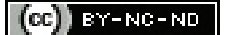


Audiological Assessment in Post COVID-19 Patients- A Cross-sectional Study

ANGELA GRACE ABRAHAM¹, RB NAMASIVAYA NAVIN², S PRABAKARAN³, S RAJASEKARAN⁴

ABSTRACT

Introduction: Hearing loss following a viral infection is a common entity. In recent studies, hearing loss has been seen among Coronavirus Disease 2019 (COVID-19) infected patients, but its association is yet to be established.

Aim: To determine the presence of hearing loss and its type in patients after COVID-19 infection.

Materials and Methods: A cross-sectional study was conducted at a tertiary health centre, Department of Otorhinolaryngology at Chettinad Academy of Research and Education, Chettinad Hospital and Research Institute, Chennai, from October 2021 to April 2022. Total of 125 patients, who had a positive history of COVID-19 infection, were reviewed in the Otorhinolaryngology Department, one month after they were tested Real Time-Polymerase Chain Reaction (RT-PCR) positive. After obtaining proper clinical history and examination, Pure Tone Audiometry (PTA) were done. Audiological report was assessed and analysed. Qualitative variables will be expressed in proportions and quantitative variables in Mean±SD/Median (IQR), Chi-square test was applied.

Results: This study included 65 (52%) males and 60 (48%) females, and the mean age was 38.44±10.9 years. Among the 125 patients, 12 (9.6%) were diabetic, 14 (11.2%) were hypertensive, 5 (4%) had dyslipidaemia, 3 (2.4%) were hypothyroid, while remaining 91 patients (72.8%) had no co-morbidities. Sensorineural Hearing Loss (SNHL) was found among 45 patients (34 with unilateral and 11 with bilateral involvement). Out of them, 2 (4.5%) were in the age group of 18-30 years, 19 (42.2%) in 31-45 years and 24 (53.3%) between 46-60 years age group. Based on the World Health Organisation (WHO) classification of hearing loss, 27 patients had mild sensorineural hearing loss, 12 patients with moderate, and six patients with moderately severe sensorineural hearing loss.

Conclusion: SNHL were found among patients who had COVID-19 infection, but due to the absence of a pre COVID-19 documented audiogram, it was difficult to conclude whether the hearing loss had occurred due to COVID-19, pre-existing hearing loss, or age-related. Further studies are required for proper understanding and correlation.

Keywords: Coronavirus disease 2019, Pure tone audiometry, Sensorineural hearing loss, Viral infections

INTRODUCTION

Hearing is one of the sensory perceptions that can get affected due to various factors such as infective, inflammatory, traumatic, or neoplastic. Some may present as congenital or idiopathic. Viral infections is one such cause that is known to affect hearing. Viruses belonging to the Herpesviridae family (such as *herpes simplex virus (HSV)*, *varicella zoster virus (VZV)*, *cytomegalovirus*), Paramyxoviridae (including *measles virus*, *mumps virus*, *rubella virus*), hepatitis virus and human immunodeficiency virus have been known to affect the audiovestibular system. According to recent discoveries, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus has been reported to cause hearing impairment among few populations [1].

Over the past two years, a novel coronavirus (SARS-CoV-2) has been infecting populations worldwide. Initially it was considered an acute respiratory disease with symptoms such as fever, myalgia, cough, sore throat and dyspnoea, and later was found to affect the neurological system, cardiovascular system, and gastrointestinal system [2,3]. Unlike anosmia and dysgeusia which were the common symptoms experienced by certain people during the epidemic, hearing loss have also been reported in many cases. However, hearing loss related to (SARS-CoV-2) infection is still under discussion [3].

