RESEARCH ARTICLE
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Tinnitus, Equilibrium Disorders, and Anxiety in COVID-19

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ABSTRACT

Objective: Researchers have previously investigated the connection between COVID-19 and equilibrium disorders (ED) and tinnitus. The present study aims to investigate the prevalence of tinnitus and ED in people post-treatment after being positive for COVID-19 and the association of these symptoms with Anxiety and demographic features.
Material and methods: Patients from two tertiary hospitals with positive reverse transcription-polymerase chain reaction (RT-PCR) tests for SARS-COV-2 between August 2020 and May 2021 were contacted by phone. The recruited patients were asked to complete our questionnaire over the phone, a developed Turkish version of a previously applied '10-item close-ended questionnaire' by Viola et al.
Results: Sixty-two patients experienced ED before COVID-19 (8%). After COVID-19, the incidence of ED sufferers increased to 178 (22%), which was statistically significant (p=0.001).
110 (25.28%) of 435 female patients and 68 (18.37%) of 370 male patients had post-COVID ED. It was significantly more common in women among COVID-19 survivors (p=0.019).
The number of patients who experienced tinnitus before COVID-19 was 64 (7%) and 105 (13%) after COVID-19. It was found statistically significant that the tinnitus increased after COVID-19 (p=0.001)
Beck's Anxiety Inventory (BAI) scores were significantly higher in the post-COVID ED and post-COVID tinnitus sufferers (p=0.001, p=0.047).
Conclusions: COVID-19 survivors had significantly suffered tinnitus or ED. BAI scores were significantly higher in post-COVID ED and tinnitus sufferers. So, it can be said that the patients with high Anxiety experienced more tinnitus and ED post-COVID period.
Keywords: Tinnitus, balance, vertigo, COVID-19, Anxiety

INTRODUCTION

The clinical symptoms of COVID-19 include fever, sore throat, cough, myalgia, and gastrointestinal infection symptoms (1). Older people with comorbidity are more susceptible to infection and prone to severe outcomes (2).

Although symptoms seen in patients with COVID-19 are primarily related to the respiratory and cardiovascular systems, neurological symptoms, such as loss of consciousness, headache, smell, and taste changes, have also been reported (3, 4). In addition, Coronavirus-related otoneurological symptoms, such as tinnitus and balance disorders, have been described (5). Regarding balance disorders, vertigo or dizziness has been defined as a clinical manifestation of COVID-19 (6).

Dizziness is one of the most common neurological signs of COVID-19, which can be related to the neuroinvasive feature of SARS-Cov-2 (7).

Different researchers have previously investigated the connection between COVID-19 and equilibrium disorders (ED) and tinnitus, and a significant connection was found between COVID-19 and balance disorders tinnitus. It has also

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been demonstrated that COVID-19-related findings, such as vertigo, were more common in women over 60 (8). Tinnitus and vertigo can be related to vascular damage because the inner ear structures are more susceptible to ischemia due to their characteristics of terminal vasculature (5).

In light of the above information, the present study investigates the prevalence of tinnitus and equilibrium disorders in people after being positive for COVID-19 and evaluates the possible relationships of these symptoms with hospitalization, Anxiety, and demographic features.

MATERIAL AND METHODS

Başkent University Ethics Committee approved this study, and 805 patients from two different University Hospitals who had positive reverse transcription-polymerase chain reaction (RT-PCR) tests for SARS-COV-2 between August 2020 and May 2021 were contacted by phone. The questionnaire was applied to the patients after the COVID-19 diagnosis. Inclusion criteria were individuals aged 18 years or older without mental problems who had a positive RT-PCR test regardless of admission history after detecting COVID-19 and the severity of their presenting

