

Original Research Article

Association of the profile of individuals with cleft lip/palate with the beginning of orthopedic/orthodontic treatment

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Abstract

Introduction: Cleft lip and palate (CLP) is the most frequent congenital malformation among the anomalies of the head and neck. The orthopedic/orthodontic treatment is included in the rehabilitation of these individuals, however there is no consensus in the literature regarding the ideal time for its beginning. **Objective:** To verify and characterize the profile of individuals with CLP treated at a reference hospital of the northeast of Brazil from 1998 to 2013 and its association with the beginning of the orthopedic/orthodontic treatment. **Material and methods:** Through direct observation of medical records, panoramic radiograph, and study casts of 323 individuals, data regarding sex, cleft type, origin and age of beginning of the orthopedic/orthodontic treatment were surveyed and analyzed using the chi-square test, considering a 5% level of significance. **Results:** Most of the individuals had trans-foramen and the unilateral cleft was the most prevalent ($p < 0.05$). Females were statistically more affected by post-foramen cleft and males by trans-foramen cleft ($p < 0.05$). Most individuals with trans-foramen cleft and post-foramen cleft started the orthopedic/orthodontic treatment between 8 and 12 years old ($p < 0.05$). No statistically significant differences occurred relating the beginning

of the orthopedic/orthodontic treatment with geographic origin and sex of, although most of them have started treatment at late mixed dentition. **Conclusion:** Regardless of gender, origin, or cleft type, most patients started orthopedic treatment up to 12 years-old, an age considered ideal by most protocols. Unilateral and trans-foramen cleft were the most prevalent cleft types. post-foramen cleft affected more females, while trans-foramen cleft affected more males.

Introduction

Cleft lip and palate (CLP) is the most common congenital malformation of the head and neck and the most studied face alteration in recent decades [8]. These malformations occur because of a sequence of changes in the development and/or aging of the embryonic processes. CLP etiology is very complex, involving the participation of genetic and environmental factors [28].

The individuals with CLP need a comprehensive and multidisciplinary care, including grafting for correction of alveolar bone defect, recommended by some authors to be held between 9 and 12 years, since the rate of clinical success is greater before the eruption of the maxillary permanent canine [13, 17]. The secondary alveolar graft is the gold standard treatment in most of the specialized centers, allowing that the teeth next to the cleft are repositioned and moved to the adequate sites without compromising the periodontal health [29].

Additionally, an orthopedic treatment previous to the secondary alveolar graft is indicated, playing a key role in the improvement of the graft access for, closing of soft tissues, correction of the central incisors' misalignment, and repositioning of the dislocated maxillary alveolar segments [13]. For this purpose, the maxillary expansion through Haas expander is one of main approaches used, aiming at reestablishing the transversal dimension of the maxilla, correcting the crossbite and to measure the cleft site [9, 30]. Compared with the slow expansion, the rapid maxillary expansion results in a shorter treatment time [1].

The protocols differ as to the ideal period for the beginning of the orthopedic treatment in individuals with cleft, although some studies indicate that the treatment onset occurs at the late mixed dentition (8 to 12 years) [9, 22] or at early mixed dentition (6 to 8 years) [3]. Although the literature lacks studies on this subject, some authors advocate that the orthopedic treatment at late mixed dentition reduces treatment time and cost, keeping the effectiveness [9, 24]. On the other hand, some treatment centers, such as the Center

for the Integrated Care of Individuals with Cleft Lip/Palate, in Curitiba (Brazil), adopts the beginning of the treatment at early mixed dentition [3]. The beginning of orthopedic therapy in individuals with CLP after the 12 years is considered inappropriate [21, 24]. The rationale behind this fact is that although the ossification of the median palatal suture is usually not finished [4], the indication of the alveolar grafting is around that age [17, 21, 24] and the peak of pubertal growth may have been taken place [20].

The literature lacks studies on the profile of patients with CLP, especially in the Northeast region of Brazil. In addition, no studies were found relating the variables sex, cleft type, and origin of the individuals with the time of beginning of the orthopedic treatment. Therefore, this observational, cross-sectional, and retrospective study aimed to verify and characterize the profile of individuals with cleft lip and palate treated in a referral hospital in the northeast of Brazil in the period from 1998 to 2013 and the association of the profile with the orthopedic/orthodontic treatment, since few studies describe such essential data for the establishment of an ideal treatment of these individuals.

Material and methods

This study was submitted and approved by the Institutional Review Board of the Albert Sabin Child Hospital of Fortaleza, under protocol #182.843.

