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Review Article

Neurological complications of COVID-19 in children and its effect on the quality of life

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ABSTRACT

Coronavirus disease 2019, a pandemic that recently enveloped the world is a highly transmissible respiratory disease leading to 2,409,011 deaths in 2021. The most prevalent clinical symptoms in coronavirus disease 2019 patients are fever, cough, shortness of breath, and other respiratory issues. Coronavirus disease 2019 exhibits various neurological manifestations and complications which are quite rare in children. The purpose of this research is to review the available information about neurological complications of Coronavirus disease 2019 in children. Coronavirus disease 2019 is linked to neurological complications in children, including headaches, encephalopathy, and certain other neurological disorders. Involvement of the nervous system in coronavirus infection is either immediate, during the progression of the disease, after recovery, or as part of multisystem inflammatory syndrome in children. The clinical manifestations of coronavirus disease in new-borns and infants with neurological complications vary and can affect the whole neuraxis, affecting the central nervous system, peripheral nervous system, or both. In addition, children with multisystem inflammatory syndrome and coronavirus had severe neurological complications such as encephalitis, epilepsy, coma, dementia, dysgeusia or ageusia, aseptic meningitis, stroke, dysarthria, dysphagia, cerebellar ataxia, axial hypotonia, and drowsiness. Seizures in children are normally reported when they are suffering from fever due to viral infection. Neurological complications in children are rare and limited literature is available in this regard. More comprehensive, clinical follow-up studies can significantly contribute to understanding the relationship among coronavirus disease effects and neurological complications among children.

Keywords: Neurological, Complication, Coronavirus, Disease

INTRODUCTION

Severe acute respiratory syndrome (SARS-CoV-2) is caused by novel coronavirus which is responsible for causing the highly contagious and infectious disease called coronavirus disease 2019 (COVID-19). The first instances of COVID-19-related infection were reported in December 2019 in Wuhan, Hubei Province, China, and were attributed to the Huanan Seafood Market. The disease has spread to over 216 nations and territories since then. COVID-19 attained pandemic status on 30 January 2020, according to the world health organization, and was declared a global pandemic in March 2020. Since then, it has been termed as the most critical global health crisis of the century and termed as the greatest challenge that humanity has faced since World War II.[1] As reported by world health organization there were 109,068,745 confirmed cases of SARS-CoV-2 by February 2021, with 2,409,011 deaths. COVID-19 mortality is linked to a number of factors, including advanced age like age greater than 60 years, gender, smoking history, pre-existing pneumonia, and presence of major concomitant diseases. Fever, cough, shortness of breath, and other respiratory difficulties are the most common clinical symptoms in COVID-19 patients, however, other nonspecific symptoms such as headache, dyspnea, fatigue, muscle pain, as well as digestive symptoms such as diarrhoea and vomiting are also reported.[2]

Children account for only 1% to 5% of all COVID-19 infections worldwide, and 80% of those infected are asymptomatic or have a moderate infection. In the largest published cohort to date, 1% of the children affected were under the age of ten, and 1% were between the ages of 10 and 18. A one-day-old baby was the youngest patient reported.[3] Children infected with the coronavirus are frequently asymptomatic or have moderate coronavirus disease, with low rates of hospitalization (2%), and death (0.03%). Adolescents, who are more frequently infected and hospitalized than younger children, have a higher disease burden. Despite the modest incidence of acute COVID-19 in children in the short term, SARS-CoV-2 infection has two long-term implications that are more concerning. The first is paediatric inflammatory multisystem syndrome which is temporally associated with SARS-CoV-2 or also called multisystem inflammatory syndrome in children. It is an immune-mediated disease that, however, affects a small percentage of children approximately 0.1% and around 2 to 6 weeks after SARS-CoV-2 infection. The second is long COVID, also known as post-COVID syndrome or SARS-CoV-2 post-acute sequelae. These phrases refer to the symptoms that continue after COVID-19. However, mostly affect adults and affect the sensory, neurologic, and cardiorespiratory systems, as well as mental health of patients.[4]

COVID-19 has been linked to a variety of neurological problems in children, including headaches, encephalopathy, and impaired mood in addition to multisystem inflammatory syndrome and respiratory disorders. In addition, children with multisystem inflammatory syndrome had severe neurological defects such as encephalitis, epilepsy, coma, dementia, dysgeusia or ageusia, aseptic meningitis, stroke dysarthria, dysphagia, cerebellar ataxia, axial hypotonia, drowsiness, and peripheral neuropathy.[5-8] Global study of approximately 1,400 paediatric patients reported prevalence of headache (4%), anosmia (2%), seizures (0.7%), and cerebrovascular stroke (0.7%). The pathophysiology of COVID-19's acute and chronic neurologic symptoms is likely complex involving direct viral invasion and replication in the central nervous system, large vessel or microvascular insufficiency due to vasoconstriction and occlusion, nonspecific effects of severe systemic COVID-19 illness or treatment, and immune system dysregulation and autoimmunity, which can all contribute to disease pattern either together or separately.[9] The purpose of this research is to review the available information about neurological complications of COVID-19 in children.

