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Olfactory Dysfunction, Dysgeusia, and Clinical Outcomes in COVID-19 Patients: An Observational Study in a Tertiary COVID Referral Center in the Philippines

ABSTRACT

Objective: To describe the prevalence, onset, associated symptoms, and clinical characteristics of COVID-19 in-patients with olfactory and gustatory dysfunction at the Philippine General Hospital from March 2021 to January 2022 and determine the number of patients with olfactory dysfunction/dysgeusia who recovered or expired.

Methods:

Design: Prospective Cohort Study
Setting: COVID-19 Referral Hospital (Tertiary National University Hospital)
Participants: COVID-19 RT-PCR positive in-patients, ages 19 and older

Results: A total of 207 patients were included. Sixty-four (64) patients reported olfactory dysfunction and 79 reported dysgeusia. Olfactory and gustatory dysfunction were observed early in the course of infection, before day 6 of illness. The average length of hospital stay was 20.36 days; those with olfactory dysfunction stayed for 17.53 days, dysgeusia for 19.92 days, and 21.09 days for those who noted neither. For those subsequently intubated, 0 had olfactory dysfunction, three reported dysgeusia, three had both and six had neither. Thirteen (13) patients in the study expired. Among them, none reported olfactory dysfunction and two had dysgeusia.

Conclusions: Our results corroborate existing literature that olfactory and gustatory dysfunction as key indicators of COVID-19 with 42.5% of participants reporting these symptoms early, often before day 6 of illness. Ninety-two percent (92%) of those affected recovered and had shorter hospital stays, emphasizing the importance of recognizing these dysfunctions for improved disease detection and outcomes.

Keywords: *anosmia; dysgeusia; olfactory dysfunction, gustatory dysfunction; COVID-19; coronavirus*

On March 11, 2020, the alarming levels of spread and severity of COVID-19 infection prompted the World Health Organization (WHO) to declare a pandemic. In the months that followed, rapidly accumulating anecdotal evidence of olfactory dysfunction and dysgeusia from around the world emerged. Olfactory dysfunction, in particular, was seen in patients ultimately testing positive for the coronavirus with no other symptoms.¹ The American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) released a statement saying that, "anosmia,

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hyposmia, and dysgeusia in the absence of other respiratory disease such as allergic rhinitis, acute rhinosinusitis, or chronic rhinosinusitis should alert physicians to the possibility of COVID-19 infection and warrant serious consideration for self-isolation and testing of these individuals.¹ After a growing body of evidence, the Centers for Disease Control (CDC) and Prevention and the WHO eventually added olfactory dysfunction and dysgeusia to their list of COVID-19 symptomatology on April 17 and May 4, respectively.¹

Impairment of olfactory and gustatory function is often neglected in clinical practice but has a great impact in the quality of life of patients. In the pilot study for the Anosmia Reporting Tool for Clinicians by the AAO-HNS, anosmia was noted in 73% of patients prior to diagnosis and was the first symptom experienced by over a quarter of them.² There is evidence from all over the globe that a significant number of proven COVID-19 patients develop olfactory dysfunction or dysgeusia, however, we see few descriptions of ENT symptoms of COVID-19 in Asian studies.³⁻⁶ A search of HERDIN Plus, the ASEAN Citation Index (ACI), and MEDLINE (PubMed) using the terms “COVID-19,” “olfactory dysfunction,” “anosmia,” “gustatory dysfunction,” and “dysgeusia” revealed no studies on the relationship between olfactory dysfunction/dysgeusia and clinical outcomes in the Philippines. There is also conflicting evidence as to whether the presence of olfactory dysfunction signals a milder or more severe clinical course of COVID-19. In a study by Karimi-Galougahi in 2020, a high proportion of patients with severe COVID-19 had isolated olfactory dysfunction as the sole initial presenting symptom.⁷ In contrast, researchers at UC San Diego Health and at a tertiary hospital in Brazil observed that the presence of olfactory dysfunction suggests a milder clinical course of the disease.^{8,9}

Since we are forced to live with SARS-CoV-2, its management relies on efficient case finding to mitigate its spread. This study aims to describe the prevalence, onset, associated symptoms, and clinical characteristics of COVID-19 patients with olfactory and gustatory dysfunction at the Philippine General Hospital from March 2021 to January 2022 and determine the number of patients with olfactory dysfunction/dysgeusia who recovered or expired.