Hearing loss may be conductive, sensorineural, and mixed type. Conductive hearing loss in a viral infection occurs as a result of middle ear effusion. However, virally induced hearing loss most commonly presents as a sensorineural hearing loss. Mechanism of sensorineural hearing loss during viral infection remains unclear but certain theories

have been postulated on either direct or indirect injury to the structures in the inner ear. An immune-mediated response can result in cytokine release, which further triggers an immune reaction, thereby damaging the inner ear structures. Ischaemic theory is another cause where there is a decrease in blood flow through the labyrinthine or cochlear artery leading to ischaemia and hearing loss [1,2,4]. Umashankar A et al., defined sudden sensorineural hearing loss as a sensorineural hearing loss of 30 dB or greater over at least three contiguous audiometric frequencies occurring over 72 hours. Unilateral presentation is seen more often but there are cases reported with bilateral involvement [5].

A recent meta-analysis reported a prevalence of 7.6% of hearing loss among patients with COVID-19 in association with audiovestibular symptoms [6]. Age, gender, co-morbidities, smoking or alcohol consumption have been assessed to determine a correlation, but only few studies have found such an association [7,8]. Hence, this study aimed at assessing the hearing of post COVID-19 infected individuals, to evaluate the presence and type of hearing impairment and to find any association of hearing loss with age, gender or co-morbidities.

MATERIALS AND METHODS

A cross-sectional study was conducted in the Department of Otorhinolaryngology at Chettinad Academy of Research and Education, Chettinad Hospital and Research Institute, Chennai, from October 2021 to April 2022. The Ethical Committee had approved the study vide letter number- IHEC – 1/0014/ 21.

Sample size calculation: Kilic O et al., reported that 40% of the patients had hearing loss in right ear [9]. Considering it as the

prevalence, with 95% confidence interval, the allowable error of 9%, the sample size was calculated as,

$$n = Z^2 pq / I^2$$

$$n = (1.96)^2 \times 40 \times 60 / (9)^2 = 114$$

The sample size was 114. To account for a non response rate of 10% (11), 125 participants (250 ears) were included in this study.

Inclusion criteria: Patients who had COVID-19 infection, and had come for follow-up in the Department of General Medicine, one-month postinfection were asked to review in the Otorhinolaryngology Department for audiological assessment. According to the National Institutes of Health (NIH) guidelines [10], patients who were either asymptomatic or those who had the milder form of the illness were selected. A total of 125 patients were included, between the age group of 18-60 years.

Exclusion criteria:

- Patients with pre-existing hearing loss based on the previous audiogram report or those using hearing aids,
- Patients with middle ear infections, tympanic membrane perforation that were identified by otoscopic examination,
- Patients who are on long term ototoxic drugs, renal failure,
- Industrial workers exposed to loud noise,
- Patient who did not give consent for the study were excluded.

Study Procedure

Patients were made aware about the purpose of the study and after obtaining informed consent, they were included in the study. Based on the proforma, a thorough history was procured along with a general and systemic examination. After a detailed otoscopic examination, serial tuning fork test was performed using a Gardiner Brown tuning fork followed by Pure tone audiometry (PTA). Pure tone thresholds were measured in both ears at 500, 1000, 2000, 4000 Hz. Results from the audiometry testing were documented.

STATISTICAL ANALYSIS

The collected data was entered in Microsoft excel and analysed with the help of Statistical Package for the Social Sciences (SPSS) version 21.0 software version 21.0. Qualitative variables will be expressed in proportions and quantitative variables in Mean±SD/Median (IQR). Chi-square test was applied to find the determinants of hearing loss, if observed. A p-value <0.05 was considered to be significant.

RESULTS

A total of 125 patients were selected for the study who were either asymptomatic or had a milder form of the illness. Among them, 65 were males (52%) and 60 were females (48%). There were 40 patients (32.0%) in the age group of 18-30 years, 53 patients (42.4%) in 31-45 years and 32 (25.6%) patients in 46-60 years age group. Among the 125 patients, 12 (9.6%) were diabetic, 14 (11.2%) were hypertensive, 5 (4%) had dyslipidaemia, 3 (2.4%) were hypothyroid, while remaining 91 patients (72.8%) had no co-morbidities [Table/Fig-1].

