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D.H.W., S.R., K.B.H. and D.J.M. conceived the ideas; K.B.H. conceived and developed the RCHM Dental Department database over the last nine years using standardised diagnostic criteria; D.H.W. collected the data; D.H.W. analysed the data; D.H.W. led the writing. All authors reviewed and approved the final version of the manuscript.

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Summary

Background: Chromosome 22q11.2 deletion syndrome (22q11.2DS) is a multifaceted syndrome with a variable phenotype. Few studies have described the associated dental characteristics and their relationship with medical co-morbidities; and no Australian data exist.

Aim: To determine the clinical manifestations and correlations between oral and medical conditions in children with 22q11.2DS.

Design: A retrospective observational study. Children genetically diagnosed with 22q11.2DS at the Royal Children's Hospital Melbourne were selected; their medical and dental characteristics were collated and analysed.

Results: The study population (n=57; mean age 11.5 y, range 2-27 y) experienced a range of medical conditions involving multiple medical systems; of whom 44 (77.2%) had caries experience, 7 (12.3%) developmentally missing teeth, and 31 (54.4%) developmental defects of enamel (DDE). Smaller proportions of primary teeth were affected by DDE in children with congenital heart disease (2.2% vs. 9.7%; p=0.02), and cardiac surgery (0.2% vs. 9%; p=0.001). Conversely, children with hypoparathyroidism (n=2) had significantly higher proportions of primary teeth affected by DDE (27.5% vs. 4%; p=0.02).

Conclusions: Significant associations existed between medical conditions (congenital heart disease, history of cardiac surgery, and hypoparathyroidism) and primary dentition DDE in children with 22q11.2 DS.

Key words:

22q11.2 deletion syndrome, DDE, enamel hypomineralisation, enamel hypoplasia

Introduction

Chromosome 22q11.2 deletion syndrome (22q11.2DS) is a multifaceted syndrome, with a vast clinical spectrum.[1] Individuals with 22q11.2DS most commonly experience a range of congenital cardiac defects (CCD), palatal anomalies, dysmorphic facial features, hypocalcaemia, T-cell mediated immunodeficiency and mild to moderate developmental delays.[1]

Nomenclature for 22q11.2DS is diverse, with clinical varied presentations that are essentially different phenotypes of a 1.5 to 3.0 megabase hemizygous deletion of chromosome 22, sometimes in conjunction with other mutations. Consequently, although "DiGeorge syndrome" and "velocardiofacial syndrome" (VCFS) have been used as 'synonyms', each syndrome should be recognised separately within the broader 22q11.2DS.[2]

The estimated prevalence of 22q11.2DS is one in 4000 live births, ranging from one in 3900 to one in 9700.[3,4] With advances in diagnosis and management, 86-96% of children with 22q11.2DS survive to adulthood; those who do not survive tend to die in early life from complex congenital heart disease, with the median age at time of death being 3.4-5 months.[5] As such, recognition and management of treatable conditions with later onset, including dental diseases, is growing in importance.[6] Recent studies have also shown the range of physical, psychological and social impacts manifest as poorer health-related quality of life in children with 22q11.2DS compared with their healthy peers.[7]

Historically, diagnosis of 22q11.2DS was made clinically therefore it is potentially under-diagnosed as it relied on clinical recognition of a combination of physical, behavioural or developmental signs.[1] Since genetic analysis became available, 20-100% of patients clinically diagnosed with DiGeorge syndrome or VCFS have the hemizygous deletion of chromosome 22q11.2 involving genes *COMT* and *TBX1*.[8] It would follow that modern genetic diagnosis is improving our understanding of the characteristics and associated oral features of 22q11.2DS.[6]

The literature consists mainly of case studies, with few cohort studies in children and adults; therefore, it is difficult to establish the prevalence of oral manifestations in children with 22q11.2DS.[9-11] Two of the larger Scandinavian cohort studies which included the oral manifestations of 22q11.2DS reported prevalence of developmental defects of enamel (DDE) of 48.3% and 66%, higher than general population estimates of 5-15% in the permanent dentition.[12,13] A range of 11.3-17% of children with 22q11.2DS have developmentally missing teeth.[9,12,13,15,16]

