



# Dental anomalies in cleft lip and palate

## A case–control comparison of total and outside the cleft prevalence

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### Abstract

This study's objective was to compare the total and outside the cleft prevalence of dental anomalies (DA) between patients with cleft lip and palate (CLP) and a control group. This retrospective cross-sectional study was done under a case–control design. The case group consisted of 192 non-syndromic patients with complete CLP, while the control group included 411 patients. All subjects had orthopantomography, intra, and extraoral photographs. The prevalence of dental agenesis, supernumerary teeth, impacted teeth, dental transposition, and microdontia were compared using a chi-squared test ( $P < .05$ ). Next, a second test was made, but only the anomalies outside the cleft were considered for this study. Total prevalence was 89.1% for cases, and 20.9% for controls ( $P < .01$ ). The prevalence of each DA was significantly higher for the case group. In the analysis of DAs outside the cleft, the total prevalence was still significantly associated ( $P < .01$ ); however, only dental agenesis was statistically significant ( $P < .01$ ). Further analysis found that a high rate of upper premolar absence ( $P < .01$ ) could explain this event. Patients with CLP have a higher prevalence of DAs compared to controls. After considering only the DAs outside the cleft, the total prevalence remains significantly higher. However, this phenomenon is explained mainly by the elevated prevalence of upper premolars' agenesis. This study's results suggest that environmental factors are behind the high prevalence of DAs in subjects with CLP.

**Abbreviations:** CI = confidence interval, CLP = cleft lip and palate, DA = dental anomalies, OR = odds ratio.

**Keywords:** cleft lip, cleft palate, tooth abnormalities

### 1. Introduction

Cleft lip and palate (CLP) is a condition of multifactorial etiology. Patients affected by oral clefts frequently present other anomalies added to this condition, like audiological,<sup>[1]</sup> ocular, central nervous system, and even gastrointestinal and urogenital alterations.<sup>[2]</sup>

Concerning the stomatological system, patients with CLP have a high prevalence of dental anomalies (DA), particularly dental agenesis, supernumerary teeth, and morphologic irregularities of the crown.<sup>[3]</sup>

Genes influence CLP and DAs development.<sup>[4,5]</sup> The available genetic data has led to the belief that a hereditary etiology could be behind the high prevalence of DAs in individuals with CLP.

However, some authors theorize that, in subjects with CLP, DAs are a physical consequence of the cleft.<sup>[6]</sup> In addition to this, it has been suggested that environmental factors such as surgical procedures performed on patients with CLP could trigger the appearance of DAs.<sup>[7,8]</sup>

This study's objective was to compare the total and outside the cleft prevalence of DA between patients with CLP and a control group. Afterward, this article discusses the findings considering the current theories for DA etiology in subjects with CLP.

### 2. Methods

This retrospective, cross-sectional study was done under a case–control design. The case group was taken from a CLP specialized clinic archives, while the controls were taken from an orthodontic clinic of a dental school; both clinics sited in Merida, Yucatan, Mexico.

The case group conformed non-syndromic patients with complete CLP (lip, alveolus, and palate); none had gone under alveolar bone graft surgery. All individuals that fulfill the above criteria were included in the case group. Controls were randomly selected. All subjects (cases and controls) had complete

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The authors report no conflicts of interest.

The datasets generated during and/or analyzed during the present study are available from the corresponding author on reasonable request.

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records, including orthopantomography and intra and extraoral photographs. None of the patients had previously undergone orthodontic treatment.

Under an Institutional Ethics Committee's approval (CEI-14-2019), subjects' data were obtained from their respective records. A total of 192 patients were included in the case group, and 411 patients were included in the control group.

Data for the study was collected and registered by a single investigator. Each patient's orthopantomography and photographs were analyzed to identify DAs and the cleft's type and location. The following DAs were considered: dental agenesis, supernumerary teeth, impacted teeth, dental transposition, and microdontia. The criteria used to identify DA are described elsewhere.<sup>[9]</sup>

The prevalence of total and individual DA was calculated for each group, and they were compared to look for associations ( $P < 0.05$ ) using a chi-squared test. Odds ratio (OR) and confidence intervals (CI) were also estimated. In the case group, a chi-square test was carried out to assess DAs by gender and compare subjects with unilateral against those with bilateral clefts.

Additionally, to identify whether patients with CLP had a higher prevalence of DA in areas non-adjacent to the cleft, a new test was performed, including only the anomalies outside the cleft. This new analysis included the total prevalence, only mandibular anomalies, and individual DAs tests. For dental agenesis, the prevalence of absent upper premolars and mandibular teeth was also calculated. In subjects with unilateral CLP, an analysis of sides was made, excluding DAs of the affected side.

