Olfactory and Gustatory Dysfunction in Pediatric Patients With Coronavirus Disease (COVID-19)

Bernaola Abraira M[1]*, Bartha De Las Peñas I[1]*, López-Araujo GA[1], Escudero Diez C[1,2,3], Rodríguez del Río P[1,2,3], Morales-Cabeza C[1], Bazire Batiz R[1,2], Ibáñez Sandín MD[1,2,3]
[1]*Servicio de Alergología, Hospital Infantil Universitario Niño Jesús, Madrid, Spain*
[2]*FibHNJ, ARADyAL-RETICs RD16/RD16/0006/0026 Instituto de Salud Carlos III, Madrid, Spain*
[3]*IIS La Princesa, Madrid, Spain*
[*]*Both authors contributed equally as first authors.*

J Investig Allergol Clin Immunol 2021; Vol. 31(3): 277-279
doi: 10.18176/jiaci.0677

Key words: COVID-19. Olfactory dysfunction. Gustatory dysfunction. Children. Pediatric population.

Palabras clave: COVID-19. Disfunción olfativa. Disfunción gustativa. Niños. Población pediátrica.

Olfactory and gustatory dysfunction (OGD) comprises relevant symptoms that may predict presence of coronavirus disease 2019 (COVID-19) in adults and are associated with mild or moderate disease [1-3]. A plausible mechanism of OGD is the direct extension of SARS-CoV-2 through the nasal mucosa, with direct damage to nonneural cells of the olfactory bulb [4]. Published data on OGD in children are scant, likely due to factors specific to the pediatric population, such as lower incidence of infection, the tendency of COVID-19 to be asymptomatic [5], and difficulties when studying childhood OGD using objective methods. Of the few case reports that have been published to date, one with 3 adolescents is particularly interesting [6]. Current data on the prevalence of OGD are based on 2 small cohorts of COVID-19–positive children [7,8] and a cross-sectional survey of Italian pediatricians [9]. In a related study, Mannheim et al [10] report that 19 of 64 (30%) infected children (0-17 years) presented nasal congestion, rhinorrhea, and total loss of smell, although they provide no data on the exact number of patients with olfactory dysfunction exclusively.

The present study, which was approved by the Ethics Committee of Hospital Niño Jesús, Madrid, Spain, aimed to evaluate OGD among symptomatic COVID-19 children seen at a referral pediatric hospital for this disease in Madrid, Spain. The database of positive SARS-CoV-2 cases diagnosed based on reverse transcription-polymerase chain reaction (RT-PCR) between March 20 and July 13, 2020 was retrospectively reviewed. Demographic information, COVID-19 symptoms, disease severity, clinical course, and comorbidities were obtained from electronic medical records. Information on smell and taste disorders and any incomplete data on other COVID-19 symptoms were obtained by telephone interview with parents and patients, who provided their oral consent to participate. The severity of COVID-19 was established according to the classification by Qiu et al [8]. Questionnaire data on onset and duration of smell and taste disorders were used, and severity was classified according to a scale modified from Izquierdo-Dominguez et al [1]. Based on the degree of loss of smell or taste, we stratified loss as normosmic-mild (0-3 points), moderate (4-6 points), or severe (7-10 points).

Qualitative variables are expressed as numbers and percentages, and the chi-square test was used for comparison. Quantitative variables are expressed as mean (SD) or median (IQR) according to their distribution. Normality of age distribution was confirmed using the Shapiro-Wilk test. The ANOVA test and the least significant difference were used as post hoc tests to compare normally distributed variables. Statistical significance was set at 95% ($P<.05$).

Ninety-two children were identified as having RT-PCR–positive SARS-CoV-2; 2 declined to participate. Asymptomatic patients were excluded. Fifty patients were diagnosed with symptomatic COVID-19 (52% male; mean age, 7 [7] years; IQR, 6 months-12 years). Patients under 6 years of age (n=20) were excluded because of the potentially poor reliability of self-reported smell function. Thirty patients were finally enrolled (Supplementary Figure). Seven patients (23.3%) presented mild COVID-19, 11 (36%) moderate disease, and 12 (40%) severe disease. Nineteen (63.33%) required hospitalization, and 11 (36.6%) were discharged after evaluation in the emergency department.

Eight of the 30 symptomatic children (26.6%) (range, 9-17 years) presented OGD; they were older than the children without OGD (12.6 [2.7] years vs 10.6 [3.1] years, respectively; $P=.045$). Five (16.6%) of the 30 COVID-19–positive children presented both smell and taste disorders, and 3 (10%) had gustatory dysfunction only (Supplementary Figure). OGD was severe in all patients (7-10 points) (Table and Supplementary Table).

