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The Assessment of Neurological Complications in Paediatric SARS-CoV-2 Infections Requires Appropriately Designed Studies

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LETTER TO THE EDITOR

We read with interest Han *et al*.'s article on a retrospective, observational, single-centre study of the neurological complications of acute SARS-CoV-2 infections in 455 paediatric patients admitted to a tertiary Hospital in Singapore from December 2021 to June 2022 [Han, V. X. *et al*., 2023]. The study is impressive, but some points require discussion.

The major limitation if the study is its retrospective design. A retrospective design does not allow control of the accuracy of the stored data, does not systematically apply the same examinations to all included patients, produces missing data, does not allow filling in missing data, and is not suitable for generating desirable new data.

A second limitation is the inclusion/exclusion criteria [Han, V. X. *et al*., 2023]. The study population is not representative because those aged >3 months to 18 years were admitted only if there was an appropriate indication (e.g. seizure, croup, dehydration, respiratory distress) [Han, V. X. *et al*., 2023]. Since neurological complications are not necessarily associated with the severity of a SARS-CoV-2 infection, it is conceivable that many neurological complications were missed. Furthermore, it is unclear why patients with MIS-C were excluded from the analysis. MIS-C is a complication of acute SARS-CoV-2 infections and can be associated with neurological impairments.

Another limitation is that no subgroup analysis of vaccinated versus unvaccinated patients was performed. It is conceivable that the frequency, spectrum, and degree of neurological complications differed between the two groups in the sense that those vaccinated had fewer and less severe neurological complications.

Since headaches can be primary or secondary, we should know the cause of headache in every patient with this symptom. How many had their headache secondary to stroke, venous sinus thrombosis, reversible, cerebral vasoconstriction syndrome, hypertension, or meningitis/encephalitis? Have these causes been adequately ruled out in all patients with headache? Were imaging and CSF tests performed on patients in whom the cause of headache remained unclear?

Since dizziness is nonspecific and multicausal, we should know in how many cases it was due to the medications used, to otological involvement, and in how many cases to central nervous system or peripheral nervous system involvement in SARS-CoV-2 infection.

It is incomprehensible how hospitalised patients could be compared with non-hospitalised patients. There were no records of nonhospitalised patients. This discrepancy should be explained.

In summary, the frequency, type, and severity of neurological complications in SARS-CoV2 infections in paediatric patients can only be reliably assessed through an appropriate prospective, multicentre design with comprehensible inclusion/exclusion criteria.

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Statement of Ethics: a) The study was approved by the institutional review board b) Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Disclosures: the author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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