RESEARCH ARTICLE

Olfactory and Taste Dysfunctions and Their Implications in Cases of Severe Acute Respiratory Syndrome Coronavirus 2: A Single-institute Study of 58 Cases

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Abstract

Importance: There is a need to identify the implications of the loss of smell and taste in cases of coronavirus disease-2019 (COVID-19).

Objective: To determine whether severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is causing isolated anosmia in adult population and whether there is a role of intranasal corticosteroids (INCs) in cases of olfactory dysfunctions (ODs).

Design: This was a prospective, cross-sectional, questionnaire-based study of 416 patients diagnosed with COVID-19 in a single institute.

Setting: Dedicated COVID-19 facility.

Participants: All patients had been tested for COVID-19 using a reverse transcription–polymerase chain reaction (RT-PCR)-based test. Patients who were hospitalized were approached in person. All patients who were discharged were then contacted by telephone up to two times to complete the study. Patients who were not reachable with two telephone calls were excluded. Demographic characteristics of the participants—age, sex, and smoking history—were collected. A standardized questionnaire was given to participants.

Result: Olfactory dysfunctions (ODs) was observed in 58 patients and isolated anosmia in 3.6% of patients; 82.7% showed complete recovery of smell, and 6.9% had partial recovery following INCs.

Conclusion: Patients reporting recent onset of anosmia should be considered positive for SARS-CoV-2 infection until proven otherwise by a screening polymerase chain reaction test. Also, ear, nose, and throat (ENT) surgeons in particular who see patients with new-onset anosmia during the COVID-19 pandemic must take safety measures to reduce the risk of exposure and infection of healthcare workers and recommend such patients for RT-PCR test. Females and young adults are more prone to SARS-CoV-2 infection. Early intervention by INCs could be beneficial in improving olfactory and taste dysfunctions (OTDs) and other post-viral neurological manifestations. It could be beneficial in improving the quality of life of elderly patients who are at a higher risk of permanent OTDs. Smokers are at a higher risk of OTDs, but this could be reversible after smoking cessation. There is a need to put SARS-CoV-2 as a differential diagnosis in cases of sudden isolated OTDs.

Keywords: Ageusia, Anosmia, COVID-19, Otorhinolaryngology, Pandemic.

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Introduction

The novel coronavirus was identified in November 2019 in Wuhan Province of China. This virus has since then spread to different parts of the world and has been declared pandemic by the World Health Organization (WHO) in March 2020. It has many constitutional symptoms, viz. fever, sore throat, dyspnea, and malaise. Additional symptoms include loss of smell, rhinorrhea, headache, and diarrhea. Coronavirus disease (COVID) has been affecting many lives in many ways. The loss of both smell and taste affects the quality of life. Viral upper respiratory tract infections (URTIs) can affect both smell and taste sensations to various degrees and duration, which can also occur in 70% of cases caused by rhinovirus, influenza and parainfluenza virus, respiratory syncytial virus, adenovirus, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

In India, cases of coronavirus disease-2019 (COVID-19) are increasing on a daily basis with more than 10 million cases by December 2020. However, it is estimated that cases may be even higher as the testing is to increase the level of virus spread in the population.

Along with many other symptoms, like cough, sore throat, and dyspnea, people have presented with olfactory and gustatory symptoms even before the molecular confirmatory tests of COVID-19. Therefore, in this study, we have made a correlation of anosmia and ageusia with other patient factors.

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Methods and Materials

This was a prospective, cross-sectional, questionnaire-based study of patients diagnosed with COVID-19. The study was commenced after approval from the Ethical Committee of the Institution in Lok Nayak Hospital, which is the largest designated COVID hospital in India. COVID-positive patients receiving medical care at the institution were identified and contacted. All patients

underwent COVID-19 detection using a reverse transcription–polymerase chain reaction (RT-PCR)-based test. Patients who were hospitalized were approached in person. All patients who were discharged were then contacted by telephone up to two times to complete the study. Patients who were not reachable with two telephone calls were excluded. Demographic characteristics of the participants—age, sex, and smoking history—were collected. A standardized questionnaire was given to participants. Participants were asked about symptoms of COVID-19 they had been experiencing and also how many days into the COVID-19 course that they began to experience OD. Then, they were asked to provide their clinical signs and the exact order in which they had experienced the symptoms. Participants were asked to rate their sense of smell and taste during the infection compared to baseline, as "normal," "decreased," or "none at all." Participants with responses of "decreased" or "none at all" were again asked about the improvement in smell during their recovery at 2 weeks. Patients who did not show any spontaneous improvement were advised to start INCs for 2 weeks. Such patients were followed up again after 2 weeks for any improvement in the OD symptoms.

