

## SPECIAL ARTICLE COVID-19

# Olfactory and Taste Disorders in Patients with SARS-CoV-2 Infection

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Int Arch Otorhinolaryngol 2020;24(3):e391–e392.

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Dear Editor,

Since December 2019, a pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread globally.<sup>1,2</sup> A spectrum of disease severity has been reported for the infection, with the main symptoms being fever, fatigue, dry cough, myalgia, and dyspnea.<sup>3</sup>

Previous strains of coronavirus have been demonstrated to invade the central nervous system through the olfactory neuroepithelium and propagate from within the olfactory bulb.<sup>4</sup> Furthermore, nasal epithelial cells display the highest expression of the SARS-CoV-2 receptor, angiotensin-converting enzyme 2, in the respiratory tree.<sup>5</sup>

It has been observed that SARS-CoV-2 does not appear to generate clinically significant nasal congestion or rhinorrhea—that is, a red, runny, stuffy, itchy nose. This observation suggests a neurotropic virus that is site-specific for the olfactory system. Although labeled as a virus that affects the respiratory system, coronaviruses are known to be neurotropic and neuroinvasive.<sup>6–9</sup>

Olfactory and taste disorders are well known to be related with a wide range of viral infections.<sup>10,11</sup> In a mice model, SARS-CoV has demonstrated a transneural penetration through the olfactory bulb.<sup>12</sup> Moreover, angiotensin converting enzyme 2 receptor, which is used by SARS-CoV-2 to bind and penetrate into the cell, is widely expressed on the epithelial cells of the mucosa of the oral cavity.<sup>13</sup> These findings could explain the underlying pathogenetic mechanism of taste and olfactory disorders in SARS-CoV-2 infection.

## Studies on Smell and Taste Dysfunction in Patients with COVID-19

Giacomelli et al<sup>14</sup> performed a cross-sectional survey of the prevalence of these alterations in the context of SARS-CoV-2 infection after some patients admitted for COVID-19 at

the Infectious Disease Department of the L. Sacco Hospital, in Milan, Italy, complained of olfactory and taste disorders (OTDs). Of 88 hospitalized patients, 59 were able to be interviewed (29 were non-respondents, of whom 4 had dementia, 2 had a linguistic barrier, and 23 were on non-invasive ventilation). Of these, 20 patients (33.9%) reported at least 1 taste or olfactory disorder, and 11 (18.6%) reported both. Twelve patients (20.3%) presented the symptoms before the hospital admission, whereas 8 (13.5%) experienced the symptoms during the hospital stay. Taste alterations were more frequently observed (91%) before hospitalization, whereas, after hospitalization, taste and olfactory alterations appeared with equal frequency. Females reported OTDs more frequently than males (10/19 [52.6%] vs 10/40 [25%];  $p = 0.036$ ). Moreover, patients with at least 1 OTD were younger than those without it (median, 56 years [interquartile range {IQR}, 47–60] vs 66 [IQR, 52–77];  $p = 0.035$ ).<sup>14</sup>

Spinato et al<sup>15</sup> evaluated the prevalence, intensity, and timing of an altered sense of smell or taste in patients with mildly symptomatic SARS-CoV-2 infection. Any altered sense of smell or taste was reported by 64.4% of the patients (95% CI, 57.3–71.0%), out of whom 34.6% also reported blocked nose. Other frequent symptoms were fatigue (68.3%), dry or productive cough (60.4%), and fever (55.5%). Among all patients, the timing of an altered sense of smell or taste onset in relation to other symptoms occurred before other symptoms in 11.9%; at the same time in 22.8%; and after other symptoms in 26.7% of cases. An altered sense of smell or taste was reported as the only symptom by 3.0% of the patients. An altered sense of smell or taste was more frequently reported by women (72.4%, 95% CI: 62.8–80.7%) than by men (55.7%, 95% CI: 45.2–65.8%;  $p = 0.02$ ).<sup>15</sup>

Xydacis et al<sup>16</sup> have observed that anosmia, with or without dysgeusia, manifests either early in the disease process or in patients with mild or no constitutional symptoms.

## Conclusion

Olfactory and taste disorders are fairly frequent in patients with SARS-CoV-2 infection and may precede the onset of full-blown clinical disease. Alterations in smell or taste were frequently reported by mildly symptomatic patients with SARS-CoV-2 infection and often were the first apparent symptom. Consideration should be given to testing and self-isolation of patients with new onset of altered taste or smell during the COVID-19 pandemic.

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