Dental caries was a common finding in individuals with 22q11.2DS.[2,10] The combined adult and child prevalence of caries in a Swedish study was 52.8%, with 46.8% prevalence in children alone.[13] Increased prevalence of DDE is associated with increased caries experience.[14]

Associations between dental findings and medical co-morbidities in individuals with 22q11.2DS have been proposed.[12,13] Enamel hypoplasia appeared to be linked with specific medical episodes, whereas enamel hypomineralisation was associated with more 'diffuse' medical conditions.[13] Associations between DDE and medical conditions including hypocalcaemia, congenital heart disease, and frequent infections have been reported, with the sole finding that individuals with 22q11.2DS and congenital cardiac anomalies had significantly fewer DDE-affected teeth (medians 15.4% vs. 29.6%); specifically, fewer teeth with enamel hypomineralisation.[12]

This study aims to further determine clinical manifestations and correlations between oral and medical conditions in children with 22q11.2DS.

Materials and methods

Ethical approval for the study was obtained from The University of Melbourne Human Research and Ethics Committee (ID 1748793.1). All individuals attended the Royal Children's Hospital Melbourne (RCHM) between 1st July 2011 to 31st January 2017, having first registered at RCHM from birth to 18 years-of-age with a genetic diagnosis of 22q11.2 DS. Individuals with complete medical and dental records were selected from a pre-existing patient database by an independent staff member. The dental records were completed by specialist paediatric dentists or paediatric dentist trainees (qualified dentists undertaking further studies to become paediatric dentists). All recorded dental diagnoses were verified by a supervising consultant specialist paediatric dentist, and records kept according to standard indexes and terminology (such as dmft/DMFT and basic DDE index terminology). That is, DDE were defined as the following:[12,13]

(1) Enamel hypoplasia: A quantitative defect of the enamel with reduced enamel thickness. The borders of the defect should be round and smooth.

(2) Enamel hypomineralisation: A defect of the enamel seen as a change in the colour and translucency of the enamel.

In addition to the written notes, at the time of visit, the dental diagnoses were charted into the electronic dental records by the head of the department (K.B.H). The records included prospective dental charting from presentation, dental radiographs (bitewing radiographs and/or panoramic radiographs), a dental history listing the previous dental provider, previous dietary practices, oral hygiene regime and fluoride exposure. Any previous dental treatment completed at RCHM was listed on the database, including historical dental charting, preventive dental care, after-hours management of facial cellulitis or dental trauma, and comprehensive dental care. Complete documentation of all dental treatment performed in the dental chair with or without local anaesthesia, inhalation sedation, or general anaesthesia at RCHM was required for inclusion in the study. Any cleft lip and palate meetings, orthodontic, periodontal, endodontic, oral maxillofacial or prosthodontic specialist consultations was also detailed on the database. De-identified demographic details, age at last dental visit, medical history and diagnoses, and dental history and diagnoses were extracted from the electronic medical and dental records.

Medical diagnoses of particular interest were the presence and absence of CCD, the types of CCD, whether cardiac surgery was performed, a diagnosis of hypoparathyroidism, hypocalcaemia or immunodeficiency before the age of 12, the presence of frequent childhood infections (FCI) [at least three recorded episodes of infection a year], cleft lip and palate (CLP), and dysmorphic facies.[17] Dental diagnoses included soft tissue findings, non-cavitated carious lesions, decayed (cavitated carious lesions), missing (due to decay) and filled permanent and primary teeth indices (DMFT/dmft), dysmorphic tooth crowns, DDE (enamel hypomineralisation and hypoplasia), developmentally missing teeth, and any other relevant dental findings in primary and permanent dentitions.

