

Cephalometric Differences in Gummy Smile and Non-Gummy Smile Children: A Case-Control Study

Stefania Mesa Beltrán¹, Lucia Victoria Bernal de Jaramillo¹, Oscar Zapata-Noreña², Mónica Patricia Giraldo-Fernández³, Diana Maria Barbosa-Liz²

¹Faculty of Dentistry, University of Antioquia, Medellin, Colombia.

²Orthodontic Postgraduate Program, Gionorto Research Group, Faculty of Dentistry, University of Antioquia, Medellin, Colombia.

³Pediatric Postgraduate Program, Gionorto Research Group, Faculty of Dentistry, University of Antioquia, Medellin, Colombia.

Corresponding author: Diana María Barbosa-Liz

E-mail: diana.barbosa@udea.edu.co

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ABSTRACT

Objective: To describe and compare children and adolescents' vertical and sagittal cephalometric characteristics with and without a gummy smile (GS). **Material and Methods:** From a population of 204 patients (7-17 years old) and after applying the selection criteria, a sample of 156 subjects were included: 37 cases (GS) and 119 controls (no GS [NGS]), in a proportion of 1:3. An operator calibrated performed linear and angular measurements on standardized digital lateral radiographs, and the skeletal, dental and soft tissue structures were then analyzed. **Results:** The mean age of the patients was 9.97 ± 2.12 . There were differences in maxillary size and position ($p < 0.05$), mandibular size and rotation ($p < 0.05$), and anterior vertical proportions between SG and NSG patients. The logistic regression model ($R^2 = 0.63$) showed that increased occlusal plane/palatal plane (OP/PP) and occlusal plane/mandibular plane (OP/MP) angles increase the possibility for GS, with an OR of 2.05 (95% CI: 1.30-3.22) and an OR of 2.32 (95% CI: 1.42-3.75), respectively. No statistically significant differences were found in sex or habits between the GS and NGS patients. **Conclusion:** Class II skeletal malocclusion with maxillary prognathism and mandibular retrognathism, the hyperdivergent growth pattern, and increased values for OP/PP and OP/PM were associated with GS in children and adolescents. This relationship was established in childhood and adolescence.

Keywords: Cephalometry; Malocclusion, Angle Class II; Case-Control Studies; Dental Occlusion.

■ Introduction

For dentofacial orthopedics and orthodontics, it is imperative not only to evaluate and correct dental malocclusions, skeletal disharmonies, and functional and soft tissue alterations but also to evaluate patients' facial aesthetic parameters, in which the smile plays a fundamental role [1].

Excessive gingival exposure is a frequent chief complaint in dentistry because many patients consider it unattractive [2]. In terms of aesthetics, the smile is generally regarded as attractive when it meets specific parameters of symmetry and proportion among its three main components: lips, gingiva, and teeth [3].

Anatomically, the smile has been classified according to the relationship between the lower edge of the upper lip and the maxillary incisors and their gingiva into three categories [4]: high, the entire dental crown and adjacent gingival band are exposed; medium, 75%-100% of the anterosuperior teeth and only the interproximal gingiva are shown; and low, less than 75% of the anterior teeth are visible, without gingival exposure.

Subsequently, the definition of a high smile has been further clarified with the concept of a gummy smile (GS) when there is more than 2 mm of gingival exposure between the upper lip and gingival margin of the upper incisors during a posed smile [5]. It has been observed that as age increases, the gingival smile decreases [6,7], and therefore, this kind of smile has been accepted as a typical characteristic in deciduous dentition [8].

Some factors associated with a GS can be evaluated clinically or using cephalometric analysis. Clinical factors include altered passive eruption [2,9], decreased upper lip length or lip elevator muscle hyperactivity [10], retrognathic mandible, maxillary excessive vertical growth [11], increased distance between the mucogingival junction and free gingival margin [9] and upper incisors with short clinical crowns [9,10], among others.

