# Evaluation of the Pandemic Normalization Process in Pediatric Surgery Operations: Tertiary Center Experience

Pediatrik Cerrahi Operasyonlarında Pandemik Normalleşme Sürecinin Değerlendirilmesi: Üçüncü Basamak Merkez Deneyimi

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#### Abstract

**Background:** The aim of this study was to evaluate pandemic normalization process in pediatric surgery operations.

**Materials and Methods:** This was a retrospective cross-sectional and comparative study conducted at a tertiary center. In our study, 917 individuals were included. It was defined as the period between June 2020, when normalization was announced after the first wave of the COVID-19 pandemic in our country, and November 2020, when the second wave of measures began [Group 1 (n=393,42.7%)]. One year later was defined as the second period [Group 2 (n=525, 57.3%)], corresponding to the same time period (June 2021-November 2021).

**Results:** The median age of Group 1 was 5 years and Group 2 was 6 years (p <0.001). Emergency surgery was more common in Group 2 (31.1% vs 35.4%). General anesthesia is the most commonly perfomed anesthesia method in both groups (98.5% vs 97.3%). Abdominal operations were the most common in both groups (48% vs 49%). While the rate of laparoscopic surgery was 62% in Group 1, it was 62.1% in Group 2. A statistically significant difference was detected in preoperative COVID-19 polymerase chain reaction (PCR) test examination Group 2 and postoperative COVID-19 PCR test examination Group 1. Lymphocyte and C-reactive protein (CRP) serum markers were similar between groups. There was no difference between the need for intensive care unit/postanesthesia care unit and mortality rates.

**Conclusions:** Although the number of pediatric surgical operations decreased during the normalization period, a successful process was managed in terms of the quality and results of the cases.

Keywords: COVID-19, Pandemic normalization process, Pediatric surgery

#### Öz

Amaç: Bu çalışmanın amacı pediatrik cerrahi operasyonlarında pandemi normalizasyon sürecini değerlendirmektir.ediatrik cerrahi operasyonlarında pandemik normalleşme sürecinin değerlendirilmesi: Üçüncü basamak merkez deneyimi

**Materyal ve Metod:** Bu, üçüncü basamak bir merkezde yürütülen retrospektif kesitsel ve karşılaştırmalı çalışmadır. Çalışmamıza 917 kişi dahil edildi. Ülkemizde COVID-19 salgınının ilk dalgasının ardından normalleşmenin açıklandığı Haziran 2020 ile ikinci önlem dalgasının başladığı Kasım 2020 arasındaki dönem olarak tanımlandı [Grup 1 (n= 393,42.7%)]. Bir yıl sonra, aynı zaman dilimine (Haziran 2021-Kasım 2021) karşılık gelen ikinci dönem [Grup 2 (n=525, %57,3)] olarak tanımlandı.

**Bulgular:** Grup 1'in ortanca yaşı 5, Grup 2'nin ortanca yaşı 6 idi (p<0,001). Acil ameliyatlar Grup 2'de daha sık görüldü (%31,1'e karşı %35,4). Genel anestezi her iki grupta da en sık uygulanan anestezi yöntemidir (%98,5'e karşı %97,3). Her iki grupta da en sık batın ameliyatları yapıldı (%48'e karşı %49). Laparoskopik cerrahi uygulanma oranı Grup 1'de %62 iken Grup 2'de %62,1 oldu. Ameliyat öncesi COVID-19 polimeraz zincir reaksiyonu (PCR) test incelemesi Grup 2'de ve ameliyat sonrası COVID-19 PCR test incelemesi Grup 1'de istatistiksel olarak anlamlı fark tespit edildi. Lenfosit ve C-reaktif protein (CRP) serum belirteçleri gruplar arasında benzerdi. Yoğun bakım ünitesi/anestezi sonrası bakım ünitesi ihtiyacı ile ölüm oranları arasında fark yoktu.

**Sonuç:** Normalleşme sürecinde pediatrik cerrahi operasyonlarının sayısı azalsa da vakaların kalitesi ve sonuçları açısından başarılı bir süreç yönetildi.

Anahtar Kelimeler: COVID-19, Pandemi normalizasyon süreci, Pediatrik cerrahi

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## Introduction

Coronaviruses, from the Coronaviridae family, are ribonucleic acid (RNA) viruses. The first descriptions of coronaviruses date back to the 1960s. Different variants are known to cause colds in humans. It was determined that a new type of coronavirus caused disease in humans on 31/12/2019 in Wuhan, China(1). In the following period, the name of the disease was defined as COVID-19 by the World Health Organization (WHO).

