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Asthma control and treatment steps in Turkish children with Asthma during the COVID-19 pandemic

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ABSTRACT

Objective: Since viral infections are one of the most important factors affecting asthma control, various precautions and recommendations for asthma patients came to the fore at the beginning of the COVID-19 pandemic. In our study, we aimed to evaluate the effects of the COVID-19 pandemic on asthma control and treatment steps of children with asthma.

Materials and Methods: The date of March 11, 2019, was accepted as the beginning of the pandemic. The application deadline to our outpatient clinic of patients within one year after the onset of the pandemic (AOP) was determined. After that, the period of the same season before the beginning of the pandemic (BOP) was determined. We recorded the asthma treatment steps, asthma control test (ACT) scores, and the number of applications to our outpatient clinic during the BOP and AOP periods of the patients.

Results: In our study, 384 patients, 64.8% of whom were male, with a median age of 11 years, were evaluated. SARS-CoV-2 PCR positivity was detected in 6 (1.6%) patients. BOP, patient treatment steps, and the number of outpatient clinic applications were higher ($p < 0.001$). AOP, there was no significant change in ACT scores ($p = 0.059$). Whereas asthma control was worse in patients susceptible to house dust mite ($p = 0.01$).

Conclusions: Although measures such as home quarantine and mask use have been reported to have positive effects on asthma control, increased exposure to house dust mites in susceptible patients may pose a risk of uncontrolled asthma.

Keywords: Asthma, pandemic, house dust mites, treatment, COVID-19, children

INTRODUCTION

COVID-19 (coronavirus disease-2019) caused by the new Coronavirus named SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2), which causes severe acute respiratory syndrome and death, was declared as a pandemic disease by the World Health Organization on March 11, 2020.

On that date, the first case was detected in Turkey (1-3). During the pandemic, various measures were taken worldwide, face-to-face education was discontinued, and curfews were imposed at intervals in our country. Asthma, one of childhood's most common chronic diseases, is most triggered by allergens, air pollution, and viral infections (4-7).

In asthma guidelines, it was recommended that patients' asthma control, treatment adherence, written asthma action plan, and spirometric measurements be evaluated every 3 to 6 months (5,7). Since the effect of Covid-19 on asthma is unknown, conflicting explanations regarding the relationship between asthma and COVID-19 in the early days of the pandemic have led to the emergence of numerous emergency precaution guidelines and new recommendations for allergy and immunology physicians (8-10).

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Although the pandemic process is discussed in many aspects in previous articles, studies investigating its effect on asthma control in children are limited. Therefore, in our study, we aimed to evaluate the effect of the COVID-19 pandemic on follow-up numbers, asthma control, and treatment steps of our pediatric patients with asthma by comparing it with the pre-pandemic period.

MATERIAL and METHODS

In this study, we included patients with asthma between the ages of 6 and 18 who were followed up in a tertiary hospital's pediatric allergy and immunology outpatient clinic between March 11, 2019, and March 11, 2021. The diagnosis and treatment steps of the patients with asthma were evaluated according to the Global Initiative for Asthma guidelines (5). Patients with additional morbidity other than allergic diseases who were followed up in an allergy center other than our clinic and whose data could not be accessed were excluded from the study.

Data collection: With reference to the pandemic start date, March 11, 2020, the 1-year period of the patients Before the Onset of the Pandemic (BOP) and After the Onset of the Pandemic (AOP) were compared.

The results of the treatment step and treatment adherence of their asthma and the Asthma Control Test (ACT) scores in their application deadline to our outpatient clinic during the period AOP were compared with the results of the same season during the year BOP. In addition, the number of applications to the allergy outpatient clinic of the patients within one year of BOP and AOP was recorded.

The most recent skin prick testing (SPT) results were recorded from the patient files. In the SPT in our department includes pollens (grasses, Artemisia vulgaris, Alnus glutinosa, Populus alba, Betula alba, Fagus sylvatica, Parietaria officinalis, Olea europaea); house dust mites (Dermatophagoides pteronyssinus, Dermatophagoides animal farinae); Felis domesticus, Canis familiaris, Blattella germanica (cockroach); molds (Alternaria alternata, Cladosporium herbarum, Aspergillus fumigatus) (Alk-Abello®, Hørsholm, Denmark). SPT was accepted as positive if the induration diameter of any allergen was 3 mm or more compared to the negative control. More than one allergen sensitivity was considered multiple sensitizations.

