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Original Article

Evaluation of taste score and fungiform papillae quantification using digital image analysis in COVID-19 patients with smell and taste dysfunction

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ABSTRACT

Background: The COVID-19 pandemic which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has created a major global health crisis in recent years. Despite this, there have been few studies that have utilized reliable methods to assess changes in taste and smell perception. Therefore, our study aims at the number of fungiform papillae and objective measures of taste perception relationship among COVID-19 patients with olfactory and gustatory disorders.

Materials and Methods: This was a cross-sectional analytical study in which 57 COVID-19 patients were recruited who confirmed the dysfunction of taste and smell. Objective assessment of the sense of taste was evaluated using four different standardized solution preparations, and the scores were given according to the patient's statements. Digitalized quantification of fungiform papillae was counted. The data were analyzed with the Pearson's correlation coefficient using the SPSS version. 23 [Licensed JSSAHER, Mysuru, Karnataka, India], and the level of significance was set at <0.001.

Results: In terms of altered or reduced taste and smell, male patients exhibited a higher incidence compared to females. Compared to the sour taste, a substantial number of COVID-19 patients have displayed a notable decrease in their ability to taste sweet, salty, and bitter flavors. However, a statistically significant positive correlation was observed between taste scores and fungiform papillae density (r = 0.518, P < 0.001).

Conclusion: Our Study demonstrated that the quantitative evaluation of taste perception and the count of fungiform papillae can serve as important indicators of SARS-CoV-2 infection, and could potentially help in the early detection and treatment of COVID-19 patients, as reduced taste function is a significant marker of the disease.

Key Words: Agnosia, COVID-19, dysgeusia, severe acute respiratory syndrome coronavirus 2, taste perception

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INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is accountable for causing COVID-19, a viral illness that began in East Asia and quickly became a global pandemic. India has been severely affected, with more than a million cases reported. Clinical investigations have identified fever, cough, difficulty breathing, arthralgia, diarrhea, sore throat, sputum production, myalgia, headache, and rhinorrhea as the most prevalent symptoms associated with the disease.[1] The occurrence and severity of smell and taste disorders are early and reliable indicators of COVID-19. A review of existing literature suggests that the prevalence of gustatory and olfactory dysfunction varies significantly across different regions, with reported rates ranging from 5.6% to 96%.

The symptoms associated with COVID-19, comprising loss of smell and taste, are not unique to the disease and can be observed in other viral infections that affect the nervous system. A Cochrane review conducted by Struyf *et al*. emphasized the limited sensitivity and specificity of these symptoms for diagnosing COVID-19 and highlighted the importance of identifying more specific indicators, such as anosmia or loss of sense of smell.[2] According to Menni *et al*., the loss of smell and taste could potentially serve as an additional indicator of COVID-19, along with other well-established symptoms. Nonetheless, while the presence of olfactory and gustatory dysfunction may assist in the early detection of the disease, they do not seem to be dependable prognostic markers of the disease.[3]

Recent research has highlighted the potential for COVID-19 to cause smell and taste disorders. An early study in Italy reported that 33.9% of COVID-19 patients who were hospitalized experienced a loss of smell or taste. Further investigations conducted across Europe revealed even higher rates, with olfactory dysfunction occurring in 75% to 85% of patients and gustatory dysfunction affecting 70% to 88% of cases. Similarly, in the United States, a high prevalence of taste and olfactory disorders has been observed in COVID-19 patients. These findings suggest that changes in smell or taste could potentially serve as a reliable indicator of COVID-19 infection and could help in the early detection of the disease.[4]

While there has been research on the loss or reduction of smell and taste during the acute phase of SARS-CoV-2 infection and the subsequent months, there is limited understanding of the qualitative symptoms of these disorders. There have been limited studies utilizing objective measures to assess gustatory function in COVID-19 patients, leaving the underlying pathophysiological mechanisms of taste disorders following the disease unclear. To improve understanding in this area, we aimed to investigate the relationship between the number of fungiform papillae and objective measurements of taste perception in COVID-19-positive patients who have experienced gustatory and olfactory dysfunctions.

MATERIALS AND METHODS

The present cross-sectional analytical study was led in JSS Hospital Mysuru, and Ethical Committee clearance has been obtained from the Institution's Ethical Committee with reference number: JSSMC/IEC/05012022/33NCT/2020-21. COVID-19 patients as the case were selected from the COVID-19 care center based on the inclusion and exclusion criteria. From these cases, individuals aged 18–60-year-old person of either sex who tested positive for coronavirus through reverse transcription–polymerase chain reaction (RT-PCR) and exhibited dysfunction in both smell and taste, were selected. A person with a history of recent (dental treatment past 1 week) or oral diseases and ear, nose, and throat infections or other communicable/systemic diseases and any drug intake and food allergies that are known to cause alteration in taste function was excluded from the study.