Statistical analysis

A descriptive analysis of the prevalence and distribution of the clinical recordings was performed in SPSS Ver. 23 (IBM Corp., NY, USA). Chi-square test or Fisher's exact test was utilised for categorical variables in 2 x 2 tables to determine whether there was a significant difference between observed and expected frequencies for those with a history of CHD, episodes of hypoparathyroidism, hypocalcemia or immunodeficiency before the age of 12, or the presence of frequent childhood infections, and dental characteristics. To assess if a history of CHD, episodes of hypoparathyroidism, hypocalcemia or immunodeficiency before the age of 12, or the presence of frequent childhood infections were associated with DDE, DMFT, or dmft in total or as a percentage of dentition, the non-parametric Mann-Whitney U test was used. A p-value below the alpha level of 0.05 was considered statistically significant.

Results

Demographic characteristics of study population

Fifty-seven children (34 boys) met the inclusion criteria (Table 1). Mean age (recorded as age at the last dental visit) was 11.5 y (SD=5; range 2 to 27; median=11). Nearly half were aged six to 12 y. All but one child resided in the state of Victoria, Australia.

Medical characteristics of study population

A range of medical conditions was present. The most common phenotypes of 22q11.2DS involved neurodevelopmental disability including global developmental delay or intellectual disability (64.9%; n=37), and cardiac issues (64.9%; n=37) of whom 27 (73%) had reparative cardiac surgery. Other affected systems included respiratory (n=26, 45.6%), endocrine (n=10, 17.5%), gastrointestinal (n=11, 19.3%), genitourinary (n=5, 8.8%) and haematological (n=7,

12.3%). For the endocrine system, six (10.5%) children were diagnosed with hypoparathyroidism and hypocalcaemia before the age of 12 y.

Ten children (17.5%; 50% female) had CLP, with two subtypes: submucous cleft (50%) and isolated clefts of the soft palate (50%).

Dental characteristics of study population

Most of the study population had healthy soft tissue or biofilm-induced gingivitis. Two children (3.5%) exhibited signs of gingival hypertrophy, secondary to anti-epileptic drugs. One child (1.8%) had a bifid uvula, without the diagnosis of CLP.

The characteristics of 1327 teeth were analysed, consisting of 913 permanent teeth (68.8%), and 414 (31.2%) primary teeth (Table 2). DDE were present in 31 individuals (54.4%); six children with enamel hypoplasia also had enamel hypomineralisation, although not necessarily affecting the same tooth (Tables 3 and 4).

A high proportion of children experienced dental caries (77.2%; mean dmft 3.5; mean DMFT 3.2). Seven children had developmentally missing teeth (12.3%), of whom six children had missing permanent teeth (10.5%).

Correlations between medical and dental characteristics of study population

As presented in Table 5, lower proportions of the number of primary teeth were affected by DDE in children with CCD when compared to those without CCD (2.2% vs 9.7%, p=0.02), and those who had reparative cardiac surgery when compared to those who did not have reparative cardiac surgery (0.2% vs 9%, p=0.001). Conversely, children with hypoparathyroidism had higher proportions of primary teeth numbers affected when compared to those without hypoparathyroidism (27.5% vs 4%, p=0.02). For all three groups (CCD, cardiac surgery, hypoparathyroidism), a difference existed in the number of primary teeth affected by enamel hypomineralisation - fewer hypomineralised teeth and CCD (p=0.049) and cardiac surgery (p=0.001), more hypomineralised teeth and hypoparathyroidism (p=0.02).

In addition, the presence of frequent childhood infection was associated with a higher dmft when compared to those without the presence of frequent childhood infection (3.91 vs 2.03, p=0.02). No other clinically or statistically significant relationships were present between other medical and dental characteristics.

Discussion

Few studies exist describing oral manifestations of children with genetically diagnosed 22q11.2DS. Excluding case studies, six studies exist in the literature investigating the prevalence of dental characteristics of 22q11.2DS. Four of these studies required the genetic confirmation of participants with 22q11.2DS prior to inclusion,[12,13,15,16,18] whilst one study included individuals who were diagnosed based on clinical phenotype alone.[9] These studies had between 29 and 53 individuals, some including adults.[9,12,13,15,16,18] To the authors' knowledge, this is the largest cohort of children with 22q11.2DS (n=57) to be studied in a major tertiary paediatric hospital to date. It is also the first to report oral health of 22q11.2DS children in Australia.

