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Review Article

Hearing Loss in Patients with Covid-19: A Narrative Review

Shaghayegh Omidvar[1,2], PhD; Afsaneh Doosti[1,2*], PhD; Zahra Jeddi[1,2], PhD; Zeinab Moradi Ganjeh[1,3], BSc

[1]Department of Audiology, School of Rehabilitation Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Rehabilitation Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[3]Student research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

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ABSTRACT

Background: Although the most common symptoms of Covid-19 are otolaryngological symptoms, including cough, sore throat, shortness of breath, and loss of sense of smell and taste, there are reports of autological and audiological manifestations of the disease such as hearing loss, tinnitus, dizziness and, etc. The present study aims to review existing studies on the occurrence of hearing loss, its types, and possible causes in Covid-19 patients.
Results: Studies have shown that the likelihood of conductive hearing loss, sensorineural hearing loss, and sudden deafness increases following Covid-19 infection. Upper respiratory tract infection, followed by acute otitis media, can significantly cause conductive hearing loss in Covid-19 people. Studies have reported various reasons for sensorineural hearing loss and sudden deafness. It contains direct viral damage to peripheral organs, vascular disorders, and the use of ototoxic drugs.
Conclusion: Because persistent hearing loss has devastating effects on quality of life, early detection and early intervention are essential. According to the available reports, hearing loss can be one of the complications of Covid-19 infection. Still, due to the lack of sufficient evidence and heterogeneity among studies, this hypothesis has not been proven yet. Therefore, longitudinal studies on a more significant number of patients using appropriate assessment instruments are recommended.

Introduction

In late December 2019, an outbreak of an unknown disease called pneumonia of unknown cause occurred in Wuhan, Hubei Province, China [1], which infected 19 other countries by January 31, 2020. Several independent laboratories identified the causative agent of this mysterious pneumonia as the new coronavirus (nCoV) [2-4]. The World Health Organization has temporarily addressed this virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the resultant infectious disease as Coronavirus 2019 (COVID-19) [5].

*Corresponding author: Afsaneh Doosti, Department of Audiology, School of Rehabilitation Sciences, Shiraz University of Medical Sciences, Shiraz, Iran. **Tel:** +98 9177165907
Email: shomidvar.audio@gmail.com

SARS-CoV-2 is a new member of coronaviruses, a large group of highly diverse, single-stranded RNA viruses [6]. Recent research has reported that SARS-CoV-2 probably originated from bats based on the similarity of its genetic sequence with other CoVs [7]. The animal host of SARS-CoV-2 infection at the human-animal interface is still unknown [8].

Commonly reported symptoms to include fever, cough, muscle aches, pneumonia, and severe shortness of breath, while less commonly reported symptoms include headache, diarrhea, bloody sputum, runny nose, and cough with mucus [9]. Patients with mild symptoms recover after one week, while severe cases have been reported to experience progressive respiratory failure due to viral alveolar damage, which may lead to death [10].

Given the prevalence of the Covid-19 virus and the lack of awareness of its adverse effects on the auditory system, the present review studies have reported hearing problems in Covid-19 patients. Due to the widespread prevalence of coronavirus and ignorance of its complications, the present study can increase knowledge about subsequent complications of the virus on the hearing system and design appropriate preventive and rehabilitation measures to reduce these complications.

Conductive Hearing Loss (CHL) in Covid-19 Patients

Any disorder with a mechanical nature that occurs when the sound cannot reach the outer ear to the inner ear is called conductive hearing loss (CHL). Common causes of CHL include otitis media with effusion (OME), cerumen accumulation in the ear canal, and otosclerosis [11].

Review of Previous Studies

Covid-19 often first appears with otolaryngological symptoms, including cough, sore throat, shortness of breath, and loss of sense of smell and taste [12, 13]. However, various auditory and vestibular symptoms have been reported in Covid-19 patients, including hearing loss (CHL and Sensorineural hearing loss/SNHL), tinnitus, vertigo, otitis externa, and unknown ear pain [14]. One of the lesser-known possible symptoms of COVID-19 is hearing loss [15], which has been studied in several studies [16-22]. Reports of CHL and mixed hearing loss (MHL) are less common than SNHL. In these cases, otitis media (OM) and ear pain are often consistent with acute OM (AOM). Because these symptoms have been reported in a few studies, they may be present under normal living conditions and may not be directly related to Covid-19 [22].

