International Journal of Multidisciplinary Research and Growth Evaluation.

Unveiling the Link between long COVID-19 and Fibromyalgia

Sidrah Parvez [1*], Ghizal Fatima [2*]
[1-2] Department of Biotechnology, Era's Lucknow Medical College & Lucknow, Era University, Lucknow, Uttar Pradesh, India

* Corresponding Author: **Dr. Ghizal Fatima & Dr. Sidrah Parvez**

Article Info

ISSN (online): 2582-7138
Volume: 06
Issue: 01
January-February 2025
Received: 07-12-2024
Accepted: 05-01-2025
Page No: 1189-1192

Abstract
The ongoing evolution of the COVID-19 pandemic has led to an increasing amount of study on Long COVID-19, defined by persistent symptoms that may remain for weeks or months following initial infection. Fibromyalgia (FM), a chronic disorder marked by pervasive pain, fatigue, and cognitive impairments, has become a notable issue among these symptoms. A literature study examining long COVID patients reveals that its predominant symptoms, such as fatigue, generalized pain, cognitive impairments, sleep problems, and mood disorders, closely resemble those associated with FM. A substantial percentage of long COVID patients fulfil the criteria for chronic overlapping pain conditions (COPCs), and the clinical progression of these illnesses is analogous. The potential mechanisms linking Long COVID-19 and FM are multifaceted, involving a combination of pathophysiological processes are discussed in this review paper.

DOI: https://doi.org/10.54660/.IJMRGE.2025.6.1.1189-1192

Keywords: COVID-19; FM; Fatigue; Stiffness; Depression

Introduction

As the epidemic evolved, an increasing number of individuals infected with SARS-CoV-2 have experienced long-lasting and persistent symptoms above the usual duration of COVID-19. Individuals with severe COVID-19 may exhibit long-term sequelae accompanied by evident underlying tissue pathology (e.g., lung scarring, vascular thrombosis, post-intensive care psychological trauma) that can be reasonably understood. Long COVID-19, or post-acute sequelae of SARS-CoV-2 infection (PASC), manifests a multitude of symptoms impacting several organ systems. Long COVID-19 is characterized by the continuation of symptoms beyond the acute phase of the infection, manifesting in numerous forms such as fatigue, respiratory complications, and neurological disorders. Estimates suggest that roughly 10-30% of patients infected with SARS-CoV-2 develop Long COVID-19 [1]. Fibromyalgia (FM) is defined by persistent pain, fatigue, sleep difficulties, and cognitive impairment. The pathogenesis is poorly comprehended, but it is thought to include dysregulation of pain pathways, genetic predisposition, and environmental influences [2-5]. Recent studies indicate a significant prevalence of FM among people with Long COVID-19. Individuals with Long COVID-19 may have symptoms similar to FM, including as persistent pain, fatigue, and cognitive difficulties. The international community of pain researchers has officially recognized FM as the exemplar for a newly identified mechanism of pain, termed nociplastic pain, characterized by pain alongside other primary symptoms such as fatigue, memory impairment, sleep disturbances, and mood disorders [6]. This study examines the correlation between Long COVID-19 and FM.

Relationship between Long COVID-19 and Fibromyalgia

FM is currently classified as a chronic overlapping pain condition (COPC), including other prevalent pain disorders such as tension headaches, irritable bowel syndrome, low back pain, temporomandibular disorders, and bladder pain syndrome [6, 7]. According to the latest International Classification of Diseases (ICD) criteria, these diseases are categorized as primary pain syndromes, indicating that pain is the principal issue and is not influenced by another disease. All these disorders primarily involve nociplastic pain, a newly identified third mechanism of pain.

