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Smell and Taste Impairment in COVID-19 Positive Pediatric Patients: A Prospective Cohort on Different Stages of The Disease

COVID-19 Pozitif Pediyatrik Hastalarda Koku ve Tat Bozukluğu: Hastalığın Farklı Evrelerinde Prospektif Bir Kohort

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Abstract

Objective: To evaluate the smell and taste impairment in Coronavirus disease-2019 (COVID-19) pediatric patients according to the disease severity.

Method: Ninety polymerase chain reaction test-confirmed COVID-19 patients were enrolled from January 2021 to July 2021. Patients were categorized into three main groups according to the stage of disease (stage 1: Outpatients, stage 2: Inpatients, stage 3: Intensive care unit patients). There were 30 pediatric patients in each group. Subjects were evaluated with a questionnaire. Visual analog scale was used to evaluate smell and taste impairment patients.

Results: The impairment of smell and taste were evaluated separately, and the rates were found to be 31.1% and 35.6%, respectively. The impairment of smell showed a statistically significant difference between the groups (p=0.002). The rate of smell impairment in the outpatients was found to be significantly higher than in the patients treated in the intensive care unit. The taste impairment did not show a statistically significant difference between the groups (p=0.109; p>0.01). Persistence of smell and taste impairment was found in 5.5% of the patients.

Conclusion: The rate of smell impairment in the outpatients was found to be significantly higher than in the cases treated in the intensive care unit.

Keywords: COVID-19, olfactory impairment, pediatrics, smell, taste

Öz

Amaç: Koronavirüs hastalığı-2019 (COVID-19) pediyatrik hastalarda koku ve tat bozukluğunu hastalığın ciddiyetine göre değerlendirmektir.

Yöntem: Ocak 2021'den Temmuz 2021'e kadar 90 polimeraz zincir reaksiyonu testi doğrulanmış COVID-19 hastası kaydedildi. Hastalar, hastalığın evresine göre üç ana gruba ayrıldı (evre 1: Ayakta tedavi olan hastalar, evre 2: Yatan hastalar, evre 3: Yoğun bakım hastaları). Her grupta 30 çocuk hasta vardı. Denekler bir anket ile değerlendirildi. Koku ve tat bozukluğu olan hastaları değerlendirmek için görsel analog skalası kullanıldı.

Bulgular: Koku ve tat bozukluğu ayrı ayrı değerlendirildi ve sırasıyla %26,7 ve %27,8 olarak bulundu. Koku alma bozukluğu gruplar arasında istatistiksel olarak anlamlı farklılık gösterdi (p=0,002). Ayakta tedavi gören hastalarda koku bozukluğu oranı yoğun bakımda tedavi edilen hastalara göre anlamlı derecede yüksek bulundu. Tat bozukluğu gruplar arasında istatistiksel olarak anlamlı bir fark göstermedi (p=0,109; p>0,01). Hastaların %5,5'inde koku ve tat bozukluğunun kalıcılığı olduğu görüldü.

Sonuç: Ayaktan tedavi gören hastalarda koku bozukluğu oranı yoğun bakımda tedavi edilen olgulara göre anlamlı derecede yüksek bulundu.

Anahtar kelimeler: COVID-19, koku, koku bozukluğu, pediatri, tat

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Introduction

Despite the increasing vaccination rates all over the world, the 2019 Coronavirus pandemic continues to affect the whole world with 254,606,286 confirmed cases and 5,122,842 deaths (as of November 16, 2021) worldwide (1). Although it presents with different symptoms, olfactory dysfunctions are the most prominent ones among ear, nose, and throat symptoms with the earlier variants (2-7). In adults, the smell and taste impairment is presented extensively in the literature. However, data on children are in limited number.

Coronavirus disease-2019 (COVID-19) has a variable course starting from asymptomatic infection to death (2,3). Previous studies have suggested that the course of disease may be adversely linked with the smell and taste impairment. In the milder forms of COVID-19, the smell and taste impairment rates were found to be high. In contrast, the smell and taste impairment rates were found to be low in critically ill patients (4). The upper respiratory tract involvement was regarded as a protective factor for lower airway involvement and more severe disease (8).

In this study, our aim is to examine the rates of smell and taste disorders in 3 groups of pediatric patients having COVID-19 with different prognosis. Although there are evaluations in terms of pediatric COVID-19 symptoms in the literature, our study differs from other studies because it examines the relationship between the stage of the disease and the olfactory disorder.

