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Effects of Covid-19 on the audio-vestibular system

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ARTICLE INFO

Keywords:
COVID-19
Hearing
Vertigo

ABSTRACT

Purpose: It was aimed to investigate the effects of COVID-19 infection on hearing and the vestibular system.

Methods: Twenty-six patients whose treatment had been completed and who had no previous hearing or balance complaints were included in the study. Patients diagnosed with the disease by PCR were included in the study. Patients with at least one month of illness were included in the study. The hearing of patients was evaluated with transient evoked otoacoustic emissions (TEOAE) and pure-tone audiometry. Bedside tests, the European Evaluation of Vertigo scale (EEV), Video Head Impulse Test (vHIT), Ocular Vestibular Myogenic Evoked Potential (oVEMP), Cervical Vestibular Myogenic Evoked Potential (cVEMP) and Videonystagmography (VNG) tests were applied to evaluate the vestibular system.

Results: A statistically significant difference was found between the COVID-19 positive and control groups according to the mean values of the 4000 Hz and 8000 Hz in both the right and left ears (p < 0.05). No statistically significant difference was found in the other frequencies and TEOAE. No statistically significant difference was found between the COVID-19 positive and control groups in terms of their normal or pathological VNG saccade, optokinetic and spontaneous nystagmus values (p > 0.05). The normal and pathological VNG head shake values were found to be significantly different between the COVID-19 positive and control groups (p < 0.05).

Conclusion: The high frequencies in audiometry in the COVID-19 positive group were worse than those in the control group. In the vestibular system, especially in oVEMP and cVEMP, asymmetric findings were obtained in comparison to the control group, and a low gain in vHIT was shown. This study shows that the audiovestibular system of people with COVID-19 infection may be affected.

1. Introduction

The novel coronavirus disease-2019 (COVID-19), which spreads rapidly around the world and appeared in the Wuhan city in the Hubei province of China in December 2019, was declared as a global pandemic by WHO in March 2020 [1]. The name of the virus that causes this disease has been determined as the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) [2]. 175 million cases and 3.7 million deaths had been reported worldwide by June 2021 [3]. Symptoms in this disease range from a mild upper respiratory tract infection to severe pneumonia. Common clinical symptoms include dry cough, fever, headache, sore throat, shortness of breath, diarrhea, vomiting and abdominal pain [4–6]. Anosmia and taste changes are common symptoms [7,8]. Studies have investigated whether the SARS-CoV-2 virus has an indirect or direct neurotrophic effect on the nervous system [9–10]. Various neurological symptoms such as loss of consciousness, headache and dizziness have been reported in COVID-19 patients [11–14]. Facial paralysis, sudden hearing loss and cases of vertigo among otologic symptoms have also been reported in relation to COVID-19 [15,16]. Whether COVID-19 has an effect on hearing and the vestibular system is still unclear. In this study, we planned to investigate whether there was any change in the hearing and vestibular system in patients with COVID-19 infection using a large battery of tests after recovery.

2. Material and method

This is a prospective study. The research was conducted in a Department of Audiology between April 2020 and June 2020. Twenty-six patients whose treatment had been completed and who had no previous hearing or balance complaints were included in the study.
Information was obtained about their complaints at the time of the disease, hospitalization and treatment that they received. Patients diagnosed with the disease by PCR were included in the study. Patients with at least 30 days of illness were included in the study. Those with severe disease or hospitalization at intensive care units were excluded from the study. Patients with previous hearing problems or balance disorders, those who had ear surgery, cardiovascular and circulatory problems, and patients using chloroquine were excluded from the study. The patients were asked whether or not they had any problems with hearing and balance before by taking a detailed anamnesis, and those who did not have any problems were included in the study. It was made sure to question the patients’ histories of exposure to noise, and those with a history of working in a loud place were excluded. To conduct the study, approval was obtained from the Ethics Committee of University Institute of Health Sciences (Decision number: 2020/1268), and consent was obtained from all individuals participating in the study. Audiometry and transient evoked otoacoustic emissions (TEOAE) to assess patients’ hearing, the European Evaluation of Vertigo scale (EEV) for vestibular system assessment, the video head impulse test (vHIT), oculomotor Vestibular Myogenic Evoked Potential (oVEMP), cervical Vestibular Myogenic Evoked Potential (cVEMP) and Videonystagmography (VNG) tests were performed.

2.1. Statistical analysis

The analysis of the data included in the study was carried out with the SPSS (Statistical Package for the Social Sciences) 25 program. The significance level (p) was taken as 0.05 for the comparison tests. Shapiro Wilk Test was used to check whether the data fit a normal distribution. Since the data were normally distributed, comparisons between the case and control (COVID (+), COVID (−)) groups were performed with the significance test (t-test) of the difference between the two means. The homogeneity of variances was checked by Levene’s test to decide which test result to look for in the comparison (p > 0.05). The values of the variables are given as frequency, percentage, mean and standard deviation. In the analysis of the categorical data, cross-tables were created, and chi-squared (χ²) analysis was carried out.

