Gustatory Dysfunction as an Early Symptom in COVID-19 Screening

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Abstract: The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from Wuhan, China in December 2019 leads to the present coronavirus disease 2019 (COVID-19) pandemic. The various symptoms identified for COVID-19 are fever, dry cough, sore throat, dyspnea, fatigue, myalgia, and headache. Olfactory and gustatory dysfunctions are emerging as a new symptom more in the European patients. Taste disturbances are common in various oral and systemic diseases. Varying severity and onset of taste disturbances are reported in COVID-19 positive patients in this pandemic. But a sudden onset of taste disturbances without an established and recognized cause should raise suspicion of COVID-19. This article will analyze the various studies focusing on taste disturbances as a reliable early symptom for COVID-19 screening.

Key Words: Coronavirus disease 2019, gustatory dysfunction, severe acute respiratory syndrome coronavirus 2, symptom, taste disturbance

Currently the identified symptoms of coronavirus disease 2019 (COVID-19) are fever, dry cough, sore throat, dyspnea, fatigue, myalgia, and headache. Olfactory and gustatory dysfunctions are emerging as a new symptom. Gustatory dysfunctions are taste disturbances varying between hypogeusia, dysgeusia, phantogeusia, and ageusia. They may occur in many situations related to nerve damage, autoimmune disease, malignancy, radiotherapy, inflammation, hormone imbalance, psychologic problems, ageing, etc. Taste loss was also reported often to occur in viral upper respiratory infections and following an influenza-like illness. It is noted that many studies in this pandemic showed the association of disturbances in smell and taste with COVID-19.

The Center for Disease Control and Prevention also added the symptom of new loss of smell or taste occurring in 2 to 14 days after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) exposure in their symptoms list. World Health Organization added these symptoms as less common for COVID-19. This article analyzes the various studies reporting these new symptoms, focusing on taste disturbances as a reliable early symptom for COVID-19 screening.

POSSIBLE MECHANISMS OF TASTE DYSFUNCTION IN COVID-19

The molecular mechanisms leading to the gustatory dysfunctions in COVID-19 are still unclear. But it is suggested that angiotensin-converting enzyme-2 (ACE2) receptor expressing cells may act as target cells for SARS-CoV-2 entry. The results from single cell RNA-seq profiles shows that the ACE2 is expressed in the epithelial cells of the oral cavity and is higher in the tongue epithelium than that of buccal and gingival tissues. This indicates that oral cavity is a high risk route of SARS-CoV-2 entry and involvement of tongue epithelium may contribute to taste disturbances.

Another common possibility is the simultaneous presence of olfactory disturbances which prevents the taste sensation, because of the intimate functional correlation between these 2 chemosensory systems. However, isolated taste dysfunctions are reported in COVID-19 which shows other mechanisms are involved. Coronavirus are known to be neurotropic and neuroinvasive. This might lead to alteration in smell or taste sensation through the cranial nerves, but still lacks enough evidence. We hope that prospective histopathologic analysis from COVID-19 autopsies will give us the understanding of pathogenesis of these chemosensitive disorders.