Nociceptive pain arises from inflammation or damage to peripheral tissues, neuropathic pain results from nerve injury, whereas nociplastic pain is mostly influenced by the central nervous system (CNS). In all these conditions there exist minor subgroups of individuals whose pain is influenced by persistent nociceptive input (e.g., peripheral inflammation or injury) or neuropathic mechanisms; nonetheless, the predominant nociplastic mechanisms in these conditions are believed to stem from the same CNS process. Nociplastic pain mechanisms frequently coexist with nociceptive pain conditions, such as autoimmune diseases, where it is estimated that one-third or more could have previously termed secondary FM and, more recently, central sensitization. The risk variables for these disorders encompass female sex (with an odds ratio of 1.5–2), socioeconomic status, inadequate sleep, physical inactivity, and cigarette smoking, which significantly corresponds with the characteristics observed in Long COVID [8]. Research on postinfectious pain associated with COVID and analogous diseases indicates that individuals with preexisting pain are predisposed to experiencing greater chronic pain as a sequela, but many also develop new pain de novo [9].

Potential Mechanisms Linking Long COVID-19 and Fibromyalgia

The relationship between Long COVID and nociplastic pain is pathophysiological. Currently, there is no consensus on a singular pathogenic mechanism for Long COVID across clinical domains, although emerging evidence suggests multiple potential pathways, including autoimmune responses, persistent viral infection or latent viral reactivation, microvascular disease, dysbiosis, and tissue damage. Evidence indicates that COVID-19 may provoke autoimmune reactions. Inflammation and immunological dysregulation may result in symptoms characteristic of FM [10]. The shared evidence of CNS dysfunction, including glial activation [11] and central sensitization [12], which are well documented across both disorders, is of particular relevance to the connection between Long COVID and FM. COVID-19 is linked to neurological symptoms resulting from viral invasion of the CNS. Neuroinflammation and neurochemical alterations may play a role in the development of FM. Employing functional neuroimaging and quantitative assessment methods in nociplastic pain conditions as FM, similar neural signatures are identified, and some of which may also be observable in children predisposed to later manifesting this range of disorders [13]. The influence of psychological factors in nociplastic situations is somewhat contested although gradually comprehended. Numerous first investigations on such conditions concentrated on psychological factors as causative, given that a significant proportion of individuals with nociplastic pain syndromes display some type of psychological discomfort. FM symptoms may be exacerbated or triggered by the psychological toll of the pandemic, which includes anxiety and depression, particularly in individuals who are predisposed to chronic pain conditions. However, more recent research indicates that a significant bidirectional relationship exists between the successful treatment of chronic pain and the rapid improvement of depression and catastrophizing in a significant number of individuals with severe pain [14]. Long COVID and FM are linked to central sensitization, a condition in which the neurological system exhibits heightened responsiveness to stimuli. Vitamin D may play a role in modulating this process [15, 16].

Moldofsky and Scarisbrick have demonstrated the significance of sleep and physical activity in relation to these conditions. A state of FM can be experimentally induced in individuals who are healthy through sleep restriction and/or absence of exercise, and was observed in 2011 in patients with severe acute respiratory distress syndrome. Sleep difficulties and decreased activity levels frequently occur with both Long COVID and FM. Research indicates that conditions similar to FM can be triggered by sleep deprivation or lack of activity. Consequently, improving sleep hygiene and promoting gradual activity may be essential elements of treatment for individuals afflicted by either condition [17]. A multitude of individuals with Long COVID experience persistent respiratory symptoms, such as cough, dyspnea, and thoracic discomfort. Steam inhalation might offer temporary relief for these symptoms, although it is not a cure. Individuals should consult healthcare professionals for comprehensive management [18]. Serotonin is essential to the body for the nociceptive pathways. Modifications in serotonin levels might affect pain perception, potentially intensifying symptoms in conditions such as FM and Long COVID. Serotonin appears to significantly impact the connection between Long COVID and FM, affecting both mood and pain perception. Comprehending this relationship can facilitate the formulation of focused therapeutic approaches that address both psychological and physical manifestations for individuals affected by these conditions. Consultation with healthcare specialists is crucial for individualized management. Frequently, when patients pursue healthcare for these non-specific symptoms, their concerns get minimized or neglected, since few professionals possess knowledge in managing this range of conditions. Consequently, it is unsurprising that numerous individuals exhibit psychiatric comorbidities that require attention, alongside their challenges related to sleep, discomfort, and functional deterioration. Recognizing that Long COVID is a clinically heterogeneous disorder with various endotypes, suggesting that Long COVID, FM, and other COPCs should be regarded as an interconnected network of disorders, potentially sharing a common pathogenic mechanism that may explain a substantial, though not exhaustive, portion of this evolving clinical spectrum. Long COVID exhibits clinical heterogeneity, characterized by a diverse array of symptoms and potential endotypes. This complexity implies that both Long COVID and FM may be more effectively comprehended within the wider framework of COPCs [19, 20].

