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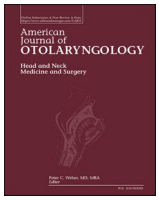

Comparison of pure tone audiometry thresholds and transient evoked otoacoustic emissions (TEOAE) of patients with and without Covid-19 pneumonia

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ABSTRACT

Objective: COVID-19 is an infectious disease caused by the new coronavirus that starts similar to an upper respiratory tract infection and causes death by causing pneumonia and vasculopathy. Many viral infections are known to cause hearing loss. In this study, pure-tone audiometry (PTA) thresholds and Transient Evoked Otoacoustic Emissions (TEOAE) results were compared across patients with COVID-19 disease and COVID-19 pneumonia, and control group patients.

Methods: The study included 240 patients in the age range of 18–50 years. The patients were divided into three groups of 80 patients as the control (no disease), COVID-19 (nonpneumonia), Covid-19 (pneumonia) groups. PTA and TEOAE tests were performed on the control group patients and the results were recorded. PTA and TEOAE tests were performed in the COVID-19 groups in the first and third months after the infection ended. Each test was performed twice; the results were recorded, and the mean of the two results was calculated.

Results: PTA results and TEOAE amplitudes in the first and third months were not significantly different between the COVID-19 non-pneumonia group and the control group ($p > 0.05$), between the COVID-19 pneumonia group and the control group ($p > 0.05$), and between the COVID-19 non-pneumonia group and the COVID-19 pneumonia group ($p > 0.05$).

Conclusions: Despite minimal impairment and minimal amplitude decreases in patients, who recovered from COVID-19, such changes were found to become restored in the third month. Furthermore, no significant changes were observed to indicate COVID-19- associated hearing loss.

1. Introduction

The new coronavirus causing COVID-19 has spread widely and resulted in the pandemic. The infection starts as an upper respiratory tract infection and may progress to death resulting from pneumonia and vasculopathy. The disease is named "coronavirus disease-2019 (COVID-19)", caused by the novel coronavirus- which is severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). The COVID-19 outbreak started in the Hubei province of China in 2019 and spread to Europe by 2020. The novel coronavirus, (SARS-CoV-2) has caused 50 million cases and approximately 1,250,000 deaths globally as of November 2020 [1]. SARS-CoV-2 starts to multiply in the nasopharynx and reaches the lungs via the oropharynx in a short time, causing acute respiratory distress syndrome. Mortality is particularly high in geriatric patients because of acute respiratory failure, cytokine storm, and vasculopathy [2].

Disease symptoms majorly include fever, cough, joint pain, and anorexia [3]. In otolaryngological practice, the loss of taste and smell, rhinorrhea, vertigo, and nasal congestions are most commonly observed as symptoms associated with COVID-19 [4]. Additionally, rarer complications of COVID-19 recently have been reported, including; hearing loss and facial paralysis [5,6]. Optimal treatment of the disease has not yet been established. The efficacy of hydroxychloroquine, favipiravir, remdesivir, ritonavir, ivermectin, convalescent plasma therapy, stem cell therapy, monoclonal antibodies, and interferons are still studied in regards to the treatment of COVID-19. Furthermore, vaccine studies are ongoing [7].

Many viral infections; including congenital infections [Cytomegalovirus (CMV) infections, Herpes Simplex Virus (HSV) infections, etc.] and acquired infections (influenza, etc.), can cause hearing loss due to the resulting injury in hair cells or neurogenic pathways in the inner ear.

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Virus-related hearing losses are mostly sensorineural, although they can also be of the conductive or mixed type. Such virus-related hearing losses can occur unilaterally or bilaterally, and can be reversible or irreversible [8,9]. The most common viral etiology of hearing loss is the measles virus causing otosclerosis. Otosclerosis can result in conductive, sensorineural, or mixed-type hearing loss [10]. Hearing loss may also be a result of bacterial and fungal infections developing secondary to immunodeficiency caused by HIV infection. Sensorineural hearing losses after influenza A (H1N1) infection, too, have been described in the literature [11].

It has recently been found out that COVID-19 causes many ear diseases and associated hearing losses [12]. In addition to the conductive hearing loss due to middle ear infections [13], several studies in the literature have reported that COVID-19 leads to high-frequency hearing loss and sudden sensorineural hearing loss (SSNHL) [14]. Studies regarding the hearing profiles of asymptomatic COVID-19 patients with positive polymerase chain reaction (PCR) test results are available but there are no studies concerning long-term hearing profiles of patients with COVID-19 pneumonia [15]. Furthermore, the effect of COVID-19 on hearing has not yet been established.

