Oral manifestations of HIV infection in children and adults receiving highly active anti-retroviral therapy [HAART] in Dar es Salaam, Tanzania

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Abstract

Background: The aim of the study was to compare the prevalence and types of HIV-related oral lesions between children and adult Tanzanian patients on HAART with those not on HAART and to relate the occurrence of the lesions with anti-HIV drug regimen, clinical stage of HIV disease and CD4+ cell count.

Methods: Participants were 532 HIV infected patients, 51 children and 481 adults, 165 males and 367 females. Children were aged 2–17 years and adults 18 and 67 years. Participants were recruited consecutively at the Muhimbili National Hospital (MNH) HIV clinic from October 2004 to September 2005. Investigations included; interviews, physical examinations, HIV testing and enumeration of CD4+ T cells.

Results: A total of 237 HIV-associated oral lesions were observed in 210 (39.5%) patients. Oral candidiasis was the commonest (23.5%), followed by mucosal hyperpigmentation (4.7%). There was a significant difference in the occurrence of oral candidiasis ($\chi^2 = 4.31; df = 1; p = 0.03$) and parotid enlargement ($\chi^2 = 36.5; df = 1; p = 0.04$) between children and adults. Adult patients who were on HAART had a significantly lower risk of oral lesions (OR = 0.32; 95% CI = 0.22 – 0.47; p = 0.005), oral candidiasis (OR = 0.28; 95% CI = 0.18 – 0.44; p = 0.003) and oral hairy leukoplakia (OR = 0.18; 95% CI = 0.04 – 0.85; p = 0.03). There was no significant reduction in occurrence of oral lesions in children on HAART (OR = 0.35; 95% CI = 0.11 – 1.14; p = 0.15). There was also a significant association between the presence of oral lesions and CD4+ cell count < 200 cell/mm$^3$ ($\chi^2 = 52.4; df = 2; p = 0.006$) and with WHO clinical stage ($\chi^2 = 121; df = 3; p = 0.008$). Oral lesions were also associated with tobacco smoking ($\chi^2 = 8.17; df = 2; p = 0.04$).

Conclusion: Adult patients receiving HAART had a significantly lower prevalence of oral lesions, particularly oral candidiasis and oral hairy leukoplakia. There was no significant change in occurrence of oral lesions in children receiving
HAART. The occurrence of oral lesions, in both HAART and non-HAART patients, correlated with WHO clinical staging and CD4+ less than 200 cells/mm³.

Background
Most African studies on HIV associated oral lesions have been done during pre-HAART era [1-11]. The relatively few studies of oral lesions in patients on HAART have been conducted elsewhere and do indicate significant differences in the influence of HAART on types of oral lesions [12-14]. For example, oral candidiasis, oral hairy leukoplakia, Kaposi’s sarcoma and HIV-associated periodontal diseases have been reported to decrease [12,13,15-22]. On the other hand, HIV-salivary gland disease, human papilloma virus (HPV)-associated oral lesions including papilloma, condylomas and focal epithelial hyperplasia [oral warts], xerostomia and recurrent oral ulceration appear to have increased [13-15,18,23-25]. There are also reports indicating no change in the occurrence of HIV associated oral lesions in children receiving HAART [26,27]. The reasons for these differences are not entirely clear. Some authors have associated these variations with differences in access to oral health care, demographic and social factors, mode of HIV transmission, types of co-infections, disease stage and immune reconstitution [18,28,29]. Nonetheless, the presence of such significant differences underlines the need for meticulous monitoring of prevalence and types of HIV associated oral lesions in every clinical setting that provide HAART [13].

As indicated earlier, most of the above-mentioned studies have been conducted in developed countries [30,31]. There is relatively little information emanating from developing countries, where particular efforts are being made to scale up provision of HAART to eligible patients [32].

The government of Tanzania, with assistance from international donor agencies, started providing HAART to HIV patients free of charge in July 2004 [33,34]. However, there is no information regarding human immunodeficiency virus (HIV)-related oral lesions of patients on antiretroviral therapy. This study aimed to determine the prevalence and types of oral manifestations of HIV/AIDS between children and adult patients on HAART and those not on HAART, and correlate clinical oral lesions with clinical stage of HIV disease, anti-HIV drug regimen and CD4+ cell count.