Table 1: The Questionnaire

Part 1: Diagnosis and Treatment	
1)	What was your first complaint to apply hospital for COVID-19?
2)	Have you stayed in the hospital during your treatment?
3)	If the answer to the 2nd question is yes: How long did you stay in the hospital (days)?
4)	If the answer to the 2nd question is yes: Have you used anticoagulant or cortisone after you have been discharged from the hospital?
5)	If the answer to the 2nd question is no: Have you used aspirin or its derivative drugs during your outpatient treatment?
6)	Have you stayed in the intensive care Unit (ICU) during COVID-19?
7)	If the answer to the 4th question is yes, how long did you stay in ICU?
Part 2: Equilibrium disorders	
1)	Have you ever experienced vertigo before the COVID-19 diagnosis? (Yes/No)
2)	If the answer to the 1st question is yes, how would you describe the characteristics of your vertigo? A) Environment (world) was spinning B) I was spinning C) It was more like dizziness D) Feeling of unsteadiness
3)	Have you ever experienced vertigo after the COVID-19 diagnosis? (Yes/No)
4)	If the answer to the 3rd question is yes, how would you describe the character of your vertigo? A) Environment (world) was spinning B) I was spinning C) It was more like dizziness D) Feeling of unsteadiness
5)	Indicate the severity of your vertigo from 1 to 10.
6)	Have you experienced nausea or vomiting during vertigo attacks?
Part 3: Tinnitus	
1)	Have you ever experienced tinnitus before the COVID-19 diagnosis? (Yes/No)
2)	If the answer to the 1st question is yes, please select the following options that fit the characteristics of your tinnitus. A) Heartbeat B) High-frequency C1) Continuous C2) Discontinuous D1) Single ear D2) Both ears
3)	Have you ever experienced tinnitus after the COVID-19 diagnosis? (Yes/No)
4)	If the answer to the 3rd question is yes, please select the following options that fit the characteristics of your tinnitus. A) Heartbeat B) High-frequency C1) Continuous C2) Discontinuous D1) Single ear D2) Both ears
5)	Indicate the severity of your tinnitus from 1 to 10.
Part 4: Migraine and comorbidities	
1)	Do you suffer from migraines/Do you experience migraine headaches? (Yes/No)
2)	If the answer to the 1st question is yes, do you have vertigo during or after your migraine attack?
3)	Do you smoke?
4)	Do you have any known diseases?
5)	Do you have any regularly used medications?

symptoms. Exclusion criteria were previous ear, brain surgery, chronic ear infections, vestibular diseases, psychiatric comorbidity, and COVID-19 vaccination. Informed consent was obtained from all participants (Figure 1).

The recruited patients were asked to fill out our questionnaire over the phone, inspired by a previously applied '10-item close-ended questionnaire' by Viola et al. (5) and evolved by the senior author, a neurotologist working in a university hospital. The language of the questionnaire was Turkish.

The questionnaire consisted of four parts, each investigating a specific condition related to COVID-19, "initial symptoms and hospitalization history," "presence and characteristics of equilibrium disorder," "presence and characteristics of tinnitus," and "presence of migraine and comorbidities" was questioned (Table 1).

In the "presence and characteristics of equilibrium disorder" part, patients were asked to characterize the equilibrium disorder in detail, as if it was spinning (self/environment) or dizziness or unsteadiness. In the "presence and characteristics of tinnitus" part, patients were asked to characterize as pulsatile or high-frequency ringing, single or both sides and continuous or not. The severity of the symptoms was also noted in each part.

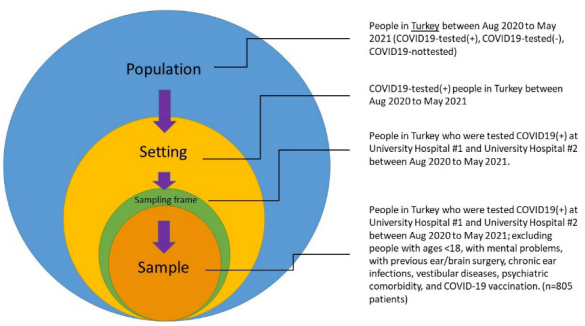

Figure 1: Target population and sampling frame

Statistical analysis

The severity of each condition was scaled from 1 (mild) to 10 (most severe). In addition to our questionnaire, the Beck anxiety scale was used to assess their anxiety levels (9). Beck anxiety inventory (BAI) is a self-reported scale that measures the level of Anxiety by scoring 21 items, which are mainly composed of somatic symptoms of Anxiety. The upper limit of the total score is 63 (10). The demographic data of the participants were recorded individually. The answers were recorded in the online Excel system, where access to the data was limited to the principal researchers.

