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# Dental development in a sample of South African HIV-positive children

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#### Abstract

**Aims:** While oral soft tissue manifestations associated with HIV-infection in children are well documented, few studies have investigated the dental development of this group. The aim of this study was to assess dental development in a sample of HIV-positive children in comparison with an age-matched HIV-negative control group.

**Methods and results:** The sample comprised 44 HIV-positive children and 44 HIVnegative children matched for age, gender, and ethnicity. An orthopantomograph (OPG) of each patient was assessed in order to calculate the dental age. The mineralization stages of teeth were used to calculate the dental age using tables formulated by Phillips and van Wyk-Kotze for this grouping. Results showed that dental development for both groups were similar to the dental age-related tables. HIV-positive children between 8 and 10 years of age showed significantly advanced dental development (p = 0.04). HIV-positive females showed significant advancement in dental age as compared to their chronological ages. Thirty-six (81.8%) HIV-positive children were on antiretroviral (ARV) drugs.

**Conclusion:** HIV-positive children presented stages of dental development in accordance with their chronological ages and in tandem with that of the HIV-negative controls.

#### **KEYWORDS**

antiretroviral therapy, dental age, human immunodeficiency virus

# **1 | INTRODUCTION**

The first cases of HIV/AIDS in children were recorded in 1983.<sup>1</sup> Since then, much advancement regarding diagnostic tools and disease management has taken place. The disease is now managed, with reasonable success, with the use of antiretroviral (ARV) drug therapy, and as such, the life expectancy of HIV-infected individuals has increased significantly.<sup>2</sup> With increased life expectancy, long-term studies on all aspects of the HIV-infected individuals have become pertinent. Documentation of the growth and development of HIV-infected children is of value as this type of information has bearing on forensic

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medicine, pediatric dentistry, and orthodontic treatment planning.  $^{\rm 3-5}$ 

Dental maturity, based on the degree of dental mineralization, is often expressed as dental age, and is one of the recognized methods of determining the biological maturity of an individual. Dental age is considered one of the best physical indicators of chronological age, as it is notably independent on the influence of external and internal factors.<sup>6</sup> Dental development is more closely related to chronological age than skeletal, somatic, or sexual maturity indicators.<sup>7</sup> The difference between dental age and chronological age indicates an advance or delay in development in comparison with the normal standard.<sup>8–10</sup> The purpose of this study was to assess the dental development of a sample of HIV-positive South African children and to compare the findings to a matched HIV-negative group.

## 2 | MATERIAL AND METHODS

#### 2.1 | Data collection

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The study was retrospective, cross-sectional in design. Ethical approval had been obtained from the University of the Western Cape's Senate Research Committee (Ref: 11/7/34) prior to conducting the study and the ethical guidelines of the World Medical Association Declaration of Helsinki (version 2002)<sup>11</sup> were strictly followed. Confidentiality was ensured by using only study record numbers on the data capturing sheets and not the patients' names. Only the two radiographic examiners (researchers) had access to patient folders.

A sample of 44 patient records of vertically infected HIVpositive children was selected from the records of Tygerberg Oral Health Centre (TOHC) of the University of the Western Cape. The study sample was randomly selected from two databases of confirmed HIV-infected children previously treated at the faculty in specialized clinics. One of the databases contained the details of children who previously formed part of a larger research project on oral mucosal lesions, while the other database was a record of all HIVinfected children treated at the Department of Paediatric Dentistry. In addition to this, a further 44 records of matched HIV-negative children were selected from the same institution (TOHC). All selected records fulfilled the criteria for inclusion.

Matching was done according to: age, gender, and ethnicity. All subjects were from similar socioeconomic backgrounds (similar educational levels, household income, and social stance within the community). Exclusion criteria included: (a) records without an orthopantomograph (OPG) and/or a medical history; (b) medical conditions other than HIV which may have had an influence on the developing dentition, e.g., Down syndrome, genetic conditions (e.g., dentinogenesis imperfecta, amelogenesis imperfecta, ectodermal dysplasia); (c) patients who were on medication which could have had an effect on the dentition, e.g., fluorides and cytotoxic agents; and (d) children with missing teeth or having multiple decayed units in the mandibular dentition.