Methods
Participants and setting
A total of 532 HIV-infected patients, 367 (69%) females and 165 (31%) males participated in the study. There were 51 children aged between 2 and 17 years, with mean age of 7.6 (SD ± 4.3) years and 481 adults aged 18–67 years, with a mean age of 38.2 (SD ± 8.9) years. Participants were recruited consecutively at the Muhimbili National Hospital (MNH) HIV clinic in Dar es Salaam, from October 2004 to September 2005. The MNH is the largest referral hospital in Tanzania and serves as a teaching facility for the Muhimbili University College of Health Sciences (MUCHS), the largest medical school in the country.

Study design and sample size calculations
This was a cross sectional study. The sample size was estimated at 336, by assuming the prevalence of oral lesions in HIV infected individuals in Tanzania to be around 30% [4] and by setting type I error at 5% and type II error at 20%. We consecutively enrolled 532 patients. None of the patients declined participation in the study, bringing the participation rate to 100%.

Investigations
Patients were interviewed using a standard structured questionnaire to obtain information regarding social and demographic details, past medical history, family history and history of previous medication. Previous episodes of oral candidiasis, other medical conditions, use of traditional medicine, anti-tuberculosis drugs, antifungal agents, and use of antiretroviral and current treatments were all recorded. Current and previous episodes of opportunistic systemic diseases related to HIV were categorized and recorded as follows: tuberculosis, pneumonia, herpes zoster infection and cryptococcal meningitis.

General examination
Clinical examination of all study patients was done by an independent physician, who categorized them in accordance with the World Health Organization (WHO) clinical staging criteria [35].

Oral examination
An oral examination was carried out by a qualified dental surgeon without knowing the HIV clinical stage and CD4+ cell count level of the patient or whether the patient was on HAART or not. A standard oral examination method recommended by WHO [36] was used to examine: (a) the extra-oral, head and neck areas; and (b), peri-oral and intra-oral soft tissues using a criteria described by Greenspan et al. [37]. Examination was conducted while the patient was seated on a chair under artificial light. The extra-oral and peri-oral tissues were examined first, followed by the intra-oral tissues, for changes in size, colour
and shape of anatomical areas as well as for clinical signs and lesions. The oral lesions associated with HIV infection were diagnosed based on their clinical presentation and where multiple sites were involved, all sites were documented.

**HIV serology and determination of lymphocytes subsets**

Blood was collected in EDTA tubes from the patients. HIV serology was determined by Vironostika HIV Uni-Form II Ag/Ab (BioMerieux, Boxtel, The Netherlands) and reactive samples were retested by Vironostika HIV Uni-Form II Plus O (BioMerieux, Boxtel, The Netherlands). Samples reactive on both tests were considered to be positive for IgG anti HIV antibodies. Enumeration of CD4+ and CD8+ T cells was done using FACS count machine after staining patients’ blood with monoclonal antibodies [38].

**HAART regimens**

In Tanzanian setting, a triple therapy consisting of 2 nucleoside reverse transcriptase inhibitors (NRTI) + 1 non-nucleoside reverse transcriptase inhibitors (NNRTI) or 2 NRTI + 1 Protease inhibitor (PI) is recommended. The first line includes four different combinations of drugs: stavudine + lamivudine + nevirapine; stavudine + lamivudine + efavirenz; zidovudine + lamivudine + nevirapine and zidovudine + lamivudine + efavirenz. The second line regimen includes the following drug combination: Abacavir + kaletra (lopinavir/ritonavir) + didanosine and abacavir + saquinavir/ritonavir + didanosine [34].

