



# Ear, Nose, and Throat (ENT) Manifestation in COVID-19 patients: A prospective, observational study

Abishesh Shakya, Subash Khadka, Sangita Regmi Chalise, Jeegyasha Thapa Bista

Department of Ear Nose Throat and Head Neck Surgery (ENT and HNS), KIST Medical College Teaching Hospital, Imadol, Lalitpur, Nepal

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## Corresponding

Abishesh Shakya  
Lecturer,  
Department of Ear Nose Throat and  
Head Neck Surgery (ENT and HNS),  
KIST Medical College Teaching  
Hospital, Imadol, Lalitpur, Nepal  
E-mail:  
abishesh.shakya1234511@gmail.com

## Introduction

The World Health Organization (WHO) declared Coronavirus disease 2019 (COVID-19) pandemic in March 2020.<sup>1</sup> The novel SARS-CoV-2 leading to COVID-19, infectious respiratory disease has affected over 0.5 million people and caused a plenty of health concerns.<sup>2</sup> Most of the people infected with the COVID-19 virus experience mild to moderate respiratory disease and recover without requiring special treatment.<sup>3</sup> The primary symptoms of COVID-19 are lower respiratory tract-related symptoms as fever, coughing, dyspnea, and tightness in the chest that could develop quickly into acute respiratory distress syndrome. An important spectrum of COVID-19 includes Ear, Nose and Throat

## Abstract

**Introduction:** The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was reported in Wuhan in China in December 2019. ENT manifestations are one of the most frequent symptoms encountered in COVID-19. Proper knowledge and study are required to know the symptoms of ENT and its relation to COVID-19. This study is undertaken to evaluate ENT manifestation in COVID-19 patients.

**Methods:** A prospective observational study was carried out on 124 patients presented to the Department of ENT-HNS, KIST Medical College, Lalitpur with diagnosed COVID-19 with ENT symptoms over a period of 1 year from 1st July 2021 to 30th June 2022. All patients with positive PCR tests for COVID-19 with ENT symptoms and age of more than 15 years, were thoroughly evaluated and an audiogram was done in patients with hearing loss.

**Result:** A total of 124 patients between the age group of 16 to 87 years were studied. Among them, most of the patients were in the age group of 16-25 years. The number of male and females were 51 (41.1%) and 73 (58.9%) respectively with male to female ratio of 0.69:1. Most common symptom of the patient with COVID-19 was Anosmia (52.5%) followed by headache (51.6%) and runny nose (48.4%).

**Conclusion:** A thorough understanding of COVID-19 and a study on ENT-related symptoms in COVID-19 should contribute to the quality of care. Sudden anosmia, dysgeusia, tinnitus, or hearing loss need to be recognized by the international scientific community as important symptoms of the COVID-19 infection

**Keywords:** COVID-19, ENT, Anosmia, Dysgeusia, Tinnitus

(ENT) symptoms like nasal discharge, nasal obstruction, sneezing, anosmia/ hyposmia, ageusia/ hypogeusia, hearing loss, and tinnitus.<sup>4</sup> The main entry points for the virus are the nasal and oral cavities, with the nasal cavity and nasopharynx being the most frequently occurring locations for virus reproduction.<sup>5</sup> There are studies that have described the loss of smell (Anosmia) and taste (Ageusia) as a manifestation of COVID-19 infection.<sup>6</sup>

This study describes the ENT manifestations of COVID-19 infection, to help physicians diagnose the COVID-19 infection at the earliest stage to better understand the epidemiology for this part of the world. Therefore, this research is designed to address the impact of this novel viral infection in ENT.

## Method

A prospective, observational, and hospital-based study was conducted from 1<sup>st</sup> July 2021 to 30<sup>th</sup> June 2022 (Duration: 1 year) at the Department of ENT-HNS, KIST Medical College and Teaching Hospital, Imadol, Lalitpur (KISTMCTH). Approval of the institutional ethics committee was obtained before the beginning of the study (Ref. 2077/78/62). Before the collection of the data, the participants were informed about the purpose and objective of the study, and written consent was obtained from each of them. The identity of the participant was kept confidential. A consecutive sampling method was used to select study participants. Based on the inclusion criteria, the total sample included during the study period comprised 124 patients. Patients with positive PCR tests for COVID-19 with an age of more than 15 years were taken. A detailed history of ENT manifestations such as runny nose, headache, nasal obstruction, tinnitus, anosmia, hearing loss, and dysgeusia documented in COVID-19 patients was taken and entered in proforma. All the included patients underwent a routine complete Ear, Nose, Throat, and Neck (ENT-HNS) examination. To measure the grading of tinnitus, Tinnitus Handicap Inventory (THI) Score was used. The grading of tinnitus was performed from the score obtained by using THI Scoring.<sup>7,8</sup>

