Clinical Oral Investigations (2023) 27:3721–3730
https://doi.org/10.1007/s00784-023-04988-2

RESEARCH

# Evaluation of the relationship between pain inflammation due to dental caries and growth parameters in preschool children

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Received: 25 December 2022 / Accepted: 28 March 2023 / Published online: 10 April 2023


## Abstract

**Objectives** To evaluate the relationship between pain inflammation due to dental caries and growth parameters, sleep disturbances, and oral health-related quality of life (OHRQoL) in preschool children before/after dental treatment and compare the results with the control group.

**Materials and methods** Study (pain inflammation due to caries) and control groups were included in this prospective clinical trial. The Child Sleep Habits Questionnaire (CSHQ) assessing sleep disturbances and the Early Childhood Oral Health Impact Scale (ECOHIS) assessing OHRQoL were applied in the corresponding time intervals to the study and control groups, respectively: baseline ($T0_{study}$), 7 days after treatment ($T1_{study}$), and following 6 months ($T2_{study}$); baseline ($T0_{control}$), and the following 6 months ($T2_{control}$). Biochemical growth parameters (insulin-like growth factor-1 and insulin-like growth factor binding protein-3) and anthropometric measurements (standard deviation score of height, weight, and body mass index) were obtained at $T0_{study}$, $T2_{study}$, and $T0_{control}$. Mann-Whitney U and the Student *t*-tests were used for statistical analyses. The significance level was set at $p < 0.05$.

**Results** Data on 45 children (mean age: 55.6 ± 10.37 months) were analyzed. $T2_{study}$ was statistically higher than $T0_{study}$ for the anthropometric measurements and biochemical growth parameters ($p < 0.05$). $T0_{study}$ was statistically higher than $T0_{control}$ for biochemical growth parameters ($p < 0.05$). CSHQ and ECOHIS scores were found statistically significant at $T0_{study}$ than $T0_{control}$ ($p < 0.05$). Statistical scores of CSHQ and ECOHIS in $T2_{study}$ were significantly reduced compared to $T0_{study}$ ($p < 0.05$).

**Conclusion** Children's growth parameters, sleep disturbances, and OHRQoL improved after the elimination of pain and inflammation.

**Clinical relevance** This study's novelty is the observation of drastically increased growth parameters and reduced sleep disturbances following dental treatment.

**Keywords** Child · Dental caries · Growth · Sleep disturbances · ECOHIS

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## Introduction

Dental caries remains a global problem that affects the quality of life in children despite preventive measures. Acute and chronic infections due to untreated dental caries may cause pain, psychological discomfort, sleep disorders, inability to eat, poor appetite, and weight loss [1]. Therefore, possible systemic effects are expected, especially in dental caries with pulpal involvement [1, 2].

Both direct and indirect effects have been claimed regarding the relationship between dental caries and growth [3]. Pulp inflammation/pain induced growth retardation because of functional limitations in chewing and calorie intake deprivation have been linked as a direct effect [3, 4]. The indirect effect is associated with the body's reactions to chronic infection [3]. Infected pulp may suppress erythrocyte production and cause anemia [1, 3]. Severe dental caries may lead to sleep disturbances. The interruption of slow-wave sleep due to pain and infection may impair growth hormone (GH) secretion [3]. In addition, pulp and periodontium pain may cause uncomfortable sleep, major stress and nervousness, increased glucocorticoid secretion, and inhibition of GH secretion, respectively [5].

Anthropometric measurements are important parameters showing the growth of children, which are widely used due to their low cost, simplicity, and strong correlation with children's nutritional status [6]. In previous studies, height, weight, body mass index (BMI), and percentile or standard deviation score (SDS) were used to evaluate the relationship between dental caries and growth [1, 4]. Unsurprisingly, height and weight in children increase through natural growth. This growth is constant over time in relation to the SDS unless growth accelerates or decelerates through external influences [7].

Insulin-like growth factor-1 (IGF-1) is an effector hormone that is essential for normal growth and has an important role in mediating the anabolic and growth-promoting effects of GH [8, 9]. Therefore, serum IGF-1 is used as a screening test for GH deficiency [9]. The bioavailability of IGF-1 is regulated by IGF-binding proteins (IGFBPs), and the most important of these is insulin-like growth factor binding protein-3 (IGFBP-3) in circulation [10]. IGFBP-3 is less age-dependent and more stable than IGF-1 [8, 11]. Serum IGF-1 and IGFBP-3 both correlate well with the physiological changes in GH secretion. They are strongly related to diurnal GH secretion, thus reflecting mean daily GH levels [9].

It is difficult to measure the pain resulting from dental caries or pulp inflammation; however, it is well-known that pain disrupts sleep [12]. Chronic pulpal or periodontal pain (nagging pain for more than 3 months) may cause poor sleep quality and reduce the benefits of sleep [12, 13].

The oral health-related quality of life (OHRQoL) is defined as the level of self-esteem and satisfaction individuals give to themselves while feeding, sleeping, or socially interacting. The perceived impact of OHRQoL on the child and parent increases in the presence of pain [14].

Previous studies have focused on the changes in anthropometric measurements following dental treatment [1, 2, 15, 16]. To our knowledge, no previous studies have evaluated the biochemical growth parameters (IGF-1 and IGFBP-3) in addition to anthropometric measurements. Moreover, studies suggest that dental caries affect sleeping habits [17, 18]. However, no other study has been found that investigates how dental caries and dental pain affect sleep habits using scales. The purpose of this study was to compare growth, sleep disturbances, and OHRQoL in preschool children with pain and inflammation due to dental caries before and after treatment in order to compare the results with the control group. The study hypothesis is that growth parameters, sleep disorders, and OHRQoL in children will improve after dental treatments.

## Materials and methods

This study was designed as a prospective clinical study. The study was conducted at Bezmialem Vakif University, Faculty of Dentistry, Department of Pediatric Dentistry, between July 2019 and March 2020. Ethical approval was obtained from the Bezmialem Vakif University Research Ethics Committee (protocol number 71306642-050.01.04). The study was registered at ClinicalTrials.gov (registration number: NCT04231383).