**Ethical issues**

The study protocol was approved by the ethics committees of the Muhimbili University of College of Health Sciences and Muhimbili National Hospital, Dar es salaam, Tanzania. Informed verbal consent was sought from participants and from parents/or guardians in case of children below eighteen years. The following information was given to ensure that parents and patients/guardians have the information needed to make an informed choice: a complete description of the aims of the study, potential benefits and risks, blood collection procedures and assurance of confidentiality of any information given as well as test results. Study personnel provided any other requested additional information. All patients seen in this study received appropriate care and treatment according to national guidelines on care and treatment of HIV infected individuals. Patients who were found to have any oral lesions were referred to the Department of Oral Surgery and Oral Pathology of the Muhimbili National Hospital where appropriate management and follow-up were given. All patients’ information and test results were confidentially kept.

**Statistical analysis**

Data were coded, entered, cleaned, validated and analyzed using the SPSS version 12.0 [39]. Patients were categorized into children (<18 years) and adults (≥18 years) and into those on HAART and those not receiving HAART. Comparison of proportions was performed using the Pearson chi-squared test and in situation where 20% or more of the cells had expected count less than 5, Fisher's exact test was used. Bivariate analysis was done using Spearman's rank correlations. A P-value of < 0.05 was considered significant. The following were determined: degree of associations between occurrence and types of oral lesions and use of anti-retrovirals, gender, smoking habits, alcohol consumption, coexistence with opportunistic systemic diseases, clinical stage of HIV disease and degree of immunosuppression. Multiple logistic regression analysis was performed to assess the association between presence of oral lesion associated with HIV and use of antiretrovirals after adjusting for CD4+ cell count.

**Results**

A total of 532 HIV-infected patients, 367 (69%) females and 165 (31%) males participated in the study (Table 1). There were 51 children aged between 2 and 17 years, with mean age of 7.6 (SD ± 4.3) years and 481 adults aged 18–67 years, with a mean age of 38.2 (SD ± 8.9) years. Overall, median CD4+ cell count was 151 cells/mm³, with values ranging from 1 to 2007 cell/mm³. The median CD4+ cell count for children was 501 cells/mm³ and 134 cells/mm³ for adults. Majority 373 (70.1%) of children and adult patients were in the WHO clinical stages II to III. Among the participants, 298 (56%) patients were on HAART, consisting of nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs). Majority 531 (99.7%) were on the first line HAART combination, of whom 229 (76.8%) were on a combination of stavudine/lamivudine/nevirapine, 32 (10.7%) on a combination of zidovudine/lamivudine/efavirenz, 26 (8.7%) on stavudine/lamivudine/efavirenz and 10 (3.4%) were on zidovudine/lamivudine/nevirapine. One patient (0.3%) was on second line combination that included protease inhibitors (Abacavir/lopinavir/didanosine). Two hundred and thirty four (44%) patients were not receiving HAART. Sixty-two patients (11.7%) reported use of traditional medicines, of whom 36 (58%) were concomitantly using traditional medicines with HAART.

A total of 237 HIV-associated oral lesions were observed in 210 (39.5%) patients. Overall, oral candidiasis was the commonest oral lesion seen in 125 (23.5%) patients followed by mucosal hyper pigmentation 25 (4.7%), parotid gland enlargement 21 (3.9%) and oral Kaposi’s sarcoma 17 (3.2%) (Table 2). In children, parotid gland enlarge-
ment was the commonest oral lesion (19.6%), followed by oral candidiasis (11.8%), oral Kaposi’s sarcoma (3.9%), oral hairy leukoplakia (3.9%), herpes simplex lesions (2.2%) and oral warts was the least (2.0%). In adults, oral candidiasis was the commonest (24.7%), followed by mucosal hyperpigmentation (5.2%), herpes zoster face and odontogenic abscess was the least (0.4% each). There was statistically significant difference in the occurrence of oral candidiasis ($X^2 = 4.31; df = 1; p < 0.05$) and parotid enlargement ($X^2 = 36.5; df = 1; p < 0.05$) between children and adults. Pseudomembranous candidiasis was the most predominant type of oral candidiasis (66.4% (83/125) followed by a combination of pseudomembranous and erythematous 12% (15/125), erythematous candidiasis 9.6% (12/125), angular cheilitis 3.2% (4/125), combination of angular cheilitis with erythematous and hyperplastic variant were the least (1.6% each). Among 125 patients diagnosed with oral candidiasis 42 (33.6%) patients had previous history of oral candidiasis, 37 (29.6%) patients presented with esophageal symptoms such as dysphagia, odynophagia and chest pain at the time of examination.

