

EDITORIAL

Unraveling Post-COVID Chronic Pain Syndrome

GP Dureja

DOI:<https://doi.org/10.62848/bjpain.v3i1.8824>

The COVID-19 pandemic had an unprecedented impact on health systems and transformed everyone's life, but the implications were most impactful for vulnerable populations, including patients with chronic pain. Another area of concern is the persistent pain reported by a notable proportion of COVID-19 survivors particularly with long COVID, now classified as post-COVID chronic pain syndrome. This condition can vary widely, affecting muscles, joints, nerves and persistent headaches and severely impacting the quality of life. New-onset chronic pain was reportedly common and likely involves multiple mechanisms; however, its prevalence decreases over time and symptoms appear to fluctuate. Broadly, mechanisms underlying pain due to SARS-CoV-2 infection could be caused by 'systemic inflammatory-immune mechanisms', 'direct neuropathic mechanisms' or 'secondary mechanisms due to the viral infection or treatment'. This editorial explores the consequences of the COVID-19 pandemic on patients already suffering from chronic pain and those with new onset chronic pain particularly in developing countries of South Asia. Existing chronic pain populations were variably impacted and social determinants of health appeared to influence the degree of effect.

There have been a number of publications related to the COVID-19 pandemic influence on the burden of chronic pain and development of new onset chronic pain particularly musculoskeletal pain, fibromyalgia and headaches¹⁻⁴. Post-COVID chronic pain syndrome is not just a physical condition; it disrupts daily activities and mental health and creates a significant burden on healthcare systems globally. The syndrome, thus, warrants a closer examination to devise effective interventions and alleviate patient suffering. Understanding the nature and prevalence of this syndrome requires a nuanced approach, especially since it often presents alongside other post-viral symptoms like brain fog and fatigue.

Amongst the Chronic Pain Syndromes, Fibromyalgia (FM) which is a complex disease with intricate pathophysiology really needs attention based on my own personal clinical experience post COVID as well as reports appearing in the international literature⁵. Although its genesis is not fully explained, but viral infections might trigger FM or worsen patients' clinical outcomes. The SARS-CoV-2 virus may affect central and peripheral nervous systems, leading to musculoskeletal, neurological, and psychological disturbances. These symptoms might persist at least 12 months beyond the recovery, often referred to as post-COVID syndrome, which resembles FM syndrome. The syndrome bears similarities to other post-viral syndromes, like chronic fatigue syndrome, where symptoms persist long after the primary infection has resolved. Patients with preexisting FM syndrome could be triggered or enhanced by COVID-19 infec-

*Director, Delhi Pain Management
Centre, New Delhi (INDIA)*

Correspondence
GP Dureja
Email: gp dureja@gmail.com

tion or by numerous and persistent stressors during the pandemic setting (isolation, depression, mental stress, generalized anxiety, and fear of the virus). Similarities between pathophysiological mechanisms and cardinal symptoms of FM and COVID-19 have been demonstrated, speculating that SARS-CoV-2 might represent a critical mediator of FM or an exacerbator of its symptoms once both syndromes share similar mechanisms and complaints⁶.

Although COVID-19 is primarily a respiratory illness, headache as an acute symptom during infection was commonly reported by a large number of our patients. Headache also has been shown to be a potential long-term problem following the acute phase of the infection. A literature review found headache and dizziness to be the most common neurological manifestation in multiple studies⁷⁻⁹. In acute COVID-19, headache is usually described as moderate or severe, diffuse and oppressive although sometimes it has been described with a migraine-like phenotype, especially in patients with a previous history of migraine. Headache intensity during acute phase seems to be the most important predictor of patients developing chronic headache post COVID. Some COVID-19 cases can be associated with cerebrovascular complications, and red flags of secondary headaches (e.g. new worsening or unresponsive headache, or new onset of neurological focal signs) should be urgently investigated with imaging. Since headaches lower a person's quality of life and depending on the severity can affect daily living activities, it is important to determine patients who are at risk for headaches long-term after contracting COVID-19 to aid in prevention of this consequence. Neuro-invasion by a corona virus could be one major causative factor in causation of this debilitating headache¹⁰.