Sample size

According to the medical literature, to investigate the loss of taste or smell with a relative precision of 15% and a 95% confidence interval, a minimum sample size of 57 subjects who tested positive for COVID-19 is required (with a compromise on the precision error). We recruited all eligible study participants consecutively from two COVID-19 sample collection centers until the desired sample size was reached.

After taking informed consent, the confirmed COVID-19 cases were clinically examined and interviewed, and data were collected on demographic details, general health information, vaccination information, drug intake, oral habits and diseases, systemic health, and the type of taste and smell changes in COVID-19-positive patients. Sample collection area, wearing appropriate personal protective equipment, and oral swab specimens are collected as per ICMR guidelines. Patients were asked to cleanse their mouths with water so that any debris from the oral cavity was wiped out. The tongue was dried with filter paper (Whatman No. 1). A cotton-tipped tweezer was used to apply a methylene blue-colored dye onto the anterior dorsal surface of the tongue, which is the area with the highest concentration of fungiform papillae. Then, the patient was asked to keep the tongue in a steady position and the image was taken using a 48-megapixel (f/2.0) Samsung S10 Lite Android phone. After transferring the images to a computer, a distinct number was assigned to each image to identify the corresponding patient. The computer-generated grid was overlaid onto the image, and the front 2 cm of the tongue was partitioned into eight 1 cm^2 sections on each side of the tongue and then counted, as shown in Figure 1. To minimize errors, the number of fungiform papillae in each section of the tongue's image of each participant was counted twice.[5]

Participants were instructed to sit comfortably and identify four basic tastes (bitter, sour, sweet, and salty) during the test. They were advised to abstain from consuming food and drinks (except water), smoking, or brushing their teeth for at least an hour before the test. The assessment of primary taste perception was conducted using Gupta *et al*.'s standardized tool.[6] The taste strips included the following concentrations and compounds: sweet (sucrose) at 0.4, 0.2, 0.1, and 0.05 g/mL; sour (citric acid) at 0.3, 0.165, 0.09, and 0.05 g/mL; salt (sodium chloride) at 0.25, 0.1, 0.04, and 0.016 g/mL; and bitter (quinine hydrochloride) at 0.006, 0.0024, 0.0009, and 0.0004 g/mL.

The filter paper strips of 8 cm in length and tip area of 2 cm^2 were dipped in the respective solutions (four concentrations of each of the four basic tastes) and placed on the dorsal surface of the anterior part of the tongue as shown in Figure 2. Taste scores were estimated for each concentration of all four basic tastants. A score of 1 was awarded for correctly identifying each taste strip, and the highest attainable score for the identification of all taste strips was 16. Fresh solutions were prepared every morning and left for 3 h before being remade. The collected data were entered into an MS Excel sheet and subjected to statistical analysis.

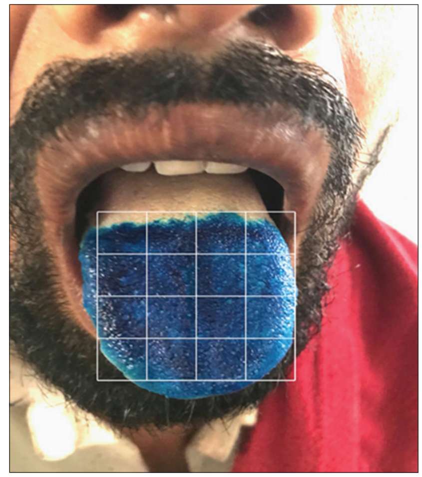


Figure 1: Stained anterior 2 cm of tongue divided into 8 areas using Adobe Photoshop.

Figure 2: The assessment of basic taste perception at the dorsal surface of the anterior part of the tongue.

Statistical analysis

Qualitative variables were articulated as frequencies and percentages, while continuous variables were expressed as mean and standard deviation. Pearson's correlation test was used to find the correlation between taste scores and fungiform density. An independent sample *t*-test was used to assess the mean difference of taste scores and fungiform density with gender. P <0.05 was considered statistically significant.

RESULTS

A total of 57 patients were included in the study. The study participants had a mean age of 42 ± 11.3 years (ranging from 19 to 60 years), with 34 females and 23 males included in the sample. Male patients exhibited changes, reductions, or losses in taste and smell in comparison to their female counterparts.

Table 1 shows that sweet, salty, and bitter tastes are more frequently affected by a loss of taste or changes in taste perception compared to sour taste. The mean and standard deviation of age, fungiform density, and taste scores (%) are 42 ± 11.3, 10 ± 1.4, and 11.7 ± 1.7, respectively, as shown in Table 2. There was no statistically significant difference in mean taste score (%) between males (10.18 ± 1.547) and females (9.74 ± 1.010, $P = 0.202$). Likewise, there was no significant difference in mean fungiform density between males (11.812 ± 1.5587) and females (11.765 ± 2.0617) ($P = 0.923$), as shown in Table 3. However, there was a positive correlation between taste scores and fungiform density, which is statistically significant ($r = 0.518$, $P < 0.001$), as shown in Graph 1.

