



Smell and Taste in Children with Covid-19

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Abstract

Objectives: To assess the frequency of loss of smell and taste in children during Covid-19 infection and their prevalence along with other symptoms, as well as the recovery of chemosensory function once healed.

Methods: To evaluate symptoms during infection, we adapted the Scandinavian adaptation of the Multi-Clinic Smell and Taste Questionnaire and the modified Monel-Jefferson questionnaire. For smell analysis we used Odor Identification (OI) and two variants of the Odor Discrimination (OD) test, and we compared the results with those of a control group.

Results: We enrolled nine patients in our experimental group and nine in our control group. Fever was the most frequent symptom (55% of cases), followed by anosmia and ageusia (44% of cases), muscle pain and asthenia (22% of cases) and diarrhea, abdominal pain, cough, and headache (11% of cases). In 11% of cases, olfactory symptoms were the only manifestation of the disease. There was no statistically significant difference in OI test and OD tests between the two groups (Children healed from Covid-19 and Control Group).

Conclusion: Loss of smell and taste are the second most common symptoms of pediatric Covid-19, and they should always be tested because they can be the only manifestations of infection. Olfactory function in Covid-19 children decreases with increasing age and improves with the passage of time after illness.

Keywords

Covid-19, Sars-Cov-2, pediatric covid-19, Covid-19 symptoms, smell, taste

Introduction

During the first wave of Covid-19 pandemic in Italy, 1.2% of cases were children.¹ It has been observed that kids are less likely to be infected and show milder disease and better prognosis than adults.^{2,3} Symptoms described in minors are typical of acute upper respiratory infections such as: fever over 37.5 °C, cough, sore throat, pharyngeal erythema, rhinorrhea, sneezing, diarrhea, vomiting, myalgia, and fatigue.^{2,4} Incubation period is longer than in adults (~6.5 vs ~5.4 days).⁵

Olfactory and taste disorders are present in upwards of 2/3 of adult patients with Sars-CoV-2 infection and may precede the onset of clinical disease.^{6,7} Empirical olfactory testing in Covid-19 cases has been performed in adults, showing smell disfunction in 98% of patients (58% anosmic, 38% severely microsmic, 27% with moderate microsmia, 13% with mild microsmia, and 2% normosmic).⁸ Decreased smell function is a major marker of Covid-19 in adults; whereby, smell testing could be used in non-pediatric patients, in some cases, to identify people in need of early treatment or quarantine.⁸

Milder symptoms, in certain circumstances, can lead to underdiagnosis.³ To avoid that, it is critical to get as much information as possible about these symptoms in children,

given the lack of communication due to age and the possibility of infection of family members together with personnel and kids in kindergarten.

Therefore, we decided to investigate smell function in children affected by Sars-Cov 2 infection, in order to add knowledge about this typical manifestation.

Materials and Methods

Population

Our population was constituted of children diagnosed with Sars-Cov 2 infection in Latina province, Italy, from March

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2020 to June 2020. Eligibility criteria were: age over five but under 18 years old, at least one positive rRT-PCR for Sars-CoV-2 on nasopharyngeal swab, at least two consecutively negative molecular swab tests for Sars-CoV-2. Exclusion criteria were: congenital or acquired conditions that lead to smell impairment, previous diagnosis of anosmia or hyposmia, lack of parental consent to participate in the study, and poor compliance during tests.

A written informed consent was signed for participation in the study. All experiments were conducted in accordance with the Helsinki Declaration. Due to the emergency condition during the experimental period, the study was authorized by Institutional Review Board of “Santa Maria Goretti” Hospital and “Sapienza University of Rome, Polo Pontino,” and it was conducted according to the World Medical Association Declaration of Helsinki.

In addition, we enrolled a control group of children of similar age and origin, with the same exclusion criteria. The study design involved two steps: an anamnestic analysis of smell and taste, referred to symptoms perceived during illness and changes in eating behavior (only in patients’ group) and the measurement of sense of smell through three different olfactometric tests.

Questionnaire

Due to the lack of pediatric questionnaires to evaluate smell and taste, we created one by adapting some questions derived from the Scandinavian adaptation of the Multi-Clinic Smell and Taste Questionnaire and the modified Monel-Jefferson questionnaire, and adding some specific questions for the pediatric age.⁹ The questions concerned: symptoms during infection, smell and taste disorders and changes in eating habits (see: “Questionnaire on loss of taste and smell in Covid-19 children,” Online material).

The compilation was carried out, whenever possible, by the patient with the supervision of the parent; otherwise, in younger, by parents only. It was performed, before olfactometry execution, at the “Santa Maria Goretti” Hospital, Latina (LT), Italy, in a private room with no time limit.

