

Original Research Article

Persistence of chemosensory deficiencies in patients of COVID-19: our experience

Vivek K. Pathak*, Pradeepti Nayak, Rohit Saxena, Rishita Kalra

Department of Otolaryngology, School of Medical Sciences and Research, Sharda University, Greater Noida, Uttar Pradesh, India

Received: 07 July 2021

Revised: 01 August 2021

Accepted: 02 August 2021

***Correspondence:**

Dr. Vivek K Pathak,

E-mail: drvkp83@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Severe acute respiratory syndrome coronavirus-2 (SARS COV-2) infection has caused a global pandemic that has spread like wildfire throughout the world over a very short period of time. Though it may present with a multitude of symptoms mainly respiratory; neurological symptoms like smell and taste disturbances have emerged with greater frequency and sometimes as the only presentation in mild and moderate cases.

Methods: This study was conducted at a tertiary hospital dedicated to COVID care in Northern India. Approval was sought from the Institutional Ethics Committee before the commencement of the study. Appropriate written and informed consent was obtained from all patients before their induction. All confirmed COVID -19 patients, previously documented to have chemosensory deficits of anosmia and dysgeusia over 3 months were followed up by over a period of 8 weeks. Data was collected on the basis of a comprehensive questionnaire telephonically at intervals of 2 weeks and 8 weeks and recorded.

Results: During the period of study, from a sample of 450 patients, a total of 199 patients complained of chemosensory dysfunction out of which 63.8% were males (Figure 1). A total of 145 patients had dysgeusia and 136 had anosmia with a male preponderance of 62% and 63.9% respectively.

Conclusions: Residual post-COVID symptoms last and whether they may permanently affect quality of life further studies are required.

Keywords: COVID-19, Anosmia, Dysgeusia

INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS COV-2) infection has caused a global pandemic that has spread like wildfire throughout the world over a very short period of time. Though it may present with a multitude of symptoms mainly respiratory; neurological symptoms like smell and taste disturbances have emerged with greater frequency and sometimes as the only presentation in mild and moderate cases.

Unlike the respiratory component of the pathology, these symptoms seem to be a part of the systemic manifestations

of a viral infection. Viruses that give rise to respiratory tract infections are well known to cause post-infectious chemosensory deficits.

The pathogenesis of these chemosensory deficits in case of Coronavirus disease 2019 (COVID-19) are not well understood. Initially it was hypothesized that they may be effects of direct viral invasion of the olfactory bulb as in cases of other viral infections. However, recent studies have indicated that it might be due to inflammation of the olfactory epithelium secondary to a high viral load. Another theory postulated that olfactory supporting cells, especially sustentacular cells, Bowman cells and

microvillar cells, expressed high density of ACE2 (Angiotensin Converting Enzyme) receptor proteins which act as an access for SARS-Cov2 to invade and infect the cells.^{1,2}

The pathogenesis of this chemosensory dysfunction has been also extensively investigated due to their prognostic significance. It has been reported that anosmia and dysgeusia usually present in patients with milder symptoms or those with early recovery and may in fact be a predictor of a favourable outcome.³

Although initially expected to be single wave, recurrence and residual infections have arisen throughout the world with greater frequency over the last few months. The disease spikes in the population have reduced over months. However, COVID-19 still poses a significant threat to the global community. Its etiopathogenesis is not fully understood and no definitive management protocol is in place. Hence further studies are imperative to understand the presentation, progression and prognosis of the disease to administer effective and prompt treatment to patients, this reducing the disease burden on the community.

Objective of this study was to estimate residual effects of chemosensory dysfunction in patients, namely anosmia and dysgeusia over a period of time.

METHODS

This descriptive study was conducted at a tertiary hospital dedicated to COVID care in Northern India from April 2020 to November 2020. Approval was sought from the Institutional Ethics Committee before the commencement of the study. Appropriate written and informed consent was obtained from all patients before their induction. Study design descriptive study All confirmed COVID -19 patients, previously documented to have chemosensory deficits of anosmia and dysgeusia over 3 months were followed up by over a period of 8 weeks. Data was collected on the basis of a comprehensive questionnaire telephonically at intervals of 2 weeks and 8 weeks and recorded.

