International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2019): 7.583

Neurology and COVID-19 in Pediatrics

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Abstract: ***The recent outbreak of corona virus infectious disease 2019 (COVID-19) has gripped the world with apprehension and has evoked a scare of epic proportion regarding its potential to spread and infect humans worldwide. As we are in the midst of the ongoing pandemic of COVID-19, scientists are struggling to understand how itresembles and differs from the severe acute respiratory syndrome corona virus (SARSCoV)at the genomic and transcriptomic level. In a short time following the outbreak, ithas been shown that, similar to SARS-CoV, COVID-19 virus exploits the angiotensin convertingenzyme 2 (ACE2) receptor to gain entry inside the cells. This finding raisesthe curiosity of investigating the expression of ACE2 in neurological tissue anddetermining the possible contribution of neurological tissue damage to the morbidityand mortality caused by COIVD-19. Here, we investigate the density of the expression levels of ACE2 in the CNS, the host−virus interaction and relate it to the pathogenesisand complications seen in the recent cases resulting from the COVID-19 outbreak. Also, we debate the need for a model for staging COVID-19 based on neurological tissue involvement.***

Keywords: Corona virus, SARS-CoV-2, COVID-19, ACE2 tissue distribution, host−virus interaction, spike protein

1. Introduction

1.1 The novel Corona Virus COVID 19

The first reports of the viral infection attracted attention in late December 2019 in Wuhan, the capital of Hubei, China. Later, it was revealed that the virus responsible for causing the infections was contagious between humans. By early January, terms like “the new corona virus” and “Wuhan corona virus” were in common use. On February 11, 2020, a taxonomic designation “severe acute respiratory syndrome corona virus 2” (SARS-CoV-2) became the official means to refer to the virus strain, that was previously termed as 2019-nCoV and Wuhan corona virus. Within a few hours on the same day, the WHO officially renamed the disease as COVID-19.[1]

1.2 The Genome of the COVID 19 Virus

The complete genome of SARS-CoV-2 from Wuhan, China was submitted on January 17, 2020 in the National Centre for Biotechnology[1] (NCBI) database, with ID NC_045512. The genome of SARS-CoV-2 is a 29,903 bp single-stranded RNA (ss-RNA) corona virus. It has now been shown that the virus causing COVID-19 is a SARS-like corona virus that had previously been reported in bats in China.

1.3 Tissue Distribution of ACE 2 in human organs and tissues

In order to discover the neurovirulence of SARS-CoV-2 and relate it to neurological tissue expression of ACE2, data retrieval was done from human protein databases. Most of the evidence of ACE2 expression in the brain comes from literature and mammalian tissue expression databases,[2] which prompted us to investigate neurotropic effects of SARSCoV- 2 and its contribution toward the morbidity and mortality of patients with COVID-19.

1.4 Evidence of the Distribution of ACE2 in the Human Brain

The brain has been reported to express ACE2 receptors that have been detected over glial cells and neurons, which makes them a potential target of COVID-19. Previous studies have shown the ability of SARSCoV to cause neuronal death in mice by invading the brain viathe nose close to the olfactory epithelium.[3] In the SARS-CoV infections that were reported in the past, autopsy findings of the patients have shown strong evidence of the presence of SARS-CoV by electron microscopy, immunohistochemistry, and real-time reverse transcription- PCR [3]. Patients with acute SARS-CoV illness have also demonstrated the presence of the virus in cerebrospinal fluid. The role of the blood-brain barrier in containing the virus and preventing it from gaining access to the neural tissues needs to be further explored in patients diagnosed with COVID-19.

1.5 Host Virus Interactions

With the mRNA encoding several other proteins,[1] theCOVID-19 virus, like SARS-CoV, uses a spike protein S1that enables the attachment of the virion to the cell membraneby interacting with host ACE2 receptor[3, 5]. A BLASTp search of the COVID-19 virus (SARS-CoV-2) receptor binding domain (RBD) subdomain-1 (319th to 591st aa) fetched a spike glycoprotein [bat corona virus RaTG13] and S1 protein partial [SARS corona virus GD322] as homologs.