Result and Analysis

The study included a total of 416 cases of confirmed COVID-19 of which 36.3% were male and 63.7% were female. The mean age was 44.92 ± 16.235 years with the range being 18–91 years. The median age was 47, and the mode was 50. Males had higher odds of OD than females [OR 1.934 (CI 1.11–3.39) $p = 0.021$]. Out of 416 patients, 70 were smokers (16.8%). The number of patients with fever was 278 (66.8%), with nasal discharge 46 (11.1%), with sneezing 28 (6.7%), with hyposmia/anosmia 58 (13.9%), with cough 206 (49.5%), with sore throat 90 (21.6%), with dyspnea 99 (23.8%), with change in taste 53 (12.7%), and with change in voice 15 (3.6%). Out of 58 patients with hyposmia/anosmia, 6 patients (10.3%) had no improvement in smell after 2 weeks, 48 patients (82.7%) had complete improvement, and 4 patients (6.9%) had partial recovery. All these 6 patients were started on INCs and showed variable degrees of improvement. In patients with symptoms of anosmia/hyposmia, 29.3% had a history of smoking, while 24.3% of all smokers had symptoms of anosmia/hyposmia (Table 1).

Anosmia was an associated symptom with fever in 10.3% of all patients, while 3.6% of patients had anosmia without fever. Ageusia was an associated symptom with fever in 10.3% of all patients, while 2.4% of patients had ageusia without fever (Table 2). Voice change was an associated symptom with fever in 2.1% of all patients, while 1.4% of patients had voice change without fever.

Table 1: Relationship between smoking and anosmia in COVID-19 patients

Smoking/Anosmia	*Yes*	*No*	*Total*
Yes	17	53	70
No	41	305	346
Total	58	358	

Table 2: COVID-19 patients with fever associated with anosmia/ageusia

	Fever	*No fever*
Anosmia	43	15
Ageusia	43	10

Patients below 40 years with anosmia were 4.8%. Patients above 40 years with anosmia were 9.1%. Patients below 40 years with ageusia were 4.3%. Patients above 40 years with ageusia were 8.4%.

Discussion

The coronavirus is spreading in different parts of India since March 2020. It has been the cause of major health issues since WHO declared it as pandemic. The rising trend of cases in India has been due to its high population density and demography. The increased number of infections due to SARS-CoV-2 in females and young adults has been shown in the current study, which is supported by Zahra et al.[1] and Vaira et al.[2] The higher infection in female patients in India could be as a result of prevalent vitamin D deficiency. In the Indian population, a high prevalence of low serum vitamin D level in women was observed.[3] Vitamin D supplementation has been proved useful in preventing acute respiratory infections.[4] This could be the case in India and countries where vitamin D deficiency is prevalent. The involvement of young adults could be because India has a higher number of individuals aged between 20 and 60 years and people of this age are more involved in socializing, which could be the cause of viral spread.

Olfactory and taste dysfunctions (OTDs) have often been ignored by many physicians, but SARS-CoV-2 has put them in the limelight. Otorhinolaryngologists see OTDs as a neurological manifestation of SARS-CoV-2. In the past, the coronavirus has been known to cause OTDs.[5] OTDs can result from rhinorrhea and nasal blockage due to multiple causes. This conductive OD results from odorants not reaching the olfactory sensory epithelium (OSE) and the patient ends up having a loss of smell. But in SARS-CoV-2, patients are having OD without rhinorrhea and nasal blockage, indicating that there is a direct involvement of OSE by SARS-CoV-2. Angiotensin-converting enzyme 2 (ACE2) has been identified as a cellular receptor for SARS-CoV-2[6] which is expressed on the nasal mucosa.[7] The virus gains entry into the nasal cavity by aerosol inhalation and reaches OSE where it attaches to ACE2 receptors. But not all patients of SARS-CoV-2 present with OTDs rather, which could be due to the invasion of supporting cells in OSE instead of sensory neurons. The higher rate of recovery in OD (82.7%) also supported by Moein et al.[8] suggests that the involvement of sensory neurons is minimal. The invasion of nonneuronal cells, like sustentacular cells, microvillar cells, basal cells, and Bowman's gland cells, by SARS-CoV-2 could be the cause of OD.

