



Neuro-otological Symptoms: An Atypical Aspect of COVID-19 Disease

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Abstract This study aimed to evaluate the various neuro-otological symptoms experienced by patients with COVID-19 disease. This is a retrospective study conducted from September 2020 to August 2021. Patients with positive RTPCR tests for COVID-19, aged between 18 and 60 years were included in the study. The patients were assessed for neuro-otological symptoms, the type, frequency, and character of these symptoms, their relation with age, gender and COVID-19 disease. Of the 286 patients, 64 (22.3%) had neuro-otological symptoms. The mean age of the patients was 36.3 ± 8.1 years. The frequency of neuro-otological symptoms was higher in females than males and was more frequent in the age group of 18–30 years as compared with other age groups. Of these 64 patients, 29 had vertigo (10.1%), 21 (7.3%) tinnitus, 16 (5.5%) experienced hearing loss. Like many viral diseases, apart from its typical prodromal symptoms, COVID-19 can also cause symptoms like tinnitus, hearing loss, and vertigo.

Keywords COVID-19 · Dizziness questionnaire · Vertigo · Tinnitus · Hearing loss

Introduction

In the realm of infectious diseases, a pandemic is the worst-case scenario. Several pandemics have emerged in the last two decades like Zika Virus, Middle East Respiratory Syndrome Coronavirus (MERS-CoV), Swine flu, Severe Acute Respiratory Syndrome (SARS) [1], COVID-19 disease is one such pandemic that barrelled through 180 countries to become a global pandemic and a public health emergency of international concern.

COVID-19 diseases, also called Severe Acute Respiratory Syndrome (SARS), was first identified in Wuhan, China. The onset of transmission is believed to have possibly started with bats, spread to cats and then to humans in China, followed by its spread across all borders [2, 3]. SARS characteristically manifests as a respiratory disease, generally 5 days after infection (1–14 days), with symptoms like dry cough, fever, headache, body aches and shortness of breath. Other symptoms can include: loss of taste or smell, headache, chest pain, conjunctivitis, nausea, vomiting, diarrhoea and rashes. It spreads through respiratory droplets and aerosols from coughs and sneezes [4–7]. The severity of COVID-19 symptoms can range from very mild to severe. Some people may have only a few symptoms, and some people may have no symptoms at all, also called asymptomatic and some people may experience worsened symptoms, such as worsened shortness of breath and pneumonia [4–7]. SARS-CoV-2 infection can also affect extrapulmonary, sensory, and neural systems, manifesting as sudden onset olfactory and/or gustatory dysfunction [8, 9], otologic symptoms [10–12], and neurological complications [13, 14]. It has been shown that the pathogenicity of SARS-CoV-2 is carried out by a surface receptor, angiotensin-converting enzyme 2, or ACE2 [15]. The ACE2 receptor is present on many cell of organs such

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as the heart, kidney, lung, central and peripheral nervous system and acts as a functional receptor for the virus [16].

While the virus is well-known for its trademark effects on respiratory function, neuro-otological damage has been reported to affect a considerable proportion of cases manifesting as vertigo, tinnitus, hearing loss [17]. The study aims is to describe uncharacteristic but not uncommon neuro-otologic manifestations of SARS-CoV-2 infection like vertigo, tinnitus, hearing loss and to study the prevalence and possible mechanisms of the onset of these symptoms.

Materials and Method

The retrospective study was conducted in the Department of ENT and HNS, GMC and SMGS hospital, Jammu from September 2020 to August 2021. Verbal consent was obtained from patients or their attendants. The study was performed in accordance with the principles of the Declaration of Helsinki. This study was approved by the Ethics Committee of our college.

Inclusion Criteria

The study group included 286 patients with a positive nasopharyngeal swab for COVID-19.

Exclusion Criteria

Hospitalization in Intensive Care Unit due to severe COVID-19 disease.

History of psychiatric or neurological disorders.

History of acoustic trauma.

History of prolonged noise exposure.

Presence of known audiological pathologies before the diagnosis of covid-19.

History of previous ear surgery.

History of treatment with chloroquine or hydroxychloroquine for their reported ototoxic effects.

Patients who refused to take part in the study.

Patients who were isolated in their homes were questioned by teleconsultation and patients who were admitted were questioned and examined by ENT doctors on COVID ward duty.

We used Dizziness Questionnaire provided by the House Ear Clinic [18].

