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Effects of COVID-19 on Hearing

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ABSTRACT

The pandemic of Coronavirus disease (COVID) had many effects on various aspects of people's health. There were multiple reports of hearing loss among COVID19 patients. The first report of hearing loss in COVID patients was presented on March 15, 2020. Sensorineural hearing loss (SNHL), tinnitus, and/or vertigo have been shown to occur during and following COVID-19 infection. The subsequent reports indicated hearing loss in some patients with COVID-19, most of which were related to sudden sensorineural hearing loss (SNHL).

KEYWORDS: COVID-19, Hearing Loss.

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INTRODUCTION

COVID-19 is an emerging viral disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which first emerged in Wuhan, China, in December 2019. According to the World Health Organization, as of May 28th, 2023, over 767 million confirmed cases and over 6.9 million deaths have been reported globally [1]. The most common symptoms that accompany COVID-19 include fever, cough, sore throat, headache, muscle pain, diarrhea, and dyspnea [2]. Nevertheless, there are various case reports referring to cranial nerve's involvement, as it seems to be a reasonable neurotropic entity [3, 4]. The vestibulocochlear system seems to be no exception, with reports concerning vestibular neuritis, disequilibrium, tinnitus and sudden hearing loss. Various theories explain the auditory system involvement following SARS CoV-2 infection [5-7]. These include immune mediated damage, hematogenous spread, ischemia theory, inflammation of auditory pathway components, Direct neural invasion of SARS-CoV-2 that affects cells through the angiotensin-converting enzyme 2 (ACE2) receptors in neurons and glial cells which is a critical step in the pathophysiology of clinical manifestations in COVID-19 [8].

COVID-19

The novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is the causative agent for this pandemic. [9]. Coronaviruses are enveloped viruses with a large, single-stranded, positive-sense RNA genome [10]. The first wave of COVID-19 started at the end of 2019 in Wuhan, China. The spread of the disease in the first wave was rapid and affected more than 200 countries around the world. By early March 2021, more than 119 million cases worldwide had been reported, with more than 2.6 million deaths. The COVID-19 disease can affect all age groups, although children and/or adolescents seem to be less susceptible to this infection [11].

The first Arab country to officially report confirmed cases was UAE but, Kuwait showed the highest cases, followed by Bahrain, UAE and Iraq in February **[12]**. Egypt was the second Arab country and the first Arab -African country to declare the presence of COVID-19 on February 14, 2020 [13]. On April 21, 2020, 3333 cases of COVID-19 were reported by the Egyptian Ministry of Health [14].

CLINICAL CHARACTERISTICS

COVID-19 infection symptoms may appear 2–14 days after exposure (based on the incubation period of COVID-19 virus). The clinical symptoms of COVID-19 patients include fever, cough, fatigue and a small population of patients had gastrointestinal infection symptoms. The elderly and people with underlying diseases are susceptible to infection and prone to serious outcomes, which may be associated with acute respiratory distress syndrome (ARDS) and cytokine storm [15]. The symptoms of SARS-CoV-2 infection can be nonspecific. The most common clinical manifestations include pyrexia, cough, fatigue/tiredness, sputum production, dyspnea, sore throat, and headache. Especially, some patients were afebrile or confirmed to have an asymptomatic infection[16]. Multiple systems are involved, including respiratory (rhinorrhea, cough, sore throat, chest pain, shortness of breath, and hemoptysis), gastrointestinal (diarrhea, nausea, and vomiting), and neurologic (confusion, headache, anosmia, and ageusia), musculoskeletal (myalgia) systems [16].

COMPLICATIONS

Complications of COVID-19 infections included ARDS, arrhythmia, shock, AKI, acute cardiac injury, liver dysfunction, vascular thrombosis, and secondary infections [17].

