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ORIGINAL ARTICLE

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Hearing profile of recovered severe acute respiratory syndrome Coronavirus-2 (SARS-COV2) patients

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Abstract

Background Coronaviruses are large, encapsulated RNA viruses that can infect both humans and animals and cause minor respiratory illnesses. In December 2019, numerous cases of pneumonia of unknown origin were reported in Wuhan, China. Coronavirus Disease 2019 (COVID-19), the cause of these cases, was discovered on January 6, 2020. The new coronavirus was declared an epidemic by the WHO on March, 2020. Several studies on COVID-19 have found that auditory complaints and hearing impairment can be detected using various tests.

Objectives Pure tone audiometry (PTA) and transient evoked otoacoustic emissions (TEOAEs) were used to assess hearing in recovered SARS-CoV-2 patients. Also, to compare the presence of patient's auditory complaints with the test findings.

Methods A case- control study was conducted, with each case and control group consisting of 58 people who were age and sex matched and ranged in age from 18 to 50 years. PTA, Extended PTA and, TEOAEs were used to evaluate hearing in both groups.

Results PTA revealed a statistically significant difference in right ear thresholds at 250 Hz, 500 Hz, 4 kHz, and 8 kHz and left ear thresholds at 250 Hz, 4 kHz, 8 kHz, and 12.5 kHz between patients and controls. Additionally, a statistically significant difference in TEOAEs' overall reproducibility and amplitude between patients and controls was discovered. Affection for PTA and TEOAEs were related to the patient's complaints of hearing loss and tinnitus, respectively.

Conclusions Whether a patient is symptomatic or not, COVID-19 may have a negative impact on their hearing.

Keywords Coronavirus 2019 (COVID-19), Severe acute respiratory syndrome coronavirus-2 (SARS-COV-2), Hearing loss, Tinnitus, Pure Tone Audiometry (PTA), Transient Evoked Otoacoustic Emissions (TEOAEs)

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Background

Coronaviruses are large encapsulated RNA viruses that can infect both humans and animals and cause a mild respiratory illness [1]. Along with the newly discovered strain, two previous outbreaks of the severe acute respiratory syndrome coronavirus (SARS-COV) and Middle East respiratory syndrome coronavirus (MERS-COV) were also connected to fatal illness [2]. In December 2019, numerous cases of pneumonia of unknown origin were reported in Wuhan, China. The culprit was determined to be a brand-new coronavirus known as severe acute respiratory syndrome corona-virus 2 (SARS-COV2) [3]. The novel coronavirus outbreak was designated Coronavirus Disease 2019 (COVID-19) by the WHO in March 2020 as a global health emergency of international concern [4].

COVID-19 symptoms are essentially respiratory, cardiologic, and gastrointestinal. Olfactory, gustatory and hearing symptoms are added to the rundown. Auditory symptoms can be caused by a variety of factors, including direct viral injury, brainstem affection, neuropathy, cytokine storm, hypoxia, and ischemia [5]. Over time, reports moved away from the potentially fatal effects of the pandemic and toward more long-term effects including hearing and balance dysfunction. Hearing loss has been documented in COVID-19 patients. Patients with COVID-19 were less likely to experience tinnitus and vertigo [6]. Multiple reports of hearing loss, tinnitus, and vertigo in patients with a spectrum of COVID-19 disease severity were mentioned [7]. Auditory thresholds starting from 1 kHz through higher frequencies were worse in COVID-19 patients when compared to controls [8]. Another study reported that patients' group significantly had worse high-frequency pure-tune audiometry (PTA) thresholds as well as the transient evoked Otoacoustic emissions (TEOAEs) amplitude in asymptomatic patients [9].

Otoacoustic emissions (OAEs) are the result of the cochlea's audio frequency signal travelling through the tympanic membrane and the middle ear's ossicular chain and entering the ear canal. They are driven by the mechanical force that the outer hair cells (OHCs) actively produce. OAEs may be induced by a broadband stimulus (a "click") or can even appear spontaneously. Due to the fact that OAEs are connected to operating OHCs, their existence is a valid predictor of the structural integrity of the cochlea, while their absence may signify a lesion. Furthermore, a preclinical cochlear lesion may also be picked up by recording OAEs because up to 30% of OHCs may suffer damage before any audiometric evidence becomes noticeable in the pure-tone audiometry [10].

Audiological symptoms are becoming more common during the pandemic, though COVID-19-associated hearing loss is still being debated, and there have been few research studies to assess the auditory system using hearing tests. We wanted to know if COVID-19 is associated with hearing loss or not by using subjective test evaluating the auditory system and objective test evaluating cochlear functions.

