

## COVID-19 Pandemic: The Concerns of Pediatric Neurologists

Dear editor,

The tsunami of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has hit hard to the world with a massive impact on healthcare system, humanity, and economy. The number of cases and deaths are overwhelming, as on May 10, 2020 there are 3,884,434 confirmed cases and 272,859 deaths globally, and 62,939 cases and 2109 deaths in India. Corona virus disease (COVID-19) has affected all age groups from adults to children and neonates. We read the AIAN supplement (2020) dedicated to COVID-19 with great interest, where most of the neurological issues related to COVID-19 pandemic have been discussed. We want to emphasize the impact of COVID-19 pandemic on children and discuss pediatric neurology perspectives related to it.

According to the literature the COVID-19 disease is mild in children and relatively a small number of pediatric cases have been reported. The largest pediatric series of COVID-19 is published by Dong *et al.* from Wuhan, China. Out of 2143 children with COVID-19, 713 were confirmed cases.<sup>[1,2]</sup> The disease was mild in 1091 (50.9%), moderate in 831 (38.8%), and 91 (4.2%) cases were asymptomatic. Among these, 43 (2%) children had severe disease and 13 (0.6%) developed acute respiratory distress syndrome and multi-organ failure. The disease was more severe in children <1 year of age.<sup>[1,3]</sup>

Ludvigsson *et al.*, in a systematic review, reported that children constituted 15% of the total COVID-19 cases.<sup>[4]</sup> In the early part of the pandemic, children get exposure at home.<sup>[4,5]</sup> In the United States, among a total of 149,760 cases, 1.7% ( $n = 2572$ ) cases were in the pediatric age group, and 398 cases were <1 year of age.<sup>[6]</sup> Among 345 pediatric cases, 23% had at least one underlying chronic disease, asthma, cardiovascular disease, and immunosuppression.<sup>[6]</sup> However, the projections for overall paediatric cases are not at all reassuring, suggesting there would be large numbers of paediatric cases with COVID-19.<sup>[7]</sup>

Healthcare issues of children with pre-existing neurological disorders are double fold, first, in the middle of healthcare crisis the usual requirements of these children are neglected, second, these children might be at a higher risk of acquiring severe COVID-19 disease. Neurological complications of COVID-19 are also increasingly recognized in adults as well as in children.

Seizures, encephalopathy, agitation, diffuse upper motor neuron signs, encephalitis, acute necrotizing encephalopathy (ANEC), stroke, anosmia, ageusia, vision loss, and Guillain-Barré syndrome (GBS) are reported in adults with COVID-19.<sup>[8-11]</sup> Mao *et al.* from Wuhan studied the neurological complication in adults with COVID-19.<sup>[8]</sup> The neurological involvement was noted in 36% of adults with COVID-19. Neurological

complications were more common in elderly patients with severe COVID-19 disease. Authors reported central nervous system manifestations (dizziness, headache, impaired consciousness, acute cerebrovascular disease, ataxia, and seizures) in 25%, peripheral nervous system manifestations (taste impairment, smell impairment, vision impairment, and nerve pain) in 9%, and skeletal muscle injury in 10.7% patients.<sup>[8]</sup> Subsequently, an autopsy report of COVID-19 patient showed brain edema and partial neuronal degeneration.<sup>[12]</sup> A case of ANEC is reported in an airline worker in her 50's with COVID-19.<sup>[13]</sup> A similar encephalopathic presentation with seizures reported in a 24-year-old male with COVID-19 pneumonia from Japan.<sup>[9]</sup> Cerebrospinal fluid (CSF) analysis showed lymphocytic pleocytosis, and CSF RT-PCR was positive for SARS-CoV-2. Magnetic resonance imaging (MRI) of brain showed T2/FLAIR hyperintensities in mesial temporal lobes with diffusion restriction.<sup>[9]</sup> Another case of mild encephalitis in an adult with SARS-CoV-2 reported from Wuhan.<sup>[14]</sup> Toscano *et al.*<sup>[15]</sup> from Italy reported five adult patients with GBS after COVID-19. Among these 5 patients with GBS, three had axonal variants, and two had acute inflammatory demyelinating neuropathy. Helms *et al.*,<sup>[16]</sup> from France reported neurological features in 49 adults with COVID-19, the most common features were agitation, confusion, and diffuse upper motor neuron signs.

Dugue *et al.* from New York reported a 6-week-old infant with fever and cough due to SARS-CoV-2 and acute life-threatening event with persistent up gaze and bilateral leg stiffening.<sup>[14]</sup> Neurological complications in other coronavirus epidemics should be known to have a better understanding of expected neurological complications with COVID-19. During SARS-CoV-1 (2003) epidemic encephalitis, polyneuropathy, and acute ischemic stroke were reported.<sup>[10,17]</sup> One-fifth of the patients with middle east respiratory syndrome virus showed neurological symptoms, including encephalopathy, seizures, stroke, GBS, and infectious neuropathy.<sup>[18-20]</sup>

