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Predisposing factors for taste loss in a group evaluated for SARS-CoV-2

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COVID-19 manifestations tend to appear approximately 2 to 14 days after virus exposure and include among others, taste, and/or olfactory impairment; the last two manifestations are considered signs of peripheral nervous system involvement. (Mao et al., 2020; CDC, 2020; Mazzatenta et al., 2020).

It has been shown that taste function can be markedly affected by changes in the form, quantity, and vascularization of taste buds or by alterations in the respiratory tract associated with smoking habits (Fraga Da Ré et al., 2018). Other factors influencing gustatory perception depend on the peripheral physical and central neural degeneration associated with aging. In fact, a decline in the sense of taste seems to occur after 60 years of age (Spence & Youssef, 2021).

Interestingly, some medications have been related to the alteration or loss of taste. (Angelo et al., 2020; Suliburska et al., 2012; Tsuruoka et al., 2005; Vaira et al., 2020). (Risso et al., 2020).

The aims of the present study were to objectively evaluate the presence of taste dysfunction and the influence that predisposing factors (age, smoking status, and medication use) have on subjects with gustatory impairment, with particular regard to those positive for SARS-CoV-2.

The present study was approved by the CU-Tonalá Ethics Committee (CEI-2020-10), Guadalajara Mexico.

A double-blind evaluation of taste function was performed. The inclusion criteria were as follows: both sexes over 18 years of age; oropharyngeal swabs were used to test for SARS-CoV-2 infection; and patient consent for participation. The exclusion criteria were invalid or indeterminate PCR results and the presence of neurological disorders or pregnancy.

For each participant, recorded data included age, sex, comorbidities (such as hypertension and/or diabetes mellitus), smoking, and medications administered.

Gustatory function was evaluated during the appointment scheduled for oropharyngeal swabs (before the results of the PCR test for SARS-CoV-2 [first blinding]) through a standardized test previously validated by Vaira, Deiana, et al. (2020).

Each dropper was covered and coded; thus, both the operator and subject were blinded to the content of each bottle (second blinding).

Taste function was evaluated in 89 participants. See clinical data (Table1). Sixteen (18%) had a smoking habit, and 31 (34.8%) were under therapy with one or more medications.

The flavorless recognized by subjects regardless of SARS-CoV-2 test status were acid and sweet. Gustatory dysfunction was not significantly different between the SARS-CoV-2-positive and SARS-CoV-2-negative groups ($p = 0.054$). Three (5.9%) subjects

Characteristics	Positive (n = 51)	Negative (n = 38)	P (CI95%)
Age, yr, Mean ± SD, range	37.5 ± 12.6 (18-82)	38.9 ± 12.6 (20-66)	0.637
Age group			
≤59 yr	47 (92.2)	35 (92.1)	1.000
>60 yr	4 (07.8)	3 (07.9)	
Sex			
Female	28 (56.0)	23 (60.5)	0.828
Male	22 (44.0)	15 (39.5)	
Smoking	9 (38.7)	7 (18.4)	0.782
Drugs intake	20 (52.6)	12 (31.6)	0.133
Predisposing factors	31 (60.8)	18 (47.4)	0.282
Flavors dysfunction			
Acid	15 (39.5)	10 (33.3)	0.192
Sweet	14 (48.3)	10 (33.3)	0.295
Bitter	8 (27.6)	5 (16.7)	0.360
Salty	11 (37.9)	5 (16.7)	0.084
Taste dysfunction			
Ageusia	3 (05.9)	2 (05.3)	0.331
Severe hypogeusia	1 (02.0)	1 (02.6)	
Moderate hypogeusia	11 (21.6)	5 (13.2)	
Mild hypogeusia	15 (29.4)	6 (15.8)	
Taste dysfunction (combined total)	30 (58.9)	14 (39.5)	0.054
Symptoms			
Headache	38 (84.4)	22 (64.7)	0.062
Sore throat	23 (41.2)	14 (51.1)	0.381
Vomiting	3 (06.7)	4 (11.8)	0.692
Diarrhea	8 (17.8)	7 (20.6)	0.779
Runny nose	15 (33.3)	10 (29.4)	0.809
Fever	27 (60.0)	19 (55.9)	0.819

TABLE 1 Characteristics of patients SARS-CoV-2 positive and negative Table 1. Characteristics of patients SARS-CoV-2 positive and negative

Note: Predisposing factors include Age ≥60 years, smoking and drugs intake. We compared categorical and numerical variables by using the χ^2 test or Fisher's exact test and Student's t-test. *p* value lower than 0.05 was considered to be statistically significant.