Aim

This study was conducted to assess hearing thresholds using both conventional pure tone audiometry (PTA) and extended high frequency audiometry. TEOAEs were used to evaluate outer hair cell function in recovered SARS-COV2 patients. A comparison of the test results with the patient's auditory complaints was also desired.

Methods

The current study is a case–control study. The study was carried out at the Audio-Vestibular Clinic, ENT Department, during the period from July 2021 to June 2022. The Research Ethical Committee and Otolaryngology Department of University' Faculty of Medicine gave their approval to the study (code:MS-251- 2021). All subjects provided their informed consent prior to participating in the study.

There were 116 participants in the study, split into two groups as follows:

- A study group (cases), which consisted of 58 post-recovery adults whose nasopharyngeal RT-PCR swabs were positive for SARS-CoV-2. The tests were done at least one month after resolution of symptoms. Their ages ranged from 18 to 50 years, with a mean age of 34.22 ± 9.31 years, and there were 28 males and 30 females.
- A control group of 58 healthy persons with a mean age of 32.28 ± 7.84 years and a range of ages from 18 to 48 years, distributed as 27 males and 31 females who were well matched in terms of age and sex to the patients and who had no prior history of auditory complaints. Controls were gathered from either relatives of the patients or colleague doctors or nurses. COVID-19 is excluded by the absence of COVID-19 symptoms (fever, cough, dyspnea, myalgia, headache, anosmia, ageusia, etc.) and no history of a previous positive PCR test.

The following conditions were excluded from the study: age over 50; any disease or condition affecting hearing, including neurotologic, vascular, autoimmune, or metabolic disorders; prior ear surgery; family hearing loss; use of ototoxic drugs; chronic noise exposure; head trauma.

Methodology

Equipment

1. Sound treated room, Amplisilence model E.
2. Pure tone audiometer: Itera II, Madsen Otometrics (GN Otometrics, Denmark) calibrated according to International Standard Organization (ISO) standards. TDH-39 head phones and radio-ear B-71 bone vibrator were used.
3. TEOAEs: Neuro-Audio (Neurosoft Ltd, Russia. Ivanovo).

Each participant was subjected to the following:

1) Taking a thorough medical history that includes: personal history, such as age, gender, occupation, and special habits of medical importance; present history: alternation in sense of hearing, tinnitus, sense of occlusion, earache, or any other otologic symptoms together with a thorough evaluation of the hearing loss and any accompanying symptoms; Past history of noise exposure, ototoxic medication use, trauma to the head or ears, and local or systemic disorders affecting hearing to help exclude any other cause of hearing affection other than the COVID-19 infection; family history of hearing loss or consanguinity. Covid-19 infection history: symptoms of the disease (fever, cough, dyspnea, myalgia, headache, anosmia, ageusia, etc.), duration of the symptoms, duration post-recovery, and period of infection (wave).
2) Otologic examination, including otoscopy and tuning fork tests.
3) Basic audiological evaluation including:
   - Air conduction thresholds in the frequency range of 250–8000 Hz, at octave frequencies. Extended high frequency audiometry was performed at 12.5 kHz.
   - Bone conduction thresholds in the frequency range of 500–4000 Hz, at octave frequencies.

Normal hearing was defined as ears with a PTA average of up to 25 dBHL (250–8000 Hz). Based on the pure tone average, the degree of hearing loss was computed as follows: Mild, 26–40 dBHL; Moderate, 41–55 dB; Moderately Severe, 56–70 dBHL; Severe, 71–90 dBHL; and Profound, more than 90 dB [11].

4) Transient Evoked Otoacoustic Emissions (TEOAEs):

   A 100 µs click stimulus at 80 dB SPL, band-pass filtered from 0.3 to 5 KHz, and a rate of 66 Hz were used to measure TEOAEs. Noise levels were under 50 dB SPL. To evaluate the reaction, 1,000 averages were gathered. Two buffers (A and B) were used to record responses, and each was averaged individually. The overall echo level was displayed in dB SPL by averaging the two waveforms' amplitudes. The software calculated the TEOAE's amplitude in five bandwidths (1, 2, 3, 4, and 5 KHz). For each frequency band, the signal-to-noise ratio (SNR) was calculated.

   The correlation between the signals from the two buffers was another way to check the repeatability of the TEOAE. All responses were saved for later examination. According to Kemp [12], TEOAE are regarded as present if the overall repeatability is 50%. The pass criteria were response SNR $\geq$ 4 dB, reproducibility in at least three frequencies $\geq$ 70%.

