

RESEARCH ARTICLE



## Influence of psychiatric symptom profiles of parents on sleep bruxism intensity of their children

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### ABSTRACT

**Objective:** The objective of this study was to evaluate the effects of parental anxiety, depression levels and psychiatric symptom profiles of parents on the occurrence of sleep bruxism in children.

**Material & Methods:** This cross-sectional study was carried out with a sample of 94 children aged 6 to 12 years, divided into two groups: with sleep bruxism (bruxism group-BG) and without sleep bruxism (control group-CG). Beck Depression Inventory (BDI), Symptom Checklist (SCL-90-R), Symptom Checklist and Screen for Child Anxiety Related Emotional Disorders-Parent (SCARED-P) scale were used to assess anxiety and depression levels of parents. All questionnaires were filled out by parents of children. Intraoral and extraoral examinations were carried out of children in the clinic and sleep bruxism was determined. All stress conditions were investigated by logistic regression analysis. In the comparison of the qualitative data, chi-square and Fisher exact tests were used.

**Results:** The data revealed that participants whose mothers had high anxiety and interpersonal sensitivity scores, and participants whose fathers had a medium level of obsessive-compulsive disorder were more likely to have an SB problem ( $p < 0.05$ ). According to the results of BDI, the fathers' results between the BG and the CG were not statistically significant ( $p > 0.05$ ). However, the mothers' results between the BG and the CG were statistically significant ( $p < 0.05$ ). When all subscales of SCARED-P were evaluated, the separation anxiety disorder subscore was statistically significant in the bruxism group.

**Conclusion:** The psychological status of parents is a significant risk factor associated with SB development in school-age children.

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## Introduction

Bruxism was defined as a repetitive activity of the jaw muscles, characterized by clenching or grinding of the teeth and/or bracing or thrusting of the lower jaw. It has been noted that the activity of masticatory muscles can occur during wakefulness (awake bruxism-AB) or sleep (sleep bruxism-SB) [1,2]. Although this definition was widely accepted worldwide, it was assessed that a new consensus was needed to further clarify this definition, to develop separate definitions for sleep and wake bruxism, to determine whether bruxism is a disorder, and to develop approaches for assessing bruxism [3]. SB is the activity of masticatory muscles during sleep, which can be rhythmic or nonrhythmic, while AB is an activity of the masticatory muscles during wakefulness which is characterized by repetitive or continuous tooth contact and/or by bracing or thrusting of the lower jaw. Rather than a disorder, bruxism should be considered a behaviour that can cause certain clinical states [3]. There is still no consensus about the etiology of SB because of its complex causes which

can be associated with local, systemic, psychological, occupational, and hereditary factors [2,4,5]. Some studies showed that genetic factors, anxiety, sleep disorders, object biting, exposure to second-hand smoke, headaches, peer problems, emotional stress, and mental problems are risk factors for bruxism [6,7]. Additionally, a disequilibrium in some neurotransmitters in the central nervous system such as dopamine and serotonin plays a role in the formation of masticatory muscle activity (MMA) and sleep bruxism [8]. Wiczorek et al. [9] reported that sleep bruxism does not significantly affect sleep duration and efficiency, however, rapid eye movement sleep might be significantly longer in SB patients. Severe sleep bruxism may cause instability in the stomatognathic system. This situation may lead to temporomandibular joint disorders with time [10–12]. It was reported that sleep habits in children were remarkably associated with sleep bruxism, temporomandibular disorders and dental caries [13]. However, whether sleep bruxism is associated with the clinical findings of temporomandibular disorders (TMD) is still controversial [14,15].

It is evaluated that the prevalence of sleep bruxism decreases with age and there are no gender differences [16]. The prevalence of sleep bruxism according to comprehensive studies performed in various populations showed around 20% in adults, but the prevalence indicated by studies that examined children only was shown to be from 19% to 40% [17,18]. SB is a very difficult condition to diagnose. It can be used non-instrumental approaches (especially self-report based on questionnaires) and instrumental approaches (especially electromyography) to evaluate bruxism [3]. It might be seen symptoms such as pain in jaw muscles, early morning pain, earache, headache and temporomandibular disorders in patients with sleep bruxism [19]. Stress has often been named as the cause of many muscle-related disorders including SB. Childhood anxiety is a general occurrence in clinical pediatric psychiatry [4,5,20]. Increasing anxiety levels of mothers or children, social and behavioural troubles, stress, and snoring improve the rate of having SB in children [21].

