



## ORIGINAL ARTICLE

# Long-term prevalence of taste and olfactory dysfunction in COVID-19 patients: A cross-sectional study

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## Abstract

**Objectives:** The objectives of the study were to investigate the long-term prevalence of taste disorder (TD) and olfactory disorder (OD) and associated risk factors in the non-hospitalized southeastern Brazil population of COVID-19 patients.

**Methods:** This cross-sectional open survey evaluated possible long-term OD and TD in non-hospitalized patients who had been diagnosed with COVID-19 for more than 30 days, through an online self-report questionnaire. Demographic data, comorbidities, symptoms, and the intensity of OD and TD at the time of diagnosis and at the time of completing the questionnaire were evaluated.

**Results:** Three hundred five responses were included. The reported prevalence of OD and TD was 72.9% and 67.4%, respectively, in the moment of diagnosis; after a mean follow-up period of 179 days, 45% and 50% still had some degree of the symptoms. There was a positive correlation between age and the high prevalence of OD ( $p = 0.02$ ). However, there was no correlation between age and TD ( $p = 0.961$ ) and weight in relation to OD/TD ( $p = 0.500$  and  $p = 0.636$ , respectively).

**Conclusion:** This study observed a high long-term prevalence of OD and TD associated with COVID-19, with a low recovery rate during the study period. There was a positive association between older participants and the prevalence of OD.

## KEYWORDS

ageusia, anosmia, COVID-19, olfactory disorder, taste disorder

## 1 | INTRODUCTION

COVID-19 is a severe acute respiratory infection caused by the SARS-CoV-2. Since 2019, scientists around the world have been challenged to understand the mechanism of action of the virus and find effective ways to prevent and treat the disease (Wynants et al., 2020). Although some patients develop the severe form of the disease, which requires hospitalization and intensive care, others have mild symptoms (87%) or are asymptomatic (50%) (Agostini et al., 2021; Gao et al., 2021). This subset of patients with mild or no symptoms can significantly contribute to the transmission of the disease.

Some symptoms of the disease, such as taste disorder (TD) and olfactory disorder (OD), deserve attention due to their high prevalence, especially in the earlier stages of the disease (Eliezer et al., 2020). A previous study observed the prevalence rates of TD and OD as 30.4% and 38.5%, respectively (von Bartheld et al., 2020). Another study conducted in North America reported a high rate of TD (53%) and OD (51%) in positive patients (Kempker et al., 2021).

In addition to the effects during the acute stage of the disease, some patients experience long-term effects of COVID-19, which persist for two or more weeks after the onset of the disease (Tenforde et al., 2020). A recent short communication reported that 18.8% and 14.1% of patients recovered from COVID-19 developed

late symptoms of OD and TD, respectively (Moraschini et al., 2021). Despite insufficient evidence to date, factors such as ethnicity, genetics, and predisposition can interfere with the virus's pathogenesis (Chopra et al., 2021). However, the prevalence of TD and OD have not been measured previously in the South American population. The objective of our study was to measure the long-term prevalence of TD, OD, and associated risk factors in the non-hospitalized population of COVID-19 patients in southeastern Brazil.

## 2 | SUBJECTS AND METHODS

### 2.1 | Study design

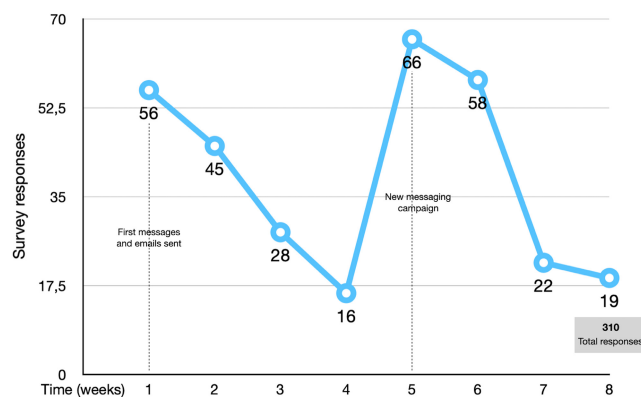
This is a cross-sectional open survey that was conducted in southeastern Brazil from September 15th to November 10th, 2021. This study evaluated, through an online self-report questionnaire, possible long-term OD and TD in patients who had been diagnosed with COVID-19 for more than 30 days. The study adhered to the principles described in the 1996 Declaration of Helsinki. The Ethics Committee of Augusto Motta University approved the research under registration number 5.098.193. The guidelines in the STROBE statement (von Elm et al., 2007) for cross-sectional studies were followed to ensure quality and transparency. In line with good practice in online research, the CHERRIES checklist (Eysenbach, 2004) was consulted.