METHODS

With University of the Philippines Manila Research Ethics Board Approval (UPMREB 2020-716-01), this prospective cohort study was conducted at the tertiary National University Hospital – a designated COVID-19 referral hospital for the National Capital Region (NCR) of the Philippines. This study included all COVID-19 RT-PCR positive patients, aged 19 years and older, who were admitted to the hospital from March 2021 to January 2022. Patients who could not be contacted remotely by phone, or had concomitant sinonasal disease, previous sinonasal surgery, previous head and neck radiotherapy, psychiatric disorders,

any pre-existing systemic disease that cause olfactory dysfunction and/or dysgeusia, who experienced olfactory dysfunction and dysgeusia prior to December 2019, or who were intubated prior to or on admission were excluded.

Patient lists were retrieved from the hospital electronic medical records (EMR) - generated daily census of all the COVID wards. Through chart review, new admissions were screened if they met the inclusion and exclusion criteria and their contact details were obtained. Those who met the inclusion criteria were contacted in their hospital beds via phone call (remote data collection was enforced to maintain isolation and protect investigators), and verbal informed consent was secured. Total population sampling, a type of purposive sampling, was employed. The principal investigator collected data by asking the questions guided by an English or Filipino screening tool based on the AAO-HNS COVID-19 Anosmia Reporting Tool and approved by the University of the Philippines Manila Research Ethics Board (UPM-REB) and the Hospital Infection Control Unit (HICU). (Figure 1)

Patient characteristics and outcomes were obtained via electronic medical record review. Outcomes were based on the discharge diagnosis on the clinical abstract of each patient upon discharge. For purposes of this study, olfactory dysfunction was defined as the complete absence or decrease in olfaction, and dysgeusia as complete absence or decrease in gustation.

Data was encoded using Microsoft® Excel for Mac Version 16.0 (Microsoft Corp. Redmond WA, USA). Data was analyzed using descriptive statistics. All continuous data were presented as means and standard deviations while categorical data were presented as frequencies and percentages. All analysis were done using R version 4.2.0 (The R Foundation, Vienna, Austria) and Rstudio 2022.02.2+485.pro2 (Posit PBC, Boston, MA, USA).

RESULTS

A total of 207 patients fulfilled the inclusion criteria and were enrolled in the study from March 2021 to January 2022. They consisted of 107 males and 100 females. Age range was from 21 to 87 years. There were 153 patients aged 19 to 59 years old, and 54 patients aged ≥ 60 years of age.

Of the 207 patients, 4% reported olfactory dysfunction, 12% reported dysgeusia, 27% experienced both, and 57% did not note either symptom. Among those with olfactory dysfunction, 29 (45%) were female and 35 (55%) were male. Among those with dysgeusia, 35 (44%) were female and 44 (56%) were male. Additionally, among those with olfactory dysfunction, 48 (75%) were in the 19 to 59 years age group and 15 (25%) were in the ≥ 60 years age group. In those with dysgeusia, 59 (75%) were in the 19 to 59 years age group and 20 (25%) were in the ≥ 60 years age group. Note that the olfactory dysfunction and dysgeusia samples are not mutually exclusive and it was possible for a person to have both.

A. Data Collection Script and Form (English)

Good morning/afternoon again! This is [insert name] from PGH Otorhinolaryngology. I was the one who contacted you earlier about a research on Anosmia, Dysgeusia, and Clinical Outcomes in COVID-19 Patients. Is this [insert name of patient]? Is now a good time to conduct the interview, ma'am/sir? I anticipate that this interview will take less than five (5) minutes to complete. I would also like to remind you, that this call will not be recorded. I will just complete a data collection form based on your answers. May we begin?

