

Persistent otorhinolaryngological symptoms in patients following COVID-19 infection

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Abstract

Background: Patients having coronavirus disease 2019 (COVID-19) may have persistent symptoms even after weeks or months of recovery. Although there are several studies on persistence of general symptoms, research primarily focussing on post COVID otorhinological symptoms are scarce.

Objectives: The aim of study was to assess the persistent otorhinolaryngological symptoms among the patients within a period of three months of recovery from COVID-19 infection.

Methods: An analytical cross-sectional study was carried out in the ENT OPD of Kathmandu Medical College Teaching Hospital Nepal from July 2021 to September 2021 after ethical clearance. Ninety-one consecutive patients who recovered from COVID-19 were evaluated. The frequency of otorhinolaryngological manifestations at the time of presentation and during the active COVID-19 illness were interpreted and classified as nasal, aural, and throat symptoms.

Results: The commonest persistent nasal symptoms was nasal obstruction in 15 out of 43 patients during COVID (15/43, 34.88 %), followed by nasal discharge (2/12, 16.66%), loss of smell (12/73, 16.43%), and frontal headache (8/40, 20%). Twenty patients had persistent aural symptoms and all of them had tinnitus (8/8, 100%) followed by earache (4/7, 57.14%), hearing loss (3/6, 50%), and dizziness (4/14, 28.57%). Thirty-four patients had persistent throat symptoms. The most common was sore throat (23/49, 46.93%) followed by itching (4/13, 30.76%), hoarseness (3/25, 12%), and dry cough (3/52, 5.7%).

Conclusion: Many ENT OPD patients had variable nasal, aural, and throat complaints at the time of infection which were still persisting in majority of them within three months of recovery from COVID-19.

Key words: Coronavirus disease 2019; Persistent otorhinolaryngological symptoms; Tinnitus.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) was declared pandemic by World Health Organisation (WHO) on March 2020.¹ An important spectrum of COVID-19 includes the otorhinolaryngological manifestations.^{2,3} This includes cough, sore throat, fever, rhinorrhea, nasal obstruction, sneezing, anosmia/hyposmia, ageusia/hypogeusia, hearing loss, tinnitus and dizziness.⁴⁻⁷

There is evidence that patients experience persistent symptoms even after weeks or months of recovery from a prior infection.⁸ The fact that symptoms during infection may not resolve spontaneously which cannot be refuted.

Although several studies on prevalence of symptoms after recovery of COVID-19 infection are available, studies specifying on persistence of otorhinolaryngological symptoms are very limited. Hence, current study, attempted to analyse the persistent otorhinolaryngological symptoms among the patients who follow in Ear, Nose, and Throat Outpatient

Department (ENT OPD) within a period of three months after the recovery from COVID-19 infection. Cognisance of all facets of the COVID-19 pandemic, including these long-term effects, enables to respond this global health crisis leading to improved public health.⁹

METHODOLOGY

An analytical cross-sectional study was carried out in the ENT OPD of Kathmandu Medical College (KMC) Teaching Hospital, Kathmandu, Nepal from July 2021 to September 2021. Ethical approval was taken from Institutional Review Committee of KMC prior to start the study (Ref. 1006202105). A written informed consent was obtained from all the research participants after explaining the objectives of the study. Provision to withdraw their participation from the study without any fear or clarification at any time during the study was informed. Precautions were taken throughout the study to safeguard the rights and welfare of all the participants.

Taking the prevalence of otorhinolaryngological symptoms in COVID-19 as 62%,¹ 91 participants were recruited for the study using Cochran formula $n = Z^2pq/d^2$; where, Z (at 95% confidence level) = 1.96; p = 0.62 (62%);¹ q (1-p) = 0.38; and d (margin of error) was taken 0.1. Consecutive sampling technique was used while selecting the research participants. Patients aged between 18-60 years visiting the ENT OPD for residual otorhinological symptoms once diagnosed with COVID-19 by positive real-time reverse transcriptase-polymerase chain reaction for SARS-CoV-2 (RT-PCR) within three months were included. Those who were unwilling to participate and/or having prior history of documented psychiatric illness were excluded from the study.