Table 3 shows no significant difference in prevalence of oral lesions among children on HAART and those not on HAART (OR = 0.35; 95% CI = 0.11 – 1.15; p > 0.05). Table 4 shows that adult patients who were on HAART had a significantly lower risk of oral lesions (OR = 0.32; 95% CI = 0.22–0.47; p < 0.01), oral candidiasis (OR = 0.28; 95% CI = 0.18 – 0.44; p < 0.01) and oral hairy leukoplakia (OR = 0.18; 95% CI = 0.04 – 0.85; p < 0.03). There was also lower prevalence of necrotizing ulcerative gingivitis, herpes simplex lesions, recurrent ulcers, Bell’s palsy and herpes zoster of face in adult patients who were on HAART.

| Characteristics                          | All patients n (%) | Patients with oral lesions n (%)* | $\chi^2$-value | p-value** |
|-----------------------------------------|-------------------|----------------------------------|----------------|-----------|
| Gender                                  |                   |                                  |                |           |
| Male                                    | 165 (31.0)        | 63 (38.2)                        | 0.17           | 0.68      |
| Female                                  | 367 (69.0)        | 147 (40.1)                       |                |           |
| Age (Years)                             |                   |                                  |                |           |
| Children 2–17                           | 51 (9.6)          | 21 (41.2)                        | 0.68           | 0.88      |
| Adults 18 – 67                          | 481 (90.4)        | 189 (39.3)                       |                |           |
| Smoking habit                           |                   |                                  |                |           |
| Current                                 | 20 (3.8)          | 14 (70)                          | 8.17           | 0.02      |
| Stopped                                 | 17 (3.2)          | 7 (41.2)                         |                |           |
| Never                                   | 495 (93.0)        | 189 (38.2)                       |                |           |
| Alcohol consumption                     |                   |                                  |                |           |
| Current                                 | 31 (5.8)          | 10 (32.3)                        |                |           |
| Stopped                                 | 37 (7.0)          | 16 (43.2)                        | 0.90           | 0.64      |
| Never                                   | 464 (87.2)        | 184 (39.6)                       |                |           |
| Traditional medicine                    |                   |                                  |                |           |
| Yes                                     | 62 (11.7)         | 25 (40.3)                        | 0.17           | 0.68      |
| No                                      | 470 (88.3)        | 183 (38.9)                       |                |           |
| Antiretroviral therapy                  |                   |                                  |                |           |
| Without therapy                         | 234 (44.0)        | 127 (54.3)                       | 38.30          | 0.00      |
| HAART therapy                           | 298 (56.0)        | 83 (27.9)                        |                |           |
| Antiretroviral types                    |                   |                                  |                |           |
| Stav/Lamiv/Nev                          | 229 (76.8)        | 9 (12.9)                         | 2.96           | 0.57      |
| Stav/Lamiv/Eff                          | 26 (8.7)          | 10 (38.5)                        |                |           |
| Zido/Lamiv/Eff                          | 32 (10.7)         | 11 (34.4)                        |                |           |
| Zido/Lamiv/Nev                          | 10 (3.4)          | 2 (20.0)                         |                |           |
| Abac/Lop/Didan                          | 1 (0.3)           | 0 (0)                            |                |           |
| WHO HIV clinical stage                  |                   |                                  |                |           |
| Stage I                                 | 70 (13.2)         | 9 (12.9)                         | 120.93         | 0.00      |
| Stage II                                | 204 (38.3)        | 38 (18.6)                        |                |           |
| Stage III                               | 169 (31.8)        | 101 (59.8)                       |                |           |
| Stage IV                                | 89 (16.7)         | 62 (69.7)                        |                |           |
| CD4* cell count (cells/mm$^3$)          |                   |                                  |                |           |
| > 500                                   | 46 (8.6)          | 10 (21.7)                        | 52.45          | 0.00      |
| 200–500                                 | 164 (30.8)        | 33 (20.5)                        |                |           |
| < 200                                   | 322 (60.5)        | 167 (31.9)                       |                |           |
| Total number of patients                | 532 (100.)        | 210 (39.5)                       |                |           |