LITERATURE SEARCH

This study is based on a comprehensive literature search conducted on June 9, 2022, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the information neurological complications of COVID-19 in children. There were no restrictions on date, language, participant age, or type of publication.

DISCUSSION

COVID-19 is a major threat to the world due to its high prevalence, severe symptoms, psychological and neurological complications, and a lack of appropriate medication. COVID-19 is thought to show minor symptoms or diseases in children. However, significant side effects, such as multisystem inflammatory syndrome, cannot be ruled out. COVID-19 causes neurological problems in children ranging from mild to severe, including stroke, encephalopathy, shortness of breath, and myalgia. Inflammatory reactions and cytokine storms are associated with the development of these disorders, altering the immune system and brain function and allowing the virus to enter the brain. These neurological disorders can be produced indirectly by significant immune responses, notwithstanding viral penetration into the brain. Infected neonates and children with SARS-CoV-2 or COVID-19 are likely to be more susceptible to inflammatory reactions that lead to more severe complications.[10] COVID-19 has a wide range of neurological complications that can be fairly severe,

however they are uncommon in children. For efficient management of these individuals, a thorough understanding of various manifestations of neurological symptoms connected to COVID-19 is essential.[11]

Neurological complications of COVID-19 in children

Neurological complications are more common in children with chronic low birth weight, new-borns and infants, and those who develop multisystem inflammatory syndrome. Fortunately, neurological symptoms, especially headaches and anaesthesia, are minor and temporary in most children, and are not significantly different from the COVID-19 study. However, more serious clinical problems may arise in some cases due to significant abnormalities in neuroimaging, electroencephalography, nerve conduction tests, and electromyography. Almost all children with COVID-19 and the symptoms found so far have fully recovered, however this has happened in some cases after a few weeks of treatment. In addition, COVID-19 infection during pregnancy is associated with an increased risk of birth defects in new-borns, which may cause severe and long-term neurological symptoms and complications. However in paediatric patients who have had multisystem inflammatory syndrome, fainting, or other neurological symptoms, as well as in pregnant women with COVID-19, monitoring of neurological growth and manifestations within a few months after treatment to detect obvious and subtle deficiency is recommended.[12]

Findings of a systematic review and meta-analysis in 2020 showed that non-specific neurological symptoms such as headache, myalgia, and exhaustion were the most common symptoms, accounting for 16.7% of all cases. A total of 42 children (1%) were found to have definite neurological complications, with 25 number of children with encephalopathy, seizure in 12, and meningeal signs among 17 children being the most common. Intracranial bleeding, cranial nerve palsy, Guillain–Barré syndrome, and visual impairments were all uncommon neurological complications. All of the children who had acute symptomatic seizures indicated a good short-term prognosis. In children with COVID-19, neurological complications are uncommon. Even so, young children are in danger of having seizures and encephalopathy, especially if they suffer from severity of disease.[13] Stafstrom states that clinical symptoms of COVID-19 in new-born and infants with neurological characteristics are diverse and can affect the entire neuraxis, affecting the central nervous system, the peripheral nervous system, or both. There were no neurological complications in some of the reported neonatal series. Irritability and lethargy are common neurological symptoms in new-borns, but they are non-specific and do not address the location of the disease process or its mechanism.[14]

Results from a case series in 2021 revealed that the most common neurologic complications in children under 5 years were seizure or epilepticus, while anosmia and ageusia were more common in patients aged 13 to 20 years. Children with COVID-19 associated with neurological complications co-versus COVID-19 had a 5% greater chance of survival and new neurologic abnormalities than non-COVID-19 associated neurologic disorders (0.2%). One male infant with COVID-19 was diagnosed with fever, fainting, and abdominal symptoms, and had a stroke and heart attack within 24 hours of admission, neuroimaging later revealed global cerebral edema. A young child with a fever and sore throat experienced a fallout, and further scan revealed brain tumours and tonsillar herniation. Following the results of the direct SARS-CoV-2 respiratory test, one primary school child met the requirements of multisystem inflammatory syndrome after one month. Shortly after his admission to the hospital, he suffered a stroke, and diagnostic neuroimaging revealed global cerebral edema and uncal herniation.[15]

