

Research Article

Relationship of Anosmia with Nasopharyngeal Swab-Based Sample Collection for Covid-19

Muneer Ahmed Solangi* and Mahvish Jabeen Channa

Institute of Biochemistry, University of Sindh Jamshoro, Jamshoro, 76080, Pakistan.

Abstract | COVID-19 caused a significant number of infections and deaths since first appearance in December 2019 in Wuhan, China. Anosmia and hyposmia had been viewed as the first signs of COVID-19. However, these could also be triggered by preceding factors in the population or those twisted during pandemic. In this prospective cohort study, respondents were surveyed with a subjective smell test to notice the incidence of smell loss after nasopharyngeal sampling. Olfactory function was evaluated multiple times with a non-specific smell test using the balm (Iodex, GSK®) and items accessible to respondents at home. Olfactory function was qualitatively categorized based on the difficulty of smelling odor such as normal (normosomia), diminished (hyposmia), and absent (anosmia). Data about manifestation, comorbidities and smell function is carefully assessed before statistical analysis. The study involved 120 individuals, of which 52 (43.3%) were female and 68 (56.6%) were male. The average age of the participants was 37 ± 15 [min 16, max 72, IQR 46.5-26=21.5]. RT-PCR revealed the presence of SARS-CoV-2 in $n = 6$ (5%), with a mean Ct-value of 30.3 ± 2.6 . Post-NPS smell loss respondents were $n=13$ (11%) among them $n=3$ (23%) had SAR-CoV-2 while $n=10$ (77%) were negative. Through Chi-square (χ^2) test, p-value was revealed ≤ 0.05 [df 1] for smell loss in negative respondents compared to positive cases which shows that they might have lost smell due to different factors other than COVID-19 which are briefly discussed.

Received | January 29, 2024; **Accepted** | May 01, 2024; **Published** | June 20, 2024

***Correspondence** | Muneer Ahmed Solangi, Institute of Biochemistry, University of Sindh Jamshoro, Jamshoro, 76080, Pakistan; **Email:** muneerahmedphd@gmail.com

Citation | Solangi, M.A. and M.J. Channa. 2024. Relationship of anosmia with nasopharyngeal swab-based sample collection for Covid-19. *Biologia (Lahore)*, 70(1): 08-15.

DOI | <https://dx.doi.org/10.17582/journal.Biologia/2024/70.1.8.15>

Keywords | Nasopharyngeal (NP), Hyposmia, Anosmia, SARS-CoV-2, COVID-19



Copyright: 2024 by the authors. Licensee ResearchersLinks Ltd, England, UK.

This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Introduction

COVID-19 has severely affected the world since its beginning in Wuhan China, on December 2019 (Wu *et al.*, 2020). Presently, pandemics have swayed 7 million people and caused 770 million infections. Several strategies have been developed to manage and diagnose disease such as before

or after the presentation of the symptoms and its development over time in patients (Tostmann *et al.*, 2020). COVID-19 cases were categorized based on indications such as symptomatic or asymptomatic. The primary objective during the pandemic was to diagnose both types of cases using COVID-19 testing (Guo *et al.*, 2020). In symptomatic, COVID-19 produces several manifestations; for instance, fever,

cough, sore throat, chills, dyspnoea, and myalgia are more regularly reported (Chen *et al.*, 2021). In the critical scenario, viral tropism into organs resulted in septic shocks, severe pneumonia, acute respiratory distress syndrome (ARDS), and death (Li *et al.*, 2021).

Subsequently, anosmia and hyposmia (smell loss) were considered as markers of COVID-19 because of their appearance before diagnostic testing and other symptoms (Moein *et al.*, 2020). During pandemic, smell loss was reported alone in 5 to 50% cases or with dysgeusia (Hopkins *et al.*, 2020). Smell loss can be caused by multiple factors that regulate or correlate with the olfactory system such as mental and physical health, age, gender or environment (Gögele *et al.*, 2024). In these factors, ageing could be the leading cause of olfactory dysfunction in individuals usually above 60 years (Doty, 2018). Other factors such as environmental, neurodegenerative diseases, and psychiatric and socio-economic issues may also manifest identical conditions (Schwartz *et al.*, 2019). Additionally, we have seen the expansion of COVID-19 and nucleic acid testing RT-PCR using swabs could impact olfactory function (Chau *et al.*, 2020).

