a hyperinflammatory state; hypercoagulability with in situ thrombosis and macrothrombosis; and maladaptation of the angiotensin-converting enzyme (ACE2) pathway 2. The evolutionary similarities between the relevant pathogenic coronaviruses explain the overlap of post-acute COVID-19 sequelae with those of SARS and MERS, and the genomic sequence identity of SARS-CoV-2 is 79 percent with SARS-CoV-1 and 50 percent with MERS-CoV. Moreover, SARS-CoV-1 and SARS-CoV-2 have the same host cell receptor: angiotensin-converting enzyme 2. There are variances, such as SARS-CoV-2 having a higher affinity for ACE2 than SARS-CoV-1, which is likely owing to changes in the receptor-binding domain of the spike protein that binds with ACE2. The spike gene has diverged in SARS-CoV-2, with only 73% amino acid similarity with SARS-CoV-1 in the receptor-binding domain of the spike protein in contrast with the other structural genes. SARS-CoV-2 has an extra S1–S2 cleavage site that allows for more efficient cleavage by host proteases and easier binding. These mechanisms are involved in the more effective and widespread transmission of SARS-CoV-2. Potential mechanisms involved in the pathophysiology of post-acute COVID-19 include: 1) virus-specific pathophysiologic changes; 2) immunologic aberrations and inflammatory damage in response to the acute infection, and 3) expected sequelae of post-critical illness. The pathophysiology of post-intensive care syndrome is multifaceted, with microvascular ischemia and damage, immobilization, and metabolic changes during critical illness all being suggested. Adding to this, prior studies of SARS survivors show that 25–30% of patients have secondary infections, suggesting that survivors of acute COVID-19 may be at higher risk of bacterial, fungal (pulmonary aspergillosis), or other pathogen infections. However, these secondary infections do SSnot account for the long-term effects of post-acute COVID-19. [18]

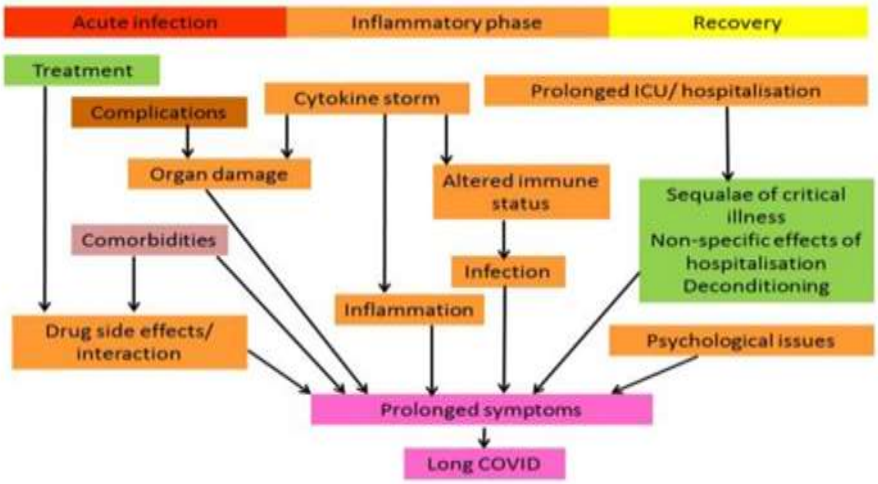

Fig.2: Various pathophysiological mechanisms of "Long COVID"[4]

The pathogenesis of post-COVID syndrome remains largely unknown and evidence states that prolonged inflammation has a key role in the pathogenesis of most post-COVID manifestations. Ortelli et al. recently studied 12 patients with a median age of 67 years, who had recovered from COVID-19 with neurological complications and who complained of fatigue had a median time from onset of COVID-19 for 12 weeks; which ranged from 9–13 weeks.[19] All 12 patients had a hyper-inflammatory acute phase with markedly elevated C-reactive protein CRP and IL-6. In comparison to 12 healthy patients who were age and gender-matched, the authors observed indications of central aberrant neuromuscular exhaustion, decreased cognitive control, diminished global cognition, apathy, and executive dysfunction in the post-COVID period, which had an impact on their everyday lives.[20] Altered neuronal function results in the profound increase of circulating cytokines, and particularly IL-6, which can penetrate the blood-brain barrier, may occur and contribute to central nervous system (CNS) complications such as altered mental status and neurocognitive disorders among others. [21]

RISK FACTORS:

