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RESEARCH NOTE

Prospective assessment of smell and taste impairment in a South-American coronavirus disease 2019 (COVID-19) cohort: Association with the need for hospitalization and reversibility of dysfunction

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anosmia, COVID-19, dysgeusia, hyposmia, olfaction disorders, risk for hospitalization, UPSIT

INTRODUCTION

Variable prevalence of smell and taste dysfunction caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection has been reported worldwide.[1,2] Although South American countries have been listed in the top ten of coronavirus disease 2019 (COVID-19) case numbers,[3,4] psychophysical data has not been reported in

these regions. This study aimed primarily to determine the frequency of self-perceived taste impairment and smell measurement in COVID-19 patients, and secondly, to assess its association with the need for hospitalization.

METHODS

We report a prospective cohort study conducted during April–October 2020, approved by our Institutional Scientific Ethics Committee (Figure S1). Cases were adults with a positive SARS-CoV-2 quantitative real-time polymerase chain reaction (qRT-PCR) and <15 days of ongoing symptoms. A chemosensory symptoms survey for self-reported olfactory and gustatory dysfunction (Table S1), and the Spanish-American version of the 40-odorant University of Pennsylvania Smell Identification Test (UPSIT) (Sensonics International, Haddon Hts., NJ, USA)[5] were applied during the recruitment process (initial UPSIT [$_{i}$UPSIT]) and repeated 30 days after symptom onset (follow-up UPSIT [$_{f}$UPSIT]). Controls were individuals without SARS-CoV-2 infection with negative qRT-PCR, immunoglobulin M (IgM)–immunoglobulin G (IgG) for SARS-CoV-2, and asymptomatic 14 days after, paired by age and sex. An UPSIT was applied in this group, to compare olfactory dysfunction prevalence in healthy subjects against cases (Figure S2).

Statistical analysis

Prospective cohort study analysis

Statistical analysis included comparisons by *t*-test and chi-square for categorical variables. Univariate linear and logistic regression models were built to assess the associations between primary outcomes: $_{i}$UPSIT score; Olfactory function improvement ($_{f}$UPSIT-$_{i}$UPSIT); outpatient or hospitalized condition (dependent variable), and each of the independent variables of interest. Multivariate linear and logistic regression models were constructed with factors significantly associated with the univariate models' dependent variable. The Hosmer-Lemeshow test was used to assess the multivariate logistic regression models goodness-of-fit. A good model fit yields a *p* value >0.05.

RESULTS

One hundred COVID-19 patients were enrolled (56 outpatients, 44 hospitalized). Five were lost during follow-up (one transferred to the intensive care unit [ICU] and four withdrew). Sixty-three controls were included. Demographics in both groups were similar (Table S2).

Self-reported symptoms in COVID-19 patients

At enrollment, smell loss was self-identified in 73 of 100 (73%) cases and was perceived at 3.4 ± 1.9 (mean ± SD) days since symptom onset. At follow-up, 23 of 94 (24.4%) persisted with olfactory dysfunction. Dysgeusia was self-perceived in 51 of 100 (51%) at enrollment. Outpatients presented dysgeusia more frequently than hospitalized individuals (36/56 [64%] vs. 15/44 [34%]; $\chi^2 = 8.99$; $p = 0.002$). At follow-up, dysgeusia decreased to 24 in 95 (25.2%).

Olfactory assessment in COVID-19 patients

$_{i}$UPSIT was obtained at 9 ± 3.2 (mean ± SD) days. Outpatients were tested at 7.5 ± 3 versus 10.8 ± 2.6 (95% confidence interval [CI], 2.09–4.40; $t = 5.584$; $p < 0.001$) days in the hospitalized group. $_{f}$UPSIT was administered on day 30.8 ± 2.2. Outpatients were tested at 30.7 ± 2 versus 31 ± 2.3 (95% CI, −0.66 to 1.15; $t = 0.532$; $p = 0.59$) days in the hospitalized group.

$_{i}$UPSIT scores were abnormal in 75 in 100 (75%) of COVID-19 patients, decreasing to 39 in 95 (41%) at $_{f}$UPSIT ($\chi^2 = 23.12$; $p < 0.001$). The $_{i}$UPSIT score was 28.07 ± 7, improving to 32.8 ± 3.4 at $_{f}$UPSIT (95% CI, 3.11–6.10; $t = 6.128$; $p < 0.001$).