Patients with severe disease, comorbidities like diabetes and other conditions which may cause neurological symptoms were excluded from the study. Also patients with conditions that may pre-dispose to rhinological symptoms, like allergic rhinitis and rhino-sinusitis were excluded. Children under the age of seven were also not included in the review.

The data collected was collated and analysed using Statistical package for social sciences (SPSS 21.0). Categorical variables are presented in number and percentage (%) and continuous variables as mean ± SD and median. Chi square test was used to evaluate the quantitative data and p<0.05 was considered statistically significant. Sample size was determined by formula

$$n = 2(Za + Z1 - b)2 \div d^2$$

RESULTS

During the period of study, from a sample of 450 patients, a total of 199 patients complained of chemosensory dysfunction out of which 63.8% were males (Figure 1). A total of 145 patients had dysgeusia and 136 had anosmia with a male preponderance of 62% and 63.9% respectively (Figure 2).

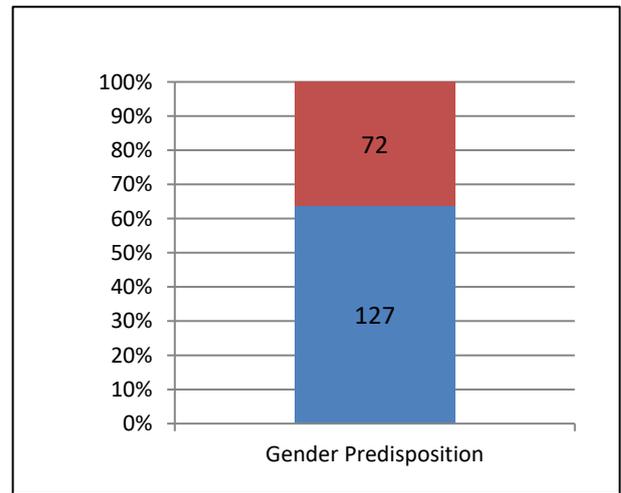


Figure 1: Gender predisposition.

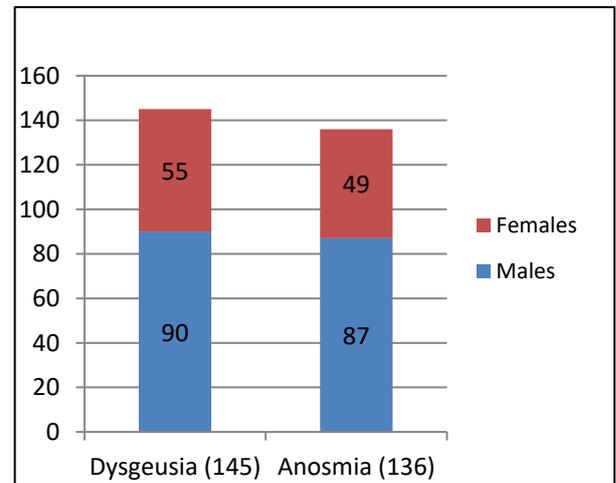


Figure 2: Gender predisposition of chemosensory dysfunction in COVID-19 patients.

Majority of the affected patients belonged to 21-50 years of age and both dysgeusia and anosmia were more common in young adults i.e. aged between 20-40 years (Figure 3).

Same sample was re-evaluated subjectively for residual dysgeusia and anosmia at 2 and 8 weeks post COVID-19 recovery.

At 2 weeks post COVID19 recovery, 15 patients (10.3% of the initially affected patients) had residual dysgeusia. However, at 8 weeks, only 4 patients (2.75%) still had symptoms. Majority of the patients were males at both 2 and 8 weeks (53% and 75% respectively) (Figure 4).