While the exact mechanisms causing post-COVID pain in various parts of the body are unknown, a phenomenon of protracted immunosuppression, known as PICS (persistent inflammation, immunosuppression, and catabolism syndrome), has been presented as a potential major contributing factor for the presentation of post-COVID symptoms¹¹⁻¹³. PICS facilitates inflammation, immunosuppression, and catabolism that may exacerbate or make patients more susceptible to the ACE2-mediated infiltration of testicular cells, instances of chronic pain, and other more common symptoms associated with

post-COVID syndrome such as fatigue and headache. PICS typically occurs following an event which prompts a systemic inflammatory response. Following the acute inflammatory response and initial infection, patients experience a compensatory anti-inflammatory response¹⁴. It is when this compensatory response is disproportionately aggressive for the amount of initial inflammation that patients experience the phenomenon of immunosuppression, known as PICS¹⁵.

Musculoskeletal pain is a common symptom experienced by almost 20% of people during the acute phase of the severe acute respiratory syndrome due to coronavirus¹⁶. Additionally, musculoskeletal pain is also a common symptom experienced during a post-COVID phase by individuals with long COVID. During the last two years, musculoskeletal involvement increased, but no clear consensus was obtained about the pathogenesis. However, there is valuable data that supports the hypothesis of angiotensin converting enzyme 2, inflammation, hypoxia, and muscle catabolism¹⁴. Additionally, medications that were used for treatment also have musculoskeletal adverse effects, such as corticosteroid-induced myopathy and osteoporosis. Symptoms that begin three months from the onset of the COVID-19 infection, continue for at least two months, and cannot be explained by another diagnosis is accepted as post/long COVID-19 syndrome. Prior symptoms may persist and fluctuate, or new symptoms may manifest. In addition, there must be at least one symptom of infection. Most common musculoskeletal symptoms are myalgia, arthralgia, fatigue, back pain, muscle weakness, sarcopenia, impaired exercise capacity, and physical performance.

The treatment for Post COVID Pain Syndrome is extremely variable and beyond the scope of this editorial; however, the treatment strategies for COVID-19-related chronic pain needs ongoing research. Further studies should determine the most efficacious way to treat COVID-19-related chronic pain and if it differs from the usual course. Diagnosing post-COVID chronic pain syndrome involves a meticulous evaluation process. Pain physicians must gather a detailed history, including pre-existing conditions and the timeline of COVID-19 infection and subsequent symptoms. Physical examinations should identify specific areas of pain and assess the severity and impact on the patient's life. Laboratory tests and imaging might be necessary to exclude other causes.

Several clinical criteria can help identify post-COVID chronic pain syndrome. Pain lasting longer than three months following COVID-19 infection and not explained by other causes is a primary marker. Moreover, pain might be accompanied by other symptoms like fatigue or cognitive impairment, further reinforcing the diagnosis. Given the multifaceted nature of post-COVID chronic pain syndrome, an interdisciplinary evaluation involving neurologists, rheumatologists, psychologists, and pain management specialists may be necessary. This holistic approach ensures that all potential contributing factors are considered and leads to a comprehensive treatment plan.

Research on post-COVID chronic pain syndrome is still in its infancy, but emerging studies are beginning to shed light on the condition. Longitudinal studies following COVID-19 survivors over time are crucial to understanding the natural progression of chronic pain and its predictors. Investigating genetic predispositions could reveal why some patients are more susceptible than others, potentially leading to targeted treatments.

Post-COVID chronic pain syndrome is a pressing issue that requires immediate attention. The syndrome's varied and persistent symptoms can profoundly affect an individual's quality of life. Recognizing and managing the condition requires a nuanced approach that encompasses a thorough understanding of the virus's long-term effects, accurate diagnostic criteria, and effective treatment modalities.

