

# Oral Manifestations in HIV/AIDS-Infected Children

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## ABSTRACT

**Objectives:** To assess factors influencing the distribution of oral manifestations in HIV/AIDS-infected children attending the Paediatric Infectious Disease Clinic in Mulago Hospital, Kampala.

**Methods:** This was a cross-sectional study comprising 237 children (males/females: 113/124) aged 1 to 12 years. The parents/guardians were interviewed to obtain demographic information, oral hygiene practices, dietary habits and health seeking behaviours as well as any medications taken. The children were clinically examined for oral lesions based on World Health Organization criteria with modifications.

**Results:** About 71.7% of the children cleaned their teeth. About 16.9% of the children had visited a dentist since birth, mainly for emergency care. One or more oral lesions were recorded in 73% of the children of whom 19.0% experienced discomfort during oral functions. Cervical lymphadenopathy, oral candidiasis and gingivitis were the most common soft tissue oral lesions: 60.8%, 28.3% and 19.0%, respectively. Except for dental caries, the overall frequency distribution of soft tissue oral lesions was significantly lower in children on highly active antiretroviral therapy (HAART) as compared to their counterparts not on HAART. The prevalence of dental caries in deciduous and permanent dentitions was 42.2% and 11.0%, respectively. Tooth brushing and previous visits to the dentist were indirectly and significantly associated with dental caries. About 5.9% (n=14) of the children had <200 CD3 + CD4 T-lymphocyte cells per  $\mu$ l of blood.

**Conclusions:** The majority of the children had one or more oral lesions, particularly in the group not on HAART. Some of the lesions were associated with discomfort during oral functions. (Eur J Dent 2011;5:291-298)

**Key words:** HIV/AIDS-infected children; Oral manifestations; Uganda

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## INTRODUCTION

Oral manifestations are often among the first symptoms in human immunodeficiency virus (HIV)-infected patients<sup>1</sup> and have been associated with immune suppression.<sup>2</sup> The distribution of some of the specific oral manifestations are reported to differ between adults and children.<sup>3</sup> The oral manifestations of oral candidiasis and oral hairy leukoplakia in particular are clinical predictors of acquired immunodeficiency syndrome (AIDS) pro-

gression and are usually associated with CD4<sup>+</sup> T-lymphocyte cell count < 200 cells/μl of blood and high viral load levels in patients.<sup>4,5</sup>

The prevalence of oral manifestations in HIV-infected adults tends to vary from country to country. Previous studies, at least in Africa, showed a wide range of prevalence rates from 1.5% up to 94%.<sup>6</sup> However, in HIV-infected children, the prevalence of oral manifestations in developed countries has been reported to be as high as 72%.<sup>7,8</sup> Comparable studies in children from developing countries, including Africa, indicated variations in the occurrence of oral manifestations, for example 61% in Brazil,<sup>9</sup> 55% in Romania,<sup>10</sup> 49% in Thailand<sup>11</sup> and 63% in South Africa.<sup>12</sup>

The introduction of highly active antiretroviral therapy (HAART) in the mid-1990s was an important landmark with therapeutic effects and dramatic changes in the clinical prospects of HIV infection. The rate of HIV-related oral manifestations has declined following the introduction of HAART.<sup>13</sup> In a prospective study, Schmidt-Westhausen et al<sup>13</sup> reported a decrease in the prevalence of soft tissue oral lesions from 34.4% to 8.2% six months following HAART. Previous studies have not reported a specific trend in the association between HAART and dental caries. In a cohort of United States HIV-infected patients receiving HAART, the prevalence of dental caries was reported to be less compared with a group not taking HAART,<sup>14</sup> whereas other reports suggested a positive correlation between HAART and caries prevalence.<sup>15</sup>

Furthermore, in a recent Brazilian study<sup>16</sup> on HIV-infected children, oral manifestations were reported to be clinical predictors of HAART failure. In Uganda, the assessment of oral manifestations in HIV-infected adults showed prevalence rates ranging from 42%<sup>17</sup> to 72%.<sup>18</sup> The only study involving Ugandan HIV-infected children, the majority of whom were on various medications including HAART, reported a prevalence of 68.6% dental caries, 40% gingivitis and 8.6% pseudomembranous candidiasis.<sup>19</sup> The objectives of the present study were to assess factors that contribute to the distribution of oral manifestations, and to establish the influence of the lesions on oral functions in HIV/AIDS-infected children attending the Paediatric Infectious Disease Clinic (PIDC) in Mulago Hospital, Kampala.

## MATERIALS AND METHODS

This was a cross-sectional survey conducted

in the Paediatric Infectious Disease Clinic (PIDC), Mulago Hospital, which used a stratified systematic random sampling technique.