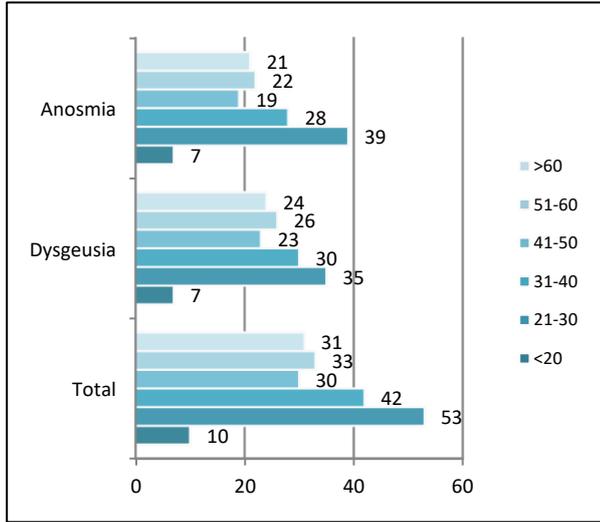


Figure 3: Age distribution amongst anosmia and dysgeusia patients.

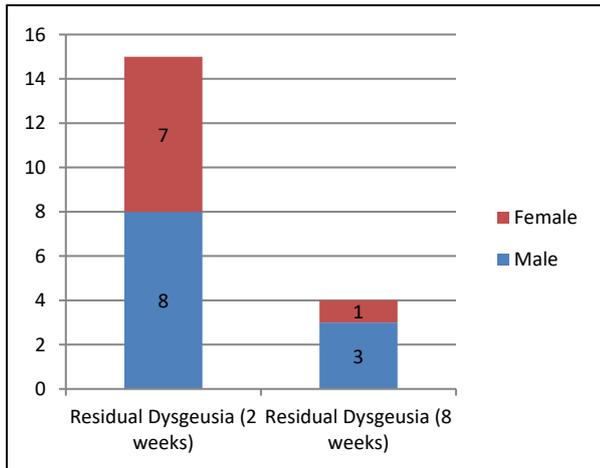


Figure 4: Residual dysgeusia at 2 and 8 weeks post COVID-19.

Patients with residual dysgeusia symptoms at both 2 and 8 weeks post infection were mostly in either in late adulthood or were elderly (Figure 5). A discrete age distribution amongst male and female patients was also done for the evaluation of prevalence of residual dysgeusia amongst different age groups of both the genders at 2 and 8 weeks post infection. (Figure 6 and 7)

Similar study for residual symptoms was done for patients with anosmia as a symptom of COVID19 infection. 9 out of 16 total patients (56.2%) who had residual symptoms at 2 weeks post infection were males (Figure 8). Interestingly, females were predominant (66.6%) for residual anosmia at 8 weeks (Figure 8).

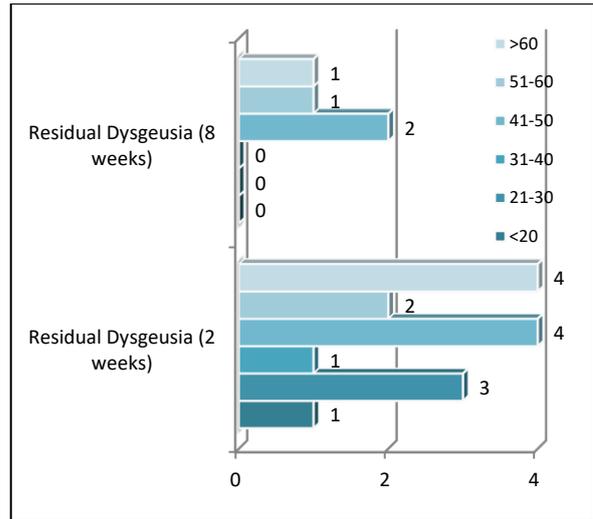


Figure 5: Age distribution amongst patients of post COVID-19 residual dysgeusia at 2 and 8 weeks.

