Published online: 2020-06-15

SPECIAL ARTICLE COVID-19

Olfaction and COVID: The little we know and what else we need to know

Fábio de Rezende Pinna[1] Deusdedit Brandão Neto[1] Marco Aurélio Fornazieri[2,3] Richard Louis Voegels[1]

[1] Division of Otorhinolaryngology, Universidade de São Paulo, São Paulo, SP, Brazil
[2] Department of Surgery, Universidade Estadual de Londrina, Londrina, PR, Brazil
[3] Pontifícia Universidade Católica do Paraná, Londrina, PR, Brazil

Address for correspondence Richard Louis Voegels, MD, PhD, Divisão de Otorrinolaringologia, Universidade de São Paulo, São Paulo, SP, Brazil (e-mail: rvoegels@gmail.com).

Int Arch Otorhinolaryngol 2020;24(3):e386–e387.

Dear Editor,

The coronavirus disease 2019 (COVID-19) is an ongoing viral pandemic that emerged from East Asia and quickly spread to the rest of the world. This infection is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Recently, there have been numerous reports in the media that anosmia occurs in patients who have contracted coronavirus disease 2019 (COVID-19) by exposure to the SARS-COV-02 virus. The COVID-19 is usually characterized by upper and lower airway symptoms, such as fever, cough, dyspnea, sputum production, myalgia, arthralgia, headache, diarrhea, rhinorrhea, and sore throat. However, the spread of the virus worldwide has shown atypical complaints, such as olfaction and gustatory dysfunction.[1–3]

In Brazil, since February 25th, there have been more than 120,000 infected individuals and 8,000 deaths until the date the present letter was written on. Self-reported anosmia has also been quite common in our country. Nowadays, there are a myriad of literature citations emerging, from single case report to self-reported surveys, from all over the world on this matter.

Subsequently, a few hypotheses have risen in the past months regarding these symptoms. Most of the studies have detected an olfactory loss prevalence higher than 60%.[2] One European multicentric survey has shown a prevalence of 85.6% of all the infected population. The same study showed that 78% of the patients have recovered in at least 8 days[3].

A methodology to decrease response bias from self-reported data is testing subjects and controls. A study from Iran tested 60 patients with COVID-19 and 60 controls with the University of Pennsylvania Smell Identification Test. They found that 98% of the patients reported some degree of olfactory deficit. Although it is hard to test large sample sizes, this manuscript depicts more precise information regarding the classification of the chemosensory loss.[2] More extensive sample sizes studies would have detected differences in subgroups that this article from the Middle East might have failed to do.

Another study from Europe hypothesized that olfactory disturbances could be highly associated with mild or moderate cases, even with a small sample size.[3] However, there is a lack of evidence that this atypical symptom could serve as a predictor of severity. Many studies support a high rate of simultaneous taste impairments. This probably should be secondary to the neuroepithelium damage.

Survey studies usually have a trend to overestimate prevalence. However, most of them agree that the prevalence of olfactory loss is higher than 60% of cases.[1–4]

Future studies should clarify whether this chemosensory loss differs according to COVID-19 severity or hospitalized and non-hospitalized patients. It is important to emphasize that survey studies, even when using smell validated tests, usually overestimate prevalence, since subjects with anosmia or hyposmia tend to participate more in these studies. It is also not known if the recovery rate prevalence or duration varies in different countries where olfaction habits may vary.

Although the association between olfaction and other nasal symptoms is not established, there is a weak association among microsmia, nasal obstruction, and rhinorrhea in this subset of patients.[3,4] Another critical topic to be verified is if reporting loss of smell could be a reliable predictor to mild or moderate COVID-19 infection.[1,2]

Small-size surveys could fail to detect differences in subgroups, such as presence of asthma, chronic nasal

published online
June 15, 2020

DOI https://doi.org/10.1055/s-0040-1713143.
ISSN 1809-9777.

symptoms, gender, and age groups. Larger sample size and well-defined strata would be the main features of the subsequent studies. All the data collected from observational studies could help us to better understand this pandemic disease.

Regarding pathophysiology, the severe inflammation due to virus infection still needs better understanding, and maybe autopsies of patients who died could compare tissue damage between the olfactory epithelium and the bulb. In addition, the olfactory epithelium expresses two host receptors, angiotensin-converting enzyme 2 (ACE2) and transmembrane protease, serine 2 (TMPRSS2) proteases, that facilitate SARS COV 2 binding, replication, and accumulation. This may be the underlying mechanism for reported cases of smell dysfunction in patients with COVID 19. It is very likely that these receptors' neurons initiate the severe inflammation.[6] As a matter of fact, histopathological analysis, including harvesting cadaveric specimen from both olfactory epithelium and bulb, will help us understand the exact virus pathway.

Finally, randomized clinical trials should also bring information on therapeutic alternatives, such as topical drugs, oral corticosteroids, and olfactory training.

References

1 Eliezer M, Hautefort C, Hamel AL, et al. Sudden and Complete Olfactory Loss Function as a Possible Symptom of COVID-19. JAMA Otolaryngol Head Neck Surg 2020; [Epub ahead of print]. Doi: 10.1001/jamaoto.2020.0832

2 Moein ST, Hashemian SMR, Mansourafshar B, Khorram-Tousi A, Tabarsi P, Doty RL. Smell dysfunction: a biomarker for COVID-19. Int Forum Allergy Rhinol 2020; [Epub ahead of print]. Doi: 10.1002/alr.22587

3 Lechien JR, Chiesa-Estomba CM, De Siati DR, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. Eur Arch Otorhinolaryngol 2020; [Epub ahead of print]. Doi: 10.1007/s00405-020-05965-1

4 Yan CH, Faraji F, Prajapati DP, Boone CE, DeConde AS. Association of chemosensory dysfunction and Covid-19 in patients presenting with influenza-like symptoms. Int Forum Allergy Rhinol 2020; [Epub ahead of print] . Doi: 10.1002/alr.22579

5 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; [Epub ahead of print]. Doi: 10.1002/hed.26204

6 Butowt R, Bilinska K. SARS-CoV-2: Olfaction, Brain Infection, and the Urgent Need for Clinical Samples Allowing Earlier Virus Detection. ACS Chem Neurosci 2020;11(09):1200–1203. Doi: 10.1021/acschemneuro.0c00172