The PIDC is a non-governmental organization health facility established under the Uganda Ministry of Health by the Baylor College of Medicine Children's Foundation (Baylor-Uganda) to enable children to live positively with HIV. It is a centre of excellence that provides medical care to the children and social support to their parents/guardians. On average, the clinic registers about 60 children per month who test positive for HIV using ELISA (HIV) and confirmed by Western blot. About 2300 of the registered children are aged between 1.5 and 12 years and of whom about 1450 are on HAART (PIDC administration, personal communication). The children report to the clinic at least once a month for the services.

The study population consisted of children registered in the PIDC who were aged between 1.5 and 12 years. The study children included those not on HAART and those who were at least 1 month on HAART. The parents/guardians of the children had to consent to participation in the study.

Children who were on HAART for less than 1 month and those younger than 1.5 years or older than 12 years were excluded.

Permission to conduct this study was obtained from Makerere University College of Health Sciences Research and Ethics Committee, Uganda National Council of Science and Technology and Baylor College of Medicine. The parents/guardians consented on behalf of the children. The consent form was translated into the local language (Luganda) for those who did not understand English. All the participants consented and were recruited into the study. During the study, the participants were treated in accordance with the Helsinki Declaration.<sup>20</sup> In consultation with the health professionals in the PIDC, advice was given to the participants regarding management of oral lesions that were observed during the study.

In September 2009, the children were selected for the study based on their medical files. With the assistance of the PIDC administration, medical files of children aged 1.5 to 12 years were sorted into two groups (strata). Group I consisted of children on HAART for at least one month and group II consisted of children who had not been started on HAART. The study sample was then obtained by a systematic random selection of files from each group using numbers. Every third file was selected until 118 files were obtained for group I and 119 files for group II. The children whose files

were selected were requested to participate in the study.

Before the main field survey, four trained dentists (CMR, AK, LM, IO) were calibrated in recording oral lesions in randomly selected children ( $n = 25$ ) in the PIDC in order to minimize intra- and inter-examiner variability. The Cohen's kappa values ranged from 0.84 to 0.89 (mean, 0.86), representing a substantial agreement in pseudomembranous, erythematous, marginal gingivitis and dental caries recordings.

A short structured questionnaire was administered to the parents/guardians of the children in the form of an oral interview in order to obtain demographic information, oral hygiene practices, dietary habits and dental care seeking behaviours in accordance with the World Health Organization (WHO) recommended form<sup>21</sup> with modifications. Some of the information such as immunological status measurement, medication and therapy history was retrieved from the children's most recent medical records.

The four trained dentists who were previously calibrated carried out clinical examinations for dental caries based on decayed, extracted/missing and filled (def/DMF) teeth indices as described by WHO criteria.<sup>21</sup> The soft tissue oral lesions were diagnosed using the classification and diagnostic criteria as described by the Collaborative Workgroup on the Oral Manifestations of Pediatric HIV Infections.<sup>22</sup> The examination was done in a well-lit room. The sun was the source of illumination. The child was seated on an office chair facing a wide open window while the examiner was seated in front of the child to fully access his/her oral cavity. The dentists worked in pairs. One dentist physically examined the child using a disposable mouth mirror, tongue depressor, dental probe, pair of tweezers and cotton wool, and then dictated the observations to the other dentist who recorded them on a WHO recommended form<sup>21</sup> with modifications. To avoid fatigue, the dentists exchanged their roles after examining every 10 children.

In order to assess the reproducibility in recording oral lesions, a blind duplicate examination of 10 children was done by each of the four examiners, after the main examination. The Cohen's kappa values ranged from 0.79 to 0.92, with no evidence of systematic errors ( $P > .05$ , paired t-test).

### Statistical analysis

The collected data were double checked for errors and completeness at the end of each day of fieldwork. The data were entered into a com-

puter using the SPSS v.15.0 (SPSS Inc., IL, USA). Frequency distributions were used to describe the material. The Student's t-test for paired observations was used to assess any systematic errors in recording oral lesions. Bivariate analyses were used to assess any associations between dependent and independent variables. The Mann-Whitney U test was used to assess any significant differences in the frequency distribution of children based on HAART and oral lesions. The probability of significance was set at the 5% level.