Given that upper lateral incisors were used to identify microdontia and that all dental transposition cases involved either the maxillary canine or the upper lateral incisors, to avoid bias, only patients with unilateral CLP were used to compare the prevalence outside the cleft for these two DAs. All statistical procedures were performed using the SPSS statistical software (Version 24.0., IBM Corp., Armonk, NY).

### 3. Results

A total of 192 patients made up the case group, 105 (54.7%) males and 87 (45.3%) females, with an average age of  $11.35 \pm 2.98$  years. Meanwhile, 411 patients were included in the control group, 274 females (66.7%) and 137 males (33.3%); their mean age was  $16.37 \pm 5.12$  years. The prevalence of DAs was significantly associated between groups; for the cases, the prevalence was 89.1% ( $n = 171$ ), and for the controls was 20.9% ( $n = 86$ ) ( $P < .01$ , OR = 30.77). Analyzing by individual DAs, all prevalence values in the case group were higher than the control's, and a significant association was found for all of them (Table 1). Dental agenesis was the most frequent DA in the case group, followed by microdontia (Table 1).

A total of 252 teeth of the patients with CLP were found missing due to dental agenesis; 60.3% of them ( $n = 152$ ) were upper lateral incisors. The most frequently impacted teeth were the upper lateral incisors (53.65%,  $n = 22$ ), followed by the maxillary canines (19.51%,  $n = 8$ ) and central incisors (19.51%,  $n = 8$ ). The most common transposition involved the upper canine with the first premolar (84.21%,  $n = 16$ ), followed by the upper canine with the lateral incisor (10.52%,  $n = 2$ ).

Concerning the comparison between genders, no statically significant associations were found for any DA (Table 2). Regarding the type of cleft, 139 subjects presented unilateral CLP (72.4%) and 53 presented bilateral CLP (27.6%); subjects with unilateral cleft had an 87.8% prevalence, while for patients with a bilateral cleft was 90.6%, no statistical association was found ( $P = .51$ ).

Once excluding DAs adjacent to the cleft, the case group total prevalence (44.3%;  $n = 85$ ) was still significantly higher than the controls ( $P < .01$ ); however, on the individual DA analysis, only dental agenesis showed a statistically significant association in the comparison between groups, 35.9% was for the case group and 5.1% for the controls' ( $P < .01$ ). Mandibular agenesis showed no significant association ( $P = .42$ ) (Table 3). The most frequently absent teeth outside the cleft were the upper second premolars (58%,  $n = 58$ ), followed by the upper first premolars (20%,  $n = 20$ ).

Finally, in the analysis by sides, the patients with right clefts showed 35% DA on the opposite side, compared with the 36.7% of the individuals with a cleft on the left side; no significant association was found ( $P = .83$ ).

## 4. Discussion

The prevalence of DAs in patients with CLP was significantly higher than in controls with elevated OR; these results concur with others reported in the literature.<sup>[3,8,10-15]</sup>

Each individual DA studied in this paper presented significantly higher prevalence values in patients with CLP than the controls. Dental agenesis (66.1%) and microdontia (26.6%) were the most prevalent DAs, which is consistent with other studies.<sup>[15,16]</sup> In the comparison by gender, no DA was significantly associated ( $P = .48$ ), as also reported in many published studies.<sup>[11,15-20]</sup> Similarly, no association was found between patients with unilateral against those with a bilateral cleft ( $P = .51$ ), an association that other authors have reported.<sup>[10,18]</sup> However, it should be noted that only patients with complete clefts were compared in the present study, and other papers report differences when comparing individuals with complete versus incomplete clefts.<sup>[21-23]</sup>

### 4.1. Dental agenesis

Dental agenesis is by far the most studied DA in patients with CLP, perhaps because it is the most prevalent.<sup>[10,15,16,18]</sup> The only

**Table 1**

Prevalence of dental anomalies in patients with cleft lip and palate compared with a control group.

Dental anomalies	CLP		Control		P	OR	CI
	N = 192	%	N = 411	%			
Total prevalence	171	89.1	86	20.9	<.01*	30.77	18.44–51.33
Agenesis	127	66.1	21	5.1	<.01*	36.28	21.33–61.71
Microdontia	51	26.6	29	7.1	<.01*	4.76	2.9–7.81
Supernumerary teeth	19	9.9	15	3.6	<.01*	2.89	1.44–5.83
Impacted teeth	33	17.2	31	7.5	<.01*	2.54	1.5–4.29
Transposition	17	8.9	10	2.4	<.01*	3.89	1.74–8.67

CI = confidence interval, CLP = patients with cleft lip and palate, OR = odds ratio.

\*Statistically significant ( $P < .05$ ).

