

COVID - 19

NEUROLOGICAL ASPECTS OF COVID-19 IN CHILDREN***Sheffali Gulati******Juhi Gupta*******Priyanka Madaan**

Abstract: *Children with COVID-19 infection may present with various neurologic manifestations. Although several neurological findings have been documented, it is not clear whether they are causally attributable to SARS-CoV-2 or just occur incidentally in children with COVID-19 infection. During the epidemic period of COVID-19, when seeing patients with neurologic manifestations, clinicians should consider SARS-CoV-2 infection as a differential diagnosis to avoid delayed diagnosis and lose the chance to treat and prevent further transmission. This article documents the various neurological features that have been reported till date due to COVID infection in children.*

Keywords: *Neurological manifestation, COVID -19, Children.*

Children under 19 years of age represented only 2% of total diagnosed cases of COVID-19 in a large cohort of 72,314 patients from China.¹ While studies in adults report up to 36.4% incidence of neurologic symptoms in COVID-19, there are no published cohorts describing neurological complications of COVID-19 in children with exception of a few case reports / series.² Moreover, whether severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is coincidental or causative for the

described neurological manifestations, is also unclear. Two routes of entry into the central nervous system have been suggested- hematogenous and via the cribriform plate. Both direct virus-induced injury and immune-mediated damage have been thought to underlie the pathogenesis of neurological complications.

Neurological manifestations

The neurological manifestations reported with COVID-19 in children include few reports of paroxysmal events (including seizures) over a wide age range encompassing a newborn and an adolescent with status epilepticus.³⁻⁵ A premorbidly normal 11 year-old boy without any prior history of seizures, presented with status epilepticus. He had a striking absence of typical respiratory symptoms except fever recorded at admission. The status epilepticus required four antiepileptic drugs. Electro-encephalography (EEG) revealed frontal intermittent delta activity and cerebrospinal fluid examination (CSF) was suggestive of meningitis/encephalitis.³ His computed tomography (CT) brain was normal. Similarly, paroxysmal events have been described in a 26 day-old neonate and 6 week-old infant, who presented with fever and mild respiratory symptoms.^{4,5} Evidence of abnormal EEG and uprolling of eyeballs in the infant points towards seizures, however normal EEG and termination of episode with stimulation raises the suspicion of non-epileptic events in the case of newborn. The CSF examination was normal in these 2 cases.

Whether COVID-19 was the culprit or an incidental finding in above cases is not clear as neither SARS-CoV-2 was demonstrated in CSF nor it was the sole pathogen detected in the respiratory samples (positive for rhinovirus/enterovirus also in case of infant and adolescent). Another report describes vague findings of axial hypotonia with drowsiness, moaning sounds in four infants (<3 months) presenting with fever and mild respiratory symptoms.⁶ Co-existing fever and dehydration suggested by presence of mottled skin (present in 3 out of 4 children) cannot be refuted as possible causes for these non-specific signs. Interestingly, all these children had a favorable outcome with complete recovery without any antiviral/immunomodulatory therapy.

* Chief, Child Neurology Division,
Center of Excellence and Advanced Research in
Childhood, Neurodevelopmental Disorders,
Department of Pediatrics,
All India Institute of Medical Sciences, New Delhi.

** Senior Resident, Child Neurology Division,
Department of Pediatrics,
All India Institute of Medical Sciences, New Delhi.

*** Senior Research Associate,
Pediatric Neurology Unit, Department of Pediatrics,
Advanced Pediatrics Centre,
Post Graduate Institute of Medical Education &
Research (PGIMER), Chandigarh.
email: sheffaligulati@gmail.com

Similar to adults, neurologic manifestations such as dizziness, headache, encephalopathy, myositis, taste and smell impairment, etc. may be seen in adolescents.² Most of these manifestations (except taste and smell impairment) were associated with severe COVID-19 in adults which are rare in children. While cerebrovascular events (both ischemic and hemorrhagic) have been associated with severe disease and lymphopenia in adults, there are no reports of cerebrovascular events in children. The striking absence of literature on cerebrovascular events in children may probably be due to the presence of proactive anti-thrombotic factors in young age and absence of comorbidities like atherosclerosis and hypertension. Other rare associations of COVID-19 in adults include Guillain Barre syndrome, meningoencephalitis, acute necrotizing encephalopathy and ataxia.⁷ These findings have not been reported in children to date except a solitary case of suspected encephalitis in an adolescent described above.³

The basis of diagnosis in these cases was RT-PCR of nasopharyngeal swab specimen for SARS-CoV-2 which appears to be a useful investigation for confirmation of COVID-19 even in children with neurological presentation. Considering the hazards of aerosol generation and low yield, CSF examination may not be a practical investigation.

Considerations in children with neurodevelopmental disorders (NDD)

Severity of the COVID-19 infection represents a major challenge to patients already afflicted with chronic and possibly acute neurological diseases and their caregivers. Children with chronic neurodevelopmental disorders (NDD) are a vulnerable population in this regard due to limited understanding of the mode of spread of COVID-19, inevitable dependency on caregivers for personal hygiene and care, and limited access to health-care facilities. Also, the NDDs are quite prevalent and afflicted children often have multiple comorbidities such as spasticity, movement disorders, gastroesophageal reflux, seizures, etc. which need to be looked after. Besides, children with specific neurological disorders may require immunosuppressive therapy such as steroids which may act as a double-edged sword. Therefore, policy-making and resource allocation should be consciously aimed at providing optimal care to children with NDDs.