### Study population

G-power software was used to compute the required sample size. The sample size was calculated with a significance level of 5%, and a test power level of 80%. The minimum sample size required to perform a valid statistical comparison that was equal for both groups was determined as 21-21 subjects with an effect size of 0.8. The children were recruited according to inclusion and exclusion criteria (Table 1). Parents of all the included subjects were informed about the study and signed an informed consent form. Children were clinically examined by a single researcher (BG) using a dental mirror and a curved explorer under a dental reflector light. The International Caries Detection and Assessment System (ICDAS II) was used for recording the stage of the carious process.

The growth parameters of children are being affected by seasonal variations [8]. The study group consisted of children who only received dental treatment under general anesthesia in order to obtain the data of all children in the same

**Table 1** Inclusion and exclusion criteria of the study

| | Study group | Control group |
|---|---|---|
| Inclusion criteria | 1. Preschool age (3–6 years)<br>2. Dental treatments to be performed under general anesthesia<br>3. Primary dentition<br>4. Early childhood caries<br>5. Symptoms of pulpitis or periapical infection in at least one tooth<br>6. Diagnosis of dental caries with ICDAS II code levels 5 and 6 in clinical and/or radiographic examination<br>7. Dental caries-related pain complaints in the previous 6 months<br>8. Consenting to participate in the study<br>9. Turkish nationality in origin | 1. Preschool age (aged 3–6 years)<br>2. Primary dentition<br>3. No symptoms of pulpitis or periapical infection on dental examination<br>4. Diagnosis of dental caries with ICDAS II code level 0, 1, 2, 3, and 4 in clinical and/or radiographic examination<br>5. No dental pain complaints in the previous 6 months<br>6. Consenting to participate in the study<br>7. Turkish nationality in origin |
| Exclusion criteria | 1. Physically and/or mentally handicapped children<br>2. Chronic and/or systemic diseases that may affect growth and development (chronic liver disease, chronic kidney disease, celiac disease, congenital heart disease, genetic syndromes, and endocrine disorders)<br>3. Corticosteroid treatment in the last 6 months<br>4. Anti-inflammatory medication use<br>5. Non-cooperation during blood sampling | |

time period and to standardize post-treatment follow-up with the completion of all treatments in a single session. Since the duration of treatment for each child would be different, children treated under local anesthesia were not included in the study to provide standardization.

## Sleep disturbances

Sleep disturbances were measured using the CSHQ. The CSHQ is a scale based on the International Classification of Sleep Disorders-R (ICSD-R). Thirty-three items were answered by parents to report the state of sleep during the previous week. Items were rated on a 3-point scale: usually (5 to 7 times per week), sometimes (2 to 4 times per week), and rarely (0 to 1 time per week). The CSHQ scores were calculated as a simple sum of the response codes. Higher scores in the CSHQ mean more sleep disturbances. The CSHQ's cutoff score is 41. Scores 41 and above indicate sleep disturbances. The Turkish reliability and validity of the CSHQ were confirmed by Fis et al. in 2010 [19].

## OHRQoL

The OHRQoL was measured using the ECOHIS. Thirteen items were answered by parents to consider the last 6 months of their child's oral health situation. Response options were scored on a scale from 0 to 4 (0 = never; 1 = hardly ever; 2 = occasionally; 3 = often; 4 = very often), with an option "don't know" scored as a non-response. The ECOHIS scores were calculated as the sum of the scores. Higher scores in the ECOHIS indicate a poorer OHRQoL. The Turkish reliability and validity of the ECOHIS were performed by Peker et al. in 2011 [20]. Question 1 (How often has your child had pain in the teeth, mouth, or jaws?) and question 6 (How often could your child not sleep because of dental problems or dental treatments?) were also recorded as well as the total score of the ECOHIS for both groups.

The CSHQ and ECOHIS were asked by the researcher and answered by parents at baseline ($T0_{study}$), 7 days after treatment ($T1_{study}$), and following 6 months ($T2_{study}$) in the study group; at baseline ($T0_{control}$) and following 6 months ($T2_{control}$) in the control group.

## Anthropometric measurements

The heights of the children were measured to the nearest 1 mm without shoes using a wall-mounted Harpenden stadiometer. Weights were measured to the nearest 0.1 kg using a clinical scale (Seca digital scales; Seca, Germany) with standard minimum clothing and without shoes. Heights and weights were measured at $T0_{study}$ and $T2_{study}$, $T0_{control}$ for the study and control group. Weight standard deviation score (weight SDS), height standard deviation score (height SDS), BMI, and BMI standard deviation score (BMI SDS) were calculated according to the national standard charts [21]. $T2_{control}$ anthropometric measurements could not be performed due to the COVID-19 pandemic.

## Serum IGF-1 and IGFBP-3—biochemical growth parameters

Venous blood samples of IGF-1 and IGFBP-3 levels were measured at $T0_{study}$, $T2_{study}$, and $T0_{control}$ in the study and control groups. Blood samples were centrifuged, and serums were stored at −80°C until analysis. IGF-1 and IGFBP-3 levels were evaluated by using the enzyme-linked immunosorbent method (Human Insulin-like Growth Factors 1 ELISA Kit-E0103Hu, Shanghai, China and Human Insulin-like Growth Binding Protein 3 ELISA Kit-E0391Hu, Shanghai, China) and measurements were recorded as ng/mL.

### Statistical analysis

Data was recorded to spreadsheets using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) for further analysis. Statistical analyses were performed using IBM SPSS Statistics 22 (IBM SPSS, Turkey). A descriptive data analysis was conducted, and the data was presented as mean, median, standard deviation, and frequency. The Shapiro-Wilk test was used for the assessment of normality. In order to compare the quantitative data, the results were compared through the Student *t*-test when they were normally distributed and through the Mann-Whitney *U* test when the data was not normally distributed. Repeated measures analysis of variance was used for intra-group comparisons of parameters with normal distribution at the baseline, following 7-day and 6-month figures; paired sample *t*-tests were used for paired comparisons. The Friedman test was used for intra-group comparisons of parameters with non-normal distribution at the baseline, following 7-day and 6-month figures, and finally, the Wilcoxon sign test was used for paired comparisons. Pearson's correlation analysis was used to study the relationships between parameters. Statistical significance was set at $p < 0.05$.