The collaboration of healthcare professionals, researchers, and patient advocates will be critical in advancing our understanding and care for this emerging syndrome. With continued research and comprehensive patient care strategies, the challenges posed by post-COVID chronic pain syndrome can be addressed more effectively.

References

- 1 Fiala K, Martens J, Abd-Elseyed A. Post-COVID Pain Syndromes. *Curr Pain Headache Rep.* 2022; 26(5):379-383
- 2 Tana C, Giamberardino MA, Martelletti P Long COVID and especially headache syndromes. *Curr Opin Neurol.* 2023; 1;36(3):168-174
- 3 Shantana H, Nelson AM, Kissoon N, Narouze S The COVID-19 pandemic and its consequences for chronic pain: a narrative review. *Anaesthesia.* 2022; 77(9):1039-1050.
- 4 Fernández-de-Las-Peñas C, Gómez-Mayordomo V, Cuadrado ML, Palacios-Ceña D, Florencio LL, Guerrero AL, García-Azorín D, Hernández-Barrera V, Arendt-Nielsen L. The presence of headache at onset in SARS-CoV-2 infection is associated with long-term post-COVID headache and fatigue: A case-control study. *Cephalalgia.* 2021; 41(13):1332-1341.
- 5 Fialho MFP, Brum ES, Oliveira SM. Could the fibromyalgia syndrome be triggered or enhanced by COVID-19? *Inflammopharmacology.* 2023; 31(2):633-651
- 6 Kocyigit BF, Akyol A. The relationship between COVID-19 and fibromyalgia syndrome: prevalence, pandemic effects, symptom mechanisms, and COVID-19 vaccines. *Clin Rheumatol.* 2022; 41(10):3245-3252
- 7 Rahman A, Niloofa R, De Zoysa IM, Cooray AD, Kariyawasam J, Seneviratne SL. Neurological manifestations in COVID-19: a narrative review. *SAGE open medicine.* 2020;8:1-10
- 8 Lahiri D, Ardila A. COVID-19 pandemic: a neurological perspective. *Cureus.* 2020; 12(4).
- 9 Desforges M, Le Coupanec A, Dubeau P, Bourgouin A, Lajoie L, Dubé M, Talbot PJ. Human coronaviruses and other respiratory viruses: underestimated opportunistic pathogens of the central nervous system? *Viruses.* 2020;12(1):14.
- 10 Bohmwald K, Galvez N, Ríos M, Kalergis AM. Neurologic alterations due to respiratory virus infections. *Front Cell Neurosci.* 2018; 12:386.
- 11 Maury A, Lyoubi A, Peiffer-Smadja N, de Broucker T, Meppiel E Neurological manifestations associated with SARS-CoV-2 and other coronaviruses: A narrative review for clinicians. *Rev Neurol (Paris).* 2021; 177(1-2):51-64.
- 12 Q, Hu B. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol.* 2020; 77(6):683-690.
- 13 Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, Tian DS. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. *Clin Infect Dis.* 2020; 71(15):762-768.

- 14 Oronsky B, Larson C, Hammond TC, Oronsky A, Kesari S, Lybeck M, Reid TR. A review of persistent post-COVID syndrome (PPCS). *Clin Rev Allergy Immunol.* 2023; 64(1): 66-74
- 15 Biradar V, Moran JL. SIRS, Sepsis and multiorgan failure. In: Fritridge R, Thompson M, editors. *Mechanisms of vascular disease: a reference book for vascular specialists* [Internet]. Adelaide (AU): University of Adelaide Press. 2011; 17.
- 16 Castaldo M, Ebbesen BD, Fernández-DE-Las-Peñas C, Arendt-Nielsen L, Giordano R COVID-19 and musculoskeletal pain: an overview of the current knowledge. *Minerva Anesthesiol.* 2023; 89(12):1134-1142.