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Hypodontia in Permanent Dentition in Patients with Cleft Lip and Palate.

Abu-Hussein Muhamad^{1*}, Abdulgani Azzadeen², and Watted Nezar³.

¹Pediatric Dentistry, University of Athens, 123 Argus Street, 10441 Athens, Greece.

²Department of Conservative Dentistry, Al-Quds University, JERUSALEM, Palestine.

³Department of Orthodontics, Arab American University, JENIN, Palestine.

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*For Correspondence

Pediatric Dentistry, University of Athens, 123 Argus Street, 10441 Athens, Greece.

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ABSTRACT

Hypodontia, also known as congenital lack of teeth or tooth agenesis, is the most common intraoral and dental anomaly. It occurs in ca. 10% of healthy people and is thought to inflict children with clefts six times more often. Occurrence of hypodontia depends on location and severity of the cleft. Unilateral complete clefts are thought to demonstrate the highest incidence of congenitally missing teeth of all the cleft groups. Mostly, in patients with cleft lip and palate, congenital lack of teeth refers to incisor region on the cleft side. A frequent lack of teeth in patients with clefts refer to premolars, usually maxillary ones. In clefts, lack of teeth usually refers to the left side of the dental arch. Even though hypodontia refers to upper lateral incisors and lower premolars mostly, it may refer to any group of teeth. Congenital lack of teeth in children with clefts needs appropriate treatment, which usually bases on orthodontic treatment followed by prosthetic reconstructions.

INTRODUCTION

Congenital lack of a tooth results from disturbances during the early stages of tooth development. A tooth is defined to be congenitally missing if it has not erupted in the oral cavity and is not visible in a radiograph. All primary teeth have erupted by the age of 3 and all permanent teeth except the third molars between the ages of 12 and 14. Therefore, 3- to 4-year-old children are suitable for diagnosis of congenitally missing primary teeth by clinical examination, and 12- to 14-year-old children, for diagnosis of permanent teeth, excluding the third molars. Radiographic diagnosis can be made at younger age depending on tooth group. The use of panoramic radiography is recommended, together with clinical examination in detecting or confirming dental development [1,2].

All primary teeth and the crypts of first permanent molars are visible by radiograph at birth. The crowns of first premolars, second premolars, and second permanent molars start to mineralize near the second birthday, and all permanent tooth crowns except the third molars have begun their mineralization by the age of six. The formation of third molars shows very large variation. Usually at the age of 8 to 10 years, the first signs of the third molars appear on a radiograph but occasionally, very late appearance (age 14 to 18) occurs [2,3]. The formation of dentition continues many years, and differences exist in mineralization stages among children depending on race, on gender, and even on family and on the individual. Especially second premolars may show late onset of mineralization, and give a false-positive diagnosis of hypodontia in radiographs.

Therefore, diagnosis of tooth agenesis in the permanent dentition should be made after the age of 6 excluding third molars, and after 10 years of age if third molars are also studied [2,4,5]. (Fig. 1) Hypodontia is the term most frequently used when describing the phenomenon of congenitally missing teeth in general. Many other terms appear in the literature to describe a reduction in number of teeth: oligodontia, anodontia, aplasia of teeth, congenitally missing teeth, absence of teeth, agenesis of teeth, and lack of teeth. Hypodontia and oligodontia are classified as isolated or nonsyndromic

hypodontia/oligodontia and syndromic hypodontia/oligodontia or hypodontia/ oligodontia associated with syndromes.

The term **hypodontia** is used in a narrow sense when the number of missing teeth is one or a few. **Oligodontia** is defined as missing a large number of teeth.

Anodontia is an extreme case, denoting complete absence of teeth. There is no clear definition in the literature concerning the limits of these classes. In the recent years, however, the following definitions have been used:

Hypodontia: 1 to 6 teeth missing (excluding the third molars)

Oligodontia: more than six teeth missing (excluding the third molars)

Anodontia: complete absence of teeth.