PREVALENCE OF TASTE DISTURBANCES IN COVID-19

One of the initial study from China by Mao et al, analyzed the neurologic manifestations in SARS-CoV-2 infected 214 patients and reported ageusia in 5.6% of patients. In contrary to this, the first European clinical series showed a high frequency of chemosensitive disorders ranging between 19.4% and 88%. They also found that the gustatory changes were frequent in the initial stages of the infection and in paucisymptomatic patients. The American academy of Otolaryngology-Head and Neck Surgery recommends that anosmia, hyposmia, or dysgeusia raises the possibility of COVID-19 suspicion and also the British Association of Otolaryngology recommends that the olfactory and gustatory disturbance symptoms (chemosensitive disorders) can be included as primary screening symptoms. The Center for Disease Control and Prevention also added the symptom of new loss of smell or taste occurring in 2 to 14 days after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) exposure in their symptoms list. World Health Organization added these symptoms as less common for COVID-19. This article analyzes the various studies reporting
features data were collected through a questionnaire from 417 mild to moderate test-confirmed COVID-19 patients. The questionnaire was based on the smell and taste component of the National Health and Nutrition Examination Survey.20 Gustatory disorders were found in 88.0% of patients out of which 78.9% had hypogeusia and 21.1% had distorted ability to taste flavors. There was a significant association between olfactory and gustatory disorders (P < 0.001). The chemosensory disorders were constant in 72.8% and fluctuated in 23.4% of patients over the days. Among the recovered patients, who had residual chemosensory disorders: isolated smell disorder was in 53.9%, isolated taste disorder in 22.5% and both in 23.6%. In this study also, females were more affected by these symptoms than males. There was no significant association between the comorbidities and the presence of these symptoms.21

Most studies were based on subjective evaluation of the patients. The first study to objectively evaluate the symptoms was conducted extensively by Vaira et al on 72 COVID-19 positive patients in the University Hospital of Sassari, Italy.21 The patients were requested to provide the timeline of the onset, duration and the regression of the chemosensitive symptoms. About 73.6% of patients reported chemosensory dysfunctions during the course of the infection. Gustatory function was evaluated by the ability to identify sweet, salt, sour, and bitter tastes. The most affected sensitivities were those for sweet and sour with no clear predominance to a specific taste. Taste scoring was carried out and found as normal in 51.4%, mild hypogeusia in 22.2%, moderate hypogeusia in 15.3%, severe hypogeusia in 9.7%, and ageusia in 1.4% of patients. Isolated taste and smell disorders were reported in 12.5% and 14.4% of patients, respectively, and both in 41.7% of patients. Complete recovery of chemosensitive symptoms was reported in 66% of patients, in which 54.3% recovered in < 5 days and 45.7% in >5 days, meanwhile 34% had persistence of smell and taste alterations. Infact, 18.1% of this series presented smell and taste alterations as the first clinical manifestation of the disease. This implies that clinicians should suspect SARS-CoV-2 infection in the differential diagnosis of such nonspecific chemosensory dysfunction.

Also, it is noted that anosmia, with or without dysgeusia, manifests earlier in the disease process or in patients with mild or no constitutional symptoms.17,22 It is commented that more evidence is needed to establish these chemosensory changes as COVID-19 symptoms.

**VARIATIONS IN THE PREVALENCE OF TASTE DISTURBANCES**

Gustatory dysfunctions are reported more in European studies and there is absence of such symptom in Asian studies. This might be due to the lack of assessment of these symptom or the Chinese patients really had insignificant taste disorders. This high regional variation might be due to the mutations of surface proteins (spike-S-protein and nucleoplasmin-N protein) in SARS-CoV-2 or due to the ACE2 polymorphisms and ACE2 expression levels between Asian and European populations.23,24 There is also a high susceptibility of females to develop these chemosensory symptoms than males. This gender-related differences would be related to the variation in the inflammatory reaction process.

**CONCLUSION**

Gustatory dysfunction symptoms are more prevalent symptoms in European COVID-19 patients as part of the chemosensory dysfunction. The sudden onset of taste disorders without any oral or systemic cause needs to be recognized by the physicians, oral-maxillofacial surgeons, craniofacial surgeons, and otorhinolaryngologists as an important suspicion for COVID-19. The relationship between the duration of the gustatory symptoms and the severity of COVID-19 disease might be associated with the viral load in the oral cavity. Future studies correlating the symptomatic condition to the viral loads from the swabs or saliva will help to verify this hypothesis. Thus, the available studies clearly show that the gustatory functions may be impaired in COVID-19 patients and would be a reliable early symptom which could be used for screening, testing and for self-isolation in this pandemic keeping in mind the regional variations.

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