## RESULTS

The study population comprised 237 children aged 1.5 to 12 (mean,  $5.9 \pm 3.8$ ) years. About 52.3% of the children were female (Table 1). The majority of the children (92.0%) had parents/guardians in the low socio-economic status category. About 87.3% of the parents/guardians had attained at least primary education (Table 1). One hundred and seventy (71.7%) children cleaned their teeth, mainly by using a plastic toothbrush (Table 1). The majority of the children (76.8%) reported consumption of sugary snacks between meals, mostly just occasionally (Table 1). Forty children (16.9%) had visited a dentist since birth, mainly for emergency care (Table 1). Most of the children ( $n=205$ ) were taking antibacterial drugs (Table 1), especially Cotrimoxazole. A small proportion of the children (9.3%) were taking their medication in the form of a syrup or suspension (Table 1). Seventy-three percent ( $n=173$ ) of the children had one or more oral lesions (Table 2). Cervical lymphadenopathy, oral candidiasis and gingivitis were the most common soft tissue oral lesions: 60.8%, 28.3% and 19.0%, respectively (Table 2). Kaposi's sarcoma, recurrent aphthous ulcerations and necrotizing gingivitis were very rare in this population: 0.4% for each of the lesions (Table 2).

Discomfort during oral functions was reported by 19.0% of the children, particularly during eating (Table 1). The discomfort was significantly associated with erythematous candidiasis, angular cheilitis, necrotizing gingivitis, recurrent herpes labialis, atypical ulcerations and dental caries ( $P < .05$ ). Generally, the frequency distribution of children with soft tissue oral lesions was significantly lower in those on HAART as compared to their counterparts not on HAART ( $P < .05$ , Table 2).

The CD3+ + CD4+ T-lymphocyte cell count values ranged from 1 to 9220 cells per  $\mu\text{l}$  of blood. About 5.9% ( $n=14$ ) of the children had  $<200$  CD3+ + CD4+ T-lymphocyte cells per  $\mu\text{l}$  of blood. The CD3+

+ CD4<sup>+</sup> T-lymphocyte cell count did not have any significant influence on the frequency distribution of oral lesions (P>.05).

Ninety-three (39.2%) children exclusively had a

deciduous dentition while 14.8% had a permanent dentition. Overall, the prevalence of dental caries was 50.2% (n=119); the values for the deciduous and permanent teeth were 42.2% and 11.0%,

**Table 1.** The frequency distribution of the children according to age, sex, level of education and socio-economic status of their parents/guardians, oral hygiene practices, dietary habits, medication and discomfort during oral functions (n=237).

Variable	Categories	n [%]
Age	1.5 - 2 years	51 (21.5)
	3 - 4 years	52 (21.9)
	5 - 6 years	42 (17.7)
	7 - 9 years	53 (22.4)
	10 - 12 years	39 (16.5)
Sex	Male	113 (47.7)
	Female	124 (52.3)
Education of parent/guardian	No formal	30 (12.7)
	Primary	112 (43.7)
	Secondary	78 (32.9)
	Tertiary	17 (7.2)
Socio-economic status of parent/guardian	Low	218 (92.0)
	Medium	17 (7.2)
	High	2 (0.8)
Tooth cleaning	Yes	170 (71.7)
	No	67 (28.3)
Device used in tooth cleaning (n=170)	Plastic toothbrush	158 (92.9)
	Chewing stick	4 (2.4)
	Others	8 (4.7)
Frequency of tooth brushing (n=170)	Once a day	52 (30.6)
	Twice a day	102 (60.0)
	> Twice a day	15 (8.8)
	Occasionally	1 (0.6)
Use of fluoride in tooth brushing (n=170)	Yes	152 (89.4)
	No	18 (10.6)
Time of brushing relative to meals (n=170)	Before breakfast	154 (90.6)
	After breakfast	15 (8.8)
	Before super	0 (0.0)
	After super	1 (0.6)
Consumption of sugary snacks	Yes	182 (76.8)
	No	55 (23.2)
Frequency of taking sugary snacks (n=182)	Once a day	12 (6.6)
	Twice a day	1 (0.5)
	> Twice a day	2 (1.1)
	Occasionally	167 (91.8)
Previous dental visits	Yes	40 (16.9)
	No	197 (83.1)
Reason for dental visits (n=40)	Routine check up	2 (5.0)
	Emergency care	38 (95.0)
Discomfort in the mouth	Yes	45 (19.0)
	No	192 (81.0)
Discomfort during function (n = 45)	Swallowing	12 (26.7)
	Speaking	8 (17.8)
	Drinking	20 (44.4)
	Eating	36 (80.0)
	Brushing	20 (44.4)
	Any other	3 (6.7)
Medication taken for HIV infection (n = 226) <sup>§</sup>	Antiretroviral	118 (49.8)
	Other antiviral	10 (4.2)
	Antifungal	8 (3.4)
	Antibacterial	205 (86.5)
	Any other	11 (4.6)
Drug preparation (n=226) <sup>§</sup>	Syrup/suspension	22 (9.3)
	Tablets	211 (89.7)