3. Results

A total of 53 people were included in the study, where 26 (49.1%) of these individuals were in the COVID-19 positive group, and 27 (50.9%) were in the control group. 36 (67.9%) of the participants were female, 17 (32.1%) were male, and the mean age of the participants was calculated as 28.98 ± 10.91 years. There were 14 (53.8%) female and 12 (46.2%) male individuals in the COVID-19 positive group, and their mean age was calculated as 34.20 ± 9.12 years. There were 22 (81.5%) female and 5 (18.5%) male individuals in the control group, and their mean age was calculated as 23.96 ± 5.92 years. The mean disease duration of the COVID-19 positive patients was found as 66.35 ± 23.51 days. The symptoms seen during the illness of the patients were evaluated. Fever was observed in 8 (30.8%) of the patients, but not in 18 (69.2%). 5 (19.2%) had respiratory distress, but none of them needed oxygen support. 21 of the patients (80.8%) had no respiratory distress. While 11 (42.3%) had joint pain and headache, 15 (57.7%) did not. The numbers of the patients with and without dizziness were equal to 13 each (50%). While there was loss of taste in 4 (15.4%) patients, this was not observed in 22 (84.6%) patients. Oxygen support and hospitalized patients were not available, and fatigue was observed in all patients (26). Favipiravir was used for treatment in 22 patients (88.5%), and no treatment was given in 3 (11.5%) (Table 1).

3.1. Audiology results

The 125 Hz, 250 Hz, 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz, 8000 Hz and PTO (average of the results for the 500, 1000, 2000 and 4000) average values of the participants were examined in both the right and left ears. No statistically significant difference was found between the COVID-19 positive and control groups in the mean values of the 125 Hz, 250 Hz, 500 Hz, 1000 Hz, 2000 Hz and PTO measurements in both the right and left ears. No statistically significant difference was found between the mean values of the 4000 Hz and 8000 Hz in both the right and left ears. No statistically significant difference was found between the mean values of the 5000 and 10000 Hz in both the right and left ears. No statistically significant difference was found between the mean values of the 125 Hz, 250 Hz, 500 Hz, 1000 Hz, 2000 Hz and PTO measurements in both the right and left ears. No statistically significant difference was found between the mean values of the 4000 Hz and 8000 Hz in both the right and left ears.

| Symptom          | Number | %     |
|------------------|--------|-------|
| Fever            | +      | 8     | 30.8 |
|                   | −      | 18    | 69.2 |
| Respiratory distress | +     | 5     | 19.2 |
|                   | −      | 21    | 80.8 |
| Oxygen support   | +      | 26    | 100.0|
|                   | −      | 26    | 100.0|
| Weakness         | +      | 26    | 100.0|
|                   | −      | 26    | 100.0|
| Joint pain       | +      | 11    | 42.3 |
|                   | −      | 15    | 57.7 |
| Headache         | +      | 11    | 42.3 |
|                   | −      | 15    | 57.7 |
| Dizziness        | +      | 13    | 50.0 |
|                   | −      | 13    | 50.0 |
| Loss of the smell| +      | 4     | 15.4 |
|                   | −      | 22    | 84.6 |
| Loss of the sense| +      | 12    | 46.2 |
|                   | −      | 14    | 53.8 |
| Treatment        | Favipiravir | 23  | 88.5 |
|                   | No treatment | 3   | 11.5 |

Table 1

Characteristics of patients with covid.

| Days of illness | Mean ± ss | 66.35 ± 23.51 day |
|-----------------|-----------|-------------------|

ss; standard deviation.

