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Smell Status in Children Infected with SARS-CoV-2

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Objectives/Hypothesis: This study aimed to evaluate the olfactory status in children with laboratory confirmed SARS-CoV-2 using subjective and psychophysical methods.

Study Design: Prospective clinical cross-sectional study.

Methods: This is a prospective clinical cross-sectional study of 79 children with COVID-19. The 21st item of SNOT-22 questionnaire and odor identification test were used for smell assessment. Children were examined twice during the hospitalization, and a telephone survey was conducted 60 days after hospital discharge.

Results: Immediately after confirmation of COVID-19, smell impairment was detected in 86.1% of children by means of the Identification test and in 68.4% of children by means of the survey (P = .010). After 5 days survey revealed a statistically significant decrease in the number of patients with hyposmia (41 out of 79, 51.9%). On the first visit, the mean Identification test score corresponded to "hyposmia" (9.5 $\pm$ 2.7), while on the second visit, the average value was 13.1 $\pm$ 1.9, which corresponded to "normosmia." According to the telephone survey, recovery of the olfactory function occurred within 10 days in 37 of 52 patients (71.2%), 11 to 29 days - in 12 children (23.1%), and later than 30 days - in three cases (5.7%).

Conclusions: In the pediatric population, olfactory dysfunction is an early and common symptom of COVID-19. There is a trend to quick recovery of olfactory function in children with COVID-19. The overwhelming majority of patients (94.3%) had no subjective olfactory complaints by the end of the first month.

Key Words: Anosmia, hyposmia, smell, children, COVID-19, SARS-CoV-2, pandemic.

Level of Evidence: 4

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INTRODUCTION

Despite local successes and loosening of restrictions in several countries, the 2019 coronavirus disease (COVID-19) pandemic continues its worldwide progression, confirming the validity and importance of scientific research regarding all manifestations of the disease. Ear, nose, and throat symptoms may precede the development of severe COVID-19. One of the most important symptoms of COVID-19 is olfactory dysfunction.

Gane et al. were among the first to report anosmia in COVID-19 patients. The authors presented a case report and case series as well as other evidence of an important fourth presenting syndrome, isolated sudden onset anosmia, which should be considered highly suspicious for COVID-19.[1] Reports of patients with olfactory dysfunction have continued to be published throughout the pandemic.

Taking into account the importance of this symptom, the American Academy of Otolaryngology-Head and Neck Surgery has developed the COVID-19 Anosmia Reporting Tool for Clinicians to allow healthcare providers of all specialties and patients worldwide to submit data for confidential reports on anosmia and dysgeusia related to COVID-19.[2] Sudden anosmia or ageusia have been recognized by the international scientific community as important symptoms of SARS-CoV-2 infection,[3] with patients having hyposmia/anosmia considered potential COVID-19 cases.[4] Printza and Constantinidis identified 18 reviewed articles and six manuscript preprints regarding anosmia in COVID-19 patients and reported that less severe COVID-19 disease was related to a greater prevalence of anosmia.[5]

The majority of publications on anosmia in COVID-19 are devoted to adult patients. Children of all ages are also susceptible to the disease. The first confirmed pediatric case of SARS-CoV-2 infection was reported in Shenzhen on January 20, 2020.[6] Clinical manifestations of COVID-19 in children are less severe than in adults, but it appears that infants in particular are more vulnerable to infections.[7]

Chang reported that disease severity was mild to moderate in 98% of pediatric patients.[8] The author named fever, cough, and rare gastrointestinal symptoms as manifestations of the disease. There were no reports of anosmia in the publications included in Chang's review,

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TABLE I.
Demographic Characteristics of Groups of Patients.

Total Number of Patients (n)	79
Age, median ± SD (years)	12.9 ± 3.4
Gender groups	
Male	37 (46.8)
Female	42 (53.2)
Age groups	
Schoolers, n (%)	31 (39.2)
Age, median ± SD (years)	9.2 ± 1.9
Adolescents, n (%)	48 (60.8)
Age, median ± SD (years)	15.3 ± 1.4
Ethnicity	
Caucasian, n (%)	74 (93.7)
Asian, n (%)	5 (6.3)

and this topic remains insufficiently explored.[8] Kaye et al. studied olfaction in 237 patients, of which only 2% were children.[2] Qiu et al., considering olfactory and gustatory dysfunction as early identifiers of COVID-19, identified anosmia in 10 of 27 children.[9]

To fill the gap in olfactory studies in children infected with SARS-CoV-2, this study aimed to evaluate the olfactory status of pediatric patients with laboratory-confirmed SARS-CoV-2 infections.