DISCUSSION

When COVID-19 first emerged, patients often reported cough, fever, and shortness of breath as the primary symptoms. The symptom of olfactory and taste dysfunction is highly variable and one of the most commonly reported during the acute phase of COVID-19. During clinical interviews, patients often describe distorted or hallucinatory perceptions of taste, while objective tests such as strip tests are typically used to diagnose loss of taste.[7,8] The clinical examination with other risk factors and the association of taste alteration symptoms with fungiform papillae count has not been reported in India.

A cross-sectional analytical study was carried out to determine the incidence of smell or taste loss based on both self-reporting and clinical examination in individuals who underwent COVID-19 RT-PCR testing at sample collection centers in Mysuru city, Southern India. The study found that a significantly higher percentage of people who tested positive for COVID-19 had experienced a loss of smell or taste in comparison to those who tested negative. Out of the 57 participants who tested positive for COVID-19 in our study, 70% reported a loss of smell and 80% had a loss of taste, with 89% of them being vaccinated. Mullol *et al*. have noted that the prevalence of smell or taste dysfunction in individuals with COVID-19 has shown a high degree of variation, ranging from 5% to 98%, which can be attributed to differences in study methodology, research design, and country of origin.[9] Carrillo-Larco and Altez-Fernandez found that the incidence of anosmia in individuals with COVID-19 varied from 22% to 68%, while the incidence of taste disorders ranged from 20% to 33%.[10] Samaranayake *et al*. conducted a meta-analysis on 11,054 COVID-19 patients across eight studies and estimated that 74.9% of mild-to-severe cases of COVID-19 patients had anosmia, while 81.3% had

Table 1: The four different types of taste perception scores between males and females among COVID-19 patients

Score	Sweet, *n* (%)	Salt, *n* (%)	Sour, *n* (%)	Bitter, *n* (%)
1	9 (15.8)	2 (3.5)	0	2 (3.5)
2	23 (40.4)	26 (45.6)	30 (52.6)	16 (28.1)
3	25 (43.9)	27 (47.4)	26 (45.6)	33 (57.9)
4	0	2 (3.5)	1 (1.8)	6 (10.5)

Table 2: The mean, standard deviation, maximum and minimum of age, fungiform density, and taste scores among COVID-19 patients

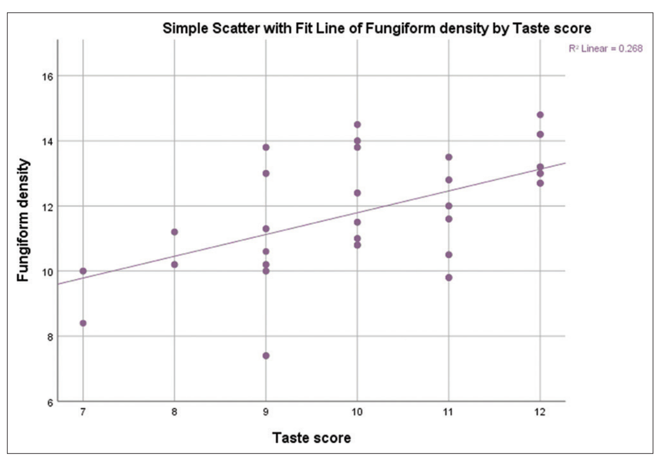
Parameters	Mean±SD	Minimum	Maximum
Age (year)	42±11.3	19.0	60
Taste score (%)	10±1.363	7	12
Fungiform density	11.793±1.7613	7.4	14.8

SD: Standard deviation

Table 3: The fungiform density and taste score between males and females among COVID-19 patients

Parameters	Sex	*n*	Mean±SD	SEM
Taste score (%)	Male	34	10.18±1.547	0.265
	Female	23	9.74±1.010	0.211
Fungiform density	Male	34	11.812±1.5587	0.2673
	Female	23	11.765±2.0617	0.4299

SD: Standard deviation; SEM: Standard error of mean



Graph 1: Correlation of fungiform papillae density and taste scores of basic tastes (sweet, salt, sour, and bitter) among COVID-19 patients.

dysgeusia.[11] As part of a European Multicenter study, Lechien *et al*. discovered that among 417 patients, olfactory dysfunction was reported among 85.6% while 88.0% reported experiencing gustatory dysfunction.[1] Jeyashree *et al*. reported that in patients with mild-to-moderate symptoms, the prevalence of self-reported alterations in the sense of smell or taste was 67%, while in patients with severe symptoms, it was 31%.[12]