At the end of the GPower 3.1.9.2 program analysis, when deciding the sample size, it was agreed to include 781 patients in the study for 81,0599 % statistical power (alpha: 0.05, beta: 0.20).

SPSS 25.0 package program was used for statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and continuous measurements as mean and standard deviation (in required parts median and minimum-maximum). Chi-square test or Fisher test statistics were used to compare categorical variables. In comparing continuous measurements between the groups, the distributions were controlled, and the dependent group t-test was used for the parameters that showed normal distribution according to the number of variables. The Mann-Whitney U test was used for the parameters that did not show normal distribution. In pre-and post-COVID-19 diagnoses, the Mc-Nemar test and intra-class correlation coefficient were used to analyze change. Binary logistic regression analysis was used to show the relationship between a dependent variable and independent variables. The statistical significance level was taken as 0.05 in all tests.

The reporting guideline that has been followed in this study was STROBE.

Table 2: Demographical Data

	n	$\bar{x}$± ±Std. Deviation	Median (IQR)	Min	Max
The interval between diagnosis and questionnaire presentation (days)	805	85.60±58.052	65 (96)	1	468
Age	805	40.77±14.441	39 (15)	18	95
ED Severity	193	5.52±2.494	5 (5)	1	10
Tinnitus Severity	122	4.93±1.976	5 (4)	1	10
Hospitalization (days)	81	9.31±9.68	6 (9)	1	67
ICU (days)	9	7.51±5.55	24 (21)	6	67
Beck's Anxiety Inventory Score	805	8.85±8.396	6 (9)	0	50

ED: Equilibrium Disorder, ICU: Intensive Care Unit, n: Number, Std: Standard deviation, IQR: Interquartile range, Min: Minimum, Max: Maximum

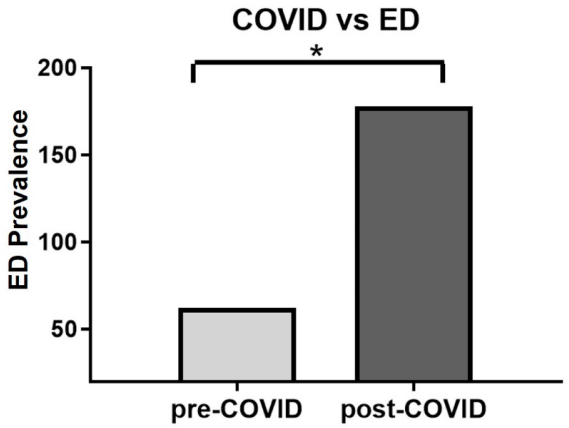

Figure 2: The Prevalence of Equilibrium Disorder pre- and post-COVID-19

RESULTS

There were 805 patients. Three hundred seventy were male (46%), and 435 were female (54%). The demographical data is shown in Table 2.

Sixty-two patients experienced ED before COVID-19 (8%). After COVID-19, ED sufferers increased to 178 (22%), which was statistically significant (p=0.001) (Figure 2). The characteristics of ED before and after COVID-19 are shown in Figure three.

The findings obtained in this study showed that 110 (25.28%) of 435 female patients and 68 (18.37%) of 370 male patients had post-COVID ED. ED was significantly more common in women among COVID-19 survivors (p=0.019).

It was found statistically significant that tinnitus increased after COVID-19 (p=0.001) (Figure 4). The number of patients who experienced tinnitus before COVID-19 was 64 (7%), and after COVID-19 was 105 (13%). The characteristics of tinnitus before and after COVID-19 are shown in Figure 5.

There was a statistically significant relationship between age and post-COVID ED (p=0.001) and post-COVID tinnitus (p=0.006).