Olfactory dysfunction severity at enrollment and follow-up was: mild microsmia in 27 in 100 (27%) versus 21 in 95 (22.1%); $\chi^2 = 0.629$; $p = 0.42$; moderate microsmia in 25 in 100 (25%) versus 15 in 95 (15.7%); $\chi^2 = 2.53$; $p = 0.11$; severe microsmia in 11 in 100 (11%) versus 3 in 95 (3.1%); $\chi^2 = 4.496$; $p = 0.03$; and anosmia in 12 in 100 (12%) versus 0 in 95 (0%); $\chi^2 = 12.15$; $p < 0.001$ of subjects.

Outpatients versus hospitalized condition

Hospitalized patients were significantly older than outpatients (51.1 ± 14.6 vs. 34.6 ± 11.5 years, 95% CI, 11.6–22.3; $t = 6.301$; $p < 0.001$). Outpatients had more frequent headache (50/56 vs. 31/44; $\chi^2 = 5.677$; $p = 0.01$), odynophagia (31/56 vs. 8/44; $\chi^2 = 14.31$; $p < 0.001$), and postnasal drip (14/56 vs. 4/44; $\chi^2 = 4.225$; $p = 0.03$). The univariate linear model (Table 1) showed that the mean $_{i}$UPSIT was significantly lower in outpatients (26.63 vs. 29.91), but lost significance in the multivariate analysis. Self-perceived dysgeusia was the only variable associated with a lower $_{i}$UPSIT score in the

TABLE 1 Univariate and multivariate linear regression analysis for factors associated with the $_{i}$UPSIT score, and olfactory improvement ($_{f}$UPSIT−$_{i}$UPSIT) measurement

	$_{i}$UPSIT				Olfactory improvement			
	Univariate		Multivariate[a,b]		Univariate		Multivariate[a,c]	
Variable	Mean difference (95% CI)	*p*	Mean difference (95% CI)	*p*	Mean difference (95% CI)	*p*	Mean difference (95% CI)	*p*
Age	0.02 (−0.04 to 0.08)	0.57			**−0.13 (−0.23 to −0.05)**	**0.003**	−0.06 (−0.11 to −0.01)	**0.03**
Gender								
Male	Reference	–			Reference	–		
Female	0.07 (−1.58 to 2.50)	0.94			0.76 (−2.12 to 3.75)	0.61		
Condition								
Outpatient	Reference	–	Reference	–	Reference	–	Reference	–
Hospitalized	**3.28 (0.94 to 5.94)**	**0.01**	0.80 (−1.69 to 3.67)	0.57	**−4.94 (−7.52 to −2.31)**	**<0.001**	−0.53 (−2.02 to 1.02)	0.51
Smoker	0.01 (−3.60 to 2.80)	1.00			1.06 (−3.62 to 7.71)	0.71		
Days of symptoms at the moment of the $_{i}$UPSIT	**0.55 (0.14 to 1.08)**	**0.02**	0.44 (−0.01 to 0.95)	0.07	**−0.80 (−1.25 to −0.32)**	**<0.001**	−0.17 (−0.36 to 0.05)	0.10
Self-perceived dysgeusia	**−4.02 (−6.46 to −1.40)**	**0.002**	**−3.52 (−5.78 to −0.61)**	**0.008**				
Persistent self-perceived nasal obstruction at day 30					**−3.70 (−6.34 to −1.10)**	**0.007**	−0.42 (−1.77 to 0.95)	0.55
$_{i}$UPSIT	–	–	–	–	**−0.91 (−0.99 to −0.82)**	**<0.001**	**−0.86 (−0.94 to −0.78)**	**<0.001**

Note: The standard error of linear regression models was estimated through bootstrapping (10,000 replications). The 95% CI were calculated using the bias-corrected and accelerated method. Variables significantly associated with the outcome are shown in bold.

Abbreviations: CI, confidence interval; $_{f}$UPSIT, follow-up University of Pennsylvania Smell Identification Test; $_{i}$UPSIT, initial University of Pennsylvania Smell Identification Test; Variance Inflation Factor (VIF), _____.

