ÖZGÜN ARAŞTIRMA ORIGINAL RESEARCH

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HEARING LOSS IN PATIENTS WITH COVID-19

COVİD-19 HASTALARINDA İŞİTME KAYBI

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Öz

Amaç
Dünya çapında bilim insanları, COVID-19'dan iyileşen hastaları takip etmeye devam ediyorlar. Bu hastalarda gözlemlenen uzun süreli kalıcı semptomları ve kalıcı hasarları yayınlıyorlar. Bu çalışma, saf ses odyometrisi kullanılarak ölçülen saf ses ortalamaları temelinde COVID-19 hastalarında işitme kaybını değerlendirmeyi amaçladı.

Gereç ve Yöntem
Bu geriye dönük veri analizi çalışmasında, COVID-19'lu hastaneye yatırılmamış hastaların saf ses ortalamaları, COVID-19'a yakalanmadan 1 yıl önce ve sonra karşılaştırıldı. Sürekli değişkenler ortalama ± standart sapma (SD) olarak, kategorik değişkenler ise sayı (n) ve yüzde (%) olarak sunuldu. Tüm veriler normal dağılım gösterdi. Bu nedenle, ölçümler arasındaki anlamlı farklılıkları belirlemek için bir parametrik test türü olan eşleştirilmiş t testi kullanılmıştır.

Bulgular
Sol ve sağ kulakların kemik ve hava yollarında ölçülen saf ses ortalamalarına göre, COVID-19 sonrası hastaların saf ses eşik değerlerinde anlamlı bir artış bulundu (tümü için p<0,001). COVID-19 öncesi ve sonrası sol kulak hava yolunun saf ton ortalamaları yaşlı erişkinlerde (41-64 yaş) genç yetişkinlere (18-40 yaş) göre daha yüksekti (p=0.040).

Sonuç
COVID-19 her iki kulağın kemik ve hava yollarını etkileyerek farklı frekanslarda farklı düzeylerde işitme kaybına neden olmaktadır. COVID-19'un komplikasyonları üzerine yapılan araştırmalar, işitme kaybı testlerini içermeli ve olası işitme kaybını önlemek için çalışmalar yapılmalıdır.

Anahtar Kelimeler: COVID-19, İşitme kaybı, Pandemi

Abstract

Objective
Worldwide, scientists continue to follow-up on patients recovered from COVID-19 and have published the long-term persistent symptoms and permanent damage observed in various tissues. The present study aimed to evaluate hearing loss in patients with COVID-19 on the basis of pure tone averages measured using pure tone audiometry.

Material and Method
In this retrospective data analysis study, pure tone averages of non-hospitalised patients with COVID-19 were compared over 1 year before and after contracting COVID-19. Continuous variables were presented as mean ± Standard deviation (SD) and categorical variables were presented as number (n) and percentage (%). All data showed normal distribution. Therefore, paired t-test, a type of

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parametric test, was used to identify the significant differences between the measurements.

Results
The pure tone threshold values of patients increased significantly after COVID-19 (p0.001 for all) based on puretone averages measured in the bones and airways of theleftandrightears. Olderadults (41–64 yearsold) had a greater difference in puretone averages of the left ear airway before and after COVID-19 (p=0.040) than younger adults (18–40 yearsold).

Conclusion
COVID-19 affects both ears' bones and airways, causing varying degrees of hearing loss at different frequencies. Hearing loss tests should be included in COVID-19 complications research, and clinicians should be given advice on how to avoid hearing loss.

Keywords: COVID-19, Hearing loss, Pandemic

Introduction

Nearly 2 years have passed since the beginning of the COVID-19 pandemic in the Chinese province of Wuhan. In the first few months of the pandemic, studies were focussed on investigating the structure of the SARS-CoV-2 virus, coronavirus disease symptoms, diagnostic tests and prognosis. Eventually, research on sequelae and disease complications were conducted. When COVID-19 was first identified, it was reported mainly as a respiratory disease that can cause damage to the lungs after recovery, leading to decreased respiratory capacity [1]. As our knowledge on the disease increased over time, it was understood that COVID-19 was primarily a disease causing endothelial damage. Although SARS-CoV-2 virus primarily affects the respiratory tract, it also had significant neurotropic effects [2]. This is why the virus affects and permanently damages many body systems. Various complications and permanent damage in different tissues in the cardiovascular, neurological and gastrointestinal systems have been reported. Several studies have since been published on the actual mechanisms underlying these damages [3–5].