There was a statistically significant relationship between age and BAI score with a positive correlation (13.3%) and between ED severity and BAI score with a positive correlation (21.3%) (p=0.001, p=0.003, respectively). BAI scores were significantly

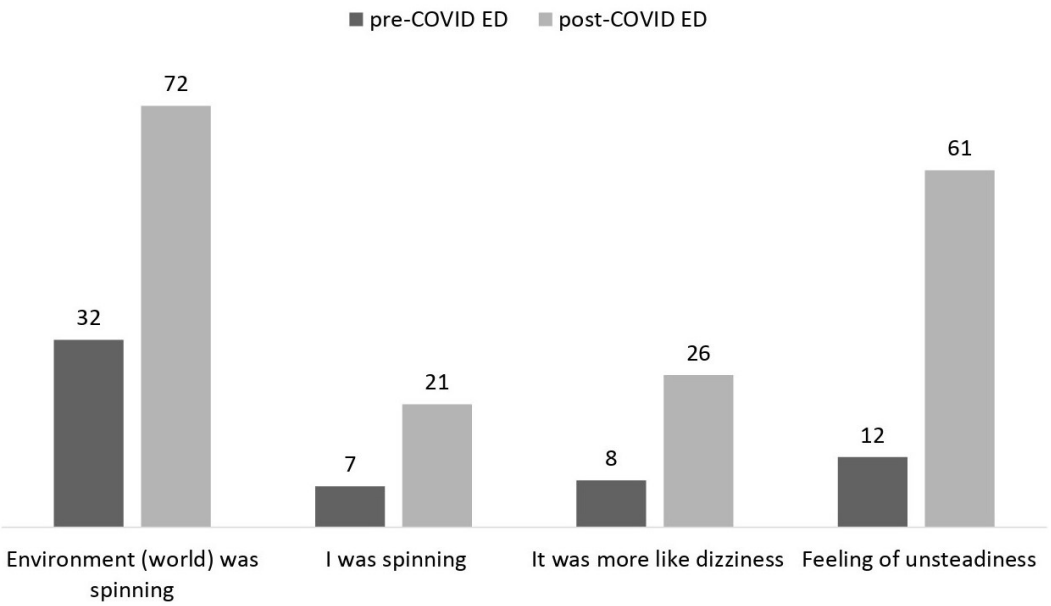

Figure 3: Characteristics of Equilibrium disorders before and after COVID-19

Table 3: Beck's Anxiety Inventory (BAI) Scores

Groups	BAI Score ±Std. Deviation	BAI Score Min-Max	BAI Score Median	*p*-value
Female	9.89±8.91	0-50	11	0.024
Male	7.64±7.58	0-48	7	
Pre-COVID ED (+)	12.02±9.01	0-33	11	0.001
Post-COVID ED (+)	13.84±9.96	0-50	14	
Pre-COVID Tinnitus (+)	12.16±7.98	2-41	11	0.047
Post-COVID Tinnitus (+)	13.44±10.06	0-50	13	
Migraine (+)	12.57±9.11	0-43	11	0.001
Migraine (-)	8.27±8.13	0-50	8	

ED: Equilibrium Disorder, STD: Standard deviation, Min: Minimum, Max: Maximum

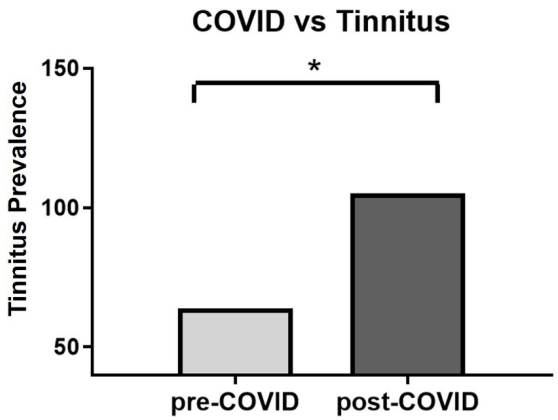

Figure 4: The Prevalence of Tinnitus pre- and post-COVID-19

higher in the post-COVID ED and post-COVID tinnitus sufferers; also, the scores were significantly higher in females and patients with migraine (Figure 6) (Table 3).