Abbreviations: CI, confidence interval; OR, Odds Ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

that tested positive for SARS-CoV-2 did not recognize any flavor (ageusia), and the percentage was similar to that of subjects with negative tests. However, moderate hypogeusia was considerably more frequent (*p* = 0.331) in the SARS-CoV-2-positive group. Interestingly, headache was present in 38 (84.4%) of the subjects that tested positive.

1.1 | Taste dysfunction according to SARS-CoV-2 status and differences between predisposing factors

An increase in approximately 25% in subjects with taste dysfunction was observed in the group of subjects positive for SARS-CoV-2 with some predisposing factors (*n* = 18, 41%) (Figure 1a).

When each evaluated factor was considered independently, no statistically significant differences were found. However, patients with taste alterations that were positive for SARS-CoV-2 were twice as frequent when some predisposing factors were found. For example, while 29.5% (*n* = 13) of SARS-CoV-2-positive participants with drug intake had taste alterations, only 13.6% (*n* = 6) of the SARS-CoV-2-negative participants showed such alterations. The same occurred in the group of smokers (9.1% vs. 4.5%, respectively). On the contrary, in the group of participants over 60 years of age, the taste alteration was very similar in both the negative and positive groups (Figure 1b). Drug intake was the most frequently present predisposing factor in this study.

If we did not take into account the status of SARS-CoV-2, no increase in taste alteration was observed due to the presence or

FIGURE 1 (a) Patients positive for SARS-CoV-2 with some of the predisposing factors show an increase in 25% in taste alterations; (b) similar frequency in the group of subjects over 60 years with taste alterations

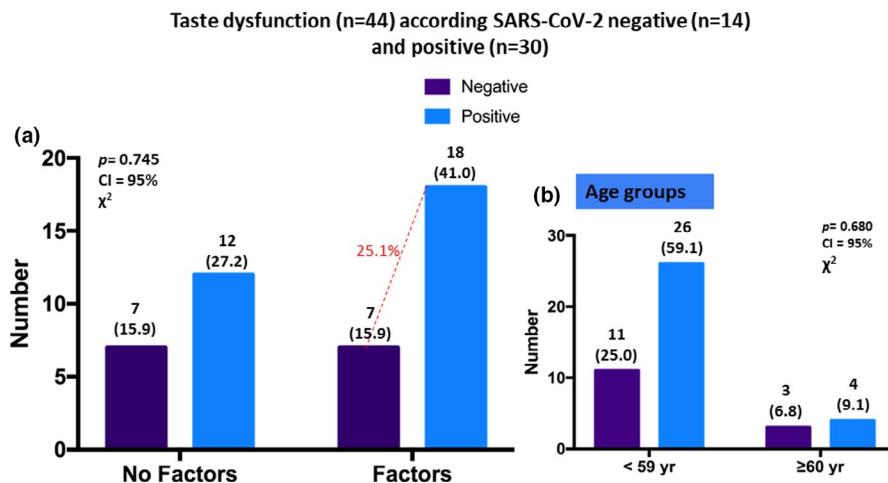
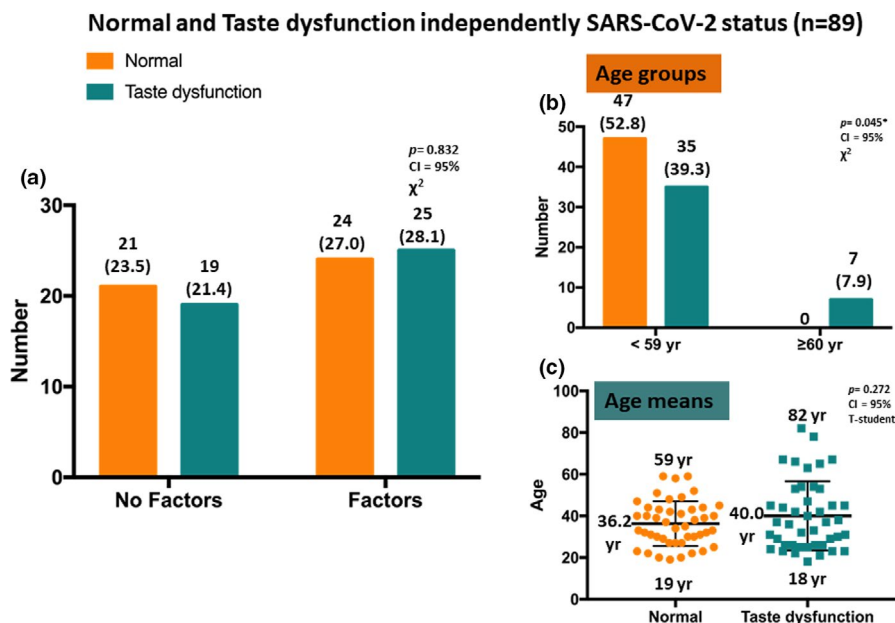


