The prevalence of HIV associated oral lesions among adults in the era of HAART

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SUMMARY

Introduction: The overall prevalence of HIV associated oral lesions among adults has decreased since the advent of highly active anti-retroviral therapy (HAART).

Aims and objectives: This study describes the prevalence and types of oral mucosal lesions in adults, who accepted a dedicated oral and dental programme for HIV-infected patients. The incidence of oral lesions and the CD4 cell counts on those patients, were related to cases receiving HAART and to those who were not.

Design: This was a retrospective, descriptive cross-sectional study.

Methods: Patients were interviewed, using a structured questionnaire to obtain information regarding medical history, current medications and demographic details. Data relating to CD4 cell counts were extracted from clinical medical records of the patient. In each case, the oral cavity of the sitting patient was examined under artificial light, by a clinician using a mouth mirror. Oral lesions were categorised in accordance with EC-Clearinghouse diagnostic criteria.

Results: The prevalence of HIV-associated oral lesions was significantly reduced ($p < 0.001$) in patients receiving HAART. There was, however, no significant difference ($p = 0.29$) in mean CD4 counts between patients receiving HAART and those not receiving HAART. The presence of oral lesions was statistically significantly, associated with both CD4 counts of <200 cells/mm^3 ($p<0.001$) and the absence of HAART ($p = 0.033$).

Conclusions: The study confirmed that the incidence of oral lesions and of pseudo-membranous candidiasis in particular, were statistically significantly reduced in patients receiving HAART.

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ACRONYMS

HAART:	Highly active anti-retroviral therapy
LGE:	Linear gingival erythema
NUG:	Necrotising ulcerative gingivitis

INTRODUCTION AND BACKGROUND

Most African studies on oral manifestations associated with HIV, were undertaken during the pre-HAART era.[1-6] The overall prevalence of oral lesions among adults has decreased since the advent, between November 2003 and March 2004,[7] of the regime of highly active antiretroviral therapy (HAART).[8] Research on the influence of HAART on types of oral lesions is important in the context of developing countries, where efforts are being made to scale up the provision of HAART to eligible patients.[9]

This study describes the prevalence and types of oral mucosal lesions in HIV-infected adults, who accepted a dedicated oral and dental programme. The occurrence of oral lesions was related to CD4 cell counts, in the presence or absence of a HAART drug regimen.

PROGRAMME DESCRIPTION

The programme was offered at the outpatient HIV clinic of Kalafong hospital, on the outskirts of Pretoria. Patients were interviewed, using a structured questionnaire to obtain information regarding medical history, current medications and demographic details. Data relating to CD4 cell count were extracted from clinical medical records of these patients. A clinician examined the oral cavity of each patient under artificial light, using a mouth mirror, the patient being seated in a chair.

The diagnostic classification and criteria for oral soft tissue lesions, associated with HIV as detailed by the EC-Clearinghouse, were used to assess and classify any presenting oral soft tissue lesions. Collected data were captured in customised Monitoring and Evaluation data capture sheets. These were filed in the office of the Programme Director.

OBJECTIVES

- To describe the demographic characteristics, treatment routines and CD4 counts of programme participants
- To describe and compare the prevalence and types of oral mucosal lesions in patients on HAART and of those not on HAART
- To assess the association between the presence of oral mucosal lesions and use of HAART, taking into account the levels of CD4 cell counts

MATERIALS AND METHODS

Study design

This was a retrospective, descriptive cross-sectional study, in which existing medical records were reviewed and a clinical examination was performed.

Study population

The study population consisted of HIV infected adults, who had attended Kalafong outpatient HIV clinic between May 2005 and April 2006. During the observation period, 541 patients visited the outpatient clinic.

Study sample

The sample size was calculated based on the prevalence of 39.3% for oral lesions in adults receiving HAART in Dar es Salaam, Tanzania, as reported by Hamza and colleagues.[11] The ideal sample size was estimated at 219 in Epi Info Version 3.3.2 software[12] at the confidence interval of 95% and absolute precision of 5%, assuming 39.3% prevalence and a total population of 541. This study finally included a sample of 203 patients.