The number of patients with a migraine history was 110 (13.6%). There were statistically significant relationships between migraine and pre-COVID ED and post-COVID ED (p=0.012, p=0.002, respectively). In the non-migraine group, the number of patients with ED before COVID was 47, and it rose to 141 after COVID. Also, in the group with migraine, ED presented in 15 patients before COVID, which rose to 37 after COVID. There was no relationship between migraine status and tinnitus before and after COVID.

The number of hospitalized patients was 81 (10%), and intensive care unit patients were nine (1%). 342 (42.4%) of the patients who were not hospitalized had a history of aspirin in their treatment. Tinnitus was statistically more common in outpatients taking aspirin or its derivative drugs (p=0.004). Comorbid disease history was present in 115 (14%) patients, and 139 patients (17%) were smokers, and there was no statistically significant relationship between comorbidity or smoking history with post covid ED or tinnitus.

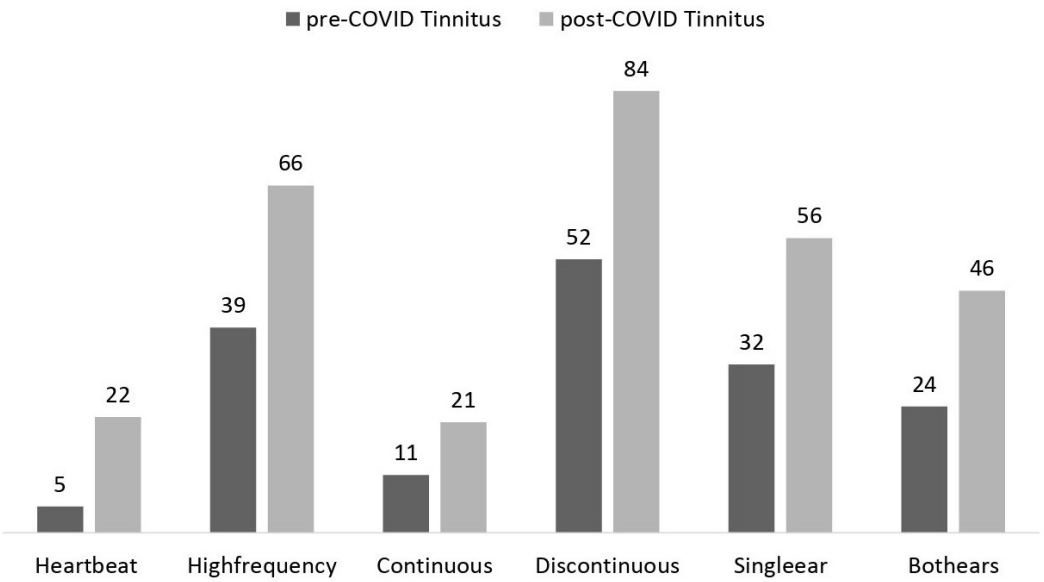

Figure 5: Characteristics of Tinnitus before and after COVID-19

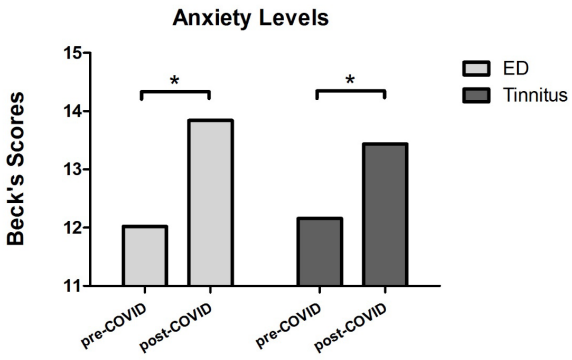

Figure 6: Beck's Anxiety Inventory Scores in Pre- and Post-COVID-19 Equilibrium Disorder and Tinnitus Sufferers

When we investigated the relationship between hospitalization and ED, post-COVID ED was observed in 26 (32%) hospitalized patients. The ED rates of hospitalized patients were significantly higher than non-hospitalized patients (p=0.014). When we looked at the post-COVID ED severity correlation, there was no statistically significant relationship with hospitalization. On the other hand, post-COVID tinnitus was observed in 16 (19.7%) hospitalized patients, and there was no statistically significant relationship between hospitalization and post-COVID tinnitus (p=0.42). However, there was a statistically significant relationship between hospitalization and tinnitus severity (p=0.001).

