Radiographic Assessment of Dental Maturation in Children With Dental Agenesis

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***Background**: Dental agenesis is the most common developmental anomaly in humans, frequently associated with disorders in dental development and maturation. **Aim**: The purpose of this study is to determine radiographic variations in dental maturation in a group of Venezuelan children with dental agenesis. **Study design:** 1,188 panoramic radiographs, from healthy patients ages 5 to 12 years old were studied for agenesis of permanent teeth. Dental maturation was assessed by relative eruption and dental age according to Nolla, comparing children affected with dental agenesis to a stratified control group selected from the same population, excluding children with premature loss of primary teeth in the left quadrants and unclear radiographs. Descriptive analysis, and differences between means and medians (Student t test, Kruskall-Wallis p=0.05) were performed. **Results**: Medians for Nolla stages were similar between groups, with delay in tooth formation in the agenesis group for second molars (p<0.05) and maxillary lateral incisors and second premolars. Dental age was significantly underestimated for both groups, -0.89 (±0.78) for the control group and -1.20 (±0.95) for the study group. Tooth eruption was similar between groups. **Conclusion**: Dental age was significantly delayed in Venezuelan children with dental agenesis, with variable significance for tooth formation of studied teeth.*

Key words: Dental agenesis, children, age determination by teeth

INTRODUCTION

Dental agenesis is the most common developmental anomaly in humans, frequently associated with disorders in dental development and maturation. [1, 2] It usually presents as an isolated anomaly, or may be associated with malformation syndromes, cleft lip/palate, reductions in tooth dimensions and morphology, taurodontism, shortened roots, delayed formation or eruption of other teeth, ectopic or included teeth, enamel hypoplasia and altered craniofacial growth. [1-3] Alternatively, it may occur as syndromic hypodontia associated with a systemic condition or with one of the large number of clinically recognized syndromes.[1]

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Prevalence of dental agenesis worldwide varies from 0.3% to 36.5% with differences between genders and ethnic groups. [4, 5] Little data regarding dental agenesis in Latin American populations has been published. [3, 6-10]

Dental agenesis may be occasionally caused by local environmental factors, such as infection, trauma, chemical substances, radiation therapy or disturbances of jaw innervations. [1, 2] Genetic factors with a marked degree of penetrance play a major role in dental agenesis. Different inheritance patterns as well as involved genes have been identified. To date, the mutation spectra of non-syndromic tooth agenesis in humans have revealed defects mainly in two genes that encode transcription factors, MSX1 and PAX9. [2, 11] Mutations in the transcription factor PAX9 have shown to be responsible for molar oligodontia, and in the transcription factor MSX1 responsible for selective posterior agenesis. Both are unrelated to isolated incisor hypodontia, where mutations in TGFα have been found responsible.[1]

Dental development is also mostly under genetic control, and may be altered in individuals with syndromes, systemic diseases, or medical treatments such as chemo or radiotherapy. Local factors such as infection, trauma, caries, pulp pathologies or premature loss of primary teeth, may also alter tooth development or eruption of succedaneum permanent teeth.[12-17] Several studies have evidenced that dental development and eruption may also be altered in individuals with dental agenesis. [6, 18-26]

Early descriptive studies have stated dental maturation delay in individuals with dental agenesis. Garn et al. in 1963 [18, 20] suggested that agenesis could be considered as the extreme expression of genes responsible for delayed calcification and eruption, as they observed significant delay in tooth formation and eruption individuals with 3rd molar agenesis, being the most posterior teeth the most delayed in formation. Bailit et al. in 1967 [19] also described that dental eruption was delayed in children with dental agenesis.

The number of teeth affected by agenesis appears to influence delays in dental development, with marked delay in formation in contralaterals to the missing tooth [21-23, 26] Gender differences have been described for these variations in dental development, affecting males for the early stages of development,[22] or females for more advanced formation stages.[6]

As a result of the above, it appears that the development of permanent teeth in children with dental agenesis may be different when compared with the general population. The purpose of this study is to determine variations in dental maturation in a group of Venezuelan children with dental agenesis.

MATERIALS AND METHOD

This study was approved by the Research and Ethics Committees of the Universidad Central de Venezuela Dental School (Nº 0101-2010) and received partial funding from the Counsel for Scientific and Humanistic Development CDCH-UCV (PI-10-7973-2011/1).