Although the symptoms of the disease are similar in children and adults, the frequency and severity of symptoms differs in children (2). A small proportion of children with COVID-19 required hospitalization (2). According to data from the Center for Disease Control and Prevention (CDC), the hospitalization rate in children under the age of 20 was reported to vary between 2.5% and 4.1% until May 2020 (3). Additionally, that report noted that among children hospitalized with COVID-19 until July 2020, around 33% needed care in an intensive care unit, and 6% needed invasive ventilation therapy (3).

The Coronavirus disease-2019 (COVID-19) outbreak was declared an "International Public Health Emergency" by the WHO on 30/01/2020, and the COVID-19 outbreak was declared a global pandemi on 11/03/2020. The Ministry of Health of the Republic of Turkey announced the measures to be taken regarding the COVID-19 epidemic on 17/03/2020. These restrictions were aimed to minimize the density in healthcare institutions and the burden on healthcare professionals. The aim of the restrictions was to use healthcare resources efficiently and rationally in extraordinary conditions caused by the pandemic and to minimize the possibility of contamination among patients and healthcare professionals. It has been pointed out that elective operations should be postponed and special attention should be paid to indication-level compatibility in the use of intensive care units (4). After the coronavirus firstiwave in our country continued from 11/03/2020 until 01/06/2020, the first normalization attempts started as of this date. For this purpose, according to declaration published by the Ministry of Health, the importance of continuity of health services other than COVID-19 was emphasized. In terms of surgical interventions, it was stated that oncological surgeries, interventions for limb loss, procedures to increase or preserve quality of life or function, and pain treatments should be planned. Additionally, it has been recommended that elective surgical operations be performed in stages. In our country, there is no published data evaluating COVID-19 and anesthesiological characteristics of pediatric surgery cases during the normalization process.

Pediatric surgical operations between "June 1, 2020, when the normalization process started, and November 9, 2020, when the second wave measures started", corresponding to the same time period one year later (June 1, 2021-November 9, 2021), were taken as basis in our study. The aim of this research is to make a detailed comparison of two different periods in terms of COVID-19, anesthesia and surgery characteristics.

## **Materials and Methods**

This was a retrospective cross-sectional and comparative research conducted at a tertiary center. The institutional ethical approval was provided (File number:6824-GOA, Registration number: 2021/36-03). Patients or their first degree relatives had signed informed consent forms, permitting their medical data to be utilized for scientific research, provided that their personal identifiers remain confidential. The research was carried out in compliance with the Helsinki Declaration Principles. In our study, 917 patients were included. It was defined as the period between June 2020, when normalization was announced after the firstiwave of the COVID-19 in our country, and November 2020, when the second wave of measures began [Group 1 (n=393,42.7%)]. One year later was defined as the second period [Group 2 (n=525, 57.3%)], corresponding to the same time period (June 2021-November 2021). Age, gender, American Society of Anesthesiologists (ASA) classification, comorbidities, clinical symptoms, fever, laboratory values, COVID-19 polymerase chain reaction (PCR) test results, radiological thorax imaging findings, type of surgery, type of anesthesia method, need for intensive care unit/postanesthesia care unit, duration of hospitalization and postoperative mortality data were obtained from hospital records. It was determined that preoperative imaging evaluation, laboratory tests and clinical symptoms' evaluations were made within 24 hours before the operation, and postoperative imaging evaluation, laboratory tests and clinical symptoms' evaluations were made within 24 hours after the operation.

Analyzes were performed with SPSS version 26.0. Normality analysis was conducted using the Kolmogorov-Smirnov test. Variables that were not normally distributed were analyzed using the Mann-Whitney U test. The results for these variables were presented asimedian (minimum-maximum) values for each group. The analysis of categorical data utilized the Chi-square test and Fisher's exact test. These were presented as counts and percentages (%).The results were 95% confidence interval (CI). The p value taken statistically significant was <0.05. The minimum number of cases required to be included in the study was determined to be 785 in order to detect a statistically significant relationship between variables with 80% power, 0.05 margin of error and 0.1 effect size. Calculations were made using the PASS program.