Our primary aim with this study is to measure the relationship between the disease severity determined by the absence or presence of pneumonia and the degree of cochlear damage in COVID-19 patients through evaluating the pure tone audiometry (PTA) and otoacoustic emission (OAE) results. The secondary aim of the study is to find out whether cochlear damage occurs due to COVID-19 and to determine the onset of hearing loss associated with the disease and the duration until the restoration of hearing.

2. Materials and methods

The study was carried out in our center between May 2020 and November 2020. A total of 240 patients; within the age range of 18–50 years, were included in the study and divided into three groups of 80 patients as the control group, non-pneumonia COVID-19 group, and COVID-19 with pneumonia group. The control group patients were selected from a population of patients who applied to the otorhinolaryngology outpatient clinic for any reason and did not have a previously known ear disease (middle ear infection, chronic otitis, Meniere's disease, etc.). PTA and Transient Evoked Otoacoustic Emissions (TEOAE) tests were performed on the patients of the control group to confirm that their hearing was normal. The diagnosis of COVID-19 was confirmed by a positive reverse transcriptase-polymerase chain reaction (RT-PCR) test result. Patients with confirmed COVID-19 but no pneumonia findings on posteroanterior (PA) lung X-rays or thoracic CT images were included in the non-pneumonia COVID-19 group. The COVID-19 pneumonia group consisted of COVID-19 patients whose diagnoses were confirmed by RT-PCR test results and who were diagnosed with pneumonia, based on findings on PA lung X-rays or thoracic CT images. Patients, included in the non-pneumonia COVID-19 group and the COVID-19 pneumonia group were randomly selected out of eligible patients that were referred to our clinic from the COVID-19 outpatient clinic.

In this study, patients with the criteria of “sudden sensorineural hearing loss” were excluded. (A commonly used criterion to qualify for this diagnosis is a sensorineural hearing loss of greater than 30 dB over 3 contiguous pure-tone frequencies occurring within 3 days' period) Patients who did not meet this criterion were used.

PTA and TEOAE tests were performed on the COVID-19 groups during the 1st and 3rd months of recovery from the infection. With these tests performed at these time points, we aimed to detect early and late cochlear damage, which could potentially occur due to COVID-19. These tests were performed for both ears during each specified time points. The averages of the two results for each time points were included in the data for statistical analysis. PTA measurements were performed using an Interacoustic AD-629® device (Denmark). TEOAE measurements were performed using a Maico-Easyscreen® device (Berlin, Germany). The frequency range of 250-8000 Hz was used in the tests. The mean frequency amplitudes were recorded. In the PTA test, bone conduction thresholds were measured in the range of 250–8000 Hz and airway thresholds were measured in the range of 250–8000 Hz. All patients underwent tympanometry. Patients with type-B and type-C tympanograms were excluded from the study. Tympanometry was performed using an Interacoustic AT235® device (Denmark) and 1000-Hz frequency.

Approvals to conduct the study were obtained from the Republic of Turkey Ministry of Health Scientific Research Committee (06.07.2020) and the Clinical Research Ethics Committee of Afyonkarahisar Health Sciences University (11.09.2020–2020/11). Informed consent was obtained from all patients.

2.1. Statistical analysis

All values were calculated as mean ± standard deviation. The SPSS 22.0 (IBM SPSS Statistics, Chicago, USA) software package was used for data analysis. A p-value of <0.05 was considered statistically significant. One-Way ANOVA was used to compare the three groups.

3. Results

The mean age was 49.28 ± 18.35 years in the control group, 51.53 ± 12.76 years in the COVID-19 non-pneumonia group, and 50.53 ± 10.26 years in the COVID-19 pneumonia group. Gender distribution was 21/19 (M/F) in the control group, 20/20 (M/F) in the COVID-19 non-pneumonia group, and 19/21 (M/F) in the COVID-19 pneumonia group.

The PTA results in the first month were not significantly different between the COVID-19 non-pneumonia group and the control group ($p = 0.079$), between the COVID-19 pneumonia group and the control group ($p = 0.082$), and between the COVID-19 non-pneumonia group and the COVID-19 pneumonia group ($p = 0.078$) (Fig. 1).