Statistical methods

The statistical package for the social sciences (SPSS) version 26 was used to code and enter the data (IBM Corp., Armonk, NY, USA). For quantitative data, the mean, SD, median, minimum, and maximum were used; for categorical data, frequency (count) and relative frequency (%) were used. The non-parametric Mann–Whitney test was used to compare quantitative variables. An analysis using the Chi square (2) test was done to compare categorical data. When the anticipated frequency was less than 5, the Fisher 's exact test was employed instead. Statistical significance was defined as a *P* value less than 0.05.

Results

The current study had two groups. The study group (cases) included 58 patients ranging in age from 18 to 50 years old, with a mean age of 34.22 ± 9.31 years. They were 28 males and 30 females. The control group included 58 healthy adults ranging in age from 18 to 48 years, with a mean age of 32.28 ± 7.84 years, distributed as 27 males and 31 females, well matched to the study group regarding age (*p* value = 0.359) and gender (*p* value = 0.852). In this study, the mean time since full recovery ranged from 4 to 44 weeks, with a mean of 18.59 ± 13.34 weeks.

Audiological symptoms among cases were distributed as follows; fourteen patients (24.1%) noticed changes in hearing sensation, eleven patients complained of tinnitus bilaterally (18.9%), three patients (5.17%) complained of right tinnitus and 2 patients (3.44%) complained of left tinnitus.

Audiometry

On PTA, all controls had bilaterally normal hearing thresholds. For recovered SARS-CoV-2 patients, PTA showed affection (threshold more than 25 dB) in 21 patients (36.2%) in the right ear and in 23 patients

(39.7%) in the left ear. Conventional PTA showed 21 of 58 patients (36.2%) had sensorineural hearing loss, which was bilateral in 13 out of 21 patients (61.9%) patients and unilateral in 8 (38.1%) patients (6 left and 2 right). The cases showed a statistical significant worse PTA thresholds in the right ear at 250 Hz, 500 Hz, 4 KHZ, and 8 kHz and in left ear thresholds at 250 Hz, 4 KHZ, 8 kHz, 12.5 kHz than controls (Tables 1, 2 and Figs. 1, 2).

TEOAEs findings

All control had bilaterally normal TEOAEs. For cases TEOAEs showed abnormal results in 45/ 58 patients (77.59%) (patients hadn't achieved the pass criteria). Out of the 45 patients presented with abnormal TEOAEs, thirty one patients had abnormal TEOAEs bilaterally (68.9%) and 14 unilateral (31.1%), which further classified into 5 patients in the right ear and 9 patients in the left ear.

TEOAEs showed affection in 36 patients (62.1%) in right ear and 40 patients (69%) in left ear. The most affected frequency bands were: 5 kHz, 4 and 5 kHz, all frequencies, 1 kHz, 1 and 5 kHz in the right ear. 5 kHz, 4 and 5 kHz, 1 and 5 kHz, all frequencies and 1 kHz in the left ear respectively. The cases showed a statistical significant worse TEOAEs overall reproducibility and amplitude Signal to Noise Ratio (SNR) at 1, 3, 4 and 5 kHz frequency bands in right ear than control (Table 3 and Fig. 3). The left ear showed a statistical significant worse TEOAEs overall reproducibility and amplitude (SNR) at all frequency bands than control (Table 4 and Fig. 4).

PTA and TEOAEs findings in comparison to hearing loss

A statistically significant higher PTA thresholds in both ears were found when the patient's complaint of hearing loss was compared to PTA thresholds. As eleven (78.6%) of fourteen patients with hearing loss had elevated PTA thresholds in the right ear, and twelve (85.7%) of the same fourteen patients with hearing loss had elevated PTA thresholds in the left ear. There was no statistically significant relationship between patient complaints of hearing loss and TEOAEs affection in both ears (Tables 5 and 6).