RT-PCR is considered a gold standard for SARS-CoV-2 detection which also assists in monitoring disease development and its severity in patients (Quraishi *et al.*, 2023). The specimen for RT-PCR is usually obtained from the oropharynx, septum, saliva, throat, or nasopharynx. These sites give significant viral load to successfully detect SARS-CoV-2. However, the nasopharyngeal specimen has a high viral load at the start of infection therefore it is preferred to collect sample. The nasopharyngeal swab (NPS) technique may cause discomfort and anxiety in individuals after testing (Kim *et al.*, 2022). Additionally, studies have reported smell loss responses before and after the NPS test using subjective response which indicates significance of NPS. Therefore, we aim to investigate the incidence of smell loss in COVID-19-negative cases after nasopharyngeal sampling and evaluate factors which might have impacted olfactory function.

Materials and Methods

Study design and sampling

The COVID-19 Sentinel facility/testing center of the outpatient department (OPD) hosted the impending

prospective cohort research (Figure 1) in June and July of 2021. This center is situated in Kotri, Pakistan, at the District Headquarters Hospital (DHQ), Jamshoro. To choose eligible participants, convenience sampling was used. Iodex (balm) was used in a non-specific smell test to measure olfactory function (OF) both before and after a 30-minute NPS test. On the following study days, the volunteers were instructed to assess the smell using the scents of objects at homes. We called the respondents to assess OF after RT-PCR. Recovery time for COVID-19 and odor loss was measured. It should be noted that following the NPS, participants evaluated their perception of smell with the items available at their homes.

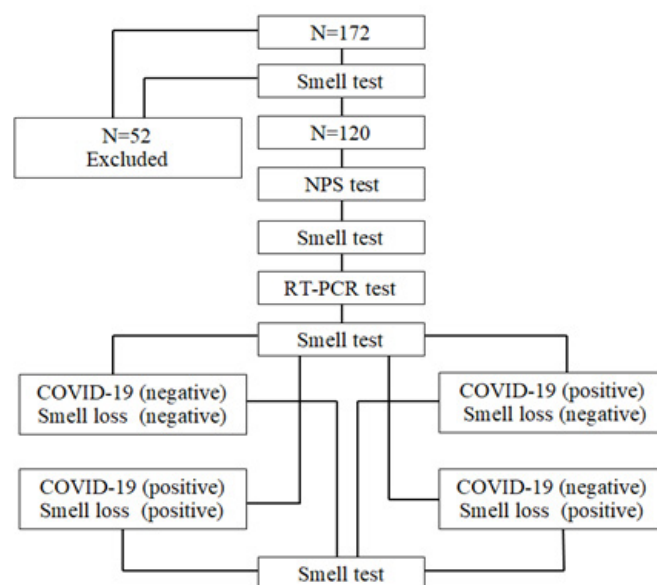


Figure 1: This flowchart shows the study design. A total of N=120 respondents went through a smell test and RT-PCR test to evaluate post-NPS smell loss. The respondents who signed consent forms were selected; they were further matched with study requirements such as normal smell function, age, and location. Smell is tested before and after nasopharyngeal sample collection.

Eligibility criteria

Respondents at least 16 years old with normal smell function who have never taken the NPS test previously were selected. Respondents with ENT (ear, nose, and throat) conditions, injuries, and olfactory dysfunction (OD) were not included.

Consumables

The disinfected swab with a flocking tip (GONGDONG®) was applied to collect nasopharyngeal (NP) specimens. For the smell test, we used Iodex (GSK®) at the testing center and

thereafter perfume, coffee, and ginger based on the respondents choice. We used Abbot Kits (Abbot Labs) to extract the viral RNA and SANSURE kits (SANSURE BIOTECH) to detect SARS-CoV-2 in specimens. The specimen was amplified on ABI Quant Studio 5.

Pre-NPS procedure

The consent form was endorsed by respondents before participating in the concurrent study according to the rules of the Hospital and the IRB of the University of Sindh, Jamshoro. We have recorded data on a structured form to input manifestations, smell loss, and COVID-19-related information. A smell test was executed with the Iodex before NP specimen collection to affirm they have an ordinary OF (Figure 2).