The cut-off for the total IgE level was determined as 100 IU/mL, and the patients were divided into two groups as normal and high (11). Absolute eosinophil counts (AEC) were recorded, and 450 cells/uL and above were considered eosinophilia (12).

The ACT is a questionnaire, and its Turkish reliability and validity have been confirmed according to age groups (4–11 years and ≥12 years) and the patients' asthma control levels were evaluated using this test (13,14). The patients with an ACT score of 20 or more points were considered to have controlled asthma.During the last three months, treatment adherence was evaluated based on self-reports and pharmacy records. The status of receiving ≥80% of the required controller medication was classified as ‘‘good adherence’’ while receiving <80% was classified as ‘‘poor adherence’’ (15).

The patients' information, such as upper respiratory tract infection (URTI) diagnosis, confirmed COVID-19 status, application to health institutions due to asthma attack, was accessed through the information registered in the hospital information system and/or through the National Health Information Bank (https://enabiz.gov.tr/) system and/or by inquiring over registered phone numbers.

Statistical analysis: Kolmogorov–Smirnov normality test was performed to select the statistical methods to be used. Pearson’s chi-square test or Fisher’s exact test was used to comparing the categorized data. Logistic regression analyses were also conducted to determine the risk factors for asthma control after the onset of the pandemic. The Wilcoxon signed-rank test, McNemar test, and ROC curve analysis were the other analysis used in the study. Statistical analysis of the study was performed using IBM SPSS Statistics for Windows, Version 25, and the statistical significance limit was determined as $p \leq 0.05$.

RESULTS

In our study, 384 patients were evaluated, 249 (64.8%) of whom were male. According to SPT, 273 (71.1%) were sensitized to at least one allergen (Table 1). The most common aeroallergens were pollens (44.3%) (**Figure 1**).

During the period BOP, the annual number of patients who applied to our outpatient clinic was 4 (min-max: 1–14), asthma treatment step was 2 (min-max: 1–5). There were 76 (19.8%) patients who applied to any healthcare facility due to an asthma attack. According to ACT scores, in 225 (58.6%) patients, asthma was under control.

During the period AOP, the annual number of patients who applied to our outpatient clinic was 2 (min-max: 1–8), asthma treatment step was 2 (min-max: AOP 1–5). There were 48 (12.5%) patients who applied to any healthcare facility due to an asthma attack. According to ACT scores, asthma was under control in 246 (64.1%) patients. 102 (26.6%) patients were diagnosed with URTI in a health institution.

When evaluated in general, there was no significant difference between the ACT scores of the patients in both periods. However, the number of applications of our patients to our clinic, their asthma treatment steps, and the number of applications to any healthcare facility due to asthma attack were significantly lower during the period AOP. Their treatment adherence increased significantly (**Table 2**).

According to AOP ACT, no significant differences were noted in asthma control and gender, presence of allergic rhinitis (AR), SPT positivity, URTI diagnosis, the presence of eosinophilia, high total IgE, admission to healthcare facilities due to asthma attack and changes in asthma treatment stepwise ($p = 0.094$, $p = 0.202$, $p = 0.106$, $p = 0.262$, $p = 0.594$, $p = 0.380$, $p = 0.809$, $p = 0.122$ respectively).

It was found that the treatment step did not change or decrease in 115 (83.3%) of 138 patients with uncontrolled asthma during the period AOP. The asthma treatment steps of these patients during the period AOP were lower than BOP ($p = 0.01$).

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During the period AOP, the patients with asthma control were older, had better treatment adherence, and had earlier admission to the outpatient clinic than patients with uncontrolled asthma (**Table 3**).

To ensure asthma control of patients, the cut-off value was determined as 4.5 months with 75.6% sensitivity and 37% specificity (95% CI 66%–76.7%) in the ROC analysis performed for the first outpatient clinic control time during the period AOP. Accordingly, in 232 (60.4%) patients who came for control earlier than 4.5 months during the period AOP, treatment adherence was better, asthma was more controlled, asthma treatment steps were higher, and the number of outpatient clinic applications was higher (p= 0.011, p< 0.001, p= 0.001, p< 0.001, respectively).