Incisors and premolars are the most frequently missing teeth. Therefore **incisorpremolar**

hypodontia (IPH) is the term that we have used to describe this form of the anomaly.

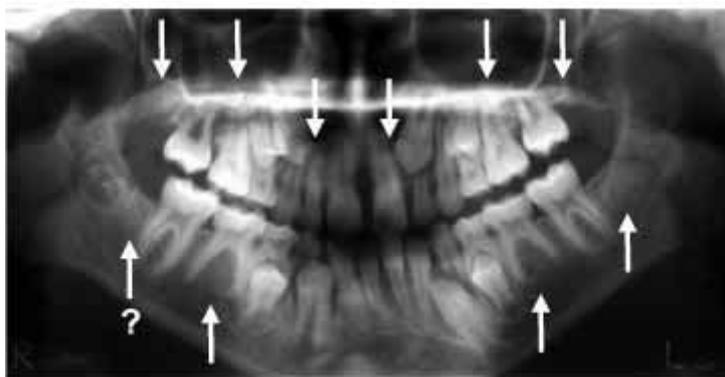


Figure 1: Congenitally missing upper second molars, second premolars, lateral incisors, lower second molar(s), and second premolars in a patient with oligodontia

DISCUSSION

Bohn was amongst the first researchers to report the prevalence of congenitally missing teeth in CL/CP patients. He investigated anomalies of the lateral incisor in cases of harelip and cleft palate. 63 patients, that were 3 to 7 years of age, were clinically and radiographically evaluated for anomalies of the lateral incisor as regards to their number. He found that 52% of missing lateral incisors were reported in the cleft lip and palate group (group B) followed by 12% in the cleft lip [6].

Olin studied the full mouth intraoral radiographs of 175 CL/CP patients, aged 3 to 23 years, at the otolaryngology and maxillofacial surgery Department, at the State University of Iowa. He found that the incidence of missing bicuspid was 24% higher in CL/CP patients than the general population. One patient in the CL group was found to have missing maxillary bicuspid, 5 patients were reported in the CP group, and 36 patients in the CL/CP had missing bicuspid [7].

Jordan et al. researched dental abnormalities associated with cleft lip and/or palate. They found 69 patients had CLP, 17 had CL, 15 CP, and 4 patients had other types of clefting. Missing teeth was much more common in the permanent dentition and it was found in 25.7% [8].

Fishman studied the factors related to tooth number, eruption time, and tooth position in 68 cleft lip and palate individuals. The patient's records (study models and radiographs) were obtained from the Cleft Palate Center, New York. Unilateral cleft on the left side occurred in 57% of the cases. He found that

unilateral complete clefts demonstrated a much higher prevalence of congenitally missing teeth with 47.6% of missing teeth reported in the right unilateral cleft lip and palate group followed by the left unilateral cleft lip and palate 26.9%. Palatal clefts reported 26.3% of hypodontia. Bilateral complete cleft cases represented with 33% of congenitally missing teeth. The most common congenitally missing tooth was the maxillary lateral incisor, particularly on the cleft side of the arch [9].

Hellquist *et al.* studied the frequency of dental abnormalities in the permanent dentition on 172 Swedish children with unilateral clefts involving the maxillary alveolar process. 58 of the patients had unilateral clefts of the lip and alveolus (UCLA), and 114 had complete unilateral cleft lip and palate (UCLP). They found out that the upper central incisor on the cleft side was congenitally missing in 1.7%. The upper lateral incisors on the cleft side was missing in 43.6%. Aplasia of the permanent teeth outside the cleft region was noted in 23.8% [10].

Ranta *et al.* examined the orthopantomograms of 251 Finnish children with isolated cleft palate patients between the ages of 6-12 years old. They found that familial history of clefting has no pronounced effect on the prevalence of hypodontia. Hypodontia was present in 31.5% of the cases. They found that the most frequent missing teeth were the maxillary lateral incisors followed by the second premolars in both arches. The prevalence of hypodontia was significantly higher in children with conical elevation of the lower lip than in those without it (25% -40%), and increased with increasing extension of the cleft [11].

