



Retrospective Observational Study

RELATIONSHIP BETWEEN MISSING TEETH AND CLEFT SIDE IN NON-SYNDROMIC CLEFT PATIENTS

B. Sayahpour¹, A. Tashakor², A. Darnahal³, S. Eslami⁴, M. Farhadi⁵, Z. Nematollahi⁶, K. Ferati⁷, A. Palermo⁸, A. Mancini⁹, E. Xhajanka¹⁰ and A. Jamilian^{11*}

¹Department of Orthodontics, Johann-Wolfgang Goethe University, Frankfurt, Germany;

²Department of Orthodontics, Faculty of Dentistry, Cranio Maxillofacial Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran;

³Harvard School of Dental Medicine, Boston, MA;

⁴International Orthodontist, Grafenberger Allee 57, 40237, Duesseldorf, Germany;

⁵Department of Orthodontics, Faculty of Dentistry, Cranio Maxillofacial Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran;

⁶Dental Research Center, Research Institute of Dental Science, Shahid Beheshti University of Medical Science, Tehran, Iran, and Craniomaxillofacial Research Center, Azad University, Dental Branch, Tehran, Iran;

⁷Faculty of Medicine, University of Tetovo, Tetovo, Macedonia;

⁸College of Medicine and Dentistry, Birmingham, UK;

⁹Interdisciplinary Department of Medicine, University of Bari "Aldo Moro", Bari, Italy;

¹⁰Medical University of Tirana, Rruga e Dibrës, Tirana, Albania;

¹¹City of London Dental School, University of Bolton, London, UK; Orthodontic Department, Dental school, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

**Correspondence to:*

Abdolreza Jamilian, DDS

Islamic Azad University, 14 Pesian Ave, Valiasr ST. Tehran, 1986944767 Iran

e-mail: info@jamilian.net

ABSTRACT

The purpose of this retrospective observational study was to evaluate the possible association between the missing teeth and the side associated with the cleft in non-syndromic patients. This study consisted of 201 cleft patients including 131 males with a mean age of 12.3 ± 4 years and 70 females with a mean age of 12.6 ± 3.9 years. 148 of the patients were affected by cleft lip and palate, while the other 53 presented only cleft lip. Charts, models, radiographs, and intraoral photographs were used for the study. T-test and chi-square tests were used for the assessment of the data. Hypodontia was found in 129 individuals (64.1%). Chi-square test showed that there was no statistically significant difference between the number of male and female patients with hypodontia ($P < 0.7$). 122 of the patients with hypodontia (60% of the total 201 subjects) had missing maxillary incisors. Totally there were 197 teeth absent in the entire cleft samples. 180 (91.3%) of these teeth were missing on the cleft side and 17 (8.7%) of them were missing on the non-cleft side. In addition, 170 (86.3%) of them were maxillary permanent

Received: 24 May, 2021

Accepted: 28 July, 2021

ISSN: 2038-4106

Copyright © by BIOLIFE 2021

This publication and/or article is for individual use only and may not be further reproduced without written permission from the copyright holder. Unauthorized reproduction may result in financial and other penalties. **Disclosure: All authors report no conflicts of interest relevant to this article.**

lateral incisors and only 27 (13.7%) of them were permanent second premolars. The frequency of missing maxillary lateral incisors in cleft lip patients was significantly higher compared with the missing second premolars in both arches. The incidence of lateral incisor missing is significantly higher on the cleft side.

KEYWORDS: *cleft lip, cleft palate, hypodontia, missing, cleft side*

INTRODUCTION

Cleft lip and/or palate (CLP) is one of the most common types of craniofacial birth defects (1). The overall prevalence rate for live births with cleft lip, cleft palate, or both has been reported at 1.39 per 1000 live births (2); it accounts for 65% of all head and neck anomalies (3). Prevalence of dental anomalies such as variations in tooth number and position and reduced tooth dimensions have always been found to be higher in CLP patients than in the whole population (4-10). Akcam et al., 2011 detected that cleft patients had at least one dental anomaly in 96.7 percent of examined subjects and many patients showed other dental and skeletal malocclusion in addition to the cleft lip and palate anomalies.