In literature, there are some researches which investigating the association between SB in children and socio-demographic factors family relationships, [5] stress, [22] and oral habits [23]. According to these researches, it was stated that a greater rate of SB among children whose mothers have a higher education level and those whose parents are divorced [5]. In another study, it was stated that children whose mothers with depressive and stressful have a greater likelihood of occurrence SB [24]. Much research has been done on children in relation to SB. Some of these studies are systematic reviews, and some have focused on the prevalence and incidence of SB or the aetiology and risk factors of SB. Additionally, there are a few studies that have examined the effects of the psychological and sociological statuses of families on children who have SB [4,5,20,21,24,25]. It is considered that the psychological status and behaviors of the family may contribute to the solution of the problem as it may be potentially related factors with sleep bruxism in children. The null hypothesis is that the psychological status of parents affects the occurrence of sleep bruxism in children. The aim of this study was to evaluate the effects of parents' psychological status and psychiatric profile symptoms on the occurrence of bruxism in school-age children.

## Materials and methods

### Participants and study design

This cross-sectional study was conducted with a sample of children between 6 and 12 years old in the mixed dentition period. The number of volunteers who would participate in this research was determined according to the results of a power analysis study made with the G\* Power software (Version 3.1.0., Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). The values of type I and type II errors were set at 0.05 and 0.20, individually. To have an 80% statistical power to detect a statistically significant difference between groups in this context, the needed sample size was 47 subjects per group.

The study sample consisted of 94 children (43 males, 51 females) who were consecutively referred to Hamidiye Faculty

of Dentistry, Department of Prosthodontics and Department of Pediatric Dentistry. Two groups of patients were determined: participants diagnosed with SB (bruxism group-BG,  $n=47$ ), and participants not diagnosed with SB (control group-CG,  $n=47$ ). The CG comprised children who were referred to the dental clinic for a routine oral inspection, without any specific dental complaint. The BG included children with symptoms of sleep bruxism such as the presence of clenching/grinding sounds during sleep and pain in the jaw muscles. The inclusion criteria were the following: children aged between 6 and 12 years, having no history of orthodontic treatment, trauma, or any psychiatric disease, and parents who signed informed consent and volunteered to participate in the study. The exclusion criteria were the following: widespread decay, premature tooth absence, systemic or mental development disorders, endocrine and metabolic disorders, presence of orthodontic treatment, trauma, and use of drugs that could affect the central nervous system.

### Psychosocial evaluation

In this study, the evaluation of psychiatric symptom profiles, anxiety, and depression levels of parents was done using the translated and validated Turkish version of the Beck Depression Inventory (BDI), Symptom Checklist (SCL-90-R), and Screen for Child Anxiety and Related Disorders-Parent (SCARED-P). All questionnaires were filled out by parents.

Beck Depression Inventory (BDI) will be used to assess depression consisting of 21 groups of four statements, the highest score for each statement is 3, and the lowest score is 0. Its original form was developed by Beck et al. [26] to determine the risk of depression in the individual and to measure the intensity of depressive symptoms and the change in severity. The BDI was developed to detect, assess, and monitor changes in depressive symptoms of individuals. Considering scores of BDI, less than 11 means minimal depressive symptoms, 12–20 means borderline results which represent mild to moderate depression, and a score higher than 21 means positive depression results and represents moderate or severe depression [27]. However, BDI cannot be used to diagnose depression.

The SCL-90-R is a 90-item multi-dimensional questionnaire designed to screen for a broad range of psychological problems. Each of the 90 items is rated on a five-point Likert scale of distress, ranging from "not at all" (0) to "extremely" (4). Subsequently, instant and continuous anxiety status, general psychological status {Somatization (S), Anxiety (A), Obsessive Compulsive Disorder (OCD), Depression (D), Interpersonal Sensitivity (IS), Psychoticism (P), Paranoid Ideation (PI), Hostility (H), Phobic Anxiety (PA), Sleep Patterns or Appetite like Additional Scales (AD), Overall Score (OS)}, and depression levels of parents were detected [28,29].