Table 1 Comparison of the right ear's PTA thresholds across frequencies in patients and controls

	Cases					Controls					*P* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Right PTA 250 Hz	18.53	6.69	17.5	10	35	12.76	3.53	10	5	20	**< 0.001**
Right PTA 500 Hz	16.29	5.89	15	10	30	12.5	3.78	15	5	20	**0.001**
Right PTA 1 kHz	13.71	4.92	15	5	20	12.93	4.09	15	5	20	0.358
Right PTA 2 kHz	12.67	5.94	10	5	40	11.72	4.14	10	5	20	0.572
Right PTA 4 kHz	16.29	8.2	15	0	40	12.5	5.15	10	5	25	**0.01**
Right PTA 8 kHz	17.76	8.12	17.5	0	45	13.88	5.85	15	5	25	**0.005**
Right PTA 12.5 kHz	26.64	17.1	20	5	70	20.78	8.73	20	5	40	0.315

Table 2 Comparison of the left ear's PTA thresholds across frequencies in patients and controls

	Cases					Controls					*P* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Left PTA 250 Hz	18.19	6.80	15.00	10.00	35.00	13.02	3.50	15.00	5.00	20.00	**< 0.001**
Left PTA 500 Hz	16.12	7.01	15.00	5.00	35.00	13.10	3.73	15.00	5.00	20.00	0.060
Left PTA 1 kHz	13.97	5.28	15.00	5.00	25.00	12.16	4.79	15.00	5.00	20.00	0.075
Left PTA 2 kHz	13.19	6.73	10.00	0.00	40.00	11.64	4.63	10.00	0.00	20.00	0.393
Left PTA 4 kHz	17.24	8.33	15.00	5.00	40.00	12.24	4.60	10.00	5.00	20.00	**0.001**
Left PTA 8 kHz	21.03	10.87	20.00	5.00	45.00	13.53	5.54	15.00	0.00	25.00	**< 0.001**
Left PTA 12.5 kHz	31.12	18.64	27.50	5.00	70.00	21.55	9.23	22.50	5.00	40.00	**0.015**

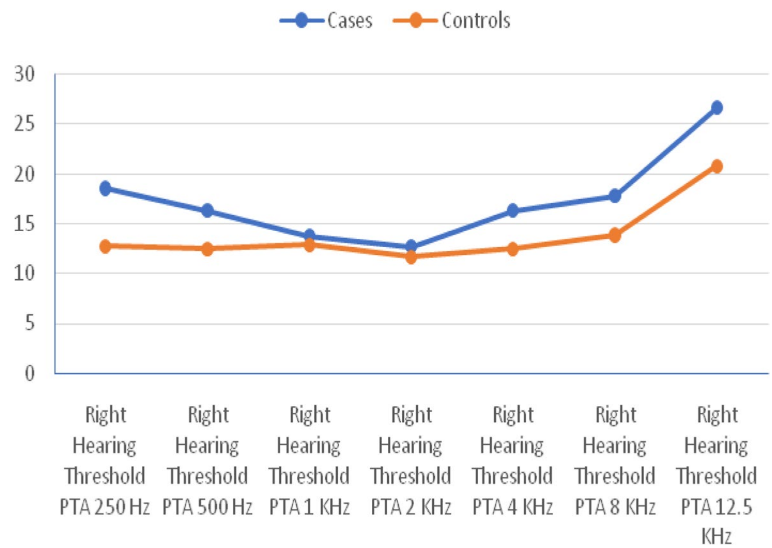

Fig. 1 Comparison between cases and controls regarding right PTA thresholds across frequencies

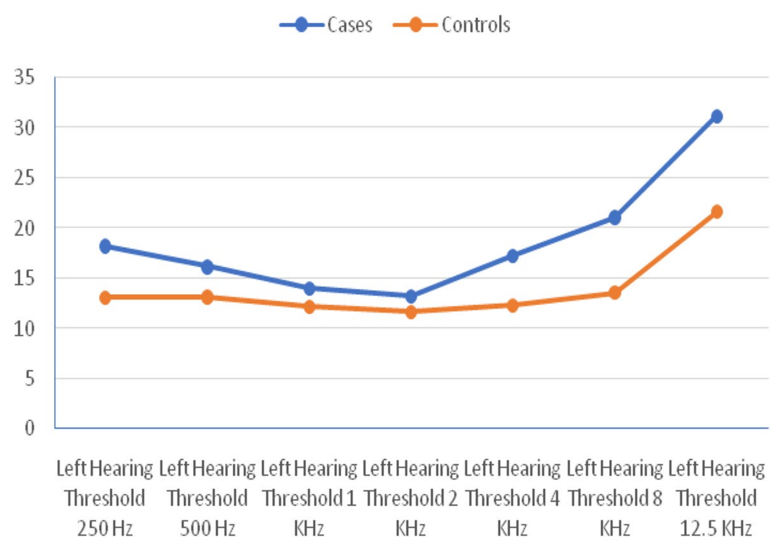

Fig. 2 Comparison between cases and controls regarding left PTA thresholds across frequencies

Table 3 Comparison of TEOAEs' overall reproducibility and amplitude (SNR) across all frequency bands in the right ear between patients and controls

