The emergence of unheeded clinical features in COVID-19 patients

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Dear Sir,

Coronavirus disease 2019 or COVID-19 was declared as a global pandemic by the World Health Organisation (WHO) on the 11th of Mar. 2020. The first suspected case of COVID-19 was reported on the 1st of Dec. 2019 in Wuhan City, the capital of Hubei province in Central China. [1, 2] To date 71,919,725 cases have been confirmed, 1,623,064 confirmed deaths, 220 countries with active cases. (16th Dec 2020). [3] The known contagion of Coronavirus Disease is SARS-CoV-2 virus. It belongs to the sabercovirus subgenera of beta coronavirus and is the 7th coronavirus which is pathogenic to humans. [4]

While conducting a systematic review of pathogenesis and clinical manifestation of COVID-19 infection, we came across many common findings. These included headaches, dry cough, myalgia, dyspnoea, pyrexia, fatigue, breathlessness, diarrhoea, and shaking chills, pharyngalgia, anorexia, arthrodynia, COVID tongue, ulcers in the mouth, dizziness, abdominal pain, nausea, and vomiting. [5] Nevertheless, a few abnormal neurological findings were also reported, although no validated studies were conducted on these symptoms. Therefore, it is crucial to comprehend the pathogenesis of SARS-CoV-2 virus in the central nervous system. Coronavirus family infections, severe acute respiratory syndrome coronavirus (SARS) and the Middle East respiratory syndrome coronavirus (MERS) has been associated with several neurological complications in the past. These viruses were neurotropic and neuroinvasive, which lead to severe inflammation and demyelination in the central nervous system. [6]

Interestingly, patients with COVID-19 are also described as similar but uncommon symptoms such as Hypogeusia (loss of taste) and Hyposmia (reduced ability to smell) or Anosmia (loss of smell). [7, 8] Currently, no tests are being performed to validate these findings, and even the pathogenesis of such neurological complications is not understood yet. [9]

According to Carod et al., coronaviruses like SARS show two propagation routes – Haematogenous route or by neuronal retrograde dissemination. In the haematogenous route, the virus can infect the blood-brain barrier’s endothelial cells or infect the macrophages and Dendritic cells, which allows their entry in the central nervous system. Another route could be through Neuronal dissemination. Upon nasal inoculation, the virus disseminates via the cribriform plate and olfactory bulb,
after that, it reaches the brain stem, piriformis cortex and spinal cord. [10] These two routes could be the possible propagation mechanisms of SAR-CoV-2 virus resulting in these neurological complications.

It is strongly recommended to consider carefully the symptoms of hyposmia and hypogeusia during the provisional diagnosis of COVID-19 infection. Doctors and nurses should collect a complete medical history of each patient, including the neurological symptoms, which would further help understand neurovirulence in SARS-CoV-2 infection.

**Keywords**
Coronavirus, COVID-19, infection, neurological, symptoms

**Abbreviations**
Coronavirus disease (COVID-19), Middle East respiratory syndrome coronavirus (MERS), Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

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