#### Results

Demographic characteristics of theigroups were given in Tablei1. The medianiage of Group 1 was 5 years and Group 2 was 6 years. There existed a difference between the groups (p <0.001). While the rate of patients aged 0-2 years was 38.8% in Group 1, it was 27% in Group 2.

This difference was significant (p<0.001). The other subgroup of ages was higher in Group 2. However, there was no statistical difference. In terms of gender, the groups were similar (p=0.09). Existence of comorbidity was found to be 27.2% in Group 2 and 21.8% in Group 1 (p=0.06).

**Table 1.** Demographic characteristics of the groups

Variables	Group 1 (n=392, 42.7%)	Group 2 (n=525, 57.3%)	p value*	
Age (years)	5 (0-18)	6 (0-18)	0.001	
Subgroups of age (n,%)			< 0.01	
0-2 years	152 (38.8%)	142 (27%)	< 0.001	
3-6 years	77 (19.6%)	122 (23.2%)	0.1	
7-11 years	78 (19.9%)	129 (24.6%)	0.09	
12-18 years	85 (21.7%)	132 (25.1%)	0.2	
Gender (n,%)				
Female	139 (35.5%)	159 (30.3%)	0.09	
Male	253 (64.5%)	366 (69.7%)		
Existence of comorbidity (n,%)	86 (21.8%)	143 (27.2%)		
Respiratory system diseases	3 (0.8%)	15 (2.9%)	0.06	
Genitourinary diseases	16 (4.1%)	20 (3.8%)		
Musculoskeletal diseases	3 (0.8%)	9 (1.7%)		
Neurological diseases	18 (4.6%)	27 (5.1%)		
Endocrine diseases	7 (1.8%)	7 (1.3%)		
Hematological diseases	17 (4.3%)	18 (3.4%)		
Cardiovascular system diseases	8 (2%)	10 (1.9%)		
Gastrointestinal system and metabolism diseases	10 (2.6%)	24 (4.6%)		
Rheumatological diseases	1 (0.3%)	1 (0.2%)		
Psychiatric diseases	3 (0.8%)	8 (1.5%)		
Genetic diseases	0 (0%)	4 (0.8%)		

\*Mann-Whitney U test was used for numerical data and Chi-square test was used for categorical data.

The surgical evaluation of groups was shown in Table 2. ASA I risk score was the subgroup with the highest frequency in both groups (76.8% vs 73.1%). On the other hand, ASA V risk score was the subgroup with the lowest rate in both groups (0.3% vs 0%). Emergency surgery was more common in Group 2 (31.1% vs 35.4%). But the groups were similar (p=0.1). General anesthesia is the most commonly perfomed anesthesia method in both groups (98.5% vs 97.3%). The groups did not differ in terms of anesthesia type (p=0.2). Regional anesthesia was not performed in any of the cases. Since regional anesthesia is not performed in any case, the type of anesthesia is not important. Abdominal operations were the most common in both groups (48% vs

49%). This group was followed by genital operations (18.5% vs 23.8%). The groups were similar regarding the type of surgery (p=0.1). While the rate of laparoscopic surgery was 62% in Group 1, it was 62.1% in Group 2 (p=0.9). When 917 patients were analyzed, it was determined that 23% (211/917) had an emergency appendectomy operation, while 18.1% (166/917) had a circumcision operation. In Group 1, the most common operation was emergency appendectomy in 19.2% (77/392), followed by circumcision in 13.5% (53/392). In Group 2, the most common operation was emergency appendectomy in 25.5% (134/525), followed by circumcision in 21.5% (113/525).

Variables	Group 1 (n=392, 42.7%)	Group 2 (n=525, 57.3%)	p value*
ASA risk score (n,%)			
I	301 (76.8%)	384 (73.1%)	0.3
II	70 (17.9%)	119 (22.7%)	
III	15 (3.8%)	16 (3%)	
IV	15 (3.8%)	6 (1.1%)	
V	1 (0.3%)	0 (0%)	
Emergency surgery (n,%)	122 (31.1%)	186 (35.4%)	0.1
Type of anesthesia (n,%)			
General	386 (98.5%)	511 (97.3%)	0.2
Sedation	6 (1.5%)	14 (2.7%)	
Type of surgery (n,%)			
Abdominal	188 (48%)	257 (49%)	
Genital	73 (18.6%)	125 (23.8%)	
Urological	44 (11.2%)	37 (7%)	
Port interventions	26 (6.6%)	34 (6.5%)	
Bronchoscopy	17 (4.3%)	14 /2.7%)	0.1
Endoscopy	8 (2%)	16 (3%)	
Anorectal	8 (2%)	12 (2.3%)	
Thoracic	8 (2%)	9 (1.7%)	
Head-neck	9 (2.3%)	5 (1%)	
Others	11 (2.8%)	26 (3%)	
Laparoscopic surgery (n,%)	243 (62%)	326 (62.1%)	0.9