Worldwide, scientists continue to follow-up on patients recovered from COVID-19 and have published the long-term persistent symptoms and permanent damage observed in various tissues. In Turkey, the isolation of patients with COVID-19 and follow-up of clinical signs and symptoms during this period are performed by family physicians in family health centres (FHCs). Although the patients diagnosed in hospitals are quarantined at home, family physicians at FHCs make daily calls to the patients they are responsible for and enquire about their general conditions and complaints. Patients whose condition worsen and need to be hospitalised are then included in this follow-up system again. Patients with various complaints and findings, especially after recovery, first visit FHCs [6]. Among all the symptoms of COVID-19, hearing loss is a subjective symptom [7]. Initial screening of patients who present with this complaint is performed using pure tone audiometry; patient swho score below the hearing loss threshold values are referred to an otolaryngologist.

The aim of the present study was to determine the incidence and level of hearing loss in patientswith COVID-19 based on pure tone averages (PTA) measured during pure tone audiometry.

Material and Method

The FHC where this study was conducted is located in a region of Turkey predominantly populated by workers of the organised industrial zone. In Turkey, pure tone audiometry is routinely performed in organised industrial zones before recruiting workers. These tests are repeated for each worker at routine periodic inspections once a year or every 3 years, depending on the hazard group of the factory [8]. This study was conducted on workers in the same factory who were diagnosed with COVID-19 and had existing routine pure tone audiometry records of each year. None of these patients were hospitalised or admitted to the intensive care unit; all patients were treated as outpatients. The aim of the study was to determine the incidence and level of hearing loss in patients with COVID-19 based on PTA measured during pure tone audiometry.

This study was as a retrospective data analysis, and all patients with COVID-19 who visited the Reşadiye Family Health Center in the Çorlu district of Tekirdağ for treatment were included. This region is located in an organised industrial zone. The factory with the largest number of workers was selected. Regular ambient noise was measured in this factory every year. In the last 3 years, all measurements were below the legal exposure limit of (Lex8 hours) 80 decibel (dB) [8]. In

this study, PTA results from 1 year before contracting COVID-19 were compared with those within 1 year after recovering from COVID-19. The inclusion criteria for the patients were as follows:

1. History of COVID-19 infection

2. Aged18≥ and ≤65 years

3. Patients with mildcourse of Covid-19 who did not require hospitalization.

4.Underwent pure tone audiometry in the last year before contracting COVID-19 (for annual routine periodic health examinations at the workplace)

5. Underwent pure tone audiometry within 1 year of recovering from COVID-19

6. Had pure tone audiometry results and consented to their use in the study

7. No history of change in working environment for the time span of these tests and during COVID-19

8. Positive result for COVID-19 on polymerase chain reaction

9. No history of a disease associated with hearingwith in the specified period

10. Not using a hearing aid

The exclusion criteria were as follows:

1. Having a congenital or known chronic ear disease

2. History and diagnosis of ear disease in the last 3 years

3. History of chloroquine or hydroxychloroquine drug use for COVID-19 treatment

4. Not consenting to participate in the study despite meeting the inclusion criteria

5. Being hospitalised or receiving intensive care due to COVID-19

Pure Tone Audiometry

All tests were performed in the sound-isolated audiology laboratory (Çorlu State Hospital audiology laboratory). Measurements were performed using Clinical Audiometer AC40 audiometry device (Inter acoustics Company, Assens, Denmark) and TDH-39P Telephonic HB-7 headphones (Telephonics Co., Farmingdale, NY, USA). Pure tone audiometry measurement is a subjective test to determine hearing threshold by giving the patient pure tone sounds. During the pure tone audiometry, the measurement in airways was started at 1000Hz in the ear with good hearing. The test was then repeated at 2000, 4000, 8000, 500 and 250 Hz. If the patient was able to hear the first stimulus at 30 dBand 1000 Hz, the sound intensity was decreased to 25 dBand below. If not, the intensity was increased to 35 dBand further until a response was received. During the measurement, all increments and decrements were at 5 dB. The lowest sound intensity where the patient was able to hear the sound was determined with this method. This minimum sound intensity was taken as the threshold value for there levant frequency. Bone conduction measurement was also performed between 250–8000 Hz. By placing a vibrator on the mastoid process of the temporal bone, the test was performed at 1000Hz and 30dB as was done for airway measurement. Sound frequency was then increased in the same manner as that during airway measurement. Evaluations were made in exactly the same manner. To calculate PTA, hearing thresholds at 500, 1000, 2000 and 4000 Hz were summed and their arithmetic average was calculated. This value was taken as the pure tone average.

Data Collection and Analysis

Age, gender and audiometric test results of the individuals were recorded after all participants who met the inclusion criteria signed the required voluntary consent form. Pure tone audiometry results were photocopied and the original test results were returned to the participants. Test results obtained within 1 year before recovering from COVID-19 were entered in an Excel sheet separately for both ears of each participant. Then, test results obtained within 1 year after recovering from COVID-19 were entered in the sheet.