The design was a retrospective, cross-sectional study of dental panoramic radiographs and dental records, taken at routine examination at the Pediatric Dentistry Postgraduate Program University Clinic (Group A) and a private pediatric dentistry practice (Group B) in Caracas.

A convenience sampling method was applied to select the panoramic radiographs from children. A total of 1,188 good quality panoramic radiographs,[27] from healthy patients ages 5 to 12 years old were studied for agenesis of permanent teeth, excluding third molars. Children were classified by age groups.

Gender and age stratification were performed to segregate the radiographs and those in compliance with the inclusion criteria (healthy children, free from any disorder affecting growth, good quality radiograph) were considered in the study.

Children with unclear or distorted panoramic radiographs, and premature loss of primary teeth in the left upper and lower quadrants were excluded in order to avoid any variation that could derive from this loss that should not be attributed to variations associated with dental agenesis;

66 children ages 5 to 12 presented with dental agenesis of one or more permanent teeth. Of these, 17 presented premature loss of primary molars leaving the study sample in N=48 children with agenesis (Table 1).

Children affected with dental agenesis were compared to a control group selected from the same population, stratified by age and gender considering 3 control individuals for each study subject.

Selected radiographs were converted into digital images and downloaded using Nikkon 10 Megapixel camera and stored as jpg files using Adobe® Photoshop® SC4. All radiographs were analyzed by one observer (ACM). Data was analyzed using SPSS® computer package.

Tooth formation was assessed observing 7 maxillary and 7 mandibular teeth (central and lateral incisors, canines, first and second premolars, first and second molars).

Dental maturation was assessed by relative eruption (1= occlusal surface covered by bone, 2= occlusal surface breaks through alveolar bone crest, 3= occlusal surface reaches occlusal plane)

Root formation according to Nolla's[28] proposed stages (0 to 10).

Statistical analysis

Data analyses was performed using PASW ® Statistics 18 (SSPS18) © 2009 SPSS Inc. USA software.

Dental agenesis was classified according to affected tooth and gender. Descriptive analysis (frequencies, means), as well as differences between means (Student T test, p=0.05) were performed.

The difference between the agenesis and the control group for tooth eruption and Nolla stages for each tooth were compared using Kruskall-Wallis test, p=0.05.

Cohen's Kappa was used to test for intra-examiner agreement, using 28 randomly selected radiographs, including subjects from each age group,

RESULTS

1.188 panoramic radiographs were observed, from children ages 5 to 12, in order to determine prevalence and distribution of dental agenesis. Prevalence of dental agenesis was 5.6%, (mean 1.64) with a female: male ratio of 1.44:1. Mean of absent teeth was higher for females (1.67) than males (1.50) without significance (student T test). Prevalence was highest for mandibular second premolars (35.17%), and maxillary lateral incisors (31.55%).

Most patients presented agenesis of 1 (56.06%) or 2 (34.85%) teeth. More severely affected patients presented with agenesis of 3 (3.03%), 4 (4.55%) and 7 (1.52%) teeth.

66 patients presented with dental agenesis, of which 15 (22.72%) were excluded from this study due to premature loss of deciduous teeth in the upper or lower left quadrants and 4 were excluded due to poor quality radiographs. Thus, 47 patients comprised the study group. For each child in the study group, 3 controls were randomly selected from the same population, matched by gender and age group. A total of 188 children completed the study and control group, mean age was for the study group was 8.13 (±1.78) and for the control group 8.12 (± 1.79), minimum 5.01, maximum 11.98.

Cohen's kappa statistic demonstrated an intra-examiner agreement of 0.77 for eruption stages and 0.82 for Nolla's tooth formation stages.

Left maxillary and mandibular teeth were observed for tooth formation (Nolla stages) And relative eruption, excluding those affected by agenesis (Table 3)

Medians for Nolla Stages were similar for most studied teeth. P values for differences between medians for each tooth were calculated using the Kruskall Wallis test. (Table 4) Differences were statistically significant, (p value <0.05), for second molars, both mandibular and maxillary. A low p value was also obtained for the difference between medians for maxillary lateral incisor and second premolar.