Olfactometry

Olfactory function was assessed using Burghart GmbH (Wedel, Germany) Sniffin’ Sticks for Odor Identification (OI) and Odor Discrimination (OD) tests.^{10,11} We performed two typologies of OD, one with pairs of pens and another with triplets of pens.^{11,12}

OI Test. OI tests require the subject to sniff an odor and then indicate what it smells like.¹¹ Odor were presented to patient with pens with everyday odors (Sniffin’ Sticks), then, were asked to indicate, among four options, which one corresponded to the smell just smelled. As described by Romeau et al., each pen was presented once, for 3 to 4 s, about 2

cm from the nostril without contact with patient’s skin.¹³ The subject was asked to sniff twice, and then the cap was immediately placed on the pen. Then an assistant, who did not know the right choice, enounced the alternative answers from a list of four choices and register on a paper patient’s choice. In this way, he gave no feedback with respect to whether the response was correct or incorrect. Between each substest we observed an interval at least of 30 s.

OD Tests. The OD tests were performed after OI. We performed two typologies of OD, one with pairs of pens and another with triplets of pens (“triangular” version).¹⁰

OD Test. In this test, we presented a pair of pens, the patient was asked to tell if the couple of odors smelled the same. The time interval between two pens was 3 s and the interval between couples was at least 30 s.

“Triangular” OD Test. Triplets of pens were presented in randomized order, with two of them with the same odor and one with a different one. The subject was required to identify which pen of the triplets had a different odor from the other two. The time interval between two pens remained 3 s and the interval between triplets was at least 30 s.^{12,13}

The same procedure, with the exception of the questionnaire, was also performed in a control group of nine children.

Statistical Analysis

Statistical analysis was performed with Statistical Package for Social Sciences 25.0 for MacOS (SPSS[®], IBM, Harmonk, NY, USA) and GraphPad Prism 8.0 for MacOS (GraphPad Inc, La Jolla, CA, USA). Quantitative variables were expressed as mean \pm standard deviation (SD) or median with interquartile range according to sample distribution; nominal variables were expressed as percentage. The prevalence of symptoms during infection was expressed as a percentage. To compare quantitative variables student’s t-test and Mann–Whitney test were performed according to sample distribution. We considered statistically significant a two-tailed p -value $< .05$.

Results

The recruitment was carried out from 1 May to 30 June 2020 through a collaboration between the Departments of Pediatrics and Otolaryngology of “Santa Maria Goretti” Hospital in Latina, LT, Italy.

In our population, all subjects came from infected households. Of the 18 patients initially eligible for the study, seven were excluded because they or a family member were still positive for nasopharyngeal swab for SARS-CoV-2 and one patient was excluded for parental refusal to participate. Since the olfactometry, as subjective tests, require the collaboration of the patient, kids who showed poor compliance

were excluded from the study population. We excluded one 4-year-old male patient for poor compliance during olfactometric tests. Therefore, our population consisted of nine children, five males and four females with a median age of 12 (4) years. The time elapsed since the diagnosis of Covid-19 consisted of a median of 64 (44.5) days.

The same olfactometric tests were administered to a control group made up of nine children, five males and three females, coming from the same geographical area and matched for age. The group had a median of 13 (4) years.

The questionnaire answers showed that all our patients, except an 11-year-old female child, were symptomatic during infection. Fever was the most frequent symptom (55% of cases), followed by anosmia and ageusia (44% of cases), muscle pain and asthenia (22% of cases) and diarrhea, abdominal pain, cough, and headache (11% of cases). In 11% of cases, olfactory symptoms were the only manifestation of the disease (Figure 1).

Parents reported that in 25% of cases of children with olfactory and gustatory dysfunctions there was a change in eating habits that returned to their previous condition after recovery. Half of kids with hypo- or anosmia and/or hypo- or ageusia were reported to have lost weight of at least 5 kg during the illness.

Among children who complained of a history of anosmia, 25% stated that, although improving, the sense of smell was not yet at the levels prior to the disease.

The two groups (children healed from Covid-19 and Control Group) did not show statistically significant difference in results between them (OI test Correct Zt = 0.97; OD test Correct Zt = 0.61; Triangular OD test Correct Zt = 0.26; all Zt were "Corrected for contiguity." $P = .3320$, $P = .5419$ and $P = .7949$, respectively; Table 1). In addition, there was no significant difference in OI test, OD test, and triangular OD test between children with and without history of anosmia during infection.