A study was performed on eight COVID-19 patients with a mean age of 30.25 years who had no history of ear problems. In these patients, OM was reported as one of the Covid-19 symptoms. Over two months during the pandemic investigated, these individuals. Six of them had ear pain, and seven had hearing loss. Middle ear fluid was evident on otoscopic examination in six patients, three patients had the usual symptoms of AOM, and one patient had AOM with a perforated tympanic membrane. Two patients had olfactory dysfunction. Results of this study showed a patient with OM in the second and third months of spring when the OM incidence is low [20]. Besides, AOM and OME are common in young children [23], while all patients in this study were adults with no history of ear, nose, and throat (ENT) problems or ENT pathology [20].

In a case report study, a 35-year-old woman was referred to the clinic with earache and tinnitus. She had none of the symptoms of COVID-19 and no comorbidities. A hyperemic and bulged tympanic membrane was seen in her otolaryngological examination. In the lower part of her chest heard the sight of wheezing. A CHL was seen in audiometry, and a type B tympanogram was observed in the right ear. Besides, a bilateral lung involvement in chest X-rays and a positive polymerase chain reaction (PCR) were reported [24].

In another study, Gunay et al. investigated a 23-year-old woman referred to the hospital with the main complaint of earache and bilateral hearing loss. Sudden bilateral hearing loss and earache were initiated three days before referring to the emergency. The PCR was positive. On otoscopic examination of bilateral serous OM and moderate MHL on audiometry, it was reasonable. Type B was seen in the tympanometry of both ears [25].

Jacob et al. reported another case of hearing loss. A 61-year-old woman presented to the hospital with increased lethargy, headache, hearing loss (to the extent that it was difficult for her to communicate), olfactory and taste disturbances, and shortness of breath. Initially, she had symptoms of ENT. Accurate hearing assessments were not performed when she was suspected of having COVID-19. She was treated in the emergency department with a short course of intravenous fluids and was admitted for supportive care. Her PCR test was positive on the third day of admission. At that time, her hearing and health status improved. On the day of discharge, hearing loss, loss of smell, and taste completely disappeared. According to Jacob et al., the elimination of hearing loss was due to supportive care, and this hearing loss might be a result of the eustachian tube involvement [26].

Sensorineural Hearing Loss (SNHL) in Covid-19 Patients

Sensory hearing loss is due to cochlear dysfunction, and neural hearing loss is due to cochlear nerve dysfunction. SNHL is a hearing disorder caused by a combination of these dysfunctions [11].

Review of Previous Studies

Preliminary observations suggest that the coronavirus may attack the vestibular and auditory nerve pathways [27]. The virus-causing vestibular neuritis or labyrinthitis can lead to vertigo or hearing loss [28]. The hearing loss resulting from viruses can be mild or severe to profound and unilateral or bilateral [29].

Gallus et al. screened forty-eight of their hospital staff (previously infected with COVID-19) for atrial symptoms and hearing defects. The control group consisted of 28 hospital staff volunteers matched with the experimental group regarding age and sex and had no previous history of atrial auditory symptoms. The mean age of the patient group was 45 years. Before the test, all patients took patient history. It identified neurologically, completed an anamnestic questionnaire, auditory-vestibular, general symptoms, manifestation, and their characteristics. Seven patients were excluded from the audiological comparison due to pre-existing hearing loss. Of the remaining 41 patients, 4 (8.3%) reported hearing loss, and 2 (4.2%) reported tinnitus. One patient with hearing loss and one patient with tinnitus reported stable symptoms. The hearing screening included pure-tone audiometry (PTA) at frequencies of 0.25 to 8 kHz for air conduction and 0.25 to 4 kHz for the bone conduction pathways. All patients who reported temporary or persistent tinnitus and hearing loss had normal hearing threshold at the test time. It compared a total of 41 patients and 28 controls. There were no differences between patients and controls

in terms of PTA. The only frequency whose threshold was significantly higher in patients was 0.25 kHz. There was no clinically significant difference between the two groups in the mentioned frequencies. At the same time, the threshold was significantly higher in the control group in terms of the two frequencies of 2 and 4 kHz [30].