This was an observational, transversal, and retrospective study characterized by the direct observation of files, panoramic radiographs, and study models of a spontaneous demand sample of individuals with CLP treated at the Section of Orthodontics of a reference northeast Brazilian hospital from the years between 1998 and 2013.

The survey of the data was carried out regarding sex, cleft type, origin, and age at the beginning of orthodontic/orthopedic treatment. The CLP presentation is very variable, and, therefore, some authors consider classifying into groups. A widely used classification employed in this study

is proposed by Spina *et al.* [26], and divides the clefts in daily pre-foramen, trans-foramen, and post-foramen. Regarding the sides, CLP is divided into unilateral, bilateral, and median, which was included by the modification by Silva-Filho *et al.* [23].

The individuals' origin was subdivided into Fortaleza capital, the metropolitan region of Fortaleza, the countryside of the state of the Ceará or other states. The individuals were divided into three groups in relation to the age at the beginning of orthodontic/orthopedic treatment: G1 - 6 to 8 years of age, early mixed dentition; G2 - 8 to 12 years of age, delayed mixed dentition; G3 - more than 12 years of age, permanent dentition.

Inclusion criteria were individuals enrolled at the institution and with files, panoramic radiograph, and study models of both jaws. Exclusion criteria include incomplete documentation, because it was not possible to verify the required information for the study. The total sample comprised 330 individuals, of which seven did not have complete documentation and were excluded, resulting in a final sample of 323 patients.

The data were submitted to the descriptive statistical analysis, through the description of the absolute and percentile frequency; and inferential statistical analysis, through chi square test, considering a level of significance of 5% (Graph Pad Prism 5.0, San Diego, CA, USA).

Results

The final sample of 323 patients was distributed according to sex. One-hundred and eighty individuals (55.73%) were of males and 143 (44.27%) females, without statistical significant differences.

In relation to the cleft type, most of the cases (77.09%) were trans-foramen ($p < 0.05$), followed by the post-foramen (13.00% of the cases) and pre-foramen cleft (9.91%) (table I).

Table I - Distribution of individuals with CLP regarding the cleft type, referral Northeast Brazilian hospital - 1998 to 2013 (n = 323)

Cleft type	N	%	p-value
Trans-foramen	249*	77.09%	<0,001*
Pre-foramen	32	9.91%	
Post-foramen	42	13.00%	
Total	323	100.00%	

Chi square test with level of significance of $p < 0.05$

* Significant difference

Table II relates the cleft type to the sex, with statistical significant prevalence for males in the trans-foramen clefts (59.04%) and females in the post-foramen clefts (59.52%). No sex predilection was verified in relation to the pre-foramen clefts.

Table II - Distribution of individuals with CLP regarding the cleft type and sex, referral Northeast Brazilian hospital - 1998 to 2013 (n = 323)

Cleft type	N	Sex		p-value
		Female N° (%)	Male N° (%)	
Trans-foramen	249	102 (40.96%)	147* (59.04%)	<0.001*
Pre-foramen	32	16 (50.00%)	16 (50.00%)	0.098
Post-foramen	42	25* (59.52%)	17 (40.48%)	0.018*

Chi square test with level of significance of $p < 0.05$

* Significant difference

Table III evaluates the pre- and trans-foramen clefts regarding to side. The total of unilateral, bilateral, and median clefts was 68.68%, 30.96%, and 0.36%, respectively. Therefore, a significantly statistical higher frequency of unilateral clefts was verified ($p < 0.001$).

Table III - Distribution of individuals with CLP regarding the cleft side, referral Northeast Brazilian hospital - 1998 to 2013 (n = 281)

Cleft side	N	%	p-value
Unilateral	193	68.68%*	<0.001*
Unilateral, left	116	60.10%	
Unilateral, right	77	39.90%	
Bilateral	87	30.96%	
Median	1	0.36%	
Total	281	100,00%	

Chi square test with level of significance of $p < 0.05$

* Significant difference

Most of the 323 individuals (42.72%) came from the countryside of the State of Ceará and 39.01% of Fortaleza, without statistically significant difference (table IV).

Table IV - Distribution of individuals with CLP regarding the origin, referral Northeast Brazilian hospital - 1998 to 2013 (n = 323)

Origin	N	%	p-value
Fortaleza	126	(39.01%)	0.795
Metropolitan region	56	(17.34%)	
Countryside of Ceará	138	(42.72%)	
Other states	3	(0.93%)	
Total	323	(100.00%)	0.144

Chi square test with level of significance of $p < 0.05$

According to table V, 53.87% of the individuals with CLP began the orthopedic/orthodontic treatment at 8 to 12 years of age. Relating the beginning of the orthodontic/orthopedic treatment with sex, it was observed that most of the males (56.11%) and females (51.05%) started the treatment at 8 to 12 years of age, without statistically significant difference.