The descriptive component of the study revealed the prevalence of CCD in individuals with 22q11.2 DS was consistent with the range between 49-83% shown in previous studies.[2,19] In the present study, there were higher rates of ventricular septal defect and tetralogy of Fallot than earlier studies of individuals with 22q11.2 DS (13-14% and 17-22% respectively). [2,19,20]

Upon analysis of the medical and dental characteristics in the present study, children with CCD or a history of cardiac surgery had a significantly lower proportion of primary, but not permanent, teeth affected by DDE when compared to those without CCD or a history of cardiac surgery. This may appear to be an unexpected finding, as the presence of CCD during early life putatively disrupts amelogenesis and therefore could result in a higher prevalence of DDE, as was found in an earlier study in Queensland, Australia.[21]

The present findings do however support the reported lower rate of DDE in permanent and mixed dentition in Norwegian individuals with CCD and 22q11.2DS.[12] Of note, is the lower number of teeth affected by hypomineralisation in children with CCD which seems to be a contributing factor when compared to the prevalence of hypomineralisation in children without CCD. [12] A recent study of children with CCD at RCHM also revealed no association between the prevalence of DDE and CCD.[14]

The reasons for these findings may relate to the distinct cardiac conditions classically found in 22q11.2DS. These are conotruncal cardiac anomalies, which include defects which are cyanotic and severe in nature, such as interrupted aortic arch, tetralogy of Fallot and truncus arteriosus.[20] It is possible that contemporary improvements in technology and medical treatment for CCD, together with earlier surgical intervention, may result in lower rates of DDE when compared to cases in the past where CCD treatment was delayed until later in life.[12]

Treatment of CCD, particularly with high severity, includes surgical management. The literature regarding a correlation between the prevalence of DDE in patients with a history of cardiac surgery is sparse. Prior to the present study, no association between DDE and cardiac surgery has been reported in individuals with 22q11.2DS. However, anaesthetic intubation, which is required for cardiac surgery under general anaesthesia, has been reported to be associated with DDE of maxillary anterior primary teeth in preterm infants.[22] In contrast, children in the present study with 22q11.2DS and a history of cardiac surgery had a significantly lower proportion of primary teeth affected by DDE when compared to those without a history of cardiac surgery. This may be explained by the severe nature of the cardiac conditions associated with the syndrome and subsequent early detection, intervention and improved oxygenation at critical stages of amelogenesis.

Hypoparathyroidism is reportedly associated with DDE in non-syndromic children.[23] The present data confirm an association in children with 22q11.2DS, specifically in the primary dentition, in which children with hypoparathyroidism and 22q11.2DS had higher proportion of primary teeth affected by DDE. A Swedish study also identified similar findings in exfoliated primary teeth of children with 22q11.2DS, where there was a high proportion of DDE in close proximity to the enamel neonatal line (23.8%).[18] These DDE were positively correlated with the children's medical histories of hypoparathyroidism and hypocalcaemia, which suggest a close aetiological relationship between development of DDE, endocrine conditions and 22q11.2DS in early childhood.[18]

The prevalence of DDE in the present study is within the range from similar populations in Norway, Sweden and Brazil (48.3-66%) and the general population (3.1-98% in the primary dentition, 20-90% in the permanent dentition).[9,12,16,24,25] In the general population, the large variation in prevalence may be attributed to differences in diagnostic criteria, study methodology and examination technique, regional or ethnic variation or true differences in the cohorts studied.[23]

The prevalence of developmentally missing teeth in the present study was within the range reported in previous studies in Norway, Sweden, Brazil, Finland (12-23.1%).[9,12,13,15] Across the board, the prevalence of developmentally missing teeth in individuals with 22q11.2DS is higher than that of the general population 2.6-11.3%.[26,27]