| Group          | Right ear | Mean ± ss | Test* p value | Left ear | Mean ± ss | Test* p value |
|----------------|-----------|-----------|---------------|----------|-----------|---------------|
| 125 Hz         | Covid (+) | 10.5 ± 2.2| p = 0.047 *   | Covid (+)| 10.4 ± 2.2| p = 0.047 *   |
|                | Covid (−) | 6.5 ± 2.0 | p = 0.059 *   | Covid (−)| 6.0 ± 2.0 | p = 0.059 *   |
| 250 Hz         | Covid (+) | 9.6 ± 1.7 | p = 0.953     | Covid (+)| 9.5 ± 1.7 | p = 0.953     |
|                | Covid (−) | 6.8 ± 1.7 | p = 0.532     | Covid (−)| 6.3 ± 1.7 | p = 0.532     |
| 500 Hz         | Covid (+) | 13.3 ± 2.2| p = 0.298     | Covid (+)| 13.2 ± 2.2| p = 0.298     |
|                | Covid (−) | 8.9 ± 2.0 | p = 0.466     | Covid (−)| 8.4 ± 2.0 | p = 0.466     |
| 1000 Hz        | Covid (+) | 9.6 ± 2.0 | p = 0.001     | Covid (+)| 9.5 ± 2.0 | p = 0.001     |
|                | Covid (−) | 5.7 ± 1.5 | p = 0.001     | Covid (−)| 5.3 ± 1.5 | p = 0.001     |
| 2000 Hz        | Covid (+) | 11.1 ± 2.0| p = 0.047     | Covid (+)| 11.0 ± 2.0| p = 0.047     |
|                | Covid (−) | 6.8 ± 2.0 | p = 0.001     | Covid (−)| 6.4 ± 2.0 | p = 0.001     |
| 4000 Hz        | Covid (+) | 13.2 ± 2.0| p = 0.001     | Covid (+)| 13.1 ± 2.0| p = 0.001     |
|                | Covid (−) | 5.1 ± 1.5 | p = 0.001     | Covid (−)| 4.7 ± 1.5 | p = 0.001     |
| 8000 Hz        | Covid (+) | 13.6 ± 2.2| p = 0.298     | Covid (+)| 13.5 ± 2.2| p = 0.298     |
|                | Covid (−) | 7.3 ± 2.0 | p = 0.001     | Covid (−)| 6.9 ± 2.0 | p = 0.001     |
| PTO            | Covid (+) | 11.2 ± 2.0| p = 0.001     | Covid (+)| 11.1 ± 2.0| p = 0.001     |
|                | Covid (−) | 5.8 ± 1.5 | p = 0.001     | Covid (−)| 5.4 ± 1.5 | p = 0.001     |

* p < 0.05 there is a statistically significant difference between groups.
ears ($p < 0.05$, Table 2).

### 3.2. TEOAE results

The TEOAE results measured in both the right and left ears of the participants were examined at 1000 Hz, 1400 Hz, 2000 Hz, 2800 Hz and 4000 Hz. No statistically significant difference was found between the COVID-19 positive and control groups according to the mean values of the 1000 Hz, 1400 Hz, 2000 Hz, 2800 Hz and 4000 Hz measurements in both the right and left ears ($p > 0.05$). Although not statistically significant, the mean values of the 1000 Hz, 1400 Hz, 2000 Hz, 2800 Hz, and 4000 Hz measurements made in both the right and left ears were found to be lower in the COVID-19 positive group in comparison to the control group ($p < 0.05$, Table 3).

### 3.3. EEV results

The mean European Evaluation of Vertigo scale (EEV) score in the COVID-19 positive group was found to be 4.5. A statistically significant difference was calculated between the COVID-19 positive group and the control group according to EEV ($p < 0.05$).

### 3.4. Bedside test results

Chi-squared ($\chi^2$) analysis was performed by creating cross-tables to compare the normal and pathological values of the bedside Romberg, tandem Romberg, Fukuda and tandem gait-tests between the COVID-19 positive and control groups. No statistically significant difference was found between the COVID-19 positive and control group in terms of the normal or pathological bedside Romberg values ($p > 0.05$, Table 4). A statistically significant correlation was found between the normal or pathological values in the tandem Romberg, Fukuda and tandem gait-tests ($p < 0.05$, Table 4).

### 3.5. VNG results

Cross-tables were created, and Chi-squared ($\chi^2$) analysis was performed to compare the normal and pathological values of VNG gaze vertical, gaze horizontal, saccade, pursuit, optokinetic, spontaneous nystagmus, head shake, Dix Hallpike and head roll between the COVID-19 positive group and the control group. Since no pathological data group was found in the VNG gaze vertical, gaze horizontal, pursuit, Dix Hallpike and head roll values, the comparison value could not be statistically calculated. No statistically significant difference was found between the COVID-19 positive and control groups in terms of their normal or pathological VNG saccade, optokinetic and spontaneous nystagmus values ($p > 0.05$). The normal and pathological VNG head shake values were found to be significantly different between the COVID-19 positive and control groups ($p < 0.05$, Table 5).

