Prevalence and Pattern of Cutaneous Lesions in Relationship to CD4 Cell Counts among Newly Diagnosed HIV Patients in University of Ilorin Teaching Hospital (UITH), Ilorin, Nigeria

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Abstract

Background: Oral lesions are among the earliest clinical manifestation of HIV infection. In developing countries like Nigeria, were sophisticated diagnostic apparatus used to monitor the immunologic status of HIV/AIDS patients is not readily available, early recognition of the commonest and specific HIV-related oral lesions can be used for diagnosis so that prompt treatment can be provided to reduce morbidity.

Objectives: To assess the prevalence and spectrum of oral lesions in relationship to CD4 cell counts among newly diagnosed HIV patients in University of Ilorin Teaching Hospital (UITH), Ilorin, Kwara State, Nigeria.

Methods: This was a hospital based, cross sectional, descriptive study of 160 newly diagnosed adult patients attending the HIV/AIDS clinic of UITH, Ilorin. The study protocol was approved by the Ethics committee of the UITH. Informed consent from all the patients was also obtained prior to data collection. All the HIV patients were treatment naïve. A questionnaire guided interview and clinical oral assessment were used.

Results: The prevalence of oral lesions was 31%. The commonest oral lesion was of fungal origin (53.1%) followed by viral (36.7%). Oral lesions of inflammatory origin (6.7%) were relatively rare while those of bacterial origin (4.1%) were not very common. None of the oral lesions detected was of neoplastic origin. Most of the oral lesions occurred when the CD4 cell counts were less than 200 cells/μl.

Conclusion: Oral lesions are common in people with HIV with very low CD4 cell counts (≤ 200 cells/μl). Oral Candidiasis is the commonest lesion in Ilorin, Kwara State, Nigeria

Key Words: HIV/AIDS, Prevalence, Spectrum, Oral Lesions, CD4 Cell Count

Introduction

Oral manifestations of HIV have been recognized since the onset of the HIV pandemic and are important indicators of the natural history of the disease, as shown by their inclusion in staging systems such as the Walter Reed Staging Classification and the system used by the Center for Disease Control and Prevention (CDC). Oral signs and symptoms are also indicators of prognosis because they are positively associated with CD4 counts and viral load [1].

The oral cavity is an important and frequently undervalued source of diagnostic and prognostic information in patients with HIV and AIDS [2]. It is like a mirror which reflects the state of health of the body since most system diseases usually manifest early in the oral tissues. Some oral lesions have been observed to be more rampant in HIV infection patients than health individuals and sometimes may be the first indication of the disease. Furthermore, the appearance of some of these lesions in an HIV infected patient may signal the deterioration of the disease [3].

Many of the clinical features of HIV infection could be attributed to the profound immunological deficiencies which develops in an inverse relationship between the level of the virus in the blood (viraema) and the CD4 lymphocyte counts (CD4 cell counts). These parameters (CD4 cell count and viral load) are the central indicators of disease progression and immune status in HIV infected individuals [1]. Therefore, factors which predispose expression of oral than lesions include CD4 counts less 200 cells/mm [3], viral load greater than 3000 copies/ml, xerostomia, poor oral hygiene and smoking [4,5].

Oral lesions are differentiated as fungal, viral and bacterial infections, neoplasms such as Kaposis sarcoma and non specific presentation such as alpthous ulceration and salivary gland tissue [6].

Prior to the introduction of combination therapy for treatment of HIV, it was estimated that up to 90 percent of HIV-infected persons would experience at least one oral manifestation during the course of the disease and up to 50 percent would experience oral ulcerations [1]. Since the introduction of combination therapy for HIV, a decrease in opportunistic oral infections such as candidiasis, oral hairy leukoplakia and Kaposi sarcoma, has been noted and is attributed to lower viral load and higher CD4 counts secondary to the use of combination antiretroviral therapy [7]. The pervasive use of ART may have also changed the patterns and rates of HIV-related oral manifestations. The effects of ART on the clinical manifestations of oral lesions have been subject to often conflicting reports, one study noted

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a reduction of oral lesions from 47.6% pre-HAART to 37.5% during the HAART era [8].

There is need for attending physicians to recognize oral lesions in HIV infection. This would lead to early detection of the infection and prompt intervention [9].

Moreover, published reports of oral lesions in HIV were mostly from the developed countries. There is paucity of data from sub-Sahara African in general and Nigeria in particular. Considering the potential geographical variability in the presentation of HIV-related oral lesions, this study aimed to determine if these lesions could same as markers of immune suppression in a developing country like Nigeria.