In a study, Mustafa et al. compared PTA thresholds and amplitude of transient evoked otoacoustic emission (TEOAE) between 20 patients with confirmed COVID-19. There were no viral infection symptoms in the experimental group, and 20 others with normal hearing (all with audiometry thresholds of 15 dBHL or better) as the control group. The experimental group was aged between 20 and 50 years. There was no significant difference between the two groups in three frequencies of 4000, 6000, and 8000 Hz. Comparing the TEOAE amplitude showed a substantial difference between the control and experimental groups [15].

In another study, 60 patients (n=120 ears) were investigated. 28 (n=56 ears) were admitted to the Covid-19 ward and were selected as the experimental group. The rest were assigned to the control group (no COVID-19).

All subjects aged less than 75 years. All patients were screened using a simple audiometric method. Patients with COVID-19 showed worse mean hearing thresholds from 1000 Hz to higher frequencies. COVID-19 seems to have detrimental effects on hearing, even by considering the age variable [31].

In a study aimed at assessing persistent self-reported changes in hearing and tinnitus, Munro et al. reviewed the history of 138 COVID-19 adults aged 44 to 82 years (mean age: 64 years) who were discharged from the hospital. They found changes in hearing or tinnitus since the diagnosis of COVID-1916 patients (13.2%). Comorbidities were common (for example, three people had diabetes). Eight people reported hearing loss, four of whom already had hearing loss, and eight reported tinnitus, three of whom already had hearing loss. One person with hearing loss had vertigo of probable vestibular origin. Another patient reported unilateral tinnitus (left ear) with a feeling of pressure in the ear. The mean age of these patients was 64 years [14].

In a study on 817 patients with a mean age of 38 years and confirmed COVID-19, Alessandro et al. investigated the neurological symptoms of COVID-19 patients. They reported hearing loss in 0.4% of patients with neurological symptoms [32].

Almufarrij et al. also conducted a rapid systematic review to investigate the presence and prevalence of atrial auditory symptoms resulting from coronavirus by reviewing 5 case reports and two cross-sectional studies. They concluded that there are rare reports of hearing loss, tinnitus, and vertigo in people with a positive PCR- result [21]. Nine months later, they updated their study and stated that the quality and quantity of the new research had increased compared to the initial survey in 2020. The authors included 28 case report series and 28 cross-sectional studies and stated that the prevalence of hearing loss, tinnitus, and vertigo was 7.6%, 14.8%, and 7.2%, respectively [22].

In a systematic review and meta-analysis, Jafari et al. reviewed twelve eligible articles related to COVID-19 patients to determine the occurrence rate of hearing loss. The results showed that the rate of Covid-19-related hearing loss is 3.1%. Slight to mild changes in hearing (especially in patients with severe disease conditions) may be overlooked [33]. SNHL is the commonly reported hearing loss in case series studies [27, 34] and case reports [17, 19, 35-37] using objective hearing assessments. According to Jafari et al., COVID-19 can cause hearing loss. However, they argue that the results should be interpreted cautiously [33].

Lamounier et al. published a report on a 67-year-old woman with SNHL after a Covid-19 infection. She reported hearing loss in her right ear after being admitted to the ICU ward. The patient's audiometry showed severe SNHL in the right ear and hearing loss at frequencies of 4 and 8 kHz with a 35-dB threshold in the left ear. The patient's previous audiometry showed hearing loss at frequencies of 6 and 8 kHz in the right ear with 45 dB and 30 dB thresholds, respectively, and normal hearing thresholds in the left ear. Another possibility that was hearing loss due to noise or acoustic trauma upon ICU admission should be considered. However, according to Lamounier et al., the audiometric findings obtained for this patient do not correspond to the classically expected changes for these cases [hearing loss upon ICU admission] [16].