Sampling method

A random sample was selected. The lottery method of random sampling[13] was used, i.e. patient files were assigned numbers and coupons with serial numbers, ranging from 1 to 541, were then thoroughly mixed in a bowl and a sufficient number drawn at random (without replacement), to provide the desired sample size. Files, corresponding to drawn numbers, were separated for analysis and the remainder (non-selected files), were returned to the archives.

MEASUREMENTS

Medical records

The filed, paper-based collected data, gathered from medical records and from both questionnaire and clinical assessments, were captured, coded and cleaned in *Microsoft Excel software*. It was then transferred and analysed in the programme, *Statistical Analysis Software* (SAS). Variables investigated included: demographic characteristics, current medication, soft tissue oral lesions and CD4 cell counts.

Definition of variables

Demographic characteristics studied, were gender and age, the latter being derived from date of birth as recorded in the file. *Current medication* was limited to categories of medications (anti-retrovirals, antifungals and antibiotics), used to treat HIV and associated opportunistic infections. *Oral soft tissue lesions* were recorded, using the EC-Clearinghouse diagnostic classification and criteria for oral soft tissue lesions, associated with HIV .[10] *CD4 cell counts* were sourced from laboratory reports. The CD4 cells were quantified in the same laboratory, using the same technique.

HAART regimens

In the South African public sector setting, recommended at the time of the study, was a triple therapy, consisting of two nucleoside reverse transcriptase inhibitors (NRTI), plus one non-nucleoside reverse transcriptase inhibitor (NNRTI), or two NRTI together with a protease inhibitor.[14] The first line regimen included = *Efavirenz; Stavudine* (d4T)+ *Lamivudine*(3TC) + *Nevirapine* (NVP). The second line regimen included the combination of *Zidovudine* (AZT), *Didanosine* (ddI) and *Lopinavir/Ritonavir.*

Ethical considerations

The study protocol was approved by the Ethics Committee of the University of Limpopo (Medunsa Campus). Permission to use medical records (programme monitoring and evaluation of records), was obtained from the Programme Director.

Statistical analysis/Hypothesis testing

Collected data were subjected to uni-variate, bi-variate and multi-variate analysis in Statistical Analysis Software (SAS) software. Frequencies, means and proportions were calculated. Patients were categorised into those on HAART and those not receiving HAART. A two-tailed Fisher's exact test was performed, to test the statistical significance of differences in the data observed between the groups and to assess the association between the presence of oral mucosal lesions and the use of anti-retrovirals, taking into account the levels of CD4 cell counts. The chosen significance level of the tests i.e. the p-value, was 0.05. Student's t-test was performed to compare CD4 means between groups.

Chi-squared test was applied to test the statistical significance of the differences in the prevalence of oral lesions between patients on HAART and those not on HAART. A multivariable logistic regression analysis was performed, to investigate the frequency of occurrence of oral lesions. The binary outcome of interest was the presence /absence of oral lesion. The dependent variable was presence of oral lesion. The explanatory variables studied were patients not on HAART and yet having CD4 counts < 200mm^3.

RESULTS

Data of a random sample of 203 patients were analysed. In a few instances the medical records of some patients were incomplete. The results and their interpretation are presented in relation to the objectives of the study.

Objective 1: Demographic characteristics

Table 1: Demography: distribution by age and gender

Age groups, years	Total no. of patients, n(%)	Gender	
		Males	Females
20-25	10 (5.0%)	1	9
26-30	33 (16.4%)	4	29
31-35	51 (25.4%)	14	37
36-40	37 (18.4%)	16	21
41-45	34 (16.9%)	12	22
46-50	16 (7.9%)	9	7
51-55	9 (4.5%)	4	5
56-60	9 (4.5%)	3	6
> 60	2 (1.0%)	1	1
TOTAL	201 (100)	64	137

* Gender and age data missing in two patients

The average age of the patients was 37 years with a range of 20 to 70 years. Two thirds were females. Just less than two thirds (65.2%) were aged between 20 and 40 years. Two patients (1.0%) were older than 60 years.