## Results

A total of 1240 children were screened for eligibility, and 63 children were enrolled in the study. Due to the dropout data of 18 children, they were also excluded. A total of 24 children (15 female and 9 male) were included in the study group and 21 children (8 female and 13 male) in the control group (Fig. 1). The mean age of the subjects was 55.6 ± 10.37 months. There was no statistical difference between the study and control groups in terms of age and gender ($p > 0.05$). The study population consisted of a similar race (Turkish nationality) without systemic disease.

Anthropometric measurements in the study and control groups are laid out in Table 2. Although the height, weight, height SDS, and weight SDS of $T0_{control}$ were higher than $T0_{study}$, this difference was not statistically significant ($p > 0.05$). BMI and BMI SDS were not significantly different between $T0_{study}$ and $T0_{control}$ ($p > 0.05$). At $T2_{study}$, height, weight, BMI, height SDS, weight SDS, and BMI SDS were significantly higher than at $T0_{study}$ ($p < 0.05$).

At $T0_{study}$, serum IGF-1 and IGFBP-3 levels were significantly higher than $T0_{control}$ ($p < 0.05$). Also, serum IGF-1 and IGFBP-3 levels at $T2_{study}$ were higher than $T0_{study}$ ($p < 0.05$; Table 3).

At $T0_{study}$, the CSHQ score was significantly higher than $T0_{control}$ and $T2_{study}$ ($p < 0.05$). The CSHQ was higher at $T0_{study}$ than $T1_{study}$ and $T2_{study}$ ($p < 0.05$). Also, the CSHQ score at $T1_{study}$ was significantly higher than $T2_{study}$ ($p < 0.05$). At $T2_{study}$, the CSHQ score was significantly higher than $T2_{control}$ ($p < 0.05$). The CSHQ score of $T0_{control}$ was higher than $T2_{control}$ ($p < 0.05$; Table 4).

Table 5 represents the ECOHIS scores in the study and control groups. The ECOHIS score of $T0_{study}$ was significantly higher than $T0_{control}$ ($p < 0.05$). The ECOHIS score of $T0_{study}$ was statistically higher than $T1_{study}$ and $T2_{study}$ ($p < 0.05$). The ECOHIS score of $T2_{study}$ was also significantly higher than $T2_{control}$ ($p < 0.05$).

The ECOHIS question 1 (Q1) score at the $T0_{study}$ was statistically significantly higher than the $T0_{control}$ ($p < 0.05$). The $T2_{study}$ Q1 score was statistically significantly higher than the $T2_{control}$ ($p < 0.05$). The $T0_{study}$ Q1 score was statistically significantly higher than $T1_{study}$ ($p < 0.05$). At $T0_{study}$, Q1 score was statistically significantly higher than $T2_{study}$ ($p < 0.05$). The ECOHIS question 6 (Q6) score at $T0_{study}$ was statistically significantly higher than the $T0_{control}$ ($p < 0.05$). The $T0_{study}$ Q6 score was statistically significantly higher than $T1_{study}$ ($p < 0.05$), and the $T0_{study}$ Q6 score was statistically significantly higher than $T2_{study}$ ($p < 0.05$, Table 6).

After the following 6 months, there was a reverse correlation of 47.5% between the CSHQ score and the height SDS in the study group ($r = 0.019$). There was a positive correlation of 46.6% between the CSHQ score and the ECOHIS score at the baseline for the children included in the study ($r = 0.001$; Table 7).

## Discussion

This prospective clinical study analyzed the changes in growth parameters, sleep disorders, and OHRQoL following treatment under general anesthesia of children with related pain and inflammation due to dental caries. The data of the study group was compared with that of a control group. In addition to anthropometric measurements, biochemical growth parameters (IGF-1 and IGFBP-3) were used to monitor the post-treatment changes in children. The data presented valuable outputs regarding the changes in growth parameters and sleep disturbances after dental treatment.

Previous studies found that pretreatment weight values were lower in the study group than in the control group [16, 22]. In this study, although the study group's height, weight, height SDS, and weight SDS were lower than those of the control group, this difference was not statistically significant.