Ranta studied hypodontia on 416 children with isolated cleft. The material for the study consisted of an orthopantomogram examination taken from patients that ranged from 6 to 12 years of age. He found no statistical significance between boys and girls, or between the cleft and non-cleft group. Ranta found that 95 children showed hypodontia of one or more second premolars. In all the studied cases, 169 (10.2%) patients had second premolars congenitally missing. Of the 95 children examined, 23 had one or more other congenitally missing teeth (a total of 41 teeth) [11].

Ranta studied the timing of tooth formation in 251 children, affected with isolated cleft palate without syndromes or other concomitant visceral anomalies (CP), was evaluated from orthopantomograms. The age range was 6–12 yr. The formation of the permanent teeth was delayed approximately 0.7 yr in CP children compared with the data on the non-cleft reference group. There were no differences in sex distribution between the CP group and the non-cleft reference group and between the CP subgroups. No significant differences in tooth formation could be detected between the subgroups; with and without positive family history of clefts, with and without conical elevation of the lower lip, and between the subgroups of submucous, partial and complete cleft of the palate. The presence of hypodontia promoted the delay significantly and the delay increased with increasing number of missing teeth per child. In the older age group of 9–12 yr, the delay was significantly longer (1.1 yr) than in the younger age group of 6–9 yr (0.6 yr). He discovered that tooth formation support the hypothesis that the genetic component in the multifactorial situation does not act directly in producing the malformation itself, but indirectly, through a reduction in buffering. Furthermore, at least some of the sporadic cases have a partly genetic etiology [12].

Ranta studied variations in tooth number in children, each of whom had supernumerary teeth and agenesis of teeth. Among the 11, seven had cleft lip and palate, and two had clefting syndromes; two children had dental anomalies only. Only children who had both supernumerary teeth and congenitally missing teeth outside the area of the cleft alveolus were included. Concomitant hypodontia and hyperdontia were observed in the same dentition in nine subjects, in the same jaw in eight subjects, and in the same jaw quadrant in only three subjects. Supernumerary teeth and agenesis of teeth were observed simultaneously more often in the permanent dentitions than in the deciduous dentitions or in both dentitions simultaneously. The overall number of supernumeraries was 10 in the deciduous dentition and 14 in the permanent dentition of the 11 subjects. The number of congenitally absent teeth was 14 in the deciduous dentition and 40 in the permanent dentition. The etiology of concomitant hypodontia and hyperdontia is difficult to explain. It may result from disturbances in migration, proliferation, and differentiation of neural crest cells or interactions between the epithelial and mesenchymal cells during the initiation of odontogenesis [13,14].

Dahloff *et al.* researched dental abnormalities in preschool children with cleft lip and /or palate, at the Department of Pedodontics at Karolinska Institute, Sweden. The patients mean age was 5.5 years. They found that hypodontia was found in 8% of the CL/CP group and did not specify the most common tooth missing [15].

Lopez *et al.* studied 86 radiographs and study models of CL/CP patients, from the Dental School of the University of Sao Polo, to identify anomalies related to the number of teeth. They identified 12 cleft lip, 16 cleft lip– alveolus, 47 cleft lip and palate, and 11 cleft palate cases.

They reported anodontia to be 23% in the studied sample. The highest prevalence for hypodontia was found for the CLP (30%), followed by lip and alveolar clefts CLA (25%), and cleft palate CP (18%). Anodontia was twice as frequent among patients with CLP. They concluded that the numerical dental anomalies are seven times more prevalent among patients with CL/CP than in the general population [16].

