

Review Article

Hearing loss, tinnitus and vertigo among pediatric patients with COVID-19 infections: a review

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is a rapidly spreading contagious respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which manifests a plethora of health concerns. It may manifest with a wide range of clinical symptoms from no symptoms to respiratory failure and even multi-organ dysfunctions. The COVID-19 infection may present with otological manifestations such as hearing loss, tinnitus, vertigo, and otalgia. The otological manifestations may be due to the involvement of the eustachian tube and cochlea by COVID-19 infections. The damaging effect of the COVID-19 infection on the inner ear is a new finding which is yet to be explored. Pure tone audiometry and impedance audiometry are two important investigations for auditory assessment among pediatric patients with COVID-19 infection. Although hearing loss, tinnitus and vertigo are not common as fever and cough in COVID-19 patients, however, auditory-vestibular symptoms significantly affect the quality of life. Additionally, the anxiety associated with COVID-19 infections may attribute to aggravation of otoneurological symptoms like tinnitus. However, these otoneurological manifestations like hearing loss will affect the speech of the pediatric patients and result in morbid life in the current COVID-19 pandemic. Clinicians or pediatricians should be aware of the otoneurological manifestation in pediatric COVID-19 patients for early identification and management. This review article discusses the details of this epidemiology, etiopathology, assessment, and management of hearing loss, tinnitus, and vertigo among COVID-19 pediatric patients.

Keywords: COVID-19, SARS-CoV-2, Hearing loss, Tinnitus, Vertigo, Pediatric patients

INTRODUCTION

COVID-19 is a contagious disease caused by a novel virus called acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ This virus is a large, encapsulated positive-strand RNA virus. COVID-19 patients usually present respiratory symptoms, however, some experience neurological symptoms.² The symptomatology of the COVID-19 patients ranges from mild respiratory symptoms to acute respiratory distress syndrome (ARDS) along with cough, fever, myalgia, olfactory and taste dysfunctions.³ The COVID-19 patients may present with both neurological symptoms respiratory problems. The neurological manifestations may affect approximately

30% of the COVID-19 patients.⁴ The neurotropic nature of SARS-CoV-2 is still being under investigation. Neurologic manifestations like headache, impaired consciousness, and dizziness have been reported in patients with COVID-19 infections.⁵ Olfactory and gustatory disturbances are two neurological manifestations found in COVID-19 patients.⁶ In addition to the variety of clinical symptoms, some COVID-19 patients present neuro-otological manifestations such as dizziness, hearing loss, tinnitus, and otalgia.⁷

The impact of SARS-CoV-2 infection on the inner ear is a new finding yet to be explored.⁸ Hearing loss, tinnitus, and vertigo are common clinical manifestations reported

in the outpatient department of otorhinolaryngology. There are numerous literatures reported regarding hearing loss, tinnitus, and vertigo associated with different viral infections. There is still debate going on about the exact etiopathology of hearing loss, tinnitus, and vertigo among pediatric patients with COVID-19 infections. There are only a few reported cases of COVID-19 infections resulting inner ear manifestations, particularly in the pediatric age group. There is not much literature for auditory-vestibular manifestations with robust epidemiological studies and management in COVID-19 pediatric patients, indicating that these medical entities are neglected in a current pandemic in the pediatric age group.

METHODS OF LITERATURE SEARCH

The research articles related to hearing loss, tinnitus, and vertigo among COVID-19 pediatric patients were searched through multiple approaches. First, we conducted an online search of the PubMed, Scopus, Google Scholar, and Medline databases with word hearing loss, tinnitus, and vertigo in COVID-19 pediatric patients, auditory-vestibular symptoms in pediatric patients infected with SARS-CoV-2, etiopathology, clinical presentations, investigations, and treatment of hearing loss, tinnitus and vertigo in pediatric patients infected with COVID-19 infection. A search strategy using Preferred Reporting Items for Systemic Reviews and Meta-analysis guidelines was developed. Randomized controlled studies, observational studies, comparative studies, case series, and case reports were evaluated for eligibility. All the articles were read and analyzed, with relevant data being extracted. A flowchart of the selected articles is in Figure 1.