Among patients with a complaint of hearing loss following a COVID-19 infection, profound cases of hearing loss who needed cochlear implantation were also observed. Degen et al. conducted cochlear implant surgery after evaluating the cochlear condition in a patient with COVID-19 [17]. Interestingly, Saki et al. ran a case report of two children undergoing cochlear implants (the first at eight years and two months, the second at 11 years and nine months). It emphasized the importance of COVID-19 screening in patients with hearing impairment, including cochlear implant recipients who experiences sudden or gradual impairment of speech clarity during the pandemic [38]. Evaluation of play audiometry of these two children (8 years and two months, 11 years and nine months) with active cochlear implantation showed a sudden decrease (minimum 20 dBHL) in hearing thresholds and the frequency range of 500 to 4000 Hz [38].

In a systematic review, Maharaj et al. identified 28 male and female patients between the ages of 20 and 60. All these patients had hearing loss (27 had audiometry), and 3 had vestibular symptoms (vertigo, earache, and tinnitus). They eventually concluded that ear-related disorders, particularly hearing loss, could be part of the clinical spectrum of COVID-19 and, in some cases, may even be a sign of disease onset [39].

Sudden Hearing Loss in Covid-19 Patients

Sudden sensorineural hearing loss (SSNHL) is a hearing loss of more than 30 dB at three consecutive frequencies over fewer than three days [40-43]. This hearing loss is a relatively common condition with an estimated incidence rate of 5-15 per 100,000 people per

year [44]. The etiology of SSNHL is unknown in up to 90% of cases [41]. The most significant improvement in SSNHL occurs within the first two weeks after its onset. A substantial percentage of patients may experience complete or partial recovery even without treatment [45]. Some viral infections can cause SSNHL, which can be congenital or acquired, unilateral or bilateral [43, 46]. Although both ears are similarly vulnerable to SSNHL, most patients develop unilateral hearing loss [41]. Since the outbreak of COVID-19, various case reports of SSNHL have been published [18, 19, 41, 47, 48].

Review of Studies

One retrospective study reviewed all medical records of SSNHL patients retrospectively between April 1 and September 30, 2020. These findings compared the medical records of SSNHL patients simultaneously in 2019. During the same period in 2020, 68 cases with a mean age of 51.7 years were referred to the ENT clinic for SSNHL (incidence rate of 8.5 per 100,000 people), while were identified only 41 patients with a mean age of 67.2 years. It is during the same time interval in 2019 (incidence rate of 5.2 cases per 100,000 people). Statistically, the incidence rate increased significantly in 2020 compared to the same period in 2019, which according to Fidan et al., is the main result of the increase in SSNHL during the outbreak of COVID-19 [49].

In their study, Kilic et al. evaluated five male patients (mean age: 40.8 years) with unilateral SSNHL for the Covid-19 infection using PCR. They reported a positive test result for one participant and that COVID-19-specific treatment decreased hearing loss [34].

Swain & Pani also investigated the prevalence of hearing loss in COVID-19 472 patients after discharge. They reported that 28 patients (5.98%) with a mean age of 28.2 years had hearing loss (22 had unilateral hearing loss, and 6 had bilateral hearing loss). Among 22 patients with unilateral hearing loss, 21 had SNHL, and one had mild CHL. Also, among 21 patients with SNHL, 17 had SSNHL [47].

Results showed a Covid-19-positive in an 84-year-old woman with acute vomiting with vertigo and SSNHL in the right ear, and an MRI assessment showed labyrinthitis in that ear [48].

Chern et al. also reported a case of bilateral SSNHL. An 18-year-old woman was referred to the otology clinic with a history of 7 weeks of bilateral SSNHL, bilateral intermittent aural fullness, and dizziness with nausea and vomiting. Her otomicroscopic examination was normal. Hearing tests showed moderate to severe SNHL in the right ear and moderate to profound hearing loss in the left ear. Her tympanometry was normal and serological testing was positive for COVID-19 (IgG) antibodies. MRI also showed bilateral intra-labyrinthine hemorrhage [18].

Lang et al. also reported that a 30-year-old woman initially had symptoms such as fever, cough, headache, and muscle aches and tested positive for COVID-19. After home quarantine, all her symptoms disappeared, but she developed sudden hearing loss (SHL) and tinnitus. The otoscopic examination was normal. Audiometry confirmed sudden high-frequency SNHL. So, MRI showed a normal inner ear [19].

