



# An Analysis of Emergency Dental Care for Primary and Permanent Teeth in Pediatric Population

## *Pediyatrik Popülasyonda Süt ve Daimi Dişler için Acil Diş Bakımının Analizi*

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### ABSTRACT

**Objective:** Teeth that priorly and urgently require emergency dental care (SOS teeth) are evaluated through clinical and radiographic exams and primarily treated with root canal therapy and/or extraction in pediatric patients. It is important both to determine the prevalence and distribution of SOS teeth in children with primary and permanent dentition and to develop an appropriate treatment plan. This study assesses the prevalence of SOS teeth among the pediatric population based on gender, as well as types of teeth and their locations in the jaw.

**Method:** A total of 1391 patients without systemic diseases at the end of primary (ages 5-6; n=215) and the beginning of permanent dentition (ages 11-12; n=169) who visited the Pediatric Dentistry Clinic of Dokuz Eylül University, between November 1, 2022, and April 30, 2023, were included in the study. To identify SOS teeth, the Caries Assessment Spectrum and Treatment code 6 were used.

**Results:** SOS teeth were found in 62.3% of 5-6, and 19.5% of 11-12 year-old children. While no statistically significant difference was observed between gender and the presence of SOS teeth in terms of primary teeth, a significant difference was found regarding permanent teeth ( $p<0.017$ ). SOS teeth appeared statistically significantly more often in the mandible than in the maxilla in terms of both primary and permanent molar teeth, ( $p=0.003$ ,  $p=0.001$ , respectively).

**Conclusion:** SOS teeth were detected at a high rate in permanent and primary molar teeth. Therefore, the detection of SOS teeth and treatment planning should be included in the agenda of dentists.

**Keywords:** Emergency dental care, primary teeth, permanent teeth, pediatric population

### ÖZ

**Amaç:** Acil diş bakımı (SOS dişleri), klinik ve radyografik olarak değerlendirilerek, çocuk hastalarda öncelikli olarak kök kanal tedavisi ve/veya çekim ile tedavi edilmesi düşünülen dişlerdir. Çocuklarda süt ve daimi dentisyon döneminde SOS dişlerinin yaygınlığını ve dağılımını belirlemek ve buna göre bir tedavi planı oluşturmak önemlidir. Bu çalışmada, çocuklarda SOS dişlerinin yaygınlığı cinsiyete, dişlere ve çenelerdeki lokalizasyonlarına göre değerlendirildi.

**Yöntem:** Dokuz Eylül Üniversitesi Çocuk Diş Hekimliği Kliniğine 1 Kasım 2022-30 Nisan 2023 tarihleri arasında başvuran, süt dişlenme döneminin sonunda (5-6 yaş) ve daimi dişlenme döneminin başında (11-12 yaş) olan ve sistemik hastalığı olmayan çocuklar çalışmaya dahil edildi. Bu dönemde kliniğimize gelen 1391 hastanın 215'i 5-6 yaşında, 169'u ise 11-12 yaşındaydı. SOS dişlerini tespit etmek için Çürük Değerlendirme Spektrumu ve Tedavi 6 kodu kullanıldı.

**Bulgular:** Beş ila altı yaş grubunda %62,3 oranında ve 11-12 yaş grubunda %19,5 oranında SOS dişleri tespit edildi. Cinsiyet ve süt dişlerinde SOS dişlerinin varlığı arasında istatistiksel olarak anlamlı bir fark bulunmazken, daimi dişlerde cinsiyetle SOS dişlerinin varlığı arasında fark tespit edildi ( $p<0.017$ ). Süt ve daimi azı dişlerinde SOS dişleri maksilladan daha fazla mandibulada görüldü ve fark istatistiksel olarak anlamlıydı (sırasıyla  $p<0.003$ ,  $p<0.001$ ).

**Sonuç:** Daimi ve süt azı dişlerinde SOS dişleri yüksek oranda tespit edildi. Bu nedenle SOS dişlerinin tespiti ve tedavi planlaması diş hekiminin tedavi planlamasında önemli bir yer almalıdır.

**Anahtar kelimeler:** Acil bakım gerektiren dişler, süt dişleri, daimi dişler, çocuk

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## INTRODUCTION

Dental caries in both primary and permanent teeth is a rising public health issue, except a few countries<sup>(1-4)</sup>. Early childhood caries, prevalent in primary teeth, can also affect permanent dentition<sup>(2)</sup>. While treating initial caries lesions in primary and permanent teeth is relatively simple, the planning, cost, and duration of treating deep dental caries involving the pulp are quite complex and lengthy<sup>(1-4)</sup>.