### 2.2 | Questionnaire content

The first page of the form contained the study title, objectives, eligibility criteria, and data confidentiality statement. It also stated that respondents would not be paid for their participation. The form was hosted on Google Forms (Google). At the end of the first page, patients had to agree to the consent form to access the full survey. The online questionnaire was adapted from Andrews et al. (2020). Research participants were asked about demographic data (age, sex, ethnicity, height, and weight) and the presence of comorbidities. The questionnaire also assessed the intensity of OD and TD at the time of diagnosis and at the time of completing the questionnaire through a visual analog scale (VAS). Survey participants could score from 0 (no OD and TD) to 10 (maximum level of OD and TD).

### 2.3 | Population and data collection

Survey participants were recruited via a form delivered using email or a messaging application (WhatsApp, Facebook). The invitation message contained a brief statement with the objective of the study, the eligibility criteria, and a website link to the questionnaire. The initial messages were sent on August 15th, 2021. The form was designed to be short and contain exclusively closed-ended questions to optimize participant adherence and reduce inconsistency in responses. The survey was primarily directed toward employees



**FIGURE 1** Responses gathered with time. Between September 15th to November 10th, 2021, 305 valid survey responses were received

of health services. The inclusion criteria for patient selection were a positive diagnosis of COVID-19 made by reverse transcription-polymerase chain reaction (RT-PCR) for at least 30 days and mild to moderate viral condition without hospitalization. Participants who were diagnosed using methods other than RT-PCR, who required hospitalization, who answered the form incompletely, or who already had a history of OD and TD were excluded.

### 2.4 | Statistical analysis

Quantitative variables were summarized using the median and standard deviation, whereas qualitative variables were described with frequency and percentage. Incomplete and inconsistent data were excluded from the analyses. Linear regression was used to determine whether baseline variables (e.g., weight and age) predicted a higher prevalence of OD and TD. First, the correlation between dependent and predictor variables was verified using Pearson's correlation. Afterward, the normality of the residuals in the data was explored using the Shapiro-Wilk test. A paired *t* test was used to check whether there was a significant difference between the level of OD and TD between the participants' diagnoses and survey responses. Statistical significance was set at  $p < 0.05$ . The Jamovi statistical software (version 1.6) was used for the analyses.

## 3 | RESULTS

### 3.1 | Response rate and demographic characteristics

Three hundred ten participants answered the questionnaire. Five participants had to be excluded for presenting incomplete or inconsistent answers. Thus, 305 responses were included in the present study. The process of capturing responses over the weeks is reported in Figure 1. The mean recovery time of post-COVID-19 patients was 179 days (range of 20–720 days). The total population consisted of 237 (78%)

women and 68 men, with a mean age of  $42 \pm 12$  years. Most participants (81.8%) reported their ethnicity as white, and these participants had a mean weight of  $74 \pm 19.7$  kg. The most common comorbidities were cardiovascular diseases (8.9%), followed by diabetes (7.2%) and respiratory diseases (6.7%). The full demographic characteristics of survey participants are reported in [Table 1](#).

### 3.2 | Olfactory and taste characteristics

The prevalence of OD and TD at the time of COVID-19 diagnosis was 72.9% ( $n = 222$ ) and 67.4% ( $n = 205$ ), respectively. Of the participants who presented with OD, 67% [VAS] ( $n = 149$ ) had a total

loss of smell (anosmia), whereas 45% [VAS] ( $n = 92$ ) of participants with TD had a total loss of taste (ageusia).

### 3.3 | Prognosis of OD and TD

When evaluating the participants who presented OD and TD at the time of diagnosis, 45% [VAS] ( $n = 100$ ) and 50% [VAS] ( $n = 102$ ), respectively, still had some degree of the symptoms after a mean time of 179 days. There was no significant difference in the level of recovery from OD ( $p = 0.251$ ) or TD ( $p = 0.503$ ) [paired *t* test] between diagnosis and the participants' survey responses. The percentage of the OD and TD levels at the time of the survey and after 179 days of follow-up can be seen in [Figures 2 and 3](#).

### 3.4 | Influence of risk predictors on OD and TD prognosis

Age and weight were tested using linear regression to determine whether they interact with an increased prevalence of OD and TD. Regarding age, there was a significant correlation between older age and OD (Coef. = 2.02; 95% CI [-0.70, -0.04];  $p = 0.02$ ). There is a 20% chance for older patients to manifest OD. However, there was no significant correlation between age and TD (Coef. = 1.93; 95% CI [-0.30, 0.32];  $p = 0.961$ ). In relation to weight, no significant correlation was observed for either OD or TD (Coef. = 3.06; 95% CI [-0.20, 0.42];  $p = 0.500$  and Coef. = 3.22; 95% CI [-0.25, 0.41];  $p = 0.636$ , respectively). The complete results of the regression analysis are reported in [Table 2](#).