MATERIALS AND METHODS

A total of 79 children aged 5 years and older with SARS-CoV-2 infections confirmed by reverse transcription polymerase chain reaction (RT-PCR)-based testing were included in this study. All children were hospitalized at the National Medical Research Center for Children's Health (Moscow, Russia) in April and May 2020. This center was reprofiled to treat children infected with SARS-CoV-2 by order of the Ministry of Health of the Russian Federation on April 2, 2020. All children with COVID-19 received treatment in accordance with the temporary national protocol adopted at that time. There was no special management of anosmia in these patients.

Children with a severe need for oxygen support or artificial ventilation were excluded, due to the difficulty of communicating with the patient to assess smell status.

Demographic characteristics of included patients are presented in Table I. We divided children into two age groups according to the classification of the American Academy of Pediatrics: schoolers (5–12 years) and adolescents (13–18 years).[10]

Study Design

A prospective clinical cross-sectional study was conducted. Each of the 79 children was examined using subjective and psychophysical methods twice during the period of hospitalization: on the day of PCR confirmation of SARS-CoV-2 and after 5 days of treatment. The second test allowed us to assess changes in olfactory function during the short-term follow-up period. Further, we conducted a telephone survey of the parents of included children 60 days after hospital discharge. During the telephone call (the third "visit"), the parents were asked to complete the SNOT-22 survey, including assessment of smell, and to answer how many days after discharge from the hospital the olfaction recovered.

Subjective Assessment of Smell

A standardized questionnaire was administered to the participants. Participants were asked to rate their sense of smell and how it worsened during the course of COVID-19 using the 21st point (sense of taste/smell) of the SNOT-22. A score of 0 to 5 was recorded, as in the SNOT-22, with 0 indicating no problem and 5 indicating a problem as bad as it can be.[11]

We used the version of the SNOT-22, which was validated and adapted to the Russian language by Eisenbach et al. (hereinafter, rSNOT-22).[12]

Psychophysical Olfactory Testing

Psychophysical testing of olfactory function was performed by means of odor identification test battery, which uses commercially available felt-tip pens.[13] Using 16 common odors, the test assesses odor identification ability. For odor presentation, the cap was removed by the experimenter for approximately 3 s. The pen's tip was placed approximately 2 cm in front of both nostrils for about 2 s before the pen was capped again. By means of a multiple-choice task, odors were identified from a list of four descriptors each. The identification score (IdS) ranged from 0 to 16.

TABLE II.
Distribution of All Patients According to the Subjective Assessment of Smell at Each Visit.

Visits	Total Number of Children	Olfactory Scores*						Middle Rank
		0	1	2	3	4	5	
Visit No. 1, number of children (%)	79	25 (31.6)	24 (30.4)	8 (10.1)	22 (27.9)	0 (0.0)	0 (0.0)	2.53
Visit No. 2, number of children (%)	79	38 (48.1)	26 (32.9)	12 (15.2)	3 (3.8)	0 (0.0)	0 (0.0)	2.05
Visit No. 3, number of children (%)	72	72 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.00
P value between visits No. 1 and No. 2†								<.001
p-value between visits No. 1 and No. 3†								<.001

*Results in scores of the answer to item 21 (sense of taste/smell) of the SNOT-22.
†Nonparametric Wilcoxon signed-rank test for dependent samples.

TABLE III.
Distribution of Patients According to the Subjective Assessment of Smell at Each Visit by Age Groups.

	Schoolers (Below 12 years old)								Adolescents (Over 12 years old)								*P* Value for the Significance of the Differences Between Age Groups*
		Olfactory Scores†								Olfactory Scores†							
Age Groups Visits	Total Number of Patients	0	1	2	3	4	5	Middle Rank	Total Number of Patients	0	1	2	3	4	5	Middle Rank	
Visit No. 1, number of patients (%)	n = 31	1 (3.2)	13 (41.9)	2 (6.5)	15 (48.4)	0 (0.0)	0 (0.0)	2.83	n = 48	24 (50.0)	11 (12.5)	6 (14.5)	7 (48.4)	0 (0.0)	0 (0.0)	2.32	.000
Visit No. 2, number of patients (%)	n = 31	12 (38.7)	13 (41.9	4 (12.9)	2 (5.5)	0 (0.0)	0 (0.0)	1.84	n = 48	26 (54.2)	13 (27.1)	8 (16.7)	1 (2.1)	0 (0.0)	0 (0.0)	2.19	.269
Visit No. 3, number of patients (%)	n = 29	29 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		n = 43	43 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
P value between visits No. 1 and No. 2‡								<.001								.017	
P value between visits No. 1 and No. 3‡								<.001								<.001	

*Nonparametric Mann–Whitney U test.
†Results in scores of the answer to item 21 (sense of taste/smell) of the SNOT-22.
‡Nonparametric Wilcoxon signed-rank test for dependent samples.