A data collection sheet was used to record relevant data from patient records. These data included date of birth, gender, date and chronological age of the patient on the day that the radiograph was taken, and whether or not the patient had been treated with ARV drugs. The dental age was calculated by applying the *Phillips and van Wyk-Kotze* (2009)<sup>13</sup> Dental Age Related Table.

### 2.2 | Radiographic examination

An OPG of each child was examined to determine the dental age by assessing the mineralization stages of the left mandibular secondary teeth. The development stage of each tooth in the lower left jaw was established by independent visual inspection by each of the examiners. The Morrees *et al.*<sup>12</sup> dental development stages were employed. This graphic illustration of tooth mineralization/development stages was used as a standard for comparison of the radiographic images. Examiners independently assessed each radiograph by comparing the specified teeth using this schematic representation of various stages of the developing tooth.<sup>12</sup>

In determining the dental age, use was made of standardized tables, as formulated by Phillips and van Wyk-Kotze.<sup>13</sup> The "*Tygerberg Table*," one of three tables formulated for dental age estimation of different ethnic groups within South Africa, was formulated primarily from a sample of patients from the TOHC. This study took place at the same oral health center at which the *Tygerberg Table* was formulated. The Phillips and van Wyk-Kotze<sup>13</sup> tables did not distinguish between gender variability, however, gender was matched for between the study group and the control group.

The examiners were blinded and thus did not know the names, age, or gender of the individuals whose radiographs were being examined. In two of the 88 OPGs examined, a discrepancy was noted. These discrepancies were resolved by joint consultation and examination of the radiographs and schematic illustration by the two examiners. Consensus was reached in both cases.

The dental age of each child was determined by adding the value of each of the secondary teeth in the left mandible, and obtaining a single value. This value was then compared with the chronological age of the child. The chronological age was noted as the age of the child on the date on which the radiograph was taken (calculated by subtracting the date on which the radiograph was taken from the date of birth). All radiographs were examined in a dark room using a viewing light box and  $3\times$  magnifier when necessary.

#### 2.3 | Statistical analysis

Data were compiled on Microsoft Excel<sup>®</sup>. The data were analyzed using Microsoft Excel<sup>®</sup> and Epi Info 2000 software. Descriptive statistics (means and standard deviations [SDs]) were calculated and the statistical comparisons between the mean chronological age and dental age were derived using the *t*-test. Results were considered as statistically significant when a *p*-value of < 0.05 was found.

**TABLE 1** Comparison of chronological and dental ages in HIV-positive children and matching controls

	Chronological age		Dental age		<i>p</i> -Value
Group	Mean	SD	Mean	SD	(t-test)
Study group	9.27	2.01	9.41	1.99	0.35
Control group	9.28	2.02	9.29	2.07	0.96



**FIGURE 1** Comparison of dental and chronological ages of males and females in HIV-positive group

# 3 | RESULTS

The sample comprised the records of 88 children. Fortyfour were vertically infected HIV-positive (study group) and 44 were matched HIV-negative controls (control group). Each group consisted of 21 (47.7%) males and 23 (52.3%) females. The chronological ages of the children in the study group ranged from 6.17 to 15.24 years (mean = 9.27 years; SD = 2.01), while the dental ages ranged from 6.09 to 15.09 years (mean = 9.41 years; SD = 1.99). Comparative differences between the chronological and dental ages of these children showed no statistical significance (Table 1), nor too, were there statistically significant differences of the dental age between children in the study group and their matched controls.

In the study group, HIV-positive males showed a dental age comparable to that of their chronological ages, while HIV-positive females showed a significantly advanced dental development as compared to their chronological ages (p < 0.05) (Figure 1).

HIV-positive children between 8 and 10 years of age (n = 20) showed significantly advanced dental development (mean = 9.32; SD = 0.99) compared to their chronological age (mean = 9.01; SD = 0.63) (p = 0.04).

Thirty-six of the 44 (81.8%) HIV-positive children were on ARV therapy. Both, children on ARVs as well as those not on ARVs showed comparable chronological and dental ages (Table 2).

