Frequency of Neurologic Manifestations in COVID-19
A Systematic Review and Meta-analysis

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Study Question
What is the frequency of neurological manifestations in patients with coronavirus disease 2019 (COVID-19)?

What Is Known and What This Paper Adds
The frequency of neurologic manifestations in patients with COVID-19 has been reported in several systematic reviews. However, associations with methodologic quality of the studies, severity of the disease, mean age, and hospitalization status of the patients have not been paid due attention. This systematic review and meta-analysis summarizes the evidence on the frequency of the full spectrum of neurologic manifestations in patients with COVID-19 in the overall, young, and elderly populations.

Methods
This systematic review and meta-analysis included studies published between December 31, 2019, and December 15, 2020, and identified by searching PubMed, EMBASE, MEDLINE, Google Scholar, Cochrane Library, and ClinicalTrials.gov. Studies that enrolled patients with probable/confirmed COVID-19 having neurological manifestations were included. Data on comorbid conditions, neurologic symptoms and diagnoses, disease severity, and hospitalization status of patients with COVID-19 were extracted from each study. Risk of bias was determined with the Joanna Briggs Institute tool. Pooled prevalence and 95% confidence interval (CI) for each neurologic manifestation were calculated with a random-effects model. Odds ratio (OR) and 95% CI were calculated to determine the association of neurologic manifestations with disease severity and mortality. The primary outcome was the frequency of neurologic manifestations in patients with COVID-19.

Results and Study Limitations
Our review included 350 studies providing data on 145,721 patients with COVID-19, 89% of whom were hospitalized. Forty-one neurologic manifestations (24 symptoms and 17 diagnoses) were identified. Pooled prevalence of the most common neurologic manifestations is provided in the table. A low risk of bias was observed in 85% of studies. Stroke was the most common neurologic diagnosis (pooled prevalence 2% [95% CI 1%–2%]). In patients with COVID-19 ≥60 years of age, the pooled prevalence of acute confusion/delirium was 34%, and the presence of any neurologic manifestations in this age group was associated with increased mortality (OR 1.80 [95% CI 1.11–2.91]). The limitations of the present study include the following: lack of data from prospective studies, vast majority of data analyzed from hospitalized cases, high heterogeneity in pooled prevalence estimates, and limited data from low- and middle-income countries.

Study Funding and Competing Interests
This review was supported in part by funding from the World Health Organization. The authors report no competing interests. Go to Neurology.org/N for full disclosures.

<table>
<thead>
<tr>
<th>Variables</th>
<th>No. of studies</th>
<th>Pooled prevalence (95% CI), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myalgia</td>
<td>207</td>
<td>20 (18–23)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>169</td>
<td>32 (30–35)</td>
</tr>
<tr>
<td>Headache</td>
<td>202</td>
<td>13 (12–15)</td>
</tr>
<tr>
<td>Smell impairment</td>
<td>51</td>
<td>19 (13–25)</td>
</tr>
<tr>
<td>Taste impairment</td>
<td>38</td>
<td>21 (15–29)</td>
</tr>
<tr>
<td>Stroke</td>
<td>29</td>
<td>2 (1–2)</td>
</tr>
</tbody>
</table>

Abbreviations: CI = confidence interval; COVID-19 = coronavirus disease 2019.
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