Scatterplot graphs with polynomial trendlines comparing Nolla stages for teeth with small p values were performed. (Fig. 1, Fig. 2,

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Table 1. Prevalence of teeth affected by agenesis

Maxillary teeth affected by agenesis (%)													
17	16	15	14	13	12	11	21	22	23	24	25	26	27
0	0	16.48	0.93	0.93	15.74	0	0	14.81	0	0.93	8.33	0	0
Mandibular teeth affected by agenesis (%)													
47	46	45	44	43	42	41	31	32	33	34	35	36	37
2.78	0	13.87	0	0	4.63	4.63	1.85	0.93	0	0.9	21.3	0	0.93

Table 2. Distribution of the study and control groups classified by gender and age

		Age							Total
Gender	Group	5.00 - 5.99	6.00 - 6.99	7.00 - 7.99	8.00 - 8.99	9.00 a- 9.99	10.00 - 10.99	11.00 - 11.99	
	Control	6	9	24	21	3	9	6	78
Female	Agenesis	2	3	8	7	1	3	2	26
	Total	8	12	32	28	4	12	8	104
	Control	15	9	9	3	15	9	3	63
Male	Agenesis	5	3	3	1	5	3	1	21
	Total	20	12	12	4	20	12	4	84

Table 3. Distribution of teeth analyzed for Nolla Stage and relative eruption

	Cases			
	Included		Excluded	
Tooth	**N**	**Percent**	**N**	**Percent**
21	188	100.0%	0	0.0%
22	177	94.1%	11	5.9%
23	188	100.0%	0	0.0%
24	187	99.5%	1	0.5%
25	181	96.3%	7	3.7%
26	188	100.0%	0	0.0%
27	188	100.0%	0	0.0%
31	188	100.0%	0	0.0%
32	188	100.0%	0	0.0%
33	188	100.0%	0	0.0%
34	187	99.5%	1	0.5%
35	171	91.0%	17	9.0%
36	188	100.0%	0	0.0%
37	187	99.5%	1	0.5%

Table 4. Medians for Nolla stages in the control and study group

Maxillary Teeth							
Tooth	21	22	23	24	25	26	27
Control	9	8	7	6	6	9	5
Agenesis	9	8	7	6	5	9	5
P value	0.714	**0.072**	0.972	0.133	**0.060**	0.816	**0.025***
Mandibular Teeth							
Tooth	31	32	33	34	35	36	37
Control	10	9	7	7	6	9	5
Agenesis	9	9	7	6	6	9	5
P value	0.481	0.467	0.852	0.143	0.368	0.534	**0.014***

*Kruskal Wallis Test p value <0.05

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Fig. 3, Fig. 4). It is evident that some cases have delayed maturation with lower Nolla Stage at higher ages for the study group. Polynomial curves for dental maturation demonstrated delayed tooth formation in the study group when compared to the control group.

Dental age using the Nolla method was calculated for the study and control groups. 31 study subjects presented with agenesis of teeth in the left quadrants, in 7 cases the affected tooth was unilateral and was substituted by the formation stage of the contralateral tooth, allowing the method application to 24 study subjects. The Nolla method underestimated dental age for both the control and the study group, with statistical significance (Student T test, p=0.01) The mean difference was -0.89 (±0.78) for the control group and -1.20 (±0.95) for the study group. Student T test was performed to determine difference in underestimation means between groups. P value was 0.70, thus failed to prove statistically significant at the p=0.05 level.

Medians for relative eruption stages were similar for all studied teeth except for the maxillary lateral incisor, accepting the null hypothesis of equality between groups. P values for differences between medians for each tooth were calculated using the Kruskall Wallis test. (Table 5) Differences were not statistically significant, (p value <0.05). A low p value obtained for the difference between medians for mandibular first molar.

DISCUSSION

Dental agenesis is the most common developmental anomaly in human and may cause malocclusion and other functional and aesthetic problems.[1, 2] Prompt diagnosis of congenitally missing teeth in children allows comprehensive treatment planning that includes all growth stages. Treatment should favor proper development of the occlusion, avoiding malocclusions and maintaining the child's self-esteem, and should be performed by a multidisciplinary team in which the pediatric dentist has utmost importance.[29]

Fig. 1. Scatterplot graph with polynomial trendline depicting the maxillary lateral incisor (22) Nolla stage according to age for the study and control group