Similarly, the proportion of individuals with 22q11.2DS with caries experience (77.2%) was higher than the general Australian paediatric population, where caries experience in the primary dentition (five to ten years) was 41.7% (95% CI 40.1-43.3), and 23.5% (95% CI 22.3-24.6) in the permanent dentition (six to 14 years).[28] Only one other

study had previously explored caries experience in children with genetically diagnosed 22q11.2DS, reporting a lower prevalence of 28.3% in Sweden, although missing teeth (possibly due to dental caries) were not considered, potentially underestimating the prevalence. Historically, management of dental caries was directed towards extraction of primary teeth, rather than restoring and retaining teeth, and a change of treatment philosophy over time may contribute to the observed lower prevalence of carious lesions.[13]

In the present study, the average dmft (3.5) was also higher than the general paediatric population (3.1, 95% CI 3.0-3.3; five to ten years), as was the average DMFT (3.2) compared with 0.7 (95% CI 0.7-0.8; six to 14 years) in the general Australian paediatric population.[28]

Forming an early dental home to maintain oral health and provide preventive dental care, modification of caries risk factors and provision of oral health education to prevent oral disease, is paramount in all children, with recommendations of the first dental visit occurring by the age of 12 months.[29,30] This is particularly important in children with medical conditions, such as CCD, as demonstrated in a recent Australian study of children at RCHM, where a large proportion of the participants with CCD experienced advanced dental caries, with mean age of presentation to the RCHM Department of Dentistry at age five years.[14] Indeed, delayed age of presentation was associated with elevated caries experience.[14] Furthermore, the repercussions of untreated carious lesions can lead to reduced oral health-related quality of life, with dental pain, infection, failure to thrive, and increased risk of infective endocarditis in children with CCD, culminating in increased psychological stress to the child and their family.[29,30] Therefore, there should be a high priority and focus on maintenance of oral health, including oral health education, as lack of relevant knowledge has been shown to be one of the most significant obstacles to maintaining good oral health.[29,30]

The presence of FCI was associated with a statistically significantly higher dmft when compared with no history of FCI in the present study.[12,17] Only one other study has collected data on FCI and dental characteristics of 22q11.2DS, but FCI was defined differently as 'frequent and prolonged infections during the first five years of life'. In this Swedish study, no relationship was found between FCI and caries experience.[13] The present data contradicts the previous findings and suggests a putative relationship between caries experience and FCI in 22q11.2DS.

A limitation of the present study is the retrospective nature. However, this study design was chosen as 22q11.2DS is a relatively uncommon condition and a convenience sample allows a larger number of participants to be enrolled. Nevertheless, the power of the

data is limited by the sample size, which is dictated by the available clinical data over the time period.

A number of clinicians were involved in data collection and entry which enabled the longitudinal nature of the data set. Although this could reduce reliability of data collection, the use of standardised criteria for diagnosis and verification by specialist consulting paediatric dentists mitigates this risk.

The age of the participants was taken at the individual's last dental visit at RCHM. Five participants last visited RCHM over age 18 years, due to 22q11.2DS being a condition (regardless of cleft status) that is eligible to receive Australian government-funded care under the Medicare Benefits Schedule 'Cleft Lip and Cleft Palate Scheme' until the age of 28. These individuals were still included in the present study as they met inclusion criteria and medical and dental data was complete from childhood.

The present study is the first to describe the dental and medical findings of children with 22q11.2DS in an Australian population and includes the largest cohort of children to be studied in a major tertiary paediatric hospital to date. It demonstrates that the medical and dental presentations of 22q11.2DS span a vast clinical spectrum. The results highlight the importance of building an awareness within the dental profession of the potential dental characteristics in this group, and the important role of early preventive dental care. There are also implications for the provision of information to parents and other caregivers regarding possible dental issues, particularly in the context of complex medical co-morbidities which may otherwise be prioritised.

An awareness of the oral health implications with certain medical co-morbidities should encourage early referral from other health professionals, by affirming children with cardiac conditions, a history of previous cardiac surgery, or hypoparathyroidism, would benefit most from early dental assessment and care. There are also opportunities for collaboration between medical and dental professionals in future research activities which could examine educational, pharmacological or surgical, multidisciplinary, or policy and advocacy interventions.