TABLE IV.
Distribution of Patients According to the Subjective Assessment of Smell at each Visit by Gender Groups.

	Male								Female								*P* Value for the Significance of the Differences Between Gender Groups*
		Olfactory Scores†								Olfactory Scores†							
Gender Groups Visits	Total Number of Patients	0	1	2	3	4	5	Middle Rank	Total Number of Patients	0	1	2	3	4	5	Middle Rank	
Visit No. 1, number of patients (%)	n = 37	11 (29.7)	14 (37.8)	4 (10.8)	8 (21.7)	0 (0.0)	0 (0.0)	2.43	n = 42	14 (33.3)	10 (23.8)	4 (9.6)	14 (33.3)	0 (0.0)	0 (0.0)	2.63	.608
Visit No. 2, number of patients (%)	n = 37	15 (40.5)	14 (37.9)	7 (18.9)	1 (2.7)	0 (0.0)	0 (0.0)	2.14	n = 42	23 (54.8)	12 (28.5)	5 (11.9)	2 (4.8)	0 (0.0)	0 (0.0)	1.96	.263
Visit No. 3, number of patients (%)	n = 36	36 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		n = 36	36 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
P value between visits No. 1 and No. 2‡								.015								<.001	
P value between visits No. 1 and No. 3‡								<.001								<.001	

*Nonparametric Mann–Whitney U test.
†Results in scores of the answer to item 21 (sense of taste/smell) of the SNOT-22.
‡Nonparametric Wilcoxon signed-rank test for dependent samples.

Normative data for normosmia, hyposmia, and anosmia are based on multicentric investigations of more than 1,000 subjects carried out by Hummel.[13] According to the mentioned study, an IdS below 8 is considered anosmia, 8 to 12 is considered hyposmia, and higher than 12 is considered normosmia.[13]

Statistical Analysis

For data processing, we used statistical parameters: mean (M), standard deviation (SD), median (Me), and 25th and 75th percentile (Q1 and Q3, respectively). The Shapiro–Wilk test was used to assess the normality of our sample of patients. The data in nominal and ordinal scales are presented as frequencies and shares.

Comparison of groups according to the subjective assessment of smell (Tables II–IV) at visits 1, 2, and 3 was carried out using the nonparametric Friedman test based on mean ranks, and pairwise comparison between visits was performed using the Wilcoxon test. Comparison at each visit between groups by age and sex was performed using the Mann–Whitney U test.

Comparison of groups based on the results of Identification test (Table V) between visits 1 and 2 was carried out using the Student's *t*-test for dependent samples. Comparison at each visit between groups by age and sex was performed using a *t*-test for independent samples.

Comparison of the methods for assessment of olfactory function (Table VI) was carried out using a Z-test.

The *P* value for statistical significance of differences was set at $P < .05$. All analyses were conducted with the use of SPSS 22.0 software (IBM SPSS Statistics, IBM Corporation).

Ethical Aspects

The study was performed in accordance with the Declaration of Helsinki and was approved by a local institutional medical ethics committee (IRB approval N6 on April 4, 2020). Written informed consent was obtained from both parents/caretakers and additional assents were obtained from participants above 15 years of age.

RESULTS

Demographic Characteristics of Study Participants

Among the 79 patients, 37 (46.8%) were boys and 42 (53.2%) were girls. All children were from 6 to 17 years of age. The largest number of patients (14) was 17 years old, and the mean age was 12.9 ± 3.4 years.

Children in the first group ("schoolers," n = 31) ranged from 6 to 12 years of age with a mean of 9.2 ± 1.9 years. The second group ("adolescence," n = 48) consisted of children aged 13 to 18 years with a mean of 15.3 ± 1.4 years.

Subjective Assessment

Due to the wide range of values and the heterogeneity of the data obtained in the subjective assessment, we decided to use nonparametric criteria and make a comparison based on the ranks.

