



# Upper airway involvement in pediatric COVID-19

Giuseppe Fabio Parisi<sup>1</sup> | Giulia Brindisi<sup>2</sup> | Cristiana Indolfi<sup>3</sup> | Lucia Diaferio<sup>4</sup> | Giuseppe Marchese<sup>5</sup> | Daniele G. Ghigioni<sup>6</sup> | Anna Maria Zicari<sup>2</sup> | Michele Miraglia del Giudice<sup>3</sup>

<sup>1</sup>Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy

<sup>2</sup>Department of Pediatrics, Allergy and Immunology Division, Sapienza University, Rome, Italy

<sup>3</sup>Department of Woman, Child and Specialized Surgery, University of Campania "Luigi Vanvitelli", Naples, Italy

<sup>4</sup>Department of Pediatrics, Giovanni XXIII Hospital, University of Bari, Bari, Italy

<sup>5</sup>Primary care pediatrician, Cedegolo, Brescia, Italy

<sup>6</sup>Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy

## Correspondence

Giuseppe Fabio Parisi, Pediatric Respiratory Unit, Department of Clinical and Experimental Medicine, University of Catania, Via Santa Sofia 78, 95123, Catania, Italy.

Email: gf.parisi@policlinico.unict.it

Editor: Philippe Eigenmann

## Abstract

The clinical spectrum of SARS-CoV-2 infection is mixed. It ranges from asymptomatic cases, medium-intensity forms with mild to moderate symptoms, to severe ones with bilateral lung involvement and respiratory distress, which can require transfer to ICUs and intubation. In most cases, the clinical picture is characterized by a persistent fever, cough, dyspnoea, expectoration, myalgias, arthralgias, headache, gastrointestinal symptoms, nasal congestion, and pharyngodynia. The spread of COVID-19 in Europe has highlighted an atypical presentation of disease involving upper airways and, above all, dysfunction of olfactory and gustatory senses. There is ample evidence that COVID-19 is significantly less severe in children than in adults. However, due to difficulties in assessing the disorder in children, especially among very young patients, the olfaction and gustatory dysfunctions remain open issues. This article sheds light on the upper airway involvement in pediatric COVID-19 subjects.

## KEYWORDS

ageusia, anosmia, Children, coronavirus, COVID-19, upper airway

## 1 | INTRODUCTION

Coronaviruses (CoVs) are a large family of viruses: some can cause diseases in humans and others in animals (such as camels, cats, and bats). Animal CoVs can rarely cause infections in humans and subsequently be transmitted between people. CoV symptoms range from a simple cold or flu-like syndrome to more serious illnesses, such as Middle Eastern respiratory syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV). On December 31, 2019, the World Health Organization (WHO) received a report from the Chinese health authorities about the presence of pneumonia cases of unknown cause in the city of Wuhan, in the Chinese province of Hubei. Subsequently, the Chinese Health Authorities identified a new CoV, SARS-CoV-2

(Severe Acute Respiratory Syndrome—CoV 2), which had never been isolated before. The SARS-CoV-2 is responsible for COVID-19, an abbreviation coined by the WHO to indicate the disease caused by the new Chinese CoV.<sup>1,2</sup>

As of May 7, 2020, there have been 3,701,257 confirmed cases of COVID-19 worldwide, including 261,097 deaths, according to the WHO.<sup>2</sup>

Italy is the third most affected country after the USA and Spain. As of May 7, 2020, in Italy, 214,103 cases and 27,955 related deaths have occurred. In particular, among the Italian pediatric population, there were 3,752 cases aged between 0 and 17 years; among these, 14.1% (529 children) were under 1 year of age, 17.0% (636 children) between 2 and 6 years, and 68.9% (2,587 children) between 7 and 17 years. A total of 3 death events were outlined among pediatric

patients. These data are provided by the Italian National Institute of Health.<sup>3</sup>

The clinical spectrum of SARS-CoV-2 infection is quite heterogeneous and ranges from asymptomatic forms to medium-intensity cases characterized by mild or moderate symptoms.<sup>4</sup>

There are also severe clinical presentations with bilateral lung involvement and respiratory distress that can evolve into critical forms, which sometimes require patient intubation and ICU transfer. About clinical studies conducted in Asia, the clinical picture in many cases is characterized by persistent fever, cough, dyspnoea, expectoration, myalgias, arthralgias, headache, gastrointestinal symptoms, nasal congestion, and pharyngodynia. In Europe, the spread of COVID-19 has sometimes highlighted an atypical clinical presentation, characterized by the involvement of upper airways and, above all, by the onset of olfactory and gustatory dysfunctions.<sup>5</sup>

There is sufficient evidence worldwide that this disease is much less severe in children than in adults.<sup>4</sup> Although very common in adults, olfactory and gustatory dysfunctions remain an open issue in children, probably due to the lack of valid methods to assess these disorders among the pediatric population. This article aims to provide a focus on the upper airway involvement in pediatric COVID-19.