1. Are you experiencing/did you experience anosmia or dysgeusia?

Anosmia	<input type="checkbox"/> YES	<input type="checkbox"/> NO
Dysgeusia	<input type="checkbox"/> YES	<input type="checkbox"/> NO

2. When was the anosmia or dysgeusia noted?
You may give the **date when** it was noted, or **how many days since your first symptom** did the anosmia or dysgeusia appear?

	Date of onset / Day of illness
Anosmia	
Dysgeusia	

3. What were the other symptoms associated with anosmia or dysgeusia?

Other symptoms	
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Thank you so much for taking the time to participate in this study, ma'am/sir.

B. Data Collection Script and Form (Tagalog)

Magandang umaga/hapon po muli! Ako ay si [insert name] mula sa PGH ENT. Ako po ang kumausap sainyo kanina tungkol sa pananaliksik ukol sa Pagbawas ng Pang-amoy, Panlasa, at ang Kinalalabasan nito sa mga Pasyente na may COVID-19. Kayo po ba ay si [pangalan ng pasyente]? Maaari po ba kayong ma-interview ngayon, ma'am/sir?

Inaasahan kong ang survey na ito ay hindi tatagal ng limang (5) minuto upang makumpleto. Gusto ko lamang po ipa-alala na ang tawag na ito ay hindi po ire-record. Itatala ko po lamang sa data collection form ang inyong mga sagot. Maaari po ba tayong magsimula?

1. Kayo po ba ay nakakaranas o nakaranas ng pagbawas ng pang-amoy o panlasa?

Anosmia	<input type="checkbox"/> OO	<input type="checkbox"/> HINDI
Dysgeusia	<input type="checkbox"/> OO	<input type="checkbox"/> HINDI

2. Kailan niyo po napansin ang pagbawas ng pang-amoy o panlasa? Maaari niyo po sabihin ang **petsa** kung kailan ito napansin o kung **ilang araw matapos ang unang sintomas** napansin ang pagbawas ng pang-amoy o panlasa.

	Petsa na napansin ang sintomas / Araw ng sakit
Anosmia	
Dysgeusia	

3. Maliban sa pagbawas ng pang-amoy o panlasa, ano pa po ang ibang sintomas na inyong naranasan kasabay nito?

Ibang sintomas	
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Maraming Salamat sa pagsali sa pananaliksik na ito, ma'am/sir.

Figure 1. Screening tool based on the AAO-HNS COVID-19 Anosmia Reporting Tool, approved by University of the Philippines Manila Research Ethics Board (UPM-REB) and the Philippine General Hospital Infection Control Unit (HICU)

