



EDITORIAL

Long COVID: A New World Post-COVID-19

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OPEN ACCESS

PUBLISHED

31 October 2024

CITATION

Camargo, JA., 2024. Long COVID: A New World Post-COVID-19. Medical Research Archives, [online] 12(10).
<https://doi.org/10.18103/mra.v12i10.5856>

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DOI

<https://doi.org/10.18103/mra.v12i10.5856>

ISSN

2375-1924

Introduction

COVID-19 has been associated with a wide range of neuronal syndromes such as encephalopathies, brain disorders, acute disseminated encephalomyelitis with hemorrhage and necrosis, transverse myelitis, Guillain-Barré syndrome, movement and behavioral disorders, cognitive decline, and Kawasaki syndrome in children.¹⁻⁶ These manifestations indicate the presence of different underlying physiological mechanisms induced by infection with SARS-CoV-2. In addition to direct viral damage, post-infection inflammation, the production of antineuronal autoantibodies, vasculitis, excessive cytokine-related inflammatory activity, and complications of cerebral hypoxia and coagulopathy have been discussed.⁷⁻¹⁰

The hyperinflammation described is related to the elevation of proinflammatory cytokines (tumor necrosis factor) and interleukins (IL) such as IL-6 as a result of an increase in the number of monocytes and macrophages. This event is called “cytokine storm”, which is added to the difficulty of eliminating SARS-CoV-2 due to the induction of apoptosis of lung endothelial and epithelial cells.¹⁰⁻¹⁸

The neurological changes alone would already be tragic, but the causative agent has a devastating effect on all organs and systems of the human body. More than 200 symptoms with impacts on multiple organ systems have been identified. It is estimated that at least 65 million people worldwide have long COVID, with the number of cases increasing daily. Medical research has made important progress in identifying various pathophysiological alterations and risk factors and in characterizing the disease. At least, based on a conservative estimated incidence of 10% of infected individuals worldwide; the number is likely to be much higher due to many undocumented cases. The incidence of long COVID is estimated at 10-30% of non-hospitalized cases, 50-70% of hospitalized cases, and 10-12% of vaccinated cases. Long COVID is associated with all ages and the severity of acute disease, with the highest percentage of diagnoses between the ages of 36 and 50 years; most cases occur in non-hospitalized patients with mild acute disease since this population represents the majority of all COVID-19 cases.^{4,16}

In contrast, there is no valid explanation for the cortical dysfunction that leads to cerebral hypometabolism, and the clinical signs observed. Similar to septic encephalopathy following bacterial infections, a systemic immune response may be suggested; this response would trigger an inflammatory reaction within the brain that disrupts the blood-brain barrier and compromises astrocyte clearance at synapses and microcirculation.^{1,15}

The fact that SARS-CoV-2 is able to replicate in neuronal cells and to infect human cerebral organoids highlights the neurotropism of this virus. Neurological and cognitive symptoms are a prominent feature of long COVID and include sensorimotor symptoms, memory loss, prolonged prostration, cognitive impairment, paresthesia, dizziness and balance problems, increased sensitivity to light and noise, loss of smell or taste, autonomic dysfunction often

affecting activities of daily living, and audiovestibular manifestations such as tinnitus, hearing loss, and vertigo.

Over time, we have seen more and more people with a wide range of short, medium and long-term complaints after infection with the virus. The systems that may be compromised during this post-illness period are well documented in the medical literature and include the cardiovascular, neurological, digestive, respiratory, endocrine, renal, immunological, dermatological, osteoarticular and muscular systems, not to mention the reproductive system, whose involvement from the beginning of the development of eggs and sperm and genetic alterations that may lead to fetal malformations or cancer have been little investigated. Finally, mood disorders, such as anxiety, depression and psychiatric disorders, attract our attention.^{11,12,17-39}

Given this bleak scenario, it would not be excessively cautious to say that all patients treated at medical services around the world should be thoroughly questioned about their health history during the pandemic, regardless of their complaints. It is very important to know, with other information, among those who tested positive for the virus, how severe the symptoms were, whether the patient required hospitalization and whether the current complaints and symptoms existed before the period of contamination.

Good assessment and detailed investigation are necessary in each case in order to establish appropriate treatment and a prognosis for the patient. This investigation often requires modern tests, which are very expensive, and is unfortunately not available for the majority of the world's population who live a low-income situation.^{1,9,12-39}

At the beginning of the pandemic, healthcare professionals were providing a wide range of viewpoints in the world's media outlets, with comments on the mechanism of action of the virus, possible treatments, and disease prognoses, in an extreme effort to alleviate suffering and to save the lives of millions of people. At that time, we already said that a deeper understanding of the causative agent could only be obtained after a period of 3 years from the beginning of the pandemic; however, today we can say with certainty that we were wrong!!!

Conclusion

Our path forward as healthcare professionals is also long. A better approach to all patients, with a detailed and thorough physical and laboratory investigation with the most appropriate tests available for each case, becomes necessary for this new scenario in global health.

More studies still need to be carried out to alleviate suffering, reduce after-effects and increase the time and quality of life of the infected population.

Conflicts of Interest:

None

Funding: None

Acknowledgements: None

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