### 3.6. vHIT results

The mean values of vHIT lateral gain, LARP gain and RALP gain measured in both the right and left ears of the participants were examined. A statistically significant difference was found between the COVID-19 positive group and the control group in terms of the mean values of the vHIT lateral gain, LARP gain and RALP gain measurements in both the right and left ears ($p < 0.05$, Table 6). The mean values of vHIT lateral gain, LARP gain and RALP gain in both the right and left ears were found to be lower in the COVID-19 positive group than the control group (Table 6). No statistically significant difference was found between the COVID-19 positive group and the control group in terms of the mean value of the vHIT lateral gain measurement ($p > 0.05$, Table 7). A statistically significant difference was found between the COVID-19 positive group and the control group in the mean values of the vHIT LARP gain and RALP gain asymmetry measurements ($p < 0.05$, Table 7). The mean values of vHIT lateral gain, LARP gain and RALP gain asymmetry were calculated to be higher in the COVID-19 positive group in comparison to the control group (Table 7). Cross-tables were created, and Chi-squared ($\chi^2$) analysis was performed to compare the values of vHIT lateral saccades, LARP saccades and RALP saccades between the COVID-19 positive and control groups. Since there was no data group with LARP saccades and RALP saccades in both the right and left ears, the comparison value could not be calculated statistically (Table 8). A statistically significant relationship was found between the presence of lateral saccades in the patients in both the right and left ears and the groups ($p < 0.05$, Table 8).

### 3.7. cVEMP results

The cVEMP P1 latency, N1 latency, P1-N1 latency and P1-N1 amplitude mean values were compared. A statistically significant difference was found between the COVID-19 positive and control groups according to the mean values of the left ear P1 latency and N1 latency measurements ($p < 0.05$, Table 9), but no statistically significant difference was found in the mean values of the P1 latency and N1 latency measurements in the right ear.

A statistically significant difference was found between the COVID positive and control groups in terms of the mean values of the right ear P1-N1 amplitude measurement ($p < 0.05$, Table 9). According to the mean values of the P1-N1 amplitude measurement in the left ear, no statistically significant difference was found between the COVID positive and control groups ($p > 0.05$, Table 9). A statistically significant difference was found between the COVID positive and control groups in the mean values of the P1-N1 latency measurement in both the right and left ears ($p < 0.05$, Table 9).

The cVEMP N1 latency, P1-N1 latency and P1-N1 amplitude mean values were found to be lower in the COVID-19 positive patients than the control group. However, the P1 Latency measurement value was calculated to be higher in the right ear in the COVID-19 positive patients in comparison to the control group, while being lower in the left ear (Table 9). A statistically significant difference was found between the COVID-19 positive and control groups according to the mean value of cVEMP asymmetry ($p < 0.05$, Table 10). It was calculated that the mean cVEMP asymmetry value was higher in the COVID-19 positive patients.

### Table 3

Comparison of groups according to the n chief values.

| Group | Right ear Mean ± ss | Test p value | Left ear Mean ± ss | Test p value |
|-------|---------------------|--------------|-------------------|--------------|
| 1000 Hz Covid (+) | 9 ± 7.2 | 12,49 | 14 ± 7,05 | 11,29 |
| Covid (-) | 7 ± 6,32 | 5,4 | 7 ± 6,32 | 5,4 |
| 1400 Hz Covid (+) | 15,16 ± 0,754 | 0,454 | 16,4 ± 0,624 | 0,536 |
| Covid (-) | 14,59 ± 0,702 | 8,69 | 14,59 ± 0,702 | 8,69 |
| 2000 Hz Covid (+) | 16,79 ± 0,897 | 0,315 | 16,37 ± 0,993 | 0,326 |
| Covid (-) | 18,56 ± 8 | 18,36 | 18,56 ± 8 | 18,36 |
| 2800 Hz Covid (+) | 18,08 ± 1015 | 0,280 | 16,63 ± 0,397 | 0,693 |
| Covid (-) | 20,33 ± 8 | 17,37 | 20,33 ± 8 | 17,37 |
| 4000 Hz Covid (+) | 14,42 ± 7,1 | 1971 ± 0,054 | 15,54 ± 0,895 | 0,375 |
| Covid (-) | 18,67 ± 8,52 | 7,9 | 18,67 ± 8,52 | 7,9 |

ss: standard deviation, a: significance test of the difference between two means (t-test).

*p < 0.05* there is a statistically significant difference between groups.
### Table 4
Comparison of Bedside Values According to Groups.