Dizziness Questionnaire

- I. When you are “dizzy” do you experience any of the following sensations?
- | | | | |
|----|---|-----|----|
| 1. | Lightheadedness or swimming sensation in the head. | Yes | No |
| 2. | Blacking out or loss of consciousness. | Yes | No |
| 3. | Tendency to fall: | | |
| | To the right? | Yes | No |
| | To the left? | Yes | No |
| | Forward? | Yes | No |
| | Backward? | Yes | No |
| 4. | Objects spinning or turning around you. | Yes | No |
| 5. | Sensation that you are turning or spinning inside, with outside objects remaining stationary. | Yes | No |
| 6. | Sensation of the environment moving up and down while you walk. | Yes | No |
| 7. | Loss of balance when walking: | | |
| | Veering to the right? | Yes | No |
| | Veering to the left? | Yes | No |
| 8. | Headache. | Yes | No |
| 9. | Nausea or vomiting. | Yes | No |

- | | | | |
|-----|---|-----|----|
| 10. | Pressure in the head. | Yes | No |
| 11. | Palpitations, perspiration, shortness of breath, or a feeling | Yes | No |

II. Please check **yes** or **no** and fill in the blank spaces.

1. My dizziness is:
 - Constant?
 - In attacks?
2. When did dizziness first occur? _____
3. If in attacks: How often? _____
 - How long do they last? _____
 - When was the last attack? _____
 - Do you have any warning that the attack is about to start?
 - Do they occur at any particular time of day or night?
 - Are you completely free of dizziness between attacks?
4. Does change of position make you dizzy?
5. Do you have trouble walking in the dark?
6. When you are dizzy, must you support yourself when standing?
7. Do you know of any possible cause of your dizziness? What? _____
8. Do you know of anything that will:
 - Stop your dizziness or make it better? _____
 - Make your dizziness worse? _____
 - Precipitate an attack? _____
 - (Fatigue? Exertion? Hunger? Menstrual Period? Stress? Emotional? Upset?)
9. Were you exposed to any irritating fumes, paints, etc., at the onset of dizziness?
10. If you are allergic to any medications, please list: _

11. If you ever injured your head, were you unconscious?
12. If you take any medications regularly, for any reason, please list: _____

13. Do you use tobacco in any form? _____ How much? _____

III. Do you have any of the following symptoms?

- | | | | |
|---|---|-------|------|
| 1. Difficult in hearing? | Both ears | Right | Left |
| 2. Noise in your ears? | Both ears | Right | Left |
| 2a. How loud is your tinnitus or head noise most of the time? | | | |
| None | No head noise. | | |
| Very Soft | Heard only in a quiet situation. | | |
| Moderate | Heard only in an ordinary situation. | | |
| Loud | Heard and noticed in all situations, even when concentrating on something else. | | |
| 2b. Describe the noise | | | |
| 2c. Does noise change with dizziness? If so, how? | | | |
| 3. Fullness of stuffiness in your ears? | Both ears | Right | Left |
| 4. Pain in your ears? | Both ears | Right | Left |
| 5. Discharge from your ears? | Both ears | Right | Left |

IV Have you ever experienced any of the following symptoms? Please check yes or no and check constant or in episodes.

- | | | |
|--|----------|-------------|
| 1. Double Vision, blurred vision or blindness. | Yes | No |
| | Constant | In Episodes |
| 2. Numbness of face. | Yes | No |
| | Constant | In Episodes |
| 3. Numbness of arms or legs. | Yes | No |
| | Constant | In Episodes |
| 4. Weakness in arms or legs. | Yes | No |
| | Constant | In Episodes |
| 5. Clumsiness of arms or legs. | Yes | No |
| | Constant | In Episodes |
| 6. Confusion or loss of consciousness. | Yes | No |
| | Constant | In Episodes |
| 7. Difficulty with speech. | Yes | No |
| | Constant | In Episodes |
| 8. Difficulty with swallowing. | Yes | No |
| | Constant | In Episodes |
| 9. Pain in the neck or shoulder. | Yes | No |
| | Constant | In Episodes |
| 10. Seasickness or car sickness | Yes | No |
| | Constant | In Episodes |

Statistical Analysis

Microsoft Excel was used to evaluate the data. Statistics for all data were presented as mean ± standard deviation, number and percentages.