	Cases					Controls					*P* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Rt Reproducibility (%)	80.43	20.02	88.65	8.10	99.40	90.12	9.16	92.45	64.50	99.60	**0.002**
Rt TEOAE 1 kHz SNR	8.31	6.82	8.00	-10.00	24.00	12.64	5.41	12.00	4.00	28.00	**0.001**
Rt TEOAE 2 kHz SNR	14.49	7.32	14.50	-9.10	28.00	16.57	5.05	16.00	6.70	27.00	0.104
Rt TEOAE 3 kHz SNR	11.15	6.76	12.00	-5.70	28.00	14.10	4.89	14.00	4.10	22.00	**0.020**
Rt TEOAE 4 kHz SNR	7.33	6.43	8.40	-17.00	19.00	10.78	3.76	11.00	4.00	22.00	**0.002**
Rt TEOAE 5 kHz SNR	1.84	6.60	3.35	-19.00	16.00	4.87	2.64	4.40	-1.90	19.00	**0.038**

Rt Right, *SNR* Signal to noise ratio

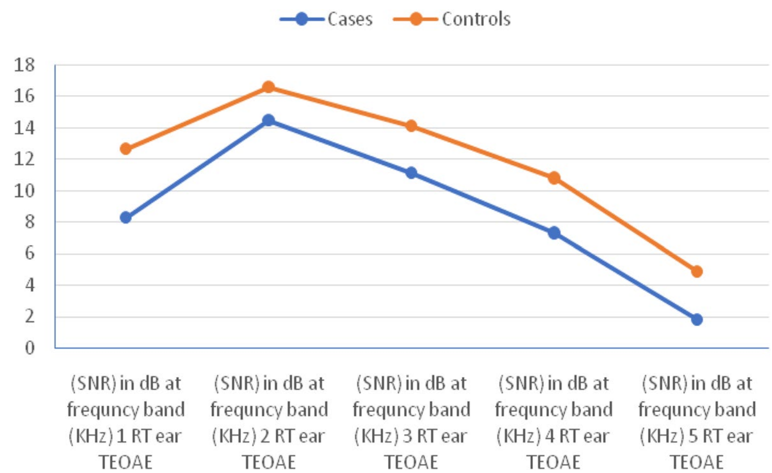

Fig. 3 Comparison of right TEOAEs amplitude (SNR) across each frequency band between patients and controls

Table 4 Comparison of TEOAEs' overall reproducibility and amplitude (SNR) across all frequency bands in the left ear between patients and controls

	Cases					Controls					*P* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Left Reproducibility (%)	78.12	22.46	85.65	1.80	99.60	91.12	9.31	95.75	66.00	100.00	**< 0.001**
Left TEOAE1 KHz SNR	8.56	7.87	8.90	-10.00	28.00	13.41	5.90	11.50	4.10	25.00	**0.001**
Left TEOAE 2 kHz SNR	13.76	6.88	14.00	-9.00	26.00	17.37	5.58	18.00	7.40	28.00	**0.005**
Left TEOAE 3 kHz SNR	9.53	5.80	9.60	-3.40	22.00	14.40	5.24	15.00	4.60	32.00	**< 0.001**
Left TEOAE 4 kHz SNR	6.51	5.65	7.20	-5.50	16.00	10.01	3.67	10.00	4.40	22.00	**0.001**
Left TEOAE 5 kHz SNR	1.35	5.79	2.55	-18.00	14.00	5.04	2.43	4.55	-0.20	15.00	**0.001**

SNR Signal to Noise Ratio

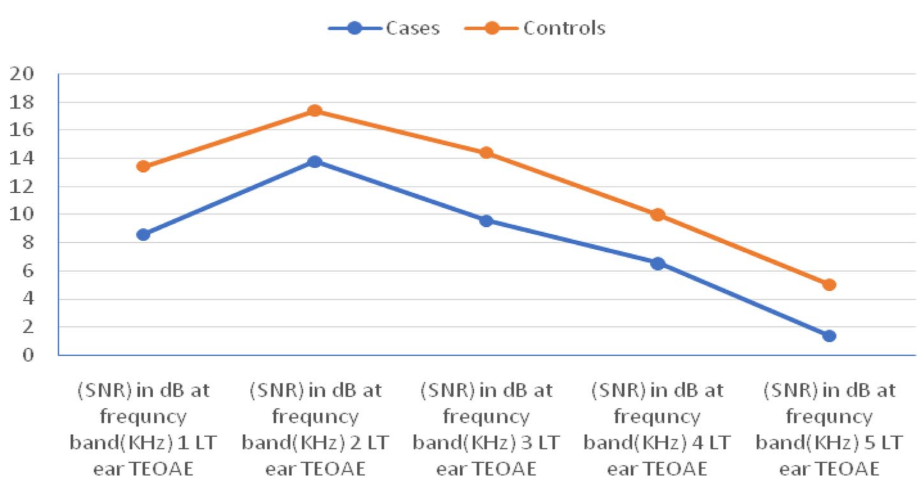

Fig. 4 Comparison of left TEOAEs amplitude (SNR) across each frequency band between patients and controls