* Row percentages; ** p-value less than 0.05 was considered significant; $\chi^2$ Chi square test
but the difference was not statistically significant (p > 0.05). After controlling for CD4+ cell count, adult on HAART had a significantly lower risk of oral Kaposi’s sarcoma compared with those not on HAART (adjusted OR = 0.29; 95% CI = 0.10–0.89; p < 0.03). The odds for oral warts and mucosal hyper pigmentation were non-significant higher in adult who were on HAART, being (OR = 1.49; 95% CI = 0.13 – 16.5; p > 0.05) and (OR = 1.62; 95% CI = 0.68 – 3.82; p > 0.05), respectively.

The duration of use of HAART ranged from 1 to 14 months, with majority (71.1%) having been on treatment for one to six months. Patients on HAART for the duration of more than six months had significantly lower prevalence of oral lesions (OR = 0.53; 95% CI 0.29–0.97; p < 0.05) and specifically oral candidiasis (OR = 0.53; 95% CI 0.29–0.97; p = 0.04).

The mean CD4+ profiles of patients on HAART and those not on HAART are shown in Table 5. Overall, the majority (67.8%) of patients who were on HAART had CD4+ cell count < 200 cells/mm^3. Only a small minority (32.2%) of the patients on HAART were found to have CD4+ counts > 200 cells/mm^3. Among those who were not on HAART 51.3% had CD4+ cell count < 200 cells/mm^3 while the rest in the group had CD4+ cell count > 200 cells/mm^3. However, the majority (70.3%) of adult patients on HAART had CD4+ cell count < 200 cells/mm^3 while only minority (36.4%) of the children on HAART had CD4+ cell count < 200 cells/mm^3. The mean difference of CD4+ cell counts

### Table 2: Occurrence of HIV-associated oral lesions among children and adults

| Oral lesion                      | Children (2–17 yrs) n (%) | Adults (18–67 yrs) n (%) | Total (n = 532) n (%) |
|---------------------------------|---------------------------|--------------------------|-----------------------|
| Oral candidiasis                | 6 (11.8)                  | 119 (24.7)               | 125 (23.5)            |
| Hyperpigmentation               | 0 (0)                     | 25 (5.2)                 | 25 (4.7)              |
| Enlarged Parotid gland          | 10 (19.6)                 | 11 (2.3)                 | 21 (3.9)              |
| Oral Kaposi’s sarcoma           | 2 (3.9)                   | 15 (3.1)                 | 17 (3.2)              |
| Necrotizing Ulcerative gingivitis| 0 (0)                     | 13 (2.7)                 | 13 (2.4)              |
| Oral hairy leukoplakia          | 2 (3.9)                   | 10 (0.6)                 | 12 (2.3)              |
| Herpes simplex lesions          | 7 (2.2)                   | 2 (2.1)                  | 9 (1.7)               |
| Recurrent ulcers                | 0 (0)                     | 4 (0.8)                  | 4 (0.8)               |
| Oral warts                      | 1 (2.0)                   | 3 (0.6)                  | 4 (0.8)               |
| Bell’s palsy                    | 0 (0)                     | 3 (0.6)                  | 3 (0.6)               |
| Herpes zoster face              | 0 (0)                     | 2 (0.4)                  | 2 (0.4)               |
| Odontogenic abscess             | 0 (0)                     | 2 (0.4)                  | 2 (0.4)               |
| All oral lesions                | 21 (41.2)                 | 189 (39.3)               | 210 (39.5)            |