Discussion

The questionnaire showed that, as described by Weil et al., Sars-CoV-2 positive infants usually come from familiar clusters.^{3,14} However, it was not possible to determine who the first case was and who was secondarily infected.

Previous studies, which did not consider anosmia and ageusia, found that the most frequent symptoms of Covid-19 in the pediatric population were fever and cough.⁵ Instead, considering what emerged from our questionnaire that investigated olfactory and gustatory disorders, in our population, the most frequent symptoms were fever and loss of smell and taste. Chemosensory loss is not only the second most common symptom of Covid-19 in pediatric patients, but, most of all, it can be the only symptom of infection (11.1% of cases). However, this finding is not in agreement with what has been observed in larger anamnestic studies; Bernaola Abaira et al. observed a prevalence of

smell and taste disorders of 26.6% (8 of 30) in 30 symptomatic infected children population, of which five had alterations in smell and taste and three only in taste. Among the patients with chemosensory disorders, two developed them before the onset of the other symptoms of COVID-19, while the others at the same time. The authors concluded, in agreement with Qui et al., Diaferio et al., and Andrade et al., that the incidence of these disorders cannot be considered an early sign of disease because in most patients their incidence is simultaneous with the onset of all symptoms.¹⁵⁻¹⁸

The early identification of symptoms is fundamental in the diagnosis of Covid-19 to limit its spread, even if the main tool remains the use of the facemask. Its use in adults has shown some undesirable effects^{19,20}; the consequences it can have on the child's respiratory physiology are yet to be investigated. So also the impact that these can have on the sense of smell and its recovery, and possibly revise or create exceptions to the laws in this sense.

We also observed that the loss of taste and smell seems to have a prevalence that increases with age.

There is consensus that, in children, relative to adults, olfactory dysfunction are uncommon.²¹ Therefore, its detection in young patients is more likely to be related to infectiousness, especially if of recent onset.

In choosing the test to use for the measurement of smell, we opted for OI and OD tests; we decided not to use threshold measurements because they have been demonstrated to be less sensitive in identifying impaired smell.²²

OI is the most popular olfactory test.¹¹ We did not use the free answer modality, but chose them from the alternatives presented because a forced choice assessment is more reliable and sensitive than non-forced-choice one.²³ The alternatives, in each olfactometric test, were presented verbally, and not in writing, since an earlier study had shown that a consistent portion of 5- and 6-year-olds were unable to read and choose between alternatives, even if they knew the correct answer.²² In order to avoid olfactory desensitization, we waited at least 30 s between each odor in the identification test and between each pair or triplet in the OD test.^{12,13}

The identification of smells by children also depends a lot on the type of smell, some are better identified than others.¹⁰ Whereas odor identification test requires the semantic ability to assign a name to the smell, this ability may not be present in younger kids. Odor discrimination tests do not require the verbal identification, but only to differentiate between different odors.¹¹ It has been observed that, when linguistic abilities are involved in the tasks, young children appeared to have less developed olfactory function; but they are able to reach similar scores when lesser degree lexical skills are required.²⁴ Therefore, younger kids that may be capable to smell an odor, but not to give it a name. For this reason, we also performed OD tests.

Previous research studied results of the OI test on healthy infants; the average scores for age were identified and an

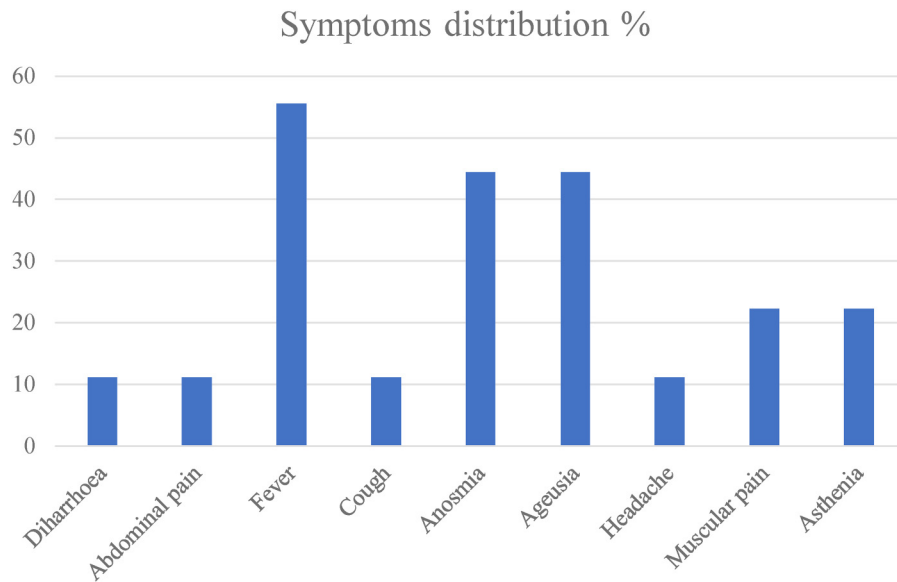


Figure 1. Sars-Cov 2 manifestations.