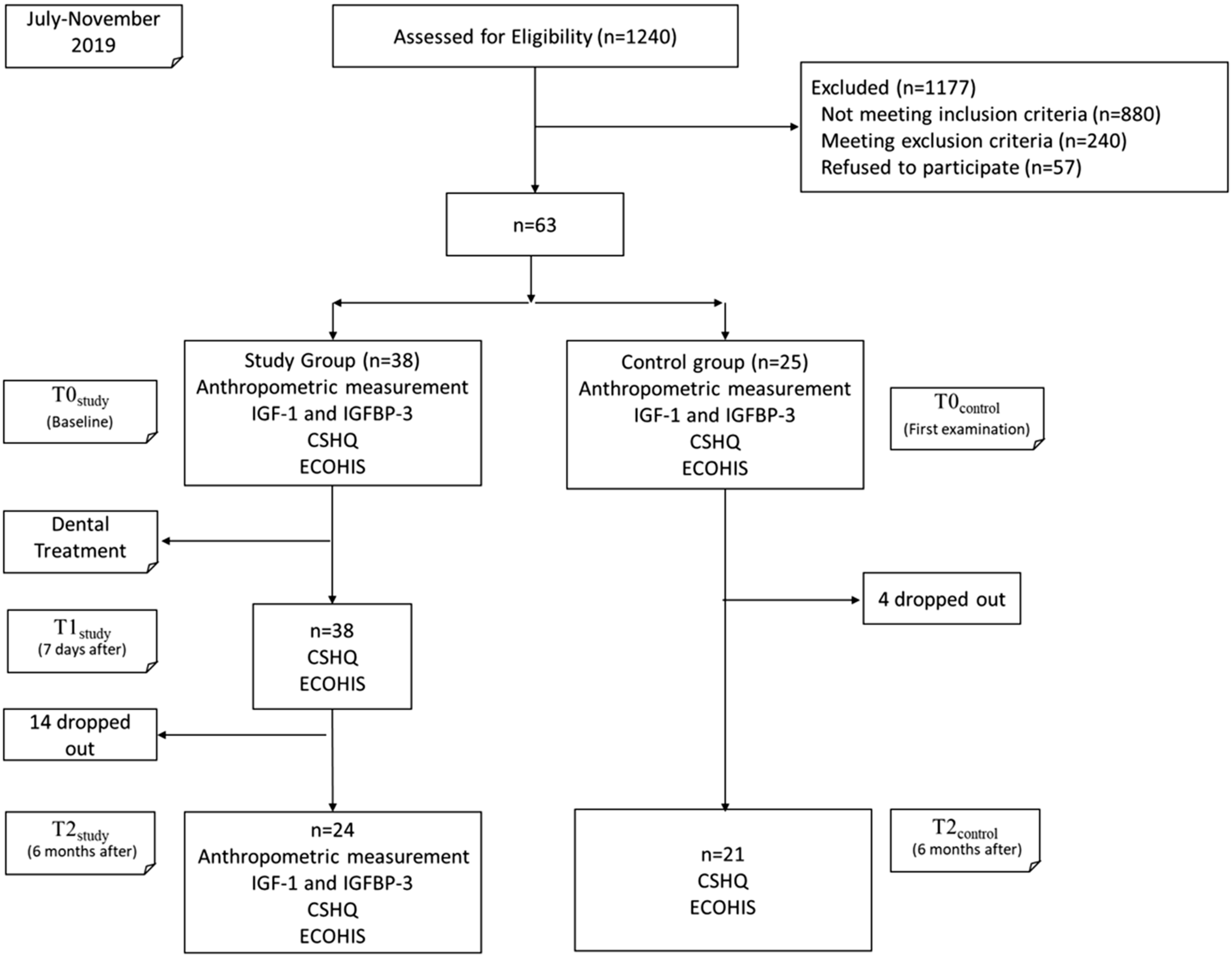


**Fig. 1** Participating children flow chart

In this research, the study population had similar demographic characteristics including age, race, and medical and dental histories.

Current study findings regarding anthropometrics revealed a significant increase in $T2_{study}$, similar to the previous studies [1, 4]. Pain and inflammation due to untreated dental caries might result in inadequate calorie intake by causing functional limitations. Chronic inflammation has been claimed to be related to conditions like anemia or metabolic disorders [3]. In addition, interruption of sleep due to dental pain might also prevent the secretion of GH at night [3, 5]. The significant increase in anthropometrics may be related to the disappearance of these negativities that affect growth as a result of dental treatment.

Another study found a significant increase in weight SDS and BMI SDS and showed a slight gain in height at the 6-month point after dental treatment under general anesthesia [7]. Monse et al. [15] found a significant increase in weight SDS and BMI SDS of low-weight children 4 months after dental treatment, while no significant increase was observed in height SDS. The authors stated that the change in height takes more time than the weight, and the follow-up period of 4 months after dental treatment is relatively short to monitor the height increase.

Reddy et al. [23] found a negative correlation between dental caries and BMI SDS. The authors reported that low-weight children had more dental caries than normal-weight and overweight/obese children. This finding has been associated with malnutrition. Researchers claimed that chronic malnutrition, especially in the first years, may increase the susceptibility to caries because of salivary hypofunction and enamel hypoplasia. Conversely, Chopra et al. [24] reported that overweight children had more dental caries than normal-weight children. The reason was argued to be linked to an increased carbohydrate intake of overweight children. Alves et al. [25] and Begum et al. [26] found no association between weight and the prevalence of dental caries. Researchers reported that many factors such as lack

**Table 2** Anthropometric measurements of the study and control groups regarding the follow-up periods

| Anthropometric measurements | Time | Study group Median ± SD | Control group Median ± SD | $p$ value[a] |
|---|---|---|---|---|
| Height (cm) | T0 | 105.15 ± 9.12 | 109.09 ± 5.23 | 0.079 |
| | T2 | 108.71 ± 8.42 | | |
| | $p$ value[b] | 0.000* | | |
| Weight (kg) | T0 | 17.37 ± 3.87 | 18.45 ± 3.24 | 0.319 |
| | T2 | 19.06 ± 4.14 | | |
| | $p$ value[b] | 0.000* | | |
| BMI | T0 | 15.59 ± 1.82 | 15.4 ± 1.73 | 0.724 |
| | T2 | 16 ± 2.01 | | |
| | $p$ value[b] | 0.016* | | |
| Height SDS | T0 | −0.15 ± 0.98 | 0.03 ± 1.1 | 0.561 |
| | T2 | −0.03 ± 0.98 | | |
| | $p$ value[b] | 0.009* | | |
| Weight SDS | T0 | −0.13 ± 1.13 | −0.07 ± 1.2 | 0.863 |
| | T2 | 0.14 ± 1.2 | | |
| | $p$ value[b] | 0.002* | | |
| BMI SDS | T0 | −0.09 ± 1.14 | −0.22 ± 1.18 | 0.722 |
| | T2 | 0.17 ± 1.21 | | |
| | $p$ value[b] | 0.018* | | |

*T0*, baseline; *T1*, following 7 days; *T2* following 6 months

*means statistically significant difference ($p < 0.05$)

[a]Student's *t*-test

[b]Paired sample *t*-test

of physical activity, unhealthy eating habits, genetics, and lifestyle may have also played a role in the etiology of childhood overweight and obesity. In the current research, the study population consists of children within normal BMI and BMI SDS averages according to the general statistics of Turkish children. No statistically significant difference was found between the study and control groups.