Among the 125 patients, 65 had history of hearing loss during the COVID-19 infection, of which 42 patients got relieved from the symptom after a few days. In this group, the hearing difficulty during COVID-19 infection had improved over time. Out of patients did not improve and the remaining 52 patients were completely cured. Other symptom such as aural fullness was seen among four patients, tinnitus in one patient and vertigo among three patients.

On an otoscopic examination, those who had ear cerumen was removed and tympanic membrane was visualised. Among them, 30 patients (24%) had a retracted tympanic membrane, while the remaining 95 (76%) had a normal tympanic membrane. Tuning fork test was done, where Rinne and Weber's test was normal. For Absolute Bone Conduction test, 88 patients (70.4%) had normal hearing while 37 patient (29.6%) had abnormal [Table/Fig-2].

Characteristics	Frequency n (%)
Age group	
18-30 years	40 (32%)
31-45 years	53 (42.4%)
46-60 years	32 (25.6%)
Mean±SD	38.44±10.9
Gender	
Male	65 (52%)
Female	60 (48%)
Chronic illnesses	
Diabetes mellitus	12 (9.6%)
Hypertension	14 (11.2%)
Dyslipidemia	05 (4%)
Hypothyroidism	03 (2.4%)
None	91 (72.8%)

[Table/Fig-1]: Characteristics of study participants.

Complaints	n (%)
History of hearing loss after COVID-19 infection	
Present	65 (52.0%)
Absent	52 (41.6%)
Time of onset of hearing loss following COVID-19 infection	
Mean±SD	5.3 ± 2.4 (days)
'Hard of hearing' post COVID-19 infection (subjective) (n=65)	
Improved	42 (33.6%)
Not improved	23 (18.4%)
Associated symptoms	
Aural fullness	04 (3.2%)
Tinnitus	12 (9.6%)
Giddiness	06 (4.8%)
Otosopic examination	
Normal	95 (76%)
Retracted tympanic membrane	30 (24.0%)
Tuning Fork test	
Rinne: Normal	125 (100%)
Weber: Normal	125 (100%)
Absolute bone conduction	
Normal	88 (70.4%)
Abnormal	37 (29.6%)

[Table/Fig-2]: Proportion of cases with Otological complaints and examination.

Audiometric assessment with PTA was tested at frequencies of 500, 1000, 2000, 4000 and 8000 Hz. Out of total, 45 patients (36%) showed SNHL of which 15 had the left ear affected and 19 having the right ear affected. Further 34 patients (27.2%) had unilateral SNHL, and 11 (8.8%) had bilateral. Remaining 80 patients (64%) have a normal PTA value. 27 (21.6%) had mild SNHL, 12 patients (9.6%) with moderate and 6 (4.8%) with moderately severe SNHL [Table/Fig-3]. Impedance audiometry for all the candidates showed a type A tympanogram, indicating a normal eustachian tube function.

Total of 45 patients had SNHL, of which majority of the patients belonged to the age group of 46-60 years of age (53.3%) (p-value=0.001). No gender-based difference was there between those with/without SNHL. SNHL was present in 11 (24.5%) out of 12 diabetic patients, however 71 (88.6%) who had no co-morbidities were found to have normal hearing (p-value=0.001). Based on the severity of COVID-19 infection, 89 patients (71.2%) were asymptomatic, among them 78 (62.4%) had normal audiogram and 11 (8.8%) had sensorineural hearing loss. Out of 125, patients had mild COVID-19 infection, among them 2 (1.6%) had normal audiogram and 34 (27.2%) had SNHL (p-value=0.01) [Table/Fig-4].