In the current pandemic, patients are clinically identified with the constitutional symptoms of the virus of which fever is the most common[9] before a molecular diagnosis is made. But in the current study, 3.6% of patients developed isolated OD and were diagnosed with SARS-CoV-2 by molecular tests. There have been similar findings in the literature by Gane et al.[10] and Hopkins et al.[11] where the predominant symptom was OD. In addition to anosmia, evidence of ageusia and dysgeusia (parageusia) was also seen in patients with COVID-19.[12] Upper respiratory viruses, such as those associated with the common cold and influenza, are considered to be the most common cause of OD in humans.[5,13] Other viruses, like human immunodeficiency virus and Creutzfeldt–Jakob disease virus,[14] can also cause OD. In this study, 10.3% of patients with OD did not improve, resulting in permanent OD, which could be an early manifestation of neurological sequelae of SARS-CoV-2. The permanent damage to OSE results from extensive loss of sensory neurons due to viral infection. This could further lead to an extension to the olfactory bulb by retrograde transport of the virus,

which is commonly seen in herpes simplex virus.[15,16] The virus may cross the inflamed blood–brain barrier and may cause neurological manifestations, like encephalitis and cerebrovascular accident. There has been evidence of SARS-CoV-2 leading to neurological manifestations.[17] This retrograde movement of SARS-CoV-2 through the olfactory nerve route and viral latency and reactivation may lead to learning and behavioral deficiencies and violent behavior in children and adults in the long term.[18]

In the protocol for treating SARS-CoV-2, patients have been given doses of oral corticosteroids to prevent acute respiratory distress syndrome. These corticosteroids may be beneficial for OSE as well as in the spontaneous recovery of OTDs. Patients with isolated OTDs are not given oral corticosteroids but can be given INCs to decrease the duration of OTDs and prevent permanent damage. A similar trial is going on to assess the efficacy of local intranasal treatment with budesonide (nasal irrigation), in addition to olfactory rehabilitation, in the management of loss of smell in COVID-19 patients without signs of severity and with persistent hyposmia for 30 days after the onset of symptoms.[19] Furthermore, studies are needed to prove the efficacy of INCs on OD due to SARS-CoV-2.

Although the mean age of patients infected with SARS-CoV-2 was 44 years in the present study, the number of patients with OTDs above 40 years was almost twice the number of patients with OTDs below 40 years. This could be due to the degenerative changes in OSE with age. Age-related deficits in smell function are well known, and decreased smell function is commonly identified in most elderly patients, including those who are not on any medications.[20] The age-related changes are due to damage to olfactory receptors and decrease in the number of glomeruli within the olfactory bulb.[21] These changes are exaggerated by the infection of SARS-CoV-2 and may lead to permanent OTDs in the elderly patients affecting their quality of life. There is a further need to study the reversibility of OTDs and the risk of permanent OTDs in elderly patients.

The correlation between smoking and OD was also assessed in the study. The number of smokers with OD (17/70 cases, 24.3%) was almost double that of nonsmokers with OD (41/346 cases, 11.9%). Patients with a history of smoking are known to develop reversible OD and rhinorrhea due to impaired mucociliary clearance of nasal mucosa.[22–24] The mucociliary impairment caused by smoking can prolong the viral infectivity time in the nasal cavity, which could result in an increased number of infected cells in OSE. Although it is not conclusively proved in the study, smoking can increase the duration of spontaneous recovery of OD, which could also result in permanent OD.