According to the SNOT-22 questionnaire, the majority of children (54 of 79, 68.4%) had olfactory disorders of different degrees immediately after receiving a positive PCR result.

The second examination, after 5 days, revealed statistically significant decrease in the number of patients with hyposmia (41 out of 79, 51.9%) and improvement in the group values (mean rank 2.05 vs. 2.53 at the first visit, $P < .001$).

Interestingly, at the first visit olfactory function suffered more in the younger age group (mean rank 2.83 vs. 2.32, $P = .000$). However, at the second examination against the background of generally positive dynamics, the values leveled off and statistically significant differences between the age groups disappeared. At the same time, there were no significant differences in the severity of hyposmia between the sexes.

TABLE V.
Odor Identification Test Scores at Each Visit in Different Age and Gender Groups, M ± SD, M ± SD, Me [Q1; Q2].

Groups	Visit No. 1	Visit No. 2	*P* Value Between Visits*
All patients, n = 79	9.5 ± 2.7	13.1 ± 1.9	<.001
	9 [8;12]	13 [11;15]	
Schoolers (below 12 years old), n = 31	8.5 ± 2.4	13.3 ± 2.0	<.001
	8 [7;9]	13.5 [11;15]	
Adolescence (over 12 years old), n = 48	10.1 ± 2.8	12.9 ± 1.8	<.001
	11 [8.5;12]	13 [11;14.5]	
P value for the significance of the differences between age groups†	0.006	0.355	<.001
Male, n = 37	9.8 ± 2.4	13.0 ± 1.8	<.001
	9 [8;12]	13 [11;14.25]	
Female, n = 42	9.3 ± 3.0	13.2 ± 2.0	<.001
	9 [7;12]	14 [11;15]	
P value for the significance of the differences between gender groups	0.381	0.568	

*t-test for dependent samples.
†t-test for independent samples.

TABLE VI.
Number of Children with Olfactory Disorders of Any Severity According to Subjective and Psychophysical Assessments at Each Visit.

Method of Assessment	Visit No. 1, Number of Patients (%)	Visit No. 2, Number of Patients (%)	Visit No. 3, Number of Patients (%)	*P* Value Between Visits No. 1 and No. 2*	*P* Value Between Visits No. 1 and No. 3*
21-st item (sense of taste/smell) of the SNOT-22†	54 (68.4)	41 (51.9)	5 (6.9)	.017	<.001
Identification score of "Sniffin' Sticks" test‡	68 (86.1)	35 (44.3)	N/A	<.001	-
P value between methods of assessments*	.010	.135	-		

*z-test.
†From "very mild problem" till "as bad as it can be."
‡IdS < 13.

On the third visit, during the telephone interview, we interviewed 72 of 79 patients. Among them, 52 children with olfactory disorders were revealed at the first visit according to the survey data. During the phone call, we asked questions from SNOT-22 regarding the sense of smell and on what day hyposmia disappeared. After 2 months, all patients had no complaints of olfactory disorders. Recovery of olfactory function occurred within 10 days in 37 of 52 patients (71.2%), within 11 to 29 days in 12 patients (23.1%), and later than 30 days in three patients (5.8%).

Psychophysical Assessment

Analysis of the results of psychophysical testing revealed that at the first visit, immediately after the confirmation of COVID, the mean identification test score in the group corresponded to "hyposmia" (9.5 ± 2.7). A 5-day interval to the second visit resulted in a statistically significant improvement in the sense of smell. The average value for the group at the second visit was 13.1 ± 1.9, which corresponded to "normosmia" according to the accepted classification.[13]

In addition, we compared the number of children with any severity of smell impairment obtained with subjective (from "very mild problem" to "as bad as it can be") or psychophysical (IdS ≤8) tests (Table VI).

We have found that smell impairment was detected more often by means of psychophysical testing than by subjective assessment (84.0% vs. 66.7%, $P = .010$), which indicates a higher sensitivity of the identification test compared to the subjective survey.

DISCUSSION

Early reports have already suggested that acute smell loss may be an early symptom associated with the worldwide pandemic known as COVID-19.[14]

There are few studies on olfactory function in children infected with SARS-CoV-2. Such studies are important since the course of COVID-19 in children is somewhat different from that in adults.