Shapira et al. (12) reported the most significant number of developmental dental abnormalities in upper lateral incisors in the cleft area, both in deciduous and permanent dentitions. Moreover, in CLP patients are frequent shape anomalies, such as enamel hypoplasia and conoid shape (13, 14). Tooth agenesis also called hypodontia or congenital absence of teeth, is the most detected developmental dental anomaly in all the cleft types (15). Furthermore, Shapira et al. (12) discovered a prevalence of 77% of hypodontia in a sample of cleft patients. Jiroutova and Mullerova (16), about the hypodontia frequency in CLP patients, found that the maxillary arch was involved more frequently in patients with this defect. The dental bud of the upper lateral incisor was often affected in both CL and CLP, while the second lower premolar was most frequently absent in the isolated cleft palate. Paranaiba et al. (17) found that in Brazilian patients with non-syndromic cleft lip and/or palate, the prevalence of agenesis of the premolars and maxillary lateral incisors is higher in unilateral complete cleft lip and palate patients. In many studies, lateral incisors are the most frequent agenesis tooth, followed by second premolars (18, 19). Whereas, in Laatikainen et al. (20) and Ranta et al. (21), the most frequently missing tooth was the upper second premolar, and to follow the maxillary lateral incisor and the lower second premolar.

However, the emerging literature evidence has always been limited to describing numbers and shape anomalies in patients with cleft. In addition, an association between anomalies with the side involved in the cleft and correlating the level of anomalies with those of the cleft has been verified only in few reports.

Considering the discrepancies in the literature, the aim of the current study was to determine the frequency of missing second premolars and lateral incisors in cleft lip/palate patients and compare it with other subjects' data to determine the possible association between the cleft side and the agenesis side.

MATERIALS AND METHODS

The study was carried out under the provisions established by the Declaration of Helsinki. Ethical approval and informed consent were obtained from each subject and a parent or trustee. 201 non-syndromic cleft lip and/or palate patients were included in the study. The patients' population was racially and ethnically similar, and all their parents were of Persian origin.

Exclusion criteria were: cleft patients with craniofacial syndrome; patients with unclear radiographs. Therefore, 201 subjects were enrolled in the study (131 males aged 12.3 ± 4 years and 70 females aged 12.6 ± 3.9 years). The gender distribution of the sample can be observed in Table I.

Table I. *Gender distribution of samples.*

Gender	N (%)	Age (year)
Male	131 (65.2)	12.3 ± 4
Female	70 (34.8)	12.6 ± 3.9

The patients were classified based on Whitaker et al. (22) classification in which the patients were divided into four groups (lip, cleft palate, cleft lip and palate, and cleft lip and alveolus), and each group was divided into two subgroups unilateral or bilateral. Dental casts, orthopantomography, and/or periapical and occlusal X-rays of the patients were used to diagnose possible agenesis (leaving out the wisdom teeth).

A thorough examination of hypodontia of permanent teeth (excluding third molars) was undertaken using panoramic, periapical, and occlusal radiographs. In addition, data regarding missing teeth inside or outside the cleft area were collected, and two observers evaluated the records simultaneously. Their outcomes were blinded to each other. Inter-observer accordance was estimated using kappa analysis. A kappa value of 1 showed perfect agreement. The Statistical Package for Social Sciences, Version 20 (SPSS Inc. Chicago, Illinois, USA) was used to examine the data. The Chi-square test was used to analyze the data, and the p-value was set at $P < 0.05$. During this research, all operators wore surgical masks to prevent the respiratory system virus (23) and to maintain office hygiene (24, 25).

RESULTS

The distribution of samples depending on the type of cleft is shown in Table II. The samples were divided into the unilateral and bilateral cleft lip, cleft lip and palate, cleft lip and alveolus, and cleft palate groups; permanent teeth agenesis was evaluated in every group. Hypodontia was found in 129 patients (64.1%) of the total sample, including 83 boys (41.3%) and 46 girls (22.8%).

Chi-square test highlighted no statistically significant difference between males and females. ($P < 0.7$) (Table II) Out of 197 teeth absent in the entire cleft sample (Table III), 180 (91.3%) teeth were missing on the cleft side, and 17 (8.7%) teeth were missing on the non-cleft side. Of these, 170 (86.3%) were upper permanent lateral incisors (160 in the cleft area and 10 in the non-cleft area), and 27 (13.7%) were permanent second premolars (20 on the cleft side and 7 on the non-cleft side) (Table IV). Statistically significant differences were detected between the lateral incisors agenesis in the cleft and non-cleft areas ($P < 0.001$).

Table II. Distribution of samples according to cleft type.

Gender	UCL	BCL	UCL and alveolus	BCL and alveolus	CP	UCLP	BCLP	Total
Male	1	1	18	8	2	64	37	131
Female	-	1	11	4	7	27	20	70
Total	1	2	29	12	9	91	57	201

Unilateral cleft lip: **UCL**; Bilateral cleft lip: **BCL**; Cleft palate: **CP**; Unilateral cleft lip and palate: **UCLP**; Bilateral cleft lip and palate: **BCLP**

Table III. Number of patients with hypodontia according to sex.

