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## Progression of Periodontal Disease in Individuals with Cleft Lip, Alveolus and Palate: 8-Year Longitudinal Study

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### Abstract

**Objective:** To compare the progression of periodontal disease of sextants in individuals with cleft lip, alveolus and palate.

**Materials and Methods:** This longitudinal, cross-section study was performed following the STROBE Statement. The sample included the study was conducted on 30 individuals, of both genders, aged 22 to 53 years, with cleft lip, alveolus and palate. The following clinical parameters were evaluated: measurement of probing depth of the sulcus or Periodontal pocket (PD), Clinical Attachment Level (CAL), Gingival Index (GI), plaque index (PI), buccal Gingival Recession (GR) in six sites of all teeth, except for the third molars. Analysis of the variation of clinical parameters of each tooth over the study period in relation to its sextant was performed by the Kruskal-Wallis and Dunn test. The variation of clinical parameters during

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the study period and the age of individuals were correlated using the Spearman correlation test. All tests considered a significance level of 5%.

**Results:** The following means were found: PD 2.4 mm, CAL 2.6 mm, GI 0.9, PI 1.0 and BR 0.3 mm. There was increase in the mean PD and CAL ( $p<0.001$ ) and reduction of mean PI and GI ( $p<0.001$ ) over time, yet the variation between sextants was not statistically significant. **Conclusion:** During the study period, there was progression of periodontal disease in all sextants, without difference between the upper anterior sextant, cleft area and the others, suggesting that the cleft, *per se*, is not a risk factor for periodontal disease. **Clinical relevance:** the epidemiology and progression of periodontal disease in individuals with cleft lip and palate must be understood in order to establish effective therapeutic approaches.

## Keywords

Cleft Lip; Cleft Palate; Periodontal Disease; Gingivitis; Periodontitis

## Introduction

Cleft lip and/or palate is a craniofacial malformation that occurs during the embryonic development of face and palate, between the 4<sup>th</sup> and 12<sup>th</sup> weeks of intrauterine life. Its etiology is multifactorial, with association of genetic and environmental factors [1]. The esthetic and/or functional changes caused by this malformation are complex and require multidisciplinary treatment [1].

According to the latest epidemiological surveys, the prevalence of cleft lip and palate in Brazil is 1 in every 650 births 16.63 in every 10,000 in China, 0.82 per 1,000 births in Canada and 1.9 per 1,000 in Iran [1-4]. The presence of cleft lip and palate causes morbidity in affected individuals and psychosocial implications in their lives [5,6]. Rehabilitation aims not only at the integration of individuals, but also to provide their full social inclusion [1,5].

Periodontal health is defined as a state free of inflammatory periodontal disease, which means absence of inflammation associated with gingivitis or periodontitis [7]. The accumulation of subgingival biofilm represents only 20% of the direct risk of developing periodontitis, and the remaining 80% are associated with direct and indirect risk factors and modifying factors that may be responsible for the development of periodontal diseases [8]. Even though oral hygiene is the most important factor for the achievement and maintenance of periodontal health, additional factors must be addressed in the search for achievement or maintenance of periodontal health [7,9].

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Most studies evaluating the periodontal status of individuals with cleft used the teeth adjacent to the cleft area as unit of analysis, as well as in the contralateral region [10-16]. However, it is relevant to evaluate the sites of all teeth to avoid underestimating the prevalence of periodontal disease in these individuals, and also to prevent the disease from progressing in affected sites located in sextants that do not include the cleft.

Studies evaluating all sites of all teeth available in the literature were cross-sectional which does not allow assessment of the progression of periodontal disease [17-19]. This study aimed to compare the progression of periodontal disease of sextants in individuals with cleft lip, alveolus and palate. The study hypothesis was that the progression of periodontal disease in the cleft sextants is not different from the other sextants.

