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Olfactory and gustative disorders for the diagnosis of COVID-19

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Dear editor

Early in the course of the still on going COVID-19 pandemic, clinicians noticed the significance of olfactory and gustative disorders [1]. A recent systematic review and meta-analysis of ten and nine available studies, reported a prevalence of 52.7% olfactory and 43.9% gustatory dysfunction respectively [2].

As soon as the outbreak reached France, we established in Marseille massive early PCR screening from a nasopharyngeal sample for patients suspected of having COVID-19, and anybody seeking treatment or SARS-CoV-2 screening [3]. Here, we questioned for recent loss of smell (LOS) and/or taste (LOT) in a cohort of patients and health care workers (HCW) before they were tested for SARS-CoV-2 by asking “have you lost your sense of smell or taste in the last 2 months?”

A total of 3497 patients were questioned between 24 March and April 25, 2020 (Table). SARS-CoV-2 was detected by PCR on nasopharyngeal swabs in 673/3497 (19.24%) of the patients tested. Of the 673 positive patients, 280 (41.6%) reported LOS and LOT, 41 (6.1%) reported LOS only, and 35 (5.2%) reported LOT only. Of the 2860 COVID-19 negative patients, 137 (4.85%) reported a LOS and LOT, 39 (1.38%) reported LOS only, and 81 (2.85%) reported LOT only. Among 2884 patients with no loss, 317 (10.99%) tested positive for COVID-19 and 2567 (89.0%) tested negative. Overall, the prevalence of LOS and/or LOT in COVID-19 patients was 356/673 (53%), which was higher than in non-infected patients (257/2824; 9.1%, $p < 0.001$; Chi-squared test). LOS and/or LOT were more frequent in female COVID-19 patients (233/401, 58.10%) than in male COVID-19 patients (123/272, 45.22%), particularly in patients under the age of 65 (women 221/361, 61.21%; men 113/231, 48.91%) ($p < 0.05$). Regarding the diagnosis of COVID-19, the positive predictive value (PPV) was 67.15% for LOS and LOT, 51.25% for LOS only, 30.17% for LOT only, and 58.08% (60% in women and 53% in men under the age of 65) for LOS and/or LOT. Overall, the negative predictive value (NPV) of smell and/or taste disorders was 89.01% (92% in men and 88% in women under the age of 65) (Table 1).

A total of 432 HCWs, including 271 women, were tested for COVID-19 using RT-PCR on nasopharyngeal swabs, in addition to an IgM/IgG antibody test (Sure Bio-Tech, Hong Kong) which was performed

according to the manufacturer's instructions, and using an in-house indirect immunofluorescence assay (IFA), as described [4], in the context of occupational medicine consultation between 17 and April 22, 2020. Among of them, 23 reported having a fever or cough in the last two months. Of the HCWs who did not report having a fever or cough ($n = 409$), seven reported LOS and LOT, and two with LOT only. Of the HCWs without a fever or cough, 10 (2.4%) reported LOS and/or LOT and all were positive for COVID-19. In addition, three HCWs without a fever or cough did not report any smell or taste loss, despite testing positive for SARS-Cov-2. In this population of HCWs, the PPV of LOS and/or LOT was 73% and the NPV was 99%.

In this study, we did not use one of the numerous tests of olfactory/gustatory function, nor did we use a score according to the number of smells recognised. We made the choice to use a single question, in order to be able to use this question in the context of real-life triage, family medicine, occupational medicine and self-evaluation, at an early stage of COVID.

To date, the exact pathogenesis responsible for olfactory or gustatory effects in COVID-19 patients is not known [2]. In acute phases of upper respiratory infection (URI), it is common to experience transient olfactory symptoms, sometimes accompanied by taste disorders, as a result of nasal inflammation, mucosal oedema, and obstruction of airflow. SARS-CoV-2 may also cause an inflammatory response in the nasal cavity that temporarily leads to the obstruction of airflow and then to anosmia/ageusia. Indeed, cells in the olfactory epithelium present the highest expression of the SARS-CoV-2 receptor, angiotensin-converting enzyme 2, making them a potential specific target [2]. Interestingly, the olfactory bulb is known as an important pathway for neurotropic viruses such as influenza viruses and previously known coronaviruses [5]. However, these disorders have not been described in previous URI epidemics, although this may be a bias of observation.