GH, IGF-1, and IGFBP-3 levels are used in the biochemical evaluation of growth. Since GH release is pulsatile and serum GH levels differ at all hours of the day, blood samples must be taken four or five times over a 12-h period in order to measure GH release. This is very time-consuming and expensive. Unlike GH, IGF-1, and IGFBP-3, which are not a pulsatile-type release and the serum levels are at the same level throughout the day, the serum IGF-1 and IGFBP-3 levels were therefore used to screen test GH levels in this study [8].

Salman et al. [27] evaluated the height SDS, weight SDS, ghrelin, and IGF-1 in children with adenotonsillar hypertrophy (ATH)-related sleep-disordered breathing (SDB) before and 3 months after surgery; the authors also compared the study group with a control group. The IGF-1, weight SDS, height SDS, and ghrelin of the study group were significantly higher than those of the control group before the surgery. Moreover, IGF-1, weight SDS, and height SDS increased significantly in the study group, and the level of ghrelin decreased. Similar to Salman et al.'s findings, the current study revealed that $T0_{study}$ serum IGF-1 and IGFBP-3 levels were significantly higher than the $T0_{control}$. Ghrelin is a peptide secreted mainly from the fundus of the stomach. It stimulates food intake, decreases energy expenditure, and supports weight gain by releasing GH [27]. Inadequate calorie intake, due to dental caries and dental pain, might increase ghrelin levels. An increase in ghrelin may also cause an increase in GH. The increase in GH may also cause an increase in serum IGF-1 and IGFBP-3 levels. The higher serum IGF-1 and IGFBP-3 levels of the study group compared to the control group may be related to the increase in ghrelin.

In medical studies, an increase in anthropometric IGF-1 and IGFBP-3 was found in children with obstructive sleep apnea syndrome OSAS or ATH after surgical treatment [11, 28, 29]. These children experienced eating difficulty, dysphagia, and high energy consumption due to obstruction of the upper respiratory tract and sleep disorders. The authors reported an increase in IGF-1 and IGFBP-3 as a result of the disappearance of these negativities after

**Table 3** Biochemical growth parameters of the study and control groups regarding the follow-up periods

| Biochemical growth parameters | Time | Study group Median ± SD | Control group Median ± SD | $p$ value[a] |
|---|---|---|---|---|
| IGF-1 | T0 | 19.69 ± 19.09 (9.9) | 5.85 ± 3.43 (4.54) | 0.006* |
| | T2 | 28.07 ± 24.46 (19.98) | | |
| | $p$ value[b] | 0.000* | | |
| IGFBP-3 | T0 | 4.58 ± 5.77 (2.48) | 2.05 ± 2.35 (1.06) | 0.027* |
| | T2 | 7.76 ± 7.35 (4.5) | | |
| | $p$ value[b] | 0.000* | | |

*T0*, baseline; *T2* following 6 months

*means statistically significant difference ($p < 0.05$)

[a]Mann-Whitney *U* test

[b]Wilcoxon's sign test

**Table 4** CSHQ scores of the study and control groups regarding the follow-up periods

| Time | Study group Median ± SD | Control group Median ± SD | $p$ value[a] |
|---|---|---|---|
| T0 | 47.29 ± 6.97 | 40.33 ± 4.98 | 0.000* |
| T1 | 44.5 ± 6.5 | - | - |
| T2 | 41.42 ± 4.94 | 38.05 ± 3.96 | 0.016* |
| $p$ value[b] | 0.000* | | |
| T0-T1 $p$ value[c] | 0.005* | - | |
| T0-T2 $p$ value[c] | 0.000* | 0.003* | |
| T1-T2 $p$ value[c] | 0.016* | - | |

*T0*, baseline; *T1*, following 7 days; *T2* following 6 months

*means statistically significant difference ($p < 0.05$)

[a]Student's *t*-test

[b]Repeated measures analysis of variance

[c]Paired sample *t*-test

**Table 5** The ECOHIS scores of the study and control groups regarding the follow-up periods

| Time | Study group Median ± SD | Control group Median ± SD | $p$ value[a] |
|---|---|---|---|
| T0 | 25.21 ± 12.15 (26) | 0.33 ± 0.86 (0) | 0.000* |
| T1 | 1.25 ± 1.65 (1) | - | - |
| T2 | 1 ± 1.74 (0) | 0.19 ± 0.68 (0) | 0.010* |
| $p$ value[b] | 0.000* | | |
| T0-T1 $p$ value[c] | 0.000* | - | |
| T0-T2 $p$ value[c] | 0.000* | 0.276 | |
| T1-T2 $p$ value[c] | 0.495 | | |

*T0*, baseline; *T1*, following 7 days; *T2* following 6 months

*means statistically significant difference ($p < 0.05$)

[a]Mann-Whitney *U* test

[b]Friedman's test

[c]Wilcoxon's sign test

surgical treatment. In this study, $T2_{study}$ serum IGF-1 and IGFBP-3 levels of the study group increased. The IGF-1 and IGFBP-3 serum levels in prepubertal children did not show a significant change depending on gender. In addition, IGF-1 and IGFBP-3 increased slowly in children until puberty [11]. Significant increases in serum IGF-1 and IGFBP-3 levels, in the short-term follow-up, might be explained by the disappearance of sleep interruptions caused by dental pain and the nutritional improvement following the treatment.