The onset of OGD was sudden in all patients; 6 developed symptoms simultaneously with the other COVID-19 symptoms, and 2 (25%) before other disease manifestations. Of the latter, one developed both symptoms, and the other only gustatory dysfunction (Supplementary Table). In no cases was OGD the only symptom. OGD was transient in all patients, with a median duration of olfactory dysfunction of 45 days (range, 15-120 days) and median duration of gustatory dysfunction of 10 days (5-120 days) (Table).

There were no significant differences in the prevalence of OGD with respect to the severity of COVID-19 (mild, 4.3%; moderate, 36.4%; severe, 25%) or in the severity of COVID-19 between patients with and without OGD (Table) ($P=.578$). Five patients with OGD (62.5%) were hospitalized (2 in the intensive care unit), 7 had digestive symptoms, 6 had fever (>37.8ºC), 4 cutaneous manifestations, 3 pneumonia, 2 odynophagia, and 1 dyspnea. All patients recovered without sequelae except for 1 asthmatic patient with exercise-induced dyspnea (case 4) (Supplementary Table).

The prevalence of OGD in this cohort was 26.6%, which is much lower than that reported in adults [1-3], including the European multicenter study by Lechien et al [3], in which 85.6% and 88.0% of COVID-19 patients reported olfactory and gustatory dysfunction, respectively, as well as a Spanish study in which 53.7% and 52.2% of patients presented

 © 2021 Esmon Publicidad

Table. Characteristics of COVID-19 Symptomatic Children Presenting With Olfactory and/or Gustatory Dysfunction

Characteristics	Children
Total no. enrolled/screened (%)	30/50 (60%)
With OGD	8/30 (26.66%)
Age Mean (SD), IQR, y	
Total children enrolled (n=30)	11.1 (3.1) y, (9-12.25 y)
Children with OGD (n=8)	12.6 (2.7) y, (11-15.25 y)[a]
Children without OGD (n=22)	10.6 (3.1) y, (10-12 y)[a]
Sex, No./total OGD (%)	
Male	6/8 (75%)
Severity of COVID-19[b] No./total (%)	
With olfactory and/or gustatory dysfunction	
Mild	1/8 (12.5%)
Moderate	4/8 (50%)
Severe	3/8 (37.5%
Without OGD	
Mild	6/22 (27.3%)
Moderate	7/22 (31.8%)
Severe	9/22 (40.9%)
Olfactory and/or gustatory dysfunction No./total OGD (%)	
Olfactory dysfunction only	0/8 (0%)
Gustatory dysfunction only	3/8 (37.5%)
Olfactory and gustatory dysfunction	5/8 (62.5)
Onset of olfactory dysfunction No./total olfactory dysfunction (%)	
As the only symptom of COVID-19	0/5 (0%)
Before onset of other COVID-19 symptoms	1/5 (20%)
At the same time as other COVID-19 symptoms	4/5 (80%)
After other COVID-19 symptoms	0/5 (0%)

Characteristics	Children
Onset of gustatory dysfunction No./total gustatory dysfunction (%)	
As the only COVID-19 symptom	0/8 (0%)
Before onset of other COVID-19 symptoms	2/8 (25%)
Concurrently with other COVID-19 symptoms	6/8 (75%)
After other COVID-19 symptoms	0/8 (0%)
Severity of olfactory dysfunction (1-10 points)[c] No./total olfactory dysfunction (%)	
Mild (1-3)	0/5 (0%)
Moderate (4-6)	0/5 (0%)
Severe (7-10)	5/5 (100%)
Severity of gustatory dysfunction (0-10 points)[c] No./total gustatory dysfunction (%)	
Mild (1-3)	0/8 (0%)
Moderate (4-6)	0/8 (0%)
Severe (7-10)	8/8 (100%)
Duration of olfactory dysfunction No./total olfactory dysfunction (%)	
1-2 wk	1/5 (20%)
3-4 wk	1/5 (20%)
4-6 wk	0/5 (0%)
≥7 wk	3/5 (60%)
→Median (IQR) 45 (18-120) d; Range, 15-120 d	
Duration of gustatory dysfunction No./total gustatory dysfunction (%)	
1-2 wk	5/7 (71.4%)
3-4 wk	0/7
4-6 wk	0/7
≥7 wk	2/7 (28.6%)
→Median (IQR) 10 (5-45) d; Range, 2-120 d	