Materials and Methods

The study was approved by our Institutional Ethics Committee University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital with study number 2021-50. According to power analysis, a total of 90 children with COVID-19 infection were enrolled. All cases were patients with definite COVID-19 infection, confirmed by real-time reverse transcriptase-polymerase chain reaction materials taken from naso-oropharyngeal swabs). Patients with asymptomatic infection, those with a known co-infection with other viruses and co-incidentally positive patients were excluded from the study. We classified the study population based on disease stage (stage 1 mild type: Outpatient, stage 2 moderate type: Inpatient, stage 3 severe type: Intensive care unit). There were 30 pediatric patients in each group.

The American Academy of Otolaryngology-Head and Neck Surgery Anosmia Reporting Tool was used as questionnaire (4). A clinical history was taken from the parents and from the patient if the patient was old enough to answer the questions. Patients' demographic data (age, gender, weight, height, body mass index) and concomitant symptoms were recorded. The patients were asked to rate their smell sensation at its worst point during the infection, as normal, partial (hyposmia), or complete (anosmia) loss of smell. All the patients were asked if they had any alteration in taste or not. Visual analog scale (VAS) was used to evaluate hyposmia and hypogeusia patients.

Power Analysis

Power Analysis was performed to determine the sample size by using G*Power (v3.1.7). According to the Cohen's effect size coefficients, assuming the evaluation being made between 3 independent groups will have a small effect size (d=0.2), the results indicated that a total sample of 90 participants with 3 equally sized groups of 30 would be required to achieve a power of 0.80.

Statistical Analysis

While evaluating the findings obtained in the study, NCSS (Number Cruncher Statistical System) Statistical Software (NCSS LLC, Kaysville, Utah, USA) program was used for statistical analysis. While evaluating the study data, quantitative variables were shown with mean, standard deviation, median, minimum, and maximum values, and qualitative variables were shown with descriptive statistical methods such as frequency and percentage. The Shapiro-Wilks test and Box Plot graphics were used to evaluate the conformity of the data to the normal distribution. The Kruskal-Wallis test was used for the comparison of the parameters that did not show normal distribution, and the Dunn test was used to determine the group that caused the difference. The Pearson chi-square test and Fisher-Freeman-Halton test were used to compare qualitative data. The results were evaluated at the significance level of $p<0.05$.

Results

The study was carried out with 90 cases, including 44.4% (n=40) female and 55.6% (n=50) male patients. The ages of the subjects participating in the study ranged from 4 to 17 ($p>0.05$) years. There was no statistically significant difference in the gender distribution, mean age, height, and body mass index of the cases according to the groups ($p>0.05$ for all comparisons). The mean weight values differed statistically significantly between the groups

(p=0.044; p<0.05). According to the pairwise comparisons made to determine the difference, the mean weight of the patients treated in the intensive care unit was found to be statistically significantly lower than that of the patients treated in the inpatient unit (p=0.021; p<0.05) (Table 1).

Of the subjects participating in the study, 72.2% (n=65) had fever, 41.1% (n=37) had fatigue, 33.3% (n=30) had headache, 37.8% (n=34) had muscle pain, 31% (n=28) had diarrhea, and 32.2% (n=29) had cough complaints. Other complaints are given in Table 2. Fever and fatigue were the most frequently reported symptoms in all study groups. In our study, the impairment of smell and taste was evaluated separately and the rates were found to be 26.7% and 27.8%, respectively.

When the smell impairment of the cases was examined, it was observed that 23.3% (n=21) could not smell (anosmia) at all, 7.8% (n=7) had a partial smell (hyposmia), and 68.9% (n=62) did not have an olfactory disorder. Hyposmia evaluation VAS scores of the subjects participating in the study ranged from 5 to 7. Smell impairment developed in 32.1% (n=9) of the cases within 1-2 days, in 39.3% (n=11) within 3-4 days, and in 28.6% (n=8) within 5 days and later. In 82.1% (n=23) of the cases with a smell disorder, this complaint was completely recovered. The impairment of smell revealed a statistically significant difference according to the groups (p=0.002). The rate of smell impairment in the outpatients was found to be significantly higher than in the patients treated in the intensive care unit.