**TABLE 2**Comparison of chronological and dental ages inHIV-positive children on ARV therapy

		Chronolo- gical age	Dental age	t	p-Value
Group 1 (ARVs)	Ν	36	36	1.45	0.15
	Mean	9.18	9.40		
	SD	1.83	1.95		
	SE	0.30	0.32		
Group 2	Ν	8	8	0.53	0.61
(not on ARVs)	Mean	9.67	9.44		
	SD	2.79	2.31		
	SE	0.98	0.81		

### 4 | DISCUSSION

Dental development and dental age in HIV-positive children remains a largely unreported area. To date there has been only few studies on this subject of which most were conducted in Brazil.<sup>3,4,10</sup> This study compared the dental development in a sample of HIV-positive children and compared it to a matched HIV-negative control group. Dental ages of HIV-positive children did not differ significantly to that of the matched control group. HIV-positive children showed stages of dental development of the secondary dentition within normal ranges. Previous studies (Table 3) vary in their findings on the topic. Triguero et  $al.^4$  and Holderbaum et  $al.^3$  both examined dental development in HIV-positive Brazilian children and concluded that these children showed delayed dental development. Fernandes et al.<sup>10</sup> also examined dental development in a sample of HIV-positive Brazilian children and reported that these patients did not show any delay in dental development. These studies were conducted on the same population group in Brazil and all three studies used the same evaluation method (i.e., Nolla's method).

It was decided to use the Moorrees *et al.*<sup>12</sup> tooth mineralization stages, in conjunction with the Phillips and van Wyk-Kotze<sup>13</sup> dental age-related table for this South African sample as it was most appropriate to this ethnic group as compared to the Nolla method, which was formulated for a Caucasian sample.

Dental age based on mineralization stages of the permanent dentition reflects the overall somatic growth and is one of the most widely used parameters to examine a patient's dental development, especially in orthodontic and forensic disciplines.<sup>14</sup> Numerous studies have reported delayed dental development in children with systemic conditions, such as fetal alcohol syndrome and leukemia.<sup>14,15</sup> It would be reasonable to expect a delay in dental development in HIV-positive children<sup>3,4</sup>; however, this was not observed in this study. The exact reasons behind this finding cannot be explained definitively but could be due to the use of ARV drugs by the

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Brazilian

100% of sample

Nolla

 Findings
 No delay in dental development
 Delayed dental development
 No delay in dental development

 majority (81.8%) of HIV-positive children in this group. It would be interesting to assess the dental development in a sample of HIV-positive children who have not had ARV drug therapy, and compare those findings to the dental development
 background and ethnicity as the c in the same geographic area. Studi ment age should factor in the ethnicity of the reference

Brazilian

100% of sample

Nolla

Population

Method used

ARV therapy

South African

81.8% of sample

of a sample of HIV-positive children on ARV drugs.

Phillips

In this study, HIV-positive children on ARVs showed similar dental ages when compared to their chronological ages. Although the toxicity of ARVs has already been linked with alterations in bone metabolism, the risk factors associated with advanced HIV infection are more strongly related to osteopenia and osteoporosis.<sup>16,17</sup> In the present study, the finding that HIV-positive children showed stages of dental development similar to their healthy counterparts can be explained by the high level of care provided for these children to avoid risk factors such as systemic infections and malnutrition. ARVs have also been shown to have positive effects on the growth of HIV-positive children despite being a risk factor for bone metabolism.<sup>18</sup> Moreover, dental tissues have been noted to be less susceptible to the negative effects of ARVs.<sup>19</sup>

Regarding the ages of HIV-positive children, there were statistically significant differences between chronological and dental ages in children between the ages of 8 and 10 years. These younger children showed advanced dental development. This finding may be a result of the recent rollout of ARVs in 2005 in public hospitals in South Africa<sup>2</sup>; hence, these younger children may have benefitted more from ARVs during the crucial dental growth periods than older children who had access to ARVs at a later stage in their lives.

Thus far, all studies documenting dental development in HIV-positive children (Table 3), 100% of the samples were on ARV drugs. In this sample, only 81.8% were on ARVs. Despite this, both Triguero *et al.*<sup>4</sup> and Holderblaum *et al.*<sup>3</sup> reported delay in dental development in HIV-positive children despite the entire sample being on ARVs.

HIV-positive females showed significantly advanced dental development, contrary to Holderbaum *et al.*<sup>3</sup> who found that HIV-positive females presented with delayed dental development.

The great similarity in the dental age and chronological age of the control group can be attributed to the fact that the Phillips and van Wyk-Kotze Dental Age-Related Tables<sup>13</sup> were formulated for children with the same socioeconomic

background and ethnicity as the control group, who also lived in the same geographic area. Studies assessing dental development age should factor in the ethnicity of the sample as compared to the ethnicity of the reference age-related tables to be used.

