

Post-COVID-19 Syndrome

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Doi: 10.47750/pnr.2022.13. S05.355

OVERVIEW

Around 117 million people have had COVID-19 diagnoses globally as of March 2021, and more than 2.6 million have died as a result (1). The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes COVID-19 is a heterogeneous virus with a wide range of symptoms, from asymptomatic to lethal conditions (2–7). One of the most prevalent symptoms of SARS-CoV-2 is interstitial pneumonia, which can be made worse by acute respiratory distress syndrome (ARDS), a condition with a high fatality rate, especially in elderly persons with several coexisting conditions (2, 3). As the COVID-19 pandemic continues, many more symptoms have been reported, including lymphopenia and elevated inflammatory markers (e.g., erythrocyte sedimentation rate, C-reactive protein, ferritin, tumor necrosis factor-, IL-1, and IL-6) as well as symptoms like fever, dry cough, shortness of breath, fatigue, myalgias, nausea/vomiting or diarrhea, headache, weakness, rhinorrhea, and (2, 3). Impaired heart, brain, lung, liver, kidney, and coagulation system functions are some other severe and life-threatening COVID-19 consequences (4–7).¹

Following COVID-19 infection, the majority of the infected patients made a full recovery. However, a sizeable fraction of SARS-CoV-2-infected patients continue to have symptoms after fully recovering from the earliest stages of COVID-19 disease. Clinicians from all around the world refer to these long-term COVID-19 effects as "Long-Haul COVID-19" or "Long-Term COVID-19" (8–11). Specifically, "long-term COVID-19" refers to people who have experienced SARS-CoV-2 infection but do not fully recover over a few weeks (often 2-3 weeks) (8–11).²

According to the COVID-19 Symptom Study, which involved more than 4 million participants in the US, UK, and Sweden and asked them to record their ongoing symptoms on a smartphone app, 10% of patients who tested positive for the SARS-CoV-2 virus continue to experience symptoms for more than three weeks, and a smaller percentage for months (8). It is now evident that some SARS-CoV-2 infection survivors, even those whose symptoms were deemed "moderate," still experience lingering or cyclical symptoms. However, the definition of post-COVID-19 symptoms is still up for debate because COVID-19 is a new condition. It is unclear whether COVID-19 can learn from MERS and SARS because long-term symptoms and complications have only been reported for other highly homologous human coronaviruses, such as Middle East Respiratory Syndrome (MERS) and severe acute respiratory syndrome (SARS). The crucial question is: "Do persistent symptoms at the post-viral stage of the disease constitute a post-COVID-19 syndrome (long-term COVID-19), and what are the main persistent symptoms?" (12–14). Research has the obvious answer, but we are unsure what to advise patients when they inquire about the trajectory and outlook of their ongoing complaints and prospective long-term symptoms. Finding a definitive response to these queries will also increase knowledge about the COVID-19 illness and allow for the development of comprehensive and focused care for survivors through the creation of preventative and efficient treatments. Although it is still too early to provide a definitive response to these issues, we think specific broad forecasts are now conceivable and would help put the proper public health safeguards in place, especially after the epidemic has passed. We conducted a systematic review of the available data, taking into account all types of papers evaluating individual persistent symptoms in mild, moderate, and severe/critical COVID-19 patients, to provide a thorough overview of the persistent symptoms at the post-viral stage of the disease. Awareness of the whole course of the disease, accurately anticipating its expanding impact beyond hospitalization and mortality, and determining whether inpatient or post-discharge-specific therapy should be assessed requires an understanding of the long-term sequelae of COVID-19.^{3,4}

Even though we are aware that there are not any long-term data on a significant number of COVID-19 patients with persistent symptoms and comparison groups and that analysis in a topic as fascinating as COVID-19 can never be updated, this review allowed us to highlight that a sizable proportion of patients have long-lasting sequelae that last for up to 6 months after COVID. These chronic symptoms can also affect people with mild, moderate, or severe COVID-19. Additionally, recent early evidence highlighted the existence of chronic COVID-19 symptoms in kids and teenagers. Some clinical studies and survey questions also revealed a potential high-risk factor for long-term COVID-19 in the female gender; among patients between the ages of 40 and 50, women appear to have a twofold increased risk of acquiring long-term COVID-19 compared to males. The risk of long-term COVID should converge between males and females after 60. This pattern appears to follow the progression of autoimmune illnesses, which are more prevalent in women until

menopause and become similar in both sexes beyond age 60. As a result, it is probable that these gender disparities in the disease and other characteristics could result from a distinct immune system response during and after COVID-19. It is not yet apparent whether this data accurately represents the community of patients with long-term COVID-19 and whether it captures the full range of the persistence and severity of long-term symptoms in these patients.⁵

