



DOES AUDIOVESTIBULAR POST-COVID SYNDROME EXIST?

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SUMMARY – The purpose of this study was to present and analyze patients with audiovestibular post COVID-19 syndrome, and highlight the most characteristic and most common findings. We analyzed 87 patients aged between 20 and 86 years who presented to the Audiology Division between February 1, 2021 and July 1, 2021 after having been isolated due to the SARS-CoV-2 infection. Study patients presented with complaints of persistent hearing loss, tinnitus, and vertigo, lasting for more than 3 months. Study results showed that there was acute sensorineural hearing loss in 4 patients during the SARS-CoV-2 infection. None of the patients experienced complete hearing recovery after 3 months. High frequency hearing loss (at 4 kHz and 6 kHz) occurred bilaterally, and was found in 52 patients. This finding of gradual hearing loss was both the most characteristic and most common in COVID patients. Extensive damage can directly occur to inner ear structures, including hair cells, the Corti organ, and the cochlear nerve because of this viral infection. A total of 73 patients had tinnitus. 68 patients had unilateral tinnitus, and only 5 patients had bilateral tinnitus. Exacerbation of tinnitus was recorded in 12 patients and new-onset tinnitus in 61 patients. Vertigo occurred in 9 patients, all of which were new-onset. A conclusion of our research is that audiovestibular post-COVID syndrome does exist. Further research with more patients and over a longer period is needed to obtain a better and longer effect on the audiovestibular system and audiovestibular complications, as well as an insight into possible recovery.

Key words: *SARS-CoV-2 infection; Audiology; Post-COVID symptoms; Hearing loss; Vertigo*

Introduction

Coronavirus disease (COVID-19) is caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Interstitial pneumonia is one of the most common complications of SARS-CoV-2, and can lead to acute respiratory distress syndrome¹. In addition to respiratory symptoms, other organ systems may be affected, such as hematologic, cardiovascular,

renal, gastrointestinal, endocrinologic, neurologic, audiovestibular, ophthalmologic, and dermatologic systems^{2,3}. At the beginning of the pandemic, focus was placed on severe and life-threatening conditions, so attention was diverted from any audiological symptoms. Later on, audiovestibular symptoms associated with COVID-19 began to be observed, including acute or gradual hearing loss, tinnitus, and dizziness. Interestingly, even audiovestibular symptoms may occur as the only symptoms of the infection^{4,5}. It has been established that some patients continue to show systematic symptoms even after recovery from the acute infection⁶. Although it has been hypothesized and proven that COVID-19, a virus with strong tropism for angiotensin-converting enzyme 2

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(ACE2) receptors, which are present in most of the organ systems of the human body, causes lasting changes on both the molecular and macroscopic level, the exact epidemiological dynamics and clinical manifestations of post-COVID have not been sufficiently researched⁷. This post-COVID syndrome was first observed in mid-2020, and by now evidence supports that 10%-35% of cases may continue as post-COVID symptoms, while hospitalized patients may have an incidence rate of as much as 85%^{8,9}. Post-COVID syndrome is defined as continuing of symptoms or complications that occur 4 weeks after the onset of the original symptoms, and it is multi-systemic in nature. Furthermore, post-COVID syndrome is differentiated into subacute (lasting for 4-12 weeks after the acute illness) and chronic (lasting for more than 12 weeks)⁹. The most common symptoms include fatigue, shortness of breath, chest pain, mental disorders, and olfactory and gustatory dysfunction^{10,11}. Although several studies have been published on the effects of COVID-19 and audiologic symptoms, a literature search did not find any studies on the post-COVID audiologic syndrome. However, in our clinical practice, we have witnessed and collected data on patients who have had audiologic symptoms even after 3 months of the infection. We believe that initial studies can help other scientists and experts in this field, and so the purpose of this study was to present and analyze patients with audiovestibular post-COVID-19 syndrome, and highlight the most characteristic and most common findings.

Materials and Methods

We analyzed 87 patients aged between 20 and 86 years who presented to the Audiologic Division between February 1, 2021 and July 1, 2021, after first having been isolated due to the SARS-CoV-2 infection, with complaints of persistent hearing loss, tinnitus, and vertigo, persisting for more than 3 months.

There were 45 male and 42 female patients (1.07:1 male to female ratio) (Table 1). All symptoms occurred during the active phase of the disease, and were present even three months after the infection, although in a milder form. All examined patients had a milder form of COVID-19 infection. According to the history, they did not use azithromycin or any other drugs that can cause tinnitus and only 4 of them had worked in noise before. Patients were selected ac-

Table 1. Number and percentage of male and female patients with audiologic post-COVID symptoms

Sex	n (%)
Male	45 (52)
Female	42 (48)
Total	87 (100)

ording to the symptoms of hearing loss, which was sudden or gradual, unilateral or bilateral, new-onset tinnitus or exacerbation of existing tinnitus, and dizziness.

