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Chronic Fatigue Syndrome After COVID-19 Infection: A Call for Action

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Dear Editor,

COVID-19 is a SARS-CoV-2 viral infection mainly affecting the respiratory system, with initial signs of fever, cough, and body ache. As of Sep 9th 2020, there have been more than 27.6 million confirmed cases worldwide, and over 898,000 died. Fatigue is a widely recorded symptom of COVID-19 (1), although observational evidence suggests that certain individuals persist in encountering intense amounts of chronic fatigue as they recuperate from this infection.

The recovery process is not yet fully understood. Some patients develop Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) after the acute SARS episode. The symptoms of CFS/ME are persistent fatigue, myalgia, depressive symptoms and nonrestorative sleep. Fatigue was one of the most often encountered consequences of the COVID-19 survivors. Approximately 53% of individuals displayed fatigue, with no marked difference in ethnicity or body mass index (BMI). There was no difference in the age within the ICU group (2, 3).

Post-infectious fatigue has likewise been witnessed after other epidemics, such as SARS-CoV1 virus, the influenza A (H1N1) and Ebolavirus infection. Given the sufficient data from earlier epidemics, many COVID-19 survivors may encounter post-viral fatigue. However, the factors which influence such development are uncertain. The recent research has demonstrated the involvement of the cytokine response. Mehta et al. (4) observed a 'cytokine storm' in patients with COVID-19. Elevated levels of IL-2, IL-7, granulocyte-colony stimulating factor, interferon- γ inducible protein10, monocyte chemoattractant protein 1, α macrophage inflammatory protein and α tumor necrosis factor were found in these patients (4). These results suggest a hyperinflammatory trend and have been correlated with complications, such as multi-organ failure. Moreover, the delays in the expression of type I interferon (IFN), an essential part of the innate defense against viral infections, are seen in COVID-19 infection (5). It has been suggested that this viral IFN development plays a crucial function in 'cytokine storm' found in patients with COVID-19 (5).

This disturbance contributes to the build-up of pro-inflammatory agents that have been postulated to influence the neurological regulation of the 'Glymphatic System' (6). The build-up of cytokines in the central nervous system may lead to post-viral symptoms. It is due to pro-inflammatory cytokines passing through the blood-brain barrier and affecting the hypothalamus leading to autonomic dysfunction.

A proportion of patients affected by COVID-19 may continue to develop a severe post-viral syndrome called 'Post COVID-19 Syndrome' – a long-term chronic fatigue condition characterised by post-exertional neuroimmune exhaustion (6). Past studies have shown that post-infectious fatigue is common for some survivors of the H1N1 influenza and Ebola virus infection (7). This study is required to examine the cytokine load of people recovering from COVID-19 to determine whether the 'cytokine storm' encountered during the disease continues and leads to more complications, including chronic fatigue.

The treatment of COVID-19 survivors is still not fully understood. Although it was originally thought to be a respiratory disorder, it affects various systems. There can be a multi-organ failure. Thus, these survivors are likely to suffer from a multi-domain injury requiring constant care. Early intervention and supportive therapies can help relieve acute phase symptoms and prevent them from being long-term. The rehabilitation community recently called for action to move rapidly to provide sufficient early and multidisciplinary treatments for a physical and psychological recovery (8). It is already well-defined that COVID-19 itself is associated with debilitating symptoms, such as myalgia, arthralgia and abdominal pain, which may lead to the use of opioids treatment (9).

In the future, researchers should investigate co-morbidities and factors that may impair immune function. It is also desirable to longitudinally follow up cases, where possible, to better understand fatigue and other symptoms.

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