We found a higher prevalence of smell and taste complaints in women than in men. In addition, we revealed that smell and taste complaints were more prevalent under the age of 65, whereas there were no difference in uninfected patients. This result is consistent with a previous cross-sectional survey [6]. Moreover, our questionnaire appeared to be very suitable for HCWs because this population in our

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Table 1

Olfactory and gustatory dysfunctions in patients seeking SARS-Cov-2 testing according to gender and threshold age 65 at the IHU Mediterranean-Infection, Marseille, France, between 24 March and April 25, 2020. CoV+ and CoV-: patients testing positive and negative for SARS-Cov-2 respectively. LOT: loss of taste; LOS: loss of smell. PPV Positive predictive value; NPV: negative predictive value.

	Total n = 3,497 [§]		Men n = 1,801 ^{§§}		Women n = 1,696 ^{§§§}		<65 n = 3223		>65 n = 274	
	CoV+	CoV-	CoV+	CoV-	CoV+	CoV-	CoV+	CoV-	CoV+	CoV-
N	673	2824	272	1529	401	1295	592	2631	81	193
LOT only	35 ^a	81 ^a	10 [*]	36 [*]	25	45	31 ^k	78 ^k	4	3
PPV (%)	30.17		21.74		35.71		28.44		57.14	
LOS only	41 ^b	39 ^b	16 ^c	14 ^c	25 ^h	25 ^h	37 ^l	35 ^l	4	4
PPV (%)	51.25		53.33		50		51.39		50	
LOS and LOT	280 ^e	137 ^c	97 ^f	55 ^f	183 ⁱ	82 ⁱ	266 ^m	133 ^m	14 ^o	4 ^o
PPV (%)	67.15		63.82		69.06		67.17		77.78	
LOS and/or LOT	356 ^d	257 ^d	123 ^g	105 ^g	233 ^j	152 ^j	334 ⁿ	246 ⁿ	22 ^p	11 ^p
PPV (%)	58.08		53.95		60.52		57.59		66.67	
No loss	317	2567	149	1424	168	1143	258	2385	59	182
NPV (%)	89.01		90.53		87.19		90.24		75.52	

[§] mean age 42.5 years, SD = 15.16 years); ^{§§} mean age 42.53 years, SD = 14.98 years; ^{§§§} mean age 42.42 years, SD = 15.35 years; *p < 0.05 ^{a-p}; p < 0.001. All statistical analyses were performed using IBM SPSS Statistics (version 20 for windows). The Chi-squared test, mean comparison, and a logistical regression were used to explore the links between olfactory or gustative disorders and variables (age, gender). For statistical significance, the p < 0.05 threshold was chosen. The performance of a binary classification of our method was measured by sensitivity and specificity percentages.

institution is mainly composed of young women.

Questioning patients and HCWs will be useful for selecting patients or HCWs to be tested in countries where access to testing is politically or technically limited, or when identifying patients to be isolated or self-isolated while awaiting testing and treatment, and with regard to taking public health measures.

Ethics

Data presented herein were collected in the context on regular care for patients, and occupational medicine for HCWs; and analysed retrospectively using the electronic health recording system of the hospital. This study is part of a non-interventional retrospective study that was approved by our institutional review board committee (Mediterranean Infection N°: 2020–021). According to European General Data Protection Regulation No 2016/679, patients were informed of the potential use of their medical data (N° MR 5010010520 in the AP-HM register) and that they could refuse the use of their data.

Transparency declaration

The authors declare no competing interests.

Author's contributions

All authors have made substantial contributions to this work and have approved the final manuscript. SB and JF contributed equally to this work. Concept and design: PP, PB. Acquisition, analysis, and interpretation of data: SB, JF, FC, LM, FF. Resources: TR, JM, HTD, MM, JCL, MM. Writing original draft: SB, JF, PP. Writing review and editing: PP. Supervision: PP.

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