

The Post-Acute COVID-19 Syndrome : A New Emerging Health Issue

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SARS- CoV-2 is a ongoing pandemic which full of mysteries, where understanding its pathogenesis and clinical features are still not clear. But post COVID-19 complications being unveiled are the next level of challenges.¹ As of 15th July, 2021 more than 189 million people have been infected and about 4 million deaths have been reported, with 170 million recovered.² According to World Health Organization (WHO) almost 80-85% of COVID-19 infections are mild or asymptomatic and resolve completely like any other uncomplicated seasonal flu, 10-15% are severe illness requiring hospitalization/ oxygen supplementation and about 5% are critical illness requiring intensive health care and mechanical ventilation.³ Generally, the majority of the patients show complete recovery within 3-4 weeks of COVID-19 infections, but few patients continue to show its lingering effects and develop protracted illness/ medical complications that can have long lasting health problems.

It is called 'Long- COVID-19'- 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 continuing symptoms of COVID-19 even after recovery. There is no clear definition of post covid syndrome. NICE guidelines arbitrarily divided COVID and its long-term effects into 3 groups: Acute COVID: Signs and symptoms of COVID-19 for up to 4 weeks, Persistent COVID: Up to 4 to 12 weeks and post-COVID-19 more than 12 weeks and not explained by other alternative diagnosis.⁴ These nomenclatures are also varies in different publications. A unified definition of long covid and characterization of its manifestations are important for early detection

There is lack of systemic reporting of the long-term consequences of COVID-19 with data still

emerging and availability of only few early studies on the subject. In a recent systematic review and meta-analysis, 80% (CI 65-92) patients with a confirmed COVID-19 diagnosis are reported to continue having at least one symptom beyond 2 weeks of acute infection.⁵ Two recent prospective studies reported persistence of symptoms in 32% of the outpatient COVID-19 subjects from Swiss (n = 669) and 83% of hospitalized COVID-19 subjects from Italy (n = 143). The UK based survey reported the prevalence of Long- COVID-19 symptoms of 1 in 5 COVID positive subjects for five weeks or longer and 1 in 10 COVID positive subjects for 12 weeks or longer.⁶

The understanding of the pathophysiology of Long- COVID-19 is important to predict, prevent and treat long-term consequences of COVID-19. It appears secondary to endotheliopathy, hypoxemic injuries, antigen- antibody reactions, or aberrant immune response.^{1,7} Reactivation or reinfection of the SARS CoV-2 is another concern in the follow-up period, with few cases being reported lately.^{8,9}

With the COVID-19 pandemic ranging across the world, many recovered patients continue to suffer the lingering effects of the infection, including respiratory, cardiac, cutaneous and nervous system impairment. Persistence of the physical symptoms seen in acute viral illness is the most common manifestation of Long- COVID-19. Sometimes, a fair of neuropsychiatric symptoms or appearance of new psychiatric symptoms is reported in 16-18% patients of Long-COVID-19, especially those who had critical illness or ICU admission.¹⁰ Long-COVID-19 subjects with persistent symptoms have reported poor quality of life and impaired functionality of 40% of the hospitalized patients even in 60 days following discharge.¹¹ There is a marked variation of post covid syndrome. The common clinical manifestations encountered in Long- COVID-19 are divided into two groups: Generalized and organ specific manifestations. In generalized manifestations, they are non-specific but often experienced persistent symptoms of COVID-19, even by patients with a milder form of the disease. Persistence of some of the acute illness physical symptoms, including dyspnea, fatigue,

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post-exertional malaise, chest pain, and cough, are the most common manifestation of the Long-COVID-19^{12,13}. Organ specific manifestations are: Neurologic: Brain fog most common, persistent loss of smell/ taste encephalopathy and stroke, Pulmonary: Dyspnea and cough, most common chest pain, Post- COVID-19 ILD, Cardiovascular: palpitations, most common myocarditis & pericarditis heart failure, Psychiatric: Most common- Depression and Post Traumatic Stress Disorder and Cutaneous: Erythematous rash and urticarial rash. Other miscellaneous manifestations like endocrinological, prothrombotic, retinal and neuromuscular complications are lately being reported in Long- COVID-19 subjects.^{14,15} The predictors of Long- COVID-19 are associated with multiple factors like older age group, middle aged women, disease severity, length of ICU stay, assisted ventilation, underlying comorbidities, abnormal lab test results like lymphopenia, thrombocytopenia, elevated D-dimer, LDH, Troponin, elevated CRP, Ferritin, IL-6 and deranged coagulation profile and miscellaneous factor like more than 5 symptoms during 1st week of infection and super added infection.¹⁶⁻¹⁹

Currently, there are no consensus guidelines for its management. Nevertheless, based on the availability of limited follow-up data, this vulnerable group of the COVID-19 recovered population requires a thorough clinical assessment to identify new, persistent or progressive symptoms; and should be appropriately investigated. The Long-COVID-19 subjects need close follow-up for monitoring early, intermediate and late complications. The requirement of oxygen supplementation, palliative care, rehabilitation, counseling, and other psycho-social needs should be assessed and addressed immediately.²⁰ The patients should be advised and prepared for self-management and supported self- management, and additional support is provided for older people and children with Long-COVID-19 symptoms. The more serious and potentially life- threatening complications like pulmonary venous thromboembolism, stroke, and acute cardiac events must be identified early and appropriately managed or referred to the care centers with subspecialty experts. The utility of steroids, anticoagulants, and other medications is yet to be explored entirely and the results of the longitudinal therapeutic clinical trials may address

this issue in the future. However, special care must be taken while prescribing steroids to avoid secondary fungal infections like aspergillosis, mucormycosis and pneumocystis pneumonia especially in diabetic and immunocompromised patients. The role of pirfenidone and nintedanib is also being evaluated in reducing lung fibrosis and further pulmonary damage.²¹ For skin lesions, authors suggest using topical steroids and oral anti-allergic drugs in mild to moderate cases and a short course of oral steroids in severe cases. A few authors have reported reduced exercise capacity in Long-COVID-19 subjects and suggested including aerobic exercises in rehabilitation of Long-COVID-19 subjects, which may boost immunity and respiratory functions.²¹ Besides, an advisory need to be given to all the patients for lifestyle modification and general preventive measures (like social distancing, hand hygiene and the wearing of a face mask) to avoid reinfection.

While managing the Long-COVID-19 subjects, care should be exercised to efficiently and optimally using the clinical, investigative and therapeutic tools.

With the re-emergence of the new waves of SARS-CoV-2 infection in many countries, it is expected that the burden of patients having long-term sequel of COVID-19 is going to be huge and it is expected to produce another public health crisis on the top of current pandemic. Thus, it is extremely important to be aware of its protean clinical manifestations, risk predictors and holistic management strategies. Further research comprising cataloging of symptoms, longer-ranging observational studies and clinical trials are critical to evaluate the long-term consequences of COVID-19 and it warrants setting-up of dedicated, post-COVID care, multi-disciplinary clinics, and rehabilitation centers.

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