Patients with long COVID are presented with a wide range of symptoms new or persistent, in both the hospitalized and non-hospitalized populations.[23] The presence of more than five symptoms during the acute stage of the disease is linked to a higher likelihood of protracted COVID. Most commonly associated symptoms with long COVID include fatigue, headache, dyspnea, hoarse voice, and myalgia. The risk of developing post-COVID syndrome increases with the presence of co-morbidities. Even those patients with mild symptoms at initial presentation developed long COVID.[24] In a prospective cohort study of confirmed COVID-19 infected adults, anosmia and dysgeusia were associated with younger age and higher heart rate at admission were considered independent predictors of Long COVID symptoms [29]. Estimated glomerular filtrate (eGFR) ≤60 mL/min/m2 and male sex were predictors of lingering abnormalities on spirometry. Moreover, a higher imaging score during the acute phase of the illness is associated with the persistence of radiologic lung involvement.[27] Another prospective cohort study showed that the oxygen supplementation duration in the acute phase of the disease is strongly associated with predicted diffusing capacity for carbon monoxide, DLCO %, and total computed tomography, CT scores 12 weeks after symptom onset. A significant association was found between dyspnea severity score on 12-week follow-up and predicted diffusing capacity for carbon monoxide, DLCO% [28]. A report of 52 cases of COVID pneumonia with at two chests computed tomography, CT scans of around 3 months apart, a higher initial CT severity score, Intensive care unit, ICU admission, longer hospitalization, other medical conditions, higher initial WBC count, and development of leukocytosis during hospitalization were considered predictors of persistent pulmonary abnormalities on the second Computed tomography scan.[29] When it comes to long-term mental health problems, there are multifold risk factors related to post-traumatic stress disorders, PTSD, and chronic psychological distress after the acute phase of COVID-19. Greater exposure to the illness was associated with a higher incidence of Post-traumatic stress disorder. Loss of loved ones, hospitalization, containment measures such as quarantine and isolation, being in low-income regions, financial stressors, having disabilities, female gender, and older age were the most common mental health risk factors reported by preliminary studies.[30] The family history of the COVID 19 positive patient turned out to be significantly associated with post-COVID 19 events in this study. Because COVID 19 spreads from person to person, family members are potential sources of infection due to the risk of the high viral load that they carry, and is a major challenge in the control of the disease.[31]

CLINICAL MANIFESTATIONS:

FATIGUE

Patients with COVID-19 may develop chronic fatigue syndrome/myalgic encephalomyelitis, present with prolonged relapse of exhaustion, cognitive dysfunction, depression, and other symptoms after a minimal amount of activity.[34] Fatigue is the most common symptom of post-COVID syndrome, with an incidence ranging from 17.5% to much higher rates for hospitalized COVID-19 patients either inwards or in intensive care units up to 60.3 and 72.0%, respectively. Fatigue is reported up to seven months by patients after the onset of COVID-19 causing disability, with many patients continuing to experience fatigue beyond seven months which requires thorough investigation. Male gender, as well as comorbidities such as hypertension and diabetes mellitus, have been linked to weariness. Because there is currently no diagnostic procedure for, any conditions with comparable symptoms must be

ruled out. Hormonal imbalances, immune system malfunction, infection, and neurological system abnormalities are all part of the disorder's etiology.[8,42] Fatigue is more profound, unrelenting exhaustion and a constant state of weariness that reduces a person's energy, motivation, and concentration.[25] It is the most commonly reported symptom with a reported frequency of 16% to 55% and is assessed using the Chalder fatigue scale. It is an 11-point questionnaire with a minimum of 0, zero, and a maximum of 11, eleven scores and a cut-off score ≥ 4. Check whether the condition fits in chronic fatigue syndrome if the symptoms persist for more than 6 months involves the three cardinal symptoms fatigue, aggravation of symptoms with exercise, and unrefreshing sleep present for more than six months. For at least 50% of the time, the severity is moderate or severe. The diagnostic criteria for Chronic

Fatigue Syndrome/Myalgic Encephalitis are as follows:

1. Chronic Fatigue Syndrome (essential criteria)
• For more than six months, significant deterioration in the capacity to execute tasks performed previous to the disease
• Profound fatigue not resolved by rest
• Discomfort or aggravation after physical effort
• Unrefreshing sleep
2. Fatigue syndrome with chronic fatigue (at least one of the two additional criteria must be present)
• Impaired cognition (impairment of executive functions or thinking that worsens with exertion, stress, or pressure)
• Intolerance to orthostatic pressure (symptoms worsen when standing and improve when lying down or raising the lower limbs)
• Patients with myalgic encephalitis must also suffer from cognitive impairment.[32]

