

## LETTER

# Post-COVID 19 neurological syndrome: A new risk factor that modifies the prognosis of patients with dementia

Dear Editor,

We read with great interest the article published by Wang et al.,<sup>1</sup> where the authors conducted a study of electronic medical records of 61.9 million patients over the age of 18 in the United States. The authors observed that patients with dementia had an increased risk of developing coronavirus disease-19 (COVID-19) compared to patients without dementia (adjusted odds ratio [AOR]: 2.00, 95% confidence interval [CI]: 1.94 to 2.06,  $P < .001$ ), with those with vascular dementia presenting severe neurological symptoms (AOR: 3.17, 95% CI: 2.97 to 3.37,  $P < .001$ ), followed by presenile dementia (AOR: 2.62, 95% CI: 2.28 to 3.00,  $P < .001$ ). Likewise, Black people with dementia had a higher risk of developing COVID-19 than White people (AOR: 2.86, 95% CI: 2.67 to 3.06,  $P < .001$ ). The risks of mortality and hospitalization at 6 months in patients with dementia and COVID-19 were 20.99% and 59.26%, respectively.<sup>1</sup> We thank Wang et al., for providing us with such valuable evidence. However, we would like to make a few comments.

There is evidence supporting the view that neurotropic respiratory viruses cause chronic brain pathology. Coronaviruses, especially  $\beta$ -coronaviruses, a group to which SARS-CoV-2 belongs, have a high affinity for the central nervous system, generating neurovascular, neurofunctional, inflammatory, and metabolic complications,<sup>2</sup> thus affecting functional capacity, especially in those with a history of chronic neurological diseases.<sup>3</sup> The inflammatory process reaction triggered by contact between the viral agent and cellular and endothelial receptors, with the release of cytokines such as IL-10 and CC14, which cause disruption of the blood-brain barrier in the central nervous system, leading to a state of hypercoagulability through microthrombotic processes.<sup>4</sup> Additionally, in response to inflammatory stimuli in neuronal tissue, the apolipoprotein  $\epsilon$ 4 genotype factors in the senescence of different cell types in the nervous system, favoring a rapidly progressive deterioration of the cognitive and motor activity of the affected person; therefore, it is to be expected that people with dementia are at increased risk of presenting an aggressive COVID-19 phenotype with obvious neurological manifestations, and furthermore, during the post-COVID neurological syndrome period (a time window lasting between months and years), a visible deterioration in the baseline dementia is observed.<sup>5,6</sup> This is without taking into account the presence of classic cardiovascular risk factors such as hypertension, diabetes mellitus, smoking, sedentary lifestyle, age and/or a history of cerebral ischemic events, which worsen the neurological prognosis of these patients.<sup>5</sup>

The neuropsychiatric manifestations of the post-COVID neurological syndrome described so far include muscle weakness and other

forms of myopathies, depression, anxiety, impaired sleep quality, post-traumatic stress syndrome, muscular pain, headache, dizziness, fatigue, and persistent anosmia,<sup>4,7,8,9</sup> and the actual impact on the progression of previously diagnosed neurodegenerative diseases is unknown. Imaging and neurofunctional studies reveal nonspecific and variable changes in the brain,<sup>10</sup> so it is essential to design and maintain ongoing prospective multicenter studies to evaluate the effect of SARS-Cov-2 neuroinvasion over time.

Considering that no study provides conclusive evidence, due to the time window of the COVID-19 pandemic course, on the association between this viral disease and dementia, we therefore suggest taking into account the post-COVID-19 neurological syndrome as an important risk factor for the progression and severity of dementia, in order to analyze and evaluate the course of those affected by COVID-19 who previously had this condition, and if necessary, to propose as well new risk stratification models to control the morbimortality of this population. To this end, we also propose the design of a specialized group to strictly monitor patients with dementia, in order to avoid the loss of data during the evaluation periods, to identify early this subgroup that is at higher risk of presenting the severe phenotype of COVID-19, and to report the specific needs in terms of socioeconomic, family and health promotion, and disease prevention aspects possibly affected by the COVID-19 pandemic.

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## ETHICS APPROVAL AND CONSENT TO PARTICIPATE/FOR PUBLICATION

Ethics approval was not necessary for this letter, and there was no outside participation. We provide consent for publication.

## CONFLICTS OF INTEREST


The authors report no declarations of interest.

## AUTHOR CONTRIBUTIONS

Each author contributed to the writing of this letter. All authors read and approved the final manuscript.

## DATA AND AVAILABILITY STATEMENT

No data were involved in this letter.

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