Table V - Distribution of individuals with CLP regarding the age at the beginning of the orthopedic/orthodontic treatment and sex, referral Northeast Brazilian hospital - 1998 to 2013 (n = 323)

Beginning of the orthopedic/orthodontic	N (%)		Sex				p-value
			Female N° (%)		Male N° (%)		
6 to 8-year-old	105	(32.51%)	54	(37.76%)	51	(28.33%)	0.159
8 to 12-year-old	174	(53.87%)	73	(51.05%)	101	(56.11%)	
After 12-year-old	44	(13.62%)	16	(11.19%)	28	(15.56%)	
Total	323	(100.00%)	143	(100.00%)	180	(100.00%)	0.144

Chi square test with level of significance of $p < 0.05$

The table VI relates the age of the orthopedic/orthodontic with the cleft type. Most of the individuals with trans-foramen clefts (53.41%) and post-foramen clefts (59.53%) started the treatment at 8 to 12 years of age ($p < 0.05$).

Table VI - Distribution of individuals with CLP regarding the age at the beginning of the orthopedic/orthodontic treatment and cleft type, referral Northeast Brazilian hospital - 1998 to 2013 (n = 323)

Cleft type	N	6 to 8-year-old		8 to 12-year-old		After 12-year-old	p-value
Trans-foramen	249	82	(32.93%)	133*	(53.41%)	34 (13.66%)	<0.001*
Pre-foramen	32	10	(31.25%)	16	(50.00%)	6 (18.75%)	0.297
Post-foramen	42	13	(30.95%)	25*	(59.53%)	4 (9.52%)	0.013*

Chi square test with level of significance of $p < 0.05$

* Significant difference

When the age of beginning of orthodontic/orthopedic treatment was related with the origin of the patients, it was observed that most individuals from Fortaleza, the metropolitan region, and the countryside of the state of Ceará started the treatment at 8 to 12 years of age, without statistically significant differences (table VII).

Tabela VII - Distribution of individuals with CLP regarding the age at the beginning of the orthopedic/orthodontic treatment and origin, N (%), referral Northeast Brazilian hospital - 1998 to 2013 (n = 323)

Beginning of the orthopedic/orthodontic	Fortaleza	Metropolitan region	Countryside of Ceará	Other states	p-value
6 to 8-year-old	42 (33.33%)	20 (35.72%)	40 (28.98%)	3 (100.00%)	0.135
8 to 12-year-old	67 (53.18%)	32 (57.14%)	75 (54.35%)	-	
After 12-year-old	17 (13.49%)	4 (7.14%)	23 (16.67%)	-	
Total	126 (100.00%)	56 (100.00%)	138 (100.00%)	3 (100.00%)	

Chi square test with level of significance of $p < 0.05$

* Significant difference

Discussion

To the best of our knowledge, the literature lacks studies on CLP incidence and prevalence in the Northeast region of Brazil, with the authors reporting a lower prevalence than that of other Brazilian regions, which can be attributed to the sub notification of the number of cases [14].

The analysis of the data of this study showed no statistically significant difference about the sex of the total sample, although males were more common (55.73%). This result corroborates the studies of Martelli-Jain *et al.* [16] and Mirfazeli *et al.* [18], who also found no statistically significant difference between the sexes. Di Ninno *et al.* [7], Takano *et al.* [27], Costa *et al.* [5] and Souza and Raskin [25] found a statistically significant higher prevalence in males.

The trans-foramen cleft was statistically more prevalent ($p < 0.05$), which confirms the findings of the literature: on the study of Cymrot *et al.* [6], 72.60% of the cases were of trans-foramen clefts; in the study of Freitas *et al.* [10], 62.00% of cases; and Di Ninno *et al.* [7], 49.00% of cases. The rationale behind this high frequency is that the environmental factors to which the embryo was exposed could affect both the primary development of lip and palate and the secondary palate, because although they are embryologically distinct processes, they occur in an approximate period.