The benchmark for measuring sleep quality is polysomnography; however, establishing sleep laboratories and spending a few nights in the sleep laboratory is difficult [30]. In this study, the CSHQ, which includes general questions about sleep habits and sleep-related difficulties, was used because it is easy to apply and is a scale applied to

**Table 6** The ECOHIS Q1 and Q6 scores of the study and control groups regarding the follow-up periods

| Question | Time | Study group Median ± SD | Control group Median ± SD | $p$ value[a] |
|---|---|---|---|---|
| Q1 | T0 | 3.08 ± 1.1 (3, 5) | 0.14 ± 0.36 (0) | 0.000* |
| | T1 | 0.25 ± 0.44 (0) | - | - |
| | T2 | 0.42 ± 0.5 (0) | 0.05 ± 0.22 (0) | 0.004* |
| | $p$ value[b] | 0.000* | | |
| | T0-T1 $p$ value[c] | 0.000* | - | |
| | T0-T2$p$ value[c] | 0.000* | 0.157 | |
| | T1-T2 $p$ value[c] | 0.157 | | |
| Q6 | T0 | 1.83 ± 1.49 (2) | 0 ± 0 (0) | 0.000* |
| | T1 | 0.08 ± 0.28 (0) | - | - |
| | T2 | 0 ± 0 (0) | 0 ± 0 (0) | 1.000 |
| | $p$ value[b] | 0.000* | | |
| | T0-T1 $p$ value[c] | 0.000* | - | |
| | T0-T2 $p$ value[c] | 0.000* | 1.000 | |
| | T1-T2 $p$ value[c] | 0.157 | | |

*T0*, baseline; *T1*, following 7 days; *T2*, following 6 months

*means statistically significant difference ($p < 0.05$)

[a]Mann-Whitney *U* test

[b]Friedman's test

[c]Wilcoxon's sign test

preschool children. Miller and Swallow [31] reported that children with dental pain woke up an average of 3 times per night, and therefore the sleep of other family members was also interrupted. Our findings showed that the study group

**Table 7** Correlation CSHQ and HEIGHT SDS, ECOHIS score, IGF-1, and IGFBP-3 of the study and control groups regarding the follow-up periods

| T0 CSHQ score | | $R$ | $p$ value[a] |
|---|---|---|---|
| Study group | T0 Height SDS | −0.032 | 0.882 |
| | T0 ECOHIS score | 0.145 | 0.499 |
| | T0 IGF-1 | −0.162 | 0.450 |
| | T0 IGFBP-3 | −0.14 | 0.515 |
| Control group | T0 Height SDS | 0.242 | 0.291 |
| | T0 ECOHIS score | −0.238 | 0.298 |
| | T0 IGF-1 | −0.396 | 0.075 |
| | T0 IGFBP-3 | 0.016 | 0.944 |
| Total | T0 Height SDS | 0.023 | 0.88 |
| | T0 ECOHIS score | 0.466 | 0.001* |
| T2 CSHQ score | | $R$ | $p$ value[a] |
| Study group | T2 Height SDS | −0.475 | 0.019* |
| | T2 ECOHIS score | 0.267 | 0.207 |
| | T2 IGF-1 | 0.301 | 0.153 |
| | T2 IGFBP-3 | 0.041 | 0.851 |

*T0*, baseline; *T2*, following 6 months

*means statistically significant difference ($p < 0.05$)

[a]Pearson's correlation analysis

had more CSHQ scores than the control group, and scores decreased at $T1_{study}$ and $T2_{study}$. The improvement of sleep patterns may be related to the disappearance of dental pain-related sleep interruptions and anxiety.

Preschool children do not have the cognitive and communication skills to provide information about their oral problems [14]. Oral health problems of a child affect not only the general health, but also the family due to the loss of working days and expenditures needed for dental treatment. Therefore, assessing parents' perceptions of how their children's oral health problems affect their lives is an important part of measuring the OHRQOL of the children. ECOHIS was administered to preschool children and answered by parents in this study.

Collado et al. [32] evaluated the OHRQoL of children with ECC treated under general anesthesia before treatment, 1 month after treatment, and 3 months after treatment; they also compared them with a caries-free control group. They reported that ECOHIS scores of children with ECC were significantly higher than the control group before treatment, and that ECOHIS scores decreased significantly at 1 month and 3 months follow-up after treatment. Cantekin et al. [33] reported a 44% reduction in ECOHIS scores after dental treatment under general anesthesia in 311 children aged 4–6 years. Almaz et al. [34] found a significant decrease in ECOHIS scores 4 weeks after dental treatment under general anesthesia in 120 preschool children. Although our study group consisted of a smaller number, we found that comprehensive dental treatments performed under general anesthesia improved the OHRQoL, which is consistent with previous studies. This finding may be related to the relief of pain, increased comfort of eating following treatment, improvement of sleep patterns, decrease in the guilt of the parents, the resolving of leave issues, and financial difficulties of the parent. The ECOHIS Q1 and Q6 scores of $T0_{study}$ were found to be significantly higher than the $T0_{control}$. In the study group, Q1 and Q6 scores were significantly decreased following treatment. This data supports the findings that children with dental caries suffer from pain, resulting in sleep deprivation at night and that this condition improves after treatment.

Kang et al. [35] reported that weight SDS and height SDS correlated with sleep questionnaire scores and IGF-1 scores in children diagnosed with SDB. Bar et al. [36] found that slow-wave sleep time in polysomnography and serum IGF-1 levels increased significantly after an adenotonsillectomy. In the present study, no significant correlation was found between the CSHQ score and the IGF-1 and IGFBP-3 levels at $T0_{study}$, $T2_{study}$, and $T0_{control}$. This finding might be linked to the fact that CSHQ is a scale which not only examines pain-related sleep disruption but also interrogates general habits related to sleep disorders. Sleep is affected by various factors such as a mother's anxiety, domestic problems, and sleep patterns provided by caregivers. Since the CSHQ scale is answered based on the situation of the previous week, there is a possibility that the child may also be affected by environmental changes that should also be considered.

At baseline, a 46.6% positive correlation was found between the total ECOHIS and CSHQ scores of the children included in the study. This finding supports the improvement of quality of life with proper childcare, regular sleep, and eating habits; vice versa is also considered true.

The research conducted had some limitations. Firstly, anthropometric measurements of $T2_{control}$ could not be obtained due to the COVID-19 pandemic. In addition, the changes in the sleep-related difficulties of the control group children may also be considered due to reasons such as the closure of schools and the absence of parents from work due to the pandemic.