SMELL AND TASTE DISTURBANCES

After the commencement of smell and taste loss, recovery of olfactory and gustatory dysfunction might take up to a month. Gender nor age are neither predictors of the olfactory result. [38] The partial loss of olfactory receptor neurons in the olfactory epithelium and cells that express two known proteins used by SARS-CoV-2 to infect human cells at the peripheral level, angiotensin-converting enzyme, ACE2, and transmembrane protease serine 2, TPMRSS2, are linked to olfactory dysfunction caused by SARS-CoV-2. The exact mechanism by which SARS-CoV-2 causes taste loss is unknown. ACE2 receptors have been found in the mouth and on the tongue, therefore it could be caused by direct injury to the gustatory organ. [8] SARS-CoV-2 infection can cause chemosensory abnormalities such as hyposmia/anosmia and ageusia/dysgeusia. There have been no reports of new-onset anosmia or ageusia during the Post-COVID era since these symptoms develop during the acute phase and persist. During the Post-COVID period, the studies found a median adjusted frequency of 23.6 percent for anosmia and 15.6 percent for ageusia or dysgeusia. According to studies, they recover in a median of 31 days, but some dysfunction may continue in around a third of the population. [32]

DYSAUTONOMIA

Dysautonomia is the dysfunction of the nerves that causes dizziness, palpitation, exercise intolerance, chest tightness, presyncope, and syncope mainly when posture changed from lying to standing. Once the cardiac and respiratory causes are ruled out, autonomic dysfunction should be ruled out. One of the reports shows abnormal autonomic function tests in 12% of patients recovering from COVID-19 and if the symptoms last more than 3 months look for the possibility of Postural orthostatic tachycardia syndrome (POTS). Check for:

1) Increase in HR >30 BPM in adults and 40 in children within 10 minutes of adopting an upright posture
2) Absence of postural hypotension
3) Symptoms of orthostatic intolerance
4) >3 months.[32]

HEADACHE

According to studies, the frequency of headaches during the post-COVID period ranges from 2 to 60%. According to a recent meta-analysis, the frequency of headaches decreases from 47 percent upon admission to 8 percent after six months. The majority of individuals suffer from tension headaches, while migraine headaches are less common. Patients having a history of migraines, on the other hand, may experience an increase in frequency. Some people may have characteristics that make them suffer from a daily headache. [32]

COGNITIVE IMPAIRMENT

Around 12-50% of patients reported that impairment of cognition persisted beyond 1 year. Impaired attention, concentration, executive function, and memory contribute to the most frequent deficits. Brain fog is another common manifestation of Long-COVID, an umbrella term used to describe the constellation of cognitive function impairment such as confusion, short-term memory loss, dizziness, and inability to concentrate. ICU admission and mechanical ventilation during acute illness contribute to long-term cognitive impairment. [32, 35]

SLEEP DISORDERS

Sleep dysfunction and insomnia can occur in around 18-30% and it persisted beyond one year in the majority. The sleep quality is assessed with the Insomnia severity index or Pittsburgh sleep quality index.[32]

NEUROMUSCULAR DISEASES

The most common triad forms where 40–70% of skeletal muscles are affected in COVID-19 cohort studies include myalgia, fatigue, and hyper creatinine kinase (CK)-emia. Quadriceps and biceps weakness is found in more than 75% of survivors of COVID-19

illness and it persists beyond one year. A COVID-19 disease requiring intensive care with invasive ventilation can lead to ICUAW, ICU (Intensive care unit) acquired weakness, a clinical picture in which CIP, critical illness polyneuropathy and CIM, critical illness myopathy intertwine. There seems to be no massively increased risk for neuromuscular patients suffering from SARS- CoV-2 infection.[32]

GUILLAIN-BARRE SYNDROME (GBS)

An acute inflammatory demyelinating polyneuritis, AIDP with neurological symptoms usually appears within 5–10 days after a COVID-19 diagnosis, although it may develop even weeks after infection. A rapid diagnosis and immediate therapy including critical care admission are recommended due to the risk of cardiovascular complications with cardiac arrhythmias and respiratory insufficiency. Clinically, mild courses up to severe tetraparesis, weakness on all the four limbs. There have also been reports of cranial nerve involvement with bilateral facial nerve palsy, ocular muscle palsy, or Miller Fisher syndrome. A rapid progression of the disease results in respiratory insufficiency and the requirement for ventilation. [32]