The THI (Newman, C. W., et al.) is a 25-item questionnaire designed to assess the effects of tinnitus on individuals. Each item is answered by circling either yes, no, or sometimes. Each yes response scores 4 points, each sometimes scores 2 points, and each no scores 0. The maximum possible score is therefore 100, and the minimum score is 0. The grading of tinnitus will be performed from the score obtained by using THI.<sup>8</sup> An audiogram test was performed in those patients who presented with otological symptoms of tinnitus and hearing loss (Model: MAICO-MA 42). The grading of hearing loss was done using the World Health Organization (WHO)'s Grades of hearing impairment.<sup>9</sup> These findings were recorded in the standard proforma. Then the data was compiled and analysed. Data including demographics, tinnitus grading, the severity of hearing loss, and concomitant diseases, were collected and categorically analyzed by using the statistical package for social sciences (SPSS) version 21.

## Results

A total of 124 participants who met inclusion criteria were included in the study, out of which 73 were females (58.9%) and 51 were males (41.1%). The study participants were in the age range between 16 and 87 years old with a mean age of  $38.31 \pm 17.28$  years. Most of the patients presented with symptoms were in the

age group under 25 years old (29.8%), followed by 26-35 years old (25.8%) as shown in Table 1.

Table 1. Sociodemographic characteristics of the respondents

Characteristics	Frequency (n)	Percentage (%)
Age (in years)		
:Mean Age $38.31 \pm 17.28$ years		
Under 25	37	29.8
26-35	32	25.8
36-45	15	12.1
46-55	19	15.3
and Older 56	21	16.9
Gender		
Male	51	41.1
Female	73	58.9
Occupation		
Medical	7	5.6
Non-Medical	117	94.4
Marital Status		
Married	82	66.1
Unmarried	41	33.1
Widow	1	0.8
Religion		
Hindu	105	84.7
Buddhist	16	12.9
Christian	2	1.6
Others	1	0.8

The distribution of patients based on the Tinnitus Grading Category is shown in Table 2. This table showed 15 (12.2%) patients were in the slight followed by 6 (4.8%) patients in the moderate, 6 patients (4.8%) in the

severe, and 4 (3.2%) patients in the mild category of Tinnitus Grading Scoring.

Table 2. Distribution of patients based on Tinnitus Grading Category

Tinnitus Grading Category	Percentage distribution of respondents in each category (%) n
Slight	(12.2) 15
Mild	(3.2) 4
Moderate	(4.8) 6
Severe	(4.8) 6
Catastrophic	0

Table 3 showed the distribution of patients based on the Grade of Hearing Impairment. As per the table, 17(13.7%) patients had no hearing impairment whereas, 8 (6.5%) patients had moderate and 5 (4%) patients had slight impairment.

Table 3. Distribution of patients based on Grade of Hearing Impairment

Grade of Hearing Impairment	Percentage distribution of respondents in each category n (%)
No impairment	(13.7) 17
Slight impairment	(4.0) 5
Moderate impairment	(6.5) 8
Severe impairment	(0.8) 1
Profound impairment including deafness	0

Table 4 showed the Age-wise distribution of patients based on ENT Manifestation. In this study, an association of age groups with ENT manifestations was done with the help of a chi-square test. Tinnitus was most common in 16 out of 33 patients (76.2%) with an age range of 56-87 years and was found to be statistically significant ( $p < 0.05$ ). Hearing loss was also found to have a statistically significant association with age and was most common in the age range of 56 and older. Anosmia was most commonly reported in 14 (73.7%) patients with age groups 46-55 years and was statistically significant.

Table 4. Age-wise distribution based on ENT Manifestation

ENT Manifestations	Age Groups (years) n (%)					Chi-Square Value	p-value
	Under 25	26-35	36-45	46-55	and Older 56		
Tinnitus	5 (13.5%)	5 (15.6%)	3 (20.0%)	4 (21.1%)	16 (76.2%)	32.294	<0.001*
Hearing Loss	0	1 (3.1%)	0	2 (10.5%)	11 (52.4%)	44.161	<0.001*
Nasal Obstruction	16 (43.2%)	15 (46.9%)	4 (26.7%)	8 (44.4%)	7 (33.3%)	2.406	0.662
Runny Nose	19 (51.4%)	16 (50.0%)	6 (40.0%)	11 (57.9%)	7 (33.3%)	3.151	0.533
Anosmia	20 (54.1%)	12 (37.5%)	11 (73.3%)	14 (73.7%)	7 (33.3%)	11.990	0.017*
Dysgeusia	15 (40.5%)	7 (21.9%)	7 (46.7%)	10 (52.6%)	7 (33.3%)	6.047	0.196
Headache	23 (62.2%)	17 (53.1%)	8 (53.3%)	(31.6%) 6	9 (42.9%)	5.538	0.253

