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# **CENTRAL NERVOUS SYSTEM MANIFESTATIONS IN PEDIATRIC PATIENTS WITH COVID-19**

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# Background

- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in Wuhan, China, in December 2019 and has become a global public health emergency
- The disease has been devastating worldwide, causing social, health, and economic crises, the effects of which will be felt for decades to come



# *Background*

- Children are less likely than adults to experience symptoms when infected with the SARSCoV-2 virus
- Current information from the pediatric populations mainly relies on case studies from individual patients



# Background

- A broad spectrum of neurological manifestations has been reported in pediatric patients, ranging from specific to nonspecific and from self-limiting to fatal
- Cases of loss of smell and taste, headache, stroke, dizziness, seizures, and ataxia have been reported



# *The Mechanism of the Neuroinvasive Potential of SARS-CoV-2*

- Virus has an affinity for angiotensin-converting enzyme 2 (ACE2) receptors normally located on the human epithelial cells of the respiratory tract
- That ACE2 receptors can also play a role in the infection of the central nervous system, which explains the neurological symptoms reported in many patients



# *The Mechanism of the Neuroinvasive Potential of SARS-CoV-2*

- Like adults, the affinity of the virus to the ACE2 receptor and subsequent disruption to normal cellular functioning, immunologically mediated cytokine storms, and increased coagulation factors have been postulated as being responsible for the neurological findings in children



# *Most Commonly Reported*

- Encephalopathy
- Headache
- Weakness
- Brainstem signs



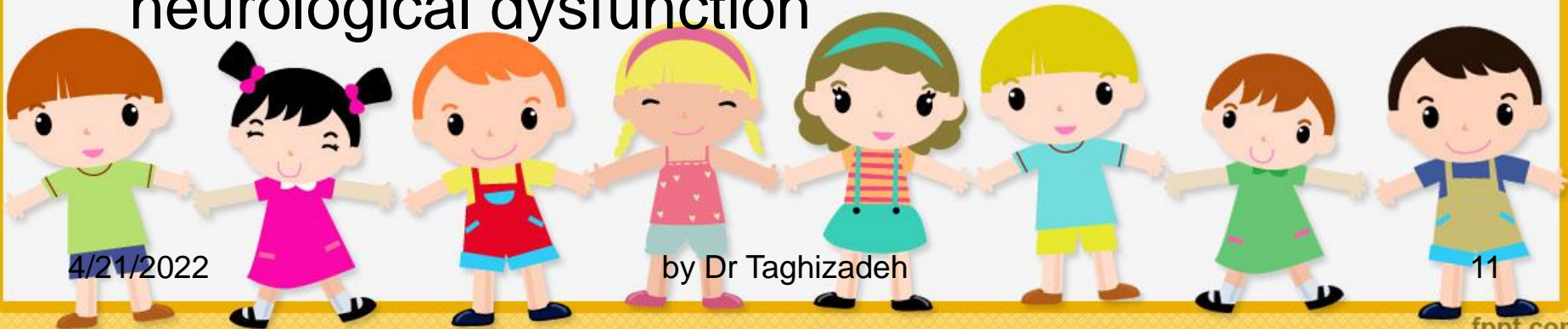
# Cerebrovascular Disease

- The most common manifestation was cerebrovascular disease (CVD), which was reported in 38 cases
- Included ischemic and hemorrhagic strokes, venous thrombosis, and cerebral arteriopathy
- Laboratory studies found increased lactate dehydrogenase (LDH), serum ferritin, and C-reactive protein (CRP)



# *Encephalopathy, Encephalitis, and Encephalomyelitis*

- Encephalopathy refers to a clinical state of altered mental status, manifesting as confusion, disorientation, behavioral changes, or other cognitive impairments, with or without inflammation of the brain tissue
- Encephalitis is characterized by the inflammation of the brain parenchyma associated with neurological dysfunction



# *Encephalopathy, Encephalitis, and Encephalomyelitis*

- ADEM, a form of autoimmune encephalitis, is an immune-mediated, inflammatory demyelinating disease of the central nervous system that can affect children and young adults after infections or immunizations
- The mean age of onset is between 3.6 and 7 years, without differences in sex