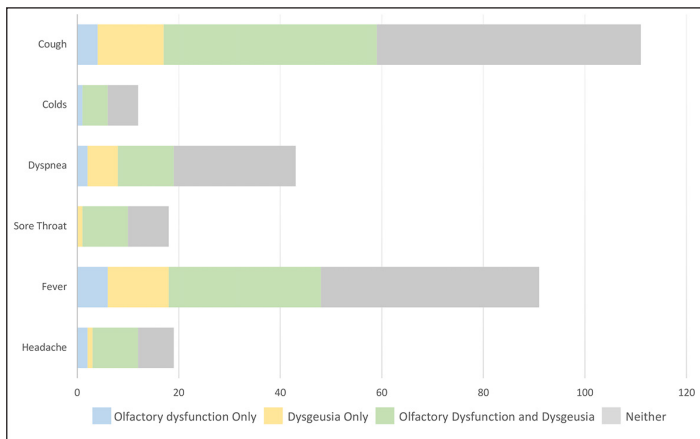


Figure 2. Other symptoms associated with olfactory dysfunction and dysgeusia

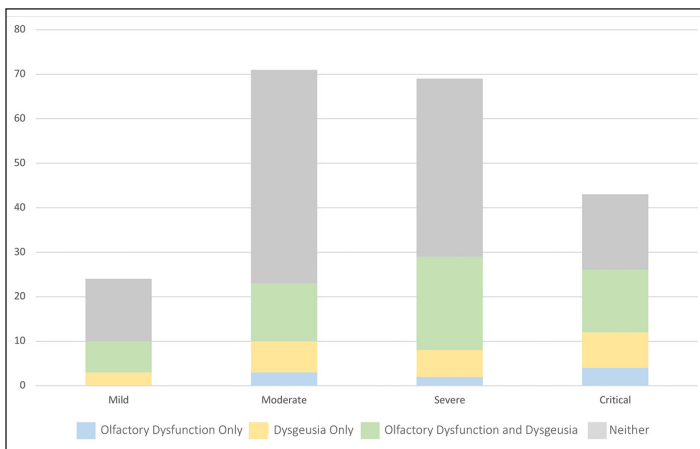


Figure 3. Distribution of COVID severity among olfactory dysfunction and dysgeusia samples

First day of onset of any symptom included in the CDC or WHO list of COVID-19 symptomatology was considered Day 1 of COVID disease. The average day of onset for olfactory dysfunction was 3.58 days \pm 1.94 days (mean day of onset \pm standard deviation) and for dysgeusia it was 3.44 days \pm 2.22 days (mean day of onset \pm standard deviation). Most patients who experienced olfactory dysfunction or dysgeusia had their onset before day 6.

Other symptoms recorded in this study were cough, colds, dyspnea, sore throat, fever, headache, generalized weakness, chest pain, nausea/vomiting, abdominal pain, and diarrhea as demonstrated in Figure 2. Among patients who presented with olfactory dysfunction only, other symptoms experienced were cough (44%), colds (11%), dyspnea (22%), fever (67%), and headache (22%) with no reports of sore throat. Among those who presented with dysgeusia only, accompanying symptoms were cough (54%), dyspnea (25%), sore throat (4%), fever (5%), and headache (4%) with no reports of colds. For those who presented with both olfactory dysfunction and dysgeusia, additional symptoms were cough (76%), colds (9%), dyspnea (2%), sore throat (16%), fever (55%) and headache (16%).

Our sample included 11.59% mild cases, 34.30% moderate cases, 33.33% severe cases and 20.77% critical cases. Figure 3 shows that there was a greater proportion of patients with either olfactory dysfunction, dysgeusia, or both with critical severity than patients with neither.

The average length of hospital stay of the sample population was 20.36 days (SD 18.39). Those who experienced olfactory dysfunction stayed for 17.53 days (SD 11.12), dysgeusia 19.92 (SD 23.68), and neither olfactory dysfunction/dysgeusia 21.09 (SD 14.51).

From the time of interview, 12 patients (6%) were eventually intubated, and 195 patients (94%) were on room air or non-invasive oxygen supplementation. Among those subsequently intubated, 0 had olfactory dysfunction only, 3 reported dysgeusia only, 3 had both olfactory dysfunction and dysgeusia, and 6 had neither.

One hundred ninety-four (194) patients (94%) were discharged, and 13 patients (6%) expired. Among those who expired, none had reported olfactory dysfunction only, two had dysgeusia only, five had both olfactory dysfunction and dysgeusia, and six had neither. Ninety-two percent (92%) of those who experienced olfactory dysfunction and/or dysgeusia were eventually discharged.

DISCUSSION

During the first few months of the pandemic, chemosensory dysfunction such as olfactory dysfunction and dysgeusia were considered rare and novel symptoms of the coronavirus. However, as more literature emerged, they were recognized as being more widespread. There is variability in the prevalence of olfactory and taste dysfunction in COVID-19 in existing literature worldwide according to a systematic review by Zahra *et al.*¹⁰

In our sample, there was an almost equal distribution among male and female patients who noted olfactory dysfunction and dysgeusia during their bout of COVID-19. Our results are similar to those reported by an Indian systematic review that did not show a significant gender predominance in the incidence rate of olfactory dysfunction.¹¹ However, several studies have found a female preponderance of olfactory dysfunction.^{5-6,12}

A European study observed that more cases with olfactory dysfunction were seen in the 22–65 years age group.¹³ In this respect, the findings are consistent with our study in which more than half of the reports of olfactory dysfunction and dysgeusia were found in those younger than 60 years of age. However, we must note that our sample's age distribution is uneven, and age-related olfactory or gustatory sensitivity has not been accounted for.