All statistical analyses were performed with IBM SPSS version 250 (SPSS Inc, Chicago, Illinois USA). Continuous variables were presented as mean ± SD while categorical variables were presented as number (n) and percentage (%). It was found that all data were normally distributed. For this reason, paired sample t-test, one of the parametric tests, was used to identify significant differences between the measurements. Independent sample t-test, one of the parametric tests, was used to determine whether there was a significant difference in PTA with respect to gender and age groups. $P<0.05$ was accepted as statistically significant in all analyses.

Results

A total of 115 people, including 47 (40.9%) women and 68 (59.1%) men, were included in the study. Of these, 33.9% (n=39) were in the 18–40-year age group and 66.1% (n=76) were in the 41–64-year age group.

There was a statistically significant difference between the pre- and post-COVID-19 PTA measurements of the right ear airway, right ear bone canal, left ear airway and left ear bone canal. A statistically significant increase was detected PTA measurements in the airway and bone canal of the right ear and the airway and bone canal of the left ear after recoveringfrom COVID-19 (p<0.001 for all) (Table 1).

There was no statistically significant difference between genders in terms of PTA measurements in both the airways and bone canals in both ears before and after recovering from COVID-19 (Table 2).

The difference in PTA in the left ear airway before and after contracting COVID-19 was higher in older adults (41–64 years old) compared to young adults (18–40 years old) (p=0.040). No significant difference was found between the left ear bone canal and the right ear airway and bone canal (Table 3).

Table 1 Comparison of pure tone average values of the right and left ear airway and bone canals pre- and post-COVID-19

Pure tone average	n	Before COVID-19 Mean ±SD	After COVID-19 Mean ±SD	p values
Right ear airway	115	26,84 ± 20,35	32,62 ± 23,30	<0.001
Right ear bone canal	115	21,70 ± 16,49	24,38 ± 17,73	<0.001
Left ear airway	115	25,97 ± 20,34	31,17 ± 22,49	<0.001
Left ear bone canal	115	21,43 ± 15,98	24,00 ± 18,46	<0.001

Paired sample t-test, p < 0.05 statistically significant
SD, standard deviation

Table 2 Comparison of the mean differences in right-left ear airway (AW) and bone canal (BC) values pre- and post-COVID-19 according to gender

Variables	Gender	n	Mean ±SD	p values
Right ear AW difference between pre- and post-COVID-19 measurement	Male	68	5,32 ± 10,95	0.589
	Female	47	6,45 ± 10,87	
Right ear BC difference between pre- and post-COVID-19 measurement	Male	68	2,25 ± 5,69	0.469
	Female	47	3,3 ± 9,75	
Left ear AW difference between pre- and post-COVID-19 measurement	Male	68	5,71 ± 9,87	0.474
	Female	47	4,47 ± 7,83	
Left ear BC difference between pre- and post-COVID-19 measurement	Male	68	2,85 ± 6,88	0.616
	Female	47	2,15 ± 8,06	

Independent sample t-test, p<0.05 indicates statistical significance
SD, standard deviation

Table 3 Comparison of the mean difference in right-left ear airway (AW) and bone canal (BC) values pre- and post-COVID-19 according to age

Variables	Age	n	Mean ±SD	p values
Right ear AW difference between pre- and post-COVID-19 measurement	18–40	39	4,10 ± 8,86	0.237
	41–64	76	6,64 ± 11,75	
Right ear BC difference between pre- and post-COVID-19 measurement	18–40	39	1,46 ± 7,63	0.220
	41–64	76	3,30 ± 7,55	
Left ear AW difference between pre- and post-COVID-19 measurement	18–40	39	3,28 ± 4,18	**0.040**
	41–64	76	6,18 ± 10,65	
Left ear BC difference between pre- and post-COVID-19 measurement	18–40	39	1,13 ± 5,78	0.134
	41–64	76	3,30 ± 7,99	

Independent sample t-test, p<0.05 indicates statistical significance
SD, standard deviation

Discussion

In the present research, hearing loss was observed in patients recovering from COVID-19 in boththerightandleftearsbased on PTA measurements in bone canals and airways of bothears. It was found that the level of hearing loss was not associated with gender and wa ssimilar between men and women. While hearing loss increased with age, it was also found that the increase in hearing loss after recovering from COVID-19 was higher in older adults compared to young adults.

In a previous study conducted on patients with COVID-19, it was shown that hearing, especially at high frequencies, was affected in a symptomatic cases where the virus load may be low. Moreover, the PTA threshold values decreased significantly. Another aspect of this study is that, in a study on 20 patients, hearing loss was significantly worse in patients with severe disease [9]. Machbooah et al. Published reports of vertigo and hearing loss they observed in patients with COVID-19. According to this previous study, although no otological findings and neurological deficits were found in the six patients that were followed up, Machbooah et al. Stated that hearing loss and vertigo developed in their cases over the course of COVID-19 infection, and hearing loss was sensorineural and unilateral [10].