Parameters	n (%)
PTA findings	
Sensorineural hearing loss	45 (36%)
Normal	80 (64%)
Level of involvement (n=45)	
Bilateral	11 (8.8%)
Unilateral	34 (27.2%)
Degree of hearing loss (n=45)	
Mild (20-40 db)	27 (21.6%)
Moderate (41-55 db)	12 (9.6%)
Moderately Severe (56-70 db)	6 (4.8%)
Severe (71-90 db)	0
Profound (71-90 db)	0

[Table/Fig-3]: The PTA findings.

Variables	Pure tone audiometry		p-value
	Normal (n=80)	Sensorineural hearing loss (n=45)	
Age (in years)			
18-30	38 (47.5%)	2 (4.5%)	0.001
31-45	34 (42.5%)	19 (42.2%)	
46-60	8 (10.0%)	24 (53.3%)	
Gender			
Male	42 (52.5%)	23 (51.1%)	0.881
Female	38 (47.5%)	22 (48.9%)	
Co-morbidities			
Nil	71 (88.6%)	20 (44.4%)	0.001
Hypothyroidism	2 (2.5%)	1 (2.2%)	
Diabetes	1 (1.3%)	11 (24.5%)	
Hypertension	5 (6.3%)	9 (20.0%)	
Dyslipidemia	1 (1.3%)	4 (8.9%)	
Severity of COVID-19			
Asymptomatic	78 (62.4%)	11 (8.8%)	0.01
Mild	2 (1.6%)	34 (27.2%)	

[Table/Fig-4]: Comparison of hard of hearing after COVID-19 infection with variables. A p-value <0.05 was considered to be significant

DISCUSSION

Hearing loss can be associated with certain viral infections such as *cytomegalovirus*, *rubella virus*, *herpes simplex virus*, *measles virus*, *varicella zoster virus*, *epstein bar virus*, *enterovirus*, *mumps virus*, *chikungunya virus*, and *human immune deficiency virus*. COVID-19 infection was mainly identified as an acute respiratory disease, where the virus is transmitted through droplet infection spread to the oral, nasal, and eye mucous membrane. The incubation period is between 2-14 days period. The virus colonises, and multiplies in the respiratory system, involving the nasopharynx, trachea, bronchi, and then lungs producing multiple symptoms. The virus then involves multiple organ systems of the body such as the gastrointestinal system, nervous system, musculoskeletal system, and renal system. Hearing loss following a COVID-19 infection may be conductive, or sudden sensorineural type, which is confirmed by audiological assessments. The cause of hearing loss may be due middle ear effusions or damage either at the level of peripheral or central auditory structures [5,11].

The pathophysiology of hearing loss in COVID-19 infection is still under investigation, however, certain theories have been postulated by various authors. According to Umashankar A et al., damage in the hearing physiology can be explained in three ways [5]. Due to the viral infection sequelae, the auditory center in the temporal lobe (Brodmann area 41,42) gets affected. There could be a thrombus or

an embolus formation caused due to changes in the microvascular structures in the inner ear thereby suppressing the blood flow to the inner ear. Another reason could be due to multiorgan involvement or can occur as a direct peripheral injury to the sensory cells of the cochlear [2,5]. Chern A et al., reported an 18-year-old woman who presented with bilateral sudden SNHL, aural fullness and vertigo. She was later diagnosed as COVID-19 RT-PCR positive. On Magnetic Resonance Imaging (MRI) scan, bilateral intralabyrinthine hemorrhage was seen and this could possibly explain the COVID-19 associated coagulopathy or direct viral insult of the cochlear nerve or labyrinth [12]. Middle ear effusion is also commonly seen during a viral infection due to the ascending infection from the nasopharynx and resulting in a conductive hearing loss. As SARS-Cov-2 virus infects and multiplies within the nasopharyngeal and oropharyngeal mucosa, this can commonly result in a middle ear infection thereby explaining the cause of a conductive hearing loss during COVID-19 infection [1,2,4,13].