Asthma was uncontrolled in 64 (56.6%) of 113 mite-sensitive patients. Treatment adherence was good in 74 (65.4%) patients. Asthma treatment step of the patients increased in 25 (22.1%), decreased or unchanged in 88 (77.9%) patients. Asthma control was lower compared to the period BOP (p= 0.01). However, there was no difference between the periods AOP and BOP in asthma treatment steps and asthma treatment adherence (p= 1.000, p= 0.099, respectively).

The change during the period AOP in asthma control of aeroallergen-sensitive patients who had controlled asthma is summarized in Table 4. Of the 158 (41.1%) patients whose asthma treatment step decreased during the period AOP, 72.2% were receiving step 1 treatment. In these patients, asthma control was increased during the period AOP compared with BOP. (47.4% vs 64.5% p< 0.001).

During the period AOP, the asthma treatment step of 48 patients who were admitted to the health institution due to asthma attack was step 2 (min-max: 1–3). Asthma was uncontrolled in 18 (37.5%) patients. There was no relationship between the application to a health institution due to asthma attack and asthma control, gender, presence of AR, and asthma treatment step change (p= 0.80, p= 0.71, p= 0.90, p= 0.06, respectively).

In patients with aeroallergen sensitivity, there was no significant difference between applications to a healthcare facility due to asthma attack during the periods BOP and AOP (15.8% vs. 12.1%, p= 0.282). However, in patients who were not aeroallergen sensitive, the number of applications to a healthcare institution due to asthma attack during the period BOP was higher than AOP (29.7% vs. 13.5%, p= 0.003).

The median age of the patients with good treatment adherence (median, min-max: 12, 6–18 years) during the period AOP was significantly higher than those with poor adherence (median, min-max: 8, 6–18 years) (p < 0.001).

It was found that advanced age, pollen sensitivity, and good treatment adherence increased the possibility of having controlled asthma (p< 0.01). In mite-sensitive patients, the probability of having uncontrolled asthma increased by 2.747 times (p= 0.013). In addition, the 1-month increase in the first outpatient clinic check-up time AOP increased the risk of uncontrolled asthma 1.4 times (p = 0.001) (**Table 5**).

The SARS-CoV-2 polymerase chain reaction (PCR) test was positive in 6 (1.6%) patients. Mild symptoms developed in all patients, and hospitalization was not required. The asthma treatment step of the patients was 2 (min-max: 2–3). The asthma treatment adherence was good for 4 (66.6%) patients. All patients were male. However, there was no correlation between SARS-CoV-2 PCR positivity and sex (p = 0.06). The mean AEC of these patients was 350 ± 242.89 /mm^3. No significant relationship was found between SARS-CoV-2 PCR positivity and presence of eosinophilia and SPT positivity (p= 0.89, p= 0.80, respectively). Asthma was uncontrolled in 5 patients according to ACT. SARS-CoV-2 PCR positivity was less in patients with controlled asthma (p= 0.024).

Table 1: Demographic, clinical and laboratory findings of the patients by age

		6-11 years	12-18 years	p	Total
Sex (n,%)	**Male**	151 (39.3)	98 (25.5)	-	249 (64.8)
	Female	69 (18)	66 (17.2)		135 (35.2)
Age (years) median (min-max)		8 (6-11)	14 (12-18)	-	11 (6-18)
AR* presence (n. %)		133 (34.6)	104 (27.1)	0.555	237 (61.7)
SPT† positivity (n. %)		147 (38.3)	126 (32.8)	0.032	273 (71.1)
SPT† multi-sensitivity (n. %)		121 (31.6)	95 (24.7)	0.161	216 (56.3)
Total IgE (IU/mL) median (min-max)		157.5 (5.7-3297)	146.5 (1.8-3200)	0.683	153 (1.8-3297)
AEC‡ (cells/uL) median (min-max)		300 (0-2100)	300 (0-2600)	0.620	300 (0-2600)