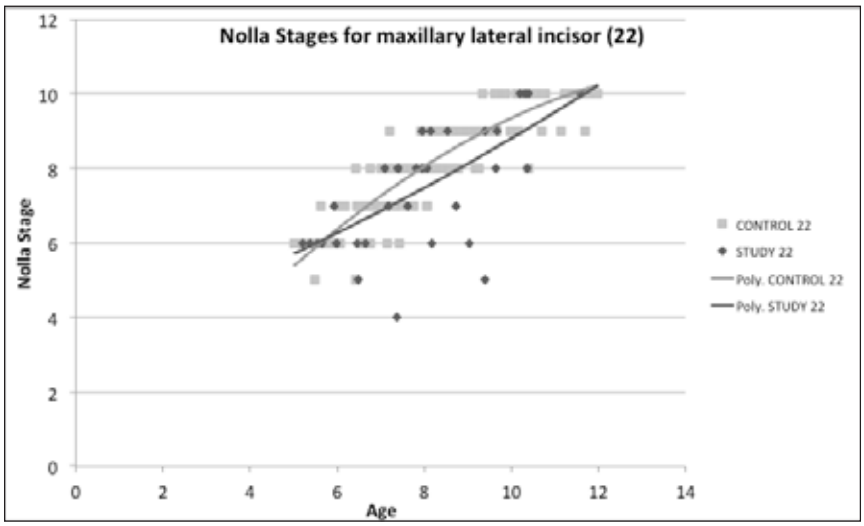
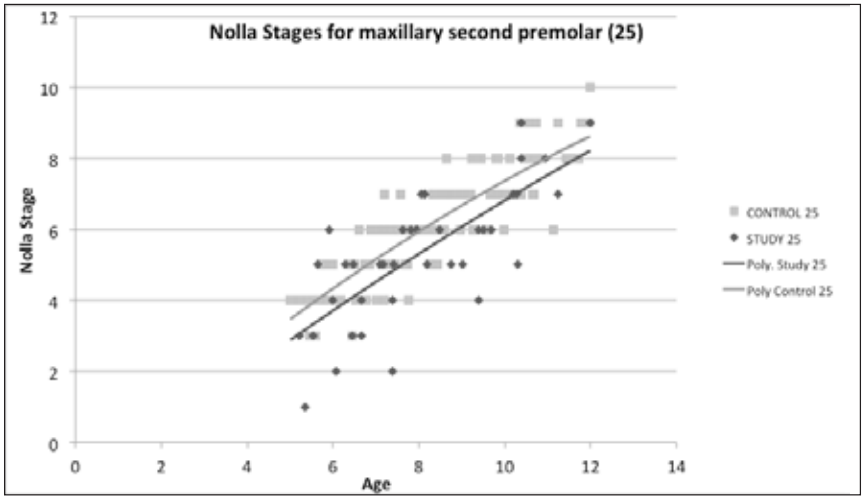


Fig. 2. Scatterplot graph with polynomial trendline depicting the maxillary second premolar (25) Nolla stage according to age for the study and control group.



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The epidemiology of dental agenesis is very variable, depending on ethnic and geographic backgrounds, with prevalence varying from 0.3 to 36.5%. [4, 5] Ethnic patterns have been reported in the prevalence and distribution of agenesis, although differences have failed to provide statistical significance. [10]

For this sample, prevalence of dental agenesis was 5.6%. This is similar to findings in Brazil, lower than that reported for European or Asian populations, and higher than other Latin American studies. [3, 5, 7, 8, 10] Teeth most affected were second mandibular premolars , followed by maxillary lateral incisors, in accordance with previous reports.[4, 5]

Females were more affected than males, (1.44:1) without significance, also being the mean number of congenitally missing teeth higher in females (1.67) than in males (1.50). This is in accordance with most studies that describe higher prevalence in females, disregarding ethnicity and geographic location. [4, 5] Most patients

Table 5. Relative eruption teeth in the control and study group

	Maxillary Teeth						
Agenesis	21	22	23	24	25	26	27
Control	3	2	1	1	1	3	1
Agenesis	3	1	1	1	1	3	1
P value	0.804	0.185	0.403	0.210	0.657	0.402	0.497
	Mandibular Teeth						
	31	32	33	34	35	36	37
Control	3	3	1	1	1	3	1
Agenesis	3	3	1	1	1	3	1
P value	0.284	0.871	0.455	0.131	0.180	**0.066**	0.639

*Kruskall Wallis Test p value <0.05

Fig. 3. Scatterplot graph with polynomial trendline depicting the maxillary second molar (27) Nolla stage according to age for the study and control group.