Figure 2: All participants were required to smell Iodex to confirm their smell status. Respondents with normal smell function before nasopharyngeal swab (NPS) testing were selected to conduct the study. Subsequently, a subjective smell test was performed after NPS to confirm the smell status of eligible participants.

NPS-testing procedure

The specimen was collected from the nasopharynx by specialists according to COVID-19 SOPs. For NPS, the respondent shifted face up at 70° and a swab was passed into the nostril delicately until reached the nasopharynx where it was rotated for 5 sec to get the maximum viral load (Figure 3). The collected specimen was placed into a viral transport medium tube for the RT-PCR. Following half-hour of the NPS test, respondents were evaluated with the Iodex to notify distinction in OF.

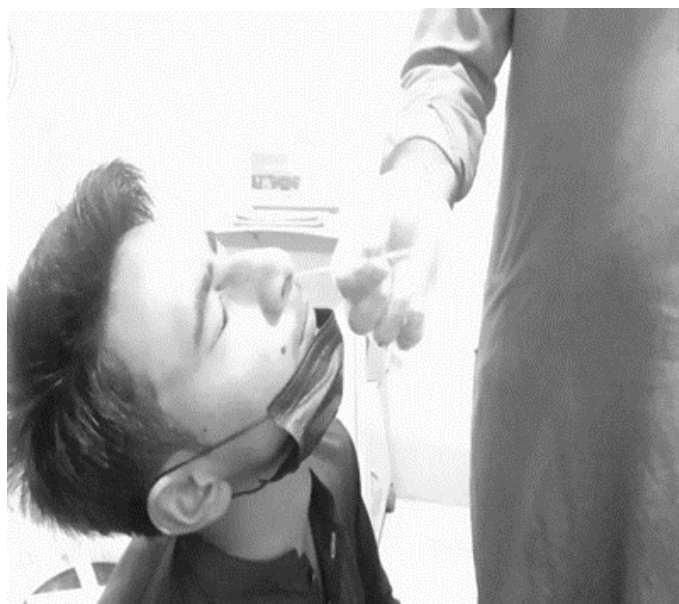


Figure 3: Sample was extracted from the nasopharynx using COVID-19 SOPs designed by CDC USA, and WHO guidelines, as a shown subject has a tilted head 70 degrees then the swab was passed into a nostril. The swab was rotated clockwise and anticlockwise for five seconds to get maximum viral load. After sample collection, respondents required to check the smell within 30 minutes to discover any change in OF.

Post-NPS procedure

RT-PCR (fluorescence testing) was performed at the Diagnostic and Research Lab LUMHS Hyderabad under COVID-19 SOPs. After NPS, we guided the respondents to assess the OF using odorants available at home. Following that, we phoned participants for correspondence after three to five days of NPS to evaluate OF. The recuperation time of cases having smell loss and COVID-19 was noted.

Statistical analysis

Chi-square test was used to measure the smell loss in COVID-19 negative cases. To comprehend the overall distribution, Binomial test on 0.50 proportions was used. The categorical data are shown as frequency and per cent (%), continuous variables are shown as mean and standard deviation (SD). Excel 365 (Microsoft Corp.) and SPSS 25.0 (IBM) used for data analysis.

Results and Discussion

To find suitable individuals for the study, 520 interviews were conducted. Those volunteered to participate were 172 (32.7%), and N= 120 (70%) of them met the eligibility requirements. Participants demographically were residents from five cities Sindh,

Pakistan; Hyderabad (n=8; 6.5%), Jamshoro (n=3; 2.5%), Sehwan (n=3; 2.5%), Thatta (n=3; 2.5%), and Kotri (n=103; 86%) (Table 2). They were 52 (43.3%) females and 68 (57.3%) males, with an average age of 37±15. The respondents belonging to the lower middle class were 90(75%) and 30(25%) to the middle-middle class. They were normosomic before and after the 30 minutes of swab test. The symptoms were reported in n=41(34%) cases including fever (n=29; 22.7%), fatigue (n=20; 15.6%), cough (n=17; 13.3%), flu (n=11; 8.6%), sore throat (n=8; 6.6%), dizziness (n=12; 9.4%), GIT complications (n=10; 7.8%), headache (n=7, 5.5%), and mild dyspnea (n=17; 13.3%) was also observed. While 79(66%) were asymptomatic at the time of the interview.