## Materials and Methods

This longitudinal, cross-section study was performed following the STROBE Statement Ethical aspects. This study was approved by the Institutional Review Board of the Hospital for Rehabilitation of Craniofacial Anomalies, University of São Paulo (HRAC/USP) (CAAE: 09990912.1.0000.5441). The patients were informed about the evaluation to which they would be submitted and signed an Informed Consent Form, confirming their agreement to participate in the study.

## Sample

400 individuals with cleft lip, alveolus and palate were examined in previous study, all non-smokers, without systemic diseases, aged 16 to 50 years, of both genders, who had no previous access to periodontal treatment [17]. After 8 years, the same individuals were contacted to participate in this study and the inclusion and exclusion factors were the same used for the previous study [17].

## Evaluation of Periodontal Status

During clinical examination, anamnesis and analysis of the medical record were performed to obtain information about each individual: age, genders, general health status, type of cleft and periodontal history. The periodontal parameters were evaluated on all teeth, except for the third molars, to diagnose the periodontal status of each individual and sextant.

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## Evaluation of Probing Depth and Clinical Attachment Level

- Measurement of probing depth of the sulcus or periodontal pocket: measured from the gingival margin to the base of the gingival sulcus/periodontal pocket. Six sites were analyzed in all teeth (MB, B, DB, ML, L, DL)
- Measurement of the clinical attachment level: measured from the cementoenamel junction to the base of the gingival sulcus/periodontal pocket. Alike the probing depth, six sites were evaluated per tooth

To achieve these measurements, a periodontal probe model COLOR CODED PROBE CP-ISUNC-PCPUNC15 (Hu-Friedy, Chicago, IL, USA) was used.

## Evaluation of Gingival Inflammation

The method used to evaluate the presence of inflammation was the Gingival Index (GI) recommended by Löe and Silness in 1963 which evaluates the gingival tissues around each tooth: distobuccal papilla, buccal margin, mesiobuccal papilla and gingival lingual margin [20]. The following criteria are used to assign the gingival index: 0= normal gingiva; 1= medium inflammation, slight color change, little edema, no bleeding on probing; 2= moderate inflammation, redness, edema and shiny surface, bleeding on probing; 3= severe inflammation, intense redness and edema, ulceration, tendency to spontaneous bleeding. The GI for each tooth is the arithmetic mean between values of each unit, and the GI for individuals is the arithmetic mean between all examined teeth.

## Evaluation of Presence of Dental Plaque

The plaque Index (PI) was assessed as described by Silness and Löe (1964), evaluating the presence of plaque in the cervical area of teeth [21]. The evaluation was performed using a dental mirror, dental explorer or periodontal probe and air drying. The following criteria are used to evaluate this plaque index: 0= no plaque in the cervical area of the tooth; 1= plaque adhered to the cervical area adjacent to the gingival margin, recognized only by running a probe over the tooth surface; 2= moderate accumulation of soft residues inside the gingival sulcus, and on the cervical area, visible with the naked eye; 3= abundance of soft matter inside the gingival pocket and on the cervical area. The PI per tooth was the arithmetic mean between scores of the different surfaces, and the PI per individual was the arithmetic mean between the plaque indices of evaluated teeth.

## Gingival Recession

Gingival Recession (GR) corresponds to the distance from the cementoenamel junction to the gingival margin in millimeters. It was evaluated on the buccal surface of all teeth with a periodontal probe model COLOR CODED PROBE CP-ISUNC-PCPUNC15.

All evaluated teeth were classified into sextants for later comparative analysis. Thus, teeth 17, 16, 15 and 14 were scored as belonging to sextant 1. Teeth 13, 12, 11, 21, 22 and 23 configured sextant 2 (cleft sextant). Teeth 24, 25, 26 and 27 were part of sextant 3. Sextant 4 was composed of teeth 37, 36, 35 and 34. Teeth 33, 32, 31, 41, 42 and 43 were included in sextant 5, while teeth 44, 45, 46 and 47 comprised sextant 6.