| Group               | Group      | Total | Test value<sup>a</sup> | p value |
|---------------------|------------|-------|-------------------------|---------|
|                     |            |       |                        |         |
|                     | Covid (+)  | Covid (-) |                        |         |
|                     | Normal     | Number | 25<sup>a</sup> | 27<sup>a</sup> | 52 | 1444 | 0.229 |
|                     | %          |         | 96.2 | 100.0 | 96,1 |
|                     | Pathological | Number  | 1<sup>a</sup> | 0<sup>a</sup> | 1 | 3,8 | 0,0 | 1.9 |
| Bedside Romberg     | Normal     | Number | 21<sup>a</sup> | 27<sup>a</sup> | 48 | 7665 | 0.006<sup>*</sup> |
|                     | %          |         | 80.8 | 100.0 | 90,6 |
|                     | Pathological | Number  | 5<sup>a</sup> | 0<sup>a</sup> | 5 | 19,2 | 0,0 | 9,4 |
| Bedside Tandem Romberg | Normal     | Number | 23<sup>a</sup> | 27<sup>a</sup> | 50 | 4,46 | 0.035<sup>*</sup> |
|                     | %          |         | 88,5 | 100.0 | 94,3 |
| Bedside Fukuda      | Normal     | Number | 23<sup>a</sup> | 27<sup>a</sup> | 50 | 4,46 | 0.035<sup>*</sup> |
|                     | %          |         | 88,5 | 100.0 | 94,3 |
|                     | Pathological | Number  | 3<sup>a</sup> | 0<sup>a</sup> | 3 | 11,5 | 0,0 | 5,7 |
|                     |            |       |                        |         |
|                     | Covid (+)  | Covid (-) |                        |         |
|                     | Normal     | Number | 26<sup>a</sup> | 27<sup>a</sup> | 53 | 2930 | 0.087 |
| Bedside Tandem Gait | Normal     | Number | 23<sup>a</sup> | 27<sup>a</sup> | 48 | 7665 | 0.006<sup>*</sup> |
|                     | %          |         | 80,8 | 100.0 | 90,6 |
|                     | Pathological | Number  | 5<sup>a</sup> | 0<sup>a</sup> | 5 | 19,2 | 0,0 | 9,4 |

<sup>*</sup> p < 0.05; different letters in the rows show the difference between the two groups, while the same letters show that there is no difference a; χ<sup>2</sup> test value.

### Table 5
Comparison of VNG values according to groups.

| Group          | Total | Test value<sup>a</sup> | p value |
|----------------|-------|-------------------------|---------|
|                |       |                        |         |
| VNG gaze vertical | Normal | Number | 26<sup>a</sup> | 27<sup>a</sup> | 53 | 3302 | 0.069 |
| VNG gaze horizontal | Normal | Number | 26<sup>a</sup> | 27<sup>a</sup> | 53 | 2930 | 0.087 |
| VNG saccade     | Normal | Number | 24<sup>a</sup> | 27<sup>a</sup> | 51 | 2930 | 0.087 |
| VNG pursuit     | Normal | Number | 26<sup>a</sup> | 27<sup>a</sup> | 53 | 2930 | 0.087 |
| VNG optokinetics | Normal | Number | 23<sup>a</sup> | 27<sup>a</sup> | 50 | 3302 | 0.069 |
| VNG spontaneous nystagmus | Normal | Number | 23<sup>a</sup> | 27<sup>a</sup> | 50 | 3302 | 0.069 |
| VNG head shake  | Normal | Number | 19<sup>a</sup> | 27<sup>a</sup> | 46 | 8735 | 0.001<sup>*</sup> |
| VNG dix halfpipe | Normal | Number | 26<sup>a</sup> | 27<sup>a</sup> | 53 | 2930 | 0.087 |
| VNG roll        | Normal | Number | 26<sup>a</sup> | 27<sup>a</sup> | 53 | 2930 | 0.087 |

<sup>*</sup> p < 0.05; different letters in the rows show the difference between the two groups, while the same letters show that there is no difference a; χ<sup>2</sup> test value.

### Table 6
Comparison of groups according to vHIT values.

| Group       | Right ear | Mean ± ss | Test | p value | Left ear | Mean ± ss | Test | p value |
|-------------|-----------|-----------|------|---------|----------|-----------|------|---------|
| vHIT Lateral Gain | Covid (+) | 0.88 ± 0.13 | −2978 | 0.005<sup>*</sup> | 0.86 ± 0.12 | −5314 | 0.001<sup>*</sup> |
|             | Covid (−) | 0.96 ± 0.06 |      |         | 1 ± 0.06 |      |      |         |
| vHIT Larp Gain | Covid (+) | 0.79 ± 0.16 | −3450 | 0.001<sup>*</sup> | 0.83 ± 0.16 | −3051 | 0.004<sup>*</sup> |
|             | Covid (−) | 0.92 ± 0.09 |      |         | 0.94 ± 0.09 |      |      |         |
| vHIT Ralp Gain | Covid (+) | 0.84 ± 0.15 | −2093 | 0.043<sup>*</sup> | 0.73 ± 0.18 | −3564 | 0.001<sup>*</sup> |
|             | Covid (−) | 0.91 ± 0.09 |      |         | 0.87 ± 0.1 |      |      |         |

<sup>ss</sup>; standard deviation, a; significance test of the difference between two means (t-test).

