Incidence of smell and taste disorders and associated factors in patients with mild to moderate COVID-19

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ABSTRACT:

Objectives: To determine the incidence of smell and taste disorders in our health department and to analyse the factors that could be associated with these symptoms in patients with COVID-19.

Methods: We conducted an observational descriptive study of all patients with COVID-19 in our health area diagnosed between 2020/03/10 and 2020/04/14. Factors related to smell and taste disorders were analysed.

Results: A total of 126 patients, 63 women and 63 men, aged 16–80 years, were included. As many as 69 patients (62.7%) presented hyposmia, and 58 (46%) of them had anosmia. A total of 75 patients (59.5%) presented hypogeusia, and 57 (45.2%) of them had ageusia. The risk factors that were most commonly associated with these disorders were the female sex (adjusted odds ratio, aOR 2.43 for smell disorders and 2.44 for taste disorders), allergic rhinitis (aOR 3.34 for smell disorders) and a younger age. A protective factor was arterial hypertension (aOR 0.51 for smell disorders and 0.35 for taste disorders). A history of tonsillectomy was the risk factor for taste disorder (aOR 5.23).

Conclusion: Our results indicate that these sensory disorders occurred more frequently in female patients and in young patients with mild to moderate COVID-19 infection who progressed with mild nasal congestion, posterior rhinorrhoea and without anterior rhinorrhoea. The recovery of taste occurred before the recovery of smell.

KEYWORDS: ageusia, anosmia, coronavirus infections, hyposmia, olfaction disorders

INTRODUCTION

SARS-CoV-2 is a coronavirus identified in December 2019 in China that causes the respiratory disease designated by the World Health Organisation as COVID-19 [1]. This virus, as with other coronaviruses, uses the angiotensin-converting enzyme 2 of the respiratory epithelium for cell entry [2].

The transmission mechanism is not completely understood, although it has been shown that person-to-person transmission is produced mainly through the respiratory pathway. Through air transmission, the virus contacts the mucous membranes of the eyes, nose and mouth. Another important transmission pathway is contact with contaminated surfaces and subsequent contact with the mucous membranes [3].

There is no one specific presentation form, although published data indicate that fever is the most common first clinical manifestation. Other common symptoms include cough, chills, sore throat, dyspnoea, vomiting, diarrhoea, dizziness and other respiratory symptoms [4]. Ophthalmologic symptoms such as dry eyes [5] and dermatological symptoms such as rashes and acrocyanotic lesions have also been reported on [6]. In China, few cases of COVID-19 associated with anosmia and ageusia have been reported on. In Europe, however, these are considered common symptoms, even as the initial manifestation of the disease [7].

Olfactory disorders due to viral infections of the upper airways are known and have been widely studied for rhinovirus, influenza, parainfluenza and other coronaviruses [8]. In addition to the dysfunction as the consequence of nasal obstruction produced by these viruses, there are other pathways by which this symptom can develop that are related to the viruses’ neurotropic and neuroinvasive capacity at the central and peripheral nervous system level [8–11]. Coronaviruses, including SARS-CoV-2, present neurotropism; therefore, direct impairment of the olfactory sensory neurons and possibly impairment of the chorda tympani, glossopharyngeal nerve and sensory branches of the vagus nerve could cause the smell- and taste-related disorders. Baig et al. [12] stated...
that olfactory colonisation is produced by hematogenous dissemination and dissemination through the cribriform plate through retrograde neuronal pathways infecting peripheral neurons.

The objectives of this study were to determine the incidence rate of smell and taste disorders in our health area and to analyse the factors that could be associated with these symptoms in patients with COVID-19.

MATERIALS AND METHODS

We conducted an observational descriptive study of all patients with COVID-19 in our health area who were diagnosed between 2020/03/10 and 2020/04/14.

We collected data on all the patients through their electronic medical history and conducted a telephone consultation one month after the date of the initial diagnosis of the disease.

The inclusion criterion was mild to moderate COVID-19 [13] diagnosed through polymerase chain reaction (PCR) tests. The exclusion criteria were a diagnosis of infection compatible with COVID-19 without PCR confirmation, no symptoms, death, hospitalisation in an intensive care unit at the time of the study (severe COVID-19), an age younger than 16 years or older than 80 years and residence in a nursing home (due to the difficulty in collecting information).

Variables collected

The electronic medical history recorded data related to the patients’ demographic characteristics, their medical and surgical history and the laboratory test results related to the PCR test’s positivity and subsequent negativity.

Each patient was located by telephone, the previously collected data was confirmed, and the patients were asked specifically about the onset and chronology of the COVID-19 symptoms.