Detailed history was taken. The frequency of otorhinological manifestations at the time of evaluation and during the active COVID-19 illness were interpreted as nasal, aural, and throat symptoms with special reference to cough, sore throat, fever, rhinorrhea, nasal obstruction, sneezing, anosmia/hyposmia, ageusia/hypogeusia, hearing loss, tinnitus, and dizziness/vertigo. Any new or the persistent symptoms within the period of three months after the recovery of COVID-19 were recorded in a predesigned proforma. Thorough examination of ear, nose, and throat were done using anterior rhinoscopy, fiber optic naso-pharyngolaryngoscopy (NPL), pure tone audiogram (PTA). CT scan or MRI was done when needed.

Statistical analysis was done using the IBM Statistical Package for the Social Sciences (SPSS) Statistics for Windows, version 20 (IBM Corp., Armonk, N.Y., USA).

Descriptive statistics was presented including mean, standard deviation, frequency, and percentage. t-test was applied and p-value less than 0.05 was considered significant.

RESULT

Out of all the outpatient visited during the data collection period, 91 participants who fulfilled the inclusion criteria of the study design were enrolled in the study. There was a slight male preponderance (50, 54.9%). In total 39 (42.9%) the patient belonged to age group of 18-34 years with mean age of 36.23 ± 12.5 years. Most (60, 65.93%) patients were from Kathmandu and least were from out of Kathmandu valley (20, 21.97%).

Among the patients having persistent nasal symptoms, the commonest was the nasal obstruction which was present in 15 out of 43 patients during active COVID (15/43, 34.88 %) followed by nasal discharge (2/12, 16.66%), loss of smell (12/73, 16.43%), and frontal headache (8/40, 20%). The likelihood of having persistent nasal obstruction was 35% lesser than who did not have it during active COVID infection (Odds Ratio = 0.65, 95% CI = 0.523- .810). Except for loss of smell, all other persistent nasal symptoms were statistically significant ($p < 0.05$), (Table 1, Figure 1).

Among the patients having persistent aural symptoms, the commonest was the tinnitus which was present in eight out of eight patients during active COVID (8/8, 100%) followed by earache (4/7, 57.14%), hearing loss (3/6, 50%), and dizziness (4/14, 28.57%). The likelihood of having persistent tinnitus was 121 times, earache was 16 times, and hearing loss was eight times higher than who did not have these symptoms during active COVID infection with Odds Ratios of 121.59 (95% CI = 14.465-1020.542), 16.4 (95% CI = 1.895- 141.910), and 8.3 (95% CI = 0.639- 107.854) respectively. Except hearing loss and aural fullness, all other persistent aural symptoms were statistically significant ($p < 0.05$), (Table 2, Figure 2)

Thirty-four patients had persistent throat symptoms. The most common was sore throat (23/49, 46.93%) followed by itching (4/13, 30.76%), hoarseness (3/25, 12%), and dry cough (3/52, 5.7%). The likelihood of having persisting sore throat was 33 times higher than who didn't have these symptoms during active COVID infection (Odds Ratio- 33.407, 95% CI = 4.249- 262.651). Throat symptoms were statistically significant for sore throat and itching ($p < 0.001$), (Table 3, Figure 3).

No new otorhinolaryngological symptoms were retrieved in any of the cases in this series.

Table 1: Distribution of nasal symptoms during and after COVID-19

| Symptoms | During COVID | Persistent symptoms | | Odds ratio | 95% Confidence interval | p-value |
|-------------------|--------------|---------------------|--------------|------------|-------------------------|---------|
| | | Yes n, (%) | No n, (%) | | | |
| Loss of smell | Yes | 12 (16.4) | 61 (83.6) | - | - | 0.114 |
| | No | - | 18 (100) | - | - | |
| Nasal obstruction | Yes | 15 (34.9) | 28 (65.1) | 0.651 | 0.523- .810 | <0.001 |
| | No | - | 48 (100) | - | Ref. | |
| Nasal discharge | Yes | 2 (16.7) | 10 (83.3) | 0.833 | 0.647- 1.073 | 0.016 |
| | No | - | 79 (100) | - | Ref. | |
| Headache | Yes | 8 (20.0) | 32 (80.0) | - | - | 0.001 |
| | No | - | 51 (100) | - | - | |
| Epistaxis | Yes | - | - | - | - | |
| | No | 2 (2.2) | 89 (97.8) | - | - | |
| Sneezing | Yes | - | 11 (100) | - | - | |
| | No | - | 80 (100) | - | - | |