Results of a European prospective cohort study in 2021 showed that 27 of 52 paediatric patients were assigned to the COVID-19 neurology group, Status epilepticus (n=7), encephalitis (n=5), Guillain-Barré syndrome (n=5), acute demyelinating syndrome (n=3), chorea (n=2), psychosis (n=2), isolated encephalopathy (n=2), and transient ischemic attack (n=1) were among the findings in the COVID-19 neurology group.[16] Results of another study in 2021 depicted that 14.8% of children with COVID-19 paediatric multisystem inflammatory syndrome who were previously healthy developed new neurological symptoms. Encephalopathy, migraines, brainstem and cerebellar indications, muscle weakness, and impaired reflexes were among the reported symptoms.[17]

Boronat stated that seizures in children caused by SARS-CoV-2 infection are frequently acute symptomatic seizures that occur primarily during feverish episodes of the viral infection. There have been two occurrences of febrile status epilepticus and two cases of status epilepticus in the setting of SARS-CoV-2-induced multisystem inflammatory syndrome. An occipital intracerebral haemorrhage was discovered in one of these patients. Seizures, with or without fever, have been observed as early as the first months of life. Fever, cough, and brief periods of reduced responsiveness with upward gaze and rigidity of both legs were seen in a 6-week-old with a positive SARS-CoV-2. The electroencephalogram revealed a delta rhythm that was intermittent. The results of all other tests, including the brain magnetic resonance imaging, were normal. Two episodes of widespread hypertonia occurred in a 26-day-old male new-born with SARS-CoV-2 infection and fever. The electroencephalogram showed no abnormalities. During SARS-CoV-2 infection, a 3-month-old girl was observed to have non-febrile focal seizures with reduced consciousness on days 6 and 9 after commencement, with normal neuroimaging.[18]

Findings of a review study in 2021 showed that 43% of paediatric patients experienced neurological

complications. Headache (34%), weariness or malaise 25%, altered mental status 23%, weakness 14%, and seizure 11% were the most prevalent symptoms. Three patients had cranial nerve VI palsy, which was noteworthy. Intracranial hypertension was also present in two of these patients. Only two individuals had dysgeusia or ageusia, and only one of them had a stroke. The median patient age was 9 years. 34% of patients with neurological symptoms exhibited polymerase chain reaction evidence of active SARS-CoV-2 infection, 54% had a positive antibody test, and 11% were polymerase chain reaction - and antibody-positive at the same time.[19] Results of a single centre study in 2021 showed that during acute COVID-19 disease, seizures, headaches, dizziness, anosmia, ageusia, and meningoencephalitis are common reported neurological symptoms. Despite the fact that seizures were the most common reason for hospitalization, meningoencephalitis was also relatively common. Children under the age of 6 years old had febrile seizures, while those beyond 6 years old had afebrile seizures. Children with febrile seizures made up half of all seizure cases. Seizures (52.9%), headache (38.2%), dizziness (11.1%), and meningoencephalitis (5.8%) were among the neurological problems that required hospitalization in 34 (8.9%) of the patients.[20]

Although some of the children with acute disease may have developed encephalopathy due to factors other than the virus's direct neurotrophic effects, such as hypoxia and septic shock, encephalopathy was determined to be the most common clear neurological complication. The disease is reported to be less severe and intense among children and neurological complications in children have been described in a small number of instances as compared to adults.[11] Involvement of the nervous system may occur spontaneously, during COVID-19 or after recovery, or as part of multisystem inflammatory syndrome in children. Cerebrovascular injuries, reversible splenial ulcers, Guillain-Barré syndrome, benign intracranial hypertension, and meningoencephalitis are the most commonly described neurological symptoms; Extreme encephalomyelitis is also a potential side effect. All neurological complications of SARS-CoV-2 infection, as well as their underlying pathogenic mechanism, require further investigation.[21]

Without an indication of respiratory symptoms, neurological manifestations could be the first sign of underlying COVID-19 infection. Also, the role of the central nervous system in COVID-19 infection must be considered, as an immune-mediated process with probable cytokine storm activation. More cases and epidemiological data are needed to support a causal relationship between COVID-19 infection and neurological involvement, especially in children who are asymptomatic or have mild respiratory symptoms from COVID-19 infection, and the neurological symptoms are the initial presentation rather than complications of underlying severe respiratory illness.[22] Due to rare occurrence of neurological complications among children literature is also very limited especially regarding the effects these neurological complications can cause in children, future comprehensive and clinical studies addressing the complications and their effects in children can be beneficial and significant.