STROKE

Ischemic strokes and intracerebral hemorrhage (ICH) occur in patients with COVID19 disease and are associated with a more severe course of the disease. Strokes are reported as Post-COVID sequelae and a confirmed or presumed infection with SARS-CoV-2 in patients with acute stroke should not lead to different treatment than for other stroke patients. They should receive the same acute diagnostics and acute treatment as all stroke patients.[32]

EPILEPSY

Since many patients with chronic epilepsy suffer from drug withdrawal attacks as a result of limited access to doctors and drugs, it is critical to ensure that patients with pre-existing epilepsy have constant access to outpatient neurological care and that adequate and timely antiepileptic drugs are prescribed to avoid supply shortages. Status epilepticus has been documented as part of the Post-COVID syndrome. [32]

CARE AND FOLLOW-UP OF POST-COVID PATIENTS:

Depending on the individual's presentation, accepted protocols for patient management and care are followed. The following are the NATIONAL COMPREHENSIVE GUIDELINES FOR Treatment OF POSTCOVID SEQUELAE issued by the Ministry of Health and Family Welfare of India.

General Consideration:

Post-acute COVID-19 syndrome is a multi-system sickness marked by respiratory, cardiovascular, hematologic, and neuropsychiatric symptoms that can occur separately or in combination. As a result, therapy should be personalized to the individual, using an interdisciplinary approach that addresses both the clinical and psychological aspects of the problem. Diabetes, chronic kidney disease, and hypertension should all be treated to the best of one's ability. [36,37] Patients should be taught how to use FDA-approved equipment such as a pulse oximeter, blood pressure monitor, and blood glucose monitor to monitor their health at home. Patients should be encouraged to consume a well-balanced diet, get adequate sleep, drink moderately, and quit smoking. [37] If needed, simple acetaminophen analgesia should be considered. If tolerated, a structured exercise program with aerobic and resistance components should be recommended. [38]

Pulmonary

Patients who have prolonged heart symptoms after recovering from COVID-19 should be followed by a cardiologist regularly. Cardiac function tests like the EKG and echocardiography must be reviewed to rule out arrhythmias, heart failure, and ischemic heart disease. A Magnetic Resonance Imaging, MRI of the heart may be performed if clinically appropriate to assess for myocardial fibrosis or scarring, given the higher risk of myocarditis in COVID-19 patients. [39]

Cardiovascular

After healing from COVID-19, patients who have persistent heart issues should be examined by a cardiologist. Cardiac function tests such as EKG and echocardiography must be assessed to rule out arrhythmias, heart failure, and ischemic heart disease. Because COVID-19 individuals have a higher risk of myocarditis, an MRI of the heart may be performed if clinically indicated to look for myocardial fibrosis or scarring. [39]

Hematologic

Despite the knowledge that COVID-19 is connected to a prothrombotic state, no consensus exists on the benefits of VTE prevention in the outpatient environment. In COVID-19 patients who develop proximal DVT or PE, the American College of Chest Physicians (CHEST) recommendations currently recommend anticoagulant treatment for at least 3 months. [40,41]

Neuropsychiatric

Patients should be tested for common psychological disorders such as anxiety, depression, sleeplessness, and post-traumatic stress disorder (PTSD), and if necessary, referred to behavioral health professionals. Because of the wide range of neurological symptoms associated with this disease, a neurology assessment should be sought as soon as possible. Additional laboratory tests, such as

hemoglobin A1C (HbA1c), TSH, thiamine, folate, Vitamin B12, and Vitamin B12, must be performed in addition to the regular laboratory checkup mentioned above to assess for any contributory metabolic disorders.[42] If there are concerns about seizures or paresthesias, EEG and EMG should be examined.[32]

Management fatigue

- Self-management and support.
- There are no official COVID guidelines.
- Look for additional systems that may be involved, such as cardiorespiratory and autonomic, and refer if needed.
- Make sure you get enough rest, sleep, and stay hydrated.
- Avoid taking over-the-counter analgesics unless necessary.
- For selected people, a management plan for chronic fatigue syndromes, such as graded exercise therapy (GET), or a self-management method, such as "pacing," in which the patient modifies their activity to prevent exertion, may be recommended.
- Supplementing with vitamin C is beneficial in some cases.
- Aerobic workouts, balancing training, breathing training, and resistance strength training should be initiated with low intensity, and progressively increasing duration and intensity can all help.[32]