Table 2: Current use of medication (antibiotics and/or ARV)

Antimicrobial types and combinations	Total no. of patients, n(%)
ARV	6 (3.0%)
Antifungal	5 (2.5%)
Antibiotics	36 (17.7%)
ARV + Antifungal + Antibiotics	10 (4.9%)
Antibiotics + ARV	119 (58.6%)
Antifungal + ARV	5 (2.5%)
Not on antimicrobials	22 (10.8%)
TOTAL	203 (100%)

Just over two thirds of the sample (69%), were receiving HAART. Antimicrobial polypharmacy was high at 66%. Antibiotic use was highest at 81%. Only a tenth (22) of the patients were not on antimicrobials. The use of antifungal medications was also limited (9.9%).

Table 3: Antiretroviral regimen

Regimen	N (%) patients
First line	131 (93.6%)
Second line	9 (6.4%)
TOTAL	140 (100%)

The majority of patients (93.6%), were on the first line combination, of whom 121 (92.4%) were on a combination of *stavudine* (d4T) + *lamivudine* (3TC) + *Efavirenz*, 10 (7.6%) on a combination of *stavudine* + *lamivudine* + *nevirapine* (NVP). Nine (6.4%) were on second line drug based combinations. Six were on 3TC/AZT (*stocrin*) and one each on 3TC/AZT/NVP, AZT (*Lopinavir/ritonavir*) and d4T/ddI. The average duration of a HAART regime was 11 months, with a range of 1 to 25 months. Half the patients had been on treatment for 4 to 14 months, with one quarter having been on treatment for 1 to 3 months and the remaining quarter 15 to 25 months.

Objective 2: Prevalence and types of oral mucosal lesions

Table 4: Comparison of oral lesions prevalence among patients on HAART and those not on HAART

Oral lesions	N (%) patients		Chi-squared test
	On HAART	Not on HAART	
Present	30 (21.4%)	34 (54%)	$p < 0.001$
Absent	110 (78.6%)	29 (46%)	
TOTAL	140 (100%)	63 (100%)	

Prevalence of oral lesions: oral lesions were absent in two thirds (139) of patients.

Oral lesions were recorded more than twice as frequently (54% vs. 21.4%) in patients not on HAART, compared with patients on HAART. There is substantial evidence ($p < 0.001$), to reject the null hypothesis of there being no difference in the prevalence of oral lesions among patients on HAART and those not on HAART.

Table 5: Lesion types and frequency of occurrence

Lesion types	n (%)
Erythematous candidiasis	15 (23%)
Pseudomembranous candidiasis	25 (38.5%)
Parotid enlargement	4 (6.2%)
Hairy leukoplakia	2 (3.1%)
LGE	6 (9.2%)
NUG	12 (18.5%)
Necrotic periodontitis	1 (1.5%)
TOTAL	65 (100%)

Candidiasis in its two forms was the most common lesion at 61.5%. NUG was the second most frequently occurring lesion at 18.5%. Multiple lesions were recorded in a lone patient (1.56%).

Table 6: Comparison of oral lesions types among patients on HAART and those not on HAART

Types	N (%) oral lesions	Fisher's exact test
Pseudo membranous candidiasis		
On HAART	10 (7.14%)	$p = 0.0020$
Not on HAART	15 (23.81%)	
Erythematous candidiasis		
On HAART	10 (7.14%)	$p = 0.7810$
Not on HAART	5 (7.94%)	
Parotid enlargement		
On HAART	2 (1.43%)	$p = 0.5895$
Not on HAART	2(3.17%)	
Hairy leukoplakia		
On HAART	0 (0)	$p = 0.3103$
Not on HAART	1 (1.59%)	
LGE (Lineal gingival erythema)		
On HAART	2 (1.43%)	$p = 0.0759$
Not on HAART	4 (6.35%)	
NUG (necrotising ulcerative gingivitis)		
On HAART	6 (4.29%)	$p = 0.1961$
Not on HAART	6 (9.52%)	
Necrotic periodontitis		
On HAART	0 (0)	$p = 0.3103$
Not on HAART	1 (1.59%)	

Pseudo-membranous candidiasis was recorded in three times as many patients not on HAART, as amongst patients on HAART(23.81% vs. 7.14%). There is substantial evidence ($p = 0.0020$) to reject the null hypothesis of there being no difference in the prevalence of pseudo-membranous candidiasis between patients on HAART and those not on HAART in the population. However, there is insufficient evidence ($p > 0.05$), to reject the null hypothesis of no difference being demonstrated in the prevalence of erythematous candidiasis, parotid enlargement, hairy leukoplakia, LGE, NUG and necrotic periodontitis, between patients on HAART and those not on HAART in the population.