Gender	No. of Patients	Patients With Hypodontia	Patients Without Hypodontia	P Value
Male	131 (65.2%)	83 (41.3%)	48 (23.9%)	0.7
Female	70 (34.8%)	46 (22.8%)	24 (12%)	
Total	201 (100%)	129 (64.1%)	72 (35.9%)	

Table V shows that 122 (60%) of the patients had missing maxillary lateral incisors, which were significantly higher than missing either maxillary or mandibular second premolars. As can be seen, 22 of the total 41 cleft lip and alveolus patients and 95 of the total 148 cleft lip and palate patients had missing laterals, while only 1 of 18 patients had missing second premolars. Table VI shows that all the patients were missing a total of 197 upper lateral incisors and upper and lower second premolars.

Table IV. Number of missing teeth according to cleft side and non-cleft side.

	Missing lateral incisor	Missing second premolars			Total missing teeth
	Maxilla N (%)	Maxilla N (%)	Mandible N (%)	Total N (%)	N (%)
Cleft side	160 (81.2)	14 (7.1)	6 (3)	20 (10.1)	180 (91.3)
Non-cleft side	10 (5.1)	6 (3)	1 (0.6)	7 (3.6)	17 (8.7)
Total	170 (86.3)	20 (10.1)	7 (3.6)	27 (13.7)	197 (100)

Table V. Number of patients with missing maxillary incisors and missing second premolars according to cleft type.

	Patients	Patients with missing Max Lateral Incisors				Patients with missing Max/Mand II Premolars			
		L	R	B	T	L	R	B	T
		Cleft lip (CL)	3	0	0	2	2	0	0
Cleft palate (CP)	9	2	0	1	3	0	0	1	2
CL and alveolus	41	10	6	6	22	0	0	0	1
Cleft lip palate (CLP)	148	30	21	44	95	4	6	8	18
Total	201	42	27	53	122	4	6	9	21

L=Left side, R=Right side, B=Both Sides, T=Total number of missing teeth

Table VI. Distribution of hypodontia in cleft patients according to number of missing teeth.

	Max Lateral Incisors				Max II Premolars				Mand II Premolars			
	L	R	B	T	L	R	B	T	L	R	B	T
Cleft lip (CL)	0	0	4	4	0	0	0	0	0	0	0	0
Cleft palate (CP)	1	0	2	3	0	0	4	4	0	0	2	2
CL and alveolus	10	6	13	29	0	1	0	1	0	0	0	0
Cleft lip palate (CLP)	29	21	84	134	2	3	10	15	0	1	4	5
Total	40	27	103	170	2	4	14	20	0	1	6	7

L=Left side, R=Right side, B=Both Sides, T=Total number of missing teeth

DISCUSSION

This study found that 129 (64.1%) of all cleft patients suffered from hypodontia. These findings correspond to the findings of Shapira et al. (12), who detect the prevalence of 77% hypodontia in their study group of subjects with cleft lip and palate, isolated or associated. These patients were missing one hundred ninety-seven upper lateral incisors and upper and lower premolars. In this study, from a total of 201 patients, 60 % of them had missing maxillary lateral incisors, similar to Suzuki et al. (26), who reported that 56.9% of their cleft lip and/or palate subjects had missing maxillary lateral incisors. Polder et al. (27), about the prevalence of permanent missing teeth in the Caucasian populations of North America, Australia, and Europe, reported that the mandibular second premolar was the most involved too, followed by the maxillary lateral incisor and the maxillary second premolar.

In the current study, 11.5% of second premolars were found to be missing, which is similar to the 18% found by Shapira et al. (12). In our study, the missing second premolars were substantially higher in the maxillary arch in all groups, with a total of 20 missing second premolars in the maxilla and 7 missing in the mandible. These numbers also correspond to the findings of Shapira et al. (28), who reported a 47-second premolars agenesis in the upper arch and agenesis in the lower arch. Nevertheless, the findings of the current study are in contrast with the findings of Laatikainen et al. (20) and Ranta et al. (21). They found that maxillary second premolars were the most frequently absent teeth, followed in order of frequency by the maxillary lateral incisors and the mandibular second premolars in cleft patients. In the current study, the absence of teeth was more frequent on the cleft side, respecting the healthy side, which agrees with the outcomes of Shapira et al. (28).