Vichi and Franchi studied abnormalities of the maxillary incisors in children with cleft lip and palate. They examined orthopantomographs of 77 patients, from the Department of Orthodontics of the University of Florence, Italy, with age range from 3 to 16 years. They found that the prevalence of congenitally missing permanent lateral incisors on the cleft side was 42.9% (22% in unilateral clefts and 20.8% in bilateral clefts), and the prevalence of missing permanent central incisors on the cleft side was 2.6% [17].

Tahir researched dental anomalies in children with cleft lip and palate in the London Hospital and St. Andrews Hospital. Children, with age range of 3 to 18 years, attended two cleft palate clinics and were examined for dental anomalies. 68.4% of the children had one or more dental anomalies. Hypodontia was present in 36.8% of the children. He also concluded that Hypodontia is more common in cleft lip and palate patients than the control sample [18].

Shapira *et al.* researched congenitally missing second premolars in cleft lip and cleft palate children. They examined 278 radiographs of CLP cases ranging from 5 to 18 years old, to determine the frequency of missing second premolars and the possible association between the cleft side and the side from which the premolar were absent. Missing premolars were found to be 18%, which was significantly higher than what is found in the general population. Higher incidence of missing second premolars was found in the maxilla (33 cases, 67%) than the mandible (16 cases, 33%). Missing second premolars were correspondent to the cleft side. They were more frequently absent on the left than on the right side both in both males and females and in both jaws [19].

Shapira *et al.* performed a research on the prevalence of hypodontia in children with various types of clefts in New York. Hypodontia was found in 213 (77%), including 127 (46%) boys and 86 (31%) girls. In total, 339 teeth were absent, including 312 (92%) teeth missing on the cleft side and 27 (8%) on the non-cleft side. They concluded that the maxillary permanent lateral incisors (269 teeth, 79%) were the most likely missing teeth on the cleft side, followed by the maxillary and mandibular second premolars (70 teeth, 21%), in both boys and girls. The teeth that were most often missing on the non-cleft side were the maxillary second premolars (12 teeth), followed by the maxillary lateral incisors (10 teeth), and mandibular second premolars (5 teeth). Hypodontia of both the maxillary lateral incisors (78 teeth) and second premolars (18 teeth) was found more frequently on the left side (35%), which is the side frequently encountered with clefting [20].

Lekkas *et al.* investigated the possible absence of teeth in the post canine region of the upper jaw of the unoperated adult cleft patient. The study was performed on 266 dental casts of fully unoperated adult cleft patients. They found that there was no absence of permanent teeth in the canine and post-canine area of the upper jaw. Tooth anomalies of number were restricted to the cleft area. They concluded that their results were in contradiction with the established hypothesis that the absence of teeth outside the cleft area of the maxilla is due to an unknown congenital factor. On the contrary, the findings support the hypothesis that surgery for the closure of the hard palate in early childhood is the most important etiological factor for the absence of teeth outside the cleft area in the early operated cleft patient. The superficial position of the tooth germs (at the time of the palatal surgery), especially those of the premolars, supports this hypothesis [21].

Reibeiro *et al.* reported the dental anomalies of the permanent lateral incisor and prevalence of hypodontia outside the cleft area in complete unilateral cleft lip and palate. They examined 203 orthopantomographs with unilateral cleft lip and palate without syndromes with an age range of 5 to 10 years. They concluded high prevalence of hypodontia of the permanent lateral incisors in the cleft side and showed that the cleft could play an important role in such absence [22,23].

Dewinter *et al.* investigated the dental abnormalities and periodontal condition of patients with unilateral cleft lip and palate (UCLP) before orthodontic treatment. They evaluated 75 individuals with

UCLP (52 males, 23 females), between the ages of 8 and 20 years. They concluded that hypodontia was found in 75.8 % of the cleft patients. Hypodontia of the lateral incisors was found in more than 50% on the cleft side. Second premolars and lateral incisors outside the cleft area were missing in 27.2% of the patients [24]

Defective gene	Type of tooth agenesis
Dlx-1 and Dlx-2	Upper molars
Activin bA, activin receptors IIA and IIB, Smad2	Incisors and lower molars
Fgf8	All but lower incisors
Msx1	All
Pax9	All

Table 1: Genes and the type of tooth agenesis seen in humans.