Assessment of a post COVID-19 patient requires detailed history taking and a clear-cut examination. An otoscopic evaluation must be done before performing an audiometric testing. Tests such as Pure tone audiometry, and otoacoustic emission tests can be done which are feasible, convenient, and sensitive. Audiometry must be assessed by an audiologist in a soundproof room which will be helpful to rule out any hearing loss. PTA measured frequencies up to 8000 Hz. Conductive and sensorineural hearing loss with its decibel can be detected. Otoacoustic Emission (OAE) which is more sensitive to sensorineural hearing loss identifies the outer and inner hair cell functioning. To assess the middle ear functions, impedance audiometry is done [14-16].

The current study aimed to assess the association between COVID-19 infection and hearing loss. As per the results obtained, 45 patients presented had SNHL (11 with bilateral, 19 with right and 15 with left SNHL). Out of the 32 patients in the age group of 46-60 years, 24 patients were found to have SNHL. From the 31-45 years age group, 19 patients had SNHL. A greater number of patients in the age group of 45-60 years had SNHL, compared with the other age groups. Few patients who had no complaints of hearing loss were found to have mild SNHL. All the patients in the study had mild symptoms of COVID-19 infection or were asymptomatic. But the majority among the mildly symptomatic group showed hearing loss.

In a case series published by Dharmarajan S et al., 53 out of 100 COVID-19 positive patients had SNHL and the study asserted that high-frequency hearing loss and referred OAE were seen in the midst of a momentous number of patients who were COVID-19 positive [17]. However, in a study conducted by Durgut O et al., the authors stated that they could not perceive the effects of SARS-CoV-2 on hearing thresholds among the 20 patients affected with mild COVID-19 disease [18]. Yet, from our study, it can be concluded that there is a possibility of SNHL associated with COVID-19 infection. Since the patients were not tested before or during the time of infection, hearing status prior to COVID-19 remains unclear. However, postinfection, we can assess whether hearing loss is persistent compared to other symptoms of COVID-19 such as anosmia or dysgeusia, which usually tends to settle once the infection has subsided. It cannot be substantiated that this hearing loss is due to COVID-19, as we are unaware of the patient's previous hearing thresholds. Since sensorineural hearing loss was seen more among patients in the 46-60 years age group, that indicates age may be associated with the hearing loss along with COVID-19 infection. However, more and detailed studies are needed to draw such conclusions.

Limitation(s)

If the audiological report prior and during the COVID-19 infection was available, that would have provided a clear idea whether the hearing

loss has occurred due to the infection. Also, if follow-up audiometric testing were done, we could have found whether the hearing loss was reversible or irreversible. The drawback of this study is that only a COVID-19 audiological assessment could have been obtained without knowing the initial hearing status of the patient.

CONCLUSION(S)

Association between COVID-19 and hearing loss requires a detailed evaluation which should include the previous hearing assessment of a patient, during the infection and postinfection follow-up. In the current study, sensorineural hearing loss was seen among 36% of the study population, whereas majority of them had mild symptoms during the active infection and belonged to 46-60 years of age group. Since we have only the post COVID-19 PTA report, we cannot justify that there is a 100% correlation between these two but can conclude that there may be an association along with the age factor.

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PARTICULARS OF CONTRIBUTORS:

1. Postgraduate, Department of ENT, Chettinad Academy of Research and Education Chettinad Hospital and Research Institute, Chennai, Tamil Nadu, India.
2. Assistant Professor, Department of ENT, Chettinad Academy of Research and Education Chettinad Hospital and Research Institute, Chennai, Tamil Nadu, India.
3. Associate Professor, Department of ENT, Chettinad Academy of Research and Education Chettinad Hospital and Research Institute, Chennai, Tamil Nadu, India.
4. Professor and Head, Department of ENT, Chettinad Academy of Research and Education Chettinad Hospital and Research Institute, Chennai, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. S Prabakaran,
3/286, Pachaiyappan Street, Periyar Salai, Palavakkam,
Chennai-600041, Tamil Nadu, India.
E-mail: somu.prabakaran@gmail.com

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