## 4 | DISCUSSION

The results of this study demonstrated a high prevalence rate of OD and TD in non-hospitalized COVID-19 patients. In addition, the study also noted that recovery from these symptoms is often delayed. A recent cohort study evaluating 150 post-COVID-19 Victorian patients observed a rate of OD and TD of 65% and 63%, respectively (Horvath et al., 2020). A study in India reported an incidence rate of 20% of OD and 45% of TD in 225 patients with COVID-19 (Panda et al., 2020). The present study observed a rate of 72.9% for OD and 64.7% for TD. The literature has not yet reached a consensus on the mechanism of action of SARS-CoV-2 in the development of OD. Some studies hypothesize that the cause may be associated with an impairment of the central nervous system (CNS) (Aragão et al., 2020; Fotuhi et al., 2020). However, autopsies failed to demonstrate the presence of the virus SARS in olfactory neurons (Gu et al., 2005). One hypothesis would be that the coronavirus impairs the olfactory pathways (Vaira et al., 2020).

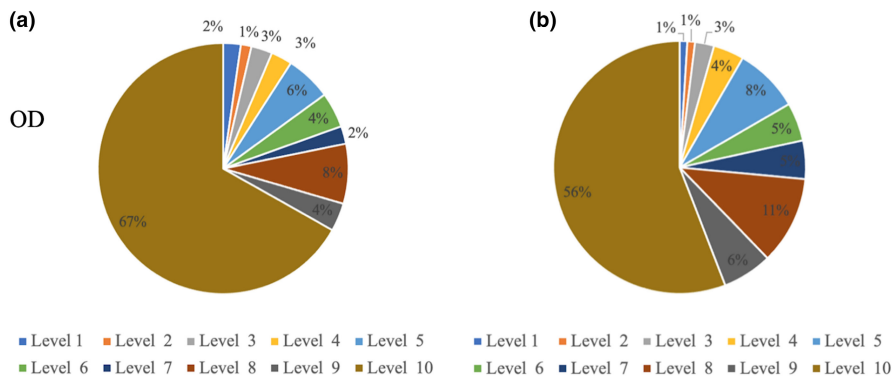
Limited data are available in the literature involving the pathogenesis of TD in COVID-19 patients (Cooper et al., 2020). RNA sequencing studies demonstrate that tongue epithelial cells express

TABLE 1 Demographic characteristics of survey participants

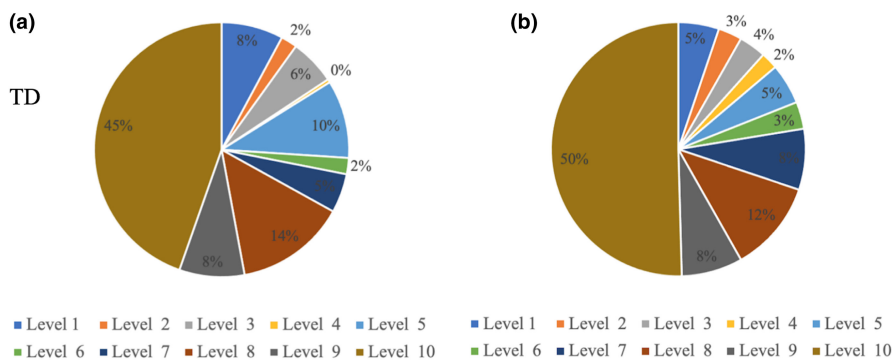
Characteristics	Value
Age, mean $\pm$ SD (range)	$42.1 \pm 12$ (14–75)
Sex, no. (%)	
Female	237 (77.7%)
Male	68 (22.3%)
Weight, $\pm$ SD (range)	$74.1 \pm 19.7$ (49–169)
Body mass index, mean <sup>a</sup>	26.8 <sup>b</sup>
Ethnicity (%)	
White	249 (81.6%)
Black	15 (4.9%)
Mixed	41 (13.4%)
Indigenous	0
Smokers, no. (%)	14 (4.6)
Systemic diseases, no. (%)	
None	233 (76.7%)
Respiratory diseases	20 (6.7%)
Cardiovascular disease	27 (8.9%)
Diabetes	22 (7.2%)
Obesity	7 (2.3%)
Thrombophilia	1 (0.3%)
Hyperthyroidism	1 (0.3%)
Arterial hypertension	1 (0.3%)
Symptoms at diagnosis, no. (%)	
Fever	105 (34.4%)
Body ache	192 (63%)
Cough	119 (39%)
Shortness of breathe	63 (14.3%)
Tiredness	154 (50.6%)
Gastrointestinal disorders	63 (20.8%)
Type of disfunction reported, no. (%)	
Olfactory disfunction	222 (72.9%)
Taste disfunction	205 (67.4%)
Both	147 (66.6%)

<sup>a</sup>Calculated as weight in kilograms divided by height in meters squared.