Methods

This study was conducted at the lentiviral clinic of the Department of the Family Medicine, University of Ilorin Teaching Hospital (UITH), Ilorin, Kwara State, Nigeria. It was a descriptive, cross-sectional study carried out from 1st of May 2009 to 30th November 2009. The inclusion criteria were newly diagnosed adult ($\geq$ 18 years) HIV/AIDS patients at the lentiviral clinic, who consented to participate in the study. Individuals on Highly Active Anti Retroviral Therapy (HAART) prior to presentation and those who refused to give consent were excluded.

The sample size was estimated using the Fisher's formula [10].

$$n = \frac{Z^2 p(1-p)}{e^2}$$

n=desired sample size

p=best estimate of prevalence of oral lesions in HIV. The prevalence rate of 90% from a previous study was used [1,11]

e= degree of accuracy desired, usually set at 0.05

Z= standard normal deviation, usually set at 1.96 which corresponds to 95% confidence level

Therefore:

$$n = \frac{(1.96)^2 0.9(1-0.9)}{(0.05)^2}$$

In order to take care of non-respondents (assuming anticipated response was 90%) then:

$$n = \frac{138.30}{0.9} = 153.664 = 160$$

Thus, an estimated sample size of 160 was used for the study. Systematic random sampling was used in recruiting respondents into the study. On average two (2) new adult HIV patients were referred daily to the family medicine HIV/AIDS clinic as obtained from the Records department. Weekly average attendances of 14 new adult HIV patients were interviewed to obtain the total sample size of 160 in 6 months.

The sampling interval was therefore 336/160 = 2:1. On every clinic day, each folder was assigned a number code from 01–14. The starting point was randomly selected by simple balloting whereby; a piece of paper was picked from folded pieces of paper bearing numbers 01–14. Therefore every 2nd folder was chosen for the study until the required

sample was obtained for the week. This procedure was repeated every week until the required total sample size was obtained. An interviewer administered questionnaire was used, with provision for interpreters in local dialect, in those without formal education.

Confirmation of HIV sero-status for all patients was by ELISA, and Western blot. CD4 cell counts were performed for all the respondent. A thorough history was taken.

Clinical oral and systemic examination was done. Oral examination was carried out in natural light using disposable wooden spatula, gloves, masks, brightly illuminating torch and sterile pieces of cotton and gauze. The oral lesions associated with HIV infection were diagnosed based on presumptive criteria given by the EEC Clearinghouse on oral problem related to HIV infection and the WHO collaborating center on oral manifestations of the HIV [12]. Proper investigations were carried out whenever required to arrive at final diagnosis. For oral candidiasis, a cytology smear was taken by scraping the oral surface. The smear was then stained with potassium hydroxide (KOH), mount followed by gram staining. For lesions where biopsy was necessary, specimens were taken after obtaining informed consent of the patient and stained with routine hematoxylin and eosin and PAS stain.

The CD4 count was recorded and correlated with the oral manifestation seen.

Respondent were grouped into different occupational classes using Oyedeji's classification [13] viz;

I. Senior public servants, professionals, managers, large scale traders, business-men and contractor, senior military officers.

II. Intermediate grade public servants, and senior school teachers, non-academic professionals e.g. Nurses, owners of medium sized business, secretaries.

III. Non-manual skilled workers including clerks, typists, telephone operators, junior school teachers, drivers, artisans.

IV. Petty traders, labourers, messengers, lower cadre civil servants.

V. Unemployed, full-time house wives, students, subsistence farmers.

The predictive value of a positive test is calculated as follow:

A/(A+B)×100, where A represents those with oral lesions, B represents those without oral lesions and A + B, the total sample respondents.

Data was entered into computer and analyze using SPSS 16.0 versions Chicago international. Results were presented in tables and charts. Categorical data was analyzed using Chi-Square P-Value was set at 0.05.