<sup>*</sup> p < 0.05 there is a statistically significant difference between groups.
Table 7
Comparison of groups according to vHIT asymmetry values.

| Group    | Asymmetry | Mean ± ss  | Test | p value |
|----------|-----------|------------|------|---------|
| vHIT lateral | Covid (+) | 4 ± 3.42   | 1071 | 0.289   |
|          | Covid (-) | 3.15 ± 2.28|      |         |
| vHIT larp  | Covid (+) | 5 ± 4.04   | 2098 | 0.041*  |
|          | Covid (-) | 3 ± 2.81   |      |         |
| vHIT ralp | Covid (+) | 8.54 ± 6.75| 3227 | 0.003*  |
|          | Covid (-) | 3.67 ± 3.77|      |         |

ss: standard deviation, a: significance test of the difference between two means (t-test).

* p < 0.05 there is a statistically significant difference between groups.

(Table 10).

3.8. oVEMP results

The mean values of the oVEMP P1 latency, N1 latency, P1N1 latency and P1N1 amplitude measurements made in both the right and left ears of the participants were evaluated. No statistically significant difference was found between the COVID-19 positive and control groups according to the mean values of the P1 latency, N1 latency, P1N1 latency and P1N1 amplitude measurements in both the right and left ears (p > 0.05, Table 9). It was found that the mean values of oVEMP P1 latency, N1 latency and P1N1 amplitude in both the right and left ears were higher in the COVID-19 positive group, and the P1N1 latency measurements were found to be higher in the control group (Table 9).

A statistically significant difference was found between the mean oVEMP asymmetry values of the COVID-19 positive group and the control group (p < 0.05). The mean oVEMP asymmetry value was found to be higher in the COVID-19 positive group in comparison to the control group (Table 10).

Table 8
Comparison of vHIT saccade values according to groups.

| Ear   | Group           | Group | Number | Number | % | % | % | % | % | % | % | % | % | ss Test | p value |
|-------|-----------------|-------|--------|--------|---|---|---|---|---|---|---|---|---|---------|---------|
| RIGHT | vHIT Lateral Saccade | +     | 42     | 0     | 84,6| 100,0 | 100,0 | 100,0 | 100,0 | 100,0 | 100,0 | 100,0 | 7,65 | 1100 | 0.281 |
|       | vHIT Larp Saccade  | +     | 260    | 27_a  | 27,4 | 53   | 100,0 | 100,0 | 100,0 | 100,0 | 100,0 | 100,0 | 92,5  |         |         |
|       | vHIT Ralp Saccade  | -     | 26     | 27_a  | 53   | 100,0 | 100,0 | 100,0 | 100,0 | 100,0 | 100,0 | 100,0 | 100,0 |         |         |
| LEFT  | vHIT Lateral Saccade | +     | 52     | 0     | 19,2 | 0,0   | 9,4   |         |         |         |         |         | 0,006* | 7665 |         |
|       | vHIT Larp Saccade  | -     | 21     | 27_a  | 48   | 100,0 | 90,6  |         |         |         |         |         |         |         |         |
|       | vHIT Ralp Saccade  | -     | 26     | 27_a  | 53   | 100,0 | 100,0 |         |         |         |         |         |         |         |         |

* p < 0.05; different letters in the rows show the difference between the two groups, while the same letters show that there is no difference a: χ2 test value.

Table 9
Comparison of groups according to cVEMP and oVEMP values.

| Group     | Right ear Mean ± ss | Test | p value |
|-----------|---------------------|------|---------|
| P1 Latans | Covid (+) 13.83 ± 1.02 | 0.585 | 0.562   |
|           | Covid (-) 13.58 ± 1.77 |      |         |
| N1 Latans | Covid (+) 20.37 ± 1.53 | -2008 | 0.050   |
|           | Covid (-) 21.36 ± 1.88 |      |         |
| cVEMP     | Covid (+) 7.78 ± 1.27 | -3280 | 0.002*  |
|           | Covid (-) 8.22 ± 1.76 |      |         |
| cVEMP     | Covid (+) 57.57 ± 25.94 | -3363 | 0.002*  |
|           | Covid (-) 82.17 ± 25.79 |      |         |
| P1 Latans | Covid (+) 10.25 ± 0.91 | 1981 | 0.053   |
|           | Covid (-) 9.82 ± 0.64 |      |         |
| N1 Latans | Covid (+) 15.24 ± 0.93 | 0.426 | 0.672   |
|           | Covid (-) 15.13 ± 0.94 |      |         |
| oVEMP     | Covid (+) 4.98 ± 0.63 | -1738 | 0.089   |
|           | Covid (-) 5.31 ± 0.69 |      |         |
| P1N1 Latans | Covid (+) 9.98 ± 0.79 | 0.551 | 0.585   |
|           | Covid (-) 8.88 ± 0.49 |      |         |

ss: standard deviation, a: significance test of the difference between two means (t-test).