Slayton et al. wanted to determine whether the candidate genes previously studied in subjects with cleft lip, cleft palate, or both area associated with hypodontia outside the region of the Literature Review 25 cleft. One hundred twenty subjects from the Iowa Craniofacial Anomalies Research Center were selected based on the availability of both dental records and genotype information.

Genotype analysis of candidate genes was performed using polymerase chain reaction/single-strand conformation polymorphism analysis. The prevalence of hypodontia in this sample was 47.5%, with 30.0% of subjects having missing teeth outside the cleft. There was a positive association between subjects with cleft lip or cleft lip and palate who had hypodontia outside the cleft region (compared with non-cleft controls) and both muscle segment homeo box homolog 1 (MSX1) (p 5 .029) and transforming growth factor beta 3 (TGFB3) [25].

Seventy-three children with submucous cleft palate were examined (38 girls and 35 boys), mean age 8.2 years (range 7.7-9.5), retrospectively from orthopantomograms. Dental abnormalities in permanent dentition were found in 26 patients (36%). Missing teeth, mainly lower 2nd premolars, upper lateral incisors, and upper 2nd premolars, were found in 12 patients (16%). Missing teeth, mainly lower 2nd premolars, upper lateral incisors, and upper 2nd premolars, were found in 12 patients (16%). Most of the patients had 1 or 2 missing teeth, 2 had 3 missing teeth. In 5 patients hypodontia was associated with another dental abnormality [26].

Aizenbud et al. investigated congenitally missing teeth in the Israeli cleft population, in Haifa. Their sample included 13 cleft lip, 25 cleft lip and alveolus, 21 cleft palate, and 120 cleft lip and palate patients. The objective of the study was to determine the prevalence of congenitally missing teeth in a group of Israeli children with various types of clefts. 67.7% of the patients presented with cleft. One hundred twenty subjects from the Iowa Craniofacial Anomalies Research Center were selected based on the availability of both dental records and genotype information [27].

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Kim & Baek in Seoul, Korea reported on the cleft sidedness and congenitally missing or malformed permanent maxillary lateral incisors in patients with unilateral cleft lip and alveolus UCLA or unilateral cleft lip and palate UCLP. The UCLP patient's demonstrated left-sided dominance. They concluded the following characteristics; malformed permanent maxillary lateral incisors were more common than congenitally missing teeth when cleft involvement was confined to the primary palate. Congenitally missing maxillary lateral incisors were significantly more in unilateral cleft lip and palate (56.7%) patients compared to unilateral cleft lip and alveolus patients (34.2%) [28].

Baek & Kim investigated the differences in the congenital missing teeth pattern in terms of tooth type (permanent maxillary lateral incisors and maxillary second premolars) and cleft sidedness between boys and girls in Korean unilateral cleft lip and alveolus UCLA and unilateral cleft lip and palate patients UCLP. The left side (58%) was predominately affected with clefing more than the right side (41%) in the UCLP. They concluded that the UCLP patients had 2.98 times more missing maxillary lateral incisors and 1.8 times more missing maxillary second premolars than did the UCLA. The maxillary lateral incisors were congenitally missing more in boys than in girls, however the maxillary second premolar showed the opposite tendency [28].