Deep dental caries involving the pulp in primary teeth negatively impacts the child's nutrition, development, and jaw structure<sup>(1,2)</sup>. Similarly, deep dental caries affecting the pulp of a permanent teeth at an early age leads to short-, medium-, and long-term problems with occlusion, chewing, and bone development, as well as economic and social difficulties<sup>(1)</sup>.

For many years, the most commonly used index for the detection of dental caries has been the decayed, missing, filled teeth (DMF-T) index, which represents the total number of decayed, missing, and filled teeth<sup>(5,6)</sup>. However, the DMF-T index does not provide sufficient information about clinical outcomes of dental caries, such as pulp involvement and tooth abscess<sup>(7)</sup>.

To identify the stage of dental caries, the Caries Assessment Spectrum and Treatment (CAST) index is utilized (Table 1)<sup>(7)</sup>. The CAST index covers all stages of caries, from sound tooth surface to enamel and dentin caries lesions, pulp and periapical inflammation, and tooth loss due to caries<sup>(7)</sup>.

This index can be applied during oral examinations to prioritize a patient's dental treatment needs and enable oral health authorities to evaluate emergency dental care. Teeth classified under CAST 6 code which identifies deep dental cavitation and pulp involvement require urgent treatment and, are considered priority teeth for treatment<sup>(8)</sup>. In recent years, teeth considered a priority for treatment and/or requiring urgent care in the literature have been defined as SOS teeth<sup>(8,9)</sup>. Unlike the CAST Index, "SOS teeth" are assessed clinically and radiographically to identify teeth that may need root canal treatment or extraction. The difference between diagnoses made based on CAST indexes, and presence of SOS teeth is revealed thorough evaluation of teeth during an oral exam, where teeth are dried with air and examined alongside clinical and radiographic findings<sup>(8-10)</sup>.

Management of such teeth is expected to produce favorable outcomes in children, including better sleep patterns, balanced nutrition, improved academic performance, and an overall higher quality of life<sup>(1)</sup>. Additionally, identifying SOS teeth during oral exams enables dentists and oral health authorities to evaluate and plan emergency dental interventions accurately. Despite the availability of abundant data on the global epidemiology of dental caries in permanent teeth of children aged 12 years in recent years, there is limited information on the prevalence of deep caries involving the pulp<sup>(11,12)</sup>. The presence of deep caries involving the pulp in children in the primary dentition prompts the European Academy of Paediatric Dentistry to develop guidelines for managing deep caries in primary teeth in pediatric dentistry<sup>(13)</sup>.

**Table 1. Description of CAST codes<sup>10</sup>**

| CAST Code | Characteristic  | Description   | Tooth             |
|-----------|-----------------|---|-------------------|
| 0         | Sound           | No visible evidence of a distinct carious lesion is present   | Healthy           |
| 1         | Sealant         | Pits and/or fissures are at least partially covered with a sealant material   |                   |
| 2         | Restoration     | A cavity is restored with an (in) direct restorative material   |                   |
| 3         | Enamel          | Distinct visual change in enamel only. A clear caries-related discolouration is visible, with or without localised enamel breakdown                                       | Reversible        |
| 4         | Dentine         | Internal caries-related discolouration in dentine. The discoloured dentine is visible through enamel which may or may not exhibit a visible localised breakdown of enamel | Irreversible      |
| 5         | Dentine         | Distinct cavitation into dentine. The pulp chamber is intact  |                   |
| 6         | Pulp            | Involvement of the pulp chamber. Distinct cavitation reaching the pulp chamber or only root fragments are present   | Serious morbidity |
| 7         | Abscess/Fistula | A pus-containing swelling or a pus-releasing sinus tract related to a tooth with pulpal involvement   | Devital           |
| 8         | Lost            | The tooth has been removed because of dental caries   |                   |

This study aims to investigate the presence of SOS teeth in patients in the final stages of primary dentition (5-6 years old) and mixed dentition (11-12 years old) and to assess their distribution and prevalence based on gender of the patients, types of teeth involved, and affected jaws.