Table 2: Distribution of Aural symptoms during and after COVID-19

| Symptoms | During COVID | Persistent symptoms | | Odds ratio | 95% Confidence interval | p-value |
|----------------|--------------|---------------------|--------------|------------|-------------------------|---------|
| | | Yes n, (%) | No n, (%) | | | |
| Earache | Yes | 2 (28.6) | 5 (71.4) | 16.400 | 1.895 - 141.910 | 0.029 |
| | No | 2 (2.4) | 82 (97.6) | - | Ref. | |
| Tinnitus | Yes | 6 (75) | 2 (25) | 121.500 | 14.465 - 1020.542 | <0.001 |
| | No | 2 (2.4) | 81 (97.6) | - | Ref. | |
| Hearing loss | Yes | 1 (16.7) | 5 (83.3) | 8.300 | 0.639 - 107.854 | 0.187 |
| | No | 2 (2.3) | 83 (97.7) | - | Ref. | |
| Dizziness | Yes | 4 (28.6) | 10 (71.4) | - | - | <0.001 |
| | No | - | 77 (100) | - | - | |
| Aural fullness | Yes | 1 (11.1) | 8 (88.9) | - | - | 0.099 |
| | No | - | 82 (100) | - | - | |

Table 3: Distribution of throat symptoms during and after COVID-19

| Symptoms | During COVID | Persistent symptoms | | Odds ratio | 95% Confidence interval | p-value |
|---------------|--------------|---------------------|--------------|------------|-------------------------|---------|
| | | Yes n, (%) | No n, (%) | | | |
| Sore throat | Yes | 22 (44.9) | 27 (55.1) | 33.407 | 4.249- 262.651 | <0.001 |
| | No | 1 (2.4) | 41 (97.6) | - | Ref. | |
| Dysphagia | Yes | - | 6 (100) | - | - | - |
| | No | - | 85 (100) | - | - | |
| Itching | Yes | 4 (30.8) | 9 (69.2) | - | - | <0.001 |
| | No | - | 78 (100) | - | - | |
| Hoarseness | Yes | - | 25 (100) | - | - | 0.559 |
| | No | 3 (4.5) | 63 (95.5) | - | - | |
| Cough | Yes | 3 (5.9) | 49 (94.2) | - | - | 0.257 |
| | No | - | 39 (100) | - | - | |
| Loss of taste | Yes | 1 (1.6) | 62 (98.4) | - | - | 1.00 |
| | No | - | 28 (100) | - | - | |

