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Original Research Article

Oto-neurological manifestation in post COVID-19 patients: a randomized prospective observational study

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ABSTRACT

Background: The corona virus disease (COVID-19) is caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) and is characterized by symptoms of the lower respiratory tract involvement, such as fever, cough, dyspnea, and chest heaviness. Sensorineural hearing loss (SNHL) is most frequent audio-vestibular symptom described, occurring alone or in association with tinnitus and vertigo.
Methods: This study was conducted in COVID-19 tertiary care center Prayagraj. COVID-19 positive patients who were included in moderate to severe category were taken up for the study and data was collected from 1st June 2021 to 1st July 2022 for audiological assessment and presence of equilibrium disorder. All patients were investigated on basis of closed ended questionnaire.
Results: Out of 1000 patients incidence of ear heaviness was found in 3.3%., decreased hearing in 0.9%., tinnitus in 1.9%., equilibrium in 0.4% and migraine in 0.4%, which was higher as compared to the normal population but not significant.
Conclusions: SARS-CoV-2 infection may cause thrombosis in audiovestibular artery and may alter the blood flow in cochlea and vestibule and cause otoneurological manifestation.

Keywords: COVID-19, SNHL, Tinnitus, Dizziness, Thrombosis

INTRODUCTION

The Coronavirus disease 2019 (COVID-19) is caused by SARS-CoV-2. SARS-CoV-2, an RNA virus of the subgenus *Sarbecovirus*, identical to SARS, and the seventh member of the human coronavirus family is the causal organism for this zoonotic infection. It induces constitutional and respiratory symptoms by binding to the human angiotensin converting enzyme (hACE-2) receptor. The median incubation period is 4 days and the major mode of transmission is human-to-human.[1] COVID-19 was declared a pandemic by word health organization (WHO) on March 11, 2020.

The COVID-19 is characterized by symptoms of the lower respiratory tract, such as fever, cough, dyspnea, and chest heaviness, which can quickly advance to ARDS.[2] However, COVID-19 also causes different upper respiratory tract related symptoms including nasal congestion, sore throat, and smell dysfunction.[3] The neurotrophic characteristics of SARS-CoV-2 are still being investigated; genome sequences were detected in the brain of affected patients, with evidence of some pathological changes in hypothalamus and cortex neurons and in the cerebrospinal fluids.[4-6] Various neurological manifestations such as impaired consciousness, headache, and dizziness have been reported in COVID-19; in addition, olfactory and taste alteration are common symptoms in COVID-19 affected patients.[7-11]

SNHL is the most frequent audio-vestibular symptom described, occurring alone or in association with tinnitus and vertigo. The etiopathogenesis of the inner ear diseases related to COVID 19 infection is still poorly understood. COVID-19 patients who reported audiovestibular disorder are on the rise; even though the

quantity of study is insufficient, the audio-vestibular disorder should still be considered as a possible symptom.[12]

The damage of the audio-vestibular system during SARS-CoV2 infection could be related to direct impairment of inner ear structure or a virus-mediated immunological response. Blood vessels, lymphatic system, nerves and in some cases meninges have been proposed as an entry route for the viruses.[13] Neuroimaging (MRI) of 10 out of 20 patients with audio vestibular disorder revealed a clear inflammatory process of the inner ear in two of them, in one case bilateral, supporting the hypothesis of a direct cochlear and labyrinthine damage.[14]

There is growing evidence of study about neurological and audio-vestibular involvement of SARS CoV-2 but oto-neurological subjective symptoms such as tinnitus and balance disorders have been marginally investigated till now.