Comparison between Tinnitus and TEOAEs findings

In both ears, there was a statistically significant TEOAE's affection in patients with tinnitus complaints. Twelve (85.7%) of fourteen tinnitus patients showed affection in TEOAEs in the right ear, and thirteen (100%) of thirteen tinnitus patients showed affection in

Table 5 Comparison between the patient's complaint of hearing loss and PTA threshold and TEOAEs affection in right ear

		Right Hearing loss				*P* value
		Yes		No		
		No	%	No	%	
Right PTA	**Affected**	11	78.6%	10	22.7%	**< 0.001**
	Normal	3	21.4%	34	77.3%	
Right TEOAEs	**Affected**	9	64.3%	27	61.4%	0.844
	Normal	5	35.7%	17	38.6%	

Table 6 Comparison between patient's complaint of hearing loss and PTA threshold affection and TEOAEs affection in left ear

		Left Hearing loss				*P* value
		Yes		No		
		No	%	No	%	
Left PTA	**Affected**	12	85.70%	11	25.00%	**< 0.001**
	Normal	2	14.30%	33	75.00%	
Left TEOAEs	**Affected**	12	85.70%	28	63.60%	0.187
	Normal	2	14.30%	16	36.40%	

Table 7 Comparison between patient's complaint of tinnitus and PTA threshold affection and TEOAEs affection in right ear

		Right Tinnitus				*P* value
		Yes		No		
		No	%	No	%	
Right PTA	**Affected**	6	42.90%	15	34.10%	0.552
	Normal	8	57.10%	29	65.90%	
Right TEOAEs	**Affected**	12	85.70%	24	54.50%	**0.036**
	Normal	2	14.30%	20	45.50%	

Table 8 Correlation between patient's complaint of tinnitus and PTA threshold affection and TEOAEs affection in left ear

		Left Tinnitus				*P* value
		Yes		No		
		No	%	No	%	
Left PTA	**Affected**	8	61.50%	15	33.30%	0.067
	Normal	5	38.50%	30	66.70%	
Left TEOAEs	**Affected**	13	100.00%	27	60.00%	**0.005**
	Normal	0	0.00%	18	40.00%	

TEOAEs in the left ear. There was no statistically significant difference between the patient's tinnitus complaint and PTA threshold affection (Tables 7 and 8).

Discussion

COVID-19 affects many body systems, and studies are being conducted to study its effect on the different systems. COVID-19 positive patients have auditory affection, according to studies. It is critical to evaluate hearing in these patients so that early identification and management of hearing loss can improve their quality of life after COVID-19.

In the current study audiological symptoms among cases were studied. Fourteen patients (24.1%) noticed changes in hearing sensation. Eleven patients complained of tinnitus bilaterally (18.9%), three patients (5.17%) complained of right tinnitus, and two patients (3.44%) complained of left tinnitus. The findings were consistent with Dharmarajan et al. [13], whose research found that the most common symptom was tinnitus in 39% of patients.

Numerous investigations have revealed a lower prevalence of auditory complaints than the current study. 8.3% of COVID-19 patients reported hearing loss, and 4.2% experienced tinnitus, according to Gallus et al. [14]. According to Bhatta et al. [15], 3.9% of people with aural symptoms had hearing loss and 1.8% had tinnitus. Almufarrij and Munro's systematic review [7] results showed that 7.6% of patients complained of hearing loss, and 14.8% from tinnitus. Jafari et al.'s. systematic review [16] reported hearing loss in 3.1% and tinnitus in 4.5% of patients. Tinnitus was reported in 11% of cases and hearing impairment in 5.1% of cases, according to Özçelik Korkmaz et al. [17]. The current study patients had higher incidence of complaints than other studies. This could be explained because the cases were recruited from Audiology clinic with patients complaining of auditory symptoms in contrast to other studies.