## 2 | UPPER AIRWAY COVID-19-RELATED DISEASE

Nasal obstruction, rhinorrhea, sneezing, pharyngodynia, olfactory, and gustatory dysfunctions could be the early symptoms of SARS-CoV-2 infection.<sup>4,5</sup>

### 2.1 | Pathophysiological mechanisms

CoVs are a family of viruses that can be associated with anosmia. As early as 2007, CoV could be detected in the nasal secretions of patients with olfactory dysfunction. This occurs because CoV can invade the olfactory bulb and, thus, the central nervous system (CNS). From a biomolecular point of view, many viruses could infect peripheral neurons using the cellular mechanism of active transport to access the CNS, through interactions with the human angiotensin-converting enzyme 2 (ACE-2) receptor. Similar to its predecessor, also SARS-CoV-2, reach the olfactory bulb, as well as some regions of the cortex, midbrain, and basal ganglia, less than 70 hours after the infection. Therefore, the neuroinvasive potential of SARS-CoV-2 seems to play a key role in the respiratory failure of COVID-19 patients.<sup>5</sup>

### 2.2 | Anosmia and ageusia

A recent study analyzed the frequency of neurological manifestations in 214 patients with COVID-19, identifying anosmia in 11 patients (5.1%) and ageusia in 12 patients (5.6%).<sup>6</sup> Indeed, it seems

### Key message

COVID-19 is a disease that involves not only the lower airways but also the upper airways and, although anosmia and ageusia are less frequent in the pediatric population, children should be investigated in any case with specific tests suitable for them.

that in subjects affected by COVID-19, anosmia, and ageusia are not accompanied by nasal obstruction or other rhinitic symptoms. This confirms that its symptomatology is linked to direct viral damage on the olfactory bulb and/or taste receptors. The importance of making a correct diagnosis stems from the consideration that in a not negligible percentage of cases, above all COVID-19 paucisymptomatic subjects, anosmia, and ageusia can represent the only symptomatic manifestation of the disease. Based on experience gained in Italy, it is essential to inform specialists, such as otolaryngologists or even allergists, to pay close attention to these possible clinical manifestations of COVID-19. Such knowledge would bring advantages in limiting the viral spread by poorly symptomatic subjects and acquiring new information on the possible pathogenesis of this new virus. Hopkins et al. have recently published a study conducted on 2,428 COVID-19 patients and concluded that anosmia in 1 out of 6 patients was the only symptom of disease<sup>7</sup>. Also, in the multicentre study published by Lechien et al., composed of 417 patients with mild or moderate COVID-19 disease, olfactory dysfunction was present in 11.8% of total cases before other symptoms. Furthermore, among 18.2% of patients without nasal obstruction or rhinorrhea, 79.7% were anosmic or hyposmic.<sup>5</sup>

### 2.3 | Diagnostic approach

In case of loss of smell, the first examination should include nasal endoscopy, usually performed by a skilled otolaryngologist, and it is expected to be normal when olfactory loss is associated with viral infections. Diagnostic imaging is rarely performed unless symptoms and examination suggest an alternative diagnosis, such as chronic rhinosinusitis or the presence of a mass. Smell tests allow to assess the precise degree of the olfactory loss, compared to the normal olfactory capacity in the general population, where an age-related decrease of smell is reported. The Smell Identification Tests and the Sniffin' Sticks test battery are the most common forms of smell tests. It is also possible to evaluate the impact of taste and smell dysfunctions on quality of life through the Questionnaire of Olfactory Disorders-Negative Statements (sQOD-NS), also available in a reduced version and translated into different languages. Focusing on pediatric population, all children with a confirmed nasopharyngeal swab for COVID-19 would be recommended to perform the "Pediatric Smell Wheel." This is a suitable game that allows to associate the proposed smell with known objects (onion, soap, popcorn,

chewing gum, banana, cherry, rose, chocolate, smoke, peppermint, and cinnamon).<sup>8</sup>

## 2.4 | Treatment

Many drugs have been proposed for the treatment of upper airway disease in COVID-19, including oral corticosteroids, topical corticosteroids, and zinc sulfate; however, a recent systematic review has failed to identify any high-level evidence to support these treatments. As for nasal corticosteroids, their use in the treatment of COVID-19 anosmia does not seem recommended; however, they must not be suspended in case of a concomitant allergic rhinitis, since the increase in sneezing could promote viral spread.<sup>9,10</sup>

## 3 | CONCLUSIONS

COVID-19 results as a disease that involves not only the lower airways, but also the upper airways, which are frequently affected by symptoms like pharyngodynia, nasal congestion, and although less frequently in pediatric population, anosmia and ageusia. However, these latter two ones should be investigated in any case in children with specific tests suitable for them.

### CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

### AUTHOR CONTRIBUTION

**Giuseppe Fabio Parisi:** Conceptualization (equal); Data curation (equal); Formal analysis (equal); Funding acquisition (equal); Investigation (equal); Methodology (equal); Resources (equal); Software (equal); Supervision (equal); Validation (equal); Visualization (equal); Writing-original draft (equal); Writing-review & editing (equal). **Giulia Brindisi:** Conceptualization (equal); Data curation (equal); Formal analysis (equal); Funding acquisition (equal); Investigation (equal); Methodology (equal); Resources (equal); Software (equal); Supervision (equal); Validation (equal); Visualization (equal); Writing-original draft (equal); Writing-review & editing (equal). **Cristiana Indolfi:** Conceptualization (equal); Data curation (equal); Formal analysis (equal); Funding acquisition (equal); Investigation (equal); Methodology (equal); Resources (equal); Software (equal); Supervision (equal); Validation (equal); Visualization (equal); Writing-original draft (equal); Writing-review & editing (equal). **Lucia Diaferio:** Conceptualization (equal); Data curation (equal); Formal analysis (equal); Funding acquisition (equal); Investigation (equal); Methodology (equal); Resources (equal); Software (equal); Supervision (equal); Validation (equal); Visualization (equal); Writing-original draft (equal); Writing-review & editing (equal). **Giuseppe Marchese:** Conceptualization (equal); Data curation (equal); Formal analysis (equal); Funding acquisition (equal); Investigation (equal); Methodology (equal); Resources (equal); Software (equal); Supervision (equal); Validation (equal);

Visualization (equal); Writing-original draft (equal); Writing-review & editing (equal). **Daniele Giovanni Ghiglioni:** Conceptualization (equal); Data curation (equal); Formal analysis (equal); Funding acquisition (equal); Investigation (equal); Methodology (equal); Resources (equal); Software (equal); Supervision (equal); Validation (equal); Visualization (equal); Writing-original draft (equal); Writing-review & editing (equal). **Anna Maria Zicari:** Conceptualization (equal); Data curation (equal); Formal analysis (equal); Funding acquisition (equal); Investigation (equal); Methodology (equal); Project administration (equal); Resources (equal); Software (equal); Supervision (equal); Validation (equal); Visualization (equal); Writing-original draft (equal); Writing-review & editing (equal). **Michele Miraglia del Giudice:** Conceptualization (lead); Data curation (equal); Formal analysis (equal); Funding acquisition (equal); Investigation (equal); Methodology (equal); Project administration (lead); Resources (equal); Software (equal); Supervision (lead); Validation (equal); Visualization (equal); Writing-original draft (equal); Writing-review & editing (equal).

### PEER REVIEW

The peer review history for this article is available at <https://publons.com/publon/10.1111/pai.13356>.

### ORCID

Giuseppe Fabio Parisi  <https://orcid.org/0000-0003-4291-0195>

Giulia Brindisi  <https://orcid.org/0000-0001-5059-6082>

Anna Maria Zicari  <https://orcid.org/0000-0002-2476-1790>

### REFERENCES

1. Chan J-W, Yuan S, Kok K-H, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet*. 2020;395:514–523.
2. World Health Organization. Coronavirus disease 2019 (COVID-19) Situation Report. [https://www.who.int/docs/default-source/coronavirus/situation-reports/20200427-sitrep-98-covid-19.pdf?sfvrsn=90323472\\_4](https://www.who.int/docs/default-source/coronavirus/situation-reports/20200427-sitrep-98-covid-19.pdf?sfvrsn=90323472_4)
3. Istituto Superiore di Sanità. Sorveglianza Integrata COVID-19 in Italia. [https://www.epicentro.iss.it/coronavirus/bollettino/Bollettino-sorveglianza-integrata-COVID-19\\_23-aprile-2020.pdf](https://www.epicentro.iss.it/coronavirus/bollettino/Bollettino-sorveglianza-integrata-COVID-19_23-aprile-2020.pdf).
4. Castagnoli R, Votto M, Licari A, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. *JAMA Pediatr*. 2020. <https://doi.org/10.1001/jamapediatrics.2020.1467>. [Epub ahead of print].
5. Lechien JR, Chiesa-Estomba CM, De Siati DR, 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):2251–2261.
6. Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol*. 2020;77(6):683.
7. Hopkins C, Surda P, Kumar N. Presentation of new onset anosmia during the COVID-19 pandemic. *Rhinology*. 2020;58(3):295–298.
8. Cameron. Olfactory perception in children. *World J Otorhinolaryngol Head Neck Surg*. 2018;212(4):57–66.
9. Bousquet J, Akdis C, Jutel M, et al. Intranasal corticosteroids in allergic rhinitis in COVID-19 infected patients: An ARIA-EAACI

- statement. *Allergy*. 2020. <https://doi.org/10.1111/all.14302>. [Epub ahead of print].
10. Licari A, Votto M, Brambilla I, et al. Allergy and asthma in children and adolescents during the COVID outbreak: What we know and how we could prevent allergy and asthma flares. *Allergy*. 2020. <https://doi.org/10.1111/all.14369>. [Epub ahead of print].

**How to cite this article:** Parisi GF, Brindisi G, Indolfi C, et al. Upper airway involvement in pediatric COVID-19. *Pediatr Allergy Immunol*. 2020;31(Suppl. 26):85–88. <https://doi.org/10.1111/pai.13356>