\* represents statistically significant at a p-value less than 0.05

Out of 124 patients, the most commonly reported ENT manifestations as shown in Fig 1, were anosmia in 64 patients (52.5%), headache in 63 patients (51.6%), runny nose in 59 patients (48.4%), nasal obstruction in

50 patients (41.0%) and dysgeusia in 46 patients (37.7%) whereas, the less common symptoms were tinnitus in 33 patients (27.0%) and hearing loss in 14 patients (11.5%).

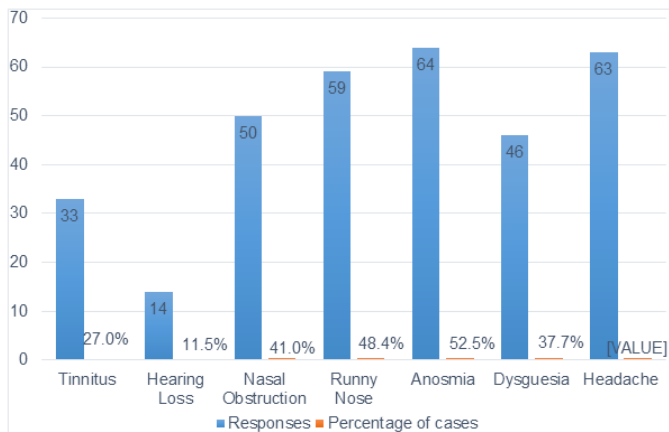


Figure 1. Percentage of ENT Manifestations as specified by respondent

## Discussion

The clinical features of COVID-19 range from asymptomatic to mild and severe disease. The most common area of infection, the primary site of the virus is the oropharyngeal and nasopharyngeal mucosa.<sup>10</sup> Most of the published research on COVID-19 has focused on the presence of lower respiratory tract infections and other common symptoms such as fever and muscle aches.<sup>1</sup> In the context of Nepal, there are very few studies related to the prevalence of ENT manifestations in COVID-19 patients. The main aim of the current research is to study the ENT manifestations of COVID-19-infected patients.

In the present study, the most common ENT-related symptoms of the patients were anosmia (52.5%) whereas, the least common symptoms were tinnitus (27.0%) and hearing loss (11.5%). The findings of this study were consistent with other literature studies by Savtale, S., et al., in which the majority of the patient had a loss of smell (53.5%), and, the least frequent symptom was tinnitus (38.5%).<sup>1</sup> In another prospective study conducted by Speth, M. M., et al., it was found that olfactory dysfunction (hyposmia/anosmia) was prevalent in 61.2 percent of patients.<sup>11</sup> With the spread of SARS-CoV-2, the number of patients developing olfactory disorders such as loss of sense of smell has increased, especially in European countries and the United States.<sup>1</sup> Although the exact cause of this is still unknown the pathogenesis of anosmia in COVID-19 appears to be related to damage to the olfactory epithelium rather than a direct result of nasal obstruction.<sup>12</sup> The olfactory system is infected by the neurotropic virus SARS-CoV-2, which enters the olfactory endothelium via angiotensin-converting enzyme-2 (ACE-2) receptors.<sup>13</sup>

A multicenter cohort study done by Ceron, D. S., et al.

showed that anosmia (100%), followed by headache (69.1%), and rhinorrhea/ nasal obstruction (40%) were the most common symptoms. This study also showed the importance of ENT symptoms for the diagnosis of COVID-19.<sup>14</sup> The results of this study resonate with the current study in which the most commonly reported ENT manifestations were anosmia (52.5%), headache (51.6%), runny nose (48.4%) and nasal obstruction (41.0%). In another study conducted by Borah, H., et al., it was found that headache is the second most common ENT manifestation which is consistent with our study.<sup>15</sup> Systemic viral infections such as influenza, and COVID-19 can irritate intracranial structures through direct invasion of virus, release of endotoxins, or immune responses of pain mediators. COVID-19 encephalitis was reported in 6% of cases.<sup>16</sup> Independent reasons for headache in COVID-19 are multifactorial, such as poor adherence to migraine medication, poor sleep, anxiety, and depression.<sup>17</sup> Even “denovo” mask-related headaches have been reported in 51.6% of healthcare workers.<sup>18</sup> The results of the present study are consistent with previous studies that reported nasal obstruction in 49.5% of the patients and runny nose in 35% of the patients.<sup>11</sup> Nasal obstruction and nasal discharge could be in fact due to Cranial Autonomic Symptoms (CAS), due to trigeminal autonomic reflex activation by central or meningeal mechanisms. Nasal obstruction and nasal discharge in COVID-19 are caused by systemic viral infection and facilitated by sinonasal mucosa inflammation. Rhinosinusitis leads to the activation of the trigeminovascular system, and hence, the activation of nociceptive pathways in the brain, leading to Nasal obstruction and nasal discharge.<sup>19,20</sup>