Menezes & Vieira studied the different types of dental anomalies as part of the cleft spectrum. The aim of the study was to determine subphenotypes of clefts based on tooth development. Records of 146 patients with oral clefts were evaluated. They reported that 32.19% presented at least one dental anomaly outside the cleft area. Individuals with complete cleft lip and palate (CLP) presented more dental anomalies than individuals with incomplete CLP ($p=.04$). Cleft palate individuals presented more dental anomalies than CLP individuals ($p=.048$). Maxillary lateral incisors and premolars were the most affected teeth. High incidence of maxillary second premolar agenesis was observed in individuals with bilateral CLP ($p=.04$). In cases with unilateral CLP, 12.5% presented dental anomalies of the maxillary lateral incisors on the non-cleft side. Cleft palate individuals presented a high incidence of mandibular premolar anomalies ($p = .004$) [29].

Da Silva *et al.* studied the dental anomalies of number in the permanent dentition of patients with bilateral cleft lip (CL). The patients were between 12 to 25 years and had no history of previous tooth extractions. The result of their study suggests that the prevalence of hypodontia was higher in patients with complete cleft lip. He also found that the most frequently affected tooth by hypodontia was the maxillary lateral incisor (26.6%), followed by the mandibular second premolar (8%), and maxillary second premolar (4.6%) [30].

Lai *et al.* performed a retrospective study on the anterior maxilla of the southern Chinese children with complete cleft lip and palate for the prevalence of different dental anomalies, position and rotation of teeth. They investigated dental records and study models of 195 CLP children aged between 3 to 17 years. They concluded that the group of Chinese children with CLP demonstrated statistically significant higher prevalence's of hypodontia. The tooth prevalence of the cleft side missing permanent lateral incisor was 19.2% in UCLP, and 20.5% in BCLP [31,32].

Galie *et al.* evaluated the dental and maxillary development and the presence of anomalies in unilateral cleft lip and alveolus patients UCLA, in the Faculty of Dental Medicine in Carol Davila University of Medicine and Pharmacy, Bucharest, Romania. Clinical and radiographic examination was carried out on 20 cases to identify hypodontia. They found out that lateral incisors on the cleft side were missing in 25%. The upper central incisor on the cleft side was missing in 15% of the cases. The second premolar was missing on the cleft side in 20%, while in only 10% cases the congenital absence was reported on both sides for the second premolars [33].

Tereza *et al.* studied the prevalence of tooth abnormalities of number and position in the permanent dentition of individuals aged 7 to 18 years old with complete bilateral cleft lip and palate. They studied 205 patients' records and panoramic radiographs. They found that hypodontia was observed in 144 patients (70.2%) and the highest prevalence was recorded for the maxillary lateral incisor teeth. When both lateral incisors were present (43%) they were located on the distal side of the cleft (25%) [34].

Treatment of Hypodontia

The congenital absence of teeth can seriously disable a young person both physically and emotionally, especially during the turbulent years of adolescence. Yet, there are reports of patients with hypodontia being referred late with all that that implies – treatment disrupting the examination years, reluctance to wear appliances because of the impact on the young person's social life [35].

Younger patients: should be reviewed regularly. Closely monitor their oral hygiene, periodontal health and caries rate as you do not want to lose the few teeth that they do have. These patients may require partial dentures which should be constructed from acrylic resin as they need to be frequently discarded as the child grows. Where there is no permanent successor to a deciduous tooth, every attempt should be made to retain the deciduous tooth. Dentures should be designed to place minimal load on deciduous teeth as this hastens root resorption [5,35].

Older patients: advanced restorative procedures are best carried out on patients in the middle to late teens. By this age, there is some stability in the dental arch, permanent teeth will have erupted, and their roots will be well formed. The patient is also beginning to take considerable interest in their dental status. Placement of implant-supported prostheses is unlikely to be considered until clinical signs of growth cessation are present. Other general factors include the ability of the patient to accept treatment; examination, work and social commitments and peer pressure [5,35].