Abbreviations: OGD, olfactory and gustatory dysfunction; PICU, pediatric intensive care unit.
[a]P=.045
[b]From Qiu et al [8], who classified the severity of COVID-19 as mild (low fever, mild cough, slight fatigue, and no evidence of pneumonia on imaging), moderate (fever, respiratory symptoms, and evidence of pneumonia on imaging), severe (dyspnea, tachypnea, desaturation, or radiologic worsening over 24-48 hours), and critical (respiratory failure, septic shock, and/or multiple-organ dysfunction).
[c]Modified from Izquierdo-Domínguez et al [1]. Normosmic-mild, 0-3 points; moderate, 4-6 points; and severe olfactory or gustatory loss, 7-10 points.

severe loss of smell or taste, respectively [1]. Furthermore, the prevalence of OGD in our study is somewhat lower than in the multicenter study by Qui et al [8], which included 27 children (6-17 years), with 10 of 27 (37%) patients (15-17 years) presenting with OGD, but similar to the Italian survey among pediatricians, in which 29% and 30% of patients with COVID-19 reported anosmia and ageusia, respectively [9]. In contrast, Erdede et al [7] detected a lower prevalence (3.7%) than we did, reporting only 1 child with taste loss from 27 COVID-19–positive children.

In our study, 10% of patients had isolated gustatory dysfunction, an uncommon but previously reported feature in adults [3] and children [7]. The degree of OGD has not been previously described in the pediatric population, and according to our findings, all patients experienced a severe symptomatic form.

We found patients with OGD to be somewhat younger than those in the study by Qui et al [8] (12.6 [2.7] vs 16.6 [0.7] years, respectively), although we found that children who developed OGD were older than those who did not, possibly because of reduced susceptibility to OGD among younger children or lower diagnostic accuracy. The patients in our study seemed to have more severe COVID-19 than in other reports in pediatric [8] and adult patients [1,3].

© 2021 Esmon Publicidad

However, severity in patients with OGD did not differ significantly from that of OGD-free individuals or among patients with OGD, although our limited sample size is a potential source of bias.

As reported by Qiu et al [8] and Diaferio et al [9], onset of OGD coincided with other symptoms in most patients, thus preventing it from being considered an early sign of COVID-19 in children. The duration of OGD was between 5 and 120 days, which is longer than that reported by Mak et al [6] (3->13 days), possibly due to the longer follow-up in our study. Interestingly, loss of smell resolved before loss of taste in our cohort.

The limitations of this study include the potential bias from selecting a population treated in a tertiary hospital, which may not reflect the entire spectrum of COVID-19 in children, particularly mild forms. Further limitations are the retrospective study design and the lack of an objective, validated method for assessing OGD.

In summary, this is one of the few reports in Europe describing OGD in children with COVID-19. In the pediatric population with predominantly moderate to severe COVID-19 presented here, OGD displayed a low prevalence, was not an early sign of disease onset, and tended to have a severe and long-lasting course.

Acknowledgments

Oliver Shaw for editorial assistance.

Funding

The authors declare that no funding was received for the present study.

Conflicts of Interest

Dr Rodriguez del Rio reports personal fees from ALK Abello, grants and personal fees from Aimmune Therapeutics, grants from Merck, personal fees from GSK, FAES, Novartis, Thermofisher, LETI Pharma, and Allergy Therapeutics outside the submitted work.

Dr Bazire reports personal fees from LETI Pharma and grants from FAES and Aimmune Therapeutics outside the submitted work.

Dr Ibáñez reports grants from Instituto Salud Carlos III, personal fees from Faes Farma, Merck, LETI, ROXALL, and CIRCASSIA, and grants from Aimmune Therapeutics outside the submitted work.

Previous Presentation

This work was accepted for presentation as a poster at the 32nd Congress of the Spanish Society of Allergology and Clinical Immunology 2020.