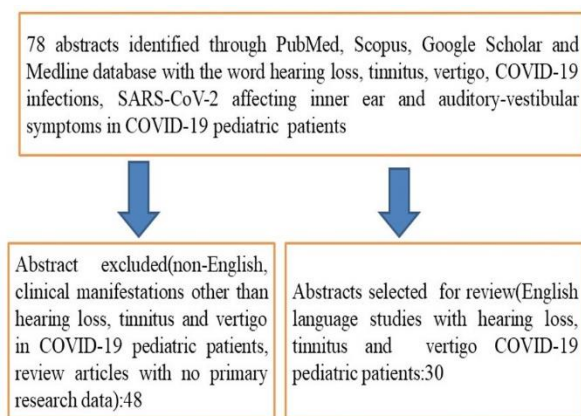


Figure 1: Flow chart showing method of literature search.

This paper focuses only on the auditory-vestibular symptoms such as hearing loss, tinnitus, and vertigo among pediatric patients infected with SARS-CoV-2. Review articles with no primary research data were also excluded. The abstracts of the published articles were identified by this search method and other articles were identified manually from the citations. This review article

reviews the epidemiology, etiopathology, clinical manifestations, investigation, and treatment of hearing loss, tinnitus, and vertigo among pediatric COVID-19 patients. This review article presents a baseline from where further prospective trials can be designed and help as a spur for further research in this important clinical aspect such as hearing loss, tinnitus, and vertigo among SARS-CoV-2 infected pediatric patients where very few studies are done in the world.

EPIDEMIOLOGY

In the last two decades, several viral epidemics like severe acute respiratory syndrome coronavirus (SARS-CoV), middle east respiratory syndrome coronavirus (MERS-CoV), and H1N1 influenza have been reported.⁹ Currently, COVID-19 infection is a highly contagious viral disease which spread to all age groups of patients and the whole world in a short period. World Health Organization (WHO) declared the COVID-19 outbreak as a global pandemic on March 11, 2020.¹⁰ There are wide ranges of symptoms in COVID-19 infection such as fever, myalgia, headache, dyspnea, loss of smell, taste dysfunction auditory-vestibular symptoms like hearing loss, tinnitus, and balance problem.^{11,12} The incidence of the audiovestibular symptoms in COVID-19 patients is still debated.¹³ Before the COVID-19 pandemic, WHO has estimated that around 360 million people with disabling hearing loss in the world which proved that more than half of the individuals with hearing impairment can be prevented by early diagnosis and treatment.¹⁴ However, the prevalence of audiovestibular symptoms in COVID-19 patients is still very low specifically in the pediatric age group. COVID-19 is more common in the adult age group than children in the early stages of the pandemic where the proportion of confirmed cases among pediatric age was relatively small. As children cannot wear masks properly or not wearing the mask and have not taken any special preventive measures, the number of pediatric patients with COVID-19 infection has increased significantly.¹⁵ The exact prevalence of audio-vestibular symptoms such as hearing loss, tinnitus, and vertigo in the current COVID-19 pandemic is not well reported. The first study by Almufarrij et al¹³ published the audio-vestibular symptoms in COVID-19 patients followed by Sanjasiaya and Maharaj et al.^{16,17} Tinnitus is the most prevalent audio-vestibular symptom (14.8%) among post-COVID-19 patients.¹³ Another study showed 7.6% of the people infected with SARS-CoV-2 experiences hearing loss, 14.8% suffered by tinnitus and 7.2% presented with vertigo.¹⁸ However, the prevalence of hearing loss, tinnitus, and vertigo among pediatric patients infected with COVID-19 infections are less studied.

ETIOPATHOLOGY

There are several viruses often associated with neuro-otological symptoms such as sensorineural hearing loss, tinnitus, and vertigo, majority of them typically damage