Why this paper is important to paediatric dentists

- The medical and dental presentations of 22q11.2DS span a vast clinical spectrum, including the presence of dental caries and developmentally missing teeth.

- There appear to be relationships between medical and dental features of 22q11.2DS, with the study confirming earlier findings of a significant positive association between hypoparathyroidism and DDE, as well as a negative association between CCD and DDE.
- The study highlights the importance of building an awareness within the dental profession of the potential dental characteristics in this population group, and opportunities for collaboration between medical and dental professionals in future research activities which could examine educational, pharmacological or surgical, multidisciplinary, or policy and advocacy interventions.

Conflict of interest

The authors declare no conflict of interest.

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Tables

Table 1 Demographic characteristics of study population.

Age in years at last dental visit (%)					
	0-5	**6-12**	**13-18**	**19-28**	**n *(%)***
Sex					
Male	3 (8.8)	18 (52.9)	9 (26.4)	4 (11.7)	34 (100)
Female	1 (4.3)	9 (39.1)	12 (52.2)	1 (4.3)	23 (100)
Total	**4 (7.0)**	**27 (47.4)**	**21 (36.8)**	**5 (8.8)**	**57 (100)**

Table 2 Summary of dental characteristics of the study population.

	Mean	**Median**	**Std Dev**	**Range**
DDE (*n* of teeth*)*	3.14	1	4.95	0-28
DDE (% of dentition)	10.59	4	17.04	0-100
DDE primary teeth (*n* of teeth)[†]	1.00	0	2.07	0-8
DDE primary teeth (% of dentition)[†]	5.01	0	10.33	0-40
DDE permanent teeth (*n* of teeth)[‡]	2.71	0	5.02	0-28
DDE permanent teeth (% of dentition)[‡]	15.08	0	24.41	0-100
Enamel hypomineralisation (*n* of teeth)	2.89	1	4.83	0-28
Enamel hypomineralisation (% of teeth)	9.91	3.12	16.91	0-100
Enamel hypomineralisation primary teeth (*n* of teeth)[†]	0.80	0	1.87	0-8
Enamel hypomineralisation permanent teeth (*n* of teeth)[‡]	2.61	0	4.91	0-28
Enamel hypoplasia (*n* of teeth)	0.25	0	0.93	0-6
Enamel hypoplasia (% of teeth)	0.68	0	2.74	0-18.75
DMFT (*n* of teeth)	3.20	0	5.92	0-26
dmft (*n* of teeth)	3.46	2	4.09	0-18
Dysmorphic crowns of teeth (*n* of teeth)	0.09	0	0.34	0-2
Dysmorphic crowns of teeth (% of dentition)	0.20	0	0.78	0-4.4
Developmentally missing teeth (*n* of teeth)	0.14	0	0.40	0-2
Developmentally missing primary teeth (*n* of teeth)	0.02	0	0.13	0-1
Developmentally missing permanent teeth (*n* of teeth)	0.12	0	0.38	0-2
Developmentally missing teeth (% of dentition)	0.48	0	1.46	0-8
		n		
Presence of CLP		10 (17.5%)		
Presence of DDE		31 (54.4%)		
Presence of dysmorphic crowns of teeth		4 (7%)		
Presence of developmentally missing teeth		7 (12.3%)		
Presence of dental caries (primary dentition)		29 (63.0%)[†]		

Presence of dental caries (permanent dentition)	24 (49.0%)[‡]

[†]A total of 46 children had complete data on primary dentition

[‡]A total of 49 children had complete data on permanent dentition

DDE = developmental defects of enamel

Std Dev = standard deviation

DMFT = permanent decayed, missing (due to decay) and filled teeth

dmft = primary decayed, missing (due to decay) and filled teeth

CLP = cleft lip or cleft lip and palate

Table 3 Distribution of teeth affected by DDE.