SUMMARY

The pediatric dentistry follows patients from growth to adolescence with the main goal of motivate breastfeeding and maintain a high level of oral hygiene. Additionally, the pediatric dentistry team must diagnose the malocclusions and refer for orthodontic treatment in adequate timing. Orthodontic diagnosis is based on conventional orthodontic records, as well as the valuable occlusal scores. The protocol of orthodontic interventions should be simplified and consistent, prioritizing the approaches that have a significant impact on the final outcome. Very early orthodontic interventions should be avoided because they present poor stability and make the rehabilitation even more exhaustive for the individuals and their families. Orthodontic treatment planning should consider the particular expectations of the individual, as well as the wide individual variability of morphological characteristics of the face and occlusion.

Congenital absence of permanent teeth has direct clinical implications. Early evaluation of the number of missing teeth and consideration of the size and number of the remaining teeth in both jaws should aid the clinician in planning and managing treatment. The high incidence of missing teeth in children with cleft lip and palate presents additional complications for treatment planning. Therefore, it is important to determine, at an early age, the presence or absence of specific permanent teeth and then to plan treatment accordingly. The type of malocclusion, degree of crowding and facial profile is of prime concern in determining the final treatment plan.



Figure 2: Van der Woude syndrome with cleft lip and palate

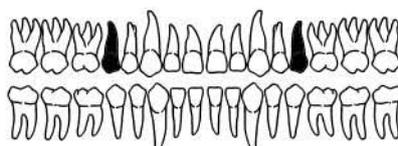


Table 2: Hypodontia

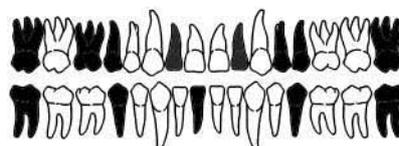


Table 3: Oligodontia refers to congenital lack of more than six teeth

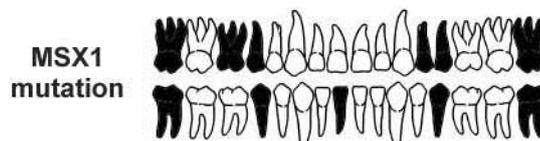


Table 4.1: Genes for congenitally missing teeth

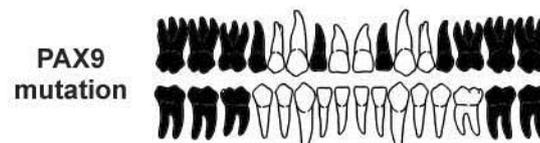


Table 4.2: Genes for congenitally missing teeth

REFERENCES

1. Adams M, Niswander J. Developmental 'noise' and a congenital malformation. *Genet Res.* 1967;10(313-317).
2. Al Omari F, Al-Omari IK. Cleft lip and palate in Jordan: birth prevalence rate. *Cleft Palate Craniofac J.* 2004;41(6):609-12.
3. Moore K, Persaud T. *The Developing Human - Clinically Oriented Embryology.* seventh ed. Philadelphia: Saunders Elsevier, 2003.
4. Kraus BS, Jordan RE, Pruzansky S. Dental abnormalities in the deciduous and permanent dentitions of individuals with cleft lip and palate. *J Dent Res.* 1966;45(6):1736-46.
5. Bishara S. *Textbook of Orthodontics.* Philadelphia: Sauders Elsevier, 2002.
6. Bohn A. Anomalies of the lateral Incisor in cases of harelip and cleft palate. *Acta Odontologica Scandinavica* 1950;9(1):41-59.
7. Olin WH. Dental anomalies in cleft lip and palate patients. *Angle Orthodontist* 1964;34:119-123
8. Jordan R, Kraus B, Neptune C. Dental abnormalities associated with cleft lip and or palate. *Cleft Palate Craniofac J.* 1966;3:22-55.
9. Fishman LS. Factors related to tooth number, eruption time, and tooth position in cleft palate individuals. *ASDC J Dent Child.*1970;37(4):303-6.
10. Hellquist R, Linder-Aronson S, Norling M, Ponten B, Stenberg T. Dental abnormalities in patients with alveolar clefts, operated upon with or without primary periosteoplasty. *Eur J Orthod.* 1979;1:169-180
11. Ranta R. Hypodontia and delayed development of the second premolars in cleft palate children. *Eur J Orthod.* 1983;5(2):145-8.
12. Ranta R. Associations of some variables to tooth formation in children with isolated cleft palate. *Scand J Dent Res.* 1984;92(6):496-502.
13. Ranta R. Numeric anomalies of teeth in concomitant hypodontia and hyperdontia. *J Craniofac Genet Dev Biol.* 1988;8:245-251.
14. Ranta R, Stegars T, Rintala AE. Correlations of hypodontia in children with isolated cleft palate. *Cleft Palate J.* 1983;20(2):163-5.