Ranta et al., in their review, showed that the prevalence of missing teeth grows according to the severity of the cleft (21). This outcome agrees with our work in which there was a high prevalence of teeth agenesis in cleft lip and palate patients and a lower prevalence in isolated cleft lip and isolated cleft palate patients. Moreover, Paranaiba et al. (17) indicated that dental abnormalities were more frequent in unilateral cleft lip and palate subjects compared with bilateral cleft lip and palate subjects. It is also reported that the majority of cleft lip and or palate patients had at least one dental anomaly, and most of the dental anomalies were observed at the side of the cleft. However, no association could be found between the type of cleft and dental anomalies (27).

Furthermore, ethnicity plays a significant part in the prevalence of cleft and associated abnormalities. Polder et al. stated that missing teeth were more frequent in Europe and Australia compared with North America (27). They also showed that the prevalence of missing teeth in females is 1.37 times higher than in males for all three continents. One of the limitations of the current study, which could affect its outcomes, is the small sample size. Moreover, associated dental disturbances and medical pathologies should be explicitly investigated in this type of frailty patient.

More multi-center works with a larger study group and different breeds are needed. In addition, future multidisciplinary studies about the genetics of cleft subjects to confirm the higher prevalence of left-sided is required.

CONCLUSION

In this study, the maxillary lateral incisor agenesis in cleft lip patients (60%) was significantly more frequent than the second premolars agenesis in both arches (11.5%). The prevalence of missing lateral incisors raises definitely according to the severity of the cleft and is significantly higher on the cleft side.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

REFERENCES

1. Baek SH . Cleft type and Angle's classification of malocclusion in Korean cleft patients. *The European Journal of Orthodontics*. 2002;24(6):647-653. doi:10.1093/ejo/24.6.647
2. Jamilian A, Sarkarat F, Jafari M, et al. Family history and risk factors for cleft lip and palate patients and their associated anom-