## **MATERIALS and METHODS**

### **Participants and Study Design**

Between November 1, 2022, and April 30, 2023, individuals who presented for dental examinations and reported other oral complaints were recruited from the Pediatric Dentistry Clinic of Dokuz Eylül. The study was approved by the Dokuz Eylül University Research Ethics Committee with protocol number 2023/19-21, date: 07.06.2023. Patients aged 5-6 and 11-12 years, without any systemic or genetic disorders, were specifically chosen for inclusion in the study. SOS teeth in the primary dentition of 5-6-year-old and in the permanent dentition of 11-12-year-old patients were assessed. An assent form and an informed consent form were signed by the children and their parents, respectively.

During this period, a total of 1391 patients visited our clinic. Of these, 215 out of 220 patients in the 5-6 age group (97.7%) and 169 out of 172 patients in the 11-12 age group (98.3%) agreed to participate in the study. Five patients were excluded from the study due to artifacts on their panoramic films. Following clinical examinations and a review of panoramic radiographic images, the presence of SOS teeth was determined. Individual forms were prepared for each patient, including age, gender, and CAST classification. Patients and their parents were informed about the study, and their signed informed consent forms were obtained.

### **Oral and Radiographic Examinations**

A total of 384 patients, aged 5-6 and 11-12 years, who presented for dental treatment, underwent thorough clinical examinations at our clinic. After drying their primary and permanent teeth with air spray, examinations were conducted using mirrors and probes. The presence of SOS teeth in both primary and permanent dentitions was confirmed using the CAST classification (code 6), and detailed observations were meticulously documented on patient forms (Table 1). Panoramic radiographic images were carefully reviewed to support clinical assessments, and all findings were recorded correctly on patient forms. Notably, the evaluation of SOS teeth in children was carried out by a specialized pediatric dentist (G.K.). To avoid bias and variability in the interobserver evaluation, the radiographs were evaluated by a single dentist.

### **Inclusion and Exclusion Criteria**

The study included children without systemic diseases aged 5-6, and 11-12 years, representing the primary, and late mixed dentition phases, respectively.

### **Statistical Analysis**

Data analysis was performed using SPSS 24.00 software (IBM, Chicago, IL, USA). Stages of dental caries in all primary and permanent teeth were evaluated separately. Numerical variables were presented as means and standard deviations, while categorical variables as frequencies and percentages. Categorical data of groups were compared using Pearson's chi-square and Fisher's exact tests. The level of statistical significance was set at  $p < 0.05$ .

## **RESULTS**

SOS teeth were found in 62.3% of 215 patients aged 5-6 years, and while in 19.5% of 169 patients aged 11-12 years. Among a total of 4300 primary teeth evaluated in the 5-6 age group, SOS teeth were recorded in 385 teeth (8.9%). In the group of patients with permanent dentition, SOS teeth were not found in incisors; however, SOS teeth were present in 44 teeth (6.5%) of the 676 permanent first molars (PFMs) examined, along with two premolars.

When assessing the relationship between gender and the presence of SOS teeth, SOS teeth were more frequently detected in women than in men across both age groups. While there was no statistically significant difference in the presence of SOS teeth in the 5-6 age group ( $p < 0.658$ ), in the 11-12 age group, greater number of SOS teeth were found in males than in females ( $p < 0.017$ ) (Table 2). Regarding the distribution of SOS teeth in the 5-6 age group, higher number of SOS teeth were noted in the upper jaw deciduous incisors than in the lower jaw incisors. However, there were statistically significantly greater number of SOS teeth in the lower jaw deciduous molars than in the upper jaw molars ( $p < 0.001$ ).

In children aged 11-12 years, SOS teeth were found in two mandibular premolars; no SOS teeth were observed in the incisors. However, a statistically significantly higher prevalence of SOS teeth was observed in mandibular first permanent molars compared to their maxillary counterparts ( $p < 0.001$ ) (Table 3). In the 5-6 age group, SOS teeth were most frequently detected in mandibular primary first molars (29.3%), followed by mandibular primary second molars (27.4%), maxillary primary first molars (20.3%), maxillary primary second molars (7.9%), maxillary primary incisors (2.0%), and mandibular primary

incisors (0.3%). The most frequently affected SOS teeth were found in both maxillary and mandibular first molars (Table 4).