Most of the COVID patients who had anosmia as one of the initial symptoms usually recover between 1 and 3 weeks spontaneously without any treatment. Treatment of COVID-19-related OD may be required if the symptoms persist for more than 3 weeks. The efficacy of any such treatment is not documented yet. We initially treated such patients with doses of intranasal steroids (fluticasone furoate nasal spray 2 puffs twice daily) with a low degree of improvement. Oral corticosteroids are not recommended because of the associated side effects. On reviewing the literature, it was found that there is a role of olfactory training which involves repeated sniffing of common odors, like lemon, coffee, rose, cloves, and eucalyptus, for 20–30 seconds each twice daily for 16 weeks.[25] Various studies have demonstrated improved olfaction in patients with post-infectious OD after olfactory training. A study by Hummel et al. found that the olfactory training appears to increase olfactory function in approximately 30% of the subjects over a period of 12 weeks compared to subjects who had no olfactory training.[26] Another study on olfactory training by Konstantinidis involving 119 patients found that 16-week short-term exposure to specific odors may increase olfactory sensitivity in patients with post-infectious and post-traumatic OD.[27] The same can be extrapolated for the management of OD associated with COVID-19. The olfactory training is very cost-effective and does not have any side effects. In this regard, it needs to be mentioned that we came across patients who used camphor, which is readily available in all Indian households, smelling it daily for a few minutes two to three times a day, and this has yielded excellent results in COVID-19 patients. As a matter of fact, some of them reported a return of camphor smell on as early as the third day and then other smells, like coffee aroma/lemon, after 3–4 days. There is no evidence regarding the use of camphor in OD, and it requires further studies. It could be acting just like olfactory training as with the other odors. Adjuvant therapies, like vitamin A, which may act to promote olfactory neurogenesis, and systemic omega-3, which may act through neuroregenerative or anti-inflammatory means, coupled with zinc 50 mg twice daily can help. The above adjuvant therapies are supposed to help in olfactory training; however, to date, there is no evidence that these therapies are effective in patients with OD related to COVID-19.

These findings are important for otorhinolaryngologists because in the post-pandemic scenario, SARS-CoV-2 will be put in the differential diagnosis of patients with OTDs. Patients presenting with isolated sudden OTDs should be looked for SARS-CoV-2 by molecular tests. There is a further need to study the presence of SARS-CoV-2 in the olfactory bulb and olfactory nerve in postmortem patients, which could enlighten us and give a better picture of neurological manifestations of this virus.

References

1. Zahra SA, Iddawela S, Pillai K, et al. Can symptoms of anosmia and dysgeusia be diagnostic for COVID-19? Brain Behav 2020;10(11):e01839. DOI: 10.1002/brb3.1839.
2. Vaira LA, Deiana G, Fois AG, et al. Objective evaluation of anosmia and ageusia in COVID-19 patients: single-center experience on 72 cases. Head Neck 2020;42(6):1252–1258. DOI: 10.1002/hed.26204.
3. Rai SK, Gupta TP, Kashid M, et al. Can self-perceived easy fatigability be a predictor of vitamin D deficiency in young Indian women? J Family Med Prim Care 2020;9(2):997–1002. DOI: 10.4103/jfmpc.jfmpc_862_19.
4. Martineau AR, Jolliffe DA, Hooper RL, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. BMJ 2017;356:i6583. DOI: 10.1136/bmj.i6583.
5. Suzuki M, Saito K, Min WP, et al. Identification of viruses in patients with postviral olfactory dysfunction. Laryngoscope 2007;117(2):272–277. DOI: 10.1097/01.mlg.0000249922.37381.1e.
6. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 2020;579(7798):270–273. DOI: 10.1038/s41586-020-2012-7.
7. Ohkubo K, Lee CH, Baraniuk JN, et al. Angiotensin-converting enzyme in the human nasal mucosa. Am J Respir Cell Mol Biol 1994;11(2):173–180. DOI: 10.1165/ajrcmb.11.2.8049077.
8. Moein ST, Hashemian SM, Mansourafshar B, et al. Smell dysfunction: a biomarker for COVID-19. Int Forum Allergy Rhinol 2020;10(8):944–950. DOI: 10.1002/alr.22587.
9. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review

