Later life depression as a risk factor for developing dementia: how much influence does the post-pandemic era have?

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By the year 2050, it is estimated that at least 20% of the world's population will be over the age of 65. Depression in late life is a serious public health problem that has a negative and substantial impact on the quality of life of older adults, their families, and their social circle. Depression, in turn, constitutes a risk and prognostic factor for the development or worsening of dementia, a condition present in about 10% of the population over 60 years of age, and which increases and intensifies with age, being up to 40% at age 90. In the context of the current COVID-19 pandemic, aspects such as persistent isolation and loneliness, socioeconomic distress, lack of family and professional support, fear of illness and death, are potential negative risk factors for developing depression and worsening the prognosis of dementia in older adults.

Keywords:
aged, dementia, dementia, depression, pandemic, risk factors

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Sir,

The rapid increase in the number of older adults around the world makes the management of mental disorders and associated complications in this age group a challenge. By the year 2050, it is estimated that at least 20% of the world's population will be over the age of 65 (Aziz and Steffens, 2013). Depression in late life is a serious public health problem that has a negative and substantial impact on the quality of life of older adults, their families, and their social circle (Ding and Kennedy, 2021). The prevalence of this condition is estimated to be 17% (McCombe *et al.*, 2018), which is closely related to suicide rates of 20% among all suicide deaths at all ages (National Institute of Mental Health, 2019). This condition carries high health costs in specialized care, medication, rehabilitation, and decompensation of previous comorbidities (Aziz and Steffens, 2013; Ding and Kennedy, 2021).

Countless risk factors have been described for the development of depression in the elderly, biological factors (mutations or genetic polymorphism, cerebrovascular disease, and coronary heart disease, among others), psychological factors (loneliness, low social support, low education, and poor nutritional status, among others), and social factors (low socioeconomic status, difficulty in accessing health services, and stressful situations, among others) (Aziz and Steffens, 2013). These factors influence neuronal dynamics, reducing the secretion of neurotropic factors and decreasing neurogenesis. In turn, neuroinflammatory signaling pathways are activated with alteration of neuroendocrine processes that do not allow the proper functioning of neurotransmitters and hinder the performance of activities of daily living, intensifying the impact of other risk factors such as cardiovascular (whose control depends on adherence to pharmacological treatment), psychological (behavior and social interaction), and social (response to stressful situations), turning this condition into a vicious circle (Fiske *et al.*, 2009). Considering also that neuroplasticity in the elderly is limited due to the presence of fragility and physiological oxidation, recovery from this pathological entity is more complex.

Depression, in turn, constitutes a risk and prognostic factor for the development or worsening of dementia (Wang *et al.*, 2021), a condition present in about 10% of the population over 60 years of age, and which increases and intensifies with age, being up to 40% at age 90 (World Health Organization, 2020).

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Currently, under the ravages of the coronavirus disease 2019 (COVID-19) pandemic, all aspects of human life have been affected (Aisenberg-Shafran *et al.*, 2021). Older adults are the population most at risk of developing the severe COVID-19 phenotype and dying, so restriction measures are more severe in them. Persistent isolation and loneliness, barriers to family support, declining socioeconomic status, difficulty of participating in recreational events, the receipt of negative news through the social media, and fear of illness and death are potential risk factors for anxiety and depression in this population at this time (Aziz and Steffens, 2013; Aisenberg-Shafran *et al.*, 2021; Ding and Kennedy, 2021; Wang *et al.*, 2021); thus, also factors to worsen the prognosis of dementia in those who already suffer from it, and in addition, have other pathological conditions that affect neurological integrity, such as silent neurovascular disease. The pathophysiological mechanism of depression in COVID-19, would be mainly related to psychological and social factors (described previously), and the acceleration in dementia due to altered control of chronic noncommunicable diseases with impact on the central nervous system, neuroinflammation due to SARS-Cov-2 infection, and the inability to stimulate neuronal activity due to confinement, constant fear, lack of social interaction, and coping with the death of loved ones and/or acquaintances (Bueno-Notivol *et al.*, 2021). This is consistent with the high overall prevalence of depression during the pandemic found in meta-analyses [25%; 95% confidence interval (CI): 18–33%] (Bueno-Notivol *et al.*, 2021). The hardest part of all this is that there is a bidirectional relationship between depression and dementia. Studies have found that patients with higher cognitive function are less likely to develop depression; however, depression as a pathological condition that inhibits cognitive functions adversely modifies the prognosis of those with dementia, thus intensifying the degree and persistence of depression, confirming the presence of a vicious cycle (Gale *et al.*, 2012).In this order of ideas, and under the modification of lifestyle in the post-pandemic era, it is valid to ask what is and will be the prognosis of depression and dementia in the coming years in this population? Even more so, when there are emerging conditions such as post-COVID-19 neurological syndrome, which results from neuroinflammation during the acute phase of COVID-19, with the potential to generate or modify the prognosis of neuropsychiatric diseases as well (Camargo-Martínez *et al.*, 2021). Wang *et al.* (2021) conducted a longitudinal study evaluating the effect of late-life depression and cognitive decline on dementia (Wang *et al.*, 2021). The authors found that presenting with depressive symptoms (aHR: 1.286; 95% CI, 1.255–1.318), having recently had depression (aHR: 1.697; 95% CI, 1.621–1.776), and presenting with subjective cognitive decline (aHR: 1.748; 95% CI, 689–1.808) substantially increased the risk of dementia, and presenting with depression and cognitive decline even more (aHR: 2.466; 95% CI, 689–1.808. 748; 95% CI, 689–1.808) (Wang *et al.*, 2021). However, Yu and Mahendran (2021) recently published a study where they showed that COVID-19 pandemic confinement negatively influenced the dynamics of affective symptoms and isolation, where symptoms of depression and anxiety were very intense and increased the risk of various affective disorders (Yu and Mahendran, 2021).

Therefore, it is necessary to modify the management and risk stratification of these patients, considering that there is a high risk of depression and possible risk of self-harm and suicide, as well as genesis of dementia and worsening of the prognosis of these patients, so it is necessary to implement strategies aimed at strict monitoring, social and family support, and comprehensive mental health care. An interesting proposal would be the implementation of post-COVID-19 centers, aimed at identifying and determining the degree of psychological and neuropsychiatric involvement of the entire population, in order to estimate with greater certainty, the overall prevalence of this type of disorders in all age groups, and to establish a personalized management.

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