The incidence of SOS teeth in maxillary first primary molars was found to be statistically significantly higher relative to the maxillary second primary molars ( $p < 0.001$ );

however, its incidence did not differ significantly in terms of mandibular primary molars ( $p < 0.366$ ). SOS teeth were more common in first and second molars in both maxillary and mandibular arches ( $p < 0.001$ ). When assessing primary molars of the right and left sides of the jaws, it was discerned that the prevalence of SOS teeth was greater on the left side ( $p < 0.003$ ).

| Children in need of emergency dental care |                 |        | SOS n (%)  | Absent n (%) | p      |
|---|-----------------|--------|------------|--------------|--------|
| Gender                                    | Primary teeth   | Female | 62 (28.8)  | 40 (18.6)    | 0.658  |
|   |                 | Male   | 72 (33.5)  | 41 (19.1)    |        |
|   |                 | Total  | 134 (62.3) | 81 (37.7)    |        |
|   | Permanent teeth | Female | 8 (4.7)    | 64 (37.9)    | 0.017* |
|   |                 | Male   | 25 (14.8)  | 72 (42.6)    |        |
|   |                 | Total  | 33 (19.5)  | 136 (80.5)   |        |

Pearson's chi-square test ( $p < 0.05$ )\*

| Affected teeth      |            | SOS n (%)  | Absent n (%) | p       |
|---------------------|------------|------------|--------------|---------|
| Primary incisors    | Maxillary  | 5 (2.3)    | 210 (97.7)   | ----    |
|                     | Mandibular | 2 (0.9)    | 213 (99.1)   |         |
| Primary molars      | Maxillary  | 87 (40.5)  | 128 (59.5)   | 0.001*  |
|                     | Mandibular | 129 (60.0) | 86 (40.0)    |         |
| Permanent incisors  | Maxillary  | -          | 169 (100.0)  | ----    |
|                     | Mandibular | -          | 169 (100.0)  |         |
| Permanent Premolars | Maxillary  | -          | 169 (100.0)  | -----   |
|                     | Mandibular | 2 (1.2)    | 167 (98.8)   |         |
| Permanent molars    | Maxillary  | 7 (4.1)    | 162 (95.9)   | 0.001** |
|                     | Mandibular | 30 (17.8)  | 139 (82.2)   |         |

Pearson's chi-square test ( $p < 0.05$ )\*, Fisher's exact test ( $p < 0.05$ )\*\*

| Primary teeth requiring emergency dental care |   | SOS n (%)  | Absent n (%) | p      |
|---|---|------------|--------------|--------|
| Maxillary first and second primary molars     | First primary molars (54-64)            | 87 (20.3)  | 343 (79.7)   | 0.001* |
|   | Second primary molars (55-65)           | 34 (7.9)   | 396 (92.1)   |        |
| Mandibular first and second primary molars    | First primary molars (74-84)            | 126 (29.3) | 304 (70.7)   | 0.366  |
|   | Second primary molars (75-85)           | 118 (27.4) | 312 (72.6)   |        |
| Maxillary primary molars                      | Right-left molars (54-55-64-65)         | 121 (14.1) | 739 (85.9)   | 0.001* |
| Mandibular primary molars                     | Right-left molars (74-75-84-85)         | 244 (28.4) | 616 (71.6)   |        |
| Maxillary-mandibular right molar              | Right primary molars (54-55-84-85)      | 158 (18.4) | 702 (81.6)   | 0.003* |
| Maxillary-mandibular left molars              | Left primary molars (64-65-74-75)       | 208 (24.2) | 652 (75.8)   |        |
| Maxillary primary incisors                    | Right-left incisors (51-52-53-61-62-63) | 17 (2.0)   | 843 (98.0)   | -----  |
| Mandibular primary incisors                   | Right-left incisors (71-72-73-81-82-83) | 3 (0.3)    | 857 (99.7)   |        |

Pearson's chi-square test ( $p < 0.05$ )\*

In children aged 11-12 years, the presence of SOS permanent teeth was most commonly observed in the mandibular right PFMs (23 teeth), followed by the mandibular left PFMs (13 teeth), maxillary left PFMs (5 teeth), and maxillary right PFMs (3 teeth). Within this age range, SOS teeth were identified in two premolar teeth in the mandible, while they were not observed in permanent incisors (Table 5).

SOS teeth were statistically significantly more often found in mandibular FPMs rather than in maxillary FPMs ( $p < 0.001$ ). Similar to the primary molar teeth of children aged 5-6 years, SOS teeth were more frequently observed on the left side of the jaws than on the right side in the 11-12 age group, but without any statistically significant difference between incidence rates ( $p < 0.061$ ).