### Table 3: Comparison of oral lesions among children on HAART (n = 22) and those not on HAART (n = 29)

| Type of oral lesion              | No. of oral lesions n (%) | Unadjusted OR (95% CI) | Adjusted OR (95% CI) | p-value |
|---------------------------------|---------------------------|------------------------|----------------------|---------|
| Oral candidiasis                |                           |                        |                      |         |
| On HAART                        | 0 (0.0)                   | 0.0 (0.0–9.20)         | 0.0 (0.0–1.80)       | 0.80    |
| Not on HAART                    | 6 (20.7)                  |                        |                      |         |
| Enlarged Parotid gland          |                           |                        |                      |         |
| On HAART                        | 4 (18.2)                  | 0.8 (0.2–3.48)         | 0.9 (0.22–3.93)      | 0.82    |
| Not on HAART                    | 6 (20.7)                  |                        |                      |         |
| Oral Kaposi’s sarcoma           |                           |                        |                      |         |
| On HAART                        | 1 (4.5)                   | 1.3 (0.08–22.6)        | 0.9 (0.05–17.4)      | 0.84    |
| Not on HAART                    | 1 (3.4)                   |                        |                      |         |
| Oral hairy leukoplakia          |                           |                        |                      |         |
| On HAART                        | 0 (0.0)                   | 0.0 (0.0–2.61)         | 0.0 (0.0–2.11)       | 0.88    |
| Not on HAART                    | 10 (6.9)                  |                        |                      |         |
| Herpes simplex lesions          |                           |                        |                      |         |
| On HAART                        | 0 (0.0)                   | 0.0 (0.0–1.52)         | 0.0 (0.0–7.30)       | 0.92    |
| Not on HAART                    | 1 (3.4)                   |                        |                      |         |
| Oral warts                      |                           |                        |                      |         |
| On HAART                        | 1 (4.5)                   | -                      | -                    | 0.91    |
| Not on HAART                    | 0 (0.0)                   |                        |                      |         |
between the adult and children on HAART and those not on HAART was statistically significant (t = 3.94; 95% CI = 42.3 – 126.3; p < 0.01). In both HAART and non-HAART receiving children and adult patients oral lesions occurred more significantly among those with CD4+ cell count less than 200 cell/mm³ (χ² = 52.4; df = 2; p < 0.01). There was a strong association between the WHO clinical stage of HIV disease with the presence of oral lesions (χ² = 52.4; df = 2; p < 0.01). There was a significant association between occurrence of pulmonary TB with oral lesions (χ² = 6.9; df = 1; p < 0.01) and oral candidiasis (χ² = 11.0; df = 1; p < 0.01) but not other systemic diseases (P > 0.05). Oral lesions were not associated with any of the investigated socio-demographic features except for tobacco smoking (χ² = 8.17; df = 2; p < 0.01).

**Discussion**

In the present study, the prevalence of HIV-associated oral lesions in adult patients receiving HAART was significantly reduced. The reduction was mainly attributed to

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**Table 4: Comparison of oral lesions among adults on HAART (n = 276) and those not on HAART (n = 205)**