The other important issue is that children with pre-existing neurological disorders might develop severe COVID-19 manifestations. Children with neuromuscular disorders are high-risk patients for severe COVID-19 disease. Respiratory muscle weakness, tracheostomy, non-invasive or invasive ventilation, weak cough, and compromised airway clearance predispose for severe COVID-19 disease. Amid the COVID-19 crisis with overwhelming numbers of patients in need of intensive care services, children with neurological disability may not feature in the priority list for intensive care services. The other group of children at risk are those on immunosuppression. Children with autoimmune encephalitis, demyelinating, paraneoplastic disorders receiving long term steroids or immunomodulators should continue the drugs as advised. In case of intercurrent illness, children

receiving steroids >20 mg/day or 12mg/m<sup>2</sup>/day prednisolone or equivalent (for methylprednisolone 15mg/m<sup>2</sup>/day) for >10 days should receive stress dose steroids. Those who are on rituximab or other biologicals should be monitored closely.<sup>[21]</sup> Children with developmental disabilities are also at high risk for COVID-19, and families of these children should follow the strict isolation measures. Because of travel restrictions supply of antiepileptics, immunotherapies and other life-saving drugs as Nusinersen, enzyme replacement therapies are compromised. Children receiving research medications as part of clinical trials/research studies are also adversely affected due to world-over travel restrictions. Health authorities should rapidly ensure that drugs are continuously available to the children in need and provide special travel permission to research medications and to the patients who require these life-saving research medications.

In conclusion, children with SARS-CoV-2 infection tend to have a milder COVID-19 disease with lower mortality. However, the presence of underlying neurological disorder or comorbid condition may predispose them for severe COVID-19 manifestations. Neurological complications seen in COVID-19 may be related to sepsis, hypoxia, or due to direct neurotropism of coronaviruses.

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### Conflicts of interest

There are no conflicts of interest.

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### REFERENCES

- Cai J, Xu J, Lin D, Yang Z, Xu L, Qu Z, *et al.* A case series of children with 2019 novel coronavirus infection: Clinical and epidemiological features. *Clin Infect Dis*. 2020. doi: 10.1093/cid/ciaa198.
- Dong Y, Mo M, Hu Y, Qi X, Jiang F, Jiang Z, *et al.* Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. *Pediatrics* 2020;1-3. doi: 10.1542/peds.2020-0702.
- Cai JH, Wang XS, Ge YL, Xia AM, Chang HL, Tian H, *et al.* [First case of 2019 novel coronavirus infection in children in Shanghai]. *Zhonghua Er Ke Za Zhi* 2020;58:E002.

- Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr* 2020;109:1088-95.
- Sun D, Li H, Lu XX, Xiao H, Ren J, Zhang FR, *et al.* Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: A single center's observational study. *World J Pediatr* 2020. doi: 10.1007/s12519-020-00354-4.
- CDC COVID-19 Response Team. Coronavirus disease 2019 in children-United States, February 12-April 2, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:422-6.
- Pathak EB, Salemi JL, Sobers N, Menard J, Hambleton IR. COVID-19 in children in the United States: Intensive care admissions, estimated total infected, and projected numbers of severe pediatric cases in 2020. *J Public Health Manag Pract* 2020. doi: 10.1097/PHH.0000000000001190.
- Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, *et al.* Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol* 2020. doi: 10.1001/jamaneuro.2020.1127.
- Moriguchi T, Harii N, Goto J, Harada D, Sugawara H, Takamino J, *et al.* A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. *Int J Infect Dis* 2020;94:55-8.
- Wu Y, Xu X, Chen Z, Duan J, Hashimoto K, Yang L, *et al.* Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav Immun* 2020. doi: 10.1016/j.bbi.2020.03.031.
- Sun WW, Ling F, Pan JR, Cai J, Miao ZP, Liu SL, *et al.* [Epidemiological characteristics of 2019 novel coronavirus family clustering in Zhejiang Province]. *Zhonghua Yu Fang Yi Xue Za Zhi* 2020;54:E027.
- Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, *et al.* Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med* 2020;8:420-2.
- Poyiadji N, Shahin G, Noujaim D, Stone M, Patel S, Griffith B. COVID-19-associated acute hemorrhagic necrotizing encephalopathy: CT and MRI features. *Radiology* 2020;201187. doi: 10.1016/j.bb.2020.03.031.
- Dugue R, Cay-Martinez KC, Thakur K, Garcia JA, Chauhan LV, Williams SH, *et al.* Neurologic manifestations in an infant with COVID-19. *Neurology* 2020. doi: 10.1212/WNL.00000000000009653.
- Toscano G, Carboni M, Rubega M, Spinelli L, Pittau F, Bartoli A, *et al.* Visual analysis of high density EEG: As good as electrical source imaging? *Clin Neurophysiol Pract* 2020;5:16-22.
- Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, *et al.* Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med* 2020. doi: 10.1056/NEJMc2008597.
- Tsai LK, Hsieh ST, Chang YC. Neurological manifestations in severe acute respiratory syndrome. *Acta Neurol Taiwan* 2005;14:113-9.
- Kim JE, Heo JH, Kim HO, Song SH, Park SS, Park TH, *et al.* Neurological complications during treatment of middle east respiratory syndrome. *J Clin Neurol* 2017;13:227-33.
- Saad M, Omrani AS, Baig K, Bahloul A, Elzein F, Matin MA, *et al.* Clinical aspects and outcomes of 70 patients with Middle East respiratory syndrome coronavirus infection: A single-center experience in Saudi Arabia. *Int J Infect Dis* 2014;29:301-6.
- Asadi-Pooya AA, Simani L. Central nervous system manifestations of COVID-19: A systematic review. *J Neurol Sci* 2020;413:116832.
- <https://www.epns.info/covid-19-and-neurological-disorders/>.

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