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Dental development in Down syndrome and healthy children: a comparative study using the Demirjian method

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Structured Abstract

Objective: In children with Down syndrome, the timing of dental eruption is important for orthodontics treatment planning. Aim of this study was to determine whether tooth eruption and development of the dentition in children with Down syndrome are impaired.

Material and Methods: Dental development was scored on orthopantomograms (OPTs) of 95 children with Down syndrome. The dental age was determined at the left mandibular side according to the Demirjian method and by converting the assigned scores to the dental maturity score. Dental development scores of control children and DS children were compared with a mixed model linear regression analysis.

Results: The model showed statistically significant changes relating to increasing age ($P<0.001$) and gender ($P<0.05$). In this comparison, the total DS group (with and without hypodontia) was not statistically significantly different from the control group. There was also no significant difference between the total sample of DS children and the control group after using the Nyström imputation (with and without hypodontia).

Conclusion: The findings showed that dental development in DS children is similar to the development of control children and that a relationship exists between hypodontia and dental development. The clinically observed late eruption is probably not due to late dental development but due to the other processes that take place during eruption, such as the possible impaired processes at the apical side and the occlusal side of an erupting element.

KEYWORDS
down syndrome, odontogenesis, regression analysis, tooth eruption

1 | INTRODUCTION

Down syndrome (DS) is one of the most common syndromes in the Netherlands, and its prevalence is 1 in 714.[1] Several dental complications are associated with Down syndrome.[2,3] The most common disturbances are agenesis of teeth, predilection for periodontitis and deviating development of both the deciduous and mixed dentition.[2] DS children show a much higher percentage of agenetic teeth than children without DS.[4,5] It is possible that in patients with DS, a relationship exists between the presence of agenesis and delayed dental development.[6]

In the general population, eruption patterns and onset of eruption are highly variable.[7] In DS children, the transition from the deciduous to the permanent dentition is slow.[4] A good indication for this slow transition is the eruption of the first molars at the age of 8-9 years in DS children compared to eruption at the age of 6-8 years in the general population.[5] From a previous study, it is known that the eruption sequence resembles the sequence in children without DS.[2] However, it is the general eruption of teeth in children with DS that seems to be disturbed and not the eruption pattern.[8] Whether these problems lie in the maturation of teeth or other mechanisms of the eruption is unclear.

Dental maturation can be established by assessing the timing of emergence of the tooth in the oral cavity. The disadvantage of this method is that the timing can be largely biased due to premature loss or ankyloses of primary teeth or tooth agenesis.[9] Dental age estimation can also be performed by measuring the open apices of seven mandibular teeth combined with a mathematical formula.[10] This method is based on measuring the completeness of apical development via a computer method determined on measurements on OPTs of patients collected in several European countries.[10] Dental development measured by the stage of root development is the most commonly known method, and the most used is the Demirjian method.[11] The Demirjian method classifies the enamel calcification in erupting and/or fully erupted teeth. It uses orthopantomograms (OPTs) to score individual teeth, and scores are combined to a maturity score.[12]

Whether a difference exists between dental development of children with DS and healthy children is still unclear. Three studies have been published with opposing views.[4,11,13] The aim of this study was to get a better understanding of dental development in DS children compared to a healthy population in relation to hypodontia. In addition, we will construct curves to illustrate dental development of DS and healthy children.

2 | PATIENTS AND METHODS

2.1 | Patients

Between November 2002 and June 2013, 94 patients (52 boys and 42 girls) diagnosed with Down syndrome were included from two centres: CBT Rijnmond, Centre for Special Dental in Rotterdam, the Netherlands, and the department of Orthodontics, Sophia Children's Hospital, Erasmus MC University Medical Center, the Netherlands. From these 94 children, 25 had one tooth missing in the mandibular left side (13 boys [52%] and 12 girls [48%]). Only patients with at least one orthopantomogram and without history of orthodontic treatment were included (N=226). Bad-quality OPTs due to inadequate compliance of subjects or OPTs of children aged outside of 2-16 year range were excluded from the study. Consequently, 130 OPTs were excluded because of the second exclusion criterion, leaving us with a total sample of 94 OPTs (42%) of children with Down syndrome. As a comparison group, we used OPTs of 451 Dutch children (225 boys and 226 girls) reported on in an earlier published study.[14] The median age at which the OPTs were taken was 7.7 year with a range from 2.9 to 16.9 years. The reference tables were adjusted according to the same calculated date of birth range of the DS sample.

The protocol for this research study was approved by the Research Ethical Committee (METC) of the Erasmus Medical Centre in Rotterdam (approval number: MEC-2011-276).

