Comparing Neuro-COVID-19 between Waves Requires Clear Cohort Selection

We read with interest the article by Sureshbabu *et al*. on a retrospective, single-center, observational study comparing first- and second-wave neurological manifestations of COVID-19.[1] A detailed questionnaire on co-morbidities, admission details, and clinical characteristics was applied to 1700 COVID-19 patients in the first and 1500 COVID-19 patients in the second wave.[1] The most common neurological manifestations of the second wave were headache, fatigue myalgia, dysgeusia, dysosmia, dizziness, encephalopathy, and stroke.[1] Dizziness, myalgia, headache, meningoencephalitis, occurred more commonly in the second wave than in the first wave. Cerebrovascular disease occurred less frequently in the second wave than in the first wave.[1] The mortality of COVID-19 patients with neurological involvement was higher in the second compared to the first wave.[1] The study is appealing but raises concerns that should be discussed.

A limitation of the study is its retrospective design. The quality of the data depends heavily on the care and accuracy with which the data were collected and documented. Missing data can no longer be added. Confirmed diagnoses can no longer be corrected.

Another limitation relates to the demarcation between first and second wave. There is no mention of how the end of the first wave and the beginning of the second wave was defined. It is therefore conceivable that an overlap occurred and some patients actually belong to the other group or vice versa.

Another limitation of the study is that the waves were defined by a time criterion and not be the presence of a specific viral mutant. Different mutants of a virus variant with different pathogenicity and therefore different tropism for the central and peripheral nervous system can circulate during a single wave. Therefore, neither patients of the first nor the second wave represent a homogenous cohort and can therefore only be compared to a limited extent.

Another limitation is that it remains unclear how the authors ruled out that neurological manifestations were not a manifestation of the infection but were actually side effects of the treatment the enrolled patients received to treat COVID-19. In particular, neuropathy and myopathy have been reported as side effects of commonly administered anti-COVID-19 drugs, such as colchicine, tocilizumab, prednisolone, or remdesivir.[2]

Surprisingly, according to Table 1, the number of imaging examinations is very small. It is therefore conceivable that a number of cerebrovascular abnormalities may actually have been missed.

Quite a few patients had to be transferred to the intensive care unit (ICU) (n = 127).[1] Because a stay in the ICU can be complicated by critical illness neuropathy/myopathy,[3] we should know how the authors ruled out that neuropathy or myopathy was actually a critical illness neuropathy/myopathy, but not due to the infection.

Another limitation is that the cerebro-spinal fluid (CSF) was obviously not examined in any of the patients.[1] We should therefore know how meningo-encephalitis was diagnosed in the five meningo-encephalitis patients listed in Table 2. Was the diagnosis established just based on the imaging or the clinical picture?

It is not comprehensible why a distinction was made between "visual impairment," "smell and taste disorder," and "altered sensorium."[1] We should know which specific sense was altered in the 40 patients with altered sensorium.

One second wave patient was diagnosed with cerebral vasculitis.[1] We should know what subtype of vasculitis was diagnosed and how. Has this particular patient had an intracranial artery biopsy or was the diagnosis suspected based on imaging criteria?

An unaccounted explanation for the difference between wave one and wave two patients is the variable availability of medical resources over time. With progression of the pandemic, there may have been significant changes in health policy, the pathogenicity of virus variants, and the availability of hospital or ICU beds.

Overall, the interesting study has some limitations and inconsistencies that call the results and their interpretation into question. Addressing these limitations could further strengthen and reinforce the statement of the study.

Ethics approval

Only secondary data were used.

Availability of data

All data are available from the corresponding author.

Author contribution

JF: design, literature search, discussion, first draft, critical comments, final approval.

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Conflicts of interest

There are no conflicts of interest.

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