When taste impairment of the cases was examined, it was detected that 17.8% (n=16) had no taste (ageusia) at all, 16.7% (n=15) tasted partially (hypogeusia), 1.1% (n=1) had different tastes (parageusia), and 64.4% (n=58) had no taste impairment. Hypogeuisa evaluation VAS scores of the subjects participating in the study ranged from 5 to 8. Taste impairment developed in 31.3% (n=10) of cases within 1-2 days, in 40.6% (n=13) within 3-4 days, and in 28.1% (n=9) within 5 days and later. In 84.4% (n=27) of the cases with a taste disorder, the taste disorder was completely recovered. Taste impairment did not show a statistically significant difference between the groups (p=0.109; p>0.05) (Table 3).

Table 2. Distribution of complaints according to groups

		Stage 1	Stage 2	Stage 3	p
		n (%)	n (%)	n (%)	
Fever	Absent	16 (53.3)	7 (23.3)	2 (6.7)	[a]**0.001 ****
	Present	14 (46.7)	23 (76.7)	28 (93.3)	
Fatigue	Absent	26 (86.7)	17 (56.7)	28 (93.3)	[a]**0.001 ****
	Present	4 (13.3)	13 (43.3)	2 (6.7)	
Feeding difficulties	Absent	27 (90.0)	25 (83.3)	26 (86.7)	[c]**0.926**
	Present	3 (10.0)	5 (16.7)	4 (13.3)	
Tiredness	Absent	15 (50.0)	15 (50.0)	23 (76.7)	[a]**0.053**
	Present	15 (50.0)	15 (50.0)	7 (23.3)	
Headache	Absent	15 (50.0)	20 (66.7)	25 (83.3)	[a]**0.024 ***
	Present	15 (50.0)	10 (33.3)	5 (16.7)	
Muscle pain	Absent	18 (60.0)	15 (50.0)	23 (76.7)	[a]**0.099**
	Present	12 (40.0)	15 (50.0)	7 (23.3)	
Stomachache	Absent	27 (90.0)	25 (83.3)	19 (63.3)	[a]**0.031 ***
	Present	3 (10.0)	5 (16.7)	11 (36.7)	
Vomiting	Absent	29 (96.7)	24 (80.0)	14 (46.7)	[a]**0.001 ****
	Present	1 (3.3)	6 (20.0)	16 (53.3)	
Diarrhea	Absent	28 (93.3)	20 (66.7)	14 (46.7)	[a]**0.001 ****
	Present	2 (6.7)	10 (33.3)	16 (53.3)	
Cough	Absent	23 (76.7)	18 (60.0)	20 (66.7)	[a]**0.380**
	Present	7 (23.3)	12 (40.0)	10 (33.3)	
Throat ache	Absent	20 (66.7)	21 (70.0)	25 (83.3)	[a]**0.303**
	Present	10 (33.3)	9 (30.0)	5 (16.7)	
Shortness of breath	Absent	29 (96.7)	25 (83.3)	20 (66.7)	[a]**0.010***
	Present	1 (3.3)	5 (16.7)	10 (33.3)	
Nasal congestion	Absent	23 (76.7)	23 (76.7)	30 (100.0)	[c]**0.008 ****
	Present	7 (23.3)	7 (23.3)	0 (0.0)	
Runny nose	Absent	27 (90.0)	25 (83.3)	30 (100.0)	[c]**0.091**
	Present	3 (10.0)	5 (16.7)	0 (0.0)	
Other	Absent	28 (93.3)	27 (90.0)	18 (60.0)	[a]**0.001****
	Present	2 (6.7)	3 (10.0)	12 (40.0)	

Other symptoms: Rash, low back pain, forgetfulness, hoarseness. [a]: Pearson chi-square test, [c]: Fisher-Freeman-Halton test, *p<0.05 **p<0.01

Table 1. Examination of demographic characteristics by groups

		Stage 1 (n=30)	Stage 2 (n=30)	Stage 3 (n=30)	p
Gender	Female	16 (53.3)	13 (43.3)	11 (36.7)	[a]0.425
	Male	14 (46.7)	15 (56.7)	19 (63.3)	-
Age	Median (Q1-Q3)	12.5 (10-15)	12 (10-13)	11 (8.5-13.3)	[b]0.266
Height	Median (Q1-Q3)	159 (147-166.5)	152.5 (142-168)	147.5 (125.5-160)	[b]0.074
Weight	Median (Q1-Q3)	50 (40-56)	51 (38-65)	41 (29-50)	[b]0.044 *
BMI	Median (Q1-Q3)	19.9 (17.2-22)	21.4 (19.2-24)	18.9 (17-22)	[b]0.088