CONCLUSION

COVID-19 is a respiratory disease that affects children less frequently and with less severity as compared to adults. Although neurologic manifestations and complications are more common in adults, they are also seen in children who have been infected with the virus, particularly those who have multisystem inflammatory syndrome. More follow-up clinical studies among children who suffered COVID-19 are needed to study the sequalae of COVID-19 among children especially who exhibited neurological manifestations.

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REFERENCES

1. Rahman S, Montero MTV, Rowe K, Kirton R, Kunik F. Epidemiology, pathogenesis, clinical presentations, diagnosis and treatment of COVID-19: a review of current evidence. Expert Rev Clin Pharmacol. 2021;14(5):601-21.
2. Halaji M, Heiat M, Faraji N, Ranjbar R. Epidemiology of COVID-19: An updated review. J Res Med Sci. 2021;26:82.
3. Govil-Dalela T, Sivaswamy L. Neurological Effects of COVID-19 in Children. Pediatr Clin North Am. 2021;68(5):1081-91.
4. Zimmermann P, Pittet LF, Curtis N. How Common is Long COVID in Children and Adolescents? Pediatr Infect Disease J. 2021;40(12):e482-7.
5. Ellul MA, Benjamin L, Singh B. Neurological associations of COVID-19. Lancet Neurol. 2020;19(9):767-83.
6. Fan S, Xiao M, Han F. Neurological manifestations in critically ill patients with COVID-19: a retrospective study. Frontiers Neurol. 2020;806.
7. Molloy EJ, Bearer CF. COVID-19 in children and altered inflammatory responses. In. Vol 88: Nature Publishing Group. 2020;340-41.
8. Diorio C, Henrickson SE, Vella LA. Multisystem inflammatory syndrome in children and COVID-19 are distinct presentations of SARS–CoV-2. J Clin Investigation. 2020;130(11):5967-75.
9. Schober ME, Pavia AT, Bohnsack JF. Neurologic Manifestations of COVID-19 in Children: Emerging Pathophysiologic Insights. Pediatr Crit Care Med. 2021;22(7).
10. Siddique R, Khan S, Shabana. Neurological complications of COVID-19 in children and the

associated immunological responses. J King Saud University Sci. 2022;34(3):101884.
11. Ahmad I, Rathore FA. Neurological manifestations and complications of COVID-19: A literature review. J Clin Neurosci. 2020;77:8-12.
12. Principi N, Esposito S. Are we sure that the neurological impact of COVID 19 in childhood has not been underestimated? Ital J Pediatr. 2021;47(1):191.
13. Panda PK, Sharawat IK, Panda P, Natarajan V, Bhakat R, Dawman L. Neurological Complications of SARS-CoV-2 Infection in Children: A Systematic Review and Meta-Analysis. J Trop Pediatr. 2020;67(3).
14. Stafstrom CE. Neurological effects of COVID-19 in infants and children. Develop Med Child Neurol. 2022;64(7):818-29.
15. LaRovere KL, Riggs BJ, Poussaint TY. Neurologic Involvement in Children and Adolescents Hospitalized in the United States for COVID-19 or Multisystem Inflammatory Syndrome. JAMA Neurol. 2021;78(5):536-47.
16. Ray STJ, Abdel-Mannan O, Sa M. Neurological manifestations of SARS-CoV-2 infection in hospitalised children and adolescents in the UK: a prospective national cohort study. Lancet Child Adolescent Heal. 2021;5(9):631-41.
17. Abdel-Mannan O, Eyre M, Löbel U. Neurologic and Radiographic Findings Associated With COVID-19 Infection in Children. JAMA Neurol. 2020;77(11):1440-45.
18. Boronat S. Neurologic Care of COVID-19 in Children. Frontiers in Neurol. 2021;11.
19. Lin JE, Asfour A, Sewell TB. Neurological issues in children with COVID-19. Neurosci Lett. 2021;743:135567.
20. Dilber B, Aydın ZGG, Yeşilbaş O. Neurological Manifestations of Pediatric Acute COVID Infections: A Single Center Experience. J Trop Pediatr. 2021;67(3).
21. Siracusa L, Cascio A, Giordano S. Neurological complications in pediatric patients with SARS-CoV-2 infection: a systematic review of the literature. Ital J Pediatr. 2021;47(1):123.
22. Aljomah L, Almedlej S, Baarmah D. Pediatrics COVID-19 and neurological manifestations: Single tertiary centre experience. e Neurological Sci. 2021;24:100355.

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