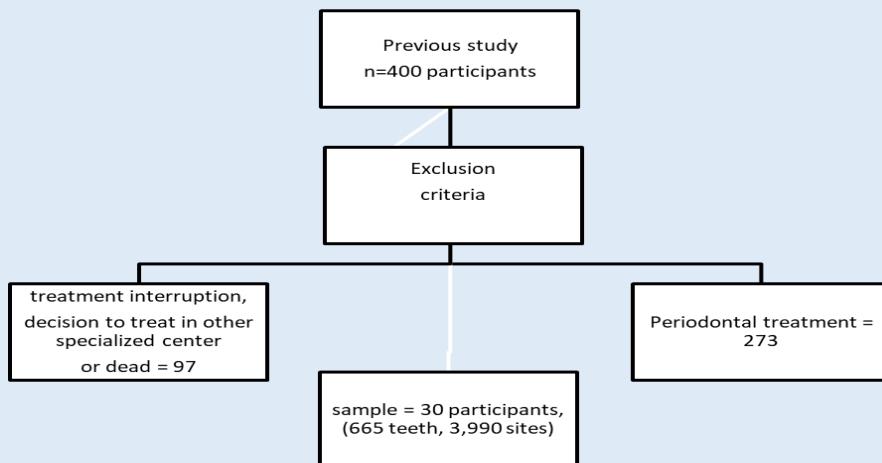
All these parameters were evaluated after 8 years (a) and initially (b) by three previously calibrated examiners. Thirty individuals were evaluated twice, with a 1-week interval. The intra and interexaminer agreement was greater than 89% (kappa test).

Analysis of the variation of clinical parameters of each tooth over the study period in relation to its sextant was performed by the Kruskal-Wallis and Dunn test.

The variation of clinical parameters during the study period and the age of individuals were correlated using the Spearman correlation test. All tests considered a significance level of 5%.

## Results

Among the 400 individuals assessed in previous study 97 did not attend to this new examination for reasons as hospital discharge, treatment interruption, decision to treat at another specialized center or death so they were excluded from the sample [17]. 273 individuals could not be included in this study because they did receive preventive procedures/periodontal surgical procedures between evaluations during last 8 years. Thus, the final sample of participants selected for this study included 30 individuals, aged 22 to 53 years, being 18 males and 12 females (Fig. 1).



**Figure 1:** Flowchart of the study.

Overall, 665 teeth (3,990 sites) were evaluated. Considering 0.861 as the largest standard deviation of evaluated parameters and a difference to be detected of 0.1 mm for alpha 5% and test power of 80%, a minimum n of 584 teeth was sufficient to perform all statistical analyses proposed. The means, medians and standard deviations of all periodontal parameters assessed after 8 years (a) and first assessment (b) are described in Table 1.

Variable	Mean	Standard Deviation	Median
PD <sub>a</sub>	2.3	0.7	2.2
PD <sub>b</sub>	2.4	0.5	2.3
CAL <sub>a</sub>	1.5	0.9	1.3
CAL <sub>b</sub>	2.6	0.8	2.5
GR <sub>a</sub>	0.2	0.8	0.0
GR <sub>b</sub>	0.3	0.8	0.0
PI <sub>a</sub>	1.5	0.6	1.0
PI <sub>b</sub>	1.0	0.8	1.0
GI <sub>a</sub>	1.7	0.4	2.0
GI <sub>b</sub>	0.9	0.9	1.0

PD= Probing Depth (mm); CAL= Clinical Attachment Level (mm); GR= Gingival Recession on buccal surface (mm); PI= Plaque Index (scores); GI= Gingival Index (scores)

**Table 1:** Means, medians and standard deviation of periodontal parameters in the evaluation after 8 years (a) and first evaluation (b).

The means and standard deviations observed per sextant in the examinations performed in 2007 and 2015 are shown in Table 2 and 3, respectively.