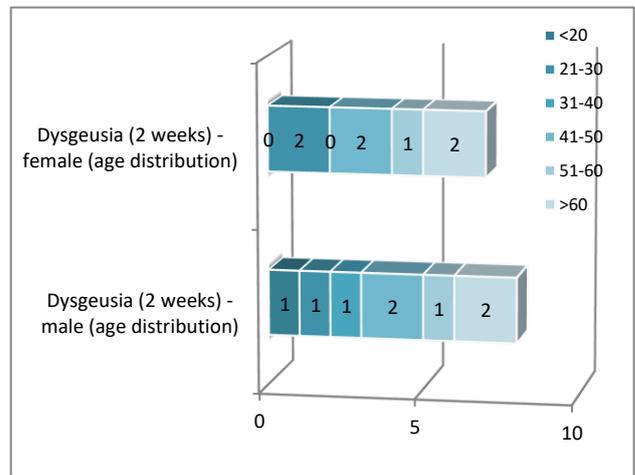


Figure 6: Age distribution amongst post-COVID-19 dysgeusia (2 weeks) patients in both genders.

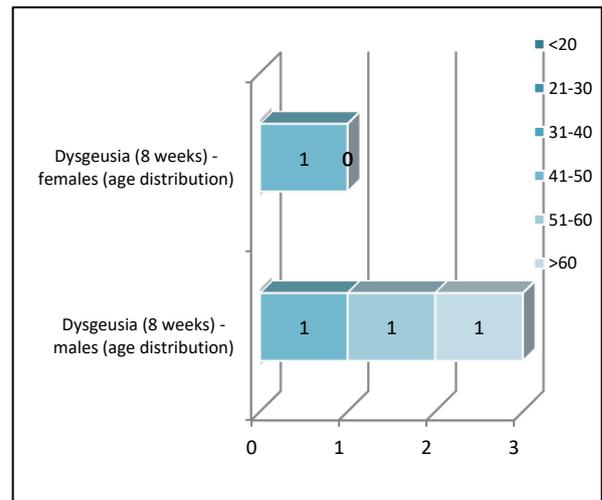


Figure 7: Age distribution amongst post-COVID-19 dysgeusia (8 weeks) patients in both genders.

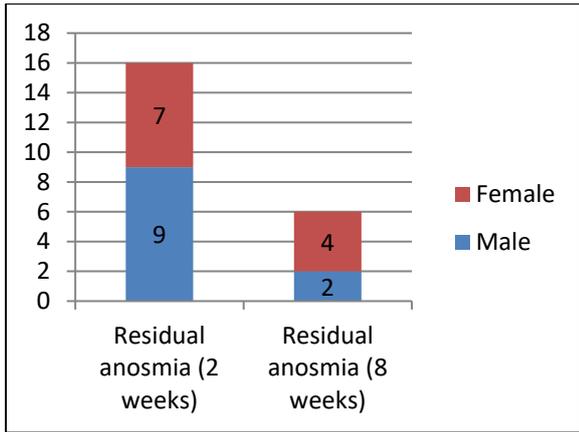


Figure 8: Residual anosmia at 2 and 8 weeks post COVID-19.

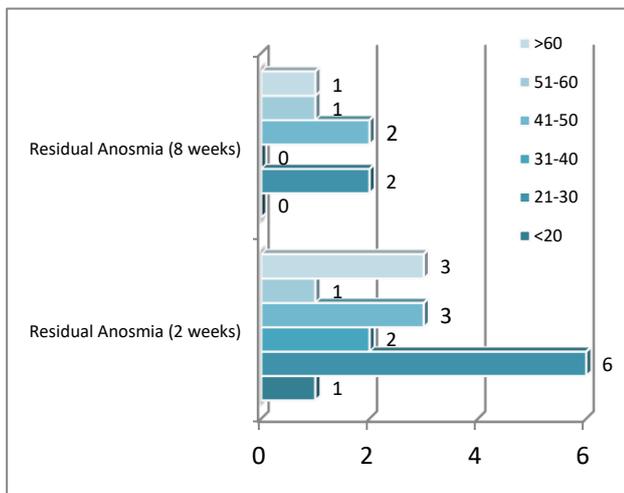


Figure 9: Age distribution amongst post COVID-19 residual anosmia patients at 2 and 8 weeks.