2.2 | Method

Dental development was scored on OPTs by determining one of the eight developmental stages (A-H) of the left-sided mandibular teeth excluding third molars, according to the Demirjian's criteria.[15] These stages were converted into numbers using French Canadian weighted scores and summed; this score is referred to as the dental maturity score (DMS), and it expresses the degree of dental development in a child.[16] Two examiners were trained using a tutorial programme, available on CD-ROM (Demirjian, 1993). To assess the interexaminer reliability, both examiners randomly rescored 20 OPTs. To assess the intra-examiner reliability, the same 20 OPTs were scored again after a period of 1 month. All 95 OPTs were scored by one examiner.

2.3 | Statistical analysis

Intra-examiner reliability and interexaminer reliability were determined using the intraclass correlation coefficient (ICC) for the DMS.[17] The ICC is comparable to the kappa coefficient. ICC values range from 0 to 1. An ICC of 0.61-0.80 is interpreted as a substantial agreement and an ICC of 0.81-1.00 as an almost perfect agreement.

Prior to the statistical analysis, the DMS was log-transformed, to obtain a more linearly distributed outcome variable. Logit transformation of the value 1 yields to $+\infty$; therefore, we used 0.997 as the maximum DMS value. We investigated the impact of Down syndrome on dental development using a mixed model linear regression, for boys and girls separately, in two steps:

In the first step, the mentioned relationship was investigated only in subjects, without hypodontia of two matching teeth in the lower jaw, as DMS could not be calculated (N=71) (Table 2 before imputation).

To increase the sample size, in the second step, we also included Down syndrome patients with hypodontia of matching teeth in the lower jaw (N=25) by imputing the scores using mathematical formulas for the assessment of developmental stages of missing teeth established by Finnish authors.[18] Differences in DMS between DS patients with and without imputation were also tested (Table 3). The group with imputed scores was referred to as "Down syndrome with imputation" in this study.

All statistical models were adjusted for age and sex. In the final model of the second step, we also adjusted additionally for the hypodontia status in children. A P value <.05 was considered as a statistically significant result. All statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

3 | RESULTS

The ICC for the intra-examiner reliability was 0.98 (95% confidence interval [CI]=0.94, 0.99). The ICC for the interexaminer reliability was 0.98 (95% CI=0.94, 0.99). Both scores are considered very high. The mean DMS for the control children was 30.07 (SD 19.89) and for DS was 15.07 (SD 11.20). To get a better insight in the crude difference in obtained DMS between compared groups, we presented the mean DMS, stratified per year of age in Table 1.

The rate of dental development in DS children was further investigated with mixed linear regression models separately for boys and girls (Tables 2 and 3). The results of the model showed that there was no significant difference between non-imputed Down

TABLE 1 Distribution of dental maturity score in controls and subjects with Down syndrome by age

	Control			Down syndrome			
Age	N*	Mean	SD	N*	Mean	SD	Difference
2	1	0.151	0.000	0	-	-	-
3	24	0.224	0.057	0	-	-	-
4	66	0.351	0.089	1	0.482	-	0.131
5	57	0.508	0.100	4	0.568	0.169	0.060
6	47	0.618	0.093	7	0.715	0.061	0.097
7	43	0.750	0.077	10	0.816	0.077	0.066
8	31	0.812	0.085	10	0.833	0.085	0.021
9	29	0.884	0.063	16	0.928	0.044	0.044
10	31	0.928	0.052	23	0.946	0.029	0.018
11	25	0.956	0.033	33	0.962	0.019	0.006
12	19	0.983	0.016	27	0.966	0.014	0.017
13	23	0.985	0.021	29	0.981	0.016	0.004
14	20	0.999	0.002	22	0.989	0.011	0.010
15	21	0.999	0.002	15	0.996	0.008	0.003
16+	14	0.999	0.004	26	1.000	0.000	0.001

*N-number of used dental panoramic radiographs.

TABLE 2 Association between dental maturity and Down syndrome using three linear mixed-effect models in boys

	Before imputation				After imputation						
	Model 1				Model 2				Model 3		
Parameter	N*	ß	95% CI	*P*-value	N*	ß	95% CI	*P*-value	ß	95% CI	*P*-value
Comparison group											
Control -ref.	225	0	-	-	225	0	-	-	0	-	-
Down syndrome	38	0.134	(−0.054, 0.323)	.160	51	0.088	(−0.086, 0.262)	.317	0.116	(−0.085, 0.318)	.256
Age	263	0.547	(0.525, 0.569)	<.001	276	0.544	(0.523, 0.566)	<.001	0.544	(0.522, 0.566)	<.001
Hypodontia status											
No ref.				262					0	-	-
Yes				14					−0.103	(−0.446, −0.240)	.550

*N-number of participating children.