Cephalometric characteristics, such as skeletal Class II and vertical growth patterns, are predisposing factors for a GS in adults [10,11]. A positive correlation between the length of the anterior facial height (nasion–menton [N–Me]), a positive correlation between the upper lip length and N–Me, and an even higher correlation with the skeletal vertical dimension, measured from the anterior nasal spine to Me (ENA–Me) have been related to a GS [12]. Additionally, proclination of the upper incisors and decreased mandibular posterior alveolar height have been seen in some adolescent patients with a GS [11].

Dental measurements that have been correlated with the presence of GS include an increased overbite (OB) and overjet (OJ) [1,10]. According to Cheng and Cheng [13], an overjet is the main influencing smile factor in different malocclusions, and it has been reported that the vestibular inclination of the upper incisors contributes dramatically to their exposure [12].

Most studies on GS and cephalometric characteristics have been carried out in adult and adolescent populations; therefore, the present study aimed to determine the relationship between a GS and some cephalometric parameters in child and adolescent populations.

■ Material and Methods

Study Design and Ethical Clearance

An analytical retrospective case-control study was performed after approval by the Ethics Committee of the Faculty of Dentistry of the University of Antioquia (Act No. 05 of 2019, 24 May 2019).

Sample

The sample was collected from three same-neighborhood private dental practices in Medellín, Colombia, between 2015 and 2020. From a population of 208 standardized lateral cephalic radiographs taken in the same radiological center (Imax®), 154 met the selection criteria and were included in the sample: 35 cases (GS) and 118 controls (NGS).

Data Collection

X-rays were captured utilizing Sirona Orthophos XG5/CEF equipment (Sirona Dental System, Bernsheim, Germany), positioned at a distance of 143.5 centimeters, voltage set between 73 and 77 Kv, 8-15 mA, exposure time ranging from 9.4 to 13.1 seconds, with the patient maintaining a natural head position and relaxed muscles.

The concept of a GS, as defined by Peck et al. [2], was used to assign individuals to groups. Those who presented a GS, defined as a gingival exposure of 2 mm or more during a posed smile, were classified as cases, and those with no gummy smile (NGS), defined as a gingival exposure <2 mm in a posed smile, were classified as controls. All participants who met the selection criteria from one of the groups were included in the analysis.

Each smile classification was obtained during clinical examination by visualization performed by a previously calibrated operator ($k > 0.8$) and then taking the measures and confirmed in photo frames taken from a video using video edition software Adobe Premier Pro version CS3® (Adobe System Incorporated, San José, CA, USA) in JPEG format. The video camera was placed 70 cm from the individual natural head position with the help of a cephalostat, following the methods reported in a previous study by the same research group [14]. This method avoided the misclassification of borderline cases.

The minimum sample size calculation was made using Epidat 4.2 (Xullo 2016, Conselleria de Sanidade, Xunta de Galicia, España; Organización Panamericana da saude; Universidade CES, Colombia) and based on a previous study [10] with a prevalence of cases of 26%, an OR of 10.4 (3.7-34.95), a 95% confidence level and a power of 80%. Using a ratio of one case for every three controls (1:3), the calculated minimum sample size required was 27 cases and 81 controls for 108 patients needed for the study. To control selection bias, we applied the following inclusion criteria: patients between 7 and 17 years of age with healthy and complete dentition, without syndromes or craniofacial anomalies, without premature loss of teeth, and with no history of dentoalveolar trauma to the anterior region. Exclusion criteria were diagnosis of any chronic systemic disease affecting craniofacial development, congenital or traumatic absence of teeth, active or previous orthopedic or orthodontic treatment, anterior restoration, and poor quality lateral cephalic radiographs in which posterior occlusion was not observed.

All patients (cases and controls) were taken in the same place and at the same time to avoid selection bias. No ethnic group restrictions were considered in this study. The parents of the participants or other responsible adults signed informed consent. After consent was obtained, each patient underwent a clinical history that included clinical examination; the type of dentition, presence of habits (digital sucking, lingual interposition, and oral breathing), and type of smile were evaluated. The clinical evaluations were done in a dental unit with sufficient illumination to avoid any bias in the classification of the patients. The 11 mm periodontal probe (Ref pcp116) Hu-Friedy® was used as the measuring instrument.