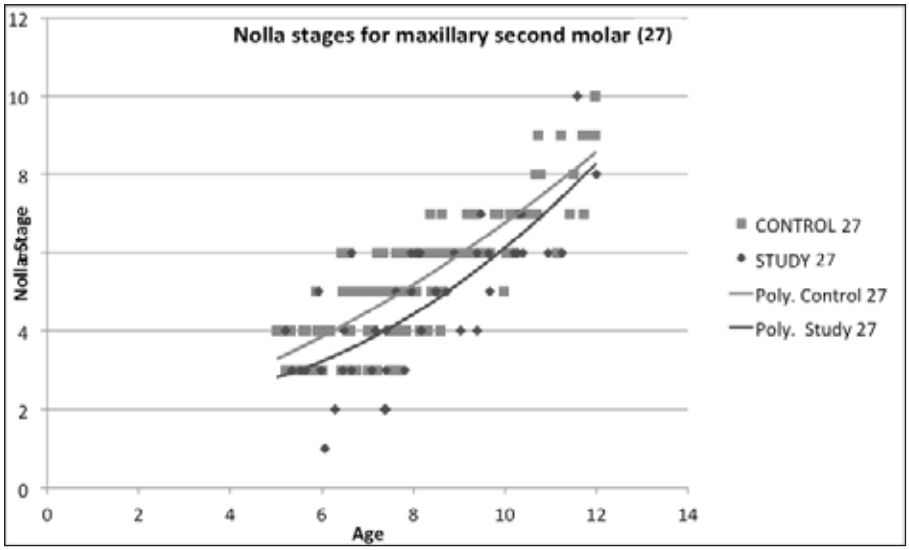
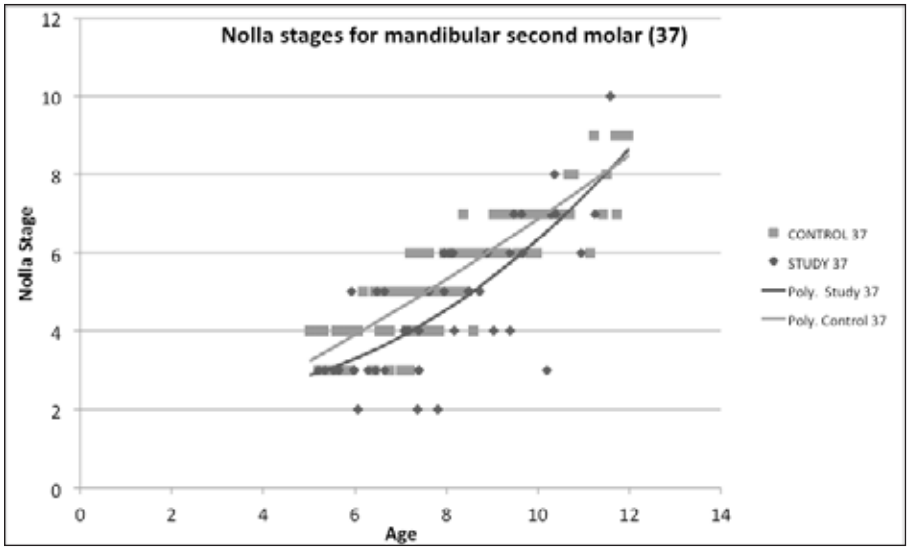


Fig. 4. Scatterplot graph with polynomial trendline depicting the mandibular second molar (37) Nolla stage according to age for the study and control group.