**Table 2**  
Prevalence of dental anomalies by gender in subjects with cleft lip and palate.

Dental anomalies	Female		Male		P	OR	CI
	N = 87	45.31%	N = 105	54.69%			
Total prevalence	79	90.8%	92	87.6%	.48	0.71	0.28–1.81
Agenesis	63	72.4%	64	61%	.09	0.59	0.32–1.09
Supernumerary teeth	5	5.7%	14	13.3%	.08	2.52	0.87–7.31
Impacted teeth	18	20.7%	15	14.3%	.24	0.63	0.3–1.35
Transposition	7	8%	10	9.5%	.72	1.2	0.43–3.3
Microdontia	18	20.7%	33	31.4%	.09	1.75	0.9–3.4

CI = confidence interval, OR = odds ratio.

exception the authors could find is a study on Colombian subjects where microdontia's prevalence was higher than agensis.<sup>[12]</sup> The prevalence for this dental abnormality ranges from 50% up to 87.8%.<sup>[10,12,13,15,16,18,19,24–26]</sup>

There is no doubt that upper lateral incisors are the most absent teeth in subjects with CLP, usually followed by upper second premolars,<sup>[10,16,21,24–27]</sup> a situation also found in the patients of this study.

Some authors believe that, due to the lack of fusion of the segments, the mesenchyme tissue in the cleft area is insufficient to support the formation of tooth buds. On the other hand, low blood supply and physical damage to the dental buds due to early surgeries are other proposed etiological factors for dental agensis, particularly in the premolar area.<sup>[28]</sup> In 2000, Lekkas et al published that they did not find absent teeth in the posterior segment of the upper arch of 266 unoperated patients with CLP in Indonesia.<sup>[7]</sup> Also, Korolenkova et al in 2019 determined that surgery type and timing are related to dental agensis in subjects with CLP.<sup>[8]</sup>

Given CLP's multifactorial etiology, complex combinations of environmental and hereditary factors may be at work to generate the different outcomes seen in each ethnic group.

Regarding the analysis of outside the cleft DAs, only dental agensis showed a significantly associated prevalence when compared with the controls. Its prevalence outside the cleft was 35.9%, similar to the 31.2% reported by Sá et al in Brazil in 2016.<sup>[22]</sup> No significant association was found regarding mandibular agensis; therefore, the upper premolars' absence mainly explains this high value, as the statistical analysis shows ( $P < .01$ ). This is an important finding because, in the Mexican population, the lower second premolar is the most frequently absent tooth.<sup>[9]</sup> The mandibular agensis comparison demonstrates that the prevalence of agensis of lower teeth is similar

between groups; meanwhile, the prevalence of upper premolars agensis is higher in subjects with CLP (OR = 47.88).

Consequently, it seems that the hereditary factors that influence the regular agensis patterns in this population are the same in the patients with CLP, at least for the lower arch. It seems unlikely that the upper premolars absence has the same etiological explanation; it is more reasonable to explain this phenomenon with environmental factors. Adding to this, all the other DAs studied did not present significant associations for their outside the cleft prevalence values, which is particularly important because some of them are genetically regulated.<sup>[29–31]</sup>

#### 4.2. Microdontia

Microdontia of upper lateral incisors was the second most prevalent DA in patients with CLP. Usually the second place in prevalence in individuals with CLP is occupied either by microdontia<sup>[15,16]</sup> or supernumerary teeth.<sup>[3,14,32]</sup>

Given that dental agensis and microdontia are different manners of dental mass reduction, the insufficient mesenchyma theory applies to both of them.<sup>[28]</sup> Some authors hypothesize that microdontia on the contralateral side of subjects with unilateral CLP is an expression of an unsuccessful bilateral cleft.<sup>[16,32]</sup> On the other hand, from a genetic point of view, microdontia is seen as a variable expression of dental agensis, and it has been proven that patients with a missing upper lateral incisor have high odds of ending up with a microdontic lateral incisor on the contralateral side.<sup>[29]</sup> Therefore, given that no significant association between groups was found when upper laterals inside the cleft microdontic were excluded, it is more likely that this high prevalence of microdontia is related to the same dental agensis hereditary mechanism, and not necessarily with the development of a cleft. Nevertheless,

**Table 3**  
Prevalence of dental anomalies outside the cleft in patients with cleft lip and palate compared with a control group.