FIGURE 2 (a) Differences between subjects with normal taste and taste dysfunction without taking SARS-CoV-2 status into account; (b) the group of subjects over 60 years had some statistically significant taste dysfunction; and (c) subjects with a wide range of age had taste dysfunction



absence of predisposing factors (Figure 2a), except for age, since the subjects older than 59 years had some degree of taste dysfunction ($p = 0.045$) regardless of SARS-CoV-2 positivity (Figure 2b). However, when considering the mean age, the results were not statistically significant ($p = 0.277$) (Figure 2c).

Taste function has widely been evaluated through subjective questions and has been found that up to 88.8% of patients with COVID-19 have hypogeusia (Amorim do Santos et al., 2021). Vaira, Deiana, et al. (2020) performed an objective evaluation on Italian patients, identifying only one case of ageusia in 72 COVID-19 patients. Similarly, applying objective methods of evaluation, we found three patients with SARS-CoV-2 that had complete loss of taste in the present study. In both studies, most of the patients had only mild-to-moderate hypogeusia.

Drug intake, along with tobacco, is considered independent factors associated with taste dysfunction. In the present study, taste disturbances were detected in subjects without SARS-CoV-2 infections who were administered drugs and/or were smokers. Moreover, there appeared to be an increase in frequency of taste dysfunction,

among subjects administered with one or more drugs, in the SARS-CoV-2-positive group. However, this was not statistically significant. Based on the very recent history of the SARS-CoV-2 virus, it is not possible to provide satisfactory explanations on how predisposing factors can contribute to or boost viral effects on the gustatory system.

According to the results of the present analysis, the frequency of taste disturbances increases when viral infection and the presence of any of the predisposing factors coexist.

We found that all patients older than 60 years had taste alterations regardless of SARS-CoV-2 status. The statistical significance highlighted for age in people over 60 years must be taken with caution in regard to the possibility of having strong statistical analysis power. In contrast, we found that gustatory dysfunction affected a wide age range of subjects, similar to the study by Vaira, Deiana, et al. (2020). In our study, it was not possible to include subjects younger than 18 years, and therefore, we cannot confirm the findings of Qiu et al. (2020), who did not observe taste dysfunctions in 27 SARS-CoV-2-positive children (age range, 6–17 years).

Taste alterations have been evaluated as a possible early clinical marker of the disease. However, to the best of our knowledge, taste dysfunction is not a reliable marker for disease progression.

In conclusion, the results of the present analysis indicate that taste dysfunction attributed to SARS-COV-2 infection may also be influenced by predisposing factors, principally by drug intake, tobacco use, and older age.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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AUTHOR CONTRIBUTIONS

Sanda López Verdín: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Resources; Validation; Visualization; Writing-original draft; Writing-review & editing. **Ronell Bologna-Molina:** Conceptualization; Funding acquisition; Investigation; Project administration; Supervision; Validation; Writing-original draft; Writing-review & editing. **Diana Aguirre-Cortés:** Data curation; Formal analysis; Investigation; Methodology; Writing-original draft. **Fernanda Corona-Meraz:** Data curation; Formal analysis; Investigation; Methodology; Writing-original draft; Writing-review & editing. **Rogelio Gonzalez Gonzalez:** Investigation; Methodology; Supervision; Writing-original draft; Writing-review & editing. **Nelly Molina-Frechero:** Methodology; Project administration; Supervision; Writing-review & editing. **Marco Meleti:** Methodology; Supervision; Validation; Writing-review & editing.

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