ASA: American Society of Anesthesiologists

\*Mann-Whitney U test was used for numerical data and Chi-square test was used for categorical data.

Clinical, laboratory and imaging features of theigroups were compared in Table 3. Theimedian preoperative fever was 36.6°C (36°C-37.6°C) in Group 1 and 36.7°C (36°C-39°C) in Group 2. This difference was statistically significant (p<0.001). But, there was no difference among the groups in the preoperative fever subgroup (>37.2°C) evaluation (44% vs 69%, p=0.3). Preoperative cough symptom was statistically significantly higher in Group 1 (7.6% vs 3.6%, p=0.01). Preoperative radiological thorax findings was 16.5% in Group 1 and 12.3% in Group 2 (p=0.07). Existence of pathological findings in preoperative radiological thorax evaluation was higher in Groupi2 (3% vs 1.5%, p=0.5). Preoperative COVID-19 PCR test examination was lower in Group 1 (89.5% vs 99.8%, p<0.001). Preoperative positive COVID-19 PCR test result was similar between groups (0.5% vs 0.3%, p=0.6). The median postoperative fever was 36.6°C (36.1°C-37.6°C) in Group 1 and 36.7°C (36.2°C-38.5°C) in Group 2. This difference was statistically significant (p=0.02). There was no difference among the groups in the postoperative fever subgroup (>37.2°C) evaluation (14% vs 24%, p=0.4). Postoperative radiological thorax evaluation was 16.5% in Group 1 and 12.3% in Group 2 (p=0.07). Existence of pathological findings in postoperative radiological thorax evaluation wasihigher in Group 2 (3% vs 4.6%, p=0.6). Postoperative COVID-19 PCR test examination wasilower in Group 2 (9.9% vs 3.4%, p<0.001). Postoperative positive COVID-19 PCR test resultiwas not different between groups (5% vs 5.5%, p=0.9). Preoperative white bloodicell (WBC), lymphocyte and c-reactive protein (CRP) parameters were similar between groups (9.4 vs 9.2, p=0.9; 3 vs 2.8, p=0.3; 3.6 vs 4, p=0.5, respectively). There existed a statistically significant difference in postoperative WBC Group 2 (10.1 vs 11, p=0.03). Postoperative lymphocyte and CRP parameters were similar among groups (1.6 vs 1.3, p=0.07; 10.2 vs 27, p=0.06, respectively).

The postoperative period of groups was evaluated in Table 4. More intensive care unit/post anesthesia care unit needs were detected in Groupi1 (6.4% vs 5%, p=0.3). Although the median duration of hospitalization was 2 days in both groups, there existed a significant difference in Group 2 (p<0.001). Three patients (0.6%) in Group 2 and one patient (0.3%) in Group 1 died. The groups were similar (p=0.4).

Table 3. The comparison of clinical, laboratory and imaging features of the group