Etiopathogenesis of otoneurological damage

An alteration of coagulation rate could cause a macro and/or micro thrombosis, with consequent transitory ischemia and hypoxia in the auditory pathways determining the onset of hearing alterations.[15] The thrombus can occlude the cochlear-vestibular artery or one of its afferent vessels, could determine transitory SSNHL or in case of extremely rapid resolution, slight hearing impairment, or tinnitus. However, despite the rapid resolution, transitory hypoxia into the cochlea could stress the inner ear cells and increase the concentration of reactive oxygen species (ROS) that could be responsible for additional damage of the hair cells. On the other hand, a thrombus in one of the vessels of the superior auditory pathways can determine central hearing loss.[16] Moreover, the presence of vertigo/dizziness in patients with COVID-19 could have the same etiopathogenesis; in fact, thrombosis in the audio-vestibular artery may alter the blood flow both in the cochlea and the vestibule explaining the presence of these symptoms.[17,18]

Thus, we aim to investigate the prevalence of otological symptoms (heaviness, decreased hearing, tinnitus) and equilibrium disorders (dizziness and vertigo) in COVID-19 patients through an online questionnaire.

Aims and objectives

Aim and objective were to investigate audio-vestibular symptoms in post COVID-19 patients in tertiary care center (MLN medical college, Prayagraj).

METHODS

This study was conducted in M L N medical college, Prayagraj, Uttar Pradesh, which was tertiary COVID-19 care center. COVID-19 positive patients with the history consistent with moderate to severe category of disease were included in the study and data was collected from 1st June 2021 to 1st July 2022 for audiological assessment and presence of equilibrium disorder. This study was done in government organization so there was no external funding.

Inclusion criteria

Non-diabetic patients with a positive nasopharyngeal swab for SARS-CoV-2, (between 30 days and 70 days of first positive swab) and patients with moderate to severe symptoms according to symptom severity of COVID-19 infection were included in the study.[19]

Exclusion criteria

History of previous ear disease (otitis media) and ear surgery, history of use of ototoxic medication, current use of hydroxychloroquine with their reported side effect, patient on invasive ventilatory support and patients with comorbidity (Diabetes, hypertension, tuberculosis and malignancy) were excluded from the study.

Symptom severity of COVID-19 infection[19]

Mild: Mild clinical symptoms meeting case definition for COVID-19 without evidence of viral pneumonia or hypoxia.

Moderate: Adolescent or adult shows lower respiratory disease on clinical assessment (fever, cough, dyspnea, fast breathing or imaging and who have saturation Spo2≥ 90 on room air but no sign of severe pneumonia.

Severe: Adolescent or adult having clinical sign of pneumonia plus any one of the criteria. 1. Severe respiratory distress, 2. SpO_2<90% on room air and 3. Respiratory rate >30 breath/minute.

*Patients showing a rapid progression (>50%) on CT imaging within 24-48 hours should be managed as severe.

Critical: Onset within one week of clinical insult (pneumonia) or new or worsening respiratory symptoms. 1. Respiratory failure, need mechanical assistance and 2. Shock.

"Extra-pulmonary" organ failure, intensive care unit is needed.

All patients included in our study gave informed consent for participating in the study and data provided in the responses to the questionnaire.

Questionnaire details

Questionnaire was designed and responses were collected telephonically. Responses recorded in an online excel spread sheet. Questionnaire composed of 5 parts, each

one investigating a specific condition and its association with COVID-19; (1) Ear fullness or heaviness, (2) Decreased hearing, (3) Presence and characteristic of tinnitus, (4) Presence and characteristic of equilibrium disorder and (5) Presence/ absence of migraine.

All patients were investigated on basis of closed-ended questionnaire as shown below and were included in the study considering the inclusion-exclusion criteria.

Closed ended questionnaire

Part 1: Ear complaints

Ear discharge

Have you ever experienced ear discharge before COVID-19 diagnosis? (Yes/No) Have you experienced ear discharge after diagnosis of COVID-19? (Yes/No)

Ear fullness/heaviness/pain

Have you ever experienced Ear fullness/ heaviness/ pain before COVID-19 diagnosis? (Yes/No). Have you experienced Ear Fullness/Heaviness/Pain after diagnosis of COVID-19? (Yes/No)

Decreased hearing

Have you ever experienced decreased hearing before COVID-19 diagnosis? (Yes/No). Have you experienced decreased hearing after diagnosis of COVID-19? (Yes/No)

Part 2: Tinnitus

Have you ever experienced tinnitus before COVID-19 diagnosis? (Yes/No). Have you started experiencing tinnitus after diagnosis of COVID-19? (Yes/No).

