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Does long-COVID really occur Less Frequently in Elderly Patients than in Younger Sufferers?

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LETTER TO THE EDITOR

We read with interest the Gaber's article on a retrospective analysis of long-COVID (LC) patents referred to an LC service in Northern England between November 2020 and November 2022 [Gaber, T. A, 2023]. It was found that of 17 patients aged >70 years with LC, only 7 had their fatigue associated with post-exertional malaise (PEM) [Gaber, T. A, 2023]. One of these 7 patients had a history of fibromyalgia and her PEM preceded a COVID-19 infection [Gaber, T. A, 2023]. Only 6 patients had significant comorbidity [Gaber, T. A, 2023]. A total of 482 of the 515 <70 year-old patients had PEM related to their fatigue (93.5%) [Gaber, T. A, 2023]. It was concluded that the prevailing hypotheses explaining the rarity of LC in the elderly population are due to data collection bias and/or biopsychosocial factors [Gaber, T. A, 2023]. The study is impressive, but some points require discussion.

The assumption that LC is less common among patients over 70 years is not supported. In support of their arguments, the author cites a meta-analysis of 45 studies in which the definition of ME, the diagnostic methods used, and the population groups varied significantly between studies ("The prevalence rates were varied by enrolled participants (gender, study participants, and population group), case definitions and diagnostic methods") [Lim, E. J. *et al*., 2020]. This suggests that individual study results are not reliable.

The author compares LC with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and emphasizes that ME/CFS requires the presence of PEM for diagnosis [Gaber, T. A, 2023]. In general, however, it is not justified to combine the terms CFS and ME. Encephalomyelitis is an inflammatory disease of the central nervous system (CNS) due to either infectious or immunological causes and is usually associated with CNS abnormalities on imaging particularly after use of contrast medium. Inflammation of the CNS can usually be documented by abnormal parameters in cerebrospinal fluid (CSF) examinations. However, none of the included 17 patients had apparent CNS imaging or CSF examinations.

A limitation of the study is it small group size (n=17) [Gaber, T. A, 2023]. From such a small number of patients, conclusions become questionable. In addition, the control group consisted of 515 patients with LC aged <70 years [Gaber, T. A, 2023]. There was also no statistical analysis. Therefore, the study design is not suitable for drawing conclusions such as those presented in the article.

It is not mentioned whether the included patients were diagnosed with depression or not. Since depression is a major cause of rest- and exercise-related fatigue [Baldwin, D. S. *et al*., 2006], it is important to know how many people had depression as a possible cause of fatigue.

Another cause of fatigue that was not taken into account in the assessment is medication. Several medications are known to cause fatigue. In particular hypnotics, sedatives, anxiolytics, benzodiazepines, neuroleptics, antidepressants, antiepileptics, immunosuppressants, steroids, and antibiotics can cause fatigue [Zlott, D. A. *et al*., 2010]. How many of the patents included were already taking medications in these classes before the COVID infection and how many received them after the onset of the infection?

It is also not considered that extensive use of electronic media could lead to increased fatigue. Since communication, education, and work have often been significantly reduced to the use of electronic media ("home office", "home schooling") and electronic media have been used more commonly since the pandemic than before

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[McClain, C. *et al*., 2021], it is conceivable that electro-smog contributed to the symptoms of LC [Kato, Y. *et al*., 2012].

In conclusion, the excellent study has limitations that should be addressed before drawing final conclusions. Clarifying the weaknesses would strengthen the conclusions and could improve the study.

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