### DISCUSSION

This study is a cross-sectional research trial aiming to determine the prevalence of SOS teeth in children aged 5-6 years with primary, and 11-12 years with permanent dentition to provide insights into this issue. We also used CAST index codes 6 and 7 to detect the presence of SOS teeth. However, there are many studies in the literature on the dental treatment of deep caries (codes 4-6) seen in primary and permanent teeth<sup>(13-16)</sup>. There are limited studies on the prevalence of urgent treatment (code 6) in primary and permanent teeth<sup>(14-18)</sup>. There are no studies in the literature on the prevalence of SOS teeth in primary and permanent teeth in the Turkish pediatric population.

Especially in developing countries, children often have SOS teeth at an early age due to inadequate, and bad oral hygiene habits. SOS teeth appear in primary and permanent dentition at an early stage and require urgent treatment, such as amputation or root canal therapy.

In this study the SOS teeth was found in 62.3% of patients with primary and in 19.5% of those with permanent dentition, indicating the need for endodontic treatment and/or extraction of one or more teeth. Generally, pulp involvement in both primary and permanent teeth is often accompanied by pain attacks, which negatively affect the child's quality of life<sup>(1,14)</sup>. Dental and developmental problems in children who experience premature loss of both primary and permanent teeth can affect their later years, leading to an increased need for complex and costly dental treatments<sup>(1)</sup>.

In our study, while a significant difference was observed between gender and SOS teeth in terms of permanent dentition, no significant difference was observed for primary dentition. Some researchers have reported lack of any correlation between gender and the number of carious lesions in primary and permanent dentitions<sup>(14-17)</sup>; while others have reported significant correlations<sup>(1,18)</sup>. Almoznino et al.<sup>(8)</sup> showed that the number of SOS teeth in permanent dentition is higher in men than in women. This finding suggests that the lower prevalence of SOS teeth among girls could be due to their earlier onset of puberty and a generally higher emphasis on personal hygiene and self-care practices.

| Permanent teeth requiring emergency dental care |                      |                                | SOS n (%) | Absent n (%) | p       |
|---|----------------------|--------------------------------|-----------|--------------|---------|
| <b>First permanent molars (FPMs)</b>            | Maxillary            | Right FPM (16)                 | 3 (1.8)   | 166 (98.2)   | ---     |
|   |                      | Left FPM (26)                  | 5 (3.0)   | 164 (97.0)   |         |
|   | Mandibular           | Right FPM (36)                 | 23 (13.6) | 146 (86.4)   | 0.077   |
|   |                      | Left FPM (46)                  | 13 (7.6)  | 156 (92.4)   |         |
|   | Maxillary            | Right-left FPM (16-26)         | 8 (2.4)   | 330 (97.6)   | 0.001** |
|   | Mandibular           | Right-left FPM (36-46)         | 36 (9.8)  | 302 (89.2)   |         |
|   | Right FPMs           | Maxillary-mandibular (16-46)   | 16 (4.7)  | 322 (95.3)   | 0.061   |
|   | Left FPMs            | Maxillary-mandibular (26-36)   | 28 (8.3)  | 310 (91.7)   |         |
| <b>Permanent premolars</b>                      | Maxillary premolars  | Right-left (14-15-24-25)       | -----     | 676 (100)    |         |
|   | Mandibular premolars | Right-left (34-35-44-45)       | 2 (0.3)   | 674 (99.7)   | ----    |
| <b>Permanent incisors</b>                       | Maxillary incisors   | Right-left (11-12-13-21-22-23) | -         | 676 (100)    | -----   |
|   | Mandibular incisors  | Right-left (31-32-33-41-42-43) | -         | 676 (100)    |         |

Pearson's chi square test ( $p < 0.05$ ), Fisher's exact test ( $p < 0.05$ )\*\*

Babaei et al.<sup>(14)</sup> evaluated the dental status of 739 primary school children aged 6-7 years according to the CAST index. In their study, they found that the indicated percentages of primary school children had dental caries CAST code 6 in their maxillary primary first molars (14.3%), maxillary primary second molars (17.9%), mandibular primary first molars (20.9%), and mandibular primary second molars (16.7%). Doneria et al.<sup>(19)</sup> evaluated the dental care status of 7-8-year-old children in India, and found CAST index code 6 dental caries in maxillary primary first molars in 29.0%, maxillary primary second molars in 15.1%, mandibular primary first molar in 23.3%, and mandibular primary second molar in 23.3% of their study participants. In line with the results obtained by the researchers mentioned above and by us, the maxillary primary second molars were the least affected teeth. In both studies the incidence rates of CAST code 6 caries were slightly lower than ours, which we attributed to the higher number of children visiting our dental clinic due to dental problems.