All cephalometric measurements were made in the morning using the same computer and software to minimize operator fatigue. Subsequently, a calibrated evaluator, blinded to the group assignment (intraclass correlation [ICC] >0.8, $k > 0.8$), performed digital linear and angular measurements of the skeletal, dental, and soft tissue structures using a VistaDent from Dentsply Sirona Orthodontics® software. Bland Altman plot was used to evaluate the agreement of the measures. The cephalometric skeletal landmarks and planes used to measure the included variables are represented in Figure 1.

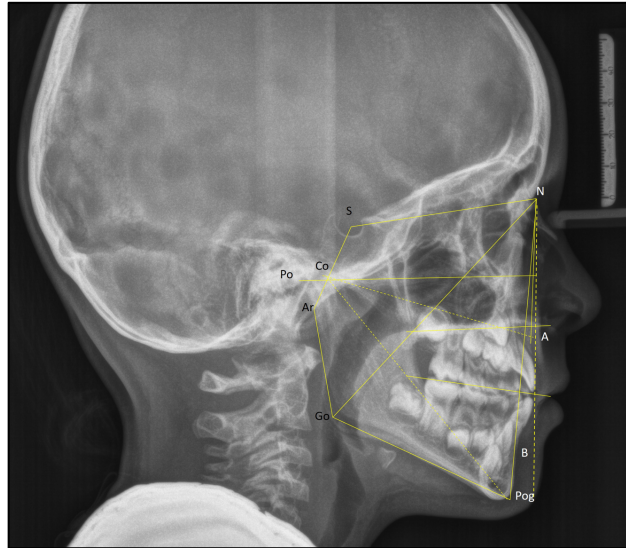


Figure 1. Cephalometric landmarks and planes.

Statistical Analysis

All statistical analyses were performed using SPSS version 17 (SPSS Inc, Chicago, IL, USA). The Kolmogorov–Smirnov test was used, and normal distributions of the continuous variables were found; therefore, parametric tests were performed. Quantitative variables were expressed as mean and standard deviation. An unpaired Student’s t-test was performed to compare quantitative variables in the two groups (GS and NGS). A bivariate analysis using Pearson's chi-square coefficient was used to compare the qualitative variables in the two groups. The significance level was set at $p \leq .05$. A multivariate analysis with binary logistic forward stepwise regression was performed to determine the influence of the cephalometric variables (cranial base, maxilla, mandible, intermaxillary, vertical, dentoalveolar, and soft tissue) on the presence or absence of a GS.

■ Results

The variables were analyzed using Bland-Altman plots, which indicated high intra-observer agreement with an average error of 0.19; SD of the difference: 0.86 (95% CI: 0.36 to 0.04). The intraoperator reproducibility (Bland-Altman plots) indicated a high concordance in the measurements.

The mean age of the patients was 9.87 ± 2.46 . The mean age for the GS group, the mean age was 8.65 ± 2.49 (95% CI: 8.12-11.21), while in the NGS group was 10.25 ± 2.29 (95% CI: 9.62-12.72; $p=0.001$). Regarding habits, no statistically significant differences were found between the two groups. The sociodemographic variables (sex, type of dentition, and habits) are described and compared in Table 1.

Table 1. Sex, type of dentition, and presence of habits in patients with and without a gummy smile.

Variables		Gummy Smile		No Gummy Smile		p-value
		N	%	N	%	
Sex	Female	23	63.9	59	50.0	0.144
	Male	13	36.1	59	50.0	
Habits	No	30	83.8	109	92.4	0.109
	Yes	6	16.2	9	7.6	
Type of Dentition	Mixed	29	80.6	63	53.4	0.04*
	Permanent	7	19.4	55	46.6	
Age Mean (SD)		8.75 (2.45)		10.29 (2.29)		0.001**

*Pearson Chi-square test; * $p < 0.05$; ** $p < 0.001$; SD: Standard Deviation.