During this consultation, we asked questions related to smell (anosmia, hyposmia and parosmia) and taste disorders (ageusia, hypogeusia and dysgeusia), as well as the duration of these disorders. We assessed the mean recovery time for the sense of smell and taste in the short (1–7 days), medium (8–30 days) and long term (>30 days).

Statistical analysis

For data management, we employed the IBM Statistical Package for the Social Sciences (SPSS)® version 25 for Mac OS X. We performed a descriptive study of the results. To determine the association between the presence of smell and taste disorders and the patients’ history and COVID symptoms, we performed a chi-squared test of independence using Fisher’s exact test when needed, which is shown along with the odds ratio (OR). We also performed a multivariate analysis using logistic regression of the main predictors. To compare the variances, we employed the Mann-Whitney U test, after confirming that the quantitative variables did not follow a normal distribution using the Kolmogorov-Smirnov test (age) or a comparison of means using ANOVA when the variable followed a normal distribution (recovery time) and the qualitative variable was polytomous.

RESULTS

The total number of patients with COVID during the established period was 205, 126 of whom met the selection criteria.

The mean age was 51.46 ± 16.47 years (range, 16–80 years), 63 patients (50%) were men, and 63 (49.2%) were women; 90.5% were nationals, 9.5% were active smokers and 17.5% had a moderate or severe drinking habit. Excess weight and obesity were present in 54% of the patients (Tab. I.).

The most common comorbidities were arterial hypertension (AHT), dyslipidaemia and allergic rhinitis (AR) (Fig. 2.).

Smell and taste disorders

Seventy-nine patients (62.7%) presented hyposmia, while 41 (32.5%) did not have this smell disorder, and 6 (4.8%) did not know or did not indicate whether they had experienced this symptom. Of the patients with smell disorders, 58 (46%) considered that they had experienced anosmia, and 17 (13.5%) had experienced parosmia during the course of the disease.

Six of the 126 patients (0.05%) experienced smell disorders and presented hyposmia prior to the infection, while four (0.03%) did not present these symptoms and had previous hyposmia; there was therefore no statistically significant difference (P = 0.701).

In terms of taste disorders, 75 patients (59.5%) presented hypogeusia, while 45 (35.7%) did not present this taste disorder, and 6 (4.8%) did not know or did not record whether they had experienced this symptom. Of the patients with smell disorders, 58 (46%) considered that they had experienced ageusia, and 17 (13.5%) had experienced parosmia during the course of the disease.

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<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
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<tr>
<td>Sex Male</td>
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<tr>
<td>Female</td>
<td>63 (50%)</td>
</tr>
<tr>
<td>Smoker No</td>
<td>75 (59.5%)</td>
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<td>Former smoker</td>
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<td>Obesity type I</td>
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<td>Obesity type II</td>
<td>7 (5.6%)</td>
</tr>
<tr>
<td>Obesity type III</td>
<td>3 (2.4%)</td>
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<tr>
<td>Alcohol No/Occasionally</td>
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<tr>
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<td>22 (17.5%)</td>
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<td>114 (90.5%)</td>
</tr>
<tr>
<td>Foreign</td>
<td>12 (9.5%)</td>
</tr>
</tbody>
</table>

Tab. I. Epidemiological characteristics of patients.
The incidence of smell disorders was higher in women (75.4%) than in men (55.9%), a difference that was statistically significant (P = 0.025). After analysing the patients’ demographic characteristics and medical history, we found that this disorder was the most common in the patients with AR (P = 0.031) and was less common in the patients with AHT (51.3% vs. 72.8% with AHT and without AHT, respectively; P = 0.02), and both associations were statistically significant (Tab. II.). The mean age was 49.39 ± 15.56 years and 56.54 ± 16.52 years for the groups with and without smell disorders, respectively, a difference that was statistically significant (P = 0.018).

The incidence of taste disorders was also higher in women (71.4%) than in men (54.2%), with a statistically significant association (P = 0.015). These symptoms were also less common in patients who had AHT (48.7%) compared with those who did not have AHT (72.8%) (P = 0.009).

However, there was no statistically significant association between taste disorders and AR (Tab. III.). The mean age was 49.74 ± 15.31 years for the group with taste disorders and 55.74 ± 17.18 years for the group without these symptoms, with a statistically significant difference (P = 0.034).

In the surgical history, there was a statistically significant association between taste disorders and a history of tonsillectomy (P = 0.046).

These symptoms were more frequent among the patients with a history of tonsillectomy (86.7%) than in those who had not undergone the procedure (61.5%) (adjusted OR, aOR 5.23; 95% CI 1.05–25.64) (Tab. III.).