Chang reviewed the characteristics of pediatric COVID-19 in a meta-analysis. The author reported a milder clinical course in children and noted that, compared with the most relevant virus SARS-CoV, SARS-CoV-2 caused less severe disease. Thus, only two children (2%) received intensive care. Fever occurred in 59% of the children, while cough occurred in 46%. Gastrointestinal symptoms were uncommon (12%), and 26% of children were asymptomatic. The most common radiographic finding was ground-glass opacities (48%). Again, no data about smell status in the patients were presented.[8]

We decided to use the facilities of the large children's state scientific medical center, which was temporarily reprofiled to treat patients with COVID-19, to conduct objective and subjective assessments of olfactory function in hospitalized children.

We are confident in the psychophysical investigation. The odor identification test has proven to be a reliable and unified method, the reproducibility of which is ensured by the availability of commercial kits.[13]

In our study, at the first visit, which corresponded to receiving the results of the SARS-CoV-2 PCR test, olfactory disorders of varying degrees were found in 84% of patients. However, olfaction tended to recover quickly in children even without specific treatment. Five days after the first visit, the mean identification score in the group increased from 9.5 ± 2.7 ("hyposmia") to 13.1 ± 1.9 ("normosmia").

There are several survey forms for the subjective assessment of smell changes. The COVID-19 Anosmia Reporting Tool for Clinicians is a great questionnaire for registering cases of post-COVID-19 anosmia and determining its prevalence in the population.[2] The contents of the tool, especially the data elements, were based on a review of multiple COVID-19 reports related to anosmia.[2] However, this form does not allow assessment of the loss of smell qualitatively and quantitatively, nor tracking of olfactory function recovery.

In our work, smell assessment was performed as a part of a comprehensive study of sino-nasal symptoms, and we decided that the application of the well-proven and commonly used Sino-Nasal Outcome Test (SNOT-22), paragraph 21 of which is devoted to olfactory/gustatory function, would be the most rational and indicative.

According to the SNOT-22 survey, olfactory disorders of different degrees were found in the vast majority of children immediately after receiving the positive PCR rest results in this study. The survey of patients at the first visit revealed signs of olfactory dysfunction in 68.4% of children (54 of 79). This percentage was slightly less than with identification test (84%), but was significantly higher than the findings of Mercante, in which I-SNOT-22 identified smell reduction in 41.7% of patients (median score, 5; range, 1–5).[11]

The subjective survey also confirmed a rapid recovery trend in olfactory function. The middle rank at the second visit was 2.05, compared with 2.53 at the first visit ($P < .001$).

We thought it interesting and valuable to determine, which of the methods for assessment of olfactory disorders produced more accurate results. When comparing the number of cases of olfactory disorder of any severity, psychophysical assessment (IdS ≤8), was significantly higher than subjective assessment (84.0% vs. 68.4%, $P = .010$).

Another very important clinical issue is the recovery period of olfactory function in different groups of patients. Kaye et al. reported that some improvement in anosmia was noted in 27% of patients, with a mean time to improvement of 7.2 days (85% improved within 10 days). However, according to the authors' comments, these data are subject to significant interpretation as many entries were submitted before long-term follow-up was achieved. There was no separate analysis in the pediatric group.[2] According to Lechien, patients with hyposmia or anosmia had the following recovery times: 1 to 4 days (33.0%), 5 to 8 days (39.6%), 9 to 14 days (24.2%), and more than 15 days (3.3%).[3]

In our study, during the telephone survey (the third "visit") we asked parents not only to complete the smell assessment point of SNOT-22 but also to define as accurately as possible the length of time anosmia persisted. The results were encouraging for the pediatric population. All patients (52 of 52, 100%) reported total recovery of olfaction within 2 months. This means that restoration of olfactory function in children occurs faster than in adults, according to the reports of Kaye and Lechien et al.[2, 3]

CONCLUSION

We understand the limitations of our study and highlight the necessity of further research in this field. In the pediatric population, olfactory dysfunction is an early and common symptom of COVID-19. Psychophysical testing was found to be more sensitive compared to the subjective survey (84.0% vs. 66.7%, $P = .010$).

Olfactory function in children with COVID-19 tends to recover quickly. On day 5, statistically significant positive dynamics were observed, the overwhelming majority of patients (94.3%) had no subjective olfactory complaints within the first month, and after 2 months normal smell function was found in all patients according to the survey.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Local Institutional Review Board of National Medical Research Center for Children's Health (N6, 14.04.2020).

Informed Consent

Informed consent was obtained from all individual participants included in this study. All authors have viewed and agreed to the submission.

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