The strengths of this study were that children with dental caries-related pain and inflammation were followed for 6 months after treatment and compared to a control group that had no significant difference in age and gender. Findings in our study suggested that the direct theory that dental caries affects growth, as a result of functional limitation and malnutrition, may have been proven to a greater degree. On the other hand, in order to prove a direct theory biochemically, an examination of ghrelin level, which increases as a result of a low-calorie diet, might also be the subject of future research. Although our study suggests that dental caries and treatments affect sleep; no correlation between sleep disturbances and growth parameters was detected. Future prospective studies may focus on evaluation against the highest standard of polysomnography regarding sleep disorders.

## Conclusion

Dental treatment due to caries is mostly neglected since the teeth of preschool children are considered temporary. The results of this study suggest that the impact of untreated dental caries extends beyond reports of pain, sleepless nights, and infection. Although pain and infection may be the most readily noticeable effects of dental caries, they may also impact upon a child's growth. The increased growth parameters (anthropometric measurements and serum IGF-1 and IGFBP-3 levels) observed in children following dental treatment suggested that untreated dental caries may affect growth. Growth parameters, sleep disturbances, and OHRQoL all improved after the elimination of pain and inflammation due to dental caries, which supports the hypothesis of the study.

**Acknowledgements** This study was supported by the Bezmialem Vakif University Scientific Research Projects Coordination Unit (Project number: 8.2019/7). This paper was based partly on a thesis submitted to the graduate faculty at Bezmialem Vakif University.

**Authors' contributions** BG conceptualized the manuscript. BG and EMG carried out the methodology. BG carried out data analysis. BG drafted the manuscript. BG and MSK edited the manuscript. All authors subsequently revised the drafts. All authors read and approved the final manuscript.

**Funding** This study was fully funded by the Bezmialem Vakif University Scientific Research Projects Coordination Unit (Project number: 8.2019/7).

## Declarations

**Ethical approval** Ethics committee approval was received for this study from the Ethics Committee of Bezmialem Vakif University (Protocol number: 71306642-050.01.04).

**Informed consent** Informed consent was obtained from all parents of participants included in the study.

**Conflict of interest** The authors declare no competing interests.

## References

1. Ferrazzano G, Sangianantoni S, Mitrano R, Ingenito A, Alcidi B, Cantile T (2019) Assessing changes in oral health-related quality of life and body growth in 3-5 years old children following dental treatment under general anaesthesia due to severe dental caries. Eur J Paediatr Dent 20:214–218
2. van Gemert-Schriks MC, van Amerongen EW, Aartman IH, Wennink JM, Ten Cate JM, de Soet JJ (2011) The influence of dental caries on body growth in prepubertal children. Clin Oral Investig 15:141–149. https://doi.org/10.1007/s00784-010-0380-3
3. Alkarimi HA, Watt RG, Pikhart H, Sheiham A, Tsakos G (2014) Dental caries and growth in school-age children. Pediatrics 133:e616–e623. https://doi.org/10.1542/peds.2013-0846
4. Duijster D, Sheiham A, Hobdell MH, Itchon G, Monse B (2013) Associations between oral health-related impacts and rate of weight gain after extraction of pulpally involved teeth in underweight preschool Filipino children. BMC Public Health 13:533
5. Vania A, Parisella V, Capasso F, Di Tanna G, Vestri A, Ferrari M, Polimeni A (2011) Early childhood caries underweight or overweight, that is the question. Eur J Paediatr Dent 12:231
6. Li LW, Wong HM, Peng SM, McGrath CP (2015) Anthropometric measurements and dental caries in children: a systematic review of longitudinal studies. Adv Nutr 6:52–63. https://doi.org/10.3945/an.114.006395
7. Mohammadi TM, Wright C, Kay E (2009) Childhood growth and dental caries. Community Dent Health 26:38
8. Yuksel B, Ozbek MN, Mungan NO, Darendeliler F, Budan B, Bideci A, Çetinkaya E, Berberoğlu M, Evliyaoğlu O, Yeşilkaya E (2011) Serum IGF-1 and IGFBP-3 levels in healthy children between 0 and 6 years of age. J Clin Res Pediatr Endocrinol 3:84
9. Ersoy B, Yuceturk AV, Taneli F, Urk V, Uyanik BS (2005) Changes in growth pattern, body composition and biochemical markers of growth after adenotonsillectomy in prepubertal children. Int J Pediatr Otorhinolaryngol 69:1175–1181. https://doi.org/10.1016/j.ijporl.2005.02.020
10. Johansson P, Aberg D, Johansson JO, Mattsson N, Hansson O, Ahren B, Isgaard J, Aberg ND, Blennow K, Zetterberg H, Wallin A, Svensson J (2013) Serum but not cerebrospinal fluid levels of insulin-like growth factor-I (IGF-I) and IGF-binding protein-3 (IGFBP-3) are increased in Alzheimer's disease. Psychoneuroendocrinology 38:1729–1737. https://doi.org/10.1016/j.psyneuen.2013.02.006
11. Nieminen P, Lopponen T, Tolonen U, Lanning P, Knip M, Lopponen H (2002) Growth and biochemical markers of growth in children with snoring and obstructive sleep apnea. Pediatrics 109:e55. https://doi.org/10.1542/peds.109.4.e55
12. Brentegani LG, Brentegani MR, Lico MC (1992) Dental pain and sleep. Experimental study on guinea pigs (Cavia porcellus). Braz Dent J 2:129–133
13. Marshansky S, Mayer P, Rizzo D, Baltzan M, Denis R, Lavigne GJ (2018) Sleep, chronic pain, and opioid risk for apnea. Prog Neuropsychopharmacol Biol Psychiatry 87:234–244. https://doi.org/10.1016/j.pnpbp.2017.07.014
14. Clementino MA, Gomes MC, de Almeida Pinto-Sarmento TC, Martins CC, Granville-Garcia AF, Paiva SM (2015) Perceived impact of dental pain on the quality of life of preschool children and their families. PloS One 10:e0130602
15. Monse B, Duijster D, Sheiham A, Grijalva-Eternod CS, van Palenstein HW, Hobdell MH (2012) The effects of extraction of pulpally involved primary teeth on weight, height and BMI in underweight Filipino children. A cluster randomized clinical trial. BMC public health 12:725. https://doi.org/10.1186/1471-2458-12-725
16. Miller J, Vaughan-Williams E, Furlong R, Harrison L (1982) Dental caries and children's weights. J Epidemiol Community Health 36:49–52. https://doi.org/10.1136/jech.36.1.49
17. Mtaya M, Astrom AN, Tsakos G (2007) Applicability of an abbreviated version of the Child-OIDP inventory among primary schoolchildren in Tanzania. Health Qual Life Outcomes 5:40
18. Heinrich-Weltzien R, Monse B, Benzian H, Heinrich J, Kromeyer-Hauschild K (2013) Association of dental caries and weight status in 6- to 7-year-old Filipino children. Clin Oral Investig 17:1515–1523. https://doi.org/10.1007/s00784-012-0849-3
19. Fis NP, Arman A, Ay P, Topuzoğlu A, Guler AS, Gokçe Imren S, Ersu R, Berkem M (2010) The validity and the reliability of Turkish Version of Children's Sleep Habits Questionnaire. Anatolian J Psychiatry 11:151–160
20. Peker K, Uysal O, Bermek G (2011) Cross-cultural adaptation and preliminary validation of the Turkish version of the Early Childhood Oral Health Impact Scale among 5-6-year-old children. Health Qual Life Outcomes 9:118
21. Neyzi O, Gunoz H, Furman A, Bundak R, Gokcay G, Darendeliler F (2008) Weight, height, head circumference and body mass index references for Turkish children. J Child Heal Dis 51:1–14
22. Acs G, Lodolini G, Kaminsky S, Cisneros GJ (1992) Effect of nursing caries on body weight in a pediatric population. Pediatric dentistry 14:302–305
23. Reddy VP, Reddy VC, Krishna Kumar RVS, Sudhir KM, Srinivasulu G, Deepthi A (2019) Dental caries experience in relation to body mass index and anthropometric measurements of rural children of Nellore district: a cross-sectional study. J Indian Soc Pedod Prev Dent 37:12–17. https://doi.org/10.4103/jisppd.Jisppd_52_18
24. Chopra A, Rao NC, Gupta N, Vashisth S, Lakhanpal M (2015) The predisposing factors between dental caries and deviations from normal weight. N Am J Med Sci 7:151–159. https://doi.org/10.4103/1947-2714.156011
25. Alves LS, Susin C, Damé-Teixeira N, Maltz M (2013) Overweight and obesity are not associated with dental caries among 12-year-old South Brazilian schoolchildren. Community Dent Oral Epidemiol 41:224–231. https://doi.org/10.1111/cdoe.12010
26. Begum MZ, Nagamalleshwari M, Srinivas P, Gadagi JS, Gadde P, Jyothirmai KJDH (2014) Is body mass index truly related to dental caries? Survey on predisposing factors for overweight among Indian school children. J Dental Hypotheses 5:150
27. Salman N, Ozturk G, Akin I, Kilicaslan S, Demirel F, Delibas N (2014) The effect of adenotonsilectomy on ghrelin, leptin, IGF-1 levels and growth parameters in children with adenotonsillar hypertrophy. J Pediatr Endocrinol Metab 27:885–890. https://doi.org/10.1515/jpem-2013-0367