Anterior cranial base length (sella–nasion) and posterior cranial base length (sella–articular) were significantly longer in the NGS patients ($p \leq 0.05$). Most of these variables presented statistically significant differences between the two groups. The comparison of the cranial, maxillary, and mandible cephalometric findings can be seen in Table 2.

Table 2. Description and comparison of the cranial base, maxillary, and mandible cephalometric characteristics in children and adolescents with and without a gummy smile.

Variables	Gummy Smile		No Gummy Smile		p-value
	Mean	SD	Mean	SD	
Cranial Base					
S-N mm	60.1	2.9	61.7	3.6	0.11
S-Ar mm	28.8	3.0	30.4	3.4	0.115
Ba-N mm	88.9	3.8	92.4	5.1	0.000***
SN / FH angle	8.2	2.7	6.9	2.9	0.017**
Ar-S-N angle	123	5.8	123.7	4.9	0.563
N-S-Ba angle	128.4	5.4	127.7	5.0	0.390
Maxillary					
SNA angle	84.9	4.6	84.1	3.6	0.379
NA/FH angle	92.9	3.6	91.0	2.9	0.007***
A to N-perpendicular line mm	2.3	2.9	0.9	2.6	0.010**
Maxillary Length (Co-A) mm	78.9	4.1	81.1	5.3	0.013*
N-ANS mm	44.4	3.5	47.0	3.9	0.000***
S – PNS mm	42.0	3.6	43.4	3.4	0.045*
SN / PP angle	6.1	3.2	6.9	3.3	0.195
FH / PP angle	-1.6	2.9	0.0	0.3	0.003**
Mandible					
SNB	78.9	3.9	79.5	3.5	0.432
Go-Gn mm	65.5	5.4	68.5	5.4	0.005**
Co-Gn mm	100.4	6.9	104.2	7.4	0.009**
Mand. length (Co-Pog) mm	97.3	6.4	101.3	7.0	0.003**
FH / MP angle	27.5	4.1	25.6	5.0	0.012*
Li-Me mm	36.7	2.6	36.7	3.5	0.898
Ar-Go mm	39.4	4.0	42.3	4.5	0.001**
Lower gonial angle	75.8	3.8	73.3	4.9	0.001**
Upper gonial angle	51.0	3.4	49.5	3.7	0.023*
Ar-Go-Me angle	126.7	4.6	122.9	6.2	0.000***
Ar angle	145.7	5.2	146.0	5.1	0.651
Pog to N-perpendicular line mm	-4.0	4.5	-4.8	4.8	0.358

Student's t-test Bonferroni correction; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; SD: Standard Deviation.

According to the analysis performed, the patients in the GS group presented higher values in the ANB angle and the Wits appraisal, with statistically significant differences ($p < 0.05$). Regarding the vertical cephalometric measurements, the variable posterior facial height (sella–gonion [S–Go]) was higher in NGS patients compared to GS patients. Likewise, the ratio of the posterior facial height to the anterior facial height showed statistically significant differences between the groups ($p < 0.05$), being lower in GS patients. In contrast, the PP/MP angle was higher in the GS patients. Regarding the cephalometric variables related to the occlusal plane, statistically significant differences were observed in the OP/PP and OP/MP variables. The anteroposterior relationships, the vertical measurements, and the variables analyzed in the occlusal plane can be seen in Table 3. An analysis was made for the mixed dentition groups only. The variables with significant differences are presented in Table 4.

Table 3. Description and comparison of anteroposterior and vertical intermaxillary relationship characteristics in children and adolescents with and without a gummy smile.