Altered taste is one of the common otolaryngological symptoms in our study. Possible explanations for loss of taste include direct viral neural invasion of smell and taste buds, viral cytotoxicity of taste buds, angiotensin II imbalance, increased pro-inflammatory cytokines, and disorders of salivary glands.<sup>13</sup>

In the study carried out by Xu, H., et al., it was found that the percentage of ACE2-positive cells was higher in taste cells, suggesting that SARS-CoV-2 may enter taste cells and cause dysgeusia in these patients.<sup>21</sup> Olfactory dysfunctions is generally found to be the initial symptom and occurs in the initial stage of the disease.<sup>22</sup>

In a systematic review done by Almufarrij, I. and K. J. Munro in December 2020 from 12 studies estimated that the prevalence of tinnitus was 14.8%, hearing loss 7.6% which slightly differs from our study which was 27.0% and 11.5% respectively.<sup>23</sup> The pathophysiology behind viral infection-related hearing loss involves multiple mechanisms and is not yet fully understood. Most hearing loss is sensorineural, possibly due to

direct damage to hair cells, the patient's inflammatory response, or the ototoxicity of drugs used to treat infections. Hearing loss due to viral infections is also associated with increased individual susceptibility to bacterial and fungal infections. Hearing loss can range from mild to severe and be temporary or permanent.<sup>24</sup>

<sup>25</sup> A study carried out by Tunkel, D. E., et al. showed a direct relationship existed between tinnitus and hearing loss, and most of the tinnitus patients have abnormal audiometry.<sup>26</sup> According to Beukes, E., et al., the experience of tinnitus was shown as the most common persistent otological presentation due to the associated stress and anxiety of the pandemic.<sup>27</sup>

The study included investigations of COVID-19 cases only from a single institute, a limited study period, and a small sample size. The findings obtained from the number of cases of a single institution may not be representative of the target population of Nepal and also limits our knowledge of geographic and institutional differences in the manifestation of COVID-19 infection. Only patients with a diagnosis of COVID-19 and visiting ENT OPD are included in the study. According to the demographic profile of the respondents, the under-twenty-five age group had the highest sample size representation, which could be the reason for the confounding effect in the study. Moreover, Tinnitus and hearing loss was more prevalent in elderly individuals, therefore it is important to assess the past history of sensorineural hearing loss in elderly patients to minimize the potential biases in the study. There were no objective scales used to certify the presence of the symptoms; rather, they were evaluated and answered on a subjective basis. Further, there was a lack of follow-up evaluation of patients which limits the detection of the recurrence of symptoms or reinfection with COVID-19. The authors recommend that large-scale studies with larger sample sizes involving multiple institutions in different geographical locations are needed to better understand the symptoms of COVID-19.

## Conclusion

The increasing cases of COVID-19 require healthcare workers to have an understanding of the disease and its symptoms. The results of this study suggest that many COVID-19 patients have ENT symptoms in addition to lower respiratory symptoms. A universal questionnaire of ENT symptoms should be developed to make diagnosis more complete and regular. A thorough understanding of the virus and a study on ENT-related symptoms in COVID-19 should contribute to the quality of care. In our study, ENT symptoms in decreasing order were Anosmia, headache, runny nose, nasal obstruction, dysgeusia, tinnitus, and hearing loss. Sudden anosmia, dysgeusia, tinnitus, or hearing loss

need to be recognized by the international scientific community as important symptoms of the COVID-19 infection. The THI and grading of hearing loss should be useful in both clinical and research settings because of its responsiveness to treatment, validity for scaling the overall severity of tinnitus, and hearing loss grading. These symptoms are likely related to the neurotropism of the virus. Additionally, Anosmia, dysgeusia, nasal obstruction, and rhinorrhea headache are early symptoms of COVID-19 and may be exploited for early quarantine and containment of viral infections.

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