Variables	Group 1 (n=392, 42.7%)	Group 2 (n=525, 57.3%)	p value*
Preoperative fever (°C)	36.6°C (36-37.6)	36.7°C (36-39)	< 0.001
Preoperative fever subgroup (>37.2°C) (n,%)	44 (11.2%)	69 (13.1%)	0.3
Preoperative cough symptom (n,%)	30 (7.6%)	19 (3.6%)	0.01
Preoperative radiological thorax evaluation (n,%)	65 (16.5%)	65 (12.3%)	0.07
Existence of pathological findings in preoperative radiological thorax evaluation (n,%)	1/65 (1.5%)	2/65 (3%)	0.5
Preoperative COVID-19 PCR test examination (n,%)	351 (89.5%)	524 (99.8%)	<0.001
Preoperative positive COVID-19 PCR test result (n,%)	2/351 (0.5%)	2/524 (0.3%)	0.6
Postoperative fever (°C)	36.6°C (36.1-37.6)	36.7°C (36.2-38.5)	0.02
Postoperative fever subgroup (>37.2°C) (n,%)	14 (3.5%)	24 (4.5%)	0.4
Postoperative radiological thorax evaluation (n,%)	65 (16.5%)	65 (12.3%)	0.07
Existence of pathological findings in postoperative radiological thorax evaluation (n,%)	2/65 (3%)	3/65 (4.6%)	0.6
Postoperative COVID-19 PCR test examination (n,%)	39 (9.9%)	18 (3.4%)	<0.001
Postoperative positive COVID-19 PCR test result (n,%)	2/39 (5%)	1/18 (5.5%)	0.9
Preoperative WBC (10X3/u/L) (n,%)	9.4 (0.2-86)	9.2 (0.3-91)	0.9
Preoperative lymphocyte (10X3/u/L) (n,%)	3 (0.1-28.4)	2.8 (0.1-45)	0.3
Preoperative CRP (mg/L) (n,%)	3.6 (0.2-369)	4 (0.1-576)	0.5
Postoperative WBC (10X3/u/L) (n,%)	10.1 (0.1-25.1)	11 (0.4-59.7)	0.03
Postoperative lymphocyte (10X3/u/L) (n,%)	1.6 (0.1-10.4)	1.3 (0-13.8)	0.07
Postoperative CRP (mg/L) (n,%)	10.2 (0.2-290)	27 (0.2-291)	0.06

COVID-19: Coronavirus disease-19; PCR: Polymerase chain reaction; WBC: White blood cell; CRP: C-reactive protein

\*Mann-Whitney U test was used for numerical data and Chi-square test was used for categorical data.

Variables	Group 1 (n=392, 42.7%)	Group 2 (n=525, 57.3%)	p value*
Need for intensive care unit/post anesthesia care unit (n,%)	25 (6.4%)	26 (5%)	0.3
Duration of hospitalization (days)	2 (1-40)	2 (1-132)	< 0.001
Mortality (n,%)	1 (0.3%)	3 (0.6%)	0.4

\*Mann-Whitney U test was used for numerical data and Chi-square test was used for categorical data.

# Discussion

In terms of gender, the groups were similar. The median age of Group 1 was found to be lower than Group 2. On the other hand, in the subgroup analysis, a higher proportion of patients in the 0-2 age subgroup was reported during the normalization period. On the contrary, older age of subgroups were at higher rates in the Group 2. This difference was statistically significant. Primarily, the fact that surgical interventions that could not be postponed during the normalization period were performed in our hospital revealed this difference. During the pandemic period, there was concern about the transmission of the disease in society. Secondly, we think that during the normalization period, younger cases were admitted to the hospital by their families. In this regard, Park P. et al. presented reports consistent with the results of our study (5).

Studies comparing pediatric surgeries with the pandemic period and after have concluded that fewer surgeries were performed during the pandemic period (6,7). In the pandemic normalization period, 31.1% of the cases were operated on emergently, and in the second period, 35.4% of the cases were operated on emergently. It can be expected that more emergency surgeries will be received at the normalization period. However, we predicted that there would be no difference between the Group 1 and Group 2, thanks to the fact that the operations of emergency cases were not ceased and did not accumulate during the pandemic period.

Considering the type of anesthesia, general anesthesia was predominantly preferred, followed by sedation anesthesia. There was no case of surgery under regional anesthesia. No significant difference was detected between anesthesia performance in both periods. In the surgical initiation guides prepared for adult cases, interventions under regional anesthesia generally come to the fore (8). In children, regional anesthesia is mostly aimed at relieving postoperative pain, and since our case population generally consists of procedures requiring general anesthesia. The general anesthesia has been the predominant practice.

Many studies in the literature have shown that laparoscopic surgery is less traumatic and causes less inflammation peroperatively than open technique surgery (9,10). It is known to shorten the hospitalization period in the postoperative period and provide a faster return to daily activities. A shorter hospital stay means less time for companions to stay in the hospital. Moreover, in a special situation such as a pandemic, the personnel and equipment requirements for laparoscopy are higher than for open surgery, and there have been concerns that the pneumoperitoneum created increases aerosol contamination (11). Laparoscopic surgeries can be performed by using special technical measures that include preventing aerosol dispersion, such as the use of filters/suction or adapted systems. Monopolar and bipolar energy use should be kept to a minimum to prevent excessive surgical smoke production and particle aerosolization (11). In our study, no difference was observed between periods. The high level of laparoscopy experience of the surgical team and careful implementation of precautions against aerosol exposure prevented differences between periods.