Audiometry

According to PTA results from the current study, there was hearing loss in the right ear in 21 patients (36.2%) and the left ear in 23 individuals (39.7%). Right ear PTA thresholds were statistically significantly poorer in the cases compared to control at 250 Hz, 500 Hz, 4 kHz, and 8 kHz, and left ear thresholds were worse at 250 Hz, 4 kHz, 8 kHz, and 12.5 kHz (Tables 1 and 2).

PTA results are in agreement with Mustafa [9], who studied twenty asymptomatic subjects positive for COVID-19 compared to twenty controls. PTA showed no significant difference at 250, 500, 750, 1000, 1500, 2000 and 3000 Hz. At 4000, 6000, and 8000 Hz, there was a significant difference (p 0.05) between the two groups. Also, Dusan et al. [18] studied 74 moderate COVID-19 patients compared to 48 controls. Thirty (40.5%) patients who tested positive for COVID-19 had sensorineural hearing loss, with 17 having unilateral hearing loss and 13 having bilateral hearing loss. Audiograms were either flat in 60% of cases or descending 40% of cases. When unilateral or bilateral groups were compared to the control group, a highly statistically significant difference was discovered at all frequencies. Sixty COVID-19 patients with moderate-severe disease were investigated in a hospital by de Sousa et al. [8]. When compared to controls, patients with COVID-19 displayed statistically significant differences (poor mean hearing thresholds) beginning at 1000 Hz and continuing through 2000, 3000, 4000, and 8000 Hz.

Dharmarajan et al. [13] studied 100 COVID-19 positive patients aged between 21 and 60 years with mild to moderate COVID symptoms. High frequency hearing loss was the most common finding. Six patients had CHL. SNHL was present in 53 patients in total. Thirty-one of the 100 patients had ear symptoms. These results match our results for the high frequency hearing loss in PTA, but in the current study, low frequency hearing loss was also detected. Furthermore, the types of hearing loss were CHL and SNHL, as opposed to the current study, in which all patients had SNHL.

Swain and Pani. [19] found that 28 (5.93%) of the 472 recovered COVID-19 patients had hearing loss. Six individuals had bilateral hearing loss, whereas twenty-two patients had unilateral hearing loss. Four (14.28%) of the 28 individuals had conductive hearing loss, whereas the remaining 24 (85.71%) had SNHL. Out of the 28 patients, 17 (60.71%) had sudden-onset hearing loss, whereas 21 (75%) had unilateral hearing loss. 16 cases (66.67%) of the 24 SNHL cases showed high-frequency SNHL in PTA.

TEOAEs

TEOAEs showed affection in 36 patients (62.1%) in right ear and in 40 patients (69%) in left ear. Cases showed a statistical significant lower overall reproducibility and amplitude (SNR) at 1, 3, 4, and 5 kHz frequency bands in right ear. The left ear showed a statistical significant lower overall reproducibility and amplitude (SNR) at all frequency bands (Tables 3 and 4 and Figs. 3 and 4).

The current TEOAEs results are in agreement with Mustafa [9], whose results showed a highly significant difference in TEOAEs amplitude among the control and test groups. Despite being asymptomatic, he came to the conclusion that the COVID-19 infection might impair cochlear hair cell function. Although all participants' hearing sensitivity was normal, TEOAEs might detect a slight decline in outer hair cell activity. The absence of overt symptoms may also mask an unidentified influence on the cochlea and other delicate sensory organs. The cause of this decline is yet unknown; however, it may be related to the harm that the viral infection caused to the outer hair cells.

Dharmarajan et al. [13] discovered that 49 of the 100 patients had referred OAEs in both ears, with the majority of the patients suffering from high-frequency hearing loss. Swain and Pani [19] look into the prevalence of hearing loss in COVID-19 patients who tested positive for RT-PCR after leaving the hospital. 28 (5.93%) of the 472 patients presented with hearing loss. TEOAE amplitude was reduced in 22 (78.57%) of the 28 patients.

In contrast to the current study, Dror et al. [20], examined 8 asymptomatic COVID-19 positive participants. They were evaluated following recovery and compared to 8 controls using ABR, OAE, and tympanometry. There were no significant differences in TEOAEs, DPOAEs, or ABR between recovered asymptomatic SARS-CoV-2 patients and controls. They used a small sample size compared to other studies; also, the results contradict Mustafa's results [9] regarding OAEs, in spite of the fact that both included only asymptomatic COVID patients.

