

Loss of Smell and Taste are Newly Emerging Symptoms in COVID-19 Patients Necessitating More Insights into their Diagnostic Evaluation

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Dear Editor,

The COVID-19 pandemic, driven by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has currently infected more than 61 million people and caused the death of more than 1.4 million around the world (November 2020 figures).¹ As a result, many countries and health organizations have had to investigate the reasons for the pandemic and improve their health care programs to cope with the emergency while trying to develop an effective vaccine. In February 2020, the World Health Organization (WHO) initially reported that the symptoms in patients with COVID-19 included fever, dry cough, sore throat, and muscle weakness. In addition, shortness of breath often indicated severe respiratory illness; however, on 4 May 2020, in a subsequent update of the presenting symptoms, the WHO indicated that loss of smell or taste could be a warning symptom for COVID-19 as many cases were being reported in different countries.¹

In the past, a few studies² have suggested an association between SARS-CoV-1 and anosmia, while the presence of SARS-CoV-1 has been reported in the nasal discharge of a patient presenting with post-viral olfactory dysfunction.³ In general, the literature, as typified by Nordin and Brämerson⁴ and Parma et al,⁵ has shown that olfactory dysfunction due to viral infections may account for 11–45% of all olfactory disorders, excluding presbyosmia. In February 2020, during the current pandemic, the presence of hyposmia was reported in China, and this was followed by multiple reports worldwide, which documented hyposmia and hypogeusia in 13–65% of cases that tested positive for COVID-19.⁶

There are anecdotal reports that indicate different patterns in the presentation of acute respiratory distress syndrome in SARS-CoV-2 compared with SARS-CoV-1. Smell and/or loss of taste have been observed in 45% of COVID-19 patients, and they were the first symptoms in 27%, even before other symptoms appeared.^{7,8} This trend is a challenge in preventing community transmission because its atypicality delays detection and treatment.

So the question becomes, why do loss of smell and taste occur?

The impact of COVID-19 on chemosensory modalities remains poorly understood. Chemosensory disturbances can result in quantitative reductions in smell (anosmia and hyposmia) and taste (ageusia and hypogeusia) or cause qualitative changes such as parosmia, dysgeusia, phantosmia, phantogeusia, etc. It seems that the mechanism that explains chemosensory disturbances in COVID-19 patients is quite different from olfactory dysfunctions in patients with rhinitis, chronic rhinosinusitis, or nasal polyps, which are primarily caused by blockages due to edema, inflammation, or the presence of toxins and microorganisms.⁹ In some recent studies, the ACE2 and TMPRSS2 receptors that bind with SARS-CoV-2 and lead to mucosal cell invasion were found to play a crucial role in affecting the neural bulbs of smell (the supporting cells) and taste neurons.⁷

Furthermore, the primary cell type affected is the supporting cell in the nasal olfactory epithelium, which is the main receiver cell for this virus. This has been reported¹⁰ in post-mortem magnetic resonance

imaging studies in patients who have died due to COVID-19. The virus's presence on ACE2 and TMPRSS2 receptors of the tongue and epithelium of the oral cavity has also been reported.¹¹

It is well known that the olfactory sensory neurons are the sensory organs for smell. Odors from the external environment are detected through the nostrils (orthonasal olfaction), and those from food or drink are detected via the nasopharynx (retronasal olfaction). The gustatory system (taste) responds to non-volatile compounds in the mouth that elicit sensations of sweet, salty, bitter, sour, and umami (savory). Chemesthesis detects other chemicals, often found in herbs or spices, that evoke sensations such as burning, cooling, or tingling. However, smell, taste, and chemesthesis are often conflated, mainly because they produce a single experience of flavor during eating, though they are separate sensory systems with distinct peripheral and central neural mechanisms.^{5,7} The modality of taste has occasionally been explored in COVID-19 patients;⁶ however, chemesthesis has still not been studied even though some authors have speculated its compromise.^{5,7,12} Clinical assessment and laboratory tests are insufficient to evaluate the chemosensory impairments and show differences in symptom severity. Therefore, the incorporation of testing of chemosensory function with the existing clinical and laboratory work-up would indeed be a stepping stone in improving our understanding of the impact of SARS-CoV-2 on olfactory cells; however, the limited availability of test laboratories and insufficient resources hinder the implementation of such an initiative in most countries.

The latest development in this regard is that a group of researchers and scientists from a combination of WHO and European-based organizations working on smell, taste, and chemosense have developed a model for the early detection of COVID-19 in patients based on questionnaires or surveys called the Global Consortium for Chemosensory Research (GCCR) questionnaires. Pennsylvania State University (Penn State) in the US has developed a model from an online survey of more than 650 members in 54 countries and 30 languages. We have contributed to the venture by adding an Arabic version, which is also available online (<https://gchemosensr.org/ar>). In addition, a clinical self-assessment tool has been developed by a group of scientists in Europe. In this, a person with suspected symptoms can choose

from four different types of taste material available at home and from this assign an analog score from 1 to 10, to evaluate the reduction or improvement in their senses.⁸ This alternative has the advantage of assessing taste without a physician being present, thus avoiding the risk of spreading infections. There have been more than 47 346 respondents to the GCCR survey to date, while 2664 respondents have completed a follow-up survey based on self re-testing. Early reports from our patients in Oman have shown that only 4–15% present with hyposmia or hypogeusia in the first three to five days of their infections, then they recover quickly. However, a small number of patients who lost their sense of smell or taste with the infection did not show any improvement until they underwent five to six weeks of smell and taste rehabilitation treatment.^{9,13,14}

In conclusion, changing the spectrum of symptoms and adding more atypical presentations of COVID-19 are challenging. The smell and taste dysfunctions have been noticed to present before more serious symptoms appear; however, further insights into the application of reduced taste and smell in diagnosing COVID-19 are lacking due to difficulties in testing olfaction and taste in the current distressing scenario. More understanding and research are needed to explore this in the future.

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