Results

There were neuro-otological symptoms in 64 (22.3%) of 286 patients. Of these 64 patients, 29 had vertigo (10.1%), 21 (7.3%) tinnitus, 16 (5.5%) experienced hearing loss (Fig. 1).

Demographics

Forty-five (70.3%) of the 64 patients with neuro-otological symptoms were females and 19 (29.6%) were males, with a male:female ratio of 2.3:1. These symptoms were seen at a higher frequency in females compared to males (Fig. 2).

The average age of the respondents was 36.3 ± 8.1 years. When patient with neuro-otological symptoms were divided into 5 age groups, it was revealed that the symptoms were mostly observed in the 18–30 years age group (Fig. 3).

Tinnitus

Twenty-one (7.4%) patients, 12 females and 7 males complained of tinnitus. The characteristics of tinnitus as described by the patient were as follows and shown in Figs. 4 and 5:

- 3 (14.2%) patients had tinnitus in both ears.
- 18(85.7%) patients had tinnitus in one ear.
- 17 (80%) had episodic.
- 4 (19%) had persistent.
- 11 (52.3%) had soft tinnitus (Heard only in a quiet situation).

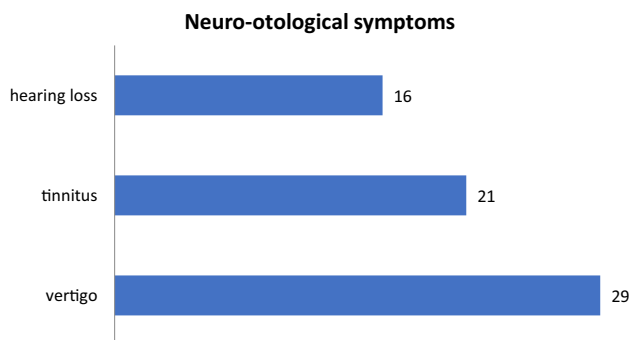


Fig. 1 Distribution of neuro-otological symptoms

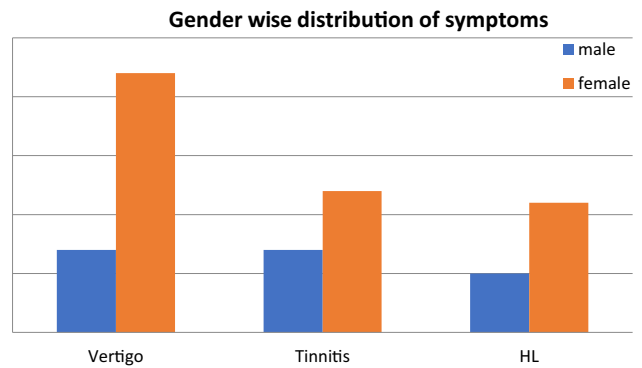


Fig. 2 Gender wise distribution of various neuro-otological symptoms

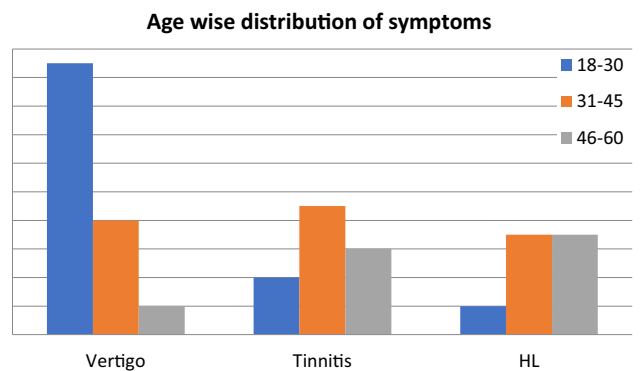


Fig. 3 Age wise distribution of neuro-otological symptoms

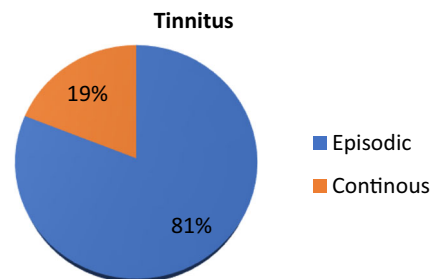


Fig. 4 Nature of tinnitus

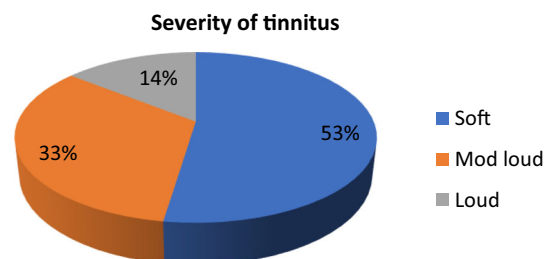


Fig. 5 Severity of tinnitus

- 7 (33.3%) had moderately loud tinnitus (Heard only in an ordinary situation).
- 3 (14.2%) had loud tinnitus (Heard and noticed in all situations).