15. Dahllof G, Ussisoo-Joandi R, Ideberg M, Modeer T. Caries, gingivitis, and dental abnormalities in preschool children with cleft lip and/or palate. *Cleft Palate J.* 1989;26(3):233-7; discussion 237-8.
16. Lopes LD, Mattos BS, Andre M. Anomalies in number of teeth in patients with lip and/or palate clefts. *Braz Dent J.* 1991;2(1):9-17.
17. Vichi M, Franchi L. Abnormalities of the maxillary incisors in children with cleft lip and palate. *J Dent Children.* 1995;62(6):412-7
18. Tahir P. Dental anomalies in children with cleft lip and/or palate or both. *Saudi Med J.* 1998;19(3):323-334.
19. Shapira Y, Lubit E, Kuftinec M. Congenitally missing second premolars in cleft lip and cleft palate children. *Am J Orthod Dentofacial Orthop.* 1999 115(4):396-400.
20. Shapira Y, Lubit E, Kuftinec M. Hypodontia in Children with various types of Clefts. *Angle Orthodontist.* 2000;70(1):16-21.
21. Lekkas C, Latief B, terRahe S, Kuijpers-Jagtman A. The adult unoperated cleft patient: absence of maxillary teeth outside the cleft area. *Cleft Palate Craniofac J.* 2000;37(1):17-20.
22. Ribeiro LL, das Neves LT, Costa B, Gomide MR. Dental development of permanent lateral incisor in complete unilateral cleft lip and palate. *Cleft Palate Craniofac J.* 2002;39(2):193-6.
23. Ribeiro LL, Neves LTD, Costa. B, Gomide MR. Dental anomalies of the permanent lateral incisors and prevalence of hypodontia outside the cleft area in complete unilateral cleft lip and palate. *Cleft Palate Craniofac J.* 2003;40(2):172-5.
24. Dewinter G, Quirynen M, Heidbuchel K, Verdonck A, Willems G, Carels C. Dental abnormalities, bone graft quality, and periodontal conditions in patients with unilateral cleft lip and palate at different phases of orthodontic treatment. *Cleft Palate Craniofac J.* 2003;40(4):343-50.
25. Slayton R, Williams L, Murray J, Wheeler J, Lidral A, Nishimura C. Genetic Association studies of cleft lip and/or palate with hypodontia outside the cleft region. *Cleft Palate Craniofac J.* 2003;40(3):274-279.
26. Heliovaara A, Ranta R, Rautio J. Dental abnormalities in permanent dentition in children with submucous cleft palate. *Acta Odontol Scand.* 2004;62(3):129-31.
27. Aizenbud D, Camasuvi S, Peled M, Brin I. Congenitally missing teeth in the Israeli cleft population. *Cleft Palate Craniofac J.* 2005;42(3):314-7.
28. Kim N, Baek S. Cleft sidedness and congenitally missing or malformed permanent maxillary lateral incisors in Korean patients with unilateral cleft lip and alveolus or unilateral cleft lip and palate. *Am J Orthod Dentofacial Orthop.* 2006;130(6):752-8.
29. Menezes R, Vieira AR. Dental anomalies as part of the cleft spectrum. *Cleft Palate Craniofac J.* 2008;45(4):414-9.