The present study showed that the mean age of patients was 42 ± 11.3 years (range: 19–60). There were 34 females and 23 males. According to Yadav *et al*., the average age of their study population was 43.03 ± 16.10 years, with 51.3% being male and 48.7% being female.[13] However, in studies conducted by Lechien *et al*. and Klopfenstein *et al*., a higher incidence of gustatory and olfactory dysfunction was reported in female patients at 63% and 67%, respectively.[1,14]

Several studies have indicated that there may be a gender-based bias in the development of chemosensory dysfunctions, possibly due to differences in the inflammatory response process between males and females. In a study by Kavaz *et al*., it was found that males exhibited a notably higher degree of dysfunction in their ability to smell and taste.[7] However, the present study revealed a significantly higher impairment of taste and smell in males when compared to females. However, there was no significant mean difference in taste score between males (10.18 ± 1.547) and females (9.74 ± 1.010, $P = 0.202$). There was no significant mean difference in fungiform density between males (11.812 ± 1.5587) and females (11.765 ± 2.0617) ($P = 0.923$). However, there was a positive correlation between taste scores and fungiform density, which is statistically significant ($r = 0.518$, $P < 0.001$).

The prevalence of taste disorders in individuals with COVID-19 was examined by Hintschich *et al*. through the application of the taste strip test, which yielded a rate of 28%.[15] In another study by Singer-Cornelius *et al*., who used Burghart taste strips to evaluate the sense of taste, the authors found the rate of taste impairment as 25% and reported that this loss was mostly in sour and salty tastes.[16] Kaya *et al*. found the most significant loss of taste in salty (27%) and sour (6%) tastes.[17] However, we found that sweet, salty, and bitter tastes are more frequently affected by changes in taste perception compared to sour tastes.

Objective gustatory assessments reveal a significantly higher prevalence of gustatory dysfunction compared to subjective measures, which may underestimate the true prevalence. Given the importance of gustatory and olfactory dysfunctions as symptoms of COVID-19, it has become necessary to investigate this area to understand the disease's pathophysiology. The neural-mucosal interface may be infiltrated by SARS-CoV-2 through transmucosal entry via regional nervous structures. If the virus gains entry into the brain, it may persist for years and induce inflammation, potentially leading to chronic neurological illnesses. The angiotensin-converting enzyme 2 (ACE2) receptor, which assists SARS-CoV-2 invasion, is found in both the olfactory neuroepithelium and the taste buds. Furthermore, an inflammatory response caused by cytokine release following ACE2 receptor binding has been proposed. Despite being more practical, subjective assessments may result in an underestimate of the prevalence of gustatory dysfunction.[18]

As far as we know, this study is one of the limited research carried out in India that has reported on the frequency of smell and taste loss in people impacted by COVID-19. We have utilized both subjective and objective assessments of taste, along with digital measurement of fungiform papillae, to confirm the loss of taste. Furthermore, the individuals being examined were unaware of their COVID-19 status, which ensured that their responses were not influenced by a positive test result. Hence, our estimates are potentially more precise. The taste solutions used in the study were chosen to be prepared appropriately for the target population and can be standardized across the country using the same concentrations.

Strength of the study

Our study has the notable feature of being prospective and conducted on a real cohort of COVID-19 patients in the Indian population. This is because all patients who tested positive for COVID-19 via RT-PCR were admitted to our hospital, regardless of the presence or absence of symptoms.

Limitation of the study

The assessment of taste sensation through clinical examination still involves a subjective element, as it relies on the participant's responses. We did not attempt to account for this bias by including a control population in our study. Additionally, our study was limited to COVID-19 patients who reported a loss of taste and smell, and we did not include all hospitalized patients being tested for the virus. As a result, we were unable to investigate the duration of the symptoms or examine the relationship between these symptoms and other risk factors, disease severity, or infection outcomes. Additionally, the number of individuals reporting these symptoms was relatively small, making it difficult to conclude. To determine whether psychophysical tests and taste dysfunction can detect subclinical dysgeusia in high-risk populations, further research is needed.

As far as we are aware, this is the first single-center cohort study in India to assess fungiform papillae count and gustatory dysfunction in COVID-19 patients with confirmed diagnoses. This could offer clinicians and dietitians a systematic approach to managing COVID-19 patients in a clinical setting.

CONCLUSION

The study of identifying and assessing the fungiform papillae density and correlating it with taste scores proved to be a noninvasive tool. As there is a strong correlation between fungiform papillae density and taste scores, this study gives a roadmap for dieticians and clinicians to promote successful guidance and management for better health care. Therefore, taste and/or smell impairment is now considered an important symptom and biomarker when screening for COVID-19.

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Conflicts of interest

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or nonfinancial in this article.

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