Equilibrium Disorder

Ninety-two patients (32.1%) reported dizziness and out of these, 29 (31.5%) patients had vertigo according to the dizziness questionnaire used, out of which, 22 females and 7 males complained of vertigo. The features associated with vertigo as described by the patient were as follows and shown in Figs. 6 and 7:

- 13 (44.8%) experienced vertigo during the COVID-19 disease isolation.
- 16 (55.2%) patients experienced after 14 days of isolation.
- 23 (79.3%) had associated mild imbalance which was more significant during initial attacks.
- 22 (75.8%) had associated nausea and vomiting.
- 11 (37.9%) vertigo was triggered by a change in head position.

In 13 (44.8%) patients, initially, the duration of an acute attack of vertigo lasted for 3 h and then the intensity was gradually improved with consecutive episodes and in 16 (55.1%) patients it was limited to minutes.

Our patients did not show any other neurologic signs and symptoms (dysarthria, dysphagia, weakness, sensory loss, vision loss, loss of consciousness or facial droop) - based on the questionnaire.

Hearing Loss

Sixteen (5.5%) patients, 11 females and 5 males experienced reduced hearing after the COVID-19 diagnosis. The characteristics of hearing loss as described by the patient were as follows:

- 5 (31%) patients had reduced hearing in both ears.

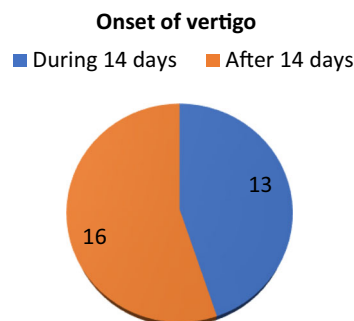


Fig. 6 Onset of vertigo

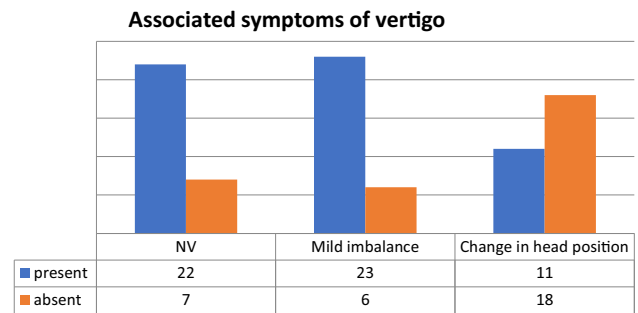


Fig. 7 Associated symptoms of vertigo

- 11(68.7) patients had reduced hearing in one ear.

Nine (14.6%) reported both vertigo and tinnitus, 11 patients (17.1%) reported both vertigo and hearing loss, 13 patients (20.3%) experienced both tinnitus and hearing loss and four patients (6.25%) reported all the three, after COVID-19 diagnosis.

Discussion

Coronaviruses (CoVs; family Coronaviridae, subfamily Coronavirinae) are enveloped, positive-stranded, RNA viruses having large genomes that are susceptible to recombination and mutations [19–21]. The mode of transmission of COVID-19 is through direct contact or respiratory droplets from an infected individual and indirect contact through fomites can also act as a vehicle of transmission [22]. As soon as the virus enters the body, the nuclear envelope is derived from the host cell's membrane. S-protein spikes (glycoprotein spikes embedded within that membrane) allow the cell to attach to a new cell and infect it [23]. S-proteins interact with the cell surface receptor, angiotensin-converting enzyme 2, or ACE2 [15]. The ACE2 receptor is present on cells of organs such as the heart, kidney, lungs, central and peripheral nervous system. S-Proteins contain an S1/S2 activation cleavage site that is activated by furin (serine endoprotease). Furin using its enzymatic activity causes irreversible cleavage of precursor proteins to enter their biologically active state. This furin autocleavage helps the S-protein's subunits to separate, and allow for the virus to enter host cells [15]. The interaction of the glycoproteins of SARS-CoV-2 to the ACE2 receptor cause subsequent cycles of viral replication, eventually leading to neuronal damage if neural tissues are involved [24]. Some viral infections are known to cause hearing loss like cytomegalovirus, rubella and measles precede sensorineural hearing loss [25, 26]. Most of them typically damaging inner ear cells [27]; however, some viruses can also affect the auditory brainstem [27]. Some studies have reported the role of some viral infectons in

vertigo pathogenesis as Epstein-Barr virus, cytomegalovirus, rubella virus, adenoviruses, influenza virus and herpes simplex virus [28].