There was no significant difference in the PTA results of the third month between the COVID-19 non-pneumonia group and the control group ($p = 0.074$), between the COVID-19 pneumonia group and the control group ($p = 0.086$), and between the COVID-19 non-pneumonia group and the COVID-19 pneumonia group ($p = 0.063$) (Fig. 2).

There was no significant difference in the TEOAE amplitudes in the first month between the COVID-19 non-pneumonia group and the control group ($p = 0.067$), between the COVID-19 pneumonia group and the control group ($p = 0.071$), and between the COVID-19 non-pneumonia group and the COVID-19 pneumonia group ($p = 0.076$) (Fig. 3).

There was no significant difference in the TEOAE amplitudes in the third month between the COVID-19 non-pneumonia group and the control group ($p = 0.072$), between the COVID-19 pneumonia group and the control group ($p = 0.069$), and between the COVID-19 non-

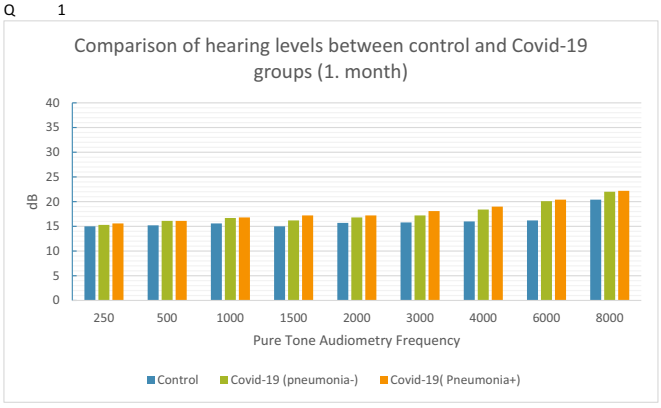

Fig. 1. Comparison of hearing levels between control and Covid-19 groups (1. Month).

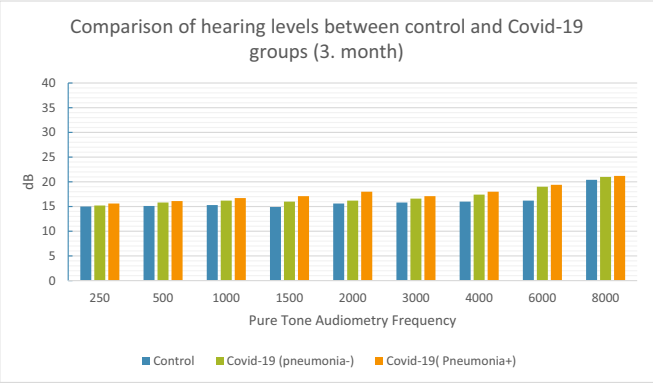

Fig. 2. Comparison of hearing levels between control and Covid-19 groups (3. Month).

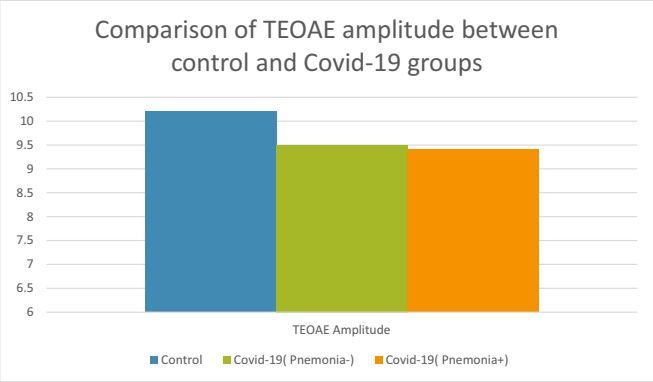

Fig. 3. Comparison of TEOAE amplitude between control and Covid-19 groups (1. Month).

pneumonia group and the COVID-19 pneumonia group ($p = 0.083$) (Fig. 3).

The intragroup comparisons of the third-month TEOAE amplitudes did not reveal any significant differences ($p = 0.086$) (Fig. 4).

These results showed that minimal impairment and minimal reductions in the amplitude occurred in high frequencies in patients, who recovered from COVID-19. However, such changes were found to be restored in the third month. No significant changes were observed to indicate a COVID-19-associated hearing loss.