Table 1: Demographic data of COVID-19 positive and smell loss respondents.

Variables	Character- istics	COVID-19	Smell loss [‡]	
		"positive (n=6)	Anosmia (n=4)	Hyposmia (n=6)
Age [†]		54.5(±10.6)	44±22.5	42±20
Gender				
	Male	4(66%)	2(50%)	2(33%)
	Female	2(34%)	2(50%)	4(67%)
Symptoms				
	Fever	4(66%)	2(50%)	5(90%)
	Cough	3(50%)	2(50%)	2(33%)
	Flu	-	2(50%)	2(33%)
	Sore throat	2(33%)	1(25%)	1(16.6%)
	Fatigue	1(16.6%)	4(100%)	2(33%)
	Dizziness	2(33%)	2(50%)	-
	Dyspnoea	3(50%)	-	1(16.6%)
	Headache	1(16.6%)	1(25%)	-
	GIT comp.	-	1(25%)	2(33%)
	Dysgeusia	-	1(25%)	-
Comorbid.				
	Nasal cong.	1(16.6%)	1(25%)	2(33%)
	Rhinorrhoea	1(16.6%)	1(25%)	2(33%)
	Depression	-	2(50%)	2(33%)
	Obesity	1(16.6%)	1(25%)	-
	Hypertension	1(16.6%)	-	2(33%)
	CVD	-	-	1(16.6%)
	Diabetes	-	1(25%)	-
Status [†]				
	Loss time	-	3.4±0.9	3.4±0.9
	Rec. time	18(±4.5)	11±3.2	9±2.7

[‡]Chi-square discovered p-value ≤0.05 with df 1, [†]Mean, ±SD and ^an=3(50%) smell loss.

Following the NPS, 13 (10.8%) respondents-male (n=6; 46%) and females (n=7; 54%) having a mean age of 42±19 lost their sense of smell in 3.4±0.9 days. In which 6 (5%) tested positive for COVID-19, had hyposmia (n=2; 33.3%) and anosmia (n=1; 16.6%). In contrast, 10 (8.3%) COVID-19 negative cases had also lost their smell, they had anosmia 4 (40%) and 6 (60%) hyposmia. Symptoms such as fever was most prevalent reported in 7 (70%) cases, least was dysgeusia (10%) (Table 1) and acute nasal congestion (30%), rhinorrhea (30%), depression (40%), hypertension (20%), obesity (10%), cardiovascular disease (10%), and diabetes (10%) were also present (Table 1).

Their average age was 54.5±10.65 years; females 2 (34%), and males 4 (66%). They also reported comorbidities such as obesity (16.6%), hypertension (16.6%), rhinorrhoea (16.6%), nasal congestion (16.6%), and symptoms such as fever (46.6%), cough (35%), sore throat (35%), fatigue (16.6%), dizziness (23.3%), headache (16.6%), and dyspnoea (35%). The recovery period for COVID-19 was 18±4.47 days. We used Chi-square test to demonstrate the relationship of smell loss in COVID-19 negative responders (n= 10) relative to all instances. The p-value of ≤0.05 with 1 df indicates that there could be other factors for the development of manifestation in COVID-19 negative cases. Additionally, the binomial test showed a p-value ≤ 0.05 for 0.50 proportions, which indicates the significance of smell loss in respondents. These findings indicate after NPS testing the prevalence of smell loss was higher in COVID-19 negative cases than positive cases. This suggests other factors also played role in olfactory dysfunction during COVID-19 pandemic.

During pandemics, there was a spike in smell loss cases. However, patients showed symptoms of olfactory dysfunction following RT-PCR status revealed or after the disease appeared (Imam *et al.*, 2020). Several investigations have demonstrated the smell loss caused by COVID-19 was often self-reported. It depends on the patient's experience of smell loss which lacks objective perception of smell (Giacomelli *et al.*, 2020). In this prospective cohort study, the olfactory function of participants was evaluated before the nasopharyngeal swab test (pre-NPS) and after the nasopharyngeal swab test (post-NPS) to differentiate normal and smell loss cases (Figure 1). A single paper questionnaire was used to record demographics, signs and symptoms, comorbidities and smell loss data.

Table 2: Prevalence of COVID-19 and smell loss in selected cities (N=120).