It is important for FM patients recovering from COVID-19 to monitor their health closely, as stress, inflammation, and medications can all impact symptom management. Similarly, patients who develops symptoms of mucormycosis (such as sinus pain, swelling, blackened tissue, or difficulty breathing) after a COVID-19 infection should seek medical attention immediately [21]. For FM patients, the physical and emotional stress of COVID-19 could worsen the symptoms by further disrupting cortisol regulation. Additionally, corticosteroid treatment for COVID-19 could have mixed effects on cortisol production, possibly making FM symptoms more challenging to manage [22]. Nebulization could be useful for FM patients who have respiratory issues or develop COVID-19. However, medications used in nebulization (especially steroids) may have side effects that can exacerbate FM symptoms [23].

Conclusion

Although both COVID and FM have distinct characteristics, their symptomatic overlap and possible common causes underscore the necessity for thorough assessment and personalized treatment strategies. Additional research is necessary to comprehensively grasp the relationship between the two. The correlation between Long COVID and FM, along with other COPCs, is robust and supported by factors that ensure both face and content validity, as evidenced by an extensive array of clinical and research data. We believe these symmetries underscore the necessity to pursue a research strategy focused on common pathways across these conditions, which may yield new insights for improved understanding and treatment of both. The association between Long COVID and FM can result from shared pathophysiological pathways, such as immunological dysregulation, CNS involvement, and psychosocial issues. Comprehending these associations helps to improve the management and treatment of individuals exhibiting symptoms of both conditions, highlighting a comprehensive and multidisciplinary approach to therapy. Understanding the links and improving results requires more research.

Conflict of interest: The authors declared no conflict of interest.