- alies. *Stomatologija*. 2017;19(3):78-83.
3. Jamilian A, Nayeri F, Babayan A. Incidence of cleft lip and palate in Tehran. *Journal of Indian Society of Pedodontics and Preventive Dentistry*. 2007;25(4):174. doi:10.4103/0970-4388.37013
 4. Lourenço Ribeiro L, Teixeira das Neves L, Costa B, Ribeiro Gomide M. Dental Anomalies of the Permanent Lateral Incisors and Prevalence of Hypodontia outside the Cleft Area in Complete Unilateral Cleft Lip and Palate. *The Cleft Palate-Craniofacial Journal*. 2003;40(2):172-175. doi:10.1597/1545-1569_2003_040_0172_daotpl_2.0.co_2
 5. Jamilian A, Jamilian M, Darnahal A, Hamed R, Mollaei M, Toopchi S. Hypodontia and supernumerary and impacted teeth in children with various types of clefts. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2015;147(2):221-225. doi:10.1016/j.ajodo.2014.10.024
 6. Grassia V, Lombardi A, Kawasaki H, et al. Salivary microRNAs as new molecular markers in cleft lip and palate: a new frontier in molecular medicine. *Oncotarget*. 2018;9(27):18929-18938. doi:10.18632/oncotarget.24838
 7. Rullo R, Festa VM, Rullo R, et al. prevalence of dental anomalies in children with cleft lip and unilateral and bilateral cleft lip and palate. *European Journal of Paediatric Dentistry*. 2015;16(3):229-232.
 8. Stahl F, Grabowski R, Wigger K. Epidemiology of Hoffmeister's "Genetically Determined Predisposition to Disturbed Development of the Dentition" in Patients with Cleft Lip and Palate. *The Cleft Palate-Craniofacial Journal*. 2006;43(4):457-465. doi:10.1597/04-156.1
 9. Perillo L, Vitale M, d'Apuzzo F, Isola G, Nucera R, Matarese G. Interdisciplinary approach for a patient with unilateral cleft lip and palate. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2018;153(6):883-894. doi:10.1016/j.ajodo.2016.12.035
 10. Martinelli M, Palmieri A, Carinci F, Scapoli L. Non-syndromic Cleft Palate: An Overview on Human Genetic and Environmental Risk Factors. *Frontiers in Cell and Developmental Biology*. 2020;8. doi:10.3389/fcell.2020.592271
 11. Akcam MO, Evirgen S, Uslu O, Memikoglu UT. Dental anomalies in individuals with cleft lip and/or palate. *The European Journal of Orthodontics*. 2010;32(2):207-213. doi:10.1093/ejo/cjp156
 12. Shapira Y, Lubit E, Kuftinec MM. Hypodontia in children with various types of clefts. *The Angle Orthodontist*. 2000;70(1):16-21. doi:10.1043/0003-3219(2000)070<0016:HICWVT>2.0.CO;2
 13. Vichi M, Franchi L. Abnormalities of the maxillary incisors in children with cleft lip and palate. *ASDC journal of dentistry for children*. 1995;62(6):412-417.
 14. Jamilian A, Lucchese A, Darnahal A, Kamali Z, Perillo L. Cleft sidedness and congenitally missing teeth in patients with cleft lip and palate patients. *Progress in Orthodontics*. 2016;17(1). doi:10.1186/s40510-016-0127-z
 15. Margareta L, Rune H, Olafur PJ. Dental abnormalities and ectopic eruption in patients with isolated cleft palate. *Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery*. 1998;32(2):203-212. doi:10.1080/02844319850158831
 16. Jiroutová O, Müllerová Z. The occurrence of hypodontia in patients with cleft lip and/or palate. *Acta Chirurgiae Plasticae*. 1994;36(2):53-56.
 17. Paranaíba LMR, Coletta RD, Swerts MSO, Quintino RP, De Barros LM, Martelli-Júnior H. Prevalence of Dental Anomalies in Patients with Nonsyndromic Cleft Lip and/or Palate in a Brazilian Population. *The Cleft Palate-Craniofacial Journal*. 2013;50(4):400-405. doi:10.1597/11-029
 18. Tortora C, Meazzini MC, Garattini G, Brusati R. Prevalence of Abnormalities in Dental Structure, Position, and Eruption Pattern in a Population of Unilateral and Bilateral Cleft Lip and Palate Patients. *The Cleft Palate-Craniofacial Journal*. 2008;45(2):154-162. doi:10.1597/06-218.1
 19. Menezes R, Vieira AR. Dental Anomalies as Part of the Cleft Spectrum. *The Cleft Palate-Craniofacial Journal*. 2008;45(4):414-419. doi:10.1597/07-064.1
 20. Laatikainen T, Ranta R. Hypodontia in twins discordant or concordant for cleft lip and/or palate. *European Journal of Oral Sciences*. 1994;102(2):88-91. doi:10.1111/j.1600-0722.1994.tb01160.x
 21. Ranta R. A review of tooth formation in children with cleft lip/palate. *American Journal of Orthodontics and Dentofacial Orthopedics*. 1986;90(1):11-18. doi:10.1016/0889-5406(86)90022-3
 22. Whitaker LA, Pashayan H, Reichman J. A proposed new classification of craniofacial anomalies. *The Cleft Palate Journal*.

- 1981;18(3):161-176.
23. Scarano A, Inchingolo F, Rapone B, Festa F, Rexhep Tari S, Lorusso F. Protective Face Masks: Effect on the Oxygenation and Heart Rate Status of Oral Surgeons during Surgery. *International Journal of Environmental Research and Public Health*. 2021;18(5):2363. doi:10.3390/ijerph18052363
 24. Scarano A, Inchingolo F, Lorusso F. Environmental Disinfection of a Dental Clinic during the Covid-19 Pandemic: A Narrative Insight. Pesce P, ed. *BioMed Research International*. 2020;2020:1-15. doi:10.1155/2020/8896812
 25. Bordea IR, Xhajanka E, Candrea S, et al. Coronavirus (SARS-CoV-2) Pandemic: Future Challenges for Dental Practitioners. *Microorganisms*. 2020;8(11):1704. doi:10.3390/microorganisms8111704
 26. Suzuki A, Watanabe M, Nakano M, Takahama Y. Maxillary Lateral Incisors of Subjects with Cleft Lip and/or Palate: Part 2. *The Cleft Palate-Craniofacial Journal*. 1992;29(4):380-384. doi:10.1597/1545-1569_1992_029_0380_mliosw_2.3.co_2
 27. Polder BJ, Van't Hof MA, Van der Linden FPGM, Kuijpers-Jagtman AM. A meta-analysis of the prevalence of dental agenesis of permanent teeth. *Community Dentistry and Oral Epidemiology*. 2004;32(3):217-226. doi:10.1111/j.1600-0528.2004.00158.x
 28. Shapira Y, Lubit E, Kuftinec MM. Congenitally missing second premolars in cleft lip and cleft palate children. *American Journal of Orthodontics and Dentofacial Orthopedics*. 1999;115(4):396-400. doi:10.1016/s0889-5406(99)70258-1