Dental anomalies	CLP		Control		P	OR	CI
	N = 192	%	N = 411	%			
Total prevalence	85	44.3	86	20.9	<.01*	3	2.07–4.35
Mandibular anomalies	9	4.7	30	7.3	.22	0.62	0.29–1.34
Agenesis	69	35.9	21	5.1	<.01*	10.41	6.13–17.67
Upper premolars	50	26.0	3	0.7	<.01*	47.88	14.7–155.93
Mandibular agensis	8	4.2	12	2.9	.42	1.44	0.58–3.59
Supernumerary teeth	12	6.2	15	3.6	.15	1.76	0.8–3.83
Impacted teeth	11	5.7	31	7.5	.41	0.74	0.36–1.51

Dental anomalies	UCLP		Control		P	OR	CI
	N = 139	%	N = 411	%			
Microdontia	6	4.3	29	7.1	.25	0.59	0.24–1.46
Transposition	8	5.8	10	2.4	.05	2.44	0.94–6.33

CI = confidence interval, CLP = patients with cleft lip and palate, OR = odds ratio, UCLP = patients with unilateral cleft lip and palate.

\*Statistically significant ( $P < .05$ ).

microdontia's prevalence in this study (26.6%), although similar to the Turkish population (25%),<sup>[16]</sup> is small compared with other studies that ranged from 34.73% to 51.9%.<sup>[12,15,17,24]</sup> So, care must be taken since each population has a different hereditary background.

#### 4.3. Supernumerary teeth

Concerning supernumerary teeth, given that no difference was found outside the cleft, the elevated prevalence must be explained by the increment inside the cleft area. Some authors believe that this could be because of a fragmentation of the dental lamina during the cleft formation.<sup>[33]</sup> There is an increase of 3.7% of total prevalence when patients with supernumerary teeth located inside the cleft are included, almost identical to the 3.8% found in a Brazilian population.<sup>[34]</sup> This increment explains the significant association between patients with CLP and controls in the overall comparison.

#### 4.4. Impacted teeth

Regarding impacted teeth, the case group's prevalence was 17.2%, similar to the 18.9% found in French patients with CLP,<sup>[10]</sup> but higher than the Colombian population (12.3%).<sup>[12]</sup> Similar to the supernumerary teeth case, impactions increment around the cleft area, concurring with the proven significant association between the presence of oral clefts and this DA.<sup>[28]</sup> Evidence shows that patients with CLP have a delay in tooth eruption due to lack of space, especially around the cleft area.<sup>[35]</sup> Another factor is the increment of supernumerary teeth in the area producing obstacles in the eruption path.

In French patients with CLP, the most frequently impacted teeth were the maxillary canines.<sup>[10]</sup> However, upper laterals occupy first place in this study. Also, central incisors have the same frequency of impaction as canines. Antunes et al (2018) recommend that secondary bone graft be done between 5 and 7 years old to promote eruption of the lateral incisor.<sup>[36]</sup> In this study, all patients with CLP lacked alveolar bone graft, explaining the high prevalence of upper laterals' impaction. The other papers that report impaction in patients with CLP do not describe this variable.<sup>[10,12,34]</sup> Above all, this DAs analysis gives a glimpse of how disruptive the cleft is to the occlusion. Just considering the number of laterals missing due to agenesis, impaction prevalence could be a lot higher.

#### 4.5. Dental transposition

Finally, dental transposition prevalence (8.9%), although high contrasted with the controls, is low compared with reports addressing patients with CLP from the United States (14.7%)<sup>[17]</sup> and Jordania (30.8%).<sup>[24]</sup> On the other hand, its prevalence inside the cleft (4.7%) is similar to that of a Brazilian population (3.4%).<sup>[34]</sup> Dental transposition etiology is multifactorial, including genetic<sup>[30,31]</sup> and environmental factors.<sup>[31]</sup> Since almost all dental transpositions affected the maxillary canines (mainly with the first premolar), only unilateral subjects were included in its analysis. The result was a marginally significant association ( $P = .05$ ) that contributes to the debate about how genes influence the presence of DAs in subjects with CLP. These results suggest the need for further studies with broader samples given dental transposition low prevalence and multifactorial etiology.

#### 4.6. Limitations of the study

The facts that only patients with complete CLP were included in the study and that all of them lacked alveolar bone graft are limitations to consider. Regarding the former, some studies have

found associations for types of cleft and DAs.<sup>[21–23]</sup> Concerning the latter, the different types of surgeries any patient with CLP is exposed to, has diverse effects, and might impact the presence of different DA.<sup>[8]</sup>

## 5. Conclusion

Patients with CLP have a higher prevalence of DA compared to controls. After considering only the DA outside the cleft, the total prevalence remains significantly higher. However, this phenomenon is explained mainly by the elevated prevalence of upper premolars' agenesis, while microdontia, supernumerary, impacted, and transposed teeth prevalence values are not different from the controls. This study's results suggest that environmental factors account for the high prevalence of DAs in subjects with CLP.

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