the inner ear hair cells; however few viruses can damage the auditory brainstem.¹⁹ Patients with COVID-19 infections are reported to be associated with neuro-otological symptoms like sensorineural hearing loss, tinnitus, and balance disorders.¹³ The neuro-invasive and neurotrophic nature of the classical features of the SARS-CoV-2.²⁰ One study revealed brain involvement by coronavirus infection and cause possible auditory-vestibular impairment.²¹ SARS-CoV-2 usually uses different receptors and pathways for its infiltration. Angiotensin-converting enzyme 2 (ACE2) is a key receptor through which the virus leads to intracellular invasion of the host.²² These receptors are commonly seen in the alveoli of the lungs. This receptor is also expressed in many cells including neurons and glial cells and result in neurological involvement.²³ The vasculopathy of the COVID-19 infection can be a direct feature of hypercoagulability.²⁴ Moreover, the relationship with COVID-19 treatment by chloroquine or hydroxychloroquine which are well-known etiology for inner ear damage and result tinnitus.²⁵ One study showed that COVID-19 infection results in deleterious effects on the outer hair cells of the cochlea.²⁶ However, the absence of the important cochlear and vestibular symptoms does not guarantee a safe healthy inner ear function. The abundant expression of ACE2 receptors in the arterial and venous endothelial cells and smooth muscles cells of the artery in different organs favors the spread of the SARS-CoV-2 throughout the body once it invades the circulation.²² By attacking the vascular system, SARS-Cov-2 can also damage the blood-brain barrier.²² Similarly the blood-labyrinthine barrier can be breached by SARS-CoV-2 and the inner invaded through infected and activated monocytes. One study on mouse cochlea showed that ACE2 expression with microarray technology and quantitative RT-PCR.²⁷ The ACE-2 expression is rich as much in the basal turn as the apical turn which corresponds to the high-frequency hearing loss in COVID-19 patients.²⁷ Damage to the auditory system often occurs by viral infections which are typically intracochlear. However, some viruses can affect the auditory brainstem as well. The viral injury to the peripheral auditory system can include damage to the organ of Corti, stria vascularis, or spiral ganglion, injury mediated by the patient's immune system against viral expressed proteins (Cytomegalovirus) and immunocompromised patient particularly children secondary to bacterial infection of the ear (human immunodeficiency virus and measles).²⁸

CLINICAL MANIFESTATIONS

The symptoms of COVID-19 infection may appear in 2 to 14 days after exposure to SARS-CoV-2.²⁹ The classical symptoms of the COVID-19 infection include fever, dry cough, fatigue, dyspnea, throat pain, headache, dizziness, myalgia, diarrhea.³⁰ There are several extrapulmonary symptoms such as the sudden onset of olfactory dysfunction and/or gustatory dysfunction.³¹ Hearing loss, tinnitus, and vertigo can affect significantly the quality of

life of children. Hearing loss is a multifaceted condition with profound medical, social and cultural manifestations. In the pediatric age group, hearing loss has an important role in communication and interaction, resulting in an invisible handicap of the affected child and also manifest psychological solitary confinement. It has been shown that the labyrinth is susceptible to ischemia and vascular damage by SARS-CoV-2 induced vasculitis which leads to hearing loss, tinnitus, and balance dysfunction.³² Acute peripheral vestibulopathy or vestibular neuritis is a viral or post-viral inflammatory disease that affects the vestibular component of the eighth cranial nerve.³³ The brainstem dysfunction due to neuroinflammatory mechanisms triggered by SARS-CoV-2 can result in sensory like auditory and vestibular dysfunctions.³⁴ In COVID-19 infection, the inflammation and edema at the nasopharynx may block the eustachian tube. The blockage of the eustachian tube results in a retracted tympanic drum with fullness in-ear and otalgia. The eustachian tube dysfunction may result in acute otitis media and cause severe otalgia and leads to hearing loss due to persistent eustachian dysfunction.³⁵ COVID-19 children may present with tinnitus. Tinnitus is defined as the perception of sound without the presence of any external or internal source. The severity of tinnitus in the COVID-19 pandemic is associated with the stress of the patient, social isolation resulting in grief, frustration, stress, and nervousness. As children are instructed to stay at home and not attending school, recreational centers, and sports or playgrounds, so increase the stress and aggravating more tinnitus.³⁶ Anxiety, depression, and irritability during pandemic further contribute to more bothersome the tinnitus

INVESTIGATIONS

Medical history taking is an important part of the diagnosis of the COVID-19 pediatric patients with hearing loss, tinnitus, and vertigo. Proper history taking must be needed in survivors of COVID-19 pediatric patients who those undertaken treatments with chloroquine or hydroxychloroquine as these may be associated with a high chance of developing auditory-vestibular symptoms.³⁷ Complete audiological assessments are needed for children with hearing loss, tinnitus, and vertigo which include tuning fork test, pure tone audiometry, and tympanometry.³⁸ Pure tone audiometry testing and tympanometry are important audiological tests usually performed in a sound-treated room. Pure tone audiometry assesses the type and degree of hearing loss whereas tympanometry evaluates the middle ear pathology and eustachian tube function. In tympanometry, type-A suggests normal middle ear, type-C indicates eustachian tube dysfunction and type-B indicates fluids in the middle ear. An otoacoustic emission (OAE) represents a type of energy produced from the outer hair cells of the cochlea. OAE may be spontaneous (SOAE), evoked by transient stimuli like clicks or tone bursts (TEOAEs). TEOAEs are not invasive tests and so can be performed easily. This test