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presented with one (56.06%) or two (34.85%) missing teeth, in accordance with previous studies. [4]

Children with syndromes, systemic diseases o premature loss of primary teeth were excluded from the study sample considering general local factors such as infection, trauma, caries, pulp pathologies or premature loss of primary teeth, may also alter tooth development or eruption of succedaneum permanent teeth. [12-16]

Dental agenesis is usually an isolated anomaly, but it may also be associated with reductions in tooth dimensions and morphology, taurodontism, shortened roots, delayed formation or eruption of other teeth, ectopic or included teeth, enamel hypoplasia and altered craniofacial growth.[1-3] Several studies have evidenced that dental development and eruption may also be altered in individuals with dental agenesis. [6, 18-26] Conclusions from comparisons between studies are difficult to make because different methods of assessing tooth developmental age have been used.[24]

One of the earliest reports regarding differences in eruption for children with dental agenesis was performed by Bailit *et al* in 1967.[19] They observed that clinical dental eruption was delayed in 177 children with dental agenesis, although these differences were not significant when compared with previous eruption data from Japan. In the present study, dental eruption was not clinically assessed but observed in panoramic radiographs, [30] thus comparison with clinical eruption means are inadequate. Nevertheless, delay for the mandibular first molar was observed. No significance was found for eruption stages in the agenesis group, due to small sample size and individual variability. Bailit *et al* [19] described delay in eruption of the mandibular central incisor in children with dental agenesis. Based on these findings, it is possible to state that the commencement of the early mixed dentition stage occurs later for children affected dental agenesis. This may have clinical importance as radiographic screening may prove necessary for children with delayed eruption in order to perform comprehensive diagnosis and treatment planning.

Nolla´s method has been previously used in several studies regarding dental development, [31-34] with variable accuracy and underestimation in most cases. In this study, dental age was significantly underestimated for both groups, -0.89 (±0.78) for the control group and -1.20 (±0.95) for the study group. Underestimation was greater for the agenesis group, although the difference in underestimation between the study and control group was not statistically significant (p=0.70), maybe due to small study sample.

Dental formation was delayed for some teeth in the agenesis group. Mandibular and maxillary second molars were significantly delayed. The study group was compared with a control group and not with Nolla's original data since these means were deemed unfit for Venezuelan population in previous studies. [32]

The data here presented suggests that in patients with dental agenesis, the most distal teeth of each dental group is more likely to present delay in formation. Also that mandibular second premolars, maxillary second premolars and maxillary lateral incisors are most likely to be absent, and, if present, are affected by delay in tooth formation.

When comparing these results to those previously published, it must be taken into account that third molar agenesis was not considered and the mean of missing teeth was lower than 2, differing from other studies that analyzed data from oligodontia patients (6 or more missing teeth) [21] or patients with third molar agenesis. [20]

Garn et al. in 1963 [18] suggested that agenesis could be considered as the extreme expression of genes responsible for delayed calcification and eruption, as they observed significant delay in tooth formation and eruption in a radiographic study comparing individuals with 3rd molar agenesis with a control group in a North American sample. Moreover, in further research Garn y Lewis [20] found that most posterior teeth were most delayed in formation. The results here presented demonstrate delay in formation of the most posterior teeth, in accordance with observations by Garn *et al.*

The number of teeth affected by agenesis may also influence delays in dental development. Rune y Sarnäs [21] studied tooth size and formation in 91 Swedish children with four or more missing teeth. Tooth formation was found to be delayed in relation to chronological age as well as compared to norms described by Haavikko (-1.8 years for boys, -2.0 years for girls). In this study, tooth development showed considerable variations between children (-2.4 to -7.8 years) with marked delay in formation in contralaterals to the missing tooth. These researchers state that there is a considerable variability between individuals and delay affects in variable degrees all teeth in all crown and root formation stages. This delay was smaller for the mandibular teeth. No specific pattern was found regarding age, gender or number of missing teeth.

The results of the present study are in accordance with those reported by Rune and Sarnäs [21] since great variability was observed and a tendency for greater delay in tooth formation was evident for the maxillary teeth when compared with the mandibular teeth.

van der Weide *et al* [22] studied 216 individuals from the Netherlands with six or more missing teeth, mean age 11.3 years, using dental development stages proposed by Demirjian. They state that dental age may not be assessed using this method for the study group because it is impossible to obtain the sum of 7 mandibular teeth due to agenesis. In order to determine the differences between the study group and the control group in formation stage for each tooth, logistic regression was used and median was calculated for each tooth determining the age at which 50% of the individuals reached each maturation stage for each tooth. These researchers found significant tendency for delay in tooth formation when comparing their sample to data from the Nijmegen Growth Study, which was more obvious in males for the early stages of development. They also found considerable variations between individuals.