[a]: Pearson chi-square test, [b]: Kruskal-Wallis test, *p<0.05, Q1-Q3: 25% percentile -75% percentile, BMI: Body mass index

Table 3. The comparison of smell and taste impairment according to groups

		Stage 1	Stage 2	Stage 3	p
		n (%)	n (%)	n (%)	
Smell impairment	**Normal (n=62)**	16 (53.3)	19 (63.3)	2 (90.0)	[c]**0.019***
	Anosmia (n=21)	11 (36.7)	8 (26.7)	2 (6.7)	
	Hyposmia (n=7)	3 (10.0)	3 (10.0)	1 (3.3)	
Recovery (n=28)	**Yes (n=23)**	11 (78.6)	9 (81.8)	3 (100.0)	[c]**1.000**
	No (n=5)	3 (21.4)	2 (18.2)	0 (0.0)	
Hyposmia VAS	**n**	3	3	1	-
	Median (Q1-Q3)	6 (5-7)	6 (6-6)	6 (6-6)	
Taste impairment	**Normal (n=58)**	18 (60.0)	15 (50.0)	25 (83.3)	[a]**0.109**
	Ageuasia (n=17)	6 (20.0)	8 (26.7)	3 (6.7)	
	Hypogeusia (n=14)	6 (20.0)	6 (20.0)	2 (10.0)	
	Parageusia (n=1)	0 (0.0)	1 (3.3)	0 (0.0)	
	Normal (n=58)	18 (60.0)	15 (50.0)	25 (83.3)	[c]**0.021***
	Abnormal (n=32)	12 (40.0)	15 (50.0)	5 (16.7)	
Hypogeuisa VAS	**n**	6	6	2	-
	Median (Q1-Q3)	5.5 (6-7)	6 (6-6)	6 (6-6)	
Recovery (n=32)	**Yes (n=27)**	10 (83.3)	12 (80.0)	5 (100.0)	[c]**0.832**
	No (n=5)	2 (16.7)	3 (20.0)	0 (0.0)	

[a]: Pearson chi-square test, [c]: Fisher-Freeman-Halton test, *p<0.05, **p<0.01, Q1-Q3: 25% percentile -75% percentile, VAS: Visual analog scale

Discussion

In the present study, our aim was to examine the rates of smell and taste disorders in 3 groups of pediatric COVID-19 patients with different stages. Overall, the rates of smell and taste impairment were found to be 31.1% and 35.6%, respectively. The rate of smell impairment in the outpatients was found to be significantly higher than in the patients treated in the intensive care unit. The taste impairment did not show a statistically significant difference between the groups.

With the progression of this pandemic, despite the constant stream of new and interesting literature, the scarcity of systematic reviews and meta-analyses on various aspects of severe acute respiratory syndrome-coronavirus-2 infection in pediatric patients (0.04%) prompted us to do this study (6).

Although the pandemic continues at full speed, the clinical course of pediatric patients is very variable. A treatment modality other than a vaccine that could be a glimmer of hope is not on the horizon. Therefore, it is important to understand the clinical course of the disease. In this study, clinical symptoms and smell and taste disorders were evaluated by survey studies according to their clinical courses in 3 groups of patients. In the literature, it has been shown that previously self-reported subjective smell impairment results are correlated with objective methods (7).

A prospective comparative study of smell and taste disorders with pediatric patients could not be found in the literature review (5). Also, information on smell and taste disorders of pediatric intensive care patients is not available in the literature. This may be due to relatively small number of critically ill pediatric patients which required intensive care unit stay. In fact, only one study has been found in the literature on adult intensive care patients. Sayın et al. (8) reported that smell and taste disorders were detected in 43.2% of the intensive care unit COVID-19 patients. Barry et al. (9) found the rate of loss of smell as 9.1% in hospitalized severely ill adult patients with COVID-19. Lechien et al. (10) reported only %38.3 smell impairment rate in severe hospitalized COVID-19 adult patients. There is a publication that argues the opposite and states that the severity of the disease is not associated with smell and taste disorders (11). It is not known whether the differences in the rapid recovery of smell and taste disorders can be attributed to the patient's forgetting the situation. Kaye et al. (12) stated that 85% of patients had anosmia healed within 10 days.