References

1. Izquierdo-Domínguez A, Rojas-Lechuga MJ, Chiesa-Estomba C, Calvo-Henríquez C, Ninchritz-Becerra E, Soriano-Reixach M, et al. Smell and taste dysfunctions in COVID-19 are associated with younger age in ambulatory settings-a multicenter cross-sectional study. J Investig Allergol Clin Immunol. 2020;30(5):1-28.
2. Kaye R, Chand CWD, Kazahaya K, Brerton J, Denneny JC 3rd. COVID-19 Anosmia Reporting Tool: Initial Findings. Otolaryngol Head Neck Surg. 2020;163(1):132-4.
3. Lechien JR, Chiesa-Estomba CM, De Siati DR, Horoi M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. Eur Arch Otorhinolaryngol. 2020;277(8):2251-61.
4. Brann DH, Tsukahara T, Weinreb C, Lipovsek M, Van den Berge K, Gong B, et al. Non-neuronal expression of SARS-CoV-2 entry genes in the olfactory system suggests mechanisms underlying COVID-19-associated anosmia. Sci Adv. 2020;6(31):eabc5801.
5. Dong Y, Mo X, Hu Y, Qi X, Jiang F. Epidemiology of COVID-19 among Children in China. Pediatrics. 2020;145(6):e20200702.
6. Mak PQ, Chung KS, Wong JS, Shek CC, Kwan MY. Anosmia and ageusia: not an uncommon presentation of covid-19 infection in children and adolescents. Pediatr Infect Dis J. 2020;39(8):e199-e200.
7. Erdede O, Sarı E, Uygur Külcü N, Yalçın EU, Sezer Yamanel RG. An overview of smell and taste problems in paediatric COVID-19 patients. Acta Paediatr. 2020;00:1-3.
8. Qiu C, Cui C, Hautefort C, Haehner A, Zhao J, Yao Qi et al. Olfactory and Gustatory Dysfunction as an Early Identifier of COVID-19 in Adults and Children: An international Multicenter Study. Otolaryngol Head Neck Surg. 2020;00:1-8.
9. Diaferio L, Parisi GF, Brindisi G, Indolfi C, Marchese G, Ghiglioni DG, et al. Cross-sectional survey on impact of paediatric COVID-19 among Italian paediatricians: report from the SIAIP rhino-sinusitis and conjunctivitis committee. Ital J Pediatr. 2020;46(1):146.
10. Mannheim J, Gretsch S, Layden JE, Fricchione MJ. Characteristics of Hospitalized Pediatric COVID-19 Cases - Chicago, Illinois, March - April 2020. J Pediatric Infect Dis Soc 2020;00:1-14.

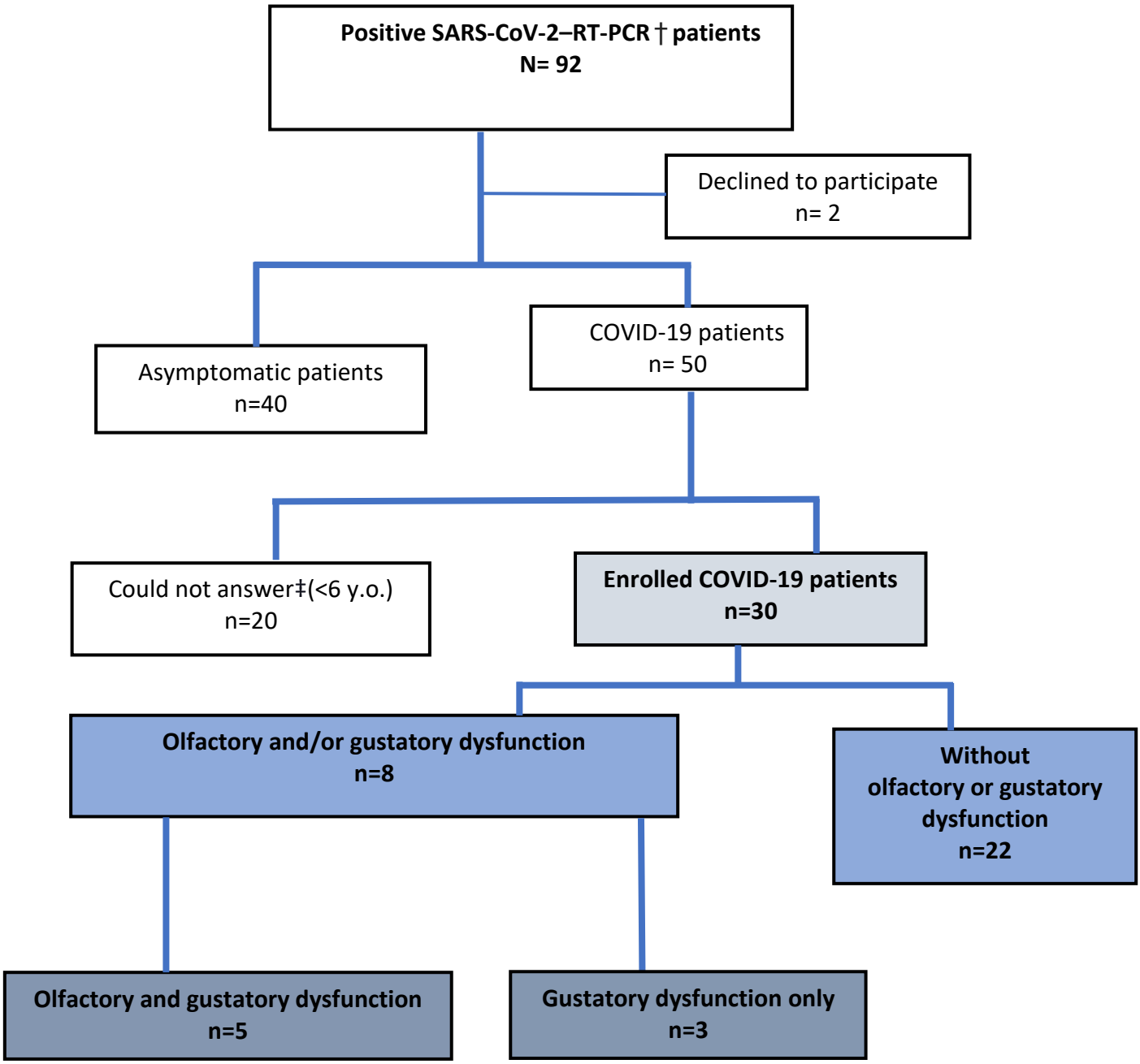
Manuscript received October 11, 2020; accepted for publication February 1, 2020.