Pure-tone audiometry was performed in all patients, while vestibulometry was only performed in those with symptoms of vertigo. Pure-tone audiometry was used to determine hearing loss and tinnitus in the ear, with hearing thresholds measured at 250, 500, 1000, 2000, 3000, 4000, 6000 and 8000 Hz. In addition to pure-tone audiometry, tympanometry was performed to rule out conductive hearing loss. The visual analog scale (VAS) from 1 to 10 (mildest to most severe) was used to determine the severity of tinnitus. The tinnitus handicap inventory (THI) method was not used, as patients in this short time frame could not judge how much and in which way tinnitus affected all aspects of their life. Instead, patients could only determine the severity of tinnitus by the previously mentioned VAS method. Classic vestibular tests were used to diagnose vertigo. These included examination of spontaneous and induced nystagmus, and the caloric test. Dix-Hallpike test was used to exclude benign paroxysmal positional vertigo (BPPV). As the available literature does not suggest new methods of the treatment of tinnitus, we treated patients with tinnitus and deafness with corticosteroids and betahistine.

Given that isolation in the COVID-19 initially lasted for 10-14 days, all patients were treated at home. Those with acute and gradual hearing loss received prednisone *per os* starting at 60 mg with gradual dose reduction for a total of 14 days with betahistine, 2x24 mg and then continued with betahistine alone for several months of follow-up.

In patients with dizziness, we used high doses of corticosteroids for a short period of 3-5 days, in combination with betahistine and sedatives, then continuing with betahistine; the length of treatment

depended on patient symptoms. Vestibular rehabilitation therapy followed initial therapy.

The study was approved by the Ethics Committee of the Split University Hospital Center.

Results

Study results showed the mean age of the patient group to be 56.23 years. Hearing loss occurred in 56 patients during the SARS-CoV-2 infection. Acute unilateral hearing loss was recorded in 3 (5.4%) patients and acute bilateral hearing loss in 1 (1.8%) patient. Only high frequency hearing loss (at 4000 and 6000 Hz) occurred bilaterally, and was found in another 52 (92.9%) patients. Patients described this hearing loss as gradual. This hearing loss was most characteristic and most common in COVID patients. The average hearing loss to high frequencies was 47 dB. None of the 56 patients experienced complete hearing recovery after 3 months, and they continued with their check-ups. Tinnitus was reported in 73, including unilateral tinnitus in 68 and bilateral tinnitus in only 5 patients. Exacerbation of tinnitus was recorded in 12 patients, including unilateral exacerbation in 1 (1.4%) patient and bilateral exacerbation in 11 (15.1%) patients. New-onset unilateral tinnitus was recorded in 61 (4 (5.5%) and new-onset bilateral tinnitus in 57 (78.1%) patients. The mean VAS score used to determine the severity of tinnitus was 7.82. Vertigo occurred in 9 patients, all of which were new-onset. Vertigo due to vestibular neuronitis was found in 7 patients and vertigo from BPPV in only 2 patients (Table 2).

Discussion

Sriwijitalai and Wiwanitkit reported on the first case of sensorineural hearing loss in a SARS-CoV-2 positive patient in April 2020¹². Since then, these audiovestibular symptoms and their etiology have been further analyzed. However, it is still not known how long these symptoms can last. Our experience and research has shown that the symptoms last for at least more than 3 months after confirmed infection, and thus we can determine this disease as audiovestibular post-COVID syndrome. Our results showed that audiologic symptoms were much more common than vestibular symptoms. Gradual symptoms were much more common than sudden ones. Both ears were affected more often than one ear. Bilaterally high frequency hearing loss (at 4 kHz and 6 kHz) was found in 52 patients and it was both the most characteristic and most common finding.