*AR, allergic rhinitis; † SPT, skin prick test; ‡AEC, absolute eosinophil count

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Table 2: Comparison of clinical findings of before and after the onset of the pandemic

	BOP*	AOP†	p
Number of applications to our outpatient clinic median (min-max)	4 (2-14)	2 (1-8)	<0.001
The first application to our outpatient clinic. AOP (month) median (min-max)	-	4 (2-11)	-
Application deadline to our outpatient clinic, AOP (month) median (min-max)	-	6 (2-12)	-
Distribution of asthma treatment steps (n, %)			
Step 1	92 (24)	159 (41.4)	
Step 2	176 (45.8)	122 (31.8)	
Step 3	101 (26.3)	88 (22.9)	<0.001
Step 4	13 (3.4)	14 (3.6)	
Step 5	2 (0.5)	1 (0.3)	
Good treatment adherence (n. %)	261 (68.0)	301 (78.4)	0.001
Controlled asthma‡ (n, %)	225 (58.6)	246 (64.1)	0.060
Number of patients with asthma attack§ (n, %)	76 (19.8)	48 (12.5)	0.006

BOP, before the onset of the pandemic; †AOP, after the onset of the pandemic; ‡Controlled asthma according to ACT scores; §Number of patients admitted to the healthcare institution due to asthma attack

Table 3: Relationship between asthma control and the other factors

Other factors	Asthma Control*		P
	Good control	Poor control	
Age (years) median (min-max)	12.5 (6-18)	8.5 (6-18)	<0.001
Pollen sensitivity (n, %)			
yes	123 (32)	47 (12.3)	0.003
no	123 (32)	91 (23.7)	
House dust mite sensitivity (n, %)			
yes	49 (12.8)	64 (16.7)	<0.001
no	197 (51.2)	74 (19.3)	
Number of applications median (min-max)	2 (1-4)	1 (1-4)	0.132
First application to our outpatient clinic, AOP† (month) median (min-max)	3 (2-11)	6 (3-8)	<0.001
Application deadline to our outpatient clinic, AOP† (month) median (min-max)	5.5 (2-11)	6.5 (3-12)	0.060
Good treatment adherence (n, %)			
yes	233 (60.7)	68 (17.7)	<0.001
no	13(3.4)	70 (18.2)	

*Asthma control according to the asthma control test; †AOP, after the onset of the pandemic

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Table 4: Change in asthma control of patients after pandemic according to aeroallergen sensitivity

		Pollens‡	House dust mites§	Molds‖	Animal danders¶
Controlled asthma (n, %)	**BOP***	113 (66.5%)	64 (56.6%)	67 (68.4%)	80 (67.8%)
	AOP†	123 (72.4%)	49 (43.4%)	68 (69.4%)	85 (72%)
p		0,123	0,01	1,00	0,44

* Before the onset of the pandemic; †After the onset of the pandemic; ‡For the 170 pollen sensitive patients; §For the 113 patients with house dust mite susceptibility; ‖For the 98 mold susceptible patients; ¶For the 118 patients with animal danders susceptibility

Table 5: Logistic regression analysis of possible risk factors for asthma control after the onset of the pandemic

Risk factors	Odds ratios (95% CI: lower- upper bound)	p
Age	0.705 (0.643-0.774)	<0.001
House dust mite sensitivity	2.747 (1.234-6.115)	0.013
Pollen sensitivity	0.290 (0.135-0.626)	0.002
First application to our outpatient clinic, AOP*	1.415 (1.160-1.727)	0.001
Application deadline to our outpatient clinic, AOP*	0.949 (0.807-1.117)	0.530
Number of applications AOP*	1.214 (0.811-1.816)	0.346