28. Cassano M, Russo G, Granieri C, Ciavarella D (2018) Modification of growth, immunologic and feeding parameters in children with OSAS after adenotonsillectomy. Acta Otorhinolaryngol Ital 38:124–130. https://doi.org/10.14639/0392-100X-1380
29. Jabbari Moghaddam Y, Golzari SE, Saboktakin L, Seyedashrafi MH, Sabermarouf B, Gavgani HA, Haghjo AG, Lotfi A, Ghabili K (2013) Does adenotonsillectomy alter IGF-1 and ghrelin serum levels in children with adenotonsillar hypertrophy and failure to thrive? A prospective study. Int J Pediatr Otorhinolaryngol 77:1541–1544. https://doi.org/10.1016/j.ijporl.2013.06.029
30. Van de Water AT, Holmes A, Hurley DA (2011) Objective measurements of sleep for non-laboratory settings as alternatives to polysomnography--a systematic review. J Sleep Res 20:183–200. https://doi.org/10.1111/j.1365-2869.2009.00814.x
31. Miller J, Swallow JN (1970) Dental pain and health. Public Health 85:46–50. https://doi.org/10.1016/s0033-3506(70)80014-2
32. Collado V, Pichot H, Delfosse C, Eschevins C, Nicolas E, Hennequin M (2017) Impact of early childhood caries and its treatment under general anesthesia on orofacial function and quality of life : a prospective comparative study. Med Oral Patol Oral Cir Bucal 22:e333–e341. https://doi.org/10.4317/medoral.21611
33. Cantekin K, Yildirim MD, Cantekin I (2014) Assessing change in quality of life and dental anxiety in young children following dental rehabilitation under general anesthesia. Pediatr Dent 36:12e–17e
34. Almaz ME, Sonmez IS, Oba AA, Alp S (2014) Assessing changes in oral health-related quality of life following dental rehabilitation under general anesthesia. J Clin Pediatr Dent 38:263–267
35. Kang JM, Auo HJ, Yoo YH, Cho JH, Kim BG (2008) Changes in serum levels of IGF-1 and in growth following adenotonsillectomy in children. Int J Pediatr Otorhinolaryngol 72:1065–1069. https://doi.org/10.1016/j.ijporl.2008.03.015
36. Bar A, Tarasiuk A, Segev Y, Phillip M, Tal A (1999) The effect of adenotonsillectomy on serum insulin-like growth factor-I and growth in children with obstructive sleep apnea syndrome. J Pediatr 135:76–80. https://doi.org/10.1016/s0022-3476(99)70331-8