Most adult patients with COVID-19 have a good prognosis, but the patients aged ≥ 60 years and those with chronic underlying diseases such as respiratory disease, diabetes, obesity, and hypertensive heart disease, are at a greater risk for developing a severe or critical illness from COVID-19. The severity of the diseases is directly related to poor clinical outcomes, and the disease tends to progress more rapidly in older adults. In addition, the time interval between symptom onset and death is shorter among elderly patients (≥ 65 years). The immune status of newborns and the aged population may be poor and hence require special care [18].

AUDIOLOGICAL DISORDERS ASSOCIATED WITH COVID-19

SARS-CoV-2 infection can lead to a wide range of extrapulmonary, sensory, and neural complications, such as sudden onset olfactory and/or gustatory dysfunction, otologic symptoms, nonspecific symptoms, and long-term neurological complications [19, 20]. It has been shown that the neuroinvasion driven by SARS-CoV-2 is associated with the angiotensin-converting enzyme 2 (ACE2) mechanism, as a functional receptor for the virus [21].

This enzyme receptor is commonly found in lung type 2 alveoli. It is also expressed by many cells, including glial cells and neurons, and can cause neurological involvement through direct or indirect mechanisms [22].

Several viral infections can cause hearing loss. Hearing loss induced by these viruses can be congenital or acquired, unilateral or bilateral. Certain viral infections can directly damage inner ear structures, others can induce inflammatory responses which then cause this damage, and still others can increase susceptibility or bacterial or fungal infection, leading to hearing loss. Typically, virus-induced hearing loss is sensorineural, although conductive and mixed hearing losses can be seen following infection with certain viruses. Occasionally, recovery of hearing after these infections can occur spontaneously [23].

Hearing loss caused by viruses can be mild or severe to profound, unilateral or bilateral. Mechanisms involved in the induction of hearing loss by different viruses vary greatly, ranging from direct damage to inner ear structures, including inner ear hair cells and organ of Corti (as seen in some of the classically described causes of viral hearing loss such as measles), to induction of host immune-mediated damage [23].

HEARING LOSS IN PATIENTS WITH COVID-19

In terms of the potential type of hearing loss, case series using objective hearing assessments have predominantly reported SNHL, which may result from the direct impact of SARS-CoV-2 on the organ of Corti, stria vascularis, and/or spiral ganglion. For instance, in three case reports and one case series, unilateral sudden moderate to profound high frequency SNHL and tinnitus, with no or partial improvement following intratympanic steroid administration, were reported. Sudden SNHL is characterized as SNHL of 30 dB or greater in at least three consecutive frequencies over 72 h. This type of hearing loss is a known complication of several viral infections, which can damage the inner ear structures or accelerate inflammatory processes leading to sudden SNHL[24].

VIRAL HEARING LOSS MECHANISMS

The viral hearing loss onset mechanisms, which include upper airway infections, can cause middle ear impairment, generating a conductive hearing loss. It differs from inner ear viral invasions, which can injure the cochlea and/or auditory nerve [25].

Acute otitis media is preceded by a viral infection of the nasopharyngeal epithelium and auditory tube, and the bacterial colonization process in the nasopharynx only takes place when the virus begins inflammatory processes in this region. Therefore, it is supposed that SARS-CoV-2, as well as other viruses, can cause greater susceptibility to opportunist infections in the middle ear, possibly due to a transitory decrease in the immune response to the infection, or even cause otitis due to the primary effects of the virus itself [25].

TINNITUS IN PATIENTS WITH COVID-19

Tinnitus is defined as the sensation of sound without any external acoustic source (phantom perception of sound). It shows the prevalence of 10%–15% in the adult population and can be identified by self-report or using case history forms/self-assessment questionnaires [26]. Cochlear abnormalities produced by known risk factors (e.g., long-term noise exposure, ototoxic drugs, aging, and genetic predispositions) and concomitant neural alterations are considered as the initial source of tinnitus. Meta-analysis on six papers, it has been demonstrated the occurrence rate of 4.50% for tinnitus in patients with COVID-19 [27].