The duration of smell disorders was less than 1 week for 18.5% of the patients, 1–4 weeks for 44.4% and longer than 4 weeks for 37%. The duration of taste disorders was less than 1 week for 27.4% of the patients, 1–4 weeks for 51.2% and longer than 4 weeks for 21.4%, with the difference being statistically significant (P < 0.001). At the time of the interview, this dysfunction persisted in 23 patients of the total who experienced a smell disorder (27.8%).

Other COVID symptoms

The most common symptoms were febricula or fever (81.7%), occasional or habitual coughing (68.2%), asthenia (66.7%) and arthralgia (61.9%) (Fig. 3.).
patients with nonsevere COVID-19 [14]. In our study, we decided to exclude patients younger than 16 years and older than 80 years due to the inability to optimally collect the information, the fact that most elderly patients presented infections of greater severity and the fact that a significant number were institutionalised in nursing homes.

The patients included in the analysis presented mild to moderate disease, i.e., the disease did not result in a respiratory distress syndrome or hospitalisation in an intensive care unit [15]. The distribution with regard to mean age, demographic characteristics and medical history agrees with the one in other published series in China [16]. AHT, dyslipidaemia and AR were the most prevalent diseases in our study population.

Sixty-eight patients (57.1%) had concomitant hyposmia and hypogeusia, a statistically significant association (P < 0.001), while 7 (5.9%) presented hyposmia but not hypogeusia, and 10 (8.4%) presented hypogeusia but not hyposmia. There was a statistically significant association between smell and taste disorders and nasal congestion (P = 0.012 and P = 0.021, respectively) and posterior rhinorrhoea (P = 0.018 and P = 0.047, respectively). Smell and taste disorders were also more frequent in patients with arthromyalgia (72% and 70.7%, respectively) and with sore throat (73.9% and 71.7%, respectively), although the association was not statistically significant. Lastly, taste disorders were more frequent in patients with dyspnoea (73.8%) and less frequent in patients with otalgia (25%) (Tab. IV.).

### Relationship between negative PCR and recovery time from smell disorders

Of the patients with smell disorders, 4 (3.2%) were treated for this symptom – 3 (2.4%) with oral corticosteroids and 1 (0.8%) with topical nasal corticotherapy.

The mean time to presenting a negative PCR was 21 ± 12.13 days for the group with a short recovery time, 18.06 ± 5.27 days for the group with a medium recovery time and 22.82 ± 9.49 days for the group with a long recovery time, with no statistically significant differences between the groups (P = 0.316). There were no differences between the recovery time and the number of PCR tests necessary to reach negativity (P = 0.596) either. The mean total number of PCR tests performed to consider the patient cured was 1.46 ± 0.82.

### DISCUSSION

In the scientific literature published to date, there has been a greater association between olfactory and gustatory dysfunction among patients with nonsevere COVID-19 [14]. In our study, we decided to exclude patients younger than 16 years and older than 80 years due to the inability to optimally collect the information, the fact that most elderly patients presented infections of greater severity and the fact that a significant number were institutionalised in nursing homes.

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The meta-analysis conducted by Wang et al. [17] found a greater association with a history of AHT, diabetes mellitus, chronic obstructive pulmonary disease, cardiovascular disease and cerebrovascular disease.
The most common symptoms of our study patients were febricula or fever (81.7%), occasional or habitual coughing (68.2%), asthenia (66.7%), smell disorder (62.7%) and arthromyalgia (61.9%). These incidence rates are higher than those published by the European Surveillance System in 14,011 cases, due to our study’s selection criteria and especially to the exclusion of asymptomatic patients with COVID-19. SARS-CoV-2 infection usually does not present the typical manifestations of nasal viral infections. Beltran et al. [35] reported that these symptoms such as fever, dyspnoea and diarrhoea were associated with the onset of severe disease, without these patients presenting a high incidence of smell and taste disorders. Mao et al. [11] found a lower prevalence of taste disorders in severe cases, with no statistically significant difference (P < 0.24), while older patients and patients with more comorbidities presented a higher incidence of severe neurological manifestations (stroke, impaired state of consciousness and musculoskeletal impairment).

