

# Delirium: A Frequent Manifestation in COVID-19 Older Patients

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**Abstract:** The authors report a high prevalence of delirium in COVID-19 old patients admitted in an academic hospital. During the recent COVID-19 period, delirium was present in 38% of old patients admitted with delirium at the COVID ward of the Erasmus MC University Medical Center of Rotterdam. We do not know in which patients COVID-19 can cause delirium; however, considering the high prevalence of delirium in COVID-19 old patients and the potential serious consequences, attention is needed in order to reduce disability and mortality in this vulnerable category of patients.

**Keywords:** delirium, old patients, COVID-19

From March until April 2020, 123 patients aged 60 years and older were admitted at the COVID ward of the Erasmus MC University Medical Center of Rotterdam, after the onset of coronavirus disease 2019 (COVID-19), the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

During this period, 47 patients (38%), 37 men and 10 women, mean age 71.3 years presented signs and symptoms of delirium. Of these, 39 patients developed a delirium during admission at the intensive care unit. Delirium screening was performed using the Delirium Observation Screening Scale (DOSS). A DOSS score  $\geq 3$  suggesting a delirium, was followed by a delirium assessment by the ward physician according to the DSM-5 criteria.<sup>1</sup> At the ICU, the Intensive Care Delirium Screening Checklist (ICDSC), based on the DSM-5 criteria, is used 3 times daily for screening for delirium.<sup>2</sup> Information on comorbidities was obtained from the medical records. Differences in baseline characteristics in patients with and without delirium were investigated by the analysis of covariance adjusted for age and sex, where appropriate (Table 1).

This prevalence of delirium is high in this novel disease which frequently presents with nasal secretions, cough, dyspnea, fever, myalgia, occasionally diarrhea and in about 15% of the patients with acute respiratory distress syndrome.

The high prevalence of delirium in COVID-19 patients at the ICU might be due to serious illness of these patients, the presence of traditional risk factors, but possibly also due to withdrawal of prolonged treatment with midazolam or clonidine. Besides, severely ill COVID-19 patients develop thromboembolic episodes, myocardial damage, kidney and liver disease. It was reported that several patients with ARDS showed cerebral hypoperfusion or small acute ischemic strokes, even with no focal neurological signs.<sup>3</sup> Neurological features such as Guillain-Barré syndrome are also described in COVID-19 positive patients;<sup>4</sup> the virus can enter the

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**Table 1** Characteristics of Patients with and without Delirium

	Delirium n=47	No Delirium n= 76	p-value
Age (years)	71.3	70.4	ns
Women (%)	10 (21.3)	25 (33)	ns
Hypertension (%)	24 (51)	25 (32)	ns
Diabetes Mellitus (%)	12 (25.5)	19 (25)	ns
Previous Stroke	5 (10.6)	7 (9.2)	ns
Admission ICU	39 (83)	31 (40.8)	0.001

**Note:** Values are means for continuous variables and percentages for dichotomous variables.

central nervous system and increase inflammatory cytokines which can be expected to lead to delirium. With the activation of brain parenchymal cells, which might express inflammatory cytokines and other inflammatory mediators in the central nervous system, the inflammatory process can lead to neuronal and synaptic dysfunction which can be expected to lead to delirium.<sup>5</sup>

Another possible explanation could be the distinct presence of hypoxia in COVID-19 patients. Studies in surgical patients found a strong correlation between intraoperative O<sub>2</sub> saturation and postoperative cognitive dysfunction.<sup>6</sup> Hypoxia and decreased brain oxygenation causes a failure in oxidative metabolism, which is associated with a strong release of neurotransmitters, especially glutamate and dopamine.<sup>7</sup> The strong release of dopamine might explain the hyperactive form of delirium with agitation and hallucinations. Hypoxia can also lead to reduced synthesis and release of acetylcholine. Cholinergic neurotransmission is sensitive to metabolic events, such as diminished availability of glucose and oxygen. Reduction in cerebral oxygen may induce delirium by impairing acetylcholine production.<sup>8</sup>

The prevalence of delirium reported in the present study is similar to the prevalence observed in other studies which have included patients of the same age but also older patients<sup>9,10</sup> and is slightly higher than the prevalence of delirium (25–31%) reported in old patients admitted with non-COVID-19 pneumonia<sup>11,12</sup> and in patients admitted with severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).<sup>13</sup> At the moment we do not know in which patients COVID-19 can cause delirium; it might be speculated that decline in physiological capacity in organ systems, with an increased susceptibility to stressors such as frailty, can play a role in these vulnerable older persons. Frailty impairs organ

reserves also at biomolecular level, due to inflammaging, immunosenescence, reduced oxygen uptake and altered energy balance which can be crucial in determining the onset of delirium in older vulnerable COVID-19 patients. Moreover, additional sensory and social deprivation, because of the specific care procedures associated with the treatment of this condition and extreme diminished, or lost, contact with relatives may have negative impact on the severity and duration of the delirium.

Delirium is an acute neuropsychiatric syndrome characterized by disturbances in attention, awareness and cognition – is a frequent disorder in older hospitalized patients. It is associated with poor clinical outcomes including prolonged hospital stay, loss of independence, admission in nursing homes and mortality. Considering the dramatic consequences of delirium and the high prevalence of delirium in COVID-19 older patients we must pay attention to early recognition of neuropsychiatric disorders in order to start with delirium-related treatment to reduce disability and mortality in this vulnerable category of patients.

## Ethics Statement

This study was conducted in accordance with the principles expressed in the Declaration of Helsinki. In The Netherlands, ethical approval and patient consent are not required for retrospective chart review studies in which data collected during routine clinical care are extracted and analyzed anonymously.

## Disclosure

The authors report no conflicts of interest.

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