<sup>b</sup>Index classified as obesity (grade I) by the World Health Organization.



**FIGURE 2** Percentage of the OD level at the time of diagnosis (a) and after 179 days of follow-up (b). Survey participants score from 0 (no OD) to 10 (maximum level of OD)



**FIGURE 3** Percentage of the TD level at the time of diagnosis (a) and after 179 days of follow-up (b). Survey participants score from 0 (no TD) to 10 (maximum level of TD)

**TABLE 2** Linear regression between risk predictors and higher prevalence of OD/TD

Risk predictor	Coef.	95% CI	p value
<b>Age</b>			
Taste	1.93	(-0.30, 0.32)	0.961
Smell	2.02	(-0.70, -0.04)	0.02*
Overall model test	0.02	(-0.70, 0.32)	0.085
<b>Weight</b>			
Taste	3.22	(-0.25, 0.41)	0.636
Smell	3.06	(-0.20, 0.42)	0.500
Overall model test	0.004	(-0.20, 0.42)	0.684

\*Statistically significant.

angiotensin-converting enzyme 2 (ACE-2) receptors significantly, indicating that the oral mucosa may be the gateway to SARS-CoV-2 (Xu et al., 2020; Zhou et al., 2020). This hypothesizes that the pathogenesis of TD may be caused by damage to taste receptors present on the tongue by infection and inflammation of epithelial cells.

Increasingly, robust evidence indicates that OD and TD manifest more strongly in patients with asymptomatic or mild COVID-19 (Giacomelli et al., 2020; Hopkins et al., 2020). To remove bias associated with severe COVID-19, this study selected only those subjects who were not hospitalized. Furthermore, to increase the accuracy of the study, only subjects diagnosed with RT-PCR were included. Tobacco is also a known risk factor for OD and TD (Da Ré et al., 2018), and 4.6% ( $n = 14$ ) of participants reported being smokers. The presence of smokers may add additional bias to the results.

After a mean follow-up period of 179 days, 45% [VAS] ( $n = 100$ ) and 50% [VAS] ( $n = 102$ ), of participants continued to experience some degree of OD and TD, respectively. In a previous study evaluating 150 patients, the authors also observed long-term effects of OD (34%) and TD (28%) of COVID-19 during a follow-up period of 83 days (Horvath et al., 2020). This suggests that the possible damage caused by the infection may require a longer period of recovery in some people and that longitudinal studies evaluating these subjects are needed in the future.

Evidence for a correlation between OD, TD, and possible associated risk predictors remains scarce in the literature. Panda et al. in 2020 evaluated 225 patients and observed that patients with comorbidities present with 2.28 times the prevalence of OD or TD (Panda et al., 2020). In the present study, age was the only variable that positively correlated ( $p = 0.02$ ) with a higher prevalence of OD. The analysis showed that there is a 20% chance for older patients to manifest OD. Because elderly patients generally have more comorbidities and, consequently, take more medications, these factors may influence the higher prevalence of OD. Another study evaluating predisposing factors for the loss of taste after COVID-19 concluded that increasing age, tobacco use, and drug intake may contribute to TD (López-Verdín et al., 2021).

The data and results observed in the present study must be interpreted with caution. First, the study was a self-administered questionnaire, which may cause bias in the patient responses. Second, it remains unknown whether regional or demographic characteristics can interfere with the prognosis of the disease. In addition, there is still no known relationship between respiratory diseases (e.g., acute respiratory diseases or allergic diseases) and a higher prevalence of

OD and TD. The relationship between OD and TD and other possible confounding factors such as medications, dry mouth, burning mouth syndrome, and neurological disorders should also be investigated in the future.

## 5 | CONCLUSIONS

In conclusion, this study observed a high long-term prevalence of OD and TD associated with COVID-19, with a low recovery rate during the study period. There was a positive association between older participants and the prevalence of OD.

### AUTHOR CONTRIBUTIONS

**Daiana Reis:** Data curation; Investigation. **Suelen Cristina Sartoretto:** Data curation; Formal analysis; Investigation; Methodology. **Monica Diuana Calasans-Maia:** Data curation; Formal analysis; Writing – review & editing. **Rafael Seabra Louro:** Formal analysis; Methodology; Writing – review & editing. **Vittorio Moraschini:** Conceptualization; Data curation; Formal analysis; Methodology; Project administration; Writing – original draft.

### PEER REVIEW

The peer review history for this article is available at <https://publons.com/publon/10.1111/odi.14231>.

### ETHICS APPROVAL

The Ethics Committee of Augusto Motta University approved the research under registration number 5.098.193.

### CONFLICT OF INTEREST

The authors declare no conflict of interest.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

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