Address	Gender			Age		Smell loss		COVID-19	
	Male	Female	Total	Male	Female	Anosmia	Hyposmia	Positive	Negative
	n(%)	n(%)	n(%)	Mean±SD		n(%)	n(%)	n(%)	n(%)
Kotri	58 (86)	45(86)	103(87)	37±16.6	37.3±14.3	5(4.7)	6(5.8)	6(5.8)	97(94.2)
Hyderabad	3(4)	5(10)	8(6)	33.7±6.5	26.4 ±6.6	*	2(25)	*	8(100)
Sehwan	3(4)	*	3(2.5)	38 ±9.9	*	*	*	*	3(100)
Thatta	2(3)	1(2)	3(2.5)	32(*)	*	*	*	*	3(100)
Jamshoro	2(3)	1(2)	3(2.5)	59 ±12.7	*	*	*	*	3(100)
Total	68(56.7)	52(43.3)	120(100)	37 ±15	36 ±14	5(4.7)	8(6.6)	6(5.8)	114(94.2)
P-value	≤0.28 [†]	≤0.3 [†]	≤0.3 [†]	<0.001 [†]	<0.001 [†]	≤0.025 [†]	≤0.004 [†]	≤0.014 [†]	*
P-value (Total)	≤0.28 [‡]			≤0.068 [‡]		<0.0001 [†]		≤0.292 [‡]	

The individuals who lost smell (n=13), recovered on average 10±3 days, anosmic in 11±3.16 days and hyposmic in 9±3 days. Six (5%) of the responders had SARS-CoV-2 with mean Ct-value of 30.3 ±2.6.

We used balm (Iodex, GSK®) which is commonly applied to relieve body pain and nasal congestion (Figure 2). RT-PCR test was conducted to detect SARS-CoV-2 with a threshold value ≤Ct30. SARS-CoV-2 was detected in 6(5%) cases with an average Ct-value of 30.3 ±2.6. RT-PCR was considered the gold standard during COVID-19 pandemic (Tombuloglu et al., 2022) and we used this test to differentiate cases who lost smell due to the COVID-19 or other factors (Table 1). Smell loss is often categorized physiologically as normal (normosomic), reduced (hyposmia), and absent (anosmia) (Marin et al., 2018). We systematically categorized smell by subjective response i.e., respondents after the smell test with Iodex were asked about smell status such as diminished (hyposmia) and vanished (anosmia) with yes/no answers. Post-NPS, we collected data on smell function through physical 47 (39%) or on the phone 73 (61%) (Figure 4). Out of N=120 respondents, post-NPS normosomic were 107 (89%) and 13 (11%) cases of smell loss in which n=10 (8.3%) were COVID-19 negative cases. These smell loss cases were hyposmic 6 (60%) and anosmic 4 (40%). A Chi-square test with a p-value ≤0.05 significantly indicates the relationship of smell loss with factors other than COVID-19. Despite the absence of SARS-CoV-2 in their samples, individuals exhibited COVID-19 symptoms (Table 1) and had comorbidities which could be the factors behind smell loss after the nasopharyngeal-based swab test. Comorbidities such as depression, flu, hypertension, non-severe nasal obstruction, and rhinorrhea could obstruct (Table 1) the odor from reaching the olfactory sensory system (Lehrich et al., 2020). Additionally, age is considered an important factor which could alter the OF, results reveal smell

loss cases had average age 42 ± 19 years (Carignan et al., 2020). In COVID-19 cases, anosmia 1 (16.6%) and hyposmia 2 (33.2%) were found with dysgeusia. However, studies have shown 5 to 50% of COVID-19 cases had anosmia or hyposmia along with dysgeusia (Hopkins et al., 2020).

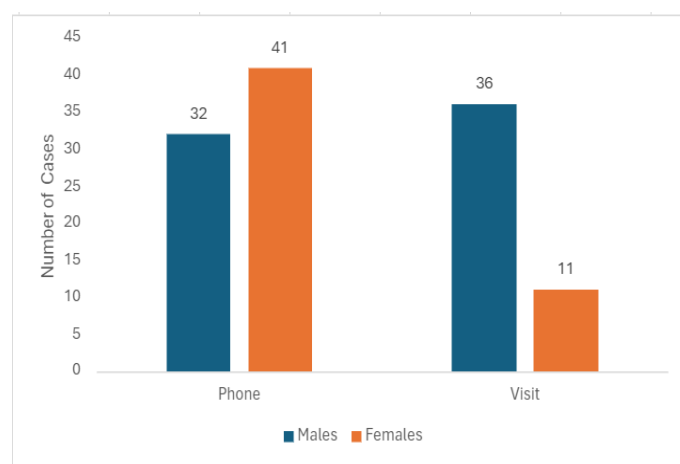


Figure 4: Post-NPS data collected through phone and visits of respondents.