TABLE 3 Association between dental maturity and Down syndrome using three linear mixed-effect models in girls

	Before imputation				After imputation						
	Model 1				Model 2				Model 3		
Parameter	N*	ß	95% CI	*P*-value	N*	ß	95% CI	*P*-value	ß	95% CI	*P*-value
Comparison group											
Control—ref.	226	0	-	-	43	0	-	-	0	-	-
Down syndrome	33	−0.019	−0.225, 0.186	.853	226	-0.054	−0.230, 0.121	.539	0.087	−0.116, 0.290	.396
Age	259	0.611	0.590, 0.632	<.001	269	0.608	0.587, 0.628	<.001	0.606	0.586, 0.626	<.001
Hypodontia status											
No—ref.					258				0	-	-
Yes					11				−0.428	−0.754, −0.103	.011

*N-number of participating children.

TABLE 4 Dental maturity differences between Down syndrome group with and without performed imputation for dental maturity score adjusted for age in boys

Parameter	N	ß	95% CI	*P*-value
Imputation				
No	263	0	-	-
Yes	13	−0.233	−0.622, 0.156	.239
Age	276	0.550	0.529, 0.571	<.001

TABLE 5 Dental maturity differences between Down syndrome group with and without performed imputation for dental maturity score adjusted for age in girls

Parameter	N	ß	95% CI	*P*-value
Imputation				
No	259	0	-	-
Yes	10	−0.128	−0.437, 0.182	.415
Age	269	0.606	0.586, 0.626	<.001

syndrome patients and controls in both boys, regression coefficient (β)=0.134, (95% CI=−0.054, 0.323, *P*=.160), and girls, β=−0.019, (95% CI=−0.225, 0.186, *P*=.853). To account for cases with DS that had missing values for DMS, we applied Finish mathematical formulas. The formulas were validated by comparing differences in DMS of DS subjects with and without imputation (Tables 4 and 5). By applying these formulas, we did not observe any significant differences between the non-imputed and imputed group of DS subjects (boys, *P*=.239 and girls, *P*=.415).

In models 2 and 3, we included also imputed DS subjects (Tables 2 and 3). The results of models 2 and 3 were consistent as regard to the differences between DS children and controls. We observed any significant differences between compared groups in males— Model 2: β=−0.088, (95% CI=−0.086, 0.262, *P*=.317), Model 3: β=−0.116, (95% CI=−0.085, 0.318; *P*=.256)—and in females, Model 2: β=−0.054, (95% CI=−0.230, 0.121; *P*=. 539), Model 3: β=0.087, (95% CI=−0.116, 0.290; *P*=.396). However, we identified that girls with hypodontia had a significantly delayed dental development: β=−0.428, (95% CI=−0.754, −0.103; *P*=.011). Figures 1 and 2 illustrate the dental development curves of DS boys and healthy boys and DS girls and healthy girls.

4 | DISCUSSION

The results of this study showed that dental development in DS children is similar to the development of normal children. This seems to contrast with some earlier findings[2,3,19,20] in which a delayed dental development was found and is in agreement with others.[13] As it is known that the clinical emergence is delayed in DS children, it is hypothesized that the dental development could be a cause for this delay; however, the results from our study did not strengthen this theory.[8,13]

Tooth eruption is a tightly regulated process involving the tooth organ (dental follicle, enamel organ) and surrounding alveolar tissues. The eruption movement results from a balance between tissue destruction (bone, connective tissue and epithelium) and tissue formation (bone, PDL and root).[21] The delay in clinical emergence probably finds its origin in the gingival tissue or another factor such as the cellular processes at the apical and occlusal side of the erupting tooth.[22]

These aberrant eruptions and shorter roots may lead to lesser vertical height development of the jaws and may result in a relatively short vertical height in the DS facial profile. It is possible that a genetic disturbance in the RANKL/RANKL/OPG system and/or the disturbance of the RUNX2 complex is a cause for the impaired eruption.[22–24] For example, in patients with cleidocranial dysostosis, delayed eruption is caused by various mutations in the gene expression, for example PAX9, MSX1, RUNX2/cbfa1 and RANK, RANKL, OPG and CSF-1.[22–27] In patients with DS, these mutations of gene expression are not known yet. The known mutations in gene expression in DS children could intervene in a yet unknown process or pathway that influences the eruption. Another factor impairing tooth eruption can be hypothyroidism seen in 50% of the DS population.[28] In contrast to the knowledge that hypothyroidism hampers the eruption of teeth, the way gene expression in DS children influences their dental development is not yet completely known.[13,28]