| Type of oral lesions        | No. of oral lesions n (%) | Unadjusted OR (95% CI) | Adjusted OR (95% CI) | p-value |
|-----------------------------|---------------------------|------------------------|----------------------|---------|
| Oral candidiasis            |                           |                        |                      |         |
| On HAART                    | 41 (14.9)                 | 0.28 (0.18–0.38)       | 0.17 (0.11–0.28)     | 0.00    |
| Not on HAART                | 78 (38.0)                 |                        |                      |         |
| Hyper pigmentation          |                           |                        |                      |         |
| On HAART                    | 17 (6.2)                  | 1.62 (0.68–3.82)       | 1.60 (0.67–3.81)     | 0.27    |
| Not on HAART                | 8 (3.9)                   |                        |                      |         |
| Enlarged Parotid gland      |                           |                        |                      |         |
| On HAART                    | 6 (2.2)                   | 0.89 (0.27–2.95)       | 0.92 (0.27–3.10)     | 0.85    |
| Not on HAART                | 5 (4.9)                   |                        |                      |         |
| Oral Kaposi’s sarcoma       |                           |                        |                      |         |
| On HAART                    | 5 (1.8)                   | 0.36 (0.12–1.06)       | 0.29 (0.10–0.89)     | 0.06    |
| Not on HAART                | 10 (4.9)                  |                        |                      |         |
| Necrotizing Ulcerative gingivitis |                     |                        |                      |         |
| On HAART                    | 5 (1.7)                   | 0.45 (0.15–1.41)       | 0.37 (0.12–1.15)     | 0.17    |
| Not on HAART                | 8 (3.4)                   |                        |                      |         |
| Oral hairy leukoplakia      |                           |                        |                      |         |
| On HAART                    | 2 (0.7)                   | 0.18 (0.04–0.85)       | 0.15 (0.03–0.70)     | 0.03    |
| Not on HAART                | 8 (3.9)                   |                        |                      |         |
| Herpes simplex lesions      |                           |                        |                      |         |
| On HAART                    | 3 (1.1)                   | 0.44 (0.10–1.86)       | 0.39 (0.09–1.69)     | 0.26    |
| Not on HAART                | 5 (2.4)                   |                        |                      |         |
| Recurrent ulcers            |                           |                        |                      |         |
| On HAART                    | 1 (0.4)                   | 0.24 (0.02–2.37)       | 0.22 (0.02–2.15)     | 0.22    |
| Not on HAART                | 3 (1.34)                  |                        |                      |         |
| Oral warts                  |                           |                        |                      |         |
| On HAART                    | 2 (0.7)                   | 1.49 (0.13–16.5)       | 1.44 (0.13–16.4)     | 0.75    |
| Not on HAART                | 1 (0.5)                   |                        |                      |         |
| Bell’s palsy                |                           |                        |                      |         |
| On HAART                    | 0 (0.0)                   | -                      | -                    | 0.84    |
| Not on HAART                | 3 (1.5)                   |                        |                      |         |
| Herpes zoster face          |                           |                        |                      |         |
| On HAART                    | 0 (0.0)                   | -                      | -                    | 0.85    |
| Not on HAART                | 2 (0.9)                   |                        |                      |         |
| Odontogenic abscess         |                           |                        |                      |         |
| On HAART                    | 1 (0.4)                   | 0.74 (0.04–11.9)       | 0.78 (0.05–13.0)     | 0.83    |
| Not on HAART                | 1 (0.5)                   |                        |                      |         |

* p-value obtained after adjusting for CD4+ cell counts.
the reduction of oral candidiasis and oral hairy leukoplakia among adult patients. This finding is consistent with observations in other studies that have shown significant reduction in these oral lesions associated with HAART usage, linked to the improved immune status of patients [12,13,15-22]. Notably, patients on HAART for the duration of more than six months had significantly lower prevalence of oral lesions (OR = 0.53; 95% CI 0.29–0.97; p < 0.05) and specifically oral candidiasis (OR = 0.53; 95% CI 0.29–0.97; p = 0.04). There was, however, no significant association between the type of HAART regimen and presence of oral lesions, most probably due to the fact that most of our patients (76.8%) were on one type of HAART consisting of stavudine, lamivudine and nevirapine, and that only one patient had a HAART combination containing PI. We found no significant difference in prevalence of oral lesions between children on HAART and those not on HAART (Table 3), similar to other studies [26,27]. The occurrence of HIV-associated oral in children is an issue that requires further investigation as the results of different studies have produced conflicting results. In one study there was no direct relationship between prevalence of oral lesions, severe immunodepression, and/or viral load > 100000 copies in children who were perinatally infected with HIV [40].

There were no significant differences in the prevalence of other oral lesions including enlarged parotid glands, necrotizing ulcerative gingivitis, recurrent ulcers, Bell’s palsy and herpes zoster of the face between HAART and non-HAART groups (p > 0.05). This could be explained by the fact that most of these lesions are classified as being less commonly associated with HIV [44] and therefore, their prevalence even in the non-HAART receiving group was small.