<b>Sext.</b>	<b>PD</b>	<b>CAL</b>	<b>GR</b>	<b>PI</b>	<b>GI</b>
1	$2.7 \pm 0.615$	$1.7 \pm 0.598$	$0.3 \pm 0.708$	$1.4 \pm 0.624$	$1.7 \pm 0.471$
2	$2.4 \pm 0.729$	$1.6 \pm 0.601$	$0.3 \pm 0.692$	$1.3 \pm 0.581$	$1.8 \pm 0.447$
3	$2.6 \pm 0.568$	$1.7 \pm 0.664$	$0.2 \pm 0.519$	$1.5 \pm 0.620$	$1.7 \pm 0.418$
4	$2.4 \pm 0.477$	$1.8 \pm 0.736$	$0.4 \pm 0.843$	$1.5 \pm 0.595$	$1.8 \pm 0.412$
5	$2.2 \pm 0.526$	$1.5 \pm 0.675$	$0.3 \pm 0.768$	$1.6 \pm 0.689$	$1.8 \pm 0.446$
6	$2.4 \pm 0.521$	$1.7 \pm 0.628$	$0.4 \pm 0.795$	$1.6 \pm 0.591$	$1.8 \pm 0.410$

Sext. = Sextant; PD= Probing Depth (mm); CAL= Clinical Attachment Level (mm); GR= Gingival Recession on buccal surface (mm); PI= Plaque Index (scores); GI= Gingival Index (scores).

**Table 2:** Means and standard deviations of periodontal parameters per sextant, evaluated after 8 years.

<b>Sext.</b>	<b>PD</b>	<b>CAL</b>	<b>GR</b>	<b>PI</b>	<b>GI</b>
1	$2.5 \pm 0.449$	$2.8 \pm 0.828$	$0.5 \pm 1.039$	$1.1 \pm 0.761$	$0.9 \pm 0.765$
2	$2.4 \pm 0.482$	$2.4 \pm 0.594$	$0.2 \pm 0.643$	$0.7 \pm 0.782$	$0.8 \pm 0.716$
3	$2.6 \pm 0.496$	$2.9 \pm 0.852$	$0.4 \pm 0.932$	$1.0 \pm 0.741$	$0.9 \pm 0.714$
4	$2.4 \pm 0.542$	$2.7 \pm 0.871$	$0.4 \pm 0.872$	$1.0 \pm 0.759$	$0.9 \pm 0.701$
5	$2.2 \pm 0.522$	$2.4 \pm 0.844$	$0.2 \pm 0.709$	$1.0 \pm 0.881$	$1.0 \pm 0.782$
6	$2.4 \pm 0.514$	$2.8 \pm 0.901$	$0.4 \pm 1.000$	$1.0 \pm 0.790$	$0.9 \pm 0.714$

Sext. = Sextant; PD= Probing Depth (mm); CAL= Clinical Attachment Level (mm); GR= Gingival Recession on buccal surface (mm); PI= Plaque Index (scores); GI= Gingival Index (scores).

**Table 3:** Means and standard deviations of periodontal parameters per sextant, initially evaluated.

Table 4 presents the comparative analysis of periodontal parameters of all sextants in the two periods evaluated. There was statistically significant difference between the parameters CAL, PI and GI in all sextants, except for PD in sextants 1, 2, 3 and 4 and GR in sextants 2, 4 and 5.

<b>Sext.</b>	<b>PD</b>	<b>CAL</b>	<b>GR</b>	<b>PI</b>	<b>GI</b>
1	0.850	<0.001*	0.048*	0.003*	<0.001*
2	0.502	<0.001*	0.186	<0.001*	<0.001*
3	0.160	<0.001*	0.021*	<0.001*	<0.001*
4	0.056	<0.001*	0.866	<0.001*	<0.001*
5	<0.001*	<0.001*	0.102	<0.001*	<0.001*

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6	0.001*	<0.001*	0.639	<0.001*	<0.001*
*p<0.05 - Statistically significant difference					

**Table 4:** Comparative analysis of means concerning the difference in Probing Depth (PD), Clinical Attachment Level (CAL), Recession on buccal surface (GR), plaque index (PI) and gingival index in the two evaluations (a and b) per sextant (sext.). p values - Wilcoxon test.