Many theories were proposed in studies that revealed significance finding in hearing among COVID-19 cases. SARS-CoV-2 can cause SNHL by inducing an inflammatory response in cochlear hair cells. The presence of ACE2 receptors in the brain, medulla oblongata, and temporal lobe aids SARS CoV2 entry into the brainstem and hearing centers, resulting in an inflammatory response via cytokine release and neurologic and otologic manifestations in COVID 19 patients [13]. SARS-CoV-2 is thought to bind to ACE-2 receptors, which are expressed in middle ear epithelial cells, the stria vascularis, and the spiral ganglion in mice [8]. Another possible mechanism, considering the neurotropic nature of SARS-CoV-2, is the ability to affect the brainstem [21].

Endothelial dysfunction and micro thrombosis have recently been highlighted as important factors in COVID-19 infection. By binding to the ACE2 receptor, viruses have been shown to affect many organs, including the cochlea, cochlear nerve, and central nervous system. Furthermore, the virus is linked to increased immune system activation, which can cause tissue damage in the patient [18].

Our results could also be explained by the previously mentioned mechanisms of hearing affection in COVID-19. The vascular theory (ischemia, endothelial dysfunction, and micro thrombosis) could explain high frequency hearing loss in the current study and other studies, which affects the basal part of the cochlea more [5]. Other explanations for hearing loss in any frequency range include brainstem damage, oxidative stress, and a cytokine storm [16].

A statistically significant difference in both ears was found between the patient's complaint of hearing loss and PTA thresholds. As eleven (78.6%) of Fourteen patients with hearing loss had an elevated PTA threshold in the right ear, and twelve (85.7%) of the same fourteen patients with hearing loss had an elevated PTA threshold in the left ear. A comparison between TEOAEs findings and the patient's complaint of tinnitus showed a statistical significant difference in both ears. As Twelve (85.7%) out of 14 patients complaining of tinnitus showed affection in TEOAEs in the right ear, and Thirteen (100%) out of the 13 patients complaining of tinnitus showed affection in TEOAEs in the left ear.

Similarly, Dharmarajan et al. [13] discovered SNHL in 53 patients in total. Hearing loss was reported as a symptom by 11 of the 53 patients, while the remaining 42 did not. compared to the current study, hearing loss was reported by only 11 patients. Among the 100 patients, 49 had referred OAE in both ears, with the majority of the patients having high frequency hearing loss. 18 of the 31 patients who complained of ear symptoms had an OAE referred to them, as did 31 of the 69 patients who never complained of ear symptoms.

A high percentage of abnormal TEOAEs in the absence of hearing loss could be attributed to a preclinical cochlear lesion, which could be evaluated by recording OAEs, as before any audiometric evidence is detectable using pure-tone audiometry, up to 30% of the OHC population may have damage [10]. In patients with normal audiograms, OAEs can be used to offer unbiased confirmation of cochlear impairment [22].

Regarding the strength points in our results, compared to most similar case -controls study, we used an equal case–control ratio with an adequate sample size in spite of the many omitted cases and controls due to commitment to the strict inclusion and exclusion criteria to avoid bias. In our humble opinion, the current study included extended audiometry (12.5 kHz). Also, we correlated patient complaints with the results of hearing tests (PTA and TEOAEs).

Regarding the limitations in the current study, the period between the patient being diagnosed by PCR and the conduction of tests was defined at 1 month with no upper limit, so other causes of hearing loss may contribute in patients coming after long period. Also, we depended on the patient's history to exclude previous hearing loss due to the absence of previous hearing records. Furthermore, despite of having COVID-19 symptoms and hearing loss, many patients were unable to participate in the study because PCR test wasn't performed routinely in all cases.

Conclusions

COVID-19 may have a negative effect on hearing, whether in patients with or without audiological symptoms. COVID-19 affects hearing thresholds at different frequencies. TEOAEs can be affected even in patients with normal PTA. There is a link between the patient's complaint of hearing loss and PTA affection, as well as tinnitus and TEOAEs affection. PTA is sensitive to hearing loss, whereas TEOAEs are sensitive to tinnitus in COVID-19 patients.

Recommendation

Patients infected with COVID-19 should have hearing tests, including PTA and OAEs, to detect and manage auditory affection early. More research is needed to address the following issues: detecting hearing affection in patients with different variants, the effect of COVID-19 vaccines on hearing affection or protection, following up on short and long periods of recovery to determine whether the affection is reversible or permanent, and assessing other aspects of the audio-vestibular system such as central and evoked potential hearing tests and vestibular tests.

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Authors' contributions
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Availability of data and materials
The datasets during and/or analyzed during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Cairo University, Faculty of Medicine, Research Ethics Committee approved the study on 25 July 2021 (MS-251-2021). All subjects provided their informed consent prior to participating in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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