A 52-year-old male physician was referred to the ENT clinic with confirmed COVID-19 due to SSNHL in the left ear and tinnitus. The patient had no earache, discharge, vertigo, or dizziness and had no history of head trauma or use of ototoxic drugs. On otoscopy, the external auditory canal and tympanic membrane were normal on both sides. Audiometry showed normal hearing in the right ear and severe SNHL in the left ear, and a type A tympanogram in both ears. Brain MRI showed no abnormality in the external auditory canal and brain cerebellopontine angle (CPA) [35].

Koumpa et al. also reported another case of SSNHL. A 45-year-old patient was admitted to the hospital's ICU due to COVID-19. She felt SSNHL and tinnitus in her left ear a week later. Ear examination showed no inflammation, and the tympanic membrane was intact. PTA showed that the frequencies 4, 3, 2, and 6 kHz were most affected, and their thresholds were 75, 75, 65, and 85 dB, respectively. MRI of the internal auditory canal ruled out other causes of unilateral hearing loss [36].

Karimi-Galougahi et al. investigated six young patients (age range 22 to 40 years) with acute-onset hearing loss and/or vertigo with a positive PCR result. They stated that since they had no relevant medical history and no history of receiving ototoxic drugs before referral. These otologic symptoms are likely to be directly related to COVID-19. In particular, PTA showed SNHL [27].

Discussion

Viruses usually cause SNHL, although some viral infections have also caused CHL and MHL. (As a viral cause has been suggested for otosclerosis, human immunodeficiency virus (HIV). It can also cause CHL through fungal and bacterial infections.) [50].

Co-occurrence of OM may be a Covid-19 manifestation or complication [20]. The sir conduction of the auditory canal can be affected following an increase in nasopharyngeal infection, which results in fluid middle ear effusion [24]. Since COVID-19 is primarily a respiratory disease, it can affect the function of the eustachian tube and the middle ear mucosa and cause CHL [31]. Due to many ciliated cells, glands, and goblet cells in the lower part of the eustachian tube [51], this part of the tube can be a susceptible route for Covid-19 infection in the middle ear. Negative intermediate ear pressure, in turn, predisposes the middle ear to the fluid formation and secondary bacterial or viral infections [52]; thus, the presence of OM may alert physicians of the possible Covid-19 disease [20] during the current pandemic.

Many hypotheses have been proposed about the pathophysiology of COVID-19 and the mechanisms that lead to unusual manifestations of the disease, such as SNHL [15, 53-55].

Possible causes could include a disorder in the auditory center in the temporal lobe as a result of viral pathophysiology due to ACE2, involvement of the microvasculature of the inner ear or auditory center, or a peripheral injury (to cochlear hair cells) due to

neurotropic characteristics of the virus [15, 53, 54].

The coronavirus possibly uses different receptors and pathways to facilitate its penetration. But ACE2 is a significant receptor used by the virus to attack a host intracellularly [56]. The coronavirus enters the cell through the ACE2 receptor [57] and can infect many organs, including the central nervous system, peripheral nervous system, and the auditory center in the temporal lobe [58]. The virus causes excessive release of cytokines and hearing damage [53], endotheliitis, and systemic dysfunction of the microcirculatory [59].

ACE2 overexpression in arterial and venous endothelial cells and arterial smooth muscle cells in many organs indicated. The coronavirus spreads quickly in the body as soon as it enters the bloodstream; it can also damage the blood-brain barrier by invading the vascular system. Similarly, it can be broken the labyrinth blood barrier and the inner ear structures attacked by infected and active monocytes [56]. Mechanisms of damage to the peripheral auditory system may include direct viral damage to the cortical organ, stria vascular is, or spiral ganglion. Following viral infections, secondary damage to the hearing system typically includes intracranial injury [15]. In this study, Mustafa et al. suggested the possibility of damage to the inner ear cells by the coronavirus. They believed that, although auditory sensitivity was normal in all participants, TEOAE showed slight impairment in the function of outer hair cells (OHCs). Besides, the high-frequency thresholds were significantly worse in the experimental group, which can be attributed to the destructive effects of viral infection on OHCs. However, its mechanism is still unknown. They stated that asymptomatic COVID-19 might obscure the strange impact of the disease on sensitive sensory organs such as the cochlea. It concluded that COVID-19 infection could have detrimental effects on the function of cochlear hair cells despite being asymptomatic. However, they believed that identifying the mechanism of these effects requires further research [15].