Variables	Gummy Smile		No Gummy Smile		p-value
	Mean	SD	Mean	SD	
Anteroposterior Relationship					
Convexity Angle	13.3	6.4	13.9	4.8	0.626
Co-A/ Co-Gn difference	21.6	5.8	23.2	4.5	0.163
Wits appraisal	-0.3	3.7	-1.5	2.8	0.050*
ANB angle	6.1	3.5	4.7	2.2	0.031*
APDI	77.1	5.4	80.4	4.9	0.002**
Vertical Relationship					
Y-axis angle	59.4	3.2	60.0	3.1	0.389
ANS-Me (Lower facial height) mm	60.4	4.3	59.6	5.6	0.340
Na-Me (Anterior facial height) mm	102.2	6.9	104.6	8.2	0.149
S-Go (Posterior facial height) mm	65.2	5.5	69.5	6.2	0.000***
Posterior facial height/ Anterior facial height %	63.9	4.0	66.4	4.4	0.002**
ODI	73.1	6.0	74.0	5.4	0.285
PP / MP angle	29.7	4.5	25.4	5.1	0.000***
SN / MP angle	35.5	5.2	32.5	5.5	0.003**
OP / PP angle	15.5	5.0	12.5	4.0	0.000***
OP / MP angle	16.2	3.9	13.4	3.8	0.000***

Student's t-test Bonferroni correction; *p<0.05; **p<0.01; ***p<0.001; SD: Standard Deviation.

Table 4. Cephalometrics variables comparison for mixed dentition.

Variables	Gummy Smile		No Gummy Smile		p-value
	Mean	SD	Mean	SD	
Age	8.0	1.9	8.9	1.8	0.024*
Cranial Base					
S- Ar mm	27.9	24.4	29.2	22.7	0.019*
Ba- N mm	88.0	30.0	90.3	39.1	0.006**
SN / FH angle	8.4	27.7	6.9	29.1	0.019*
Maxillary					
NA/FH angle	93.7	30.0	90.8	26.6	0.000***
A to N- perpendicular line mm	3.0	2.3	0.7	22.6	0.000***
N-ANS mm	43.6	32.4	45.1	33.2	0.038*
S - PNS mm	41.0	32.7	42.3	2.5	0.041*
FH/PP angle	-1.8	31.5	0.03	0.2	0.000***
Mandible					
Ar-Go mm	38.4	34.8	40.7	36.8	0.006**
Lower goniac angle	76.0	3.7	72.9	54.4	0.008**
Upper goniac angle	51.6	32.8	50.0	36.0	0.039*
Ar-Go-Me angle	127.5	45.8	122.9	65.3	0.001**
PP/ MP angle	30.0	47.6	26.0	56.8	0.001**
Anteroposterior Relationship					
Wits appraisal	-0.01	38.6	-1.7	25.9	0.015*
ANB angle	6.6	3.5	4.8	21.8	0.004**
APDI	105.7	40.9	90.8	76.5	0.006**
Vertical Relationship					
ANS - Me (Lower facial height) mm	59.6	38.7	57.6	48.4	0.046*
S-Go (Posterior facial height) mm	63.4	38.2	66.9	42.6	0.000***
Posterior facial height / Anterior facial height %	63.1	38.7	66.6	48.0	0.001**
SN / FH angle	8.4	27.7	6.9	29.1	0.019*
FH / PP angle	-2.3	35.2	-0.4	25.9	0.006**
SN / MP angle	36.2	51.9	32.2	61.0	0.003**
FH / MP angle	27.7	39.1	25.2	5.1	0.024*
PP / MP angle	30.0	47.6	25.7	5.4	0.000***
OP / MP angle	16.2	41.5	12.4	39.1	0.000***
OP/ PP angle	15.6	61.3	13.5	51.4	0.087
OP / SN angle	17.0	50.5	13.1	38.8	0.000***

Student's t-test Bonferroni correction; *p<0.05; **p<0.01; ***p<0.001; SD: Standard Deviation.

The logistic regression analysis performed in the present study used the “forward technique” to explore the influence of cephalometric variables on a GS; Step 5 found that an increased OP/PP angle (OR=2.05, 95% CI: 1.30-3.22) and increased OP/MP angle (OR=2.32, 95% CI:1.42-3.75) can explain or influence 63% of the GS behavior (R²). The various models of the regression analysis are shown in Table 5.

Table 5. Logistic regression analysis.