When we look at the logistic regression analysis, the equation was statistically significant (-2 LL=69.803; Cox & Snell R2=0.185; Nagelkerke R^2=0.249; *X*2=12.305 p=0.041).

Binary logistic regression analysis revealed that males were 3.514 times more affected than females from ED before COVID. In addition, the patients with lower BAI scores were unaffected by ED before COVID ($p< 0.05$). The other parameters did not have a significant effect.

DISCUSSION

Our survey study presented that; COVID-19 increases the prevalence of tinnitus and ED, negatively affecting the quality of life and increasing anxiety levels with advanced age. Hospitalization significantly increases the prevalence of ED. Migraine has a clear relationship with ED regardless of COVID. Some of our findings, the prevalence of ED in females with advanced age with COVID-19, were consistent with the literature (8, 11). The new findings were that; hospitalization significantly increased the prevalence of ED in COVID-19 survivors; the presence of migraine was significantly related to ED regardless of COVID, and BAI scores were significantly higher in females, patients with migraine, and the post-COVID ED and tinnitus sufferers.

Hospitalization could increase stress and Anxiety not only in COVID-19 patients but also in patients with severe illnesses that require hospitalization. Coping support interventions can alleviate psychological distress during hospitalization. These interventions could prevent severe and bothersome symptoms like tinnitus and ED in COVID-19 survivors. More evidence is needed to determine if such interventions benefit patients with COVID-19 during their hospitalization. Migraine is a multifactorial disorder, with genetic, hormonal, environmental, dietary, sleep, and psychological aspects playing different roles in each individual. Studies reported that mood and anxiety disorders are two to ten times more common in migraineurs than in the general population(12). Our study also showed a positive correlation between migraine and BAI scores.

Many studies have been conducted on clinical findings resulting from COVID-19, and dizziness has been accepted as a significant symptom (13-16). Mao et al.(7) have found neurological findings in 76 of 214 hospitalized patients with COVID-19. The most common symptoms in patients with CNS findings have been dizziness (16.8%) and headache (13.1%). In another study, dizziness has been more common in intensive care unit patients than in non-ICU patients (17). None of the survivors had dizziness as a presenting symptom in our study. On the contrary, most of the patients had presented with fever, sore throat, and headache simultaneously (75%), and 10% had presented with loss of smell and taste sensation. There was not any statistically significant relationship between presenting symptoms and post-COVID symptoms. Also, in the present study, true vertigo was more pronounced within ED disorders before and after COVID-19.

Waissbluth et al.(11) have observed an increase in the prevalence of benign paroxysmal positional vertigo after COVID-19. Compared to our study, their patients were generally younger and usually female. However, they have stated that the incidence by sex was not as striking as in the previous year.

In the study conducted by Özçelik et al., one hundred sixteen hospitalized patients with COVID-19 were questioned regarding otolaryngological symptoms associated with COVID-19. Additionally, clinical evaluations were conducted (8). The rate of otological/vestibular symptoms was dizziness (31.8%), tinnitus (11%), true vertigo (6%), and hearing impairment (5.1%), respectively. Unlike our study, these symptoms were observed more in patients under 60. Concerning gender distribution, dizziness was statistically higher in women in their study.

Freni et al.(18)used tinnitus handicap inventory (THI) on 50 patients with COVID-19. They applied the THI test to the patients twice after 15 days of RT-PCR SARS-COV-2 negativity. According to the results, tinnitus appeared or worsened in 10 patients (20%). In the second test, tinnitus persisted in five patients. They also evaluated hearing loss with Hearing Handicap Inventory for Adults. The current study showed that COVID-19 caused some deleterious effects on cochlear cell functions even if the disease process passed.