While it is already established that viral infections such as herpes viruses, rubella, cytomegalovirus, measles and mumps may cause both congenital and acquired loss of hearing and balance, it may be that COVID-19 should be added to this list¹³. These listed viruses often cause sensorineural damages to hearing and balance, leading to further patient suffering by deteriorating social and psychological health^{14,15}. Three mechanisms are involved in the occurrence of sensorineural hearing loss associated with viral infections, i.e., neuritis caused by viral infection of the cochlear nerves, cochleitis due to viral infection of the cochlea and perilymphatic tissues, and stress response

Table 2. Number and percentage of patients with specific audiologic post-COVID symptoms

Disorder	Type of disorder	n (%)	Total
Hearing loss	Sudden unilateral	3 (5.4)	56
	Sudden bilateral	1 (1.8)	
	Gradual unilateral	0 (0)	
	Gradual bilateral	52 (92.9)	
Tinnitus	New-onset unilateral	57 (78.1)	73
	New-onset bilateral	4 (5.5)	
	Exacerbation unilateral	1 (1.4)	
	Exacerbation bilateral	11 (15.1)	
Vertigo	BPPV	2 (22.2)	9
	Vestibular neuronitis	7 (77.8)	

resulting from cross-reaction of the inner ear antigen with viral infection¹⁶. Animal studies on various viruses have reported inductive hearing loss either by direct effects on the inner ear structures, or by indirect effects through the cerebrospinal fluid¹⁷. Hearing and balance disorders may depend on vascular damage, as the inner ear structures are particularly sensitive to ischemia due to their characteristic terminal vasculature and large energy requirements¹⁸.

Mustafa found that SARS-CoV-2 positive patients had significantly poorer pure tone audiometry thresholds at high frequencies and transient evoked oto-acoustic emission amplitude¹⁹. This indicates a potential relationship between COVID-19 and cochlear damage. SARS-CoV-2 causes an inflammatory response and increase in cytokines such as tumor necrosis factor, interleukin 1 and interleukin 6. Direct cochlear entry and inflammation leading to cellular stress are the mechanisms that can cause permanent sensorineural hearing loss, and could occur in case of SARS-CoV-2 infection²⁰. A problem with this research was that there were no hearing thresholds prior to COVID infection available, so it could be that some of those high frequency losses had existed previously. The main limitation of the study was that we did not have the patient hearing thresholds before COVID-19 infection to compare them with hearing thresholds after the infection. It is possible that some of the patients had hearing loss prior to the infection that was similar or the same as the high frequency hearing loss recorded in the study.

Conclusion

A conclusion of our research is that audiovestibular post-COVID syndrome does exist. SARS-CoV-2 infection has shown new clinical manifestations, which may also be the only manifestations of the disease and can last for more than 3 months. Although we found a link between coronavirus and hearing loss, tinnitus and vertigo, we still do not know the prevalence because the focus is still on more severe and life-threatening conditions, so hearing and balance disorders have been neglected. At the same time, it was a short period of patient monitoring to get a definitive insight into the results of treatment. Further research with more patients and over a longer period is needed to obtain a better and long-term effect on the audiovestibular system and audiovestibular complications, as well as an insight into the possible recovery.

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Sažetak

POSTOJI LI AUDIOVESTIBULARNI POST-COVID SINDROM?

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Svrha ovog istraživanja bio je prikazati i analizirati bolesnike s audiovestibularnim post-COVID-19 sindromom te istaknuti karakteristične i najčešće nalaze. Analizirali smo 87 bolesnika u dobi od 20 do 86 godina koji su se od 1. veljače 2021. do 1. srpnja 2021. godine javili u Audiološki odjel nakon što su prvi put izolirani zbog infekcije SARS-CoV-2, s pritužbama na trajni gubitak sluha, tinitus i vrtoglavicu koji su trajali dulje od 3 mjeseca. Rezultati studije pokazuju da je došlo do akutnog gubitka sluha kod 4 bolesnika tijekom infekcije SARS-CoV-2. Niti jedan od bolesnika nije doživio potpun oporavak sluha nakon 3 mjeseca. Visokofrekventni gubitak sluha (na 4 kHz i 6 kHz) dogodio se obostrano, a pronađen je u 52 bolesnika. Ovaj nalaz gubitka sluha bio je i najkarakterističniji i najčešći u bolesnika s infekcijom COVID. Tinitus je imalo 73 bolesnika. Jednostrani tinitus imalo je 68 bolesnika, a bilateralni tinitus samo 5 bolesnika. Pogoršanje tinitusa zabilježeno je u 12 bolesnika, a novonastali tinitus u 61 bolesnika. Vrtoglavica se pojavila u 9 bolesnika, od kojih su svi bili novonastali. Zaključak našega istraživanja je da audiovestibularni post-COVID sindrom postoji. Potrebna su daljnja istraživanja s više bolesnika kroz dulje vrijeme kako bi se dobio bolji i dugotrajniji učinak na audiovestibularni sustav i audiovestibularne komplikacije, kao i uvid u mogući oporavak.

Ključne riječi: Infekcija SARS-CoV-2; Audiologija; Simptomi post-COVID; Gubitak sluha; Vrtoglavica