Objective 3: Association between the presence of oral mucosal lesions and use of HAART, taking into account the CD4 cell count

Table 7: CD4 cell counts of patients on HAART and those not on HAART

	Patients on HAART			Patients not on HAART			Student's t-test
	n (%)	Mean	SD	n (%)	Mean	SD	
CD4							
<100	38 (30)	40.24	28.38	22 (42)	42.50	28.60	
100 -200	27 (21)	148.00	26.05	25 (47)	148.12	30.02	$p = 0.293$
>200	63 (49)	3180.38	22636.73	6 (11)	328.83	25.69	
TOTAL	128 (100)	1608.51	15892.57	53(100)	124.74	93.49	

* HAART status data missing in 22 patients

There is insufficient evidence (p = 0.293) to reject the null hypothesis of there being no difference in mean CD4 count between patients on HAART and those not on HAART in the population.

Table 8: Comparison of incidence of oral lesions among patients with CD4 < 200 and those with CD4 > 200

Lesion presence	Cd4<200 n (%)	Cd4>200 n (%)	Fisher's exact test
No	64 (57.1%)	61 (88.4%)	$p < 0.001$
Yes	48 (42.9%)	8 (11.6%)	
TOTAL	112 (100%)	69 (100%)	

Oral lesions were recorded in more than three times the numbers of patients with CD4 < 200, as patients with CD4 > 200 (42.9% vs. 11.6%). There is substantial evidence (p < 0.001), to reject the null hypothesis of there being no difference in the proportion of individuals with oral lesions, among patients with a CD4 count < 200 and those with CD4 counts > 200 in the population.

Table 9: Association in the occurrence of oral lesions and HAART in patients having CD4 counts of less than 200/mm^3

Patients with Cd4<200	Lesions, n (%)			Fisher's exact test
	Yes	No	Total	
On HAART	22 (33.8%)	43 (66.2%)	65 (100%)	$p = 0.0331$
Not on HAART	26 (55%)	21 (45%)	47 (100%)	
TOTAL	48 (42.9%)	64 (57.1%)	112 (100%)	

Oral lesions were recorded in more than half (55% vs. 33.8%), as many patients not on HAART with levels of CD4 cells < 200, as patients on HAART. There is some evidence ($p = 0.0331$) to reject the null hypothesis of no association between HAART use and a decreased prevalence of oral lesions, among patients with a CD4 count < 200 in the population (Table 10).

Oral lesions were recorded in more than three times (33.3% vs. 9.5%) as many patients on HAART with CD4 cell > 200, as patients not on HAART. There is insufficient evidence (p=0.1398) to reject the null hypothesis of no association between HAART use and occurrence of oral lesions among patients with a CD4 count > 200 in the population (Table 10).

The results in Table 11 indicate that a CD4 count < 200 (p = 0.0011) and not on HAART ($p = 0.0084$), are independently associated with the occurrence of oral lesions. Individuals who have a CD4 count < 200, have 4.211 times the odds of having oral lesions, as those who have CD4 > 200 and who are not on HAART. In other words, the odds of having oral lesions in these individuals are increased by 321%. The upper limit of the confidence interval for this odds ratio, shows the increased odds could be as high as 897%.

Table 10: Association in occurrence of oral lesions and use of HAART amongst patimets having CD4 counts greater than 200/mm^3

Patients with Cd4>200	Lesions, n (%)			Fisher's exact test
	Yes	No	Total	
On HAART	2 (33.3%)	4 (66.7%)	6 (100%)	$p = 0.0331$
Not on HAART	6 (9.5%)	57 (90.5%)	63 (100%)	
TOTAL	48 (42.9%)	64 (57.1%)	112 (100%)	

Individuals who are not on HAART, have 2.650 times the odds of having oral lesions, as those who are on HAART and have CD4 counts less than 200 cells per Individuals who are not on HAART have 2.650 times the odds of having oral lesions as those who are on HAART and have CD4 counts less than 200 cells per mm^3.

In other words, the odds of having oral lesions in these individuals are increased by 165%. The upper limit of the confidence interval for this odds ratio, shows the increased odds could be as high as 447%.