Variables	Crude OR				Full Model Adjusted OR				Final Model OR			
	OR	p-value	95% CI		OR	p-value	95% CI		OR	p-value	95% CI	
FH / PP angle	0.52	0.045*	0.32	0.84	0.39	0.048*	0.17	0.89	0.37	0.036**	0.11	1.24
OP / PP angle	1.28	0.008**	1.13	1.45	2.01	0.007**	1.33	3.06	2.05	0.003**	1.30	3.22
PP / MP angle					0.58	0.032*	0.39	0.88	0.54	0.025	0.34	0.85
OP / MP angle	1.28	0.004**	1.11	1.47	2.02	0.008**	1.33	3.06	2.31	0.002**	1.42	3.75
Constant					0.00	0.035*			410.2	0.032		0.26

*p<0.05; **p<0.01; OR = Odds Ratio; 95%CI = 95% Confidence Interval; FH: Frankfort Plane; PP: Palatal Plane; OP: Conventional Occlusal Plane; MP: Mandibular Plane.

■ Discussion

This investigation sought to identify which cephalometric characteristics differed in children and adolescents with and without gummy smiles (GS and NGS, respectively). Identifying these differences in this population may help clinicians develop diagnostic protocols, allowing the early intervention of possible associated risk factors. Thus, early treatment could avoid the persistence of GS in adults and reduce the biological cost of some treatments, such as maxillofacial surgery, periodontal surgery, and botox [15-18].

It is vital to consider both clinical evaluation and cephalometric analysis when searching for factors related to GS [11,12,15,19-21]. Our study found that GS patients presented shorter angular and longitudinal skull base measurements than NGS patients. Regarding the maxilla, patients with GS presented maxillary prognathism. This finding was supported by some authors who indicated the presence of a GS and maxillary prognathism was strongly related [19,22,23].

GS patients were found to have structurally shorter mandibles. Additionally, the GS group presented mandibular retrognathism with a smaller SNB and an increased ANB angle. This finding relates the GS to Class II malocclusion, as other authors have found [22,14]. According to some authors [11,22,23], an increased ANB angle is mainly related to mandibular retrognathism. Based on the above, it is suggested that combined skeletal distocclusion (with maxillary and mandibular involvement) plays an important role in the presence of a GS in children and adolescents. This finding is similar to the reports of other authors [23,14], in which an association was found between Class II dental malocclusion and a GS. To the best of our knowledge, the present study is the first to evaluate these cephalometric characteristics in child and adolescent patients with and without a GS. This finding is of great clinical relevance because skeletal Class II malocclusion may be a factor for a more substantial possibility of GS in children and adolescents.

The relationship between vertical growth and patients with a GS has been previously reported [14,24,25]. From a vertical point of view, the negative value of the Frankfort horizontal (FH)/PP angle in patients with a GS suggests more cranial anterior rotation of the palatal plane in this group. In these patients, there is likely dental compensation with extrusion of the upper incisors that favors the development of a GS. Anti-clockwise rotation of the maxilla decreased PP/SN value in patients with an open bite [26]; vertical excess of the maxilla [2,27] and greater anti-clockwise rotation of the PP [28] have been found in patients with a GS. Our findings suggest that palatal rotation could constitute an important aspect of diagnosing GS.

In our study, GS patients had increased gonial angles and FH/MP and SN/MP angles, while the ramus height was shorter, suggesting that children and adolescents with GS appear to have a vertical growth pattern. This finding is related to studies by several authors [11,25,26,29,30] who also found vertical excesses in adult patients with a GS.

The occlusal plane is another critical variable involving dentoalveolar structures [31-33]. This investigation found statistically significant increases in OP/MP and OP/PP for patients in the GS group. Kaya and Uyar [34] found a statistically significant relationship between OP inclination and the amount of gingival visualization. Additionally, according to Câmara and Martins [33], the perception of smile attractiveness according to the amount of gingival display changes depending on the OP inclination. Therefore, assessing the OP in patients with a GS is essential and can help determine possible treatment plans.