References

1. Altmann DM, Whettlock EM, Liu S, Arachchillage DJ, Boyton RJ. The immunology of long COVID. Nature Reviews Immunology. 2023;23(10):618-34.
2. Parvez S, Fatima G, Mahdi F, Fedacko J, Hadi NR. Unraveling the clinico-genetic association of catechol-O-methyltransferase-rs4680 G> A gene polymorphism in women with fibromyalgia syndrome. Wiadomości Lekarskie Monthly Journal. 2022;75(10):2439-44. DOI:10.36740/WLek202210123.
3. Parvez S, Fatima G, Mehdi F, Hadi NR, Fedacko J. Relationship between vitamin D receptor gene BsmI polymorphism and fibromyalgia syndrome. Cureus. 2022;14(7). DOI:10.7759/cureus.27113.
4. Parvez S, Fatima G, Mahdi F, Hadi NR, Fedacko J. Assessment of the association of serotonin transporter gene (5-HTTVNTR & 5-HTTLPR) polymorphism in patients with fibromyalgia syndrome. Wiadomości Lekarskie Monthly Journal. 2023;76(6):1378-84. DOI:10.36740/WLek202306108.
5. Parvez S, Dzupina A, Fatima G, Fedacko J, Magomedova A, Mehdi AA. Unveiling the role of human PER3 gene polymorphism (rs57875989) as a potential risk factor in fibromyalgia syndrome patients. Cureus. 2024;16(12):e75210. DOI:10.7759/cureus.75210.
6. Fitzcharles MA, Cohen SP, Clauw DJ, Littlejohn G, Usui C, Häuser W. Nociplastic pain: towards an understanding of prevalent pain conditions. The Lancet. 2021;397(10289):2098-110.
7. Proal AD, VanElzakker MB, Aleman S, Bach K, Boribong BP, Buggert M, Cherry S, Chertow DS, Davies HE, Dupont CL, Deeks SG. SARS-CoV-2 reservoir in post-acute sequelae of COVID-19 (PASC). Nature Immunology. 2023;24(10):1616-27.
8. Möller M, Borg K, Janson C, Lerm M, Normark J, Niward K. Cognitive dysfunction in post-COVID-19 condition: mechanisms, management, and rehabilitation. Journal of Internal Medicine. 2023;294(5):563-81.
9. Choutka J, Jansari V, Hornig M, Iwasaki A. Unexplained post-acute infection syndromes. Nature Medicine. 2022;28(5):911-23.
10. Peluso MJ, Ryder D, Flavell RR, Wang Y, Levi J, LaFranchi BH, Deveau TM, Buck AM, Munter SE, Asare KA, Aslam M. Tissue-based T cell activation and viral RNA persist for up to 2 years after SARS-CoV-2 infection. Science Translational Medicine. 2024;16(754):eadk3295.
11. Leng A, Shah M, Ahmad SA, Premraj L, Wildi K, Li Bassi G, Pardo CA, Choi A, Cho SM. Pathogenesis underlying neurological manifestations of long COVID syndrome and potential therapeutics. Cells. 2023;12(5):816.
12. Khoja O, Silva Passadouro B, Mulvey M, Delis I, Astill S, Tan AL, Sivan M. Clinical characteristics and mechanisms of musculoskeletal pain in long COVID. Journal of Pain Research. 2022:1729-48.
13. Pinto AM, Geenen R, Wager TD, Lumley MA, Häuser W, Kosek E, Ablin JN, Amris K, Branco J, Buskila D, Castelhano J. Emotion regulation and the salience network: a hypothetical integrative model of fibromyalgia. Nature Reviews Rheumatology. 2023;19(1):44-60.
14. Clauw DJ, Calabrese L. Rheumatology and long COVID: lessons from the study of fibromyalgia. Annals of the Rheumatic Diseases. 2024;83(2):136-8.
15. Parvez S, Fatima G, Al-Awaida W, Hussien YA, Tamam SA, Hadi NR. Vitamin D: implications in COVID-19. Latin American Journal of Pharmacy. 2021;40:23-6.
16. Parvez S, Fatima G, Das SK, Ahmad I. Positive and negative association of vitamin D with fibromyalgia syndrome. Era's Journal of Medical Research. 2020;7(1):126-33. DOI:10.24041/ejmr2020.21.
17. Clauw DJ, Häuser W, Cohen SP, Fitzcharles MA. Considering the potential for an increase in chronic pain after the COVID-19 pandemic. Pain. 2020 Aug 1;161(8):1694-7.
18. Parvez S, Fatima G, Hadi NR, Jha H. Early steam inhalation: the first crucial step in combating evil—the COVID-19. Era's Journal of Medical Research. 2021;8(1):82-4. DOI:10.24041/ejmr2021.15.
19. Davis HE, Assaf GS, McCorkell L, Wei H, Low RJ, Re'em Y, Redfield S, Austin JP, Akrami A. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. EClinicalMedicine. 2021;38.
20. Parvez S, Fatima G, Das SK, Ahmad I. Serotonin role in fibromyalgia. Era's Journal of Medical Research. 2021;8(1). DOI:10.24041/ejmr202L10.
21. Fatima G, Parvez S, Raza AM, Fedacko J, Hadi NR. COVID-19 and mucormycosis: a short report from India. Era's Journal of Medical Research. 2021;8(2). DOI:10.24041/ejmr2021.38.
22. Parvez S, Fatima G. Mini review: association between serum cortisol levels and COVID-19 disease. Era's Journal of Medical Research. 2021;8(2). DOI:10.24041/ejmr2021.35.
23. Singh RB, Fatima G, Parvez S, Halabi G, Hadi N. Safety and efficacy of nebulization for reducing the intensity of viral load and clinical manifestations in patients with COVID-19. In: Features, Transmission, Detection, and Case Studies in COVID-19. 2024. Academic Press. p.

507-14. DOI:10.1016/B978-0-323-95646-8.00054-8.