The Screen for Child Anxiety Related Emotional Disorders - Parent (SCARED-P) is a 41-item brief self-report scale that screens for anxiety in children and adolescents aged 9–18 and specifically assesses five main anxiety disorders: Panic Disorder or Somatic Symptoms, Generalized Anxiety Disorder, Separation Anxiety Disorder, Social Anxiety Disorder and

Significant School Avoidance [30]. The SCARED provides severity scores for anxiety symptoms; while a definitive diagnosis cannot be extrapolated from such scores, they constitute an initial screen that would need to be confirmed with further clinical assessments. The scale is available in both child- and parent-report versions (SCARED-C and SCARED-P), with moderate inter-rater correlation ( $\rho=0.32$ ,  $p=0.0001$ ). Both versions of the SCARED have high internal consistency and test-retest reliability. It was accepted that scores over 25 points indicate evidence of anxiety disorders.

### Procedure

This cross-sectional study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Gulhane Military Medical Academy Haydarpaşa Training Hospital, Istanbul, Turkey (approval number 1491-66-16/1539).

Parents were informed about the purpose and benefits of the study, and an informed consent form was obtained from parents. All questionnaires were filled out by parents. Data were collected by the Turkish version of the questionnaire using the instruments mentioned above from the parents. The socio-demographic data included data on age, gender, history of systemic or psychological disorders, and educational status of parents. Additionally, the presence of SB in the children was determined with questions and clinical examination based on the International Classification of Sleep Disorders diagnostic criteria prepared by the American Academy of Sleep Medicine. These criteria are the occurrence of audible grinding/clenching sounds during sleep, abnormal tooth wear, morning pain in masticatory muscles and jaw locking [31,32]. In the evaluation of sleep bruxism, it was asked whether they had their child clenching/grinding their teeth during sleep and whether their child had pain in the jaw muscles to the parents. Clinical examinations were performed by a prosthodontist. The type of tooth wear was determined (Erosion, Attrition, Abrasion or Abfraction) [33]. Toothwear was evaluated using by Smith and Knight index [34]. The occurrence of wear on the occlusal surfaces of three teeth or more (incisors and molars) was considered a symptom of probable sleep bruxism. The masticatory muscle discomfort was assessed by asking whether the child felt pain during palpation [35]. Children who had an incomplete medical examination or missing questionnaire form, and parents who lacked a signed consent form, were not included in the study. The effects of parents' anxiety, depression levels, and psychiatric symptom profiles on the formation of SB in children were evaluated.

### Statistical analysis

In this study, frequency distribution showing the distribution of demographic characteristics, Cronbach alpha coefficient of scale reliability, factor analysis of distributions, frequency, and percentage of distribution of cut data, and mean and standard deviation of distribution of continuous data were used.

Logistic regression analysis was used to determine the associations between psychiatric disorders and sleep bruxism. In the comparison of the qualitative data, Chi-square and Fisher exact tests were used. The chi-square test was utilized to analyze the different variables investigated in the study at a confidence level of 95%. Statistical significance was set at  $p<0.05$ . All statistical analyses were performed with the Number Cruncher Statistical Systems 2007 software package (NCSS, Kaysville, UT, USA).

### Results

Ninety-four children within the age range of 6–12 years (43 boys and 51 girls) met the inclusion criteria, and both the children and their parents were included in this study. Of the children included in the study, 45.75% were boys and 54.25% were girls, with an average age of  $9.12\pm 1.08$  for boys and  $9.18\pm 1.17$  for girls. When the SCL-90-R values of parents of the bruxism group and those of the control group were compared; the OCD, IS, and AS values of fathers and the A, OCD, D, IS, H, and OS values of mothers were statistically significant ( $p<0.05$ ) (Table 1).

According to the statistical review of the final equation, it is statistically significant and an important factor if the participant mothers have a high score for the level of A and a medium or high score for the level of IS. Participants whose mothers had high anxiety scores were 7.59 times more likely to have SB problems than those mothers who had no anxiety. Participants whose fathers had a moderate level of OCD were 1.85 times more likely to have an SB problem than those whose fathers did not have this level (Table 2).

According to the results of BDI, the fathers' results between the BG and the CG were not statistically significant (chi-squared test). In terms of the mothers, the results between the BG and the CG were statistically significant ( $p<0.05$ ) (Fisher's exact test) (Table 3).