In a case report, Koumpa et al. Stated that sudden onset neurosensory type hearing loss developed in a patient hospitalised due to COVID-19. In this study, the authors reported that the hearing loss was unilateral (left ear) [11]. In another study conducted with 82 patients with COVID-19, neurosensory type hearing loss was detected in only one patient and hearing loss was bilateral [12]. In a case report published in Turkey, it was reported that a patient with COVID-19 developed unilateral neurosensory hearing loss during hospitalisation [13]. Although there limited reports in the literature, we detected hearing loss even in non-hospitalised individuals with a good prognosis in the present study, unlike previous studies. This loss was shown to be bilateral and occurred in both the bone canals and airways.

Hearing loss may ocur due to Viral or vascular causes, cellular stres response or a mechanism mediated by the immune complex. Herpes virus and cytomegalo virus are the most important viruses associated with hearing loss. The most well-known Viral effect on the audiovestibular system is herpes zoster oticus, also known as Ramsey Hunt's disease, caused by varicella zoster. In this disease, mild to moderate sensorineural hearing loss at high frequencies develop due to retrocochlear involvement in addition to varying degrees of vestibular symptoms due to vestibula rnerve involvement [14,15]. SARS-CoV-2 reaches the central nervous system via two important routes. First, SARS-CoV-2 damages the capillary endothelium with the help of slow flow and pass from the systemic circulation to the cerebralcirculation. Direct passage through the cribriform wall and olfactory bulb is these condroute [16]. Many studies have shown that the critical target of SARS-CoV-2 is angiotensin-

converting enzyme-2 (ACE-2) [17]. The receptors for this enzyme are found in many organs in the body, including endothelial cells, enterocytes, kidney cells, hepatocytes, smooth muscles and nevre cells, which are also found in the central and peripheral nervous system [18]. There is abundant ACE-2 expression in the brain, medulla oblongata and temporal lobe. Therefore, it can be speculated that SARS-CoV-2 virus can easily affect the central auditory pathways in both the brain stemand the auditorycortex [19,13]. Another way SARS-CoV-2 virus reaches the nervous system is transneuronal transition to the nervous system along the olfactory epithelial axons by directly invading the olfactory receptors via inflammation in the nasal epithelium [20]. Some researchers claims that CoV-2, like other neurotropic viruses, causes Viral damage in the organ of Corti and hair cells, which is demonstrated by the effect on otoacoustic emission results. Considering all these mechanisms, hearing loss caused by COVID-19 is expected. In the present research, however, the mechanisms by which this virus causes hearing loss were not investigated. Possible causes of hearing loss were excluded, and only people with mild COVID-19 were included in the study. Bilateral hearing loss in both bone canals and airways were demonstrated in these patients. Therefore, conducting further studies on the aetiology and mechanisms of hearing loss based on disease prognosis will shed more light on the subject.

Studies examining the relationship of hearing loss with age have been mostly performed in young patients and a symptomatic cases, trying to exclude age-related hearing loss from the samples [21,22]. Even though our results showed that hearing loss increased with age, patients from similar age groups were investigated since age-related hearing loss was not the focus of the study. Considering that the prognosis of the disease is quite severe over the age of 65 years and age-related hearing loss is more common over that age, further studies investigating the relationship between age and hearing loss due to COVID-19 are warranted.

Although there are no studies investigating the relationship between COVID-19 related hearing loss and gender, it is known that hearing loss is generally more common among men, independent of COVID-19 [23]. The results of the present study indicated that the rate of hearing loss was similar in terms of gender in patients with COVID-19. There are many studies in the literature reporting that the incidence of COVID-19 is higher in men compared to women and the course of thedisease is more severe in men [24,25].

Conclusions

Given that COVID-19 is a novel disease and its complications are yet to be revealed in detail, similar studies should be conducted on larger patient groups. Were commend adding pure tone audiometry to the routine tests for COVID-19 in patient follow-up centres, regardless of diseases everity. Furthermore, patients with hearing loss should be further evaluated with advanced hearing tests.

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Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Ethical Approval
This study was approved by Tekirdağ Namık Kemal University Non-interventional Clinical Research Ethics Committee (No: 2021.172.06.02). All study participants provided informed consent in compliance with the Helsinki Declaration.

Consent to Participate and Publish
Written informed consent to participate and publish was obtained from all individual participants included in the study.

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Availability of Data and Materials
The authors undertake that all data of this article can be made accessible at any time by protecting the personal rights of the patients participating in the study.

Authors Contributions
GÖ: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft.
DT: Conceptualization; Methodology; Writing-review & editing

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