Table 1. OI test result, percentage of correct answers in OD and triangular OD test in each study group.

Covid-19 group				
Nr.	Sex	OI score	% OD2 score	% OD3 score
1	M	10	100	100
2	M	9	81	94
3	F	11	81	94
4	F	5	94	75
5	M	8	88	88
6	F	4	75	75
7	F	9	88	83
8	M	9	100	100
9	M	10	100	50
Control group				
Nr.	Sex	OI score	% OD2 score	% OD3 score
1	F	8	67	67
2	F	8	67	67
3	M	10	83	67
4	M	7	67	67
5	M	8	67	100
6	M	9	100	100
7	M	9	100	100
8	M	10	100	100
9	F	9	100	100

Abbreviations: OI, odor identification; OD, odor discrimination.

improvement in the score with increasing age was demonstrated.^{22,25} Analyzing the results of our infected population, it emerged that 44.4% of children were below the average values indicated in literature for age-matched kids. The average age of this subpopulation is 14.25 years, while that of children not below the average age values is 9.4 years. Contrary to what happens in the healthy, the kids below

the threshold, despite being older, have a lower average score (6.75) than the younger population above the threshold (9.4). This contrasts with what emerged in the literature with respect to age scores on the OI test.^{5,23}

Among children who had a chemosensory deficit, a quarter of them said that the sense of smell, although it had improved, did not have the same sensitivity as it had before Covid-19. But analyzing test results of all children who experienced chemosensory disorders compared to the average age, only 25% reach a sufficient score. The remaining 75% has an average difference of -2.67 compared to the reference one.^{22,25}

Of the total, 44.4% of the Covid-19 positive children were below the average values indicated in the literature for kids of the same age, with a mean score of 6.75. This group has an average age of 14.25, against the 9.4 years of the normosmic group, which totaled an average score of 9.6.

Children below the average values for age are also those with the most recent diagnosis of the disease with an average of days elapsed from the first diagnosis 56.75 against 73.6 in the group of kids who did not go below the average values for age. Our observations are similar to those emerged in several studies concerning smell and taste in children with Covid-19 which stated that they have high severity and long duration.^{16,18}

In conclusion, our data indicate that olfactory performance in children with Covid-19 decreases with increasing age and improves with the passage of time after illness (Figure 2).

OD test scores have a linear correlation with OI test score in both standard and triangular modality (Figure 3).

In subjects with chemosensory impairment, it could be useful to perform a follow-up for smell and taste, and, in case of persistent alterations, diet should be monitored. In fact, olfaction is essential to achieve a balanced diet for proper nutrition.^{26,27} For a young person, during the crucial

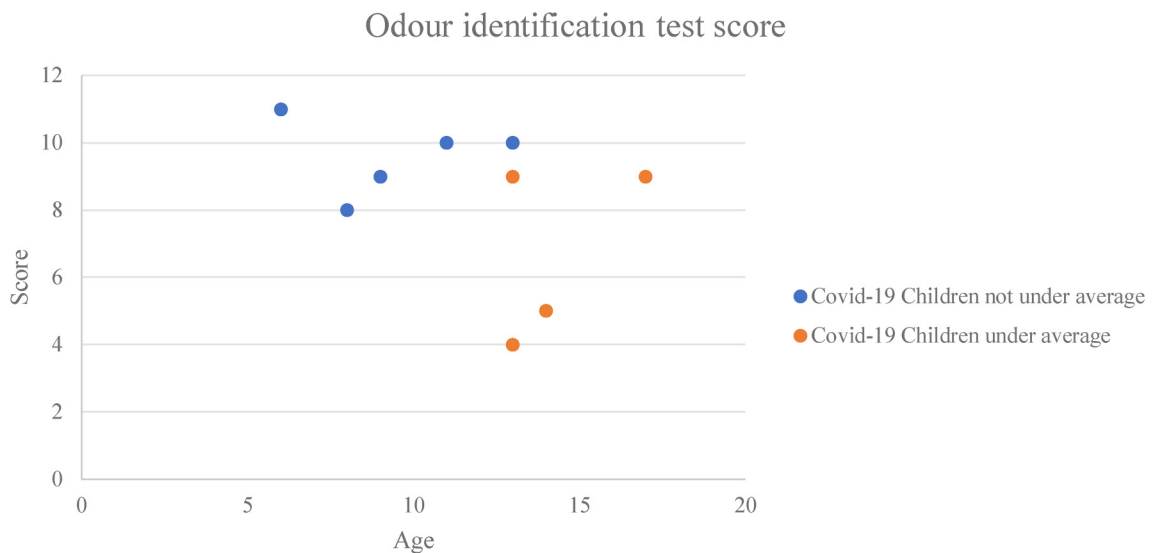


Figure 2. Odor identification test score.