The internal consistencies of the SCARED-P were represented by Cronbach's alpha values of 0.92 and 0.91, the BG and the CG, respectively. No statistically significant difference was found between the BG and the CG in all subscales of SCARED-P, except for the separation anxiety disorder ( $p=0.023$ ). On the other hand, the total mean SCARED-P scores revealed significant differences between the BG and the CG ( $p<0.05$ ) (Table 4). Logistic regression analyses of SCARED-P are shown in Table 5. In the bruxism group, it was found that only the separation anxiety disorder subscore was statistically significant and 62% lower than the control group.

### Discussion

The aetiology of bruxism is not known exactly. However, the most noted causes are considered to be lifestyle, quality of life, habits, nutrition, and other medical conditions, as well as emotional states such as stress and anxiety [36,37].

It is well known that the presence of SB in families predicts higher levels of psychological strain in parents. It is considered that the psychological status and behaviours of the parents may be potentially related factors to sleep bruxism in

**Table 1.** Self-assessment SCL-90-R scores (%) of psychosocial symptoms in parents.

	Symptoms	BG		CG		<i>p</i> value*		
		Moderate problem (0.5–1)	Psychological distress present (1>)	Moderate problem (0.5–1)	Psychological distress present (1>)	BG vs Control Common	Normal problem	Moderate problem
F	S	31.91	14.89	21.28	12.77	0.420	0.20	0.55
	A	25.53	2.13	10.64	4.26	0.160	0.06	0.99
	OCD	48.94	19.15	25.53	19.15	0.041*	0.01*	0.33
	D	17.02	19.15	27.66	6.38	0.120	0.38	0.12
	IS	23.40	21.28	23.40	4.26	0.041*	0.59	0.02*
	P	17.02	4.26	8.51	6.38	0.440	0.23	0.99
	PI	38.30	10.64	27.66	6.38	0.330	0.19	0.45
	H	21.28	25.53	19.15	12.77	0.230	0.51	0.09
	PA	14.89	4.26	6.38	0.00	0.130	0.19	0.22
	AS	19.15	25.53	23.40	4.26	0.015*	0.89	0.006*
M	OS	25.53	12.77	21.28	6.38	0.450	0.49	0.45
	S	27.66	23.40	25.53	12.77	0.330	0.52	0.14
	A	21.28	27.66	8.51	6.38	0.002*	0.02*	0.002*
	OCD	44.68	29.79	46.81	8.51	0.018*	0.27	0.008*
	D	31.91	27.66	17.02	14.89	0.027*	0.02*	0.03*
	IS	36.17	21.28	12.77	14.89	0.009*	0.003*	0.11
	P	19.15	4.26	10.64	6.38	0.481	0.26	0.73
	PI	36.17	14.89	34.04	10.64	0.761	0.68	0.48
	H	29.79	23.40	21.28	8.51	0.047*	0.13	0.02*
	PA	8.51	14.89	6.38	6.38	0.356	0.59	0.17
AS	31.91	23.40	27.6	8.51	0.082	0.29	0.04*	
OS	29.79 (51.06)	19.15	12.77	10.64	0.034*	0.02*	0.10	

\**p* < 0.05 Chi-square test.

BG: SB group; CG: Control group; F: father; M: mother; S: somatization; A: anxiety; OCD: obsessive-compulsive disorder; D: depression; IS: interpersonal sensitivity; P: psychoticism, PI: paranoid ideation; H: hostility; PA: phobic anxiety; AS: sleep patterns or additional scale; OS: overall score.

**Table 2.** Logistic regression analysis results of SCL-90-R between BG and CG in parents.

Symptom	$\beta$	SE ( $\beta$ )	Wald	<i>p</i>	Exp( $\beta$ )	95% CI for Exp( $\beta$ )	
						Lower	Upper
M A	Not at all		8.78	0.01			
	Moderate	-0.09	0.55	0.03	0.87	0.91	2.68
	Problem present	2.03	0.87	5.42	0.02	7.59	41.82
IS	Not at all		7.94	0.02			
	Moderate	1.5	0.54	7.70	0.01	4.49	12.98
	Problem present	-1.79	0.87	4.25	0.04	0.17	0.92
F OCD	Not at all		6.22	0.05			
	Moderate	0.62	0.31	4.11	0.04	1.85	3.37
	High level	-0.03	0.35	0.01	0.92	0.97	1.93

M: mother; F: father; A: anxiety; IS: interpersonal sensitivity; OCD: obsessive-compulsive disorder;  $\beta$ : regression coefficient in multiple analysis; SE: standard error; Exp( $\beta$ ): odds ratio; CI: confidence interval.**Table 3.** Comparison of BDI scores (N %) between groups.

