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Utility of hyposmia and hypogeusia for the diagnosis of COVID-19

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For the Rennes-Angers-Nantes (RAN) COVID Study Group

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Early and accurate diagnosis of patients infected with human coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is key in the management of the current pandemic. Following its emergence in China, coronavirus disease 2019 (COVID-19) has spread in the northern hemisphere during the winter season, while other respiratory viruses co-circulate, notably influenza. This epidemiological conjunction complicates clinical diagnosis of COVID-19, as patients often present with influenza-like illness (ILI). Consequently, the definite diagnosis of COVID-19 mostly relies on positive RT-PCR on respiratory samples, although discriminant features have been reported on thoracic CT-scan.¹ However, access to these diagnostic tests is limited in the context of this large-scale pandemic. Distinctive clinical features would be welcome, to better select patients who require investigations. During the early phase of COVID-19 outbreak in France, we noticed that many COVID patients reported loss of smell (hyposmia), and taste (hypogeusia). We aimed to investigate the diagnostic value of these symptoms.

Rennes, Angers, and Nantes are referral centers for emerging infectious diseases in Western France (population catchment area, 5 million inhabitants). The study was carried out from 15th to 18th March, 2020, while there was no public awareness of the potential link between taste or smell disorders, and COVID-19. All patients who underwent tests for SARS-CoV-2 by RT-PCR on nasopharyngeal samples since February 16th were contacted by e-mail or phone to fill in a web-based questionnaire, with four questions: i) have you been diagnosed with COVID-19 following diagnostic screening; ii) did you notice a loss of smell during your disease; iii) did you notice a loss of taste; iv) do you regularly suffer from ear, nose, and throat (ENT) disorders. The study was approved by the Rennes University Hospital institutional review board.

Of the 452 patients contacted, 259 (57%) replied, of whom 68 (26%) reported positive test for SARS-CoV-2. Hypogeusia was reported by 63 patients (24%), hyposmia by 51 patients (20%), both by 43 patients (17%), and ENT disorders by 82 patients (32%). Hypogeusia and hyposmia were strongly associated with COVID-19 diagnosis, separately and combined, in patients with and without medical

history of ENT disorders (table). The best performance was obtained with the combination of hypogeusia and hyposmia in patients with no medical history of ENT disorders, with a sensitivity of 42% [27-58], and a specificity of 95% [90-98].

To our knowledge, this is the first report of discriminant clinical features that may be used for the diagnosis of COVID-19 in patients with ILI. These symptoms, easy to collect, could be used for mass screening, by professionals with limited medical knowledge, and through telemedicine. Taste and smell disorders have been associated with herpes zoster and HIV.^{2,3} Neuroinvasive potential of SARS-CoV-2 may play a role in the pathophysiology of hypogeusia and hyposmia.⁴ As the olfactory mucosa is located in the upper region of the nasal cavity, direct or indirect effect of SARS-CoV2 in situ may be an explanation as well. The prevalence of taste and smell disorders in COVID-19 patients was estimated at 5%, but data were retrospectively collected from medical files, which may underestimate the real prevalence.⁵ Indeed, these symptoms may not be spontaneously reported if not searched for.

This study has limitations: Firstly, data were retrospectively collected, through web-based questionnaire, and we collected no data on age, sex, or other symptoms. Secondly, data were collected anonymously, so that we could not check the accuracy of the diagnosis reported by patients. Thirdly, sample size was limited, and the response rate sub-optimal. Finally, as the diagnosis relied on detection of SARS-Cov-2 by RT-PCR on nasopharyngeal samples, sub-optimal sensitivity of this test (as low as 60% in some reports) may lead to misclassification, and diagnostic bias.⁶ However, this preliminary report of a strong association between hypogeusia/hyposmia, and COVID-19 diagnosis, in patients with ILI suggests that these symptoms, easy to collect, may be a precious tool for initial diagnostic work-out in patients with suspicion of COVID-19. Larger prospective studies are required to confirm these preliminary findings.

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	Patients with SARS-Cov-2 (n=68)	Patients without SARS- Cov-2 (n=189)	Odds Ratio [IC95]	P value	Sensitivity [IC95]	Specificity [IC95]	Positive likelihood ratio [IC95]	Negative likelihood ratio [IC95]
All patients								
Hypogeusia (%)	42 (62%)	20 (11%)	13.4 [6.61-28.3]	<0.0001	62% [49-73]	89% [84-93]	5.8 [3.7-9.1]	0.43 [0.31-0.58]
Hyposmia (%)	31 (45%)	19 (10%)	7.44 [3.63-15.6]	<0.0001	46% [33-58]	90% [85-94]	4.5 [2.7-7.5]	0.6 [0.48-0.76]
Hypogeusia and hyposmia (%)	29 (43%)	13 (7%)	9.94 [4.54-22.9]	<0.0001	43% [31-55]	93% [88-96]	6.2 [3.4-11.2]	0.61 [0.50-0.76]
ENT history								
Hypogeusia (%)	14 (56%)	8 (14%)	7.55 [2.31-26.7]	0.0002	56% [35-76]	86% [74-93]	4.0 [1.9-8.2]	0.51 [0.32-0.80]
Hyposmia (%)	12 (48%)	8(14%)	5.51 [1.68-19.3]	0.0002	48% [28-69]	86% [74-94]	3.4 [1.6-7.3]	0.60 [0.41-0.89]
Hypogeusia and hyposmia (%)	11 (44%)	7 (12%)	5.47 [1.6-20.1]	0.0003	44% [24-65]	88% [76-95]	3.6 [1.6-8.1]	0.64 [0.44-0.91]
No ENT history								
Hypogeusia (%)	28 (65%)	12 (9%)	18.2 [7.27-48.6]	<0.0001	65% [49-79]	91% [85-95]	7.1 [4.0-12.8]	0.38 [0.25-0.57]
Hyposmia (%)	19 (44%)	11 (8%)	8.56 [3.38-22.7]	<0.0001	44% [29-60]	92% [86-96]	5.3 [2.7-10.2]	0.61 [0.46-0.80]
Hypogeusia and hyposmia (%)	18 (42%)	6 (5%)	14.8 [5.02-50.2]	<0.0001	42% [27-58]	95% [90-98]	9.2 [3.9-21.7]	0.61 [0.47-0.79]

ENT: ear, nose, and throat

Table 1. Diagnostic value of hypogeusia, hyposmia, and both, for the diagnosis of COVID-19