María Dolores Ibáñez Sandín
Allergy Department
Hospital Infantil Universitario Niño Jesús
Avda/ Menéndez Pelayo, Nº 65
28009 Madrid, Spain
E-mail: mibanezs@salud.madrid.org

 © 2021 Esmon Publicidad

SUPPLEMENTARY MATERIAL

SUPPLEMENTARY FIGURE: Flowchart of the study.



† Exclusion criteria previously established.
‡ RT-PCR reverse transcription-polymerase chain reaction

J Investig Allergol Clin Immunol 2021; Vol. 31(3): 277-279
doi: 10.18176/jiaci.0677
© 2021 Esmon Publicidad

SUPPLEMENTARY MATERIAL

Supplementary Table. Description of patients with COVID-19 and olfactory and /or gustatory dysfunction.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Age (years)	13	17	12	9	16	11	11	12
Sex	Female	Female	Male	Male	Male	Male	Male	Male
Comorbidities	No	No	No	Allergic rhinitis, asthma, and food allergy.	Allergic rhinitis and hypertension	No	No	No
Olfactory and gustatory dysfunction								
Onset relative to other symptoms	**OD:** Concomitant **GD:** Concomitant	**OD:** Concomitant **GD:** Before	**OD:** Concomitant **GD:** Concomitant	**OD:** Concomitant **GD:** Concomitant	**OD:** Before **GD:** Before	**OD**: N/A **GD:** Concomitant	**OD:** N/A **GD:** Concomitant	**OD**: N/A **GD:** Concomitant
Severity (0–10) †	**OD:** 10 **GD:** 10	**OD**: 10 **GD:** 10	**OD:** 9 **GD:** 10	**OD:** 9 **GD:** 10	**OD:** 10 **GD:** 10	**OD:** N/A **GD:** 9	**OD:** N/A **GD**: 7	**OD:** N/A **GD:** 8
Duration (days)	**OD:** 45 **GD:** 45	**OD:** 120 **GD:** 5	**OD:** 15 **GD:** 15	**OD:** 21 **GD:** 10	**OD:** 120 **GD:** 120	**OD:** N/A **GD:** 2	**OD:** N/A **GD:** NA	**OD:** N/A **GD:** 7
COVID-19								
Symptoms								
Fever	Yes	Yes	No	Yes	Yes	Yes	Yes	No
Respiratory	No	Dyspnea	Pneumonia	Pneumonia	Odynophagia	Pneumonia	No	Odynophagia
Gastrointestinal	Vomiting and diarrhea	Vomiting, diarrhea, and abdominal pain.	Vomiting and diarrhea	Vomiting	No	Vomiting and diarrhea	Diarrhea	Vomiting and diarrhea
Cutaneous	No	No	Dryness	Generalized rash	No	No	Generalized rash	Generalized rash
Grade of severity ‡	Moderate	Moderate	Severe	Moderate	Mild	Severe	Severe	Moderate
Management	Home	Hospitalization	PICU	Hospitalization	Home	PICU	PICU	Home

OGD: Olfactory and gustatory dysfunction; GD: Gustatory dysfunction; OD: Olfactory dysfunction; N/A: Non applicable; NA: Not available; PICU, Paediatric intensive care unit.
† Modified from reference 1. Izquierdo-Domínguez A, et al.
‡ From reference 8. Qiu C, et al.

doi: 10.18176/jiaci.0677
© 2021 Esmon Publicidad