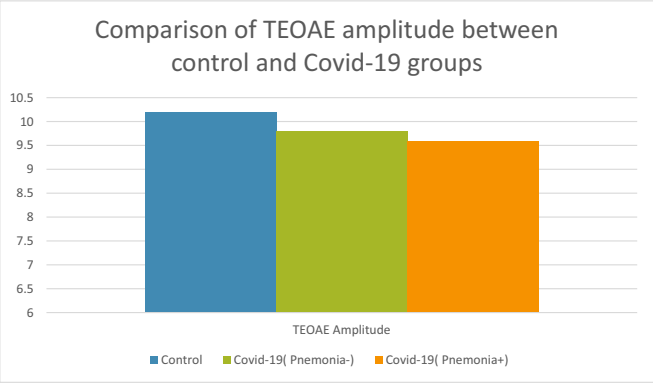

Fig. 4. Comparison of TEOAE amplitude between control and Covid-19 groups (3. Month).

4. Discussion

Otologic complications of COVID-19 have recently been reported. Furthermore, rare complications such as conductive hearing loss, SSNHL, and facial paralysis due to middle ear infections have been reported [4,14].

Viral infections lead to hearing loss possibly by causing damage to the inner ear. The most well-known virus associated with hearing loss is the measles virus, which causes sensorineural hearing loss resulting from cochlear otosclerosis. Herpesviruses and cytomegalovirus have also been found to cause sensorineural hearing loss due to their damaging effects on the inner ear. These viruses cause hearing loss through direct damage to the spiral ganglion, the organ of Corti, and stria vascularis, or they cause damage via proteins synthesized against such structures. Additionally, these viruses can cause further damage by leading to immunodeficiency resulting in secondary bacterial infections [8,10].

It can be predicted that the novel coronavirus disease too can cause hearing loss similar to the effects of the aforementioned viruses. Indeed, some recent studies have reported that coronavirus can cause hearing loss. After the report of the first case in the world in April 2020 [15], many sensorineural hearing loss cases associated with COVID-19 were reported [16]. In a study about the pathophysiology of COVID-19-associated hearing loss, it has been reported that there are ACE-2 receptors in the temporal lobe and SARS-CoV-2 binds to these receptors unfavorably acting on the auditory center [17].

The first study about this subject matter in the literature is similar to our study and that study has reported that the virus causes sensorineural hearing loss at high frequencies as detected by TEOAE and PTA. The hearing loss was associated with cochlear damage potentially occurring in asymptomatic COVID-19 patients. However; in that study, the measurements were performed only in the first month and only in asymptomatic individuals, obtaining controversial results [13]. Another matter of discussion is that the cause of the anticipated hearing loss in coronavirus disease may be the drugs used in the treatment. Among such drugs, especially, hydroxychloroquine has long been known to be ototoxic. Therefore, the use of hydroxychloroquine may explain the high-frequency hearing loss observed in COVID-19 patients [18]. Similar results were obtained in another study, showing that coronavirus damaged outer hair cells of the cochlea [19]. It was found in our study that, although mild distortion occurred at high frequencies in both TEOAE and PTA, such changes were not significant. Furthermore, such mild distortions were found to become close to normal in the control tests performed in the third month. The severity of hearing loss did not increase as the disease progressed to pneumonia. Therefore; based on our study results, it cannot be argued that the novel coronavirus causes significant hearing loss.

Although our study is valuable in terms of determining the absence of hearing loss in COVID-19 patients, the results of the study are limited due to the absence of long-term results and the small number of individuals participating in the study. Future studies are needed to be conducted in more than one center on a larger patient population without the use of ototoxic drugs.

5. Conclusion

The novel coronavirus disease causes many otological symptoms. The most likely of such symptoms is sensorineural hearing loss. Although it was observed that the disease caused mild hearing loss at high frequencies in our study, it was determined that the observed changes were not statistically significant and that they were transient. Furthermore, it was determined that progressed disease did not contribute to hearing loss. However, further studies are needed to evaluate the matter of hearing in COVID-19.

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Ethics

Ethics committee approval was received from Afyonkarahisar Healthy Science University Clinical Research Ethic Committee. (11.09.2020–2020/11).

Consent

Consent was obtained from of the patients.

Info

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Declaration of competing interest

No conflict of interest was declared by the authors.

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