It is often postulated that infection with neurotropic viruses can cause vestibular neuritis which occurs due to chronic inflammation of nerve. Also, vestibular nerve degeneration with sparing of the peripheral receptor structure has been suggested. Some authors opine that the superior vestibular nerve is more commonly involved in this disease as compared to the inferior one; this may be attributed to the longer and narrower bony canal traversed by the superior nerve, making it more susceptible to compressive swelling [29]. Direct vestibular nerve infection by the virus is a possible mechanism as proposed by some studies [30]. Milionis et al. linked vestibular neuritis to the increase in levels of Plasma fibrinogen and C-reactive protein (CRP) as a result of the inflammatory event of the viral infection [31]. Bumm et al. supported the immunological theory in vestibular neuritis pathogenesis. They detected the presence of T4 T-helper and T8 T-suppressor cells by specific monoclonal antibodies in inner ear diseases (e.g., vestibular neuritis, sudden hearing loss, Bell's palsy, and Meniere's disease) [32].

Coronavirus related neuro-otological symptoms, such as tinnitus and balance disorders, have been described [10, 23, 33–37], as neurotrophic and neuroinvasive capabilities are typical of some coronaviruses [38]. Moreover, a novel and interesting link between COVID-19 and newly diagnosed hearing loss, vertigo and tinnitus have been reported [12]. Some reports linked vertigo to post-covid infection [39, 40]. This association is not elucidated sufficiently and the published studies about it are few. The mechanism of vestibular neuritis in SARS-COV-2 is probably by viral or post-viral inflammatory disorder [41].

Demographics

Our study results are congruent with the previous study in regards with the demographics; neuro-otological symptoms were common in the young adult age group and in females.

Hearing Loss

Our results show 4.8% of the included patients had hearing loss, which is congruent with the previous studies. Hearing loss has been reported in previous studies [16, 23, 33, 38, 42–44]. Sriwijitalai and Wiwanitkit first reported neurosensory hearing loss in one patient (1.22%) out of 82 patients [38]. Elibol et al. studied 155 patients, out of which 89 (57.4%) patients had otolaryngological symptoms. Of these 89 patients, 2 (1.2%) tinnitus, 1 (0.6%) had Bell's palsy, 1 (0.6%) had sudden hearing loss problems [33]. These studies also provide no evidence

considering the severity (i.e., slight to profound) and the type of the hearing loss (i.e., sensory-neural hearing loss (SNHL), conductive hearing loss (CHL), or mixed hearing loss), or the potential pathology involved. A study by Mustafa et al. reported high-frequency pure tone thresholds and TEOAE amplitudes were significantly worse in COVID-19 patients [43]. Regarding the potential type of hearing loss, few case series [37, 45] and case reports [34, 45–48] have reported SNHL as the type of HL in COVID-19 patients and theorized that it results from the direct impact of SARS-CoV-2 on the organ of Corti, stria vascularis, and/or spiral ganglion [43, 49].

Vertigo

Dizziness is an umbrella term in medicine that is classified using patients' history into vertigo, disequilibrium, presyncope, and lightheadedness [50, 51]. Vertigo is a false sensation of whirling or rotation originating from the vestibular system, the main causes of vertigo are benign paroxysmal positional vertigo, Ménière's disease, vestibular neuritis, and labyrinthitis [52]. Disequilibrium is feeling off-balance or wobbly, the main causes are Parkinson's disease and diabetic neuropathy. Presyncope is the feeling of losing consciousness or blacking out. Lightheadedness is feeling disconnected from the environment, is commonly associated with psychogenic or psychiatric origins such as anxiety, depression, and somatoform disorders [53]. The inner ear structures are susceptible to ischemia and vascular damage, which eventually leads to auditory and balance dysfunction [41]. It has been studied that vasculitis also is one of the clinical manifestations of COVID-19 [54] which can be a possible mechanism of auditory and balance dysfunction.