If yes, please specify characteristics of your tinnitus (occasional/ continuous floating/ persistent/ pulsatile/ continuous.

Part 3: Equilibrium disorders (vertigo/dizziness)

Have you ever experienced vertigo/dizziness before COVID-19 diagnosis? (Yes/No). Have you started experiencing dizziness/ vertigo after diagnosis of COVID-19? (Yes/No).

If yes, please describe characteristics of your symptoms (violent vertigo attacks/ chronic dizziness/instability).

Part 4: Migraine

Do you suffer from migraine prior to diagnosis of COVID? (Yes/No). Have you experienced migraine after the diagnosis of COVID? (Yes/No).

If yes: Is the pain associated in half portion of head? (Yes/No). Pain is associated with intolerance to light or sound? (Yes/No) and does vomiting starts before or after onset of headache? (Yes/No).

RESULT

A total no. of 1040 patients with no h/o diabetes data collected by on line telephonic survey. The maximum number of patients in this survey (Figure 1) belonged to 40-50 year of age groups. Male:female-1.9:1 (668:332). Out of total 1040 patients 744 belongs to moderate and 296 belongs to severe symptoms (Figure 2).

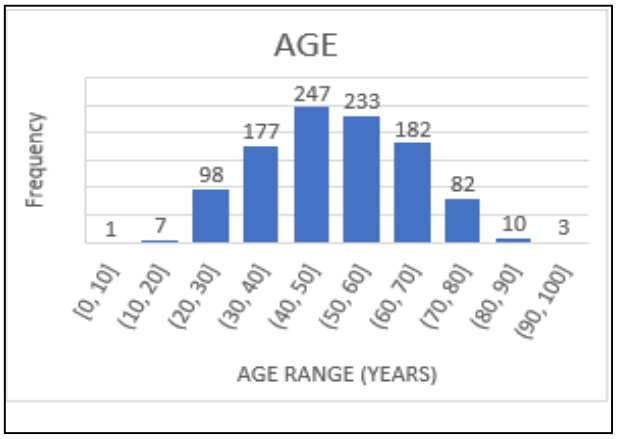

Figure 1: Age distribution of patients.

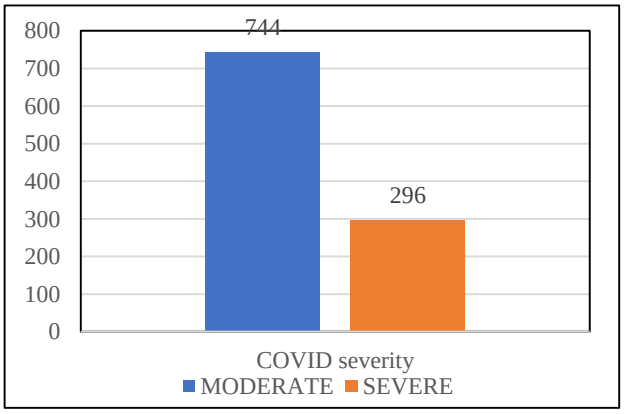

Figure 2: COVID severity amongst COVID-19 positive patients (n=1040).

In our study (Table 1) out of 1040 non-diabetic COVID-19 patients with moderate to severe illness, 1000 patients were studied on basis of closed-ended questionnaire by a telephonic survey. 40 patients were excluded from the study out of which 8 patients were diagnosed as early diabetics, 5 patients had a past history of ear disease, 2 patients had a history of ear surgery, 4 patients had a history of use of ototoxic medication, 1 patient had a history of anti-tubercular drug treatment, while 20 patients were having multiple systemic illnesses. Hence, 40 patients were excluded from our study i.e. For a total of 1000 patients further, detailed study was done.