Our findings regarding the incidence of olfactory dysfunction in COVID-19 recapitulate other Asian studies which show a lower incidence of olfactory dysfunction and dysgeusia compared to Western nations. A study in a Singaporean Community Care Facility which included Indian, Chinese, Bangladeshi, and other ethnicities,

observed olfactory dysfunction in 3.0% of their patients and ageusia in 2.6%.¹⁴ Additionally, there were no reports of olfactory dysfunction in a systematic review of 5 articles about the presenting symptoms of COVID-19 conducted in China.¹⁵ In contrast, a large multicenter study from Europe found that 85.6% of COVID-19 patients reported olfactory dysfunction and 88.0% reported gustatory dysfunction.⁶ On an even larger scale, a meta-analysis involving COVID positive patients worldwide found that 44.1% had olfactory deficits and 43.3% had some form of taste deficit, and also demonstrated how Caucasians have 3-6 times higher prevalence of chemosensory deficits than East Asians.¹⁶ Klopfenstein, *et al.*⁵ theorized that these differences may be due to a possible mutation of the SARS-CoV-2 viral genome or the affinity of SARS-CoV-2 for angiotensin converting enzyme-2 of a specific ethnic group.

Our data showed that 9 patients reported olfactory dysfunction only, 24 patients reported dysgeusia only and 55 patients reported experiencing both. This can indicate that it is more likely that someone positive for SARS-CoV-2 can present with both symptoms rather than only one.

The most commonly reported symptoms in our study were cough (53%) and fever (44%) which is consistent with nearly all international publications.¹⁰ However, these contrast with the findings of Avci *et al.*,¹⁷ wherein the most prominent symptoms were olfactory dysfunction (44.2%), dysgeusia (43.9%), and fever (38.7%). It is interesting to note that among those with olfactory dysfunction, only 9% (six) also reported experiencing colds. And among those with dysgeusia, only 6% (five) experienced concomitant colds while 12% (10) experienced sore throat. This supports the theory that among those with COVID-19, the mechanism of olfactory dysfunction and dysgeusia is unique and not just secondary to other rhinologic or oral cavity symptoms. In a study by Hopkins, Surda and Kumar,¹⁸ the proportion of COVID-19 patients reporting olfactory dysfunction remained high despite the absence of nasal obstruction. Anecdotal evidence also cites abrupt onset and the absence of nasal symptoms as suspicious features of SARS-CoV-2 etiology.¹² Comparing the different hypotheses on the mechanism of olfactory dysfunction in COVID-19, the most viable one is that of the virus having effects on the sustentacular cells of the olfactory epithelium, rather than the olfactory neurons.¹⁹⁻²⁰ It may be direct by reducing their odorant clearing function, or indirect by extinguishing their protective abilities for olfactory neurons causing metabolic dysfunction.¹⁹⁻²⁰

Our present study included hospitalized patients who suffered from mild to severe forms of COVID-19. We found that 88 patients (42.51%), less than half of our sample size, suffered from olfactory dysfunction and/or dysgeusia. A study done in Istanbul to determine the relationship between olfactory dysfunction and hospital admission demonstrated olfactory dysfunction in 462 patients (47%) of the

out-patient group, and 67 (31.20%) in the in-patient group.¹⁷ Their regression analysis revealed a lower hospitalization rate in patients with olfactory dysfunction. Since our study only recruited in-patients, this could contribute to the lower reports of olfactory dysfunction and dysgeusia.