[a]Multivariate regression model constructed with all the significant variables.

[b]Mean VIF value = 1.32.

[c]Mean VIF value = 1.36.

multivariate model. Olfactory improvement was inversely associated with age and the $_{i}$UPSIT score in the multivariate analysis.

Olfaction impairment and hospitalization

Univariate and multivariate regression models (Table 2) showed that anosmia and odynophagia had a protective Odds Ratio (OR), while older age and a higher $_{i}$UPSIT score were associated with a greater risk for hospitalization.

DISCUSSION

We show a prevalent and partially reversible smell dysfunction, as reported elsewhere.[6] Age and better smell function were associated with a higher risk for hospitalization, whereas odynophagia decreased that risk. The inclusion of a matched control group validated our results, because control subjects had higher UPSIT scores, suggesting that the results observed in the COVID-19 cohort were not due to sociocultural reasons.

Our findings are similar to two European studies,[7–9] which found that patients reporting smell loss were less

TABLE 2 Univariate and multivariate logistic regression model for factors associated with admission

	Univariate		Multivariate[a]	
Variable	**Odds ratio (95% CI)**	***p***	**Odds ratio (95% CI)**	***p***
Age	**1.09 (1.05–1.13)**	**<0.001**	**1.09 (1.05–1.13)**	**<0.001**
Gender				
Male	**Reference**	–		
Female	**0.82 (0.37–1.82)**	0.63		
iUPSIT	**1.08 (1.02–1.14)**	**0.006**	**1.10 (1.02–1.19)**	**0.01**
Anosmia (score <18)	**0.08 (0.01–0.62)**	**0.02**		
Odynophagia	**0.18 (0.07–0.46)**	**<0.001**	**0.18 (0.06–0.58)**	**0.004**
Smoker	**0.81 (0.24–2.81)**	**0.74**		
Goodness-of-fit of the multivariate logistic regression models				**0.59**

Note: Variables significantly associated with the outcome are shown in bold. The outcome variable is dichotomic: outpatients versus hospitalized.
Abbreviations: CI, confidence interval; iUPSIT, initial University of Pennsylvania Smell Identification Test.
[a]Multivariable logistic regression model including all significant variables (except anosmia, because of collinearity with baseline UPSIT).

likely to be admitted for COVID-19 than those with normosmia. Self-perceived dysgeusia may represent the loss of flavor perception secondary to smell dysfunction or a direct injury to taste buds.

Age was associated with a lesser improvement in olfaction, as expected due to the decrease of olfactory neurons and a diminished renewal capacity of the olfactory epithelium with increasing age.[10] iUPSIT score was inversely associated with improvement in olfaction: patients with a higher iUPSIT score (better olfaction) have a smaller improvement after 1 month.

The present study has the following limitations: (1) patients with smell impairment could have been more prone to participate; and (2) outpatients had greater smell loss and were tested with the UPSIT earlier than hospitalized patients. It is possible that due to a rapid recovery of smell function, the UPSIT scores were higher in hospitalized patients.

CONCLUSION

SARS-CoV-2 induced disease produces a prevalent but highly reversible olfactory and taste dysfunction. Age and better olfactory function are associated with a greater risk for hospitalization, while odynophagia, as a symptom of COVID-19, appears to be a protective factor.

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CONFLICT OF INTEREST

The authors have declared no conflicts of interest.

AUTHOR CONTRIBUTIONS

Claudia González G. helped with the study design, recruited patients, collected and analyzed data, made figures and tables, interpreted data, and wrote the paper. Francisco Gustavo García-Huidobro, and Antonia Elisa Lagos recruited patients, collected clinical data, and wrote the paper. Erick Salinas, Adriana Toro, Rodrigo Aliaga, Luis Antonio Díaz, and Tamara García-Salum recruited patients, collected clinical data, and revised the paper. Eduardo Fuentes-López analyzed data, interpreted data, and wrote the paper. Claudio Andrés Callejas interpreted data and revised the paper. Arnoldo Riquelme helped with the study design, recruited patients, and revised the paper. Rafael A. Medina recruited patients, collected, analyzed, and interpreted data, provided funding for the study, and wrote the paper. James N. Palmer provided funding for the study, helped with the study design, analyzed and interpreted data, and wrote the paper.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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