The comparisons between the two evaluations did not evidence statistical difference in parameters regarding their variation over time, except for CAL (p=0.011) (Table 5).

Variable	p
PD	0.145
CAL	0.011*
GR	0.139
PI	0.156
GI	0.683

\*p<0.05 - Statistically significant difference

**Table 5:** Comparative analysis of means concerning the difference in Probing Depth (PD), Clinical Attachment Level (CAL), Recession on buccal surface (GR), Plaque Index (PI) and gingival index concerning the variation over time (Kruskal-Wallis test).

In Table 6, the mean values of each parameter obtained after 5 years were compared with means of the same parameters obtained in the initial evaluation and there was a statistically significant increase in probing depth and clinical attachment level. The measurements of buccal recession did not show statistically significant difference. The plaque index and gingival index scores were significantly lower.

Variable	N	Mean	Standard Deviation	p
PD <sub>a</sub>	665	2.3	0.567	<0.001
PD <sub>b</sub>	665	2.4	0.519	
CAL <sub>a</sub>	665	1.4	0.752	<0.001
CAL <sub>b</sub>	665	2.6	0.839	
GR <sub>a</sub>	665	0.3	0.796	0.653
GR <sub>b</sub>	665	0.3	0.861	
PI <sub>a</sub>	665	1.4	0.579	<0.001
PI <sub>b</sub>	665	1.0	0.806	
GI <sub>a</sub>	665	1.6	0.309	<0.001
GI <sub>b</sub>	665	0.9	0.738	

**Table 6:** Comparison of means obtained for Probing Depth (PD) (mm), Clinical Attachment Level (CAL) (mm), Buccal Recession (GR) (mm), Plaque Index (PI) (score) and Gingival Index (GI) (score) in the periods after 5 years (a) and first evaluation (b) -Wilcoxon test.

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## Discussion

The longitudinal evaluation of clinical parameters over time in the two study periods showed significant increase in the clinical attachment levels and probing depth in that period. However, the plaque and gingival indices were significantly lower.

It is possible to correlate signs and symptoms of periodontal disease with factors that predispose to tissue destruction using parameters based on the degree of inflammation and involvement of the supporting tissue, besides indicators of the oral hygiene level. The most commonly used in epidemiological studies are probing depth, clinical attachment level, plaque and gingival indices [10,11,22,23].

The therapies performed for the treatment of cleft lip and palate can cause some harmful effects in the oral cavity, such as presence of multiple scars, shallow vestibule, absence of keratinized mucosa and deficiency of bone tissue in teeth close to the cleft area, usually accompanied by recession [16,24-27]. Some authors have demonstrated that individuals with cleft lip and palate are more susceptible to the development of periodontal diseases, and that the cleft per se would be a risk factor for the development of periodontal disease. Conversely, other authors reported that teeth adjacent to the cleft do not differ in the prevalence of periodontal disease compared to the others [10,11,17,23,28,29].

This study included only individuals with cleft affecting the alveolar ridge, to assess if the cleft per se would be associated with the occurrence of periodontal changes over time. Regarding the methodology, it was decided to assess the periodontal parameters in all teeth, with six sites per tooth, avoiding overestimating the prevalence [30].

Another factor that increases the sensitivity of analysis is the use of gingival index proposed by Löe and Silness [20] and the plaque index proposed by Silness and Löe [21]. Unlike the dichotomous index used in the study of Huynh-Ba, which only identifies the presence or absence of plaque and bleeding on probing, the indices used in the present study are divided into scores from 0 to 3, which qualify the presence of plaque or gingival inflammation depending on the severity of each case [15].

The use of mean of clinical parameters for each tooth in the statistical analyses rather than a general mean for each patient is also a methodological aspect of this study that favors the sensitivity of results. According to Eke and collaborators the use of mean values in statistical analyses tends to underestimate the true prevalence of the phenomenon studied [30,31]. The fact that periodontal pathologies do not affect all teeth equally is also a reason for individualized analysis per tooth, since values outside the normal standard in specific sites may

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be diluted and masked when the individual's mean values are obtained. Even though a more detailed methodology has the benefit of greater accuracy in results, it also poses difficulty in the comparison with results from studies with less detailed methodology [32].