For both olfactory dysfunction and dysgeusia, we observed that the average day of onset was around day 3 to 4, with majority occurring before day 6 of illness. The findings in our study are consistent with those of a retrospective study by Klopfenstein *et al.*,⁵ where patients developed olfactory dysfunction 4.4 ± 1.9 days after the onset of infection. An Italian study confirmed that olfactory dysfunction and dysgeusia are early symptoms of COVID-19, generally occurring within the first 5 days of the clinical onset and tending to decrease or disappear over time.¹² Olfactory dysfunction peaks slightly earlier than gustatory dysfunction according to several studies in Europe.¹² A study of 135 COVID patients which aimed to characterize the temporal relationship of olfactory dysfunction to other clinical symptoms found that 10.4% had isolated sudden onset olfactory dysfunction, 31.1% had sudden onset olfactory dysfunction followed by other COVID symptoms, 17.8% had other COVID symptoms followed by gradual onset olfactory dysfunction, and 40.7% did not present with olfactory dysfunction.¹³

It appears that those with olfactory dysfunction and dysgeusia have shorter average lengths of stay. As of writing, we found no published study exploring the length of hospital stay and the presence of olfactory or gustatory dysfunction, based on a search of HERDIN Plus, the ASEAN Citation Index (ACI), and MEDLINE (PubMed). Although it is an interesting statistic, care must be used as it may just be due to the smaller samples from the olfactory dysfunction and dysgeusia samples.

From our study population, it was evident that most patients have moderate to severe disease. There were quite a bit more patients with critical status than mild, indicating that the sample contains more "high stakes" COVID statuses. Despite this, of those who reported olfactory dysfunction/dysgeusia, 81 patients were discharged and seven expired. This study is consistent with several reports that have surmised that olfactory dysfunction may be a marker for a milder form of COVID-19.⁹ Some even go as far as to suggest that patients with olfactory dysfunction have the immune competence to contain SARS-CoV-2 in the upper airways only. Moreover, lesser hospitalizations rates were also observed in those with olfactory dysfunction or hyposmia.⁷ The observations in this study could be attributed to the disparity in COVID severity status in the sample.

Although most with olfactory or gustatory dysfunction were categorized as having critical COVID status, majority (92%) were eventually sent home stable. In the olfactory dysfunction and dysgeusia group, only three and six patients, respectively, were eventually intubated. Moreover, only 8% of those who experienced olfactory dysfunction and dysgeusia expired.



Our study has several limitations. Despite the significant sample of patients, our study was carried out in a single hospital and included only in-patients. The lack of out-patient managed cases and geographical limitations may have had an impact on our results. It is also important to note that several COVID-19 surges occurred in the Philippines during the data collection period which forced hospitals to prioritize more severe cases for admission affecting our study sample. Our use of purposive sampling is prone to observer bias. Moreover, the representativeness of the sample may be difficult to defend. Future studies should attempt stratified sampling or other non-purposive sampling methods. As sample size can be a significant limitation, more studies or a larger sample size should be carried out in the future to validate the findings of this study.

Another limitation of this study was the absence of physical contact with the patients. Data was gathered remotely via phone calls and those who could not be contacted via phone were not included. The absence of full objective olfactory assessment and nasal endoscopy (which was contraindicated in the current situation), remains a limitation of this study as we could not rule out all possible etiologies

of olfactory dysfunction and dysgeusia. More objective assessment of olfactory dysfunction/dysgeusia using reporting tools were not done due to lack of Filipino validated reporting tools. Further studies should include patients managed at home or those sent to community quarantine sites to account for the milder form of COVID-19. It is also highly encouraged for subsequent studies to have larger cohort sizes by including multiple hospitals in the Philippines. Utilizing a validated AAO-HNS COVID-19 Anosmia Reporting Tool in the local language would also be more reflective of the actual prevalence of olfactory and gustatory dysfunction in the country.

In conclusion, this study highlights the significant role of olfactory and gustatory dysfunction as indicators of COVID-19 with 42.5% of participants reporting either of these symptoms. Olfactory and gustatory dysfunction were observed early often occurring before day 6 of illness. 92% of those affected recovered and experienced shorter duration of hospitalization. This underscores the importance of recognizing olfactory and gustatory dysfunction in improving disease detection and outcomes for both the public and the scientific community.

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