Smell difficulties might be caused by different factors such as genetic, physiological, psychological health, or socioeconomic status (Elkholi et al., 2021). Similarly, the nasopharyngeal technique for obtaining the COVID-19 sample could impact OF or an incorrectly collected sample might damage the sensory epithelium of the nasopharynx which could result in partial or complete smell loss (Guimarães et al., 2022). We hardly ever encounter objects that travel profoundly in the nose touching the oropharynx or olfactory sensory region. It has been reported during nasopharyngeal testing, the contact between swabs and epithelial surfaces can cause pain or sneezing

(Abdelrahman *et al.*, 2020). It makes sense this interaction might partially inhibit the conduction of chemosensory signals. It is unclear whether this effect can cause smell dysfunction or in the presence of comorbidities or symptoms as reported in this study. Additionally, a person who has experienced trauma and mental anguish typically exhibits impaired smell and cannot accurately separate odors (De Luca *et al.*, 2023). Similar conditions have been seen throughout the COVID-19 pandemic for instance, there was a spike in depression, physical inactivity, hypertension, and neuropsychiatric illness (Roy *et al.*, 2021). The world already had epidemics of fever, cough, flu, and upper respiratory tract illnesses and COVID-19 pandemics elevated them to another level. Smell loss can be caused by the degeneration of the components that control smell function or olfactory system few of them discussed above. Therefore, it is essential to monitor smell function carefully and consider different factors such as gender, age, genetics, mental and physical health while treating smell loss or other associated illnesses such as COVID-19.

Conclusions and Recommendations

Through this prospective cohort study, we conclude that smell loss can be caused by different factors that regulate olfaction. Post-NPS smell loss shows that different factors such as manifestations, comorbidities, psychological disorders, socio-economic status and testing procedures might have impacted the olfactory function of COVID-19-negative cases. Alteration in these factors can impact olfaction and due to its multi-perspective nature, smell function should be tracked analyzing epidemiological history, demographic, mental and physical condition of cases. Our research shows the incidence of smell loss after NPS in COVID-19 negative cases was statistically significant with a p-value $7 \leq 0.05$.

Smell function could be assessed using objective or semi-objective tests. Olfactory distortion should be studied using specific tests such as UPSIT or Sniff-in's stick; however, disease-induced smell loss should be considered after finding disease specific markers. The results of this study will help to manage smell loss in clinical settings and to investigate smell using study design. This study will also help physicians to sort the olfactory disorders at different stages of development and researchers to assess olfactory function through non-specific means. Finally, it is required to investigate

the impact of swabs on the sensory epithelial layer of the nasopharynx.

Acknowledgment

We express our gratitude to the physicians and technical personnel of DHQ Hospital Jamshoro at Kotri collaborated with us during this study. Also, we acknowledge HEC Pakistan for the award of PhD fellowship.

Author's Contribution

Muneer Ahmed Solangi: Research design, concept, methodology, sampling, data analysis and first draft writing.

Mahvish Jabeen Channa: Result validation, interpretation of results, final draft writing.

Funding

We want to thank the Higher Education Commission of Pakistan for financial support to complete research work under the Indigenous 5000 PhD Fellowship Program phase II (batch VI).

Limitations

We have not used advance methods such as the UPSIT and Sniff-in's stick test due to the inaccessibility of resources and lack of funding.

Conflict of interest

The authors have declared no conflict of interest.