Li Xia et al.(19) have examined the relationship between Anxiety and tinnitus using a Self-Rating Scale system and have performed THI and test of loudness on the patients. During the COVID-19 Pandemic, they observed that tinnitus's severity increased in the presence of Anxiety, even if Sound Therapy and Educational Counselling treatment was performed. The first study confirmed Anxiety's causative/promotive role on tinnitus during COVID-19. Our study had a statistically significant relationship between tinnitus, ED, migraine, and BAI scores. Anxiety plays a critical role in these multifactorial symptoms in COVID-19 survivors.

Eldre Beukes et al. have conducted a systemic review of 33 studies published regarding tinnitus during COVID-19 (20). Twenty-eight studies have examined the effects of the Sars-Cov-2 virus; five studies have examined the impact of the Pandemic on tinnitus. COVID-19 impact studies have failed to find a consistent pattern of presentation of tinnitus or additional factors that may contribute to the development of tinnitus. For pandemic impact studies, it has been suggested that stress and Anxiety associated with the Pandemic consistently contribute to tinnitus experiences. Consistent with our study, they have underlined that stress affects the development of tinnitus.

Viola et al.'s study applied the online questionnaire to 185 patients with COVID-19 (5). Thirty-four (18.4%) stated they had an equilibrium disorder after COVID-19. Of these, 32 patients had dizziness, and two had acute vertigo attacks. Forty-two patients (23.2%) stated that they experienced tinnitus after COVID-19, and 14 (7.6%) experienced tinnitus and equilibrium disorders. This study was a survey study like ours.

Ototoxic drugs, such as azithromycin and hydroxychloroquine, frequently used in pandemics, may also be associated with equilibrium disorders. Post-COVID ED and tinnitus have been lately observed besides the COVID-19 findings. Considering the progression of the Pandemic, the number of these cases

will gradually increase; thus, the differential diagnosis of post-COVID ED from diseases, such as acute neuritis, should be made in the future. Since much data, including the pattern of balance disorder and the sound heard in tinnitus, may be helpful in further studies, the characteristics of ED and tinnitus and the effects on the individual should be examined in further studies.

Our study was a cross-sectional questionnaire study and had some potential limitations. Since we could not contact the patients face to face due to the Pandemic, we reached the patients through phone calls. Thus, clinical evaluation could not be performed. In addition, this was a survey study, and the data consisted of subjective patient-reported symptoms. Therefore, unpredictable factors, such as the patient's psychological state, could affect the data and the result of the study. Nevertheless, our survey consisted of a significant number of patients and the subjective symptoms like tinnitus and ED could be evaluated through questionnaires at some level. The number of patients evaluated in this study is the principal strength that helps us conclude.

CONCLUSIONS

COVID-19 survivors had significantly suffered tinnitus or ED with a positive correlation with age. Also, post-COVID ED was seen more in women than men. Hospitalization has significantly increased the prevalence of ED, and the presence of migraine before and after COVID-19 has a significant relationship with ED. Beck's Anxiety Inventory scores were significantly higher in female patients with migraine and post-COVID ED and tinnitus sufferers. It can be said that the patients with high Anxiety experienced more tinnitus and ED in the post-COVID period.

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Ethics Committee Approval: This study was approved by Başkent University Ethics Committee (Date: 28.04.2021, No: 21/81).

Informed Consent: Written informed consent was obtained.

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- S.E., D.T., S.N.B., D.T.D., P.D., P.K.; Data Acquisition- S.E., D.T., S.N.B., D.T.D., P.D.; Data Analysis/Interpretation- S.E., D.T., S.N.B., D.T.D., P.D., P.K.; Drafting Manuscript- S.E., D.T., S.N.B., D.T.D., P.D., P.K.; Critical Revision of Manuscript- P.K.; Final Approval and Accountability- S.E., D.T., S.N.B., D.T.D., P.D., P.K.

Conflict of Interest: The authors have no conflict of interest to declare.

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