* p < 0.05 there is a statistically significant difference between groups.
4. Discussion

The SARS-CoV-2 pandemic that started in December 2019 has caused the deaths of over 2 million people. Fever, cough, sore throat, respiratory failure, taste and smell disorders are common clinical symptoms in patients [16]. Neurotrophic features for the coronavirus family have been described so far [15]. Among otoneurological symptoms, patients with hearing loss, tinnitus and dizziness have been reported. This situation may be directly related to neural tissue invasion or vasculitis [17]. Although the average of all frequencies was found within the normal limits in the hearing assessment of patients by audiological and TEOAE performed in patients who had had COVID-19 and recovered, a significant difference was found, especially at 4000 Hz and 8000 Hz, in comparison to the control group. Although the SSO value was 11.12 ± 5.78 dB for the right ear and 8.58 ± 5.32 dB for the left ear within normal limits, it was calculated higher than the control group. In the TEOAE results, no significant difference was found in the control group in the mean frequency measurements of 1000 Hz, 1400 Hz, 2000 Hz, 2800 Hz and 4000 Hz, but the mean values were found to be low at all frequencies. When we look at the published literature, sudden hearing loss was shown in a 67-year-old COVID-19 patient, and it was treated with steroids [18]. In another study, audiometry and TEOAE were performed on patients with asymptomatic COVID-19. Significant results were obtained at 4000 Hz, 6000 Hz and 8000 Hz in audiometry. The decrease in TEOAE was found to be significant in comparison to the control group [19]. These studies similarly supported the information that cochlear hair cells may be affected by COVID-19 infection. COVID patients may have disturbances in the vestibular system. In the VNG tests of the COVID-19 positive patients, pathological findings were found in 3 patients in the head shake test. In the vHIT test, the gain was found to be lower in all channels in comparison to the control group. The RALP and LARP symmetry among the vHIT asymmetry values were found to be significantly different in comparison to the control group. When we look at the saccades in vHIT, a significant difference between the groups was found only in the lateral canal. The fact that saccades were seen together with the losses in the VOR gains suggested that there was a significant influence in the semicircular canals or afferent ways [20]. In cVEMP, a significant difference was found based on the value of the control group in the asymmetry values. Additionally, a statistically significant difference was found between the groups’ P1, N1 and P1-N1 latencies and p1-n1 amplitudes. A significant difference was found in the asymmetry values in oVEMP, but no significant changes were observed in the amplitude and latency values. Changes in the cVEMP latencies and amplitudes of the patients with COVID suggested that COVID affects the brainstem and vestibulocollic arc and slows down the communication on the arc. These impacts were shown to occur in the retro-labyrinth lesions in the vestibulospinal pathway in the literature. The lack of large differences in the gain asymmetries in VEMPs revealed the importance of the compensation mechanism of the central vestibular system [21,22]. Moreover, the difference in the patients with COVID in the bedside tests drew attention to the effect of COVID on the vestibulospinal arc and postural balance. When we look at COVID-19 and vestibular system evaluation in the literature, in a study evaluating the vestibular system in 185 patients through online questions, balance disorders were detected in 34 patients after their diagnosis of COVID-19. Among these patients, 32 patients reported dizziness (94.1%), and 2 (5.9%) reported acute vertigo attacks. For balance disorders, the mean VAS score was calculated as 5 [17]. In another case report, a case of vestibular neuritis that could be associated with COVID-19 with nausea and vomiting was presented [23]. In another review article, vestibular complaints were reported in 7 patients diagnosed with COVID-19 infection, but a direct vestibular origin was not mentioned [24]. Although scientific knowledge on COVID-19 is increasing, the information in the audiovestibular literature is still limited. Researchers have not been able to address the life-threatening symptoms of COVID-19, as well as associated hearing and balance problems. The former members of the coronavirus family (MERS and SARS) have had effects on the hearing and balance system. SARS-CoV-2 may have direct neurological involvement or inner ear involvement due to widespread hypercoagulation recently seen in COVID-19 patients. Vascular involvement may be one of the clinical signs of COVID-19 such as various viral infections including hepatitis B and C vasculitis [25]. Audiovestibular system disorders may occur due to vascular damage because the inner ear is very sensitive to ischemia [26]. Primary and secondary vasculatures may be associated with hearing and vestibular symptoms [27]. This study is a comprehensive study which evaluated both the auditory and vestibular systems and included a control group. The vestibular system was evaluated with a large battery of tests. In terms of hearing, statistically significant results were obtained at higher frequencies in comparison to the control group. In the vestibular system, especially in oVEMP and cVEMP, asymmetric findings were obtained in comparison to the control group, and a low gain in vHIT was shown.