References

- Abdelrahman, Z., Li, M. and Wang, X., 2020. Comparative review of SARS-CoV-2, SARS-CoV, MERS-CoV, and influenza a respiratory virus. *Front. Immunol.*, 11: 552909. <https://doi.org/10.3389/fimmu.2020.552909>
- Carignan, A., Valiquette, L., Grenier, C., Musonera, J.B., Nkengurutse, D., Marcil-Héguy, A., Vettese, K., Marcoux, D., Valiquette, C., Xiong, W.T., Fortier, P.H., Gagnéux, M. and Pépin, J., 2020. Anosmia and dysgeusia associated with SARS-CoV-2 infection: An age-matched case-control study. *Can. Med. Assoc. J.*, 192(26): E702-e707. <https://doi.org/10.1503/cmaj.200869>
- Chau, C.H., Strobe, J.D. and Figg, W.D., 2020. COVID-19 clinical diagnostics and testing

- technology. *Pharmacotherapy*, 40(8): 857-868. <https://doi.org/10.1002/phar.2439>
- Chen, Y., Klein, S.L., Garibaldi, B.T., Li, H., Wu, C., Osevala, N.M., Li, T., Margolick, J.B., Pawelec, G. and Leng, S.X., 2021. Aging in COVID-19: Vulnerability, immunity and intervention. *Ageing Res. Rev.*, 65: 101205. <https://doi.org/10.1016/j.arr.2020.101205>
- De Luca, R., Bonanno, M., Rifici, C., Quartarone, A. and Calabrò, R.S., 2023. Post-traumatic olfactory dysfunction: A scoping review of assessment and rehabilitation approaches. *Front. Neurol.*, 14. <https://doi.org/10.3389/fneur.2023.1193406>
- Doty, R.L., 2018. Age-related deficits in taste and smell. *Otolaryngol. Clin. North Am.*, 51(4): 815-825. <https://doi.org/10.1016/j.otc.2018.03.014>
- Elkholi, S.M.A., Abdelwahab, M.K. and Abdelhafeez, M., 2021. Impact of the smell loss on the quality of life and adopted coping strategies in COVID-19 patients. *Eur. Arch. Otorhinolaryngol.*, 278(9): 3307-3314. <https://doi.org/10.1007/s00405-020-06575-7>
- Giacomelli, A., Pezzati, L., Conti, F., Bernacchia, D., Siano, M., Oreni, L., Rusconi, S., Gervasoni, C., Ridolfo, A.L., Rizzardini, G., Antinori, S. and Galli, M., 2020. Self-reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: A cross-sectional study. *Clin. Infect. Dis.*, 71(15): 889-890. <https://doi.org/10.1093/cid/ciaa330>
- Gögele, M., Emmert, D., Fuchsberger, C. and Frasnelli, J., 2024. Factors influencing olfactory function in an adult general population sample: The CHRIS study. *Chem. Senses*, 49. <https://doi.org/10.1093/chemse/bjae011>
- Guimarães, T.C., Marques, B.B.F., Tinoco, J.M.M., Porto, L., Tinoco, E.M.B. and Fischer, R.G., 2022. SARS-COV-2 detection in saliva and nasopharyngeal swabs using RT-PCR was similar. *Braz. Dental J.*, 33(2): 68-72. <https://doi.org/10.1590/0103-6440202204591>
- Guo, G., Ye, L., Pan, K., Chen, Y., Xing, D., Yan, K., Chen, Z., Ding, N., Li, W., Huang, H., Zhang, L., Li, X. and Xue, X., 2020. New insights of emerging SARS-CoV-2: Epidemiology, etiology, clinical features, clinical treatment, and prevention [Review]. *Front. Cell Dev. Biol.*, 8. <https://doi.org/10.3389/fcell.2020.00410>
- Hopkins, C., Surda, P. and Kumar, N., 2020. Presentation of new onset anosmia during the COVID-19 pandemic. *Rhinology*, 58(3): 295-298. <https://doi.org/10.4193/Rhin20.116>
- Imam, S.A., Lao, W.P., Reddy, P., Nguyen, S.A. and Schlosser, R.J., 2020. Is SARS-CoV-2 (COVID-19) post viral olfactory dysfunction (PVOD) different from other PVOD? *World J. Otorhinolaryngol. Head Neck Surg.*, 6(S1): S26-S32. <https://doi.org/10.1016/j.wjorl.2020.05.004>
- Kim, D.H., Kim, D., Moon, J.W., Chae, S.W. and Rhyu, I.J., 2022. Complications of nasopharyngeal swabs and safe procedures for COVID-19 testing based on anatomical knowledge. *J. Korean Med. Sci.*, 37(11): e88. <https://doi.org/10.3346/jkms.2022.37.e88>
- Lehrich, B.M., Goshtasbi, K., Raad, R.A., Ganti, A., Papagiannopoulos, P., Tajudeen, B.A. and Kuan, E.C., 2020. Aggregate prevalence of chemosensory and sinonasal dysfunction in SARS-CoV-2 and related coronaviruses. *Otolaryngol. Head Neck Surg.*, 163(1): 156-161. <https://doi.org/10.1177/0194599820929278>
- Li, Y., Ji, D., Cai, W., Hu, Y., Bai, Y., Wu, J. and Xu, J., 2021. Clinical characteristics, cause analysis and infectivity of COVID-19 nucleic acid repositive patients: A literature review. *J. Med. Virol.*, 93(3): 1288-1295. <https://doi.org/10.1002/jmv.26491>
- Marin, C., Vilas, D., Langdon, C., Alobid, I., López-Chacón, M., Haehner, A., Hummel, T. and Mullol, J., 2018. Olfactory dysfunction in neurodegenerative diseases. *Curr. Allergy Asthma Rep.*, 18(8): 42. <https://doi.org/10.1007/s11882-018-0796-4>
- Moein, S.T., Hashemian, S.M., Mansourafshar, B., Khorram-Tousi, A., Tabarsi, P. and Doty, R.L., 2020. Smell dysfunction: A biomarker for COVID-19. *Int. Forum Allergy Rhinol.*, 10(8): 944-950. <https://doi.org/10.1002/alr.22587>
- Quraishi, E., Jibuaku, C., Lisik, D., Wennergren, G., Lötvall, J., Nyberg, F., Ekerljung, L., Rådinger, M., Kankaanranta, H. and Nwaru, B.I., 2023. Comparison of clinician diagnosis of COVID-19 with real time polymerase chain reaction in an adult-representative population in Sweden. *Respirat. Res.*, 24(1): 10. <https://doi.org/10.1186/s12931-023-02315-7>
- Roy, D., Ghosh, R., Dubey, S., Dubey, M.J., Benito-León, J. and Ray, K.B., 2021. Neurological and neuropsychiatric impacts of COVID-19