Lozada and Infante [6] also used Demirjian's stages to compare dental development in 56 Colombian children with dental agenesis with a control group. They found a tendency for delayed tooth formation, and that females evidenced delayed eruption, (0.7 years for males, 1 year for females) particularly for more advanced formation stages, although this was not statistically significant.

Slayton [24] reviewed the research published by Usleghi *et al* [23] determining that it was a well-designed study with an accepted method for quantifying dental development using radiographs with an evidence level of 3a (Systematic review with homogeneity of case-control studies).

In the present study, over 90% of the children presented with agenesis of 1 or 2 teeth, the correlation between delay and number of affected teeth was not found as reported by other studies.[21, 23]

Ruiz-Maelin *et al* [26] studied a sample composed by 139 ages 9 to 18, white and non-white patients from the United Kingdom, using the above mentioned methods (Demirjian, Haavikko). For each subject the mean and standard error of the age of attainment of

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each tooth stage were calculated using the weighted average method to estimate dental age. Significant delay in dental age was found in the dental agenesis group when compared to a control group. Dental age presented delay in comparison to chronologic age of -1.64 (±1.75) years (Demirjian) and -1.20 (±1.74) (Haavikko), and -0.60 to -0.88 years compared to the control group. The delay was greater in males, but without significance. This study found no evidence to suggest that sex or ethnicity has an effect in the delay in dental age for agenesis patients. Results in the present study using the Nolla method (-0.89 (±0.78) for the control group and -1.20 (±0.95) for the study group) are very similar to those obtained by Ruiz-Maelin et al. [26] using the Haavikko method.

Ruiz-Maelin and Cols. [26] grouped agenesis individuals in three categories (mild 1-2 missing teeth, moderate 3-5 missing teeth, severe 6 or more missing teeth) and found a statistically significant association between number of affected teeth and delay in dental age, whereas as the number of absent teeth increased so did the difference between dental and chronological age in a rate of 0.13 *per* year. The severity of the hypodontia affected the magnitude of the delay and the teeth adjacent to the site of the agenesis were significantly delayed compared to the corresponding teeth in the matched group.

Uslenghi *et al* [23] assessed dental development according to Haavikko's method in 135 UK children, mean age 10.38, with agenesis of one or more permanent teeth. Mean dental age was calculated using all developing teeth and compared to chronological age. Significant delay (1.51 years) in dental development was observed in children with dental agenesis. Also, teeth adjacent to the site of the agenesis were most delayed. These researchers found the delay in dental development to be significantly correlated to the severity of agenesis and that the greatest deviation in dental age was observed for the older children.

In the present study almost all patients presented mild hypodontia (1-2 missing teeth), and the association between number of affected teeth and delay in dental age was not observed.

Great variability in dental maturation was observed between all individuals in this study group. Some patients presented with normal maturation while others presented with great delay. Such observations are in accordance with most published data [22] This variability determines that, in each case, dental age assessment must be performed on an individual basis before commencing comprehensive orthodontic/prosthetic treatment. Common methods of assessing dental age may be unfit for children with dental anomalies such as agenesis.[23] Research with larger samples and collaborative studies using the same methodology may be necessary in order to determine if these methods are applicable, and to determine if differences observed are significant.

Children with hypodontia have malocclusions and functional problems. Self esteem related with qualitative assessment of esthetics may also be affected, especially when anterior teeth are missing. Treatment planning that includes tooth replacement and/or orthodontic space closure is a complex process that must take into account the patient's overall characteristics.[29, 35] For the clinician, it is important to consider that patients with dental agenesis may have a generalized delay in dental development, and that this delay seems to be more pronounced in severely affected patients. In some cases, it may be necessary to postpone treatment decisions to confirm which teeth are really missing or present with severe delay. [24]

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CONCLUSION

Prevalence of dental agenesis in this Venezuelan sample (5.66%) is similar to that reported in other populations. 91% presented with one or two missing teeth being the mandibular second premolar and the maxillary lateral incisor most frequently affected. Females were more affected than males (1.44:1).

Dental eruption failed to demonstrate difference between the study and control group.

Dental age was significantly underestimated for both groups, and was delayed in children with dental agenesis (-1.20) when compared to the control group (-0.80),

Tooth formation had a tendency to be delayed in the agenesis group with evident variation between individuals. This delay was significant for the mandibular and maxillary second molar.

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