Vestibular neuritis or acute peripheral vestibulopathy is a viral or post-viral inflammatory disease, which involves the vestibular part of the eighth cranial nerve [55]. The disease is clinically diagnosed with vertigo and develops acutely over minutes to hours, accompanied by nausea and vomiting, possibly due to irritation of the emetic tracts which are in proximity with the vestibular nerve/nuclei [56].

In our study, vertigo was present in 9.4% of cases which is similar to the percentage of vertigo reported in some studies [11, 16, 43, 58] but some studies have results incongruent with ours [42, 57, 58]. Various case reports [37, 39, 59–63] have been published describing acute vertigo attacks in COVID-19 patients. Viola et al. did a multicentre study that included 15 hospitals using an online 10-item close-ended questionnaire developed to identify the presence of tinnitus and balance disorders in patients with COVID-19. Thirty-four patients (18.4%) reported equilibrium disorders after the COVID-19 diagnosis. Of

these, 32 patients reported dizziness (94.1%) and 2 (5.9%) reported acute vertigo attacks. Forty-three patients (23.2%) reported tinnitus; 14 (7.6%) reported both tinnitus and equilibrium disorders [42]. Some authors have presented results different from ours like Panda et al., who evaluated 145 patients with mild COVID-19 to report that 96 patients (66.2%) had ENT manifestations, out of which 7 (1%) patients accounted for vertigo [57]. Picciotti et al. studied eight patients (4 F, 4 M, aged between 44 and 69 years) with COVID-19 infections complaining of vertigo and concluded the cause to be benign paroxysmal positional vertigo (BPPV). He has stated that vestibular evaluation showed involvement of posterior semicircular canals in five patients and horizontal in three. They hypothesized that BPPV in COVID-19 infections can be related to drugs, prolonged bed rest and direct damage by a viral infection on the peripheral vestibular system and in particular on the otolithic membrane due to the cytopathic effect of the virus and to the inflammatory response [58]. Mao et al. studied 214 hospitalized patients with laboratory confirmed diagnosis of severe acute respiratory syndrome coronavirus-2 infection, 78 patients (36.4%) had neurologic manifestations, out of which 36 (16.8%) had dizziness however, they have not described the type or cause of dizziness [14]. Han et al. has reported a case study of a 47-year-old man who came to the emergency department with a chief complaint of fever, cough, stuffy nose, nausea and vertigo. [59]. Karam et al. reported a case study of 60-year-old diabetic and hypertensive female patient with a 9-days history of COVID-19 symptoms who presented to the emergency department with acute vertigo attack without nausea or vomiting [60].

Tinnitus

In our study, tinnitus was present in 7.4% of cases which corresponds to the percentage reported in few studies [11, 16, 23] but some studies have results incongruent with ours [7, 33, 42, 57, 64]. Elibol et al., Lechien et al. and Kardas et al. have reported tinnitus in 1.2, 0.3 and 2% while Viola et al. has reported 23.2% cases complaining of tinnitus. Tinnitus in patients with COVID-19 has been attributed to SARS-CoV-2 on the auditory system and also to the anxiety caused by the unpredictability of the disease [65].

Limitations of the Study

Our study has several limitations which may have affected the outcome of the study. It has a small population size as compared with some other studies which have done multicentric research over a larger geographical area. We have not assessed the type of hearing loss and have not

compared the severity of COVID-19 with neuro-otological symptoms. Also, the patients who were home isolated during the COVID-19 infection could not be assessed and evaluated clinically.

Conclusion

COVID-19 is a viral infection that affects respiratory, gastrointestinal, cardiac and nervous systems varying from person to person. There is no doubt it primarily affects the respiratory tract but this study along with many other studies prove the diverse manifestations of COVID-19, among which include vertigo, tinnitus and hearing loss. This is the first study from our region focussing only on neuro-otological symptoms of COVID-19 and unlike many other studies; we have not used online reporting forms. We have used the teleconsultation facility of our department for home isolated patients and the hospitalized patients were assessed by ENT surgeons on COVID duty.

Authors' Contributions All authors contributed to the study conception and design. Material preparation, data collection, analysis and the first draft of the manuscript was written by Dr. Faizah Deva and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

Conflict of interest None.

Ethics Approval Approval was obtained from the ethics committee of our college. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

Consent to Participate Informed consent was obtained from all individual participants included in the study.

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