A logistic regression analysis was performed to determine which variables might influence the presence of a GS in children and adolescents; it was found that the OP/PP angle and OP/MP angle influenced the presence of a GS. Patients with an increased OP/PP have twice the possibility of developing a GS than patients with an angle in regular measurements (OR 2.05, 95% CI: 1.30-3.22). Similarly, having an increased OP/MP angle twice the chance of developing GS as those with a normal angle (OR 2.32; 95% CI: 1.42-3.75). This suggests the etiological role of vertical alterations in a GS [14,24-26,35,36]. Clinicians should be attentive to the vertical relationships of their patients, as vertical excesses may be risk factors for a GS. It is essential to mention that this regression model explains 63% of the variation in the GS variable, leaving 37% of the variation explained by variables other than those studied in the present investigation. This may be a limitation, but simultaneously, it motivates the search for explanations other than cephalometric factors that may influence a GS.

Regarding sociodemographic variables, it has been found that GS is more common in women [7,19]. However, in our investigation, this difference by sex was not statistically significant, similar to previously conducted research with children and adolescents [10,21]. The age of the patients could be a determining factor for not finding the sexual dimorphism seen in adults. Differences in age in GS and NGS patients SG were found. Although in a case-control study, the groups should ideally be similar in all variables, the age difference suggests a decrease in the GS during the transition from mixed to permanent dentition. Other authors have reported this finding, and it has been associated with the development of perioral soft tissues [6,7].

Regarding habits, we found no direct relationship between its presence and the appearance of a GS; this differs from other findings in which a relationship was observed between the presence of a GS, oral breathing, and lingual interposition [28,36]. However, one limitation of the present study was that it was not possible to specify each habit due to the small number of patients in the sample with habits. Additionally, the study's retrospective design could cause some memory bias and under-registration of the habits. Another of the limitations of this study is that since it includes patients ranging from mixed dentition to permanent dentition, the age range is extensive (from 7 to 17 years old). This leads to a possible underrepresentation of any group, decreasing the possibility of comparisons between groups. To address this limitation, we analyzed only mixed dentition, in which we found significant differences similar to those in the entire population (Table 4). This finding suggests that the cephalometric differences between patients with and without a gummy smile are established since mixed dentition.

Although some of the statistically significant differences found may not be clinically relevant, major differences were found in the maxillary upper position, decreased mandibular size, mandibular retruded position, and hyperdivergent intermaxillary relationships. Multiple researchers have reported these differences [11,24] and suggest a correlation between hyperdivergent skeletal class II malocclusion and gingival smile.






Consequently, clinicians should prioritize preventive intervention targeting gingival smile management in individuals exhibiting this skeletal pattern.

In summary, the cephalometric differences in patients with and without a GS could be established in childhood and adolescence. The clinical implication of these findings is that it may be possible to detect, since mixed dentition, possible related factors for GS development, provide early diagnosis and treatment, and decrease the biological and economic cost of late corrective treatment.

■ Conclusion

Evidence of association between Class II skeletal malocclusion with maxillary prognathism - mandibular retrognathism and GS in children and adolescents was found. A hyperdivergent growth pattern in patients with a palatal plane rotating up and forward, posterior mandibular rotation, shorter ramus, or bigger gonial angle increases the possibility for GS. Finally, children and adolescents with increased OP/PP or increased OP/MP have twice the odds of developing GS compared to those with typical values.

■ Authors' Contributions

SMB		https://orcid.org/0009-0008-2484-2639	Investigation and Writing - Original Draft.
LVBJ		https://orcid.org/0000-0003-0612-4779	Conceptualization, Methodology, Writing - Original Draft, Writing - Review and Editing, and Project Administration.
OZN		https://orcid.org/0000-0003-4088-7753	Conceptualization and Methodology.
MPGF		https://orcid.org/0009-0000-4133-3256	Conceptualization, Methodology, and Data Curation.
DMBL		https://orcid.org/0000-0003-3679-1142	Conceptualization, Methodology, Formal Analysis, Data Curation, Writing - Original Draft, and Writing - Review and Editing.

All authors declare that they contributed to a critical review of intellectual content and approval of the final version to be published.

■ Financial Support

None.

■ Conflict of Interest

The authors declare no conflicts of interest.

■ Data Availability

The data used to support the findings of this study can be made available upon request to the corresponding author.

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