*AOP, after the onset of the pandemic

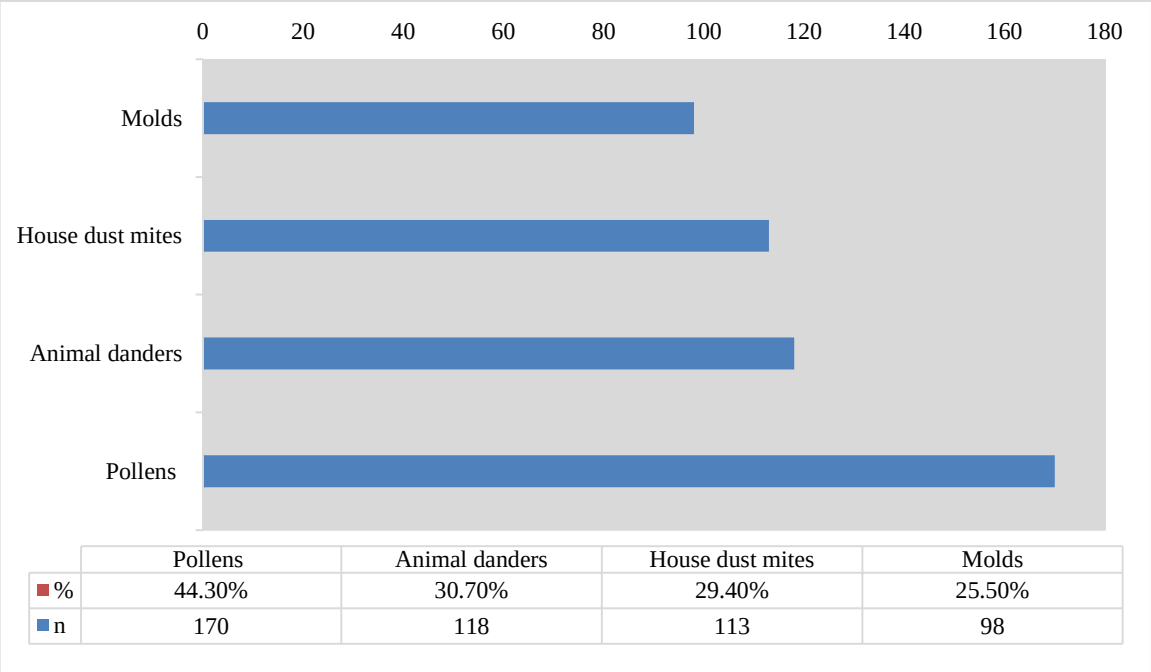

Figure 1: Distribution of aeroallergens according to skin prick test results

DISCUSSION

The COVID-19 pandemic has affected asthma control by causing changes in asthma follow-up and treatment plans due to the measures taken for the pandemic. Because of the important role of viral infections in triggering asthma attacks, it has been thought that patients with asthma may be more susceptible to SARS-CoV-2 infection, and asthma controls may be affected during infection (16,17).

COVID-19 is rare in children (16). In parallel with the prevalence of asthma in pediatric patients with COVID-19, there are few studies evaluating the prevalence of COVID-19 in children with asthma. The prevalence of asthma in 115 children with COVID-19 was 13%, and asthma was reported as the most common comorbidity (18). In a study evaluating 182 pediatric patients with COVID-19 who were hospitalized, asthma was reported in only one patient (19).

Another study reported that uncontrolled and severe asthma might pose a risk of COVID-19 mortality and morbidity (10).

In our past study conducted on the pediatric population, 45 (18.9%) of 237 patients were positive for SARS-CoV-2 PCR (20). In our current study, 6 (1.6%) of 384 children with asthma were found to be PCR positive, and asthma was uncontrolled in most of the patients. When comparing both of our studies, we found that the prevalence of COVID-19 in children with asthma was much lower than in the general pediatric population. SARS-CoV-2 PCR sampling was performed in both of our studies when patients were contacted or symptomatic. The lower SARS-CoV-2 PCR positivity in pediatric asthmatic patients may have a protective effect on families' stricter implementation of preventive measures and treatments given for asthma.

Some researchers have argued that eosinophilia in patients with asthma may be protective against COVID-19 infection and may lead to a mild course of the disease (21, 22). In one study, no significant effect of the presence of atopy on clinical symptoms and complications in COVID-19 was found (19). We did not find a relationship between SARS-CoV-2 PCR positivity and the presence of eosinophilia or atopy in our patients. None of our asthmatic COVID-19 patients had signs of severe illness.