In this study, a statistically significant greater prevalence ($p < 0.05$), of males were found in trans-foramens clefts, result that is consistent with several other studies [7, 15, 16, 18]. This sex-dependent susceptibility has been related to different gene expression between the sexes. Blanco *et al.* [2] found results that support the hypothesis that genetic variation in the MSX1 gene may be linked

to this higher susceptibility of males. Kumari *et al.* [11] suggested that homocysteine level threshold necessary to manifest cleft lip with or without cleft palate in female is much higher than in males, which may be one reason why the frequency of females is smaller than in males. However, further molecular and genetic studies are necessary for a better understanding of the differences between the cleft types and gender.

The post-foramen cleft was significantly more frequent in females, which is reinforced by the findings of several studies [6, 7, 10, 18]. Cymrot *et al.* [6] found that 61.70% of post-foramen clefts occurred in the female gender, as well as Di Ninno *et al.* [7] that reported 59.5% of prevalence. According to Lary and Paulozzi [12], this higher incidence could be explained by the fact that the palate of a female embryo delay approximately one week more to close than the palate of a masculine embryo, extending the time in which the mothers are exposed to the environmental agents that associated with the genetic factors can increase the probability of failure in the fusing of the palatal processes.

A vast number of studies prove a predominance of the unilateral clefts in relation to the bilateral [10, 15, 16], coinciding with the observed in this study, in which the unilateral clefts were statistically more frequent. A side pattern is already known for many anomalies, and, although many genes have been described with symmetrical expression at the two sides of the vertebrates, the metabolic effect had been not yet discovered. This differentiated expression of genes during different periods of development may result in different potential of cellular proliferation, adhesion, and migration [19].

A discreet prevalence of residents in the countryside of the State of Ceará (42.72%), followed by individuals from Fortaleza (39.01%). Although

no statistically significant difference was found, a hypothesis for the largest number of patients from the countryside of the State would be the shortage of reference centers for the treatment of cleft lip and palate in Ceará. This slight predominance was also found by Di Ninno *et al.* [7], who observed that 38.50% of individuals with clefts came from the countryside of Minas Gerais.

In this study, it was observed that more than half of the individuals started the orthodontic/orthopedic treatment at late mixed dentition (8 to 12 years). The Hospital for Rehabilitation of Craniofacial anomalies of the University of São Paulo (HRAC-USP), center of reference in the treatment of individuals with cleft in Brazil, states the beginning of the orthodontic treatment approximately at 8 years, in late mixed dentition [9]. Most of patients with trans-foramen cleft and post-foramen clefts also started the treatment at this age group. Then, some individuals started treatment at 6 to 8 years-old, an age range also found in orthodontic treatment protocols for individuals with cleft [3]. Other individual with clefts started treatment after 12 years of age, a late period from the orthopedic point of view in relation to bone grafting [21, 24]. Few studies in the literature reported this subject, such as Ribeiro *et al.* [21], who found that 90% of the studied individuals had already finished the growth at the beginning of the orthodontic treatment, impairing the rehabilitation and prognosis of the treatment.

The relation between the beginning of the orthodontic/orthopedic treatment with sex showed that most of the males (56.11%) and females (51.05%) started the treatment at 8 to 12 years of age, without statistically significant difference. When the age of beginning of orthodontic/orthopedic treatment was related with the origin of the patients, most individuals from Fortaleza, the metropolitan region, and the countryside of the state of Ceará started the treatment at 8 to 12 years of age, without statistically significant differences (table VII). As far as we are concerned, the literature lacks studies similar to this present study.

Authors highlighted that very early interventions, such as those at deciduous dentition or at early mixed dentition, often result in relapse and add more procedures in the long and complex rehabilitating process [19]. However, late orthodontic/orthopedic (after the 12 years of age) can compromise the result of treatment [3, 9, 27]. Thus, an intervention in a period considered more appropriate, for example, in late mixed dentition (8-12 years of age), as in most of the individuals of the present study, is defended by some authors [9].

Conclusion

Regardless of gender, origin, or cleft type, most patients started the orthopedic treatment up to 12 years of age, an age considered ideal by many of the protocols. This fact reveals the effectiveness of the treatment even in more severe cases and in patients who need to move from the countryside to the capital. This analysis of the relationship between the profile of individuals with cleft lip and palate with the beginning of the orthopedic treatment makes this study pioneer. The most frequent clefts were unilateral and trans-foramen cleft ($p < 0.05$). The post-foramen cleft was more prevalent in females, while trans-foramen clefts were in males ($p < 0.05$). The knowledge of the profile of the individuals with CLP allows to clarify this congenital alteration still more and to trace strategies to assure the integral treatment to this individuals.

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