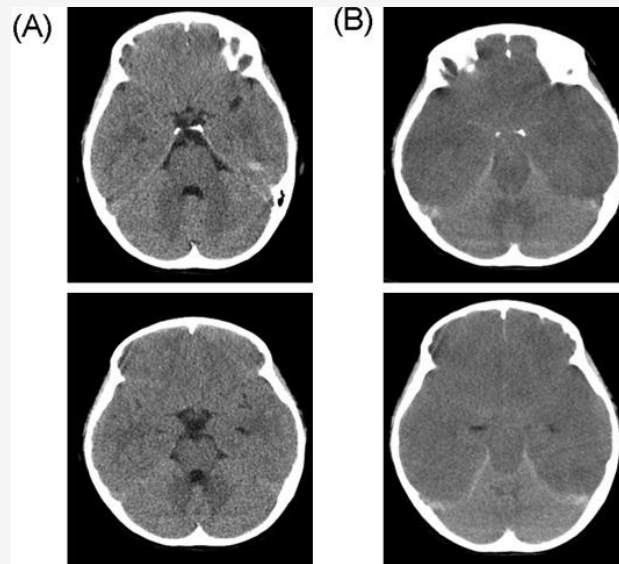
# *Encephalopathy, Encephalitis, and Encephalomyelitis*

- Two reports of anti-NMDA receptor encephalitis associated with SARS-CoV-2 infection in children were found
- The most common symptoms were dyskinesia, personality change, seizures, and cognitive disorders
- This type of encephalitis has also been reported in adults



# *Acute Fulminant Cerebral Edema*

- This complication has had high mortality



# Seizures, Status Epilepticus

- Seizures were reported in five patients as the primary neurological manifestation of children with SARS-CoV-2 infection
- Three of those cases were self-limited seizures in afebrile and previously healthy children
- *The 24-h EEG indicated a diffuse cerebral dysfunction of non-specific etiology*



# *Acute Myelitis*

- A three year-old girl, previously healthy, presented progressive muscle weakness and decreased sensation
- The patient evolved to flaccid quadriparesis and respiratory failure requiring intubation.
- The neurologic exam showed the absence of cough and gag reflexes, with all other cranial nerves intact, flaccid quadriparesis with areflexia, and no response to pain below the neck



# *Acute Myelitis*

- Initial MRI of the cervical spine revealed T2-hyperintense edema involving most of the transverse aspect of the spinal cord from the lower medulla to midthoracic level
- CSF showed mild pleocytosis
- SARS-CoV-2 test was positive in the nasopharyngeal swab
- CSF was negative for SARS-CoV-2 by PCR



# Discussion

- During the last 20 years, the world has experienced three epidemics linked to coronaviruses:

1- severe acute respiratory syndrome (SARS) in 2002

2- the Middle East respiratory syndrome (MERS) in 2012

*3- severe acute respiratory syndrome  
coronavirus 2 (SARS-CoV-2)*



# Discussion

- The novel SARS-CoV-2 causes a clinical syndrome with pulmonary manifestations that have been well characterized
- There are reports of neurological manifestations in patients with SARS-CoV-2 infection in both adult and pediatric populations



# Discussion

- COVID-19 usually courses with mild symptoms in children; however, serious complications may occur during both acute infection and the multisystem inflammatory syndrome in children (MIS-C)
- The neurological manifestations related to the central nervous system elucidated in the present review include strokes encephalopathy, encephalitis, seizures, acute cerebral edema, acute transverse myelitis, acute myelitis, and cerebellar ataxia



# Discussion

- SARS-CoV-2 could also indirectly damage the central nervous system via activation of the immune response, damaging the neuronal tissue
- SARS-CoV-2 affects the CNS via systemic and local inflammatory response causing cytokines storming and immune cell reactivation



# Discussion

- The rarity with which the virus has been found in the CSF in patients with clinical evidence of brain inflammation linked to SARS-CoV-2 implies that *immunemediated damage is more important* than viral replication in neurons



# Discussion

- *Stroke and encephalopathy* were the predominant neurological syndromes associated with SARS-CoV-2 infection in children
- Hypercoagulable states indicated by elevated D-dimer, prolongation of prothrombin time (PT), activated partial thromboplastin time (aPTT), and thrombocytopenia have been observed with the SARS-CoV-2 infection



# Discussion

- *The interaction between the virus and the ACE2 receptors* expressed on vascular endothelial cells may trigger a pro-inflammatory response and a procoagulable state by initiating vasculitis and disruption of vascular integrity, with subsequent activation of the clotting cascade



THANKS FOR  
YOUR  
ATTENTION



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