The significant increase in the clinical attachment values and probing depth in the study period showed worsening of the main periodontal characteristics. These results were also found by Salvi, et al., who suggested that this worsening of periodontal health is related to the lack of frequent preventive programs and treatments. In addition to plaque control, the repetition of oral hygiene instructions and patient motivation is more efficient to improve the periodontal clinical parameters and the more periodontal maintenance sessions, the better the values of clinical parameters evaluated [23,33,34].

The scores of plaque and gingival indices in this study showed significantly lower values over time. This possibly occurred because the first measurements were obtained without any specialized periodontal care. In the first evaluation, the patients received oral hygiene instructions.

The regular interruption and frequent removal of bacterial deposits accumulated in the gingival margin are fundamental for the prevention of plaque-induced periodontal diseases [35]. Even though oral hygiene remains the most important factor for the achievement and maintenance of periodontal health, it should not be the only focus of attention, and it is also important to consider additional factors [7,9]. This can be observed in the present study, in which even though there was a reduction in plaque and gingival indices, it was not enough to avoid the progression of periodontal disease.

Another hypothesis for this difference in results is the fact that plaque and gingival indices represent a momentary and easily reversible condition, while the presence of destruction of periodontal supporting tissues, identified mainly in the measurements of clinical attachment level, represent the true sequel of an existing or previous disease [35]. The mean score of the gingival index corresponds to mild gingivitis, as also reported by Teja, et al., [13].

The comparison of variations in clinical parameters between sextants for each tooth showed no statistically significant difference for any parameter, except for the clinical attachment level. The sextants 6 and 3 showed significantly higher values than sextant 2. That is, not only the cleft sextant shows no increase in the values of parameters evaluated in relation to the others, but also presents a significant decrease in the clinical attachment level in relation to sextants 6 and 3 (Table 2,3). This agrees with other studies, even though some present different methodologies impairing any direct comparisons [11,12,17,18,28].

Similar to other studies in which there is a tendency to increase in periodontal disease with the increase in age [17,30]. This study revealed a tendency to increased values of clinical attachment level over the years. The comparisons between all sextants showed that the cleft per si is not a risk factor for decrease of clinical attachment level, but clinical studies with longitudinal follow-up with a larger sample should be performed.

## Conclusion

During the study period, progression of periodontal disease was observed in all sextants, without difference between the sextant of the cleft area and the others, suggesting that the cleft itself is not a risk factor for periodontal disease.

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## Authors Contributions

Conception: Ana Lúcia Pompéia Fraga de Almeida, Methodology: Bruno Nicoliello Moreira, Ana Lúcia Pompéia Fraga de Almeida, Formal analysis and investigation: Bruno Nicoliello Moreira, Bárbara Fortunato Prohmann, Ana Lúcia Pompéia Fraga de Almeida, Writing - original draft and preparation: Bruno Nicoliello Moreira, Ana Lúcia Pompéia Fraga de Almeida, Writing - review and editing: Nicole Rosa de Freitas, Luisa Belluco Guerrini, Gisele da Silva Dalben, Ana Lúcia Pompéia Fraga de Almeida, Funding acquisition: Ana Lúcia Pompéia Fraga de Almeida, Bárbara Fortunato Prohmann, Bruno Nicoliello Moreira, Resources: Ana Lúcia Pompéia Fraga de Almeida, Supervision: Ana Lúcia Pompéia Fraga de Almeida.

## Ethics Approval

This study was approved by the Institutional Review Board (CAAE: 09990912.1.0000.5441) and was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki. The patients were informed about the evaluation to which they would be submitted and signed an Informed Consent Form was obtained from all subjects involved in the study.

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## Conflict of Interest

The authors declare non-financial conflict of interest.

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