Likewise, there was insignificant increase in oral papillomatous [oral warts] in patients on HAART as compared to the non-HAART group. The increase in oral warts among patients on HAART has been associated with immune reconstitution [18,23-25]. The lack of significant association between oral wart and HAART usage observed in the present study could be due to the short period of the administration of HAART as majority of patients were on HAART for one to six months.

Mucosal hyperpigmentation, which was the second most prevalent oral lesions after oral candidiasis with a prevalence of 4.7%, occurred at higher, but non-significant magnitude, among adult patients who were on HAART. The reported prevalence of mucosal hyperpigmentation compares with a prevalence of 6% among HIV/AIDS patients in Kenya [9]. The higher prevalence of mucosal hyperpigmentation in patients on HAART has been linked with increased melanin production in the epithelium associated with increased release of α-melanocyte-stimulating hormone (α – MSH) [41] as a result of systemic ketoconazole and zidovudine therapy [42,43]. In the present study 20% (5/25) of patients with mucosal hyperpigmentation were on HAART combination containing zidovudine.

Table 5: CD4+ cell counts of Patients on HAART and those not on HAART

| CD4+ cell count (cells/mm³) | Patients on HAART (n = 298) | Patients without HAART (n = 234) |
|---------------------------|-----------------------------|---------------------------------|
|                           | n (%)                       | Mean ± SD                       | n (%)                       | Mean ± SD                       |
| <200                      | 202 (67.8)                  | 84.0 ± 62.1                     | 120 (51.3)                  | 65.2 ± 57.0                     |
| 200–500                   | 80 (26.8)                   | 296.0 ± 75.0                    | 84 (35.9)                   | 314.4 ± 90.2                    |
| >500                      | 16 (5.4)                    | 714.1 ± 207.1                   | 30 (12.8)                   | 879.9 ± 415.2                   |
| Total                     | 298                         | 174.8 ± 177.5                   | 234                         | 259.1 ± 310.0                   |

Student’s t-test for comparing means; (t = 3.94; 95% CI = 42.3 – 126.3; p = 0.00).
Table 6: Association in the occurrence of oral lesions and opportunistic systemic diseases among HIV-infected patients expressed as Odds ratios (OR) with 95% Confidence intervals

| Systemic disease          | n (%)   | OR (95% CI)       | χ²-value (p-value) |
|---------------------------|---------|-------------------|--------------------|
| Tuberculosis              |         |                   |                    |
| All oral lesions          | 62 (11.7)| 2.02 (1.19–3.46)  | 6.9 (0.008)        |
| Oral candidiasis          | 34 (54.8)| 2.50 (1.44–4.34)  | 11.0 (0.001)       |
| Pneumonia                 | 14 (2.6)| 0.61 (0.19–1.96)  | 0.71 (0.40)        |
| All oral lesions          | 4 (28.6)| 0.54 (0.12–2.42)  | 0.68 (0.41)        |
| Oral candidiasis          | 2 (14.3)|                   |                    |
| Herpes zoster             | 8 (1.5)| 0.51 (1.01–2.53)  | 0.71 (0.32)        |
| All oral lesions          | 2 (25.0)| 1.08 (0.22–5.45)  | 0.01 (0.00)        |
| Oral candidiasis          | 2 (25.0)|                   |                    |

(55x99) undesca. (55x111) oc-occurrence of oral lesions in children receiving HAART.  

(55x123) tion, while the prevalence of other oral lesions was unchanged. However there was no significant change in occurrence of oral lesions in children receiving HAART.

More studies preferably longitudinal need to be conducted for longer periods of time in order to get a better picture on the efficacy of HAART in reducing oral lesions in both children and adults in our setting.

**Competing interests**

The author(s) declared that they have no competing interests.

**Authors’ contributions**

All authors were involved in designing the study. OIMH and FM took part in data collection, data handling and preparation of manuscript. MINM, ENMS, MJM, FHM, PEV and AJAM participated in preparation of the manuscript. EK participated in data analysis and preparation of the manuscript. Finally, all authors read and approved the final manuscript.

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