Brazilian

100% of sample

Delayed dental development

Nolla

In conclusion, HIV-positive children presented with dental ages comparable to their chronological ages and to the dental ages of the HIV-negative controls. HIV-positive females showed advanced dental development compared to their chronological ages. The findings could be of significance to patients undergoing orthodontic treatment and for forensic purposes.

#### ETHICS STATEMENT

The ethical approval for the study was obtained from the senate research ethic committee of the University of the Western Cape.

#### **CONFLICTS OF INTEREST**

The authors declare that they have no conflict of interest for this study.

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#### REFERENCES

- 1. Oleske J, Minnefor A Jr, Cooper R, et al. Immune deficiency syndrome in children. *JAMA*. 1983;249:2345–2349.
- Johnson LF, Keiser O, Fox MP, et al. Life expectancy trends in adults on antiretroviral treatment in South Africa. *AIDS*. 2016;30:2545–2550.
- Holderbaum RM, Veeck EB, Oliveira HW, Silva CL, Fernandes A. Comparison among dental, skeletal and chronological development in HIV-positive children: a radiographic study. *Braz Oral Res.* 2005;19:209–215.
- Trigueiro M, Tedeschi-Oliveira SV, Melani RF, Ortega KL. An assessment of adverse effects of antiretroviral therapy on the development of HIV positive children by observation of dental mineralization chronology. *J Oral Pathol Med.* 2010;39:35–40.

- Bolanos MV, Manrique MC, Bolanos MJ, Briones MT. Approaches to chronological age assessment based on dental calcification. *Forensic Sci Int.* 2000;10:97–106.
- Rózyło-Kalinowska I, Kiworkowa-Raczkowska E, Kalinowski P. Dental age in Central Poland. *Forensic Sci Int.* 2008;30:207– 216.
- Davidson LE, Rodd HD. Interrelationship between dental age and chronological age in Somali children. *Community Dent Health*. 2001;18:27–30.
- Liversidge HM, Speechly T, Hector MP. Dental maturation in British children: are Demirjian's standards applicable?. *Int J Paediatr Dent*. 1999;9:263–269.
- Ramos-Gomez FJ, Petru A, Hilton JF, Canchola AJ, Wara D, Greenspan JS. Oral manifestations and dental status in paediatric HIV infection. *Int J Paediatr Dent*. 2000;10:3–11.
- Fernandes A, Cherubini K, Veeck EB, Grando LJ, Silva CL. Radiographic evaluation of the chronological development of permanent dentition in children infected with HIV. *Clin Oral Investig.* 2007;11:409–413.
- World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. J Postgrad Med 2002;48:206–208.
- Moorrees CF, Fanning EA. Formation and resorption of three deciduous teeth in children. Am J Phys Anthropol. 1963;21:205– 213.
- Phillips VM, van Wyk Kotze TJ. Dental age related tables for children of various ethnic groups in South Africa. J Forensic Odontostomatol. 2009;27:20–28.

- Naidoo S, Norval G, Swanevelder S, Lombard C. Foetal alcohol syndrome: a dental and skeletal age analysis of patients and controls. *Eur J Orthod*. 2006;28:247–253.
- Martin MB, Li CS, Rowland CC, Howard SC, Kaste SC. Correlation of bone age, dental age, and chronological age in survivors of childhood acute lymphoblastic leukaemia. *Int J Paediatr Dent*. 2008;18:217–223.
- Kühne CA, Heufelder AE, Hofbauer LC. Bone and mineral metabolism in human immunodeficiency virus infection. J Bone Miner Res. 2001;16:2–9.
- Mondy K, Yarasheski K, Powderly WG, et al. Longitudinal evolution of bone mineral density and bone markers in human immunodeficiency virus-infected individuals. *Clin Infect Dis.* 2003;36:482– 490.
- McKinney RE, Johnson GM, Stanley K, et al. A randomized study of combined zidovudine–lamivudine versus didanosine monotherapy in children with symptomatic therapy-naive HIV-1 infection. The Pediatric AIDS Clinical Trials Group Protocol 300 Study Team. *J Pediatr.* 1998;133:500–508.
- Merwin DR, Harris EF. Sibling similarities in the tempo of human tooth mineralization. *Arch Oral Biol.* 1998;43:205–210.

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