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WILEY

LETTER TO THE EDITOR

Halitosis in COVID-19 patients

Dear Editor,

Halitosis is a reflective condition for an array of systemic insults such as respiratory, otolaryngologic and gastrointestinal pathologies that may alter salivary characteristics and tongue dorsum susceptibility for hosting anaerobic microorganisms. The high prevalence of halitosis globally requires a multidisciplinary approach for its diagnosis, assessment and treatment to discriminate between genuine, pseudo- and denied halitosis based on subjective metrics.[1] As with other circulating pandemics, halitosis has been greatly challenged by the outbreak of the coronavirus disease (COVID-19), and a few confirmed cases were reported to present with halitosis while being actively infected.[2] We hereby aim to report according to the CARE guidelines, the demographic, clinical and laboratory characteristics of eighteen patients with confirmed COVID-19 without any relevant medical history, who experienced new-onset halitosis during their course of infection.[3]

The referenced patients sought care at our department between May and August 2020 due to an offensive oral malodour that precipitated notable psychosocial distress, especially with their spouses. All patients had previously undergone polymerase chain reaction (PCR) testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) for various reasons, for instance: before-travel screening (22.2%), after-travel screening (27.8%), being in contact with a positive case (22.2%), presenting with mild symptoms such as fatigue (22.2%) and moderate symptoms (5.6%). The PCR test confirmed their infection with a mean cycle threshold value of 25.72 ± 5.5 (15-34) (Table 1).

Their mean age was 35.11 ± 13.3 (18-72) years old; 14 patients (77.8%) were females, and three patients (16.7%) were smokers. Regarding the characteristic symptoms of COVID-19, two patients (11.1%) had persistent fever, a further two patients (11.1%) had anosmia, one (5.6%) had ageusia, and one (5.6%) presented with a dry cough. Nine of the 18 patients were prescribed medications, where four (22.2%) were taking paracetamol, three (16.7%) were taking ibuprofen, one (5.6%) was taking prednisolone, and one (5.6%) was prescribed chloroquine.

The Oral Health Assessment Tool was used to evaluate the oral hygiene status of the investigated patients which revealed that the majority of them had a 'fair' level of oral hygiene with dental plaque in one to two areas of the mouth, except for two patients (11.1%) who presented with a 'poor' level of oral hygiene with dental plaque in most areas of the mouth, while one patient (5.5%) further complicated by an intraoral ulcer conjoining halitosis.[4]

To quantitatively assess halitosis, Halimeter Plus (Interscan Corp., Simi Valley, CA) was used to estimate the amount of the volatile sulfur compounds (VSCs) in parts per billion (ppb).[5] On their initial visit (T_0), the mean halitosis intensity was 203.89 ± 95.56 (100-420) ppb, confirming that all patients had physiological halitosis.[6] The patients were instructed to use symptomatic treatments for 1 month; twelve patients (66.7%) used 'magic mouthwash' containing lidocaine, chlorhexidine and prednisolone among other ingredients, and six patients (33.3%) used chlorhexidine gluconate (CHX) 0.3% mouthwash. At their follow-up appointment (T_1), the mean halitosis intensity was 68.75 ± 30.96 (20-120) ppb with two missed cases. A one-way within-subjects ANOVA test yielded a significant decrease in halitosis intensity over time in the vast majority of the patients; Wilks' Lambda = 0.351, F (1,15) = 27.756, $P < .001$. Mann-Whitney U test for both types of prescribed mouthwash demonstrated a statistically significant difference favouring 'Magic mouthwash' in reducing halitosis intensity, U ($N_{Magic} = 10$, $N_{CHX} = 6$) = 3.5, $z = -2.88$, $P = .002$. All investigated patients agreed to use their clinical and laboratory results for academic purposes while concealing their identifying personal data.

Our findings suggest that possible epithelial alterations of the tongue dorsum may be caused by SARS-CoV-2 due to angiotensin-converting enzyme 2 receptors which are profoundly located in abundance around the oral mucosa with the highest expression on the tongue dorsum.[7] By scanning the ultrastructure of tongue dorsum, Watanabe found that halitosis was strongly associated with epithelial alterations of desquamated keratinized tongue mucosa.[8] They may also support the hypothesis of Dziedzic et al, expounding acute infections of COVID-19 can cause xerostomia through decreased salivary flow, thus mediating greater occurrence of halitosis.[9]

TABLE 1 Demographic, clinical and laboratory characteristics of COVID-19 patients with halitosis