In our study, the rate of SOS teeth (CAST index code-6) in permanent teeth was 19.5%. Que et al.<sup>(20)</sup> reported the first permanent molar CAST index code 6 in 16.9% of their pediatric patients aged 11-14 years. In our research, the incidence rates of SOS in permanent maxillary right and left first molars (1.8% vs 3.0%), permanent mandibular left, and right first molars (13.6% vs 7.9%) were as indicated. Gudipaneni et al.<sup>(21)</sup> identified dental caries (CAST index code-6) in permanent first molars of children aged 7-9 in the maxillary right, and left first molars (5.9% vs 3.1%), in the mandibular left, and right first molars (9.0% vs 8.5%). Although the children's age range in their study was younger than ours, the rate of SOS teeth was quite similar. In our study, the prevalence of SOS teeth was 9.9% in mandibular FPMs,

compared to 2.4% in the maxillary FPMs. Among children in this age group, no SOS teeth were found in permanent incisors, but two mandibular premolar teeth required emergency dental treatment.

Similar to our study, in their study of 11-12-year-old children, Oter et al.<sup>(17)</sup> reported that maxillary FPMs require more intensive treatment than mandibular FPMs. Consistently, existing literature suggests a higher susceptibility of mandibular first permanent molars to decay compared to their maxillary counterparts<sup>(17-19)</sup>.

In our study, although there was no statistically significant difference between permanent molar teeth of both sides of the upper and lower jaws in terms of

the presence of SOS teeth ( $p < 0.061$ ), SOS teeth were more commonly observed in both primary molars ( $p < 0.003$ ) and permanent molar teeth on the left side rather than the right side. While most studies report no difference in the number of decayed and extracted teeth between the right and left sides of the jaws<sup>(21-23)</sup>, Oter et al.<sup>(17)</sup> have reported a higher incidence of deep dentin caries and apical lesions on the left side of the jaws.

The study group showed a high occurrence of caries-prone primary molars and decayed, missing, or filled primary teeth, highlighting the critical importance of pulpal intervention as the main treatment for these dental problems. Since primary teeth play a crucial functional role in children's dental health and greatly influence the health of permanent teeth later on, the study emphasizes the need to focus on preventive care at an early stage in both primary and permanent dentitions.

We believe that applying preventive treatments such as fluoride and fissure sealants to primary and permanent teeth starting from an early age, while emphasizing timely prophylactic intervention may help prevent the formation of SOS teeth.

In our opinion, conduction of larger, multicenter, population-based studies is necessary to determine the prevalence of SOS teeth in primary and permanent dentitions.

### Study Limitation

The limitation of the study is that it is a single-center study conducted on a small number of patients who applied to our clinic.

### Conclusion

In summary, this study revealed the presence of SOS teeth in the primary teeth of children aged 5-6 years and in the permanent teeth of those aged 11-12 years. SOS teeth were more prevalent in males in the 11-12 age group. They were also quite common in especially mandibular primary molars and permanent first molars. These data have highlighted the importance of preserving primary molars and permanent first molars, especially in the early period, as well as the need for root canal treatment. Further research with a large population is needed to raise awareness on this critically important issue.

## Ethics

**Ethics Committee Approval:** The study was approved by the Dokuz Eylül University Research Ethics Committee with protocol number 2023/19-21, date: 07.06.2023.

**Informed Consent:** An assent form and an informed consent form were signed by the children and their parents, respectively.

## Footnotes

### Author Contributions

Surgical and Medical Practices: G.K., G.B., S.E.G., E.T., Concept: G.K., G.B., Design: G.K., G.B., Data Collection or Processing: G.K., S.E.G., E.T., Analysis or Interpretation: G.K., G.B., Literature Search: G.K., G.B., S.E.G., E.T., Writing: G.K., G.B., S.E.G., E.T.

**Conflict of Interest:** The authors disclose no potential conflicts of interest.

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