requires lesser time, lesser cost, and higher sensitivity.³⁹ The viral injury to the outer hair cells is evidenced by the reduced amplitude of the TEOAEs and DPOAEs. Reduced amplitude in TEOAE indicates subtle deterioration of the outer hair cells of the cochlea. As SARS-CoV-2 virus has deleterious effects on the outer hair cells of the cochlea, may affect the low-frequency threshold of pure tone audiogram, and also has an impact on TEOAE and DPOAE low-frequency amplitudes. The injury to outer hair cells of the cochlea is evidenced by decreased amplitude of TEOAEs and DPOAEs. Magnetic resonance imaging (MRI) is useful to rule out any lesions in the brain and inner ear. The middle ear status and eustachian tube functions are evaluated with impedance audiometry. Type-A tympanogram indicates normal middle ear. Type-C indicates eustachian tube dysfunction and Type-B indicates fluids in the middle ear. Videonystagmography (VNG) is an important test for investigating vertigo.

TREATMENT

Currently, there is no effective treatment for COVID-19 infections and the treatment is still under investigation.⁴⁰ Presently there is no evidence of randomized clinical trials for specific treatment which improves the patient outcome in COVID-19 infection.⁴¹ As there is complex pathophysiology of the inner ear or labyrinthine manifestations, definitive treatment is yet to be developed. It is often challenging for clinicians to detect the etiology of COVID-19 infections for hearing loss, tinnitus, and vertigo and start appropriate treatment for getting maximum clinical recovery with minimal adverse effects and complications in children. Corticosteroid is an important medication for the treatment of sudden onset of neuro-otological symptoms like sensorineural hearing loss.⁴² COVID-19 pandemics forced each of us to maintain social distancing measures for limiting the spread of infection. So, adequate treatment can be provided to the children which affect the communication, auditory linguistic, and learning development. The use of face masks, social distancing, and the implementation of online classes affect children's lives. The sensorineural hearing loss in COVID-19 pediatric patients requires hearing health care such as hearing aids and hearing protection. Those with tinnitus furthermore need social support and education from the parents of the children regarding the impact of tinnitus.⁴³ Drugs like lidocaine, antidepressants, benzodiazepines, and caroverine are tried and given some benefit for managing tinnitus. Ginkgo biloba is also a popular complementary alternative medicine prescribed by many physicians for the treatment of tinnitus.⁴⁴ There are several nonpharmacological treatment options available such as tinnitus retraining therapy (TRT), masking, amplification, and limiting inducing agents and environmental factors. Masking often covers or partially covers the tinnitus with an external sound. TRT includes counseling and sound generator therapy and is more effective than masking. The use of self-guided coping methods such as exercising

outdoors, relaxation, and spending time outdoors are important strategies for the reduction of tinnitus distress during a pandemic. The most commonly used resource for coping with tinnitus during the current pandemic is contact with family members and friends. Other resources which increase coping include spending time in outdoors and in nature. Exercises, relaxation, and mindfulness are considered as useful coping during a pandemic. Aggravation of tinnitus in social isolation can be managed by online interventions such as internet-based cognitive behavioral therapy.

CONCLUSION

Pediatric patients with COVID-19 infections have a chance of hearing loss, tinnitus, and vertigo. The exact role for pathogenesis of sensorineural hearing loss and tinnitus in children infected with SARS-CoV-2 is not well defined. There is a large gap in the understanding of the etiopathogenesis, clinical manifestations like hearing loss, tinnitus, and vertigo, and human transmission of this disease. There should be continuous monitoring of the cochlear symptoms in pediatric COVID-19 patients is required to ensure a detailed understanding of this inner ear pathogenesis. Routine screening for hearing loss, tinnitus, and vertigo should be recommended among COVID-19 positive pediatric patients with help of clinical examinations, tuning fork tests, pure tone audiometry, and otoacoustic emission for early diagnosis and appropriate rehabilitation. Awareness regarding hearing loss, tinnitus, and vertigo among COVID-19 pediatric patients are usually crucial in the current pandemic. Early diagnosis of auditory-vestibular symptoms with early initiation of targeted treatment for pediatric patients helps to reduce the incidence of morbidity.

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