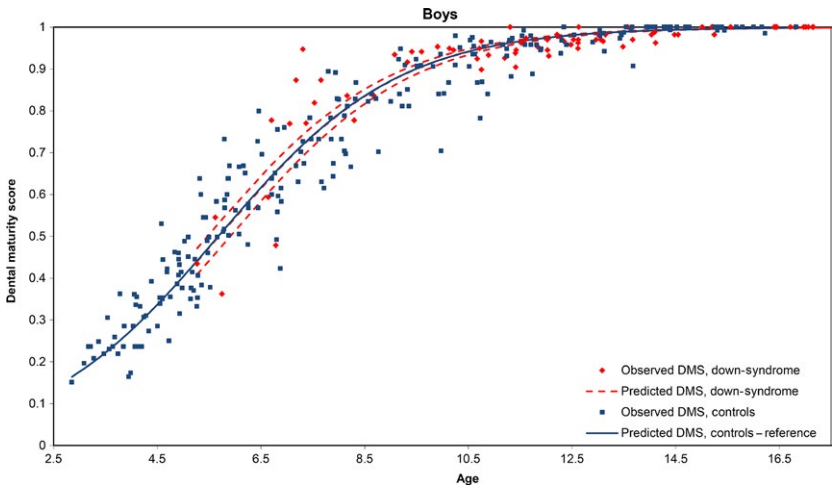

FIGURE 1 DMS vs Age (boys)

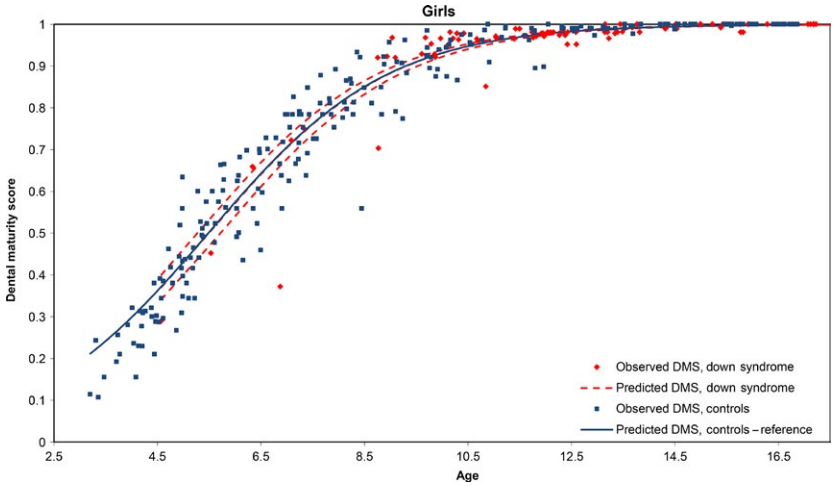

FIGURE 2 DMS vs Age (girls)

The Demirjian method of assessing dental age is the most precise and accurate method as compared to other dental age estimation methods at this time.[29,30] In our study, the younger DS children were the most difficult to because of the less cooperativeness of the DS children when making an OPT. In older more cooperative children and in adolescents, it was easier to obtain good OPTs and thereby determining a DMS score. The scoring was also difficult due to the different form (shorter and blunter) of the roots.

The subjects of our study were all collected from the Rotterdam region, the Netherlands, and therefore, a regional bias may exist. On the other hand, a general population study which was performed lately[31] showed no regional differences compared to the rest of the country. The inter-regional differences found until now may be better explained by secular trends in dental development found in previous studies.[32] Secular variations have been observed in sexual development and physical growth due to continuous changes in genetic, epigenetic and environmental factors.[33–36] Lately, a Dutch population study showed a positive secular trend in accelerated dental development in Dutch children born between 1961 and 1994,[31] although researchers earlier believed that secular trends did not influence dental development. In the light of these studies, we need to control for secular trends. In our study, the data were consistent with the used comparison tables (Amsterdam and Nijmegen)[14,31] but only after the results were compensated for a secular trend by transforming age to the same date of birth range.

As DS children are known to have a higher prevalence of agenetic teeth, we needed to address agenetic teeth in our study. If there were one or more agenetic teeth, we used a correction based on a mathematical formula.[18] The tooth that was most absent was the P2, and the formula for the imputation of the P2 has a probability of 70% and therefore be less accurate but still acceptable. Our study showed that both in the normal and DS population, a significant difference existed in dental development between patients with hypodontia and without hypodontia in the DS group. This agrees with other studies reporting on non-syndromic hypodontia.[19,20] We expected to find a difference within the DS population between patients with and without agenesis when tested separately. However, we did not find a statistically significant difference, and this may be due to the sample size in relationship to the effect size.

This study showed no differences in dental development in children with DS compared to control children. The clinical relevance of this study lies in the impaired clinical emergence with a seemingly normal eruption pattern and dental development in DS children. Clinicians may be late in the follow-up of dental development, as patients with DS are relatively late with other problems.

5 | CONCLUSION

This study shows that the dental development in subjects with and without DS is comparable. The late emergence in the oral cavity is probably not due to late dental development but due to other processes that take place during eruption, such as possible impaired processes at the apical and occlusal side of an erupting tooth. Clinicians should be aware that they should intervene at an age that normal dental development takes place because clinical emergence may be late.

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