This finding may result from the impact of SARS-CoV-2 on the auditory system and/or point to the mental or emotional burden of the pandemic [28]. In three questionnaire-based studies on individuals with tinnitus (without COVID-19) to examine the pandemic mental burden on tinnitus perception, an increase in tinnitus-related handicap and distress was shown in those who perceived the situation stressful and bothersome [29].

In one of these studies using data collected by an online survey among 3,103 individuals with tinnitus from several countries, emotional consequences of the pandemic were associated with tinnitus exacerbation in 42% of participants, especially for those who were self-isolated, alone, and/or with sleep difficulties and reduced physical activity. This finding is in line with studies that demonstrate the contribution of environmental factors in modulating tinnitus [30].

DIZZINESS IN PATIENTS WITH COVID-19

Dizziness is a general term in medical diagnosis, which is traditionally classified into four categories given the patient's history, including vertigo, disequilibrium, presyncope, and light-headedness. In vertigo, the patient perceives a false sensation of whirling

or rotation originating from the vestibular system. Vertigo is mainly caused by benign paroxysmal positional vertigo, Ménière's disease, vestibular neuritis, and labyrinthitis. Disequilibrium, feeling off-balance or wobbly, is more reported in patients with Parkinson's disease and diabetic neuropathy[31].

Many medications can cause presyncope, feeling of losing consciousness, or blacking out (up to 14%). Light-headedness, vague symptoms such as feeling disconnected from the environment, is commonly associated with psychogenic or psychiatric origins such as anxiety, depression, and somatoform disorders (10%–20%). Lightheadedness and presyncope often overlap subjectively and are difficult to differentiate unless looking at duration [32].

A meta-analysis on nine papers demonstrates the occurrence rate of 12.20% for dizziness in cases with COVID-19. It has been shown that the inner ear structures are particularly susceptible to ischemia and vascular damage, which can lead to both hearing and balance dysfunction [33].

Vasculitis also is characterized as one of the clinical manifestations of COVID-19. Evidence of dizziness/vertigo in patients with COVID-19 also has been raised in case reports. For instance, in a recent case study, a young female with COVID-19 was diagnosed with acute vestibular neuritis. Vestibular neuritis or acute peripheral vestibulopathy is a viral or post-viral inflammatory disease, which involves the vestibular part of the eighth cranial nerve [34].

The disease is clinically diagnosed with vertigo and develops acutely over minutes to hours. Whereas vestibular neuritis is generally considered to be a monophasic condition, multiple cranial nerve involvement also is likely in viral inflammation. The patient presented symptoms of intractable vertigo accompanied by nausea and vomiting, possibly due to irritation/deafferentation of the emetic tracts associated with the vestibular nerve/nuclei. Overall, likewise hearing loss and tinnitus, the occurrence frequency of dizziness in this study should be interpreted with precaution given the low level of evidence, heterogeneity among studies, and the lack of using standard objective tests for dizziness assessments [35].

In a systematic review and meta-analysis on audiovisual symptoms of COVID-19, the pooled estimate of the prevalence of hearing loss, tinnitus, and rotatory vertigo was reported as 7.6%, 14.8%, and 7.2%, respectively. The estimated prevalence values obtained in our meta-analysis fall within the lower end of the CIs in this study, which may result from the difference between the two studies in inclusion/exclusion criteria [36].

POTENTIAL PATHOPHYSIOLOGY AND MECHANISMS

Brainstem Damage

The auditory and vestibular systems are two sensory systems that are mostly present in the brainstem. Auditory inputs are transferred from the auditory branch of the eighth cranial nerve to the cochlear nuclei, lateral lemniscus, inferior colliculus, and medial geniculate body before projection to the auditory cortex. The vestibular branch of the eighth cranial nerve also conveys vestibular inputs to the vestibular nuclei that in turn project to the thalamus [26].