There is a rising concern about initiating and continuing immunosuppressive therapies like adrenocorticotrophic hormone (ACTH) or steroids in

children with infantile spasms, Duchenne muscular dystrophy (DMD), etc. Current guidelines advocate continuing standard therapy (steroids / ACTH/ Vigabatrin) for infantile spasms.⁸ Similarly children with DMD can continue steroids which may be converted to stress dose in case of acute illness based on the judgement of treating physician.⁹ Intravenous immunoglobulin (IVIg) and azathioprine may also be initiated and continued with routine precautions and careful monitoring of lymphocyte counts in the case of azathioprine.¹⁰ However, the risk-benefit ratio should be carefully considered before rituximab initiation.¹⁰

Children with disabilities and their families frequently require medical support as compared with typically developing children. Also, their rehabilitation needs may further be heightened with lockdowns due to restricted mobilization and closure of special schools and early intervention centers. Continual provision of medical services (including rehabilitation) by telemedicine is the need of the hour.

Conclusion

A high index of suspicion and characterization of clinical features by the neurologists on the frontline are key to diagnosis which should be aided by the provision of appropriate PPE. For outpatient care and rehabilitation of children with NDD, teleconsultation may be a beneficial approach.

Points to Remember

- *Neurological manifestations are reported in pediatric COVID-19 albeit in lower frequency than that in adults.*
- *Symptoms range from mild ones like headache to full blown meningoencephalitis.*
- *Whether the SAR-CoV-2 virus is the etiologic or an incidental accompaniment is yet to be elucidated.*

References

1. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA 2020; 323(13):1239.
2. 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 [Internet]. 10th Apr, 2020 [cited 2020 Apr 22]; Available from <https://jamanetwork.com/journals/jamaneurology/fullarticle/2764549>.

3. McAbee GN, Brosgol Y, Pavlakis S, Agha R, Gaffoor M. Encephalitis Associated with COVID-19 Infection in an 11 Year-Old Child. *Pediatr Neurol* 2020 Apr; S0887899420301430.
4. Dugue R, Cay-Martínez KC, Thakur K, Garcia JA, Chauhan LV, Williams SH, et al. Neurologic manifestations in an infant with COVID-19. *Neurology*. 23rd Apr, 2020; 10.1212/WNL.0000000000009653.
5. Chacón-Aguilar R, Osorio-Cámara JM, Sanjurjo-Jimenez I, González-González C, López-Carnero J, Pérez-Moneo-Agapito B. COVID-19: Fever syndrome and neurological symptoms in a neonate. *Anales de Pediatría (English Edition)*. 2020 Apr; S2341287920300661.
6. Nathan N, Prevost B, Corvol H. Atypical presentation of COVID-19 in young infants. *Lancet* 2020; 395(10235):1481.
7. Herman C, Mayer K, Sarwal A. Scoping review of prevalence of neurologic comorbidities in patients hospitalized for COVID-19. *Neurology* 2020 Apr 28. DOI:https://doi.org/10.1212/WNL.0000000000009673.
8. Child neurology society statement for release_Management of Infantile spasms (IS) during COVID-19 pandemic. April 2020 [Internet]. [Last accessed on 15th May, 2020]. Available from: [https://www.childneurologysociety.org/docs/default-source/2020-cns-/cns-statement-for-release_management-of-infantile-spasms-during-the-covid-19-pandemic-\(4-6-20\).pdf?sfvrsn=435065b8_2](https://www.childneurologysociety.org/docs/default-source/2020-cns-/cns-statement-for-release_management-of-infantile-spasms-during-the-covid-19-pandemic-(4-6-20).pdf?sfvrsn=435065b8_2).
9. Veerapandian A, Wagner KR, Apkon S, McDonald CM, Mathews KD, Parsons JA, et al. The care of patients with Duchenne, Becker, and other muscular dystrophies in the COVID 19 pandemic. *Muscle Nerve* 2020 May 5; mus. 26902.
10. Manji H, Carr AS, Brownlee WJ, Lunn MP. Neurology in the time of COVID-19. *J Neurol Neurosurg Psychiatry* 2020; 91(6):568-570.

CLIPPINGS

Ignaz Semmelweis : Father of hand hygiene.

Handwashing has been a central component of personal hygiene for many years. However, the link between handwashing and health was first made by Ignaz Semmelweis, a Hungarian doctor working in Vienna General Hospital, who is known as the father of hand hygiene. In 1846, he noticed that the maternal mortality in / doctor-run maternity ward in his hospital were much more than the adjacent midwife-run maternity ward. He investigated and noticed that doctors often visited the maternity ward directly after performing an autopsy. Based on this observation, he developed a theory that those performing autopsies got ‘cadaverous particles’ on their hands, which they carried from the autopsy room to maternity ward and this is responsible for fatal puerperal fever. Midwives were not exposed to these particles.

As a result, Semmelweis imposed a new rule mandating handwashing with chlorine for doctors. The rates of death in his maternity ward fell dramatically from 10 percent to 2 percent This was the first proof that cleansing hands could prevent infection. However, the innovation was not popular with everyone. In 1861 he published his principal work - The Etiology, Concept, and Prophylaxis of Childbed Fever. Later he was dismissed from the hospital for political reasons, harassed by the medical community and contemporaries. Later abandoned by his wife, believing that he was losing his mind, and in 1865 he was committed to an asylum. He died there of septicemia only 14 days later, possibly as a result of being beaten up by guards. He died for the cause he promoted.

Only years after his death, Louis Pasteur developed the germ theory of disease, offering a theoretical explanation for Semmelweis’s findings. After 150 years, it was the Semmelweis University (SU) in Budapest that first adapted a digital tool to teach hand disinfection technique. Now washing hands with soap and water is universally agreed to be the most effective method to prevent the spread of the new coronavirus, SARS-CoV-2,

Global Handwashing Partnership. <http://globalhandwashing.org/abouthandwashing/historyofhandwashing/> Accessed on 14th June 2020.