and meta-analysis. Int J Infect Dis 2020;94:91–95. DOI: 10.1016/j.ijid.2020.03.017.
10. Gane SB, Kelly C, Hopkins C. Isolated sudden onset anosmia in COVID-19 infection. A novel syndrome? Rhinology 2020;58(3):299–301. DOI: 10.4193/Rhin20.114.
11. Hopkins C, Surda P, Kumar N. Presentation of new onset anosmia during the COVID-19 pandemic. Rhinology 2020;58(3):295–298. DOI: 10.4193/Rhin20.116.
12. Mehraeen E, Behnezhad F, Salehi MA, et al. Olfactory and gustatory dysfunctions due to the coronavirus disease (COVID-19): a review of current evidence. Eur Arch Otorhinolaryngol 2021;278(2):307–312. DOI: 10.1007/s00405-020-06120-6.
13. Jafek BW, Hartman D, Eller PM, et al. Postviral olfactory dysfunction. Am J Rhinol 1990;4(3):91–100. DOI: 10.2500/105065890782009497.
14. Mueller C, Temmel AF, Quint C, et al. Olfactory function in HIV-positive subjects. Acta Otolaryngol 2002;122(1):67–71. DOI: 10.1080/00016480252775760.
15. Bearer EL, Breakefield XO, Schuback D, et al. Retrograde axonal transport of herpes simplex virus: evidence for a single mechanism and a role for tegument. Proc Natl Acad Sci U S A 2000;97(14):8146–8150. DOI: 10.1073/pnas.97.14.8146.
16. Diefenbach RJ, Miranda-Saksena M, Douglas MW, et al. Transport and egress of herpes simplex virus in neurons. Rev Med Virol 2008;18(1):35–51. DOI: 10.1002/rmv.560.
17. Ahmad I, Rathore FA. Neurological manifestations and complications of COVID-19: a literature review. J Clin Neurosci 2020;77:8–12. DOI: 10.1016/j.jocn.2020.05.017.
18. Becker Y. HSV-1 brain infection by the olfactory nerve route and virus latency and reactivation may cause learning and behavioral deficiencies and violence in children and adults: a point of view. Virus Genes 1995;10(3):217–226. DOI: 10.1007/BF01701811.
19. Daval M, Corré A, Palpacuer C, et al. Efficacy of local budesonide therapy in the management of persistent hyposmia in COVID-19 patients without signs of severity: a structured summary of a study protocol for a randomised controlled trial. Trials 2020;21(1):666. DOI: 10.1186/s13063-020-04585-8.
20. Doty RL, Shaman P, Applebaum SL, et al. Smell identification ability: changes with age. Science 1984;226(4681):1441–1443. DOI: 10.1126/science.6505700.
21. Meisami E, Mikhail L, Baim D, et al. Human olfactory bulb: aging of glomeruli and mitral cells and a search for the accessory olfactory bulb. Ann N Y Acad Sci 1998;855:708–715. DOI: 10.1111/j.1749-6632.1998.tb10649.x.
22. Ajmani GS, Suh HH, Wroblewski KE, et al. Smoking and olfactory dysfunction: a systematic literature review and meta-analysis. Laryngoscope 2017;127(8):1753–1761. DOI: 10.1002/lary.26558.
23. Ramos EM, De Toledo AC, Xavier RF, et al. Reversibility of impaired nasal mucociliary clearance in smokers following a smoking cessation programme. Respirology 2011;16(5):849–855. DOI: 10.1111/j.1440-1843.2011.01985.x.
24. Rodrigues FM, Ramos D, Xavier RF, et al. Nasal and systemic inflammatory profile after short term smoking cessation. Respir Med 2014;108(7):999–1006. DOI: 10.1016/j.rmed.2014.04.020.
25. Whitcroft KL, Hummel T. Olfactory dysfunction in COVID-19: diagnosis and management. Journal of the American Medical Association 2020;323(24):2512–2514. DOI: 10.1001/jama.2020.8391.
26. Hummel T, Rissom K, Reden J, et al. Effects of olfactory training in patients with olfactory loss. Laryngoscope 2009;119(3):496–499. DOI: 10.1002/lary.20101.
27. Konstantinidis I, Tsakiropoulou E, Bekiaridou P, et al. Use of olfactory training in post-traumatic and postinfectious olfactory dysfunction. Laryngoscope 2013;123(12):E85–E90. DOI: 10.1002/lary.24390.