<sup>§</sup> Some children were taking different medications

respectively (Table 2). Tooth decay was the most common condition in the deciduous and permanent teeth: 40.5% versus 9.7% (Table 2). Generally, there was a tendency for children on HAART to have a higher frequency of dental caries as compared to their counterparts not on HAART (Table 2), although the difference was not statistically significant ( $P>.05$ ). Gender, consumption of sugary snacks, socioeconomic status and drug preparation did not have any significant influence on dental caries ( $P>.05$ ). Age was directly associated with dental caries while tooth brushing and previous visits to the dentist were indirectly associated with dental caries ( $P<.05$ ).

## DISCUSSION

The study population comprised children aged 1.5 to 12 years who were stratified and randomly selected based on their medical files. This method of sample selection minimizes any chances of selection bias. Most of the children ( $n=205$ ) were found to be taking antibacterial drugs (Table 1), especially Co-trimoxazole. As a policy, patients with AIDS disease in stage 2 to stage 4, according

to World Health Organization definition criteria, should be on Co-trimoxazole prophylaxis to prevent *Pneumocystis carinii* pneumonia and other opportunistic infections.<sup>6</sup>

The oral lesions may have had a negative impact on the nutritional health of the children<sup>23,24</sup> by reducing food intake as a result of discomfort during eating. In another review of published reports, Enwonwu<sup>25</sup> revealed that malnutrition may induce mucosal disruptions predisposed to candidiasis and severe periodontal disease. Moreover, protein/energy malnutrition in particular may result in hypofunction of the salivary glands with a consequence of xerostomia as well as failure to protect the oral mucosa against the numerous potentially pathogenic oral microbial agents. In the present study, 73% of the children had one or more of the oral lesions and 19.0% ( $n=45$ ) admitted experiencing discomfort during oral functions, particularly during eating (Table 2).

Appropriate treatment of the lesions may improve food intake thereby improving quality of life, yet only 2.5% of the study children were taking medication specifically for soft tissue oral le-

Table 2. The frequency distribution of children on highly active antiretroviral therapy (HAART) and not on HAART, according to type of oral lesions ( $n=237$ ).

Variables	Children on HAART ( $n=118$ )		Children not on HAART ( $n=119$ )	Total ( $n=237$ )
Are oral lesions present?				
Yes	80 (67.8)	S	93 (78.2)	173 (73.0)
No	38 (32.2)		26 (21.8)	64 (27.0)
Type of lesion ( $n = 173$ ) <sup>ø</sup>				
Oral candidiasis	23 (19.5)	S	44 (37.0)	67 (28.3)
Pseudomembranous	16 (13.6)	S	22 (18.5)	38 (16.0)
Erythematous	3 (2.5)	S	8 (6.7)	11 (4.6)
Angular cheilitis	4 (3.4)	S	12 (10.1)	16 (6.8)
Gingivitis	16 (13.6)	S	29 (24.4)	45 (19.0)
Erythema gingival banding	0 (0.0)	NS	2 (1.7)	2 (0.8)
Necrotising gingivitis	0 (0.0)	NS	1 (0.8)	1 (0.4)
Marginal gingivitis	16 (13.6)	S	26 (21.8)	42 (17.7)
Recurrent herpes labialis	1 (0.8)	NS	2 (1.7)	3 (1.7)
Recurrent aphthous ulceration	1 (0.8)	NS	0 (0.0)	1 (0.4)
Atypical oral ulcerations	0 (0.0)	NS	2 (1.7)	2 (0.8)
Oral Kaposi's sarcoma	0 (0.0)	NS	1 (0.8)	1 (0.4)
Salivary gland disease	3 (2.5)	S	10 (8.4)	13 (5.5)
Molluscum contagiosum	7 (5.9)	NS	4 (3.4)	11 (4.6)
Cervical lymphadenopathy	64 (54.2)	S	80 (67.2)	144 (60.8)
Deciduous teeth*				
Total caries (def <sup>t</sup> )	51 (43.2)	NS	49 (41.2)	100 (42.2)
Decayed teeth	49 (41.5)	NS	47 (39.5)	96 (40.5)
Extracted teeth due to caries	5 (4.2)	NS	2 (1.7)	7 (7.5)
Filled teeth due to caries	0 (0.0)	NS	1 (0.8)	1 (1.1)
Permanent teeth*				
Total caries (DMFT)	17 (14.4)	NS	9 (7.5)	26 (11.0)
Decayed teeth	16 (13.6)	S	7 (5.9)	23 (9.7)
Missing teeth due to caries	1 (0.8)	NS	1 (0.8)	2 (0.8)
Filled teeth due to caries	0 (0.0)	NS	2 (1.7)	2 (0.8)