DISCUSSION

An interpretation and review of the results is preceded by a brief summary *(in italics)*. The objectives of the study organize the discussion. The clinical range and prevalence of oral lesions are discussed, in relation to a sample of previous African studies (Table 12). A considerable regional variation in the prevalence of HIV associated oral lesions has been established.[15,16] The latest review hints that lesions other than candidosis have a low prevalence in industrialised countries.[8] Most African studies on HIV associated oral lesions have been done during the pre-HAART era. Literature in this field in the HAART era is woefully lacking. The results of the current study are compared with the seminal work of Hamza and colleagues in Tanzania.[11]

Table 11: Logistic regression analysis of oral lesion occurrence in HIV-infected patients

Variable	Parameter estimate	Standard error	Wald Chi-square	*p*- value	Estimated odds ratio	95% CI for odds ratio
Intercept	-0.9422	0.2257	17.4318	<0.0001	-	-
CD4 <200	0.7189	0.2199	10.6855	0.0011	4.211	(1.778 – 9.973)
Not on HAART	0.4872	0.1849	6.9453	0.0084	2.650	(1.284-5.469)

Table 12: Review of a Reference group of Studies Examining Prevalence of HIV-related oral lesions

Author Site	Cohort	Oral lesions %	Most Prevalent Lesions	Oral Candidiasis	HL	KS	PD	PE/SG
Wanzala, Kenya [16]	Women prostitutes N = 334 80.5% HIV positive	15.6	OC 13.1	OC 13.1 EC 10.1 PC 0.4 AC 1.5 HC 1.1	0.4	0	0	0
Hodgson, Zambia[4]	Adults N =107	HIV 40 AIDS 55	HIV OC 25.2 AIDS OC 33.4	HIV/AIDS OC 25.2/33.4 EC 6.5/11.8 PC 18.7/21.6 AC None	HIV 4.7 AIDS 5.8	HIV 8.4 AIDS 11.8	HIV 2.8 AIDS 3.9	0
Tukutuku, Zaire [17]	Adult patients with AIDS N = 83	94	OC 94	OC 94 EC 22.8 PC 32 AC 32.5 HC 6	14	12	16	2
Itula, Namibia[5]	HIV +ve/ HIV –ve adults and children 29/376 N = 405	21	PD 33.3	OC 0 EC 0 PC 0 AC 0	16.7	16.7	33.3	0
Matee, Tanzania[6]	HIV positive patients >18 years old N= 192	HIV +ve/ AIDS 10.4/36.8	HIV +ve HL 3.0 AIDS OC 17.6	OC 1.5/17.6 EC PC AC	HIV+ve/ AIDS 3.0/7.2	0	0	HIV +ve/ AIDS PE 11.9/20 SG 43.2/49.6
Schiodt, Tanzania[18]	Aids patients/ medical non-suspected patients/dental outpatient/ patients with STD's 39/44/53/50 N= 186	19	OC 15 HL 11	OC 15 EC 9 PC 8 AC 3	11	1	NA	0
Matee, Tanzania[19]	HI +ve/ HIV –ve adult patients 103/22 N= 125	80.24	OC 35.2 KS 30.4	OC 35.2 EC NI PC 25.6 AC 9.6	0	30.4	2.4	0
Kamiru, [20] Lesotho	N= 270	73	OC 54	OC 54 EC 26 PC 27 AC 14	14	<1	8	0
Adurogban, Nigeria [21]	HI +ve/ HIV –ve adults 81/598 N= 679	HIV +ve/ HIV -ve 56.8/14.2	HIV +ve/ HIV -ve OC 54.3/6.1	HIV +ve/ HIV -ve OC 54.3/6.1 EC PC 33.3/4.3 AC 21.0/1.8	HIV +ve/ HIV -ve 0/0	HIV +ve/ HIV -ve 0/0	HIV +ve/ HIV -ve 3.7/6.7	0.1
Butt, Kenya[3]	N= 61	100	OC >80	OC >80 EC 21.3 PC 19.7 AC 27.9 HC 52.5	0	13	100	0