1.6 A proposed cascade of CNS involvement in COVID 19 infection

The dissemination of COVID-19 in the systemic circulation or across the cribriform plate of the ethmoid bone during an early or later phase of the infection can lead to cerebral involvement as has been reported in the past for SARS-CoV affected patients.[3] The presence of the COVID-19 virus in the general circulation understandably enables it to pass into the cerebral circulation where the sluggish movement of the blood within the microcirculation could be one of the factors that may facilitate the interaction of the COVID-19 virus spike protein with ACE2 expressed in the capillary endothelium. Subsequent budding of the viral particles from the capillary endothelium and damage to the endothelial lining can favour viral access to the brain. Once within the milieu of the neuronal tissues, its interaction with ACE2 receptors expressed in neurons[2] can initiate a cycle of viral

budding accompanied by neuronal damage without substantial inflammation as has been seen with cases of SARS-CoV3 in the past. The movement of the COVID-19 virus to the brain via the cribriform plate close to the olfactory bulb can be an additional pathway that could enable the virus to reach and affect the brain. Additionally, the findings like an altered sense of smell or hyposmia in an uncomplicated early stage COVID- 19 patient should be investigated thoroughly for CNS involvement.

1.7 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.[6 to 8]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 many cases.

Table 1: CNS manifestations of COVID 19 in pediatrics

Dizziness
Headache
Encephalopathy
Seizures
Altered sensorium
Myositis
Encephalitis
Taste and smell impairment
Neuropathy
GBS
Stroke (very rare in pediatrics)
Brainstem signs
Cerebellar signs
Miller Fisher syndrome
Polyneuritis cranialis
Meningism
Ataxia
Dysarthria
Dysphagia
Confusion

Table 2: Peripheral Nervous system manifestations

Generalised proximal weakness
Urinary retention
Bilateral proximal leg weakness
Global flaccid weakness
Reduced reflexes

Table 3: Associated co morbidities

Neurodevelopment delay
Spasticity
DMD
Myopathies
Multisystem involvement

2. Conclusions and Future Directions

Autopsies of the COVID-19 patients, detailed neurological investigation, and attempts to isolate SARS-CoV-2 from the endothelium of cerebral microcirculation, cerebrospinal fluid, glial cells, and neuronal tissue can clarify the role played by this novel COVID-19 causing corona virus in the ongoing mortalities as has been in the recent outbreak. It is important to mention here that although the cerebral damage may complicate a COVID-19 infection, it appears that it is the widespread dysregulation of homeostasis caused by pulmonary, renal, cardiac, and circulatory damage that proves fatal in COIVD-19 patients.

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.

3. Acknowledgements

To The Dean BJGMC, Pune
To the Head of the Paediatrics Department Dr Aarti Kinikar BJGMC, Pune
To all staff and residents who manage pediatric Covid cases in the hospital.

4. Conflicts of Interest

None

5. Funding and sponsorship

Not required for the same.

References

[1] Wuhan seafood market pneumonia virus isolate Wuhan-Hu-1, complete genome. Nucleotide, National Centre for Biotechnology Information (NCBI), National Library of Medicine (US), National Centre for Biotechnology Information, Bethesda, MD, https://www.ncbi.nlm.nih.gov/nuccore/1798174254 (accessed on 8/08/2020).
[2] Palasca, O., Santos, A., Stolte, C., Gorodkin, J., and Jensen, L. J. (2018) TISSUES 2.0: an integrative web resource on mammalian tissue expression. Database 2018, No. bay003.
[3] Netland, J., Meyerholz, D. K., Moore, S., Cassell, M., and Perlman, S. (2008) Severe acute respiratory syndrome corona virus infection causes neuronal death in the absence of encephalitis in mice transgenic for human ACE2. J. Virol. 82 (15), 7264–75.
[4] Li, Y. C., Bai, W. Z., and Hashikawa, T. (2020) the neuro invasive potential of SARS-CoV2 may be at least partially responsible for the respiratory failure of COVID-19 patients. J. Med. Virol., DOI: 10.1002/jmv.25728.
[5] Wrapp, D., Wang, N., Corbett, K. S., Goldsmith, J. A., Hsieh, C. L., Abiona, O., Graham, B. S., and McLellan,

J. S. (2020) Cryo-EM structure of the 2019-nCoV spike in the perfusion conformation. Science, No. eabb2507.

[6] 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.

[7] 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.

[8] Chacón-Aguilar R, et al. COVID-19: Fever syndrome and neurological symptoms in a neonate. Anales de Pediatría(English Edition). 2020 Apr; S2341287920300661.