During the pandemic, some measures have been taken, such as using masks, staying at home, and decreasing school days. As a result, it has been reported that risk factors for asthma attacks, such as viral infections, air pollution, and outdoor allergens have been avoided. Thus asthma control has improved (23). In our study, no significant increase was found in asthma control during the pandemic. We thought that patients not being able to manage their asthma treatment steps well, their poor treatment adherence, and their sensitivity to household allergens might be effective in this situation.

The AOP period treatment adherence of our patients was approximately 80%, it was increased compared to the BOP period, and asthma control was better in patients with good treatment adherence. Another factor that we thought could be effective was whether stepwise asthma treatment changes were made appropriately. Approximately 75% of our patients whose AOP step treatment decreased were receiving the first step asthma treatment, and their asthma controls were better than BOP. This made us think that our patients generally managed the decrease in the treatment steps correctly. However, the expected increase in asthma treatment steps was not found in patients with uncontrolled asthma and mite-sensitive patients with reduced asthma control. This suggests that according to their own perceptions, patients reduce their treatment when symptoms are mild but cannot increase treatment when symptoms increase.

In current guidelines, it has been recommended to increase telemedicine applications, reduce allergy clinic applications, continue asthma medications, and use written asthma action plans to increase treatment adherence and reduce contact (5, 24).

Our clinic is a tertiary hospital, and the rate of use of telemedicine applications in hospitals with similar conditions has been reported to be 13% (25). However, we do not know how many patients in our study could benefit from telemedicine services. Perhaps in line with the recommendations, or perhaps due to the fear of COVID-19, the outpatient clinic applications of the patients decreased significantly. We found that delaying AOP control is a risk factor for uncontrolled asthma. Although asthma control was worse in patients who applied late to the first outpatient clinic control during the pandemic, their asthma treatment steps were lower. This suggests that some patients may not have been managed the treatment properly on their own without medical assistance.

Studies during the pandemic reported that children with asthma were not adversely affected by the virus, and there was a 76% decrease in emergency room visits (26).

In our study, in general, applications to the health institution due to asthma attack decreased during the pandemic. This was evident in patients without aeroallergen sensitivity. Due to pandemic measures, the decrease in viral infections, which are the most important risk factors for asthma attack in non-atopic patients, may affect this situation.

The effects of allergens on asthma control and attack development have been discussed in studies. It has been reported in the studies conducted during the BOP period that measures to reduce mite exposure are insufficient in providing asthma control (27). During the pandemic, it has been reported that restrictions cause patients to be exposed to more domestic allergens, such as molds and mites, which may aggravate their asthma (28). A recent study from our country reported that despite domestic allergens, asthma control was better than before the pandemic (29). In our study, mite sensitivity was present in approximately 1/3 of our patients, and we found that asthma control of these patients decreased after the pandemic. Although there was no significant change in stepwise asthma treatments and treatment adherence was good, the decrease in ACT scores was significant. The presence of house dust mite sensitivity was the most important risk factor for uncontrolled asthma in our patients.

Our data consist of only a cluster of patients whom we follow. Therefore, it may fall short of demonstrating the ultimate effects of universal changes on childhood asthma. In addition, another limitation was that we evaluated the asthma controls of the patients only based on ACT scores and could not benefit from spirometric measurements or other parameters indicating inflammation.

CONCLUSION

As a result, this study is one of the rare studies evaluating the effects of the COVID-19 pandemic on the control, stepwise management, and exacerbation of asthma in children with asthma. Thanks to the measures taken during the pandemic, it is thought that the effect of viral infections on asthma attacks has lost its importance. Considering that restrictions may continue in this period, it would be beneficial to take domestic precautions in patients susceptible to house dust mites, which are found to pose a risk of uncontrolled asthma. Particular care should be taken to ensure adherence of young patients with treatment and change the treatment steps of uncontrolled asthma patients. Although asthma guidelines recommend minimizing face-to-face meetings, we think that it would be appropriate to evaluate more frequently uncontrolled asthma patients who have not been able to or who have been late to create asthma treatment plans during the pandemic process.

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Ethical approval: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by Local Ethical Committee. All procedures performed in studies with human participants met the ethical standards of the Institutional Research Commission and the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards. Ethics committee approval was received for this study from the Local Ethics Committee of Dokuz Eylül University, School of Medicine (Approval number: 2021/14-34)

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