Percentage is given in parentheses; <sup>ø</sup> Some of the children had more than one oral lesion and \* others had both decayed (d/D), extracted (e) missing (M) and filled (f/F) teeth (t/T); S, significant; NS, not significant.

sions. This implies that the majority of the lesions remain unattended, which is similar to previous findings in Ugandan HIV-infected adults.<sup>18</sup> In comparison with a previous study on paediatric HIV-infected Ugandans,<sup>19</sup> these children also had unmet restorative dental treatment needs indicated by the high proportion of children with decayed teeth: 40.2% and 9.7% out of 42.2% and 11.0% of the total caries prevalence in the deciduous and permanent teeth, respectively (Table 2).

In the present study, cervical lymphadenopathy, oral candidiasis and gingivitis were the most common oral soft tissue lesions (Table 2). This finding corroborates previous reports on paediatric HIV infection.<sup>1,7,19</sup>

It should be noted that regular dental care in HIV-infected individuals results in better oral health with no greater cost than regular attendance.<sup>26</sup> Although as many as half of the children (n=119) in the present study had dental caries, only 16.9% had previously visited a dentist since birth, although this was mainly for emergency care (Table 1). Whereas, Okunseri et al<sup>27</sup> indicated that as many as 50% of paediatric HIV-infected medical patients (n=102) in the United States had visited a dentist in the past twelve months, studies<sup>28</sup> in sub-Saharan Africa revealed a limited access to and utilization of dental care among the black population, especially in rural areas and areas of extreme poverty. In the present study, the majority of the children (92%) were from families of low socio-economic status (Table 1), which may partly explain the poor dental care seeking behaviour of this population.

Generally, the frequency distribution of children with soft tissue oral lesions was significantly lower in those on HAART as compared to their counterparts not on HAART (Table 2). This is in agreement with the previous finding by Schmidt-Westhausen and co-workers.<sup>13</sup> On the other hand, children on HAART had a higher frequency of dental caries as compared to their counterparts not on HAART (Table 2), although the difference was not statistically significant. Some anti-retroviral drugs are sucrose based in the form of a syrup or suspension, such as Zidovudine,<sup>3</sup> and others may lead to decreased salivation, which makes them potentially cariogenic. About 9% of children in the present study were taking their medication in form of a syrup or suspension (Table 1). However, the drug preparation did not significantly influence the development of dental caries, probably due to limited variability. The incidence of dental caries was found to increase with age, which is in

agreement with previous studies<sup>29-31</sup> on Ugandan children. This upward trend of dental caries with age is a result of the disease being a cumulative phenomenon.

The present study supported the notion of a negative association between tooth brushing and the development of dental caries,<sup>32</sup> particularly with the regular use of fluoride toothpaste. About 71.7% of the children reported cleaning their teeth and 92.9% of these reported using a plastic toothbrush (Table 1). These values are much higher than previous findings recorded in 10 to 14-year-old rural Ugandan school children,<sup>30</sup> which were 32% and 7%, respectively.

In support of the previous study<sup>30</sup> in rural Ugandan school children, consumption of sugary snacks was not significantly associated with the development of dental caries. It should be noted that more than 90% of the children who gave a positive response were taking the snacks occasionally (Table 1), which may have had a limited impact on the development of dental caries.

It was not possible to perform an immunological measurement of the children in the present study because of limited funding and PIDC does not routinely assess the viral load levels of its patients. The immunological measurement values employed in the analyses were retrieved from the most recent medical records and were a composite of CD3<sub>+</sub> and CD4<sub>+</sub> T-lymphocyte counts. Contrary to Howell et al,<sup>33</sup> but in agreement with Gaitán-Cepeda et al,<sup>34</sup> the CD3<sub>+</sub> + CD4<sub>+</sub> cell count did not have any significant influence on the frequency distribution of oral lesions. Some of the available CD3<sub>+</sub> + CD4<sub>+</sub> values were recorded as much as 6 months prior to the present study, thus such a time lag renders caution in the interpretation of this finding.

## CONCLUSIONS

The majority of the HIV/AIDS-infected children in the PIDC had one or more oral lesions. Except for dental caries, the oral lesions were more frequently recorded in children not on HAART. Some of the lesions were associated with discomfort during oral functions. There is a need to integrate oral health care into the general medical care of these children to ensure regular screening for oral lesions and appropriate early management.

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