Some viruses can affect the auditory brainstem [15]. Wege et al. reported brainstem involvement in Covid-19 patients [60]. Various theories have been put forward about the mechanism of hearing loss after infection. One of these theories is the transmission of virus-infected blood to the temporal lobe in this group of patients. SARS binds to hemoglobin via the β chain and enters red blood cells, acting as a vector and infecting all tissues by binding to the ACE2. Since ACE2 has been reported to be abundant in the brain, medulla oblongata, and temporal lobe, the auditory center is affected, leading to hearing loss. SARS-CoV-2 triggers the release of cytokines upon binding to the ACE2 receptor. Thus, the auditory center is affected after attaching the released inflammatory mediators to the receptors in the temporal lobe. Besides, the coronavirus, by deoxygenated red blood cells, may have caused a lack of oxygen in the auditory center, resulting in permanent hearing loss [55].

According to Wilson et al., three mechanisms are involved in the occurrence of SSNHL following viral infections: neuritis/inflammation of the nerve due to viral involvement of the cochlear nerves, cochlear inflammation due to viral involvement of the cochlea and pre-lymphatic tissues, and the reaction of inner ear antigens to viral infections [61].

Venous disorders are another possible cause of SSNHL following COVID-19 [54]. The coronavirus can infect the veins that feed the auditory center and create a new clot in these arteries or move it by replacing a pre-existing clot. This clot can block the veins that feed the auditory center and cause ischemic damage. Impairment of auditory function in COVID-19 is not a predicted finding, but due to impaired venous structure and thrombosis sensitivity in elderly patients, hearing problems may occur through the mechanism above [53]. The elderly group, the main target population for acute COVID-19, is prone to hearing loss, especially following the ischemia theory [55]. Marcucci et al. and Yang et al. also reported increased laboratory risk factors for atherosclerosis (cholesterol, triglyceride, and homocysteine) in SSNHL patients [62, 63].

Serotonin is also a sensitive and specific marker for diagnosing SSNHL and possibly activates platelets in microcirculation. The coronavirus seems to cause endotheliitis in the auditory center of the temporal lobe, cochlear nerve, and cochlear tissues. Releasing serotonin and SARS-CoV-2 infection leads to platelet activation and causes SSNHL [54].

Besides, since this neuro-invasive virus can cause peripheral neuropathy, the coronavirus also has the potential to cause auditory neuropathy spectrum disorder (ANSD), a disorder in which OHCs have a proper function in the cochlea. Still, auditory transmission is disrupted along the ascending neural pathway. Neural auditory defects may appear over a long period. Interestingly, some neurological symptoms of SARS-CoV-2 and MERS-CoV infections, such as peripheral neuropathy, encephalitis, and Guillain-Barré syndrome (GBS), occur two to three weeks after the onset of respiratory symptoms. GBS is an acute immune-mediated disease with central and peripheral neurological manifestations that are theoretically possibly associated with auditory neuropathy [56].

Another critical issue is that many drugs are consumed to treat COVID-19. It includes chloroquine, hydroxychloroquine, azithromycin, lopinavir-ritonavir, interferon, ribavirin, and ivermectin, which have ototoxic effects. However, these effects may be reversible [64].

Conclusion

Since February 2020, the COVID-19 pandemic has affected the capacity of healthcare systems in most countries, even the most organized ones. Evaluation of hearing thresholds in positive cases of Covid-19 infection is critical, especially in patients who have recovered from it. Since persistent hearing loss has devastating effects on the quality of life, early detection and intervention are essential for preventing Covid-19-related hearing loss. Despite all the reports that reinforce the relationship between COVID-19 and hearing changes, it is still unclear whether COVID-19 affects the hearing system.

Therefore

1. Covid-19 disease should be diagnosed using

appropriate tests.
2. There must be a temporal correlation between infection and the onset of hearing loss.
3. It should seek related signs and symptoms (related to labyrinthitis or neuritis).
4. Other causes that can cause SNHL should be ruled out

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