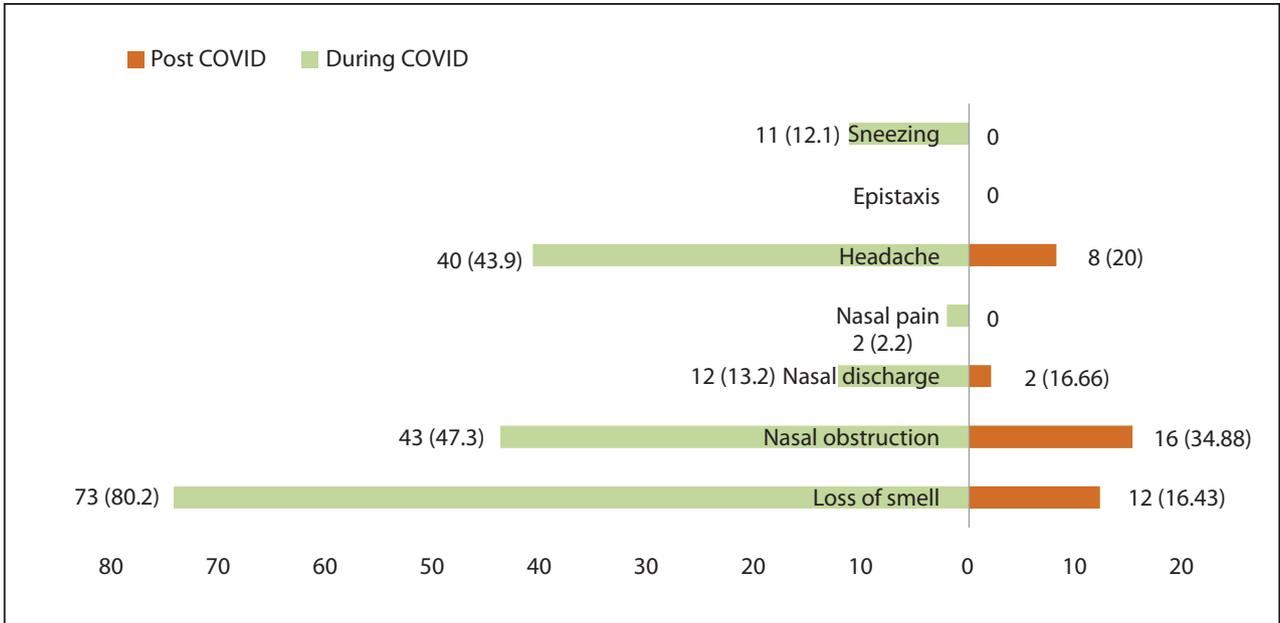


Figure 1: Nasal symptoms, n (%)