Management dysautonomia

• Patient education
• Structured aerobic and resistance training, as well as non-orthostatic workouts like recumbent bicycling and swimming.
• Supplementing with fluids (2-3 L/day) and salt (1-2 tbsp)
• Avoid triggering factors such as caffeine, alcohol, prolonged standing, hot humid conditions, and dehydration, as well as medications like duloxetine and nortriptyline.
• Compression clothing
• Fludrocortisone and midodrine are pharmacological medications.[32]
Management headache
• Look for the red flags
• Treatment varies depending on the nature and frequency of the headache. [32]

Management cognitive dysfunction

- There is no defined COVID procedure.
- Assess the patient using validated tests and try to rule out treatable causes of cognitive impairment, as is standard clinical practice.
- It requires a holistic approach. Patients should be assured that most of them will recover.
- Repeated cognitive exercises, stress reduction, coping skills, and, if available, the assistance of speech, language, and occupational therapists may be beneficial.
- Crossword puzzles, simple number games (such as sudoku), reading newspapers, and reading books can all aid to improve cognitive ability. [32]

Management of sleep dysfunction

- Those who are experiencing trouble sleeping should practice good sleep hygiene.
- Avoid coffee and alcohol before bedtime, and don't use your phone or computer too late at night.
- In a quiet, dimly lit room, soothing or tranquil sleep music may aid in improving sleep latency.
- Self-medicating with benzodiazepines should be avoided. It is preferable to seek medical advice rather than self-medicate. [32]

Management Guillain-Barre Syndrome (GBS)

NCS - nerve conduction investigations - usually show a demyelinating pattern of damage, while axonal processes are also seen. To rule out an infectious etiology, a cerebrospinal fluid investigation is required. A cytoalbuminous dissociation appears in the majority of instances. The treatment is identical to the standard GBS treatment. Intravenous immunoglobulins (2 g/kg BW) are recommended, however, plasma exchange is also an option. Corticosteroids should be avoided if at all possible. [32]
Management stroke
It is important to recognize stroke symptoms and initiate a Protocol Based Stroke Management Some of the warning signs are

- Sudden onset
- Difficulty in speaking or understanding words
- Strange feeling or loss of feeling on one side of the body
- Face, arm, or leg weakness
- Unexplained dizziness or loss of balance
- Decreased or blurred vision
- Severe unexplained headache

Since the window for thrombolysis is 4.5 hours a quick assessment should be made fast.

- Ask the patient to smile

- Ask the patient to raise arms
- Ask the patient to say a phrase and
- Ask about the onset of symptoms and its time

Refer the patient to a center with a stroke management facility.[32]

Management of Status Epilepticus:

When compared to normal management, the Post-COVID management plan is the same.

- Anti-N-methyl-D-aspartate (NMDA) antibody and Anti-voltage gated potassium channel antibody may be effective in cases where the etiology is uncertain and CSF does not reveal the infection.
- CSF, brain imaging, EEG, and drug monitoring, among other tests, should be utilized judiciously.
- First line agents Lorazepam/Diazepam/Midazolam Agents.
- In the second tier, Lacosamide/Levetiracetam/Phenobarbitone phenytoin/phosphenytoin/sodium valproate phenytoin/phosphenytoin/sodium valproate phenytoin/phosphenytoin/sodium valproate phenytoin/ SE refractory SE that persists despite adequate delivery of benzodiazepines and at least one antiepileptic medicine is referred to as refractory SE, regardless of the timing (RSE).
- Intubation and mechanical ventilation of the patient, as well as frequent hemodynamic support with pressors or inotropes, are more aggressive interventions that should be used.
- Propofol, Thiopentone, Ketamine, and Midazolam are some of the drugs that may be employed. If a patient is not responding, they may be sent to a higher level of care. [32]

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Nothing to disclose

CONCLUSION:

Patients with COVID-19 require long-term monitoring and management of their post-COVID symptoms, even after they have recovered. During their stay and discharge, such patients require a complete rehabilitation program. However, a great population in the post-COVID condition requires continuous surveillance. Patients who exhibit symptoms such as weariness, cough, and shortness of breath early in their condition are more prone to develop the post-COVID syndrome. The most common long-term symptoms identified based on various studies include fatigue, headache, myalgia, joint pain, and exertional dyspnea. Understanding the long-term implications of COVID 19 is critical in primary care since post-COVID symptoms will account for a major portion of morbidity during and after the pandemic.

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