- pandemic. *Can. J. Neurol. Sci.*, 48(1): 9-24. <https://doi.org/10.1017/cjn.2020.173>
- Schwartz, J.S., Tajudeen, B.A. and Kennedy, D.W., 2019. Chapter 18 - diseases of the nasal cavity. In: R.L. Doty (Ed.), *Handbook of Clinical Neurology*. Elsevier. 164: 285-302. <https://doi.org/10.1016/B978-0-444-63855-7.00018-6>
- Tombuloglu, H., Sabit, H., Al-Khallaf, H., Kabanja, J.H., Alsaeed, M., Al-Saleh, N. and Al-Suhaimi, E., 2022. Multiplex real-time RT-PCR method for the diagnosis of SARS-CoV-2 by targeting viral N, RdRP and human RP genes. *Sci. Rep.*, 12(1): 2853. <https://doi.org/10.1038/s41598-022-06977-z>
- Tostmann, A., Bradley, J., Bousema, T., Yiek, W.-K., Holwerda, M., Bleeker-Rovers, C., ten Oever, J., Meijer, C., Rahamat-Langendoen, J., Hopman, J., van der Geest-Blankert, N. and Wertheim, H., 2020. Strong associations and moderate predictive value of early symptoms for SARS-CoV-2 test positivity among healthcare workers, the Netherlands, March 2020. *Eurosurveillance*, 25(16): 2000508. <https://doi.org/10.2807/1560-7917.ES.2020.25.16.2000508>
- Wu, F., Zhao, S., Yu, B., Chen, Y.M., Wang, W., Song, Z.G., Hu, Y., Tao, Z.W., Tian, J.H., Pei, Y.Y., Yuan, M.L., Zhang, Y.L., Dai, F.H., Liu, Y., Wang, Q.M., Zheng, J.J., Xu, L., Holmes, E.C. and Zhang, Y.Z., 2020. A new coronavirus associated with human respiratory disease in China. *Nature*, 579(7798): 265-269. <https://doi.org/10.1038/s41586-020-2008-3>