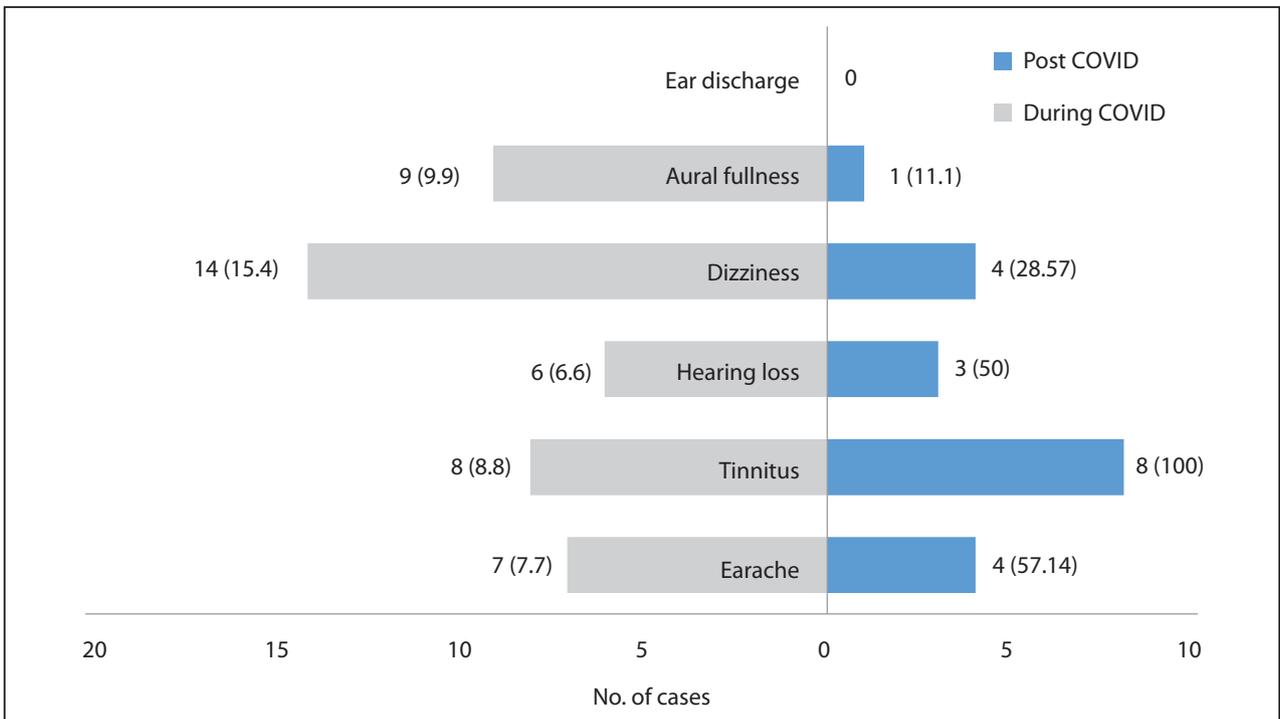


Figure 2: Aural symptoms, n (%)

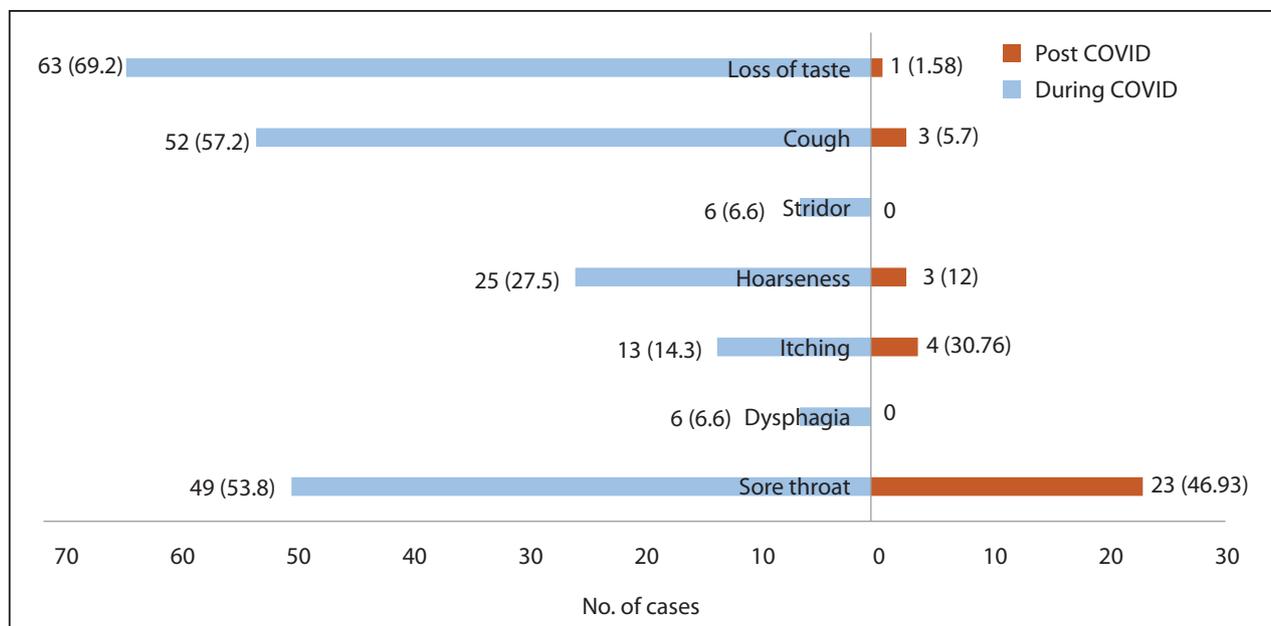


Figure 3: Throat symptoms, n (%)

DISCUSSION

Clinicians and researchers have focussed on the acute phase of COVID-19, but continued monitoring for long-lasting effects is needed.¹⁰ It has been evident that many patients continue to experience symptoms weeks and months after the onset of COVID-19, regardless of disease severity. Most published COVID-19 research are focussed on the lower respiratory tract manifestations and its sequel due to their life-threatening nature but the literature on the multiple facets of otorhinological manifestation within three months of recovery from COVID-19 is scarce. Since the authors have included the persistent post COVID-19 ear, nose and throat symptoms within three months of the infection, the authors want to term it as "Persistent post-acute COVID-19 Otorhinological syndrome".