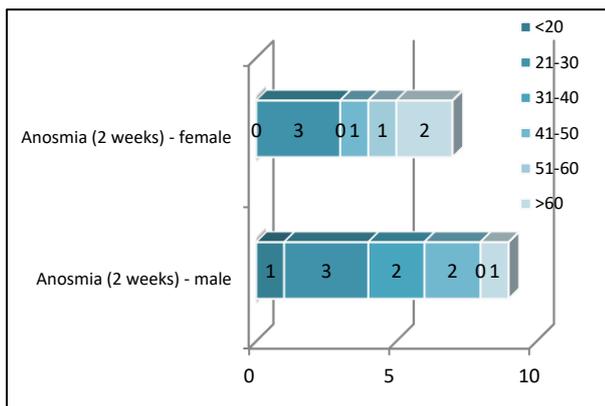


Figure 10: Age distribution amongst post-COVID-19 anosmia (2 weeks) patients in both genders.

Residual anosmia at 2 weeks was highest in the patients between 21-30 years of age whereas, at 8 weeks, was uniformly dispersed amongst all age groups (Figure 9). Age grouping amongst both genders at 2 weeks post COVID19 showed that both of them had more patients

belonging to third decade of life such that 33.3% of males and 42.9% of females were in that age group as shown below (Figure 10).

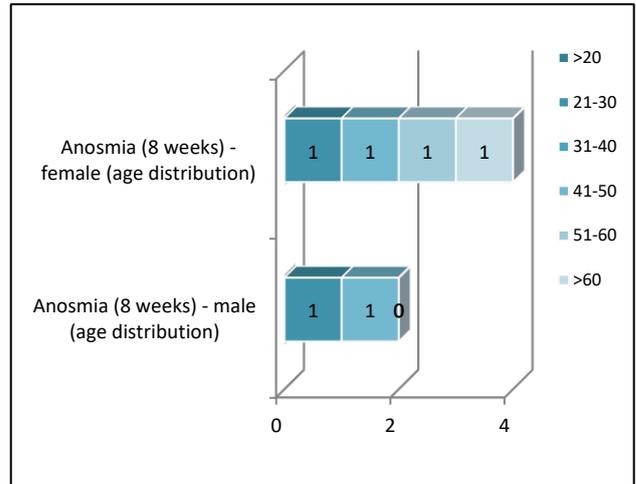


Figure 11: Age distribution amongst post-COVID-19 anosmia (8 weeks) patients in both genders.

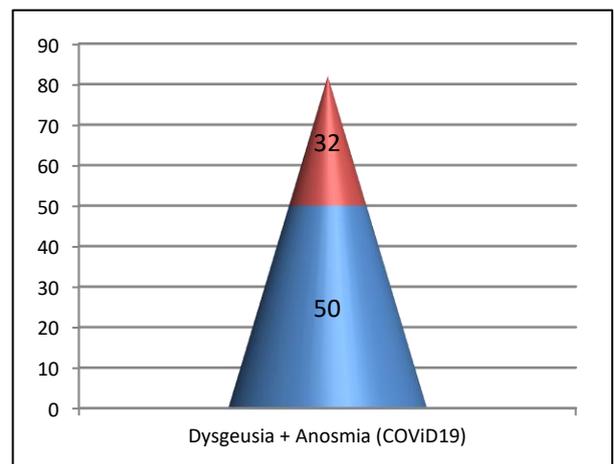


Figure 12: Symptom distribution according to sex.