Table 1: Comparative study of oto-vestibular symptoms before COVID-19 and after one month from COVID-19 infections.

Symptoms	Before COVID (out of 1000)		After 1 month of COVID (out of 1000)	
	Yes	No	Yes	No
Ear heaviness/ fullness/ pain	08	992	33	967
Decreased hearing	05	995	09	991
Tinnitus	Occ (2) Pul (0) Per (0) Cf (1) Cont. (1)	996	Occ (13) Pul (3) Per (2) Cf (0) Cont. (1)	981
Equilibrium	Vva (1)	999	Cd (3) Vva (1)	996
Migraine	Hemi (0) Ha (1)	999	Hemi (2) Ha (2)	1037

The maximum of cases before COVID-19 and after COVID-19 were asymptomatic. Out of 1000 patients 8 patients suffered from ear heaviness, 5 patients had decreased hearing, 4 patients had tinnitus,1 patient had dizziness and 1 patent had migraine before COVID-19 infection. Whereas after one month of COVID-19 patients 33 patients suffered from ear heaviness, 9 patients decreased hearing, 19 patients with tinnitus, 4 patients with dizziness and 4 patients suffering with migraine.

COVID-19 positive patients with a history of moderate to severe category of symptoms were included in the study and data was collected for audiological assessment and presence of equilibrium disorder.

In our study, the following observation was recorded.

Table 2: Incidence of ear heaviness in the post-COVID.

Gender	Diseased	Non-diseased
Male	21	647
Female	12	320

According to Fischer exact test p=0.709 (Statistically not significant) i.e., incidence of ear heaviness was higher as in post COVID-19 compared to before the COVID-19 infect.

Table 2: Incidence of decreased hearing in post-COVID.

Gender	Diseased	Non-diseased
Male	06	662
Female	03	329

According to Fischer exact test p=1.00 (Statistically not significant) i.e., incidence of decreased hearing was higher as in post COVID-19 compared to before COVID-19 infection.

Table 3: Incidence of tinnitus in post-COVID.

Gender	Diseased	Non-diseased
Male	12	656
Female	07	32

According to Fischer exact test p=0.80 (Statistically not significant) i.e., incidence of tinnitus was higher as in post COVID-19 compared to before COVID-19 infection.

Table 4: Incidence of equilibrium disorder in post-COVID.

Gender	Diseased	Non-diseased
Male	1	667
Female	3	329

Fischer exact test, p=0.950 statistically not significant.

Table 5: Incidence of migraine in post-COVID.

Gender	Diseased	Non-diseased
Male	1	667
Female	3	329

Fischer exact test, p=0.109 statistically not significant.

Incidence of ear heaviness=3.3%, incidence of decreased hearing=0.9%, incidence of tinnitus=1.9%, incidence of equilibrium=0.4% and incidence of migraine=0.4%.

DISCUSSION

This study was performed to evaluate the symptomatic effect of COVID-19 oto-vestibular system before COVID-19 and after one month from COVID-19 infection and to compare the outcome. It has been observed that viral infections are a known cause of hearing loss, mostly by damaging inner hair cells; however, some viruses can also affect the auditory brain stem.[20,21] As neurotrophic and neuro-invasive capabilities are typical of some coronaviruses, previous studies on other coronavirus infections showed a brain involvement, focusing attention on the possible neuro-auditory impairment following this infection.[22-24]

CONCLUSION

In our study audio vestibular symptoms were found to be more common amongst post COVID-19 patients as compared to the general population but there is no significant difference in the incidence of the audio vestibular symptoms. This may be due to SARS-CoV-2 infection may causing thrombosis in audiovestibular artery and may alter the blood flow in cochlea and vestibule and cause otoneurological manifestation.

Limitation

Our study is based on subjective feedback of patients; some patient gives poor response based on questionnaire.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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