The conclusion drawn from this review is that aberrant lung functions, frequently accompanied by persistent dyspnea, general neurological degradation, smell and taste problems, and chronic exhaustion, are the most frequently reported symptoms following COVID-19. Joint discomfort and chest pain are some other typical symptoms. After early recuperation, these symptoms may persist or return for weeks or months. For people with mild-to-moderate COVID-19, chronic fatigue, anosmia/ageusia, and dyspnea are the most frequent long-term symptoms, along with concentration problems, memory loss, and disorientation. These symptoms appear to be more prevalent in patients who were initially worse. Additional long-term symptoms in COVID-19 patients with critical to the severe disease include lung fibrotic-like alterations up to 6 months after infection and a significant decline in lung diffusing capacity for DLCO, which frequently requires oxygen use even after release from the hospital. The general cognitive decline appears to be more closely associated with critical-to-severe forms of COVID-19 but is also present in people with mild-to-moderate COVID-19. In light of the complete picture of pervasive long-term symptoms described in this research, chronic fatigue is unquestionably the one that affects mild-to-critical COVID-19 patients the most frequently. This is consistent with another study that showed that people who survived epidemics like SARS and the Ebola virus experienced high levels of post-infectious weariness.⁶

Additionally, illnesses like mononucleosis that do not reach epidemic or pandemic levels have been linked to weariness. At this time, it is unclear why certain COVID-19 patients continue to experience persistent fatigue and other long-term problems. However, most scientists and medical professionals concur that the long-term COVID-19 symptoms are linked to the coronavirus' capacity to instigate a significant inflammatory response in order to determine if the "cytokine storm" that existed during COVID-19 remains and contributes to these long-term problems, analysis of cytokine networks in individuals who recover from the disease will thus be required.⁷

The study's key strength is its emphasis on several chronic symptoms that may make it challenging to restore functional capacity from before the COVID-19 infection. While some of the studies included in this review concentrated on a single population of COVID-19-infected patients, i.e., mild/moderate and severe/critical, many studies included heterogeneous populations, from mild to critical, without taking into account disease severity as well as preexisting co-morbidities, treatment regimens, mean ages, gender, and other aspects. This bias may change how the data are evaluated and analysed, which can impact the outcomes. Data from future designs, which were created by analysing homogeneous populations of COVID-19 patients and were able to take into account their characteristics both before and during infection, may offer new and in-depth knowledge about the risk factors that contribute to long-term COVID-19 symptoms. Another bias that needs to be considered is that many studies have used self-administered questionnaires and scores, telephone/online interviews, and phone applications, even though in some studies, the long-term COVID-19 sequelae were evaluated through clinical visits and specific instrumental analyses. This is because entry limitations within the COVID-19 departments make it challenging to assess the patient in the hospital. On the other hand, in an emergency medical situation like the one we are in, inspecting and analyzing them at home poses logistical challenges that are nearly insurmountable. This sort of self-evaluation, however, draws attention to bias in the recognition of symptoms because patients may be psychologically and emotionally affected by the disease itself.⁸

To prevent the probable persistent symptoms reported in the current evaluation, a thorough analysis and comprehension of all the factors related to long-term COVID-19 are currently required. Future research should examine the following topics:

- The full spectrum of COVID-19-related disorders and their long-term manifestations
- The underlying relationships between viral spread, related pro-inflammatory changes, and long-term disease pathogenesis
- The duration and severity of long-term symptoms about the resolution of the disease
- The relationship between disease severity and long-term dysfunctions
- The impact of specific antiviral therapies and in vitro vaccines