5. Conclusion

The high frequencies in audiometry in the COVID-19 positive group were worse than those in the control group. In the vestibular system, especially in oVEMP and cVEMP, asymmetric findings were obtained in comparison to the control group, and a low gain in vHIT was shown. This study shows that the audiovestibular system of people with COVID-19 infection may be affected. However, the support of this study with series with higher numbers of patients will be thanks to future studies.

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Acknowledgements

We would like to thanks, our patients who participated in our study for their contribution to the studies.

Funding

No financial supporter.

References

[1] Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet 2020;395:470–3.
[2] World Health Organization. WHO characterizes COVID-19 as a pandemic. March 11, 2020. Published.
[3] Johns Hopkins University and Medicine. Coronavirus resource center, https://coronavirus.jhu.edu/; 2020.
[4] Chaves S, Long B, Koyzman A, Liang SY. Coronavirus disease (COVID-19): a primer for emergency physicians [published online ahead of print, 2020 Mar 24]. Am J Emerg Med 2021;44:220-9.
[5] Chen G, Wu D, Guo W, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest 2020;130(5):2620–9.
[6] Wong SH, Lui RN, Sang JJ. Covid-19 and the digestive system. J Gastroenterol Hepatol 2020;35(5):744-8.
[7] Lechier JR, Chiesa-Estomba CM, De Sisti DR, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. Eur Arch Otorhinolaryngol 2020;277(1):2251-61.
[8] Giacomelli A, Pezzati L, Conti F, et al. Self-reported olfactory and taste disorders in COVID-19 patients in Italy: a national survey. J Neurol Sci 2020;411:116884.
[9] Román GC, Spencer PS, Reis J, et al. The neurology of COVID-19 revisited: a proposal from the environmental neurolgy specialty Group of the World Federation of neurology to implement international neurological registries. J Neurol Sci 2020;414:116894.
[10] Niazkar HR, Zibaee B, Nasimi A, Bahri N. The neurological manifestations of COVID-19: a review article. Neurol Sci 2020;41(7):1667–71.

[11] Ahmad I, Rathore FA. Neurological manifestations and complications of COVID-19: a literature review. J Clin Neurosci 2020;77:8–12.

[12] Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with Coronavirus disease 2019 in Wuhan China. JAMA Neurol 2020;77(6):683–90.

[13] Morisuchi T, Hori N, Goto J, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. Int J Infect Dis 2020;94:55–8.

[14] Özçelik Korkmaz M, Egilmez OK, Özçelik MA, Güven M. Otolaryngological manifestations of hospitalized patients with confirmed COVID-19 infection [published online ahead of print, 2020 Oct 3]. Eur Arch Otorhinolaryngol 2020:1–11.

[15] Sriwijitalai W, Wiwanitkit V. Hearing loss and COVID-19: a note. Am J Otolaryngol 2020;41(3):102473.

[16] Vaira LA, Salzano G, Deiana G, De Riu G. Anosmia and ageusia: common findings in COVID-19 patients. Laryngoscope 2020;130(7):1787.

[17] Viola P, Ralli M, Pisani D. Tinnitus and equilibrium disorders in COVID-19 patients: preliminary results [published online ahead of print, 2020 Oct 23]. Eur Arch Otorhinolaryngol 2020:1–6.

[18] Lamounier P, Franco Gonçalves V, Ramos HVL, et al. A 67-year-old woman with sudden hearing loss associated with SARS-CoV-2 infection. Am J Case Rep 2020;21:e927519.

[19] Mustafa MWM. Audiological profile of asymptomatic Covid-19 PCR-positive cases. Am J Otolaryngol 2020;41(3):102483.

[20] Jacobson GP. Balance function assessment and management. P hurl publishing; 2020.

[21] Murofushi T, et al. Diagnostic value of prolonged latencies in the vestibular evoked myogenic potential. Arch Otolaryngol Head Neck Surg 2001;127(9):1069–72.

[22] Heide G, et al. Brainstem representation of vestibular evoked myogenic potentials. Clin Neurophysiol 2016;127(7):1102–8.

[23] Malayala SV, Raza A. A case of COVID-19-induced vestibular neuritis. Cureus 2020;12(6):e8918. Published 2020 Jun 30.

[24] Almufarrij I, Uus K, Munro KJ. Does coronavirus affect the audio-vestibular system? A rapid systematic review. Int J Audiol 2020;59(7):487–91.

[25] Roncati I, Ligabue G, Fabbiani L, et al. Type 3 hypersensitivity in COVID-19 vasculitis. Clin Immunol 2020;217:108487.

[26] Ralli M, Campo F, Angeletti D, et al. Pathophysiology and therapy of systemic vasculitides. EXCLI J 2020;19:817–54.

[27] Ralli M, Di Stadio A, De Virgilio A, Croce A, de Vincentiis M. Autoimmunity and otolaryngology diseases. J Immunol Res 2018;2018:2747904.