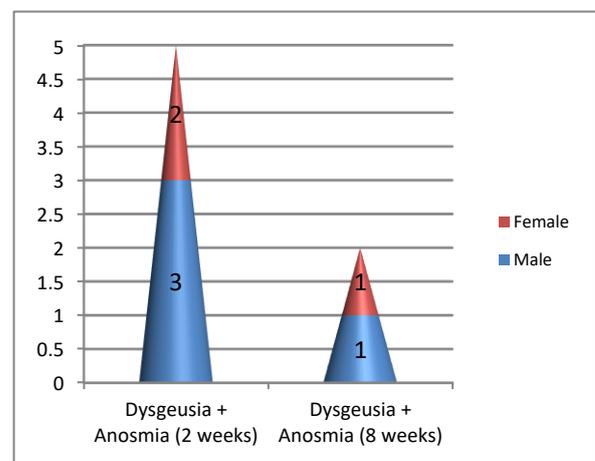


Figure 13: Patients with both, anosmia and dysgeusia, during COVID-19, at 2 and 8 weeks post COVID-19.

Results showed varied dispersal amongst different age groups in both genders at 8 weeks post COVID-19 (Figure 11).

82 patients of 199 had an overlap between both the chemosensory symptoms i.e. dysgeusia and anosmia. In such a presentation, male patients were either higher in number or equal to females at all stages of subjective evaluation such that 60.9%, 60% and 50% were males at the time, post 2 weeks and post 8 weeks of COVID-19 infection respectively. (Figure 12, 13)

DISCUSSION

Post-viral chemosensory dysfunction has been long confirmed in various viral illnesses. According to reports It accounts for almost 40% of patients presenting with anosmia in clinical settings.⁴ It can therefore be theorized that patients infected by SARS CoV-2 will also present with anosmia and dysgeusia. This chemosensory alteration has been attributed to various factors including olfactory neuropathy and conductive olfactory loss.

The European Rhinology Society has reported that a significant number of the COVID-19 patients (20-60%) had loss of smell and that, in a few, it occurred before other more frequently encountered symptoms like cough/fever.⁵

Kaye et al analyzed 237 cases of COVID 19 where anosmia was noted in 73% of patients prior to COVID-19 diagnosis and was the initial symptom in 26.6%. An improvement in the symptom was observed improvement was noted in 27% of patients within a mean of 7.2 days. 85% improved within 10 days.⁶

Heidari et al reported significant improvement in olfactory function after 2 weeks of follow up in in about 75 % (17/23) of patients in the study.⁷

Tsvigoulis et al found that the mean duration of self-reported olfactory dysfunction using Q-SIT™ and SNOT-22 assessment was 70.5 (60–74) days.⁸

Klein et al in their study, deduced that taste and smell changes were the longest-lasting symptoms (17.2±17.6 and 18.9±19.7 days, durations censored at 60 days). Longer smell recovery correlated with smell change severity. Change in taste and smell persisted after negative RT-PCR tests (26% and 29% of the patients respectively). At six-months follow-up, chemosensory changes persisted in 14% of the subjects.⁹ Kandemirli et al also reported persistence of symptoms for upto 4 months post COVID.¹⁰

Hopkins et al conducted a study on 382 patients. 86.4% reported complete anosmia and a further 11.5% had severe hyposmia at the outset. At follow-up 1 week later, 80.1% reported lower severity scores at follow-up, 17.6% remained unchanged and 1.9% of the patients had worsened. 11.5% already reported complete resolution, while 17.3% reported persistent and total anosmia, with

reported duration being between 1 to 4 weeks. The overall cumulative improvement rate of patients was 79% patients.¹²

General consensus is that spontaneous improvement occurs within a mean duration of 2–3 weeks.¹ However cases of persistent anosmia have also been reported where the chemosensory deficit has lasted for more than a month.⁸⁻¹⁰ This may be due to the fact that olfactory epithelium regenerates in 6–8 weeks. Therefore any epithelial damage caused by the SARS COV-2 virus may persist for as long.¹³ Kandemirli et al and Klein et al reported cases with persistent anosmia at 4-months and 6-month period, respectively, suggesting that there might be other potential mechanisms beyond epithelial damage that lead to permanent anosmia. Further data on this permanent anosmia are important to highlight the pathogenesis of COVID-19 anosmia.