When postoperative PCR test data was examined; during the pandemic normalization period, 2 out of 39 cases that underwent post-operative PCR testing were found to be positive. When the second period was examined, postoperative PCR test was performed to 18 cases and the postoperative PCR test of 1 case was found positive. In both groups, the cases with PCR positivity in the postoperative period are the same as the cases with PCR positivity in the preoperative period. No new cases with PCR positivity were detected in the postoperative period in either Group 1 or Group 2. In the systematic review by Prasad et al., it was reported that even with preoperative COVID-19 screening, the risk of complications continued in cases with positive COVID infection within one month after electiveisurgery (12). Therefore, there is a need for more rigorous preoperative screening and vigilant postoperative monitoring in these individuals. The stress induced by surgery might theoretically render individuals with weakened immune systems more susceptible to contracting COVID-19 infection either in the hospital or within the community during the immediate postoperative period (12). However, there was no increase in test positivity in our study cohort. This situation can be interpreted as the effectiveness of inspection, sanitation and isolation mechanisms. A statistically significant difference was detected in preoperative COVID-19 PCR test examination Group 2 and postoperative COVID-19 PCR test examination Group 1. We think that the reason why the preoperative COVID-19 PCR test examination rate is higher in Group 2 is the effect of the anxiety caused by coronavirus on healthcare professionals and patients. On the other hand, we hypothesize that the lower rate of postoperative COVID-19 PCR test examination in Group 2 is due to the approach of clinical finding follow-up instead of test-based applications.

According to Jackson et al.'s study, fever (58%) and cough (50%) were the two most often reported symptoms in pediatric COVID-19 patients who were exhibiting symptoms (13). In Group 2, preoperative and postoperative fever were statistically significantly different. However, fever rates above >37.2°C did not differ between groups in both the preoperative and postoperative periods. Additionally, the rate of cough symptoms in Group 1 was more than twice that of Group 2. Radiological thorax evaluations (direct thorax radiography or thorax computed tomography) performed for various indications before and after surgery were 16.5% in Group 1 and 12.3% in Group 2 for both periods. Pathological radiological findings due to COVID-19 in the preoperative and postoperative periods were found to be similar between the groups.

Since the course of COVID-19 disease is atypical in the pediatric population and PCR results can be misleading, lymphopenia, leukopenia and high CRP levels have become important in the diagnosis of the disease (14–16). In this current research, there existed no difference among the groups regarding preoperative WBC, lymphocyte, and CRP. Similarly, postoperative lymphocyte and CRP were similar between groups. Postoperative WBC was statistically significantly different in Group 2, but this could not be primarily attributed to coronavirus infection.

More intensive care unit/postanesthesia care unit needs were detected in Group 1. Although in both groups the median duration of hospitalization was 2 days, there existed a significant difference in Group 2. Three patients (0.6%) in Group 2 and one patient (0.3%) in Group 1 died. We think that these differences in our study are related to the heterogeneous patient population rather than COVID-19.

The retrospective design, heterogeneous population and heterogeneous surgery typeof the study cohort were the limitations of our study. On the other hand, the large number of our study cohort, the lack of studies evaluating the normalization process in the literature, and the fact that it includes experiences in tertiary care center were the strengths of our study.

In conclusion, despite the decrease in the number of pediatric surgical operations during the normalization period, a successful process was observed in the tertiary center. It is very important to share our experiences against this pandemic and future pandemics that threaten human life.

**Ethical Approval:** All procedures performed were in accordance with the ethical standarts of the institutional committee (File number:6824-GOA, Registration number: 2021/36-03) and with the Helsinki declaration and its later amendments or comparable ethical standards.

#### Author Contributions:

Concept: B.M.Y., V.H., Ç.G.O. Literature Review: B.M.Y., D.G.İ. Design : B.M.Y. Data acquisition: B.M.Y., O.Y. Analysis and interpretation: B.M.Y., V.H., İ.E.İ. Writing manuscript: B.M.Y., O.Y. Critical revision of manuscript: Ç.G.O. **Conflict of Interest:** The authors have no conflicts of interest to declare. **Financial Disclosure:** Authors declared no financial support.

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