	BG (n=47)	CG (n=47)	<i>p</i> value*
	Depression present (17 $\geq$ )	Depression present (17 $\geq$ )	BG vs. CG
Father	10.64	8.51	NS
Mother	21.28	0.00	0.001*

\**p* < 0.05 (Chi-square test, Fisher's exact test).

BG: SB group CG: Control group NS: no significance.

children. Based on the results obtained, data support the null hypothesis that the psychological status of parents affects the occurrence of sleep bruxism in children.

The quality of life in children with SB, their parents' psychological status and family functioning have been studied extensively [5,20,23,38]. However, no research has been found that examines the relationship between children with sleep bruxism and family dynamics using different psychological tests. Therefore, the present study provides preliminary evidence concerning SB in children related to the

presence of psychiatric disorders and higher anxiety and depression symptoms in families. The study also produced data indicating that SB is related to higher additional score levels in parents, regardless of the severity of anxiety or depressive symptoms. It is important to note that psychological scales alone are not capable of making a diagnosis of anxiety. However, in this study, a wide range of scales served to make comparisons between the groups and indicate that symptoms may be more prominent in one group than another.

Lobbzoo et al. [39] emphasized that SB should be identified with questionnaires, oral history taking, anamnesis, and extraoral and intraoral examination. Moreover, in some situations, there also needs to be an electromyographic recording of the activity of the masticatory muscles and a polysomnographic recording of the sleeping children. Furthermore, the authors noted that these diagnostic options should be used together, as patients who suffer from SB may not be aware of the presence of SB [39].

**Table 4.** Comparison of Parent's SCARED-P score means between BG and CG participants.

	CG				BG			p value	
	Mean (SD)	Med	Fr	Per	Ort	Med	Fr		Per
PD	1.85(2.52)	1.00			2.81(2.66)	2.00			NS
(+)			44	93.6%			43	91.5%	NS
(-)			3	6.4%			4	8.5%	
GAD	2.26(3.14)	1.00			3.13(3.25)	2.00			NS
(+)			45	95.7%			44	93.6%	NS
(-)			2	4.3%			3	6.4%	
SAD	4.00(3.38)	4.00			5.21(3.26)	5.00			NS
(+)			16	34.0%			27	57.4%	0.023*
(-)			31	66.0%			20	42.6%	
SOD	3.81(2.98)	3.00			4.89(3.45)	4.00			NS
(+)			42	89.4%			39	83.0%	NS
(-)			5	10.6%			8	17.0%	
SA	.83(1.22)	0.00			1.06(1.39)	1.00			NS
(+)			40	85.1%			41	87.2%	NS
(-)			7	14.9%			6	12.8%	
TOTAL	12.74(10.42)	11.00			17.26(10.85)	13.00			0.043*
(+)			44	93.6%			37	78.7%	0.036*
(-)			3	6.4%			10	21.3%	

BG: SB group; CG: Control group; SD: standard deviation; Med: median; Fr: frequency; Per: percentage; PD: panic disorder; GAD: generalized anxiety disorder; SAD: separation anxiety disorder; SOD: social anxiety disorder; SA: significant school avoidance; NS: no significance ( $p > 0.05$ ).

**Table 5.** Logistic regression analysis results of SCARED-P between BG and CG.

	B	SE ( $\beta$ )	Wald	p	Exp( $\beta$ )	95% CI for Exp( $\beta$ )	
						Lower	Upper
PD	.155	.397	.153	.695	1.168	.537	2.541
GAD	.214	.469	.209	.648	1.239	.494	3.103
<b>SAD</b>	<b>-0.481</b>	<b>.213</b>	<b>5.085</b>	<b>.024</b>	<b>.618</b>	<b>.407</b>	<b>.939</b>
SOD	.272	.306	.791	.374	1.313	.721	2.391
SA	-0.089	.300	.089	.765	.914	.508	1.645
TOTAL	.689	.348	3.926	.048	1.991	1.008	3.934

PD: panic disorder; GAD: generalized anxiety disorder; SAD: separation anxiety disorder; SOD: social anxiety disorder; SA: significant school avoidance;  $\beta$ : regression coefficient in multiple analysis; SE: standard error; Exp( $\beta$ ): odds ratio; CI: confidence interval.