Author Site	Cohort	Oral lesions %	Most Prevalent Lesions	Oral Candidiasis	HL	KS	PD	PE/SG
Jonsson, Zimbabwe[2]	HIV positive adults N = 100	92	KS 72	OC 22 EC 5 PC 2 AC 5	none	72	3	0
Arendorf, South Africa[1]	HIV Positive Men & Women N = 600	60.4	OC 37.8	OC 37.8 EC 15.7 PC 15.5 AC 6.7	19.7	1.5	8.5	0.8
Hamza, Tanzania[9]	HIV positive adults and children 481/51 N = 532	Adults/ Children 39.3/ 41.2	Adults OC 24.7 Children EP 19.6 OC 11.8	Adults/ Children OC 24.7/11.8 EC PC AC	Adults/ Children 0.6/3.9	Adults/ Children 3.1/3.9	Adults/ Children 2.7/0	2.3
Current Study South Africa	N =203	31.8	OC 61.5	OC 61.5 EC 23 PC 38.5 AC	3.1	0	29.2	6.2

Key: **HL:** Hairy leukoplakia **EC:** Erythematous Candidiasis **PM:** Pseudomembranous Candidiasis **KS:** Kaposi sarcoma **PD:** Periodontal & gingival lesions **OC:** Oral Candidiasis **AC:** Angular cheilitis **HP:** Hyperplasic Candidiasis **PE/SG:** Parotid Enlargement/Salivary gland enlargement

Objective 1: Demographic characteristics

Anti-retroviral and antibiotic use was high i.e. 69% and 81% respectively, among patients in this study. These findings are not unexpected. The research sites pioneered HAART use in public service.[23] Anti-retroviral and antibiotic uses were associated. Antibiotic use was commenced when the CD4 count dropped below 200cells/mm^3, or when there were clinical signs of advanced immune deficiency for pneumocystis carini pneumonia prophylaxis.[14] *The majority (93%) of patients were on the first line combination of anti-retrovirals consisting of stavudine (d4T) + lamivudine (3TC) + Efavirenz.* This result differs considerably from that of Hamza and colleagues[11], who reported that 76.8% of their patients received a combination of *stavudine* (d4T) + *lamivudine* (3TC) + *Nevirapine*.

Objective 2: Prevalence and types of oral mucosal lesions

*The prevalence of oral lesions was 31.8%.*The present findings seem to be consistent with other research which found that the incidence of oral lesions has declined in the era of HAART.[24-27] Variation in the reported prevalences (31.8% vs.39.3%), between this study and that of Hamza and colleagues, may be explained by the share of non-group 1 lesions, in the total prevalence of oral lesions. Non-group 1 lesions accounted for 6.2% in this study, compared with 12.4% in that of Hamza and colleagues.[11] The prevalence of oral lesions in the pre-HAART era reference group of studies averaged 55.2/58.6 with a range of 15.6%[17] and 100%.[3] Variation in the prevalence of oral lesions, may have been due to a range of factors such as the composition of the sample (cohort, stages of disease), socio-demographic factors, diagnostic criteria, sample size and sample selection.[28] *The prevalence of HIV-associated oral lesions was significantly ($p < 0.001$) reduced in patients receiving HAART.* This study produced results which corroborate the findings of a great deal of the previous work in this field. A significant reduction in the frequency of oral lesions following the introduction of HAART has been reported in industrialised countries.[29-33]

Oral candidiasis

Oral candidiasis was the most prevalent oral lesion in both this study (61.5%) and that of Hamza and colleagues (24.7%).[11] Pseudo-membranous candidiasis (62.5% vs. 66.4%) was more prevalent than the erythematous form (37.5% vs.9.6%) and angular cheilitis (0 vs. 3.2%). These findings are consistent with those of other studies.[1, 4, 20, 21] Oral candidiasis was the most prevalent oral lesion in a majority of pre-HAART era reference group of studies. Contrary to expectations, Kaposi sarcoma and periodontal and gingival lesions were predominant oral lesions in a two studies.[2,5]

Hairy leukoplakia

The prevalence of hairy leukoplakia in this study (3.1%) and in that of Hamza and colleagues (0.6%), compares poorly with the mean prevalence of the condition (7.4%) in the pre-HAART era reference group of studies. These findings seem to be consistent with other research, which found a significantly lower prevalence of hairy leukoplakia.[30] The data suggests that HAART reduces the incidence of hairy leukoplakia. However, with insufficient regional studies, caution must be applied. Further work is required to establish this.