SARS-CoV-2 levels (detection, load) in patients and how this links to long-term symptoms are another crucial factor that should be evaluated. It is currently unknown if the initial viral load, per se, may significantly impact long-term symptoms, particularly in patients with mild-to-moderate COVID-19. The clinical interpretation of COVID-19's long-term symptoms will be aided by knowing SARS-CoV-2 detection and viral load at various periods of infection. Similarly, more research is required to offer reliable information on the relationship between viral shedding and long-term COVID-19. There is evidence that continuous viral shedding in SARS-CoV-2 may be longer in faeces than in respiratory secretions, notwithstanding claims suggesting the median length of viral shedding ranges from 12-to-20 days. Despite not being contagious, the persistent viral gene fragments may still be causing a severe immune overreaction, which could account for the continuation of symptoms in COVID-19-free patients. Alternately, even if the infection is eradicated, the immune system may still be overactive or unbalanced, similar to the long-term disability following glandular fever. The knowledge

of the causes of long-term symptoms, the role played by the immune system, and the likelihood of transmission may be improved with a better understanding of these last two areas.^{9,10}

Funding: There was no outside support for this study.

Conflicts of Interest: There are no conflicts of interest declared by the authors.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This evaluation does not require ethical approval because no patient data will be collected. Plagiarism, confidentiality, malfeasance, data falsification and/or falsification, double publishing and/or submission, and duplication are among the ethical problems examined in this study.

ACKNOWLEDGMENTS

First and foremost, I want to express my gratitude to God for allowing me the opportunity to conduct and complete this research project for my academic achievement. I'd want to thank and show gratitude to my mentor for encouraging and guiding me during the process of writing this post. who had devoted their valuable time to guide me, either directly or indirectly, during the journey I'd want to express my heartfelt gratitude to all of my friends for their unwavering support and aid in completing this study. Finally, I'd like to express my gratitude to my family for their love, patience, and support throughout the study process.

REFERENCES

1. Salamanna, F., Veronesi, F., Martini, L., Landini, M. P., & Fini, M. (2021). Post-COVID-19 syndrome: the persistent symptoms at the post-viral stage of the disease. A systematic review of the current data. *Frontiers in medicine*, 8, 653516.
2. COVID-19 Dashboard by the Center for Systems Science Engineering (CSSE) at Johns Hopkins University (JHU). Available online at: <https://coronavirus.jhu.edu/map.html> (accessed December 17, 2020).
3. Levi M, Thachil J, Iba T, Levy JH. Coagulation abnormalities and thrombosis in patients with COVID-19. *Lancet Haematol*. (2020) 7:438–40. doi: 10.1016/S2352-3026(20)30145-9.
4. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol*. (2020) 77:1–9. doi: 10.1001/jamaneurol.2020.1127
5. Chen YT, Shao SC, Hsu CK, Wu IW, Hung MJ, Chen YC. Incidence of acute kidney injury in COVID-19 infection: a systematic review and meta-analysis. *Crit Care*. (2020) 24:346. doi: 10.1186/s13054-020-03009-y.
6. Correia AO, Feitosa PWG, Moreira JLS, Nogueira SÁR, Fonseca RB, Nobre MEP. Neurological manifestations of COVID-19 and other coronaviruses: a systematic review. *Neurol Psychiatry Brain Res*. (2020) 37:27–32. doi: 10.1016/j.npbr.2020.05.008.
7. Hui DS, Joynt GM, Wong KT, Gomersall CD, Li TS, Antonio G, et al. Impact of severe acute respiratory syndrome (SARS) on pulmonary function, functional capacity and quality of life in a cohort of survivors. *Thorax*. (2005) 60:401–9. doi: 10.1136/thx.2004.030205.
8. Ngai JC, Ko FW, Ng SS, To KW, Tong M, Hui DS. The long-term impact of severe acute respiratory syndrome on pulmonary function, exercise capacity and health status. *Respirology*. (2010) 15:543–50. doi: 10.1111/j.1440-1843.2010.01720.x.
9. Hertting O. More research is needed on the long-term effects of COVID-19 on children and adolescents. *Acta Paediatr*. (2021) 110:744–5. doi: 10.1111/apa.15731
10. Moldofsky H, Patcai J. Chronic widespread musculoskeletal pain, fatigue, depression and disordered sleep in chronic post-SARS syndrome; a case-controlled study. *BMC Neurol*. (2011) 11:37. doi: 10.1186/1471-2377-11-37.