LETTER TO THE EDITOR



High prevalence of olfactory and taste disorder during SARS-CoV-2 infection in outpatients

To the Editor,

We read with interest the meta-analysis by Sun et al and their conclusion on the most prevalent symptoms based on 10 reports weighted prevalently on Chinese patients.¹ The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) epidemic initiated in China in December 2019 has drawn relevant attention to respiratory symptoms and to clinical pictures dominated by severe respiratory engagement leading to noninvasive and invasive ventilation.^{2,3} After China, Italy has experienced the second wave of epidemic spread and also has a high case-fatality rate attributed to multiple factors.⁴ In their report, the authors align with the vast majority of reports from the far East conveying the notion that coronavirus disease 2019 (COVID-19) is predominantly related to respiratory symptoms thus confirming the need for preparedness to respiratory support/ intensive care unit.^{5,6}

We note, however, that this analysis is based exclusively on hospitalized patients, which only represent a minor proportion (about 20%) of all infected symptomatic patients, and may thus represent a relevant bias. Limited or no information has been so far gathered on the majority of milder cases of SARS-CoV-2-disease that are cared for at home since they are not progressing to respiratory insufficiency and hospitalization/ventilation.

In addition, profound olfactory and taste disorder (OTD), that has been reported to be frequent in hospitalized patients in Italy,⁷ is not reported in China or other areas,^{2,3,5} and correspondingly fails to be reported in the meta-analysis.¹

To investigate OTD in outpatients, a questionnaire was administered at our institute to physicians caring for patients with COVID-19 at home. A total of 95 patients have been observed independently (Table 1). Patients had been followed up in five different independent areas, without epidemiological relationship. All had confirmed SARS-CoV-2 infection as determined by nasopharyngeal swab polymerase chain reaction (NFS), had mild symptomatic disease with fever and without respiratory distress nor need for hospitalization/respiratory oxygen support.

Notably, 48 of 95 (50.5%) patients had extensive taste disorder (>8 on a 10-grade Likert scale) and had an associated self-assessed olfactory dysfunction compared to their experience before onset of fever and COVID-19 symptoms (grade > 6, Likert scale) (Table 1). ODT was reported to occur very early on during disease (within 5 days from the onset of fever). All patients reported loss of taste to the otherwise lively variety of regional Italian dishes. In all cases, OTD was reported as a first-in-life event. All patients had other complaints leading to NFS including influenza-like illness with fever (37.5°C-38°C), myalgias, fatigue, nausea, and diarrhea. From onset of symptoms, no patient had progression to polypnea severe cough and/or oxygen desaturation over a mean observation of 10 days (range: 5-18).

Mild olfactory dysfunction may occur in some patients with common cold and chronic rhinitis and may occur with considerably lower incidence in peak influenza season (12%),⁸ while profound taste dysfunction is quite unusual during viral infections.

A limitation of the meta-analysis by Sun et al¹ and of other reports on hospitalized patients^{2,3,5,6} is represented by an unexplained biased reporting on ODT, which in Italy represents a prevalent symptom not only in hospitalized patients with respiratory insufficiency,⁷ but also in the majority of outpatients, as reported here.

Reasons underlying failure to report this clinical picture so far may include failure to detect, recognize or report these signs, different population genetics of chemosensors, or differences in regional cuisine habits. SARS-CoV-2 infection determines a surprisingly high and widespread incidence of OTD which appears to be pathognomonic. This high frequency of ODT can be used to help identify SARS-CoV-2 outpatient cases without respiratory involvement in western countries.

For these reasons, we suggest that meta-analyses that are performed on exclusively hospitalized populations with patient selection

TABLE 1	Taste and odor alterations in nonhospitalized
mild-modera	ate asymptomatic patients with positive nasal/throat
SARS-CoV-2	2 detection

Independent patient group	SARS-2+	Mild/ moderate ILI	OTD disorder n (%)
1	14	14	6 (43)
2	30	30	7 (23)
3	13	13	6 (46)
4	7	7	6 (86)
5	31	31	23 (74)
Total	92	95	48 (51)

Note: Fever <38.5°C; myalgias, fatigue, nausea, vomiting, diarrhea, cough. Abbreviations: ILI, influenza-like illness; OTD, olfactory and taste disorder; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.

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skewing based on ethnicity or country of origin and without consideration of ODT need to account for the above limitation.

We suggest that taste and smell disorder in COVID-19 patients should be considered and included in disease definitions. This would be beneficial to the diagnosis of COVID-19 patients with inconspicuous symptoms. In fact, at this stage of the pandemic, the number of asymptomatic SARS-CoV-2 infections is increasing, and any clinical symptom that had not been previously noticed is beneficial to the diagnosis of COVID-19.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

All authors have visited patients, and contributed to write the manuscript.

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