Self-report psychological inventories are commonly used by both clinicians and researchers to collect information about patients' emotional states. In the clinician-based scales, the data comes directly from the patients who reflect their perceptions of distress [28]. The subscale study reliability results were satisfactory as defined in the results section.

It is important to determine the relationship between sleep bruxism and psychological disorders. Smardz et al. [40] reported that there was no statistically significant correlation between the severity of sleep bruxism with self-reported perceived stress and depression. However, in another study showed that anxiety may be an effective factor for SB in children [36]. According to Luecken and Lemery, [38] disrupted parent-child relationships lead to the development of negative psychological and social features. The findings of this study are in agreement with previous studies, which suggested that children whose parents have psychological problems may develop emotional defence mechanisms and may have parafunctional habits such as teeth grinding and clenching [5]. In addition, there is an increased risk of the development of physical disorders.

At this time, available evidence suggests that adverse childhood experiences (ACEs) have been associated with chronic diseases, premature death, smoking, substance abuse, alcohol abuse, anxiety, and depression [39]. Research has also put forward the idea that exposure to maltreatment in childhood is associated with lower educational access,

more antisocial behaviours, more frequent absence from work, poor job performance, and retirement due to handicaps [39]. Therefore, the idea that adverse childhood experiences can lead to anxiety and depression in children suggests that these children may experience an increased likelihood of SB due to depression.

According to Rossi et al. [5] although there is not a very close relationship, it has been stated that the divorced parental status may be a decisive factor connected to SB. Seraj et al. [25] examined 600 children aged 4 to 12 years and found that children whose mothers did not work were less prone to sleep bruxism than children whose mothers worked all day; they also stated that spending time with their mothers reduces the susceptibility to sleep bruxism. Serra Negra et al. [23] released a study about the effect of the structure and social behaviour of the family on the emotional development of children, and this emotional state should be considered in terms of SB. These results confirm the relationship between psycho-emotional problems and SB. According to the current study, the final regression model demonstrated that, in this sample, the presence of SB in children was affected by their parents' psychological situations and that these can be considered factors in the protection of school children with SB. When the results of this study were compared with the other studies mentioned above, it was determined that psychological disorders were examined individually, and the generalization of the results obtained regarding the emotional

behaviours of mothers and fathers who were dominant in SB was also consistent. In addition, the interactions with parents' mental status with the SB cases, which were considered within normal limits but still in the risk group, were extremely striking in this study.

There are several methodological limitations within the current questionnaire-based study that are the average sample size, and the absence of sleep recordings. Although parentally reported SB is considered valid, future research may benefit from an objective measure of SB and detailed clinical evidence of its association with specific health conditions. Another limitation of this study is the lack of research on respiratory and sleep disorders such as obstructive sleep apnea, upper airway obstruction, insomnia, and parasomnia. The relationship between respiratory and sleep disorders and sleep bruxism can be examined by planning a study in which children with these disorders will be included.

## Conclusions

Within the limitations of this clinical study, the following conclusions were drawn:

1. The psychological status of parents seems to be associated with SB development in school-age children.
2. High levels of anxiety in mothers and high levels of obsessive-compulsive disorder in fathers are factors that increase the risk of bruxism in children.
3. The high level of depression in mothers has an important effect on the formation of sleep bruxism in children.
4. In the diagnosis of sleep bruxism in children, it will be useful for clinicians to evaluate the psychiatric symptom profiles of the parents, to determine the source of the problem.

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## Ethical statement

This cross-sectional study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Gulhane Military Medical Academy Haydarpaşa Training Hospital, Istanbul, Turkey (approval number 1491-66-16/1539).

## Patient consent

Parents were informed about the purpose and benefits of the study, and an informed consent form was obtained from parents.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

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