Enamel hypomineralisation		
	Permanent teeth (% of hypomineralised permanent teeth)	**Primary teeth (% of hypomineralised primary teeth)**
Incisors	44 (34.4)	8 (21.6)
Canines	8 (6.3)	13 (35.1)
Premolars	17 (13.3)	n/a
Molars	59 (46.1)	16 (43.2)
Total	128 (100)	37 (100)
Enamel hypoplasia		
	Permanent teeth (% of hypoplastic permanent teeth)	**Primary teeth (% of hypoplastic primary teeth)**
Incisors	3 (60)	0
Canines	0	2 (22.2)
Premolars	1 (20)	n/a
Molars	1 (20)	7 (77.8)
Total	5 (100)	9 (100)

Table 4 Prevalence of DDE in individuals with 22q11.2 DS of different populations.

Country	22q11.2DS Diagnosis	Sample size	Females	Males	Ages* (Years)			DDE (%)	Enamel hypomineralisation (%)	Enamel hypoplasia (%)	Both enamel hypomineralisation and hypoplasia (%)
					Range	Mean	Median				
Australia (Melbourne) [†]	Genetic	57	23	34	2 - 27	11.5	11	54.5[∝]	54.5	10.5	10.5
Norway (Oslo) [12]	Genetic	50	27	23	1.5-44	[‡]	10	66[∝]	58	42	34
Sweden (Goteborg) [13]	Genetic	29	30	23	2 -43	11.1	8	48.3[∝]	[‡]	[‡]	[‡]
Brazil (Sao Paulo) [9]	Phenotype (VCFS)	26	15	11	7 - 48	18.3	[‡]	16[°]	57.7	15.4	11.5

[*]Age at last presentation

[†]The present study

[‡]Data unavailable

[∝]Criterion used for DDE: basic DDE index terminology (presence or absence of enamel hypomineralisation or enamel hypoplasia)

[°]Criterion used for DDE: basic DDE index terminology (the presence or absence of enamel opacities/hypomineralisation or enamel hypoplasia)

Table 5 Correlations between medical and dental characteristics which were statistically significant.

Congenital Heart Defects					
Dental characteristics	**CHD**	**Mean**	**Std Dev**	**P value**	**Statistical test**[†]
DDE primary teeth (*n)*	Y	0.45	1.12	0.025	MWU
	N	1.94	2.88		
DDE primary teeth (%)	Y	2.2	5.6	0.024	MWU
	N	9.7	14.4		
Enamel hypomineralisation primary teeth (*n*)	Y	0.27	0.80	0.049	MWU
	N	1.35	2.56		
Cardiac Surgery					
Dental characteristics	**CS**[‡]	**Mean**	**Std Dev**	**P value**	**Statistical test**[†]
dmft	Y	1.48	2.93	0.001	MWU
	N	4.14	4.38		
DDE primary teeth (*n)*	Y	0.05	0.22	0.001	MWU
	N	1.80	2.55		
DDE primary teeth (%)	Y	0.2	1.0	0.001	MWU
	N	9.0	12.7		
Enamel hypomineralisation primary teeth (*n*)	Y	0.03	0.18	0.001	MWU
	N	1.29	2.27		
Immune Findings					
Dental characteristic	**FCI**[‡]	**Mean**	**Std Dev**	**P value**	**Statistical test**[†]
dmft	Y	3.91	4.46	0.021	MWU
	N	2.03	3.36		
Endocrine Findings					
Dental characteristics	**HP**[‡]	**Mean**	**Std Dev**	**P value**	**Statistical test**[†]
DDE primary teeth (*n)*	Y	5.50	2.12	0.017	MWU
	N	0.79	1.84		
DDE primary teeth (*%)*	Y	27.5	10.6	0.017	MWU

	N	4.0	9.2		
Enamel hypomineralisation	Y	4.50	3.54	0.015	MWU
primary teeth (*n*)	N	0.51	1.49		

* MWU = Mann-Whitney U test

†MWU = Mann-Whitney U test

‡CS = Presence of cardiac surgery

HP = Presence of hypoparathyroidism

FCI = Presence of frequent childhood infection