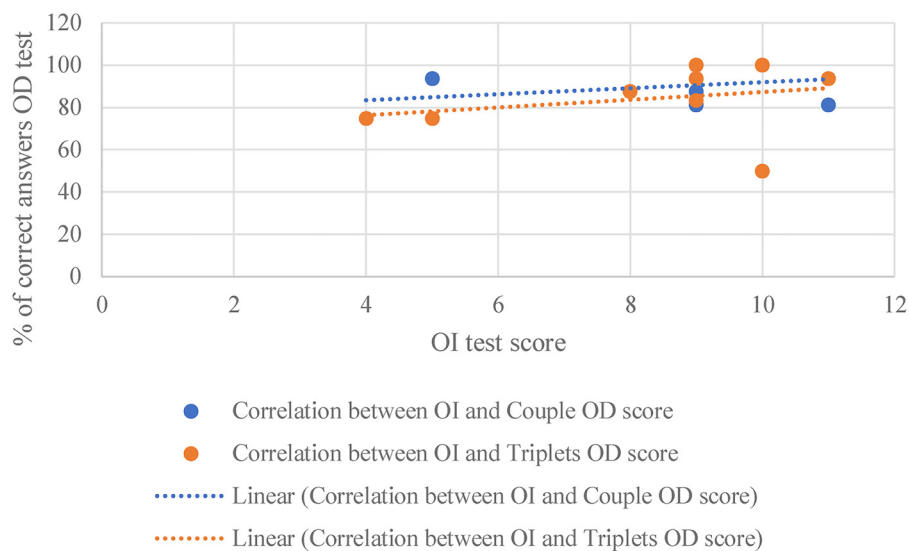


Figure 3. Correlation between OI score and OD scores.

Abbreviations: OI, odor identification; OD, odor discrimination.

years of their psychophysical development, proper nutrition is essential.

The recognition of smells depends on the children's familiarity with them. To make sure we did not have low scores for cultural, regional, and local food habits bias, we compared the results with those of a control group. It was selected so as to have the same geographical origin, cultural background, and dietary habits of the experimental group. By comparing the results with the Mann–Whitney test, we can state that there is no statistically significant difference between the groups under study. Therefore, the cut-offs expressed in the literature cannot be taken as a reference for our population.

But the reduction of the olfactory capacities with increasing age and proximity to the disease remains confirmed. As well as the presence of 22% of patients with significantly hyposmic values (scores of 4 and 5) at the odor identification test is confirmed.

Further studies, on larger populations, are needed to better define the behavior of Covid-19 and, although our populations did not have a statistically significant difference, we can affirm that the olfactory sequelae of Sars-CoV-2 remain, in isolated cases, even after healing.

The main limitation of our study is the sample size. The low number of patients recruited is mainly due to the

difficulty of enrolling children and carrying out all the clinical tests required by our protocol. We hope to be able to share data on larger populations in the future. Furthermore, it would be useful to extend the follow-up of patients already enrolled and to measure their olfactometric outcomes over time.

However, this study remains the first in the literature to perform a clinical test for the measurement of smell in children, not collecting data only with anamnesis or questionnaires. Whereby, we find it useful to share our current observations.

Conclusion

Loss of smell and taste should be considered a pediatric symptom of Covid-19 and it should always be tested because it can be the only manifestation of infection. Olfactory function in Covid-19 children decreases with increasing age and improves with the passage of time after illness.

In some cases, olfactory sequelae can remain even longer after healing, the usefulness of a follow-up of the olfactory and gustatory functions should be evaluated.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author contribution(s)

Piero Giuseppe Meliante: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Software; Writing – original draft; Writing – review & editing.

Alessia Marcellino: Investigation; Methodology; Project administration; Writing – review & editing.

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Alessia Testa: Investigation; Methodology; Project administration; Writing – review & editing.

Andrea Gallo: Conceptualization; Formal analysis; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Writing – review & editing.

Riccardo Lubrano: Conceptualization; Formal analysis; Methodology; Project administration; Supervision; Validation; Writing – original draft; Writing – review & editing.

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Supplemental Material

Supplemental material for this article is available online.

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