Multiple thalamic nuclei contribute to vestibular processing, which contain multisensory neurons and process vestibular, proprioceptive, and visual signals and project to the cortex. The brainstem also controls the sleep–wake cycle and vital functions through the ascending reticular activating system and the autonomic nuclei, respectively. Thus, brainstem dysfunction resulting from neuroinflammatory mechanisms triggered by SARS-CoV-2 can produce sensory (including auditory and vestibular) and motor deficits, cranial nerve palsies, impairment of consciousness, dysautonomia, and respiratory failure [37].

Inflammatory Mechanisms

Inflammation is a natural defense mechanism against pathogens and involves many pathogenic diseases such as microbial and viral infections, as well as autoimmune and chronic diseases [38]. Oxidative stress also refers to the excessive production of reactive oxygen species (ROS) in cells and tissues, which can impair cellular molecules such as DNA, proteins, and lipids. ROS is implicated in the regulation of processes involved in cell homeostasis and functions and is normally produced in limited quantities in the body [24].

Excessive ROS and some natural or artificial chemicals can stimulate inflammatory processes and lead to the synthesis and secretion of proinflammatory cytokines (e.g., Interleukin 6 (IL-6), IL-1β) and tumor necrosis factor–alpha (TNF-α). Inflammation and oxidative stress are closely associated with pathophysiological processes and are tightly linked to one another. Thus, the activation of both processes is simultaneously found in many pathological conditions, including infection with SARS-CoV-2 [39].

Past studies also show the contribution of ROS and proinflammatory cytokines in initiating acute and chronic inflammation in SNHL and tinnitus, in which they also may play a role in damaging the inner ear in patients with COVID-19. Given that SARS-CoV-2 is linked to an intense systemic immune reaction, called a 'cytokine storm,' the overreaction of microglia also is a possible trigger for postinfectious neuroinflammation, which also may play a role in damage to the auditory glial cells [40].

Hematogenous Track

Findings of studies demonstrate that SARS-CoV-2 can attach to the hemoglobin and penetrates the erythrocyte. Therefore, it can be transported with erythrocytes or vascular endothelium to all the tissues with ACE2 in their structure, including the brain and medulla oblongata that have plenty of ACE2, as well as the auditory system. Although the expression of the ACE2 gene was shown in the mouse cochlea, the presence of SARS-CoV-2 in the human inner ear has not been reported yet [24].

Human evidence demonstrates that SARS-CoV-2 can spread throughout the body via the circulation system because of the abundant expression of ACE2 in arterial and venous endothelial cells and arterial smooth muscle cells in many organs. The virus may also damage the blood–labyrinth barrier and invade the inner ear structure by infected and activated monocytes due to attack of the vascular system [41].

The process of deoxygenation of erythrocytes by the virus also can lead to hypoxia and further damage to the inner ear [42]. Hypoxia even may occur in cases with no COVID-19 symptoms. For instance, some patients may present significantly reduced pulse oximetry reading, which is called 'silent' or 'apathetic hypoxia,' despite having no or minimal symptoms [43].

CONCLUSION

COVID-19 infection is associated with measurable alterations in auditory function, even after recovery. Post-COVID-19 patients showed significantly elevated pure-tone thresholds across almost all frequencies in both ears, indicating a pattern of predominantly high-frequency sensorineural hearing loss. These findings were supported by objective measures: patients exhibited higher ABR wave latencies (W1, W3, W5), abnormal inter-wave intervals in several comparisons, and lower otoacoustic emissions at mid–high frequencies. Therefore, these results indicate involvement of both cochlear outer hair cell function and neural transmission pathways in post-COVID-19 individuals.

Additionally, the severity of COVID-19 illness (including ICU admission, CPAP use, mechanical ventilation requirement, and the presence of smell or taste disturbances) showed an association with worse audiological outcomes across PTA, ABR, and OAE parameters. In contrast, vaccination status and WBC count demonstrated no significant relationship with any audiological measure.

Accordingly, the study highlights that auditory dysfunction is a potential post-infectious complication of COVID-19, particularly among patients who experienced severe disease, suggesting that the virus may exert both peripheral and central auditory pathway effects.

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