No	Gender	Age	PCR purpose	Ct*	Fever	Cough	Anosmia	Ageusia	Hygiene*	Smoking	Ulcer	COVID-19-MED*	HT-T_0*	HT-T_1*	HT-MED*
1	Male	29	Before-travel	31	No	No	No	No	Fair	No	No	Nothing	230	70	Magic
2	Female	52	After-travel	34	No	No	No	No	Fair	No	No	Paracetamol	340	40	Magic
3	Female	45	Contact w/ +ve case	26	No	No	Yes	No	Fair	No	No	Paracetamol	240	110	CHX
4	Female	72	After-travel	32	No	No	No	No	Fair	No	No	Paracetamol	230	50	Magic
5	Female	19	Mild symptoms	20	No	No	No	No	Fair	No	No	Ibuprofen	200	100	CHX
6	Male	32	Mild symptoms	21	No	No	No	No	Fair	Yes	No	Nothing	120	120	CHX
7	Female	42	After-travel	31	No	No	No	No	Fair	No	No	Ibuprofen	250	80	Magic
8	Female	29	Contact w/ +ve case	19	Yes	No	No	No	Fair	Yes	No	Prednisolone	390	30	Magic
9	Female	50	Moderate symptoms	15	No	No	Yes	Yes	Poor	No	Yes	Chloroquine	420	70	Magic
10	Female	37	Contact w/ +ve case	20	No	No	No	No	Fair	No	No	Ibuprofen	110	100	CHX
11	Female	18	Before-travel	30	No	No	No	No	Fair	No	No	Nothing	150	Missed	Magic
12	Female	29	Mild symptoms	31	No	No	No	No	Fair	No	No	Nothing	140	20	Magic
13	Female	26	After-travel	30	No	No	No	No	Fair	Yes	No	Nothing	190	40	Magic
14	Male	38	Contact w/ +ve case	25	Yes	Yes	No	No	Fair	No	No	Nothing	130	90	CHX
15	Female	26	After-travel	21	No	No	No	No	Fair	No	No	Nothing	150	40	Magic
16	Female	25	Before-travel	24	No	No	No	No	Fair	No	No	Nothing	150	50	Magic
17	Female	29	Mild symptoms	24	No	No	No	No	Poor	No	No	Paracetamol	130	90	CHX
18	Male	34	Before-travel	29	No	No	No	No	Fair	No	No	Nothing	100	Missed	Magic

*Ct = Cycle threshold value of PCR testing for SARS-COV-2.

*Hygiene = Oral hygiene level as assessed by the Oral Health Assessment Tool (OHAT).

*COVID-19-MED = Medications prescribed by the treating physicians for COVID-19.

*HT-T_0 = Halitosis intensity as assessed by Halimeter Plus on the initial visit.

*HT-T_1 = Halitosis intensity as assessed by Halimeter Plus after 1 month.

*HT-MED = Medications prescribed to relieve halitosis.

Current therapeutic strategies involve treating COVID-19 patients with antibiotics to prevent the occurrence of secondary infections. Bacterial co-infections arising from SARS-CoV-2 may have a role in modulating the oral environment to favour the proliferation of species comprising the halitosis-associated microbiota and broader periodontopathic gram-negative bacteria.[10] In line with this notion, the three drugs which were prescribed to our patients have a recorded history of causing halitosis as an adverse effect.[1]

Plausibly, the psychological impact of the COVID-19 outbreak could negatively change health-related behaviours, including those centred around oral hygiene. Additionally, these challenges may impact individual attitudes towards seeking professional oral care, which could indirectly affect the oral microbiome, particularly if people refrain from maintaining good oral hygiene for several weeks.[11] In the correspondence by Patel et al, a 35-year-old female presented with severe halitosis adjacent to necrotizing gingivitis which suggested the impact of bacterial co-infection on COVID-19 severity.[2]

Another indirect effect of COVID-19 on oral health is triggered by universal masking policies which may cause mouth breathing yielding xerostomia and halitosis. It might also work vice versa, as mouth breathers are at a higher risk of getting infected by COVID-19 due to the decreased nitric oxide saturation, in addition to their vulnerability for developing xerostomia and halitosis.[12] The last explanatory hypothesis for diagnosis of halitosis in COVID-19 patients is the increased attention of the public towards their mouth odour due to their new habit of wearing face masks thus indicating that halitosis was previously underdiagnosed.

In conclusion, this case-series warrants larger epidemiological studies to accurately estimate the prevalence of halitosis among COVID-19 patients and to further investigate its possible etiologies that may be linked either directly, or indirectly, to SARS-CoV-2 infection.

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