The demographic profile of the patients included in this series was similar to few published research.^{4,11-13} Most of the patients were from the Kathmandu district, this might be due to easy accessibility.

There are very few published results on the persistent otorhinological symptoms. The commonest persisting nasal symptom was the nasal obstruction (15/43, 34.8%) followed by headache (8/40, 20%), nasal discharge (2/12, 16.66%) and loss of smell (12/73, 16.43%). Other nasal symptoms like nasal pain, epistaxis and sneezing were completely recovered during the presentation. In a similar study done in Netherland and Belgium

by Facebook survey for general and otorhinological symptoms during three months post recovery from COVID-19 illness, anosmia was found to be persistent in 39.7% and sneezing in 31.6%.¹⁴ The exact cause for this is yet not known but infection of the olfactory system by neurotropic virus the SARS-CoV-2 which enters the olfactory endothelium via Angiotensin-converting enzyme 2 (ACE-2) receptors could be the possible explanation.¹⁵ The different finding with regards to the frequency of persistent symptoms in this study might have some genetic implication.

Tinnitus, hearing loss and the vertigo were the most common audio-vestibular symptoms studied in COVID-19. A systematic review done by Almufarrij et al.¹⁶ in December 2020 from 12 studies estimated that the prevalence of tinnitus was 14.8%, hearing loss 7.6% and dizziness 7.2% but slightly different results were observed in this study which were 8.8%, 6.6%, and 15.4% respectively. The persistent audio-vestibular symptom which was most difficult to resolve within 3 months after recovery from COVID-19 was tinnitus (100%) followed by hearing loss (50%) and dizziness (28.57%) which was a similar observation in another study.¹⁷ This is plausible as several other viral infections like measles, rubella, and cytomegalovirus have been identified to directly damage the inner ears.¹⁸ The authors agree with Beukes et. al.¹⁹ for tinnitus experience as the most common persistent post COVID otological presentation due to associated stress and anxiety of the pandemic. This needs long

term follow-up regarding the recovery or the persistence of tinnitus for better understanding of its impact in COVID-19 and its treatment. The earache was the second most common persistent otological symptom in this study (57.14%) which might be due to eustachian tube dysfunction secondary to the nasal or nasopharyngeal involvement of COVID-19.

Alteration of the taste sensation is the second most common otorhinological symptoms after smell disorders which have been studied in many studies during COVID-19 pandemic. Though there were high percentage of patients having loss of taste sensation during active COVID-19 (63, 69.2%), its persistence was observed in only one (1.5%) patient within three months of recovery in this study. The possible explanation behind the loss of taste sensation could be direct viral neural invasion to olfactory and gustatory nerves, viral cytotoxicity to taste buds, angiotensin II imbalance, augmented pro-inflammatory cytokines, and disturbances in salivary glands and sialic acid.²⁰

The most frequent persistent post COVID-19 throat symptoms were sore throat (23/49, 46.93%) and itching (4/13, 30.76%). Symptoms like those have been termed as atypical otolaryngologic manifestation of COVID-19 in the literature and its exact cause is not known.²¹

The lack of data variation due to the involvement of single institute, small sample size, shorter evaluation of only three months, lack of in-depth analysis of individual symptom and interpretation of results with respect to mild or severe COVID were felt to be the primary shortcomings of this study. The authors, therefore recommend for larger multicentre studies with longer follow-ups. Yet, the current findings are eye opening as the authors attempted to bridge the gap in the existing knowledge with regards to persistent post-acute COVID-19 otorhinological symptoms.

CONCLUSION

It was found that many ENT OPD patients had various nasal, aural, and throat complaints at the time of infection which was still persisting in majority of them within three months of recovery from COVID-19. The most frequent Persistent post-acute COVID-19 Otorhinological symptoms in decreasing order were tinnitus, earache, hearing loss, sore throat, nasal obstruction, throat itching, dizziness, nasal discharge, and loss of smell.

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