The low mortality rate (0.1%) in pediatric patient groups and the clinical picture are different from those in adults, which is being tried to be explained by various hypotheses (13). The exact pathophysiology of smell and taste impairment in COVID-19 patients is still unknown (14). Human angiotensin-converting enzyme 2 (ACE 2) is the important key factor for entering coronaviruses.

Although low *ACE 2* gene expression has been implicated in children, a prospective observational cohort study found no age-related differences (15). One of the other blamed factors is the immaturity of immunological development in children, which is important in the milder course of the clinical course (16). Except that the immune system is immature, the lack of maturity in the receptors, to which ACE 2 binds, is used to explain the fact that pediatric taste and odor disorders are less frequent than in adults (16). Another implicated hypothesis is that smoking increases the expression of ACE 2, thus facilitating the entry of the coronavirus into the pulmonary epithelium (17). There is no doubt that the smoking rate of adults is higher than that of pediatric patients, which protects children from serious infections (13).

Two forms of COVID-19 infection were hypothesized in the literature. One is the "nasal form" and the other is "pulmonary form" (8). In early variants of COVID-19 infection, the characteristic of infection is the presence of smell and taste impairment in the absence of nasal blockage (3,4). The presence of smell and taste impairment was the sign of upper respiratory tract involvement and when this occurred, the nasal as well as systemic responses were triggered. In the absence of smell and taste impairment, immune responses may not be triggered. Second mechanism is that the lungs may be the first reservoir and the upper respiratory involvement may not be the case (18). Yan et al. (18), in their study, published that partially mild outpatient cases might be a result of nasal-centered viral spread, while patients requiring hospitalization might be experiencing a more pulmonary-centered infection. However, very few data are available regarding the effect of disease severity on chemosensory findings (19).

Saniasiaya et al. (5) were able to include only 9 studies in their systematic review between December 1, 2019 and April 30, 2021, examining COVID-19 positive pediatric patients with olfactory dysfunction. Only one of the studies included in this review studied on 141 patients, which is higher than our number of patients. In their study, they reported the prevalence of smell and taste disorders in children and adolescent patients to be 28.4% in COVID-19 (14). Rusetsky et al. (2) stated that, in the pediatric population, olfactory dysfunction was an early and warning symptom. Within a month, 93.4% of patients' complaints regress. Sayin et al. (4) reported changes in smell and taste in children aged 7-15 years at the rate of 10.4-13.1%. When the smell and taste impairment develops, it mostly occurs as partial loss and recovers early and spontaneously (20).

Our prospective study was the first study that evaluated smell and taste impairment according to different stages of COVID-19 infection. This study also serves as the first study that evaluated COVID-19 pediatric patients that required intensive care unit stay. Our findings were consistent with the literature which highlighted that the presence of smell and taste impairment was related to milder disease. There are some limitations of this study. First, we did not use an objective testing method. However, using objective testing in a pediatric group of patients was challenging, and it is also not the case for the patients that required ICU stay. Second, we performed the present study with a small effect size. This is why pediatric patients requiring ICU stay are in a limited number. The fact that the intensive care data of pediatric patients are not included in the previous papers on this topic in the literature makes it difficult to interpret our own data in light of the literature. Although we could evaluate the smell with the questions that we asked the children, we had difficulties in the evaluation of taste. Finally, we could not present the long-term outcomes for those who did not experience a recovery in smell and taste impairment.

Conclusion

In our study, smell and taste impairment was evaluated in different stages of COVID-19 pediatric patients. The rate of smell impairment in the outpatients was found to be significantly higher than in the patients treated in the intensive care unit. Further studies will clarify the relationship between smell and taste impairment and disease severity.

Ethics

Ethics Committee Approval: The study was approved by our Institutional Ethics Committee University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital with study number 2021-50.

Informed Consent: Written informed consent for publication was obtained from the parents on behalf of the patients.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.A., B.M., N.S., Concept: Z.M.Y., N.S., N.A., B.M., N.H., Design: Z.M.Y., N.S., N.A., B.M., Data Collection or Processing: N.S., N.A., B.M., Analysis or Interpretation: Z.M.Y., İ.S., Critical Review: İ.S., E.Ş., N.S., Writing: Z.M.Y., E.Ş., N.H., Supervision: E.Ş., N.H., İ.S., Z.M.Y.

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