In our study, we observed that AHT was a protective factor for presenting smell and taste disorders (OR, 0.39; 95% CI 0.17–0.87; and OR, 0.35; 95% CI 0.15–0.83%) respectively. This finding was probably due to the fact that the patients with smell and taste disorders were younger (with a mean difference of 7.5 years and 6 years, respectively), while the patients who presented AHT were usually older and had a greater risk of developing a more severe disease. There was also a statistically significant association between smell disorders and AR (P = 0.031), with an OR of 3.34 (95% CI 1.06–10.53), a value that remained after adjusting through logistic regression. AR is the most significant aetiological factor that contributes to the onset of smell disorders [29]. Inflammation of the nasal mucosa added to the neurotropic characteristics [12, 30–32] of SARS-CoV-2 explains this greater association in patients with AR.

The incidence of smell and taste disorders in our study was similar to that in a systematic review by Muhammad Aziz et al. [26] where almost 50% of the patients presented taste perception disorders. This high incidence of taste disorders has motivated several authors to propose the oral cavity as a possible gateway for the infection, given that a high expression of angiotensin-converting enzyme receptors has been observed on the lingual surface and oral mucosa [26, 27].

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A higher incidence of taste and smell disorders has been observed in paucisymptomatic patients and can be the only manifestation of the disease [14]. In a meta-analyses conducted by Ji et al. [28], symptoms such as fever, dyspnoea and diarrhoea were associated with the onset of severe disease, without these patients presenting a high incidence of smell and taste disorders.

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The incidence of smell and taste disorders was similar to that found by Padermo et al. [33]. As with our study, the incidence of smell disorders in the authors’ series was higher among women (75.4%) than among men (55.9%), with a statistically significant association (P = 0.025).

Xydakis et al. [34] suggested that, in the current context of the pandemic, the onset of smell and taste disorders without accompanying nasal congestion (as happens with other upper airway viruses) is suggestive of SARS-CoV-2 infection, given that SARS-CoV-2 infection usually does not present the typical manifestations of nasal viral infections. Beltran et al. [35] reported that these smell disorders were only associated with 12.9% of cases of nasal
obstruction. Unlike other series in which the infection in patients with anosmia did not produce congestion [33], our series observed a statistically significant association between smell and taste disorders and nasal congestion (P = 0.012 and P = 0.047, respectively) and with posterior rhinorrhea (P = 0.018 and P = 0.047, respectively), without previous symptoms of mucus discharge. This result suggests that although the manifestations in the upper airways can be highly diverse, there is a certain degree of inflammatory disease in the nostrils.

Therefore, these sensory disorders occurred more frequently in female patients and in young patients with mild to moderate COVID-19 infection who progressed with mild nasal congestion, posterior rhinorrhea and without anterior rhinorrhea.

In the series by Beltran et al., the complete recovery time from smell disorders was 1 week ± 3.5 days for 40% of their patients; however, the follow-up time was shorter than in our study, in which we observed a recovery time of less than 1 week for 18.5% of the patients, 1–4 weeks for 44.4% and longer than 4 weeks for 37%. The recovery time for taste disorders was shorter than the recovery time for smell disorders, with a statistically significant difference (P ± 0.001), similar to the findings of a study by Lechien et al. [36].

In our study, we observed a statistically significant association between a history of tonsillectomy and taste disorders (P = 0.046) (OR, 5.23; 95% CI 1.05–25.64). These patients had not experienced taste disorders before the pandemic, after tonsillectomy, or during a common cold. We have found no studies to date in the published literature that referred to this association. The tonsillectomy procedure can cause subsequent taste disorders due to injury to the glossopharyngeal nerve [37]. In patients who underwent tonsillectomy, the nerve trajectory is closer to the pharyngeal mucosa due to the elimination of tonsillar lymphoid tissue. These patients might therefore more easily present an injury to this nerve due to the direct action of the virus that can use the oral cavity as a gateway [26].

There was no statistically significant difference between the recovery time for smell disorders and time to negativisation of the PCR test or the number of PCR tests until negativisation. We cannot draw solid conclusions, due to the fact that a structured and homogeneous protocol was not followed given the lack of materials that occurred during this phase of the pandemic. Additionally, there are authors who have reported obtaining positive PCR results after a negative result in a previous PCR test [38]. Therefore, further studies are needed to determine the associations between these variables, so that we can establish a standardised management protocol for international implementation.

CONCLUSIONS

The incidence rate of smell and taste disorders in our area was 62.7% and 59.5%, respectively. The risk factors that were most associated with these disorders were the female sex, AR and younger age. A protective factor was AHT. The history of tonsillectomy was a risk factor for presenting taste disorders. Taste and smell disorders are the most common presentation of mild SARS-CoV-2 infections and are sometimes the only manifestation of the disease. In most cases, the patients completely recover their olfactory and gustatory capabilities.

Marina Andreu Gálvez and Alberto J. Guillén Martínez should be considered joint first author because they had contributed equally to this work.

REFERENCES