Periodontal and gingival lesions

In contrast to earlier findings, which reported a significant decrease in industrialised countries[29-31, 34] and the results of Hamza and colleagues (2.7%),[11] periodontal and gingival lesions were the second most prevalent lesions in this study (29.2%). The reason for this is unclear, but it may have something to do with the observation that large numbers of NUG cases among patients of indeterminate HIV status, presented at dental clinics.[35] The prevalence of periodontal and gingival lesions in the pre-HAART era reported in the reference group of studies ranged between 0%[17] and 100%.[5]

Parotid enlargement

Parotid enlargement is common in HIV infected children.[11,36-38] It was not documented in two-thirds of the pre-HAART era reference group of studies. Conflicting

results about the prevalence of salivary gland disease in adult patients receiving HAART in industrialisd countries, have been reported. Earlier findings of a rising trend[30,39] were not supported by a later study.[33] The prevalence of parotid enlargement in this study was 6.2%. Hamza and colleagues reported a prevalence of 2.3%.[11] Future studies on the trends of the prevalence of parotid enlargement in Africa are recommended.

Kaposi sarcoma

Kaposi sarcoma was not documented in this study. Kaposi sarcoma was the third most common oral lesion in a majority of pre HAART era reference group studies.

Hamza and colleagues reported a prevalence of 3.1%.[11] Conflicting results have been reported in industrialised countries where the prevalence is low. Whereas the results in Germany supported an association between a significant decrease in the prevalence of Kaposi sarcoma and the initiation of HAART,[25] Patton in the USA[30] and Ceballos-Salobrena[31] in Mexico found no significant occurrence of Kaposi sarcoma with HAART.

Seven types of oral lesions were observed (EC, PM, PE, HL, LGE, NUG, NUP). In contrast to earlier findings[11, 25, 27] the clinical range of lesions seen in this study is narrow. This study is biased towards group 1 lesions. Very few non-group 1 lesions were recorded. It is somewhat surprising that oral warts were not documented, considering the duration of HAART use. The reason for this is not clear. Numerous studies have detected oral warts in patients on HAART.[30, 32, 39, 40] Hamza and colleagues reported a prevalence of 0.6%.[11] *Multiple lesions per patient were observed in a lone patient*. The simultaneous occurrence of two different types of lesions was rare in this study. This may be related to the common use of HAART. *Pseudo-membranous candidiasis was significantly reduced (p<0.0020) in patients receiving HAART*. The present findings and those of Hamza and colleagues[11] seem to be consistent with other research, attributing the reduction in prevalence of oral lesions to a reduction of Pseudo-membranous candidiasis.[26, 34, 41]

Objective 3: Association between the presence of oral mucosal lesions and the use of ARV, after adjusting for CD4 cell count

There was no difference (p = 0.29) in mean CD4 counts between patients receiving HAART and those not receiving HAART. This study confirms that HAART increases the CD4 cell count.[30, 42] This is demonstrated by the rise in half the patients of the mean CD4 count, from 200 cell/mm^3 to 3180.38 cell/mm^3. Government policy at the time directed that ART therapy be initiated at CD4 count < 200 cell/mm^3 [43] *The presence of oral lesions was associated with CD4 counts <200 cells (p<0.001) and non-use of HAART (p = 0.033).* The present findings seem to be consistent with other research, which found that a CD4 count <200 cell/mm^3 predispose to the expression of oral lesions[44, 45] and that HAART reduces their occurrence.[26]

3.6 Limitations of the study

The occurrence of oral lesions could not be related to viral load. High viral load has been associated with oral lesions.[44,46,47] Different techniques of quantifying viral load were utilised i.e. quantitative RNA-PCR, branched DNA (bDNA) and nucleic acid sequence based amplification (NASBA). The RNA-PCR assay can detect as few as 40 copies of HIV RNA per millilitre and is positive in >98% of patients. The bDNA assay can detect as few as 500 copies of HIV RNA per millilitre and is positive in >90% of patients.[48]

CONCLUSION

Oral lesions and pseudo-membranous candidiasis, in particular, were significantly reduced in patients on HAART in the present study.

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