In a study by Altundag et al 135 patients of COVID 19 suffering from anosmia and hyposmia were evaluated.¹ Olfactory scores were seen to have completely reverted to normal in 51.2% of patients (with a mean duration of 7.8±3.1 (2–15) days. Recovery of 75–100% was observed in 75% of patients with a mean duration of 8.4±3.4 days. Rate of olfactory dysfunction recovery was seen to be higher in patients with initial COVID-19 related complaints and gradual development of olfactory dysfunction as compared patients who presented with isolated or initial of the sense of olfaction. Duration of the chemosensory deficit was longer in patients with isolated anosmia or initial presentation of anosmia.

Limitations of the study more such types of studies are required.

CONCLUSION

Further studies are imperative to deduce the cause of these protracted symptoms and their consequences to the patient. Burning questions include whether it indicates a continuing damage to patients otherwise thought to be cured or if it is a consequence of weakened immunity due to the disease. Also important is that we be aware as to how long these residual post-COVID symptoms last and whether they may permanently affect quality of life. This may determine the likelihood of short-term and long-term physical and psychological effects on the patient, whether the period set for social isolation by general consensus is sufficient and the possible complications after the patient has been discharged. Undoubtedly, more in-depth research is necessary to understand how this disease develops, its complications and the ideal way to manage with minimum repercussion for the patient and society.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Altundag A, Saatci O, Sanli DET. The temporal course of COVID-19 anosmia and relation to other clinical symptoms. *Eur Arch Otorhinolaryngol*. 2020.
2. Gori A, Leone F, Loffredo L. COVID-19-Related Anosmia: The Olfactory Pathway Hypothesis and Early Intervention. *Front Neurol*. 2020;11:956.
3. Foster KJ, Jauregui E, Tajudeen B, Bishehsari F, Mahdavinia M. Smell loss is a prognostic factor for lower severity of coronavirus disease 2019. *Ann Allergy Asthma Immunol*. 2020;125(4):481-3.
4. Pang KW, Chee J, Subramaniam S. Frequency and Clinical Utility of Olfactory Dysfunction in COVID-19: a Systematic Review and Meta-analysis. *Curr Allergy Asthma Rep*. 2020;20:76.
5. European Rhinologic Society (ERS). COVID-19: What's NOW? ERS members email. <https://mailchi.mp/4c241a511c2d/important-info-on-covid-19?e=d610a2d247>. Accessed on 4th November, 2020.
6. Kaye R, Chang CWD, Kazahaya K, Brereton J, Denny JC. COVID-19 Anosmia Reporting Tool: Initial Findings. *Otolaryngology–Head and Neck Surgery*. 2020;163(1):132-4.
7. Heidari F, Karimi E, Firouzifar M. Anosmia as a prominent symptom of COVID-19 infection. *Rhinol*. 2020;58:302-3.
8. Tsvigoulis G, Fragkou PC, Lachanis S. Olfactory bulb and mucosa abnormalities in persistent COVID-19 induced anosmia: a magnetic resonance imaging study. *Eur J Neurol*. 2020.
9. Klein H, Asseo KN. Onset, duration, and persistence of taste and smell changes and other COVID-19 symptoms: longitudinal study in Israeli patients. *medRxiv*. 2020.
10. Kandemirli SG, Altundag A, Yildirim D, TekcanSanli DE, Saatci O. Olfactory Bulb MRI and paranasal sinus CT findings in persistent COVID-19 anosmia. *AcadRadiol*. 2020;1:1076-6332.
11. Hopkins C, Surda P, Whitehead E. Early recovery following new onset anosmia during the COVID-19 pandemic – an observational cohort study. *J of Otolaryngol - Head & Neck Surg*. 2020;49:26.
12. Bonenberger A. Anosmia: COVID-19's mysterious side effect. *Yale Medicine*. <https://medicine.yale.edu/news/yale-medicine-magazine/anosmia-covid19s-mysterious-side-effect/>. Accessed on 5th November, 2020.

Cite this article as: Pathak VK, Nayak P, Saxena R, Kalra R. Persistence of chemosensory deficiencies in patients of COVID-19: our experience. *Int J Otorhinolaryngol Head Neck Surg* 2021;7:1426-31.