Results

Table 1 displays the socio-demographic characteristics of the respondents. Out of the 160 subjects studied 120 (75%) were females while 40 (25%) were male. The male: female ratio was 1:3. A greater number of the respondents were

Table 1. *Socio – demographic characteristics of respondents (n=160).*

Variable	n	%
Age group (years)		
20 – 29	92	57
30 – 39	56	35
> 40	12	8
Sex		
Female	120	75
Male	40	25
Ethnicity		
Yoruba	121	76
Igbo	18	11
Hausa	13	8
Fulani	2	1
Others	6	4
Religion		
Islam	111	69
Christianity	47	30
Others	2	1
Educational Level		
No formal education	28	18
Primary	63	39
Secondary	41	26
Tertiary	28	17
Residential location		
Urban	108	68
Rural	52	32
Social Class		
Group I		4
Group II		17
Group III	14	9
Group IV	21	13
Group V		104

Table 2. *Prevelence of Oral lesions among the respondents (N=160).*

Oral Lesions	n	(%)
Oral lesion present	49	30.6
Oral lesion absent	111	69.4

Table 3. *Classification of oral lesion based on aetiology.*

Oral Lesions	n	(%)
Fungal	26	53.1
Viral	18	36.7
Inflammatory	3	6.1
Bacterial	2	4.1
TOTAL	49	100
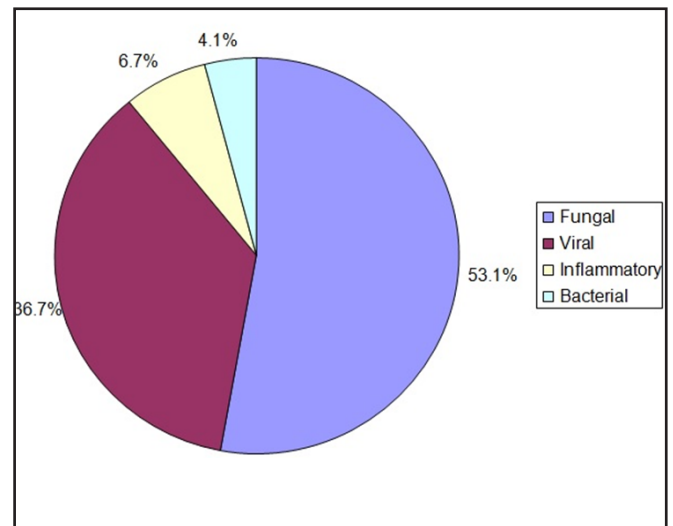
Figure 1. *The commonest etiology of oral lesions was fungal (53.1%), closely followed by viral (36.7%). Oral lesions of inflammatory origin were not very common (6.7%), while Bacteria (4.1%) were the least cause of oral lesions in the study.*

Table 4. *Spectrum of oral lesions among the respondents (n = 49).*

Fungal		
Pseudomembranous candidosis	13	26.5
Angular cheilitis	8	16.3
Erythematous candidosis	3	6.1
Hyper-plastic candidosis	2	4.1
Viral		
Herpetic stomatitis	13	26.5
condyloma acuminata	4	8.2
oral hairy leukoplakia	1	2.0
Inflammatory		
Recurrent apthous ulcerations	3	6.2
Bacteria		
HIV gingivitis	2	4.1
TOTAL	49	100

Muslim 111 (69%) compared to Christians 47 (30%). Most of the respondents 120 (76%) were of Yoruba extraction. Predominantly, 108 (68%) lived in an urban setting. The majority 63 (39%) of the respondents had primary while 41 (26%) had secondary education. Seventeen percent (n=28) had tertiary education and the remaining had no formal education. Majority 104 (65%) were in Social Class V. These comprised the unemployed, students and those involved in unskilled occupations.

Table 2 shows the prevalence of oral lesions among the respondents. Forty nine (36.6%) had oral lesions while 111 (69.4%), did not.

Table 3 shows that oropharyngeal candidiasis 26 (53.1) was the most common oral infection, followed by viral infections 18 (36.7%) (*Figure 1*).

Table 4 shows that, the commonest type of candidosis in our patients was pseudomembranous candidosis seen in 13 (26.5%), followed by angular cheilitis 8 (16.3%), erythematous candidosis 3 (6.1%), while hyper-plastic variety was the least 2 (4.1%).

Table 5 shows the CD4 cell counts of the respondents in the study. 32.5% had CD4 cell counts <200 cells/µl while 67.5% had CD4 cell counts between 200 and 500 cells/µl. None had CD4 cell counts greater than 500.

Table 6 shows the association between CD4 cell counts

with oral lesions, in HIV/AIDS patients. Most of the oral lesions occurred when the CD4 cell counts were less than 200 cells/µl. There was a strong association (p = 0.03) between CD4 cell count and occurrence of oral lesions in HIV/AIDS patients. $X^2 = 4.949$, df = 1, p = 0.03.

Discussion

There was a female preponderance 75% compared with 25%

Table 5. *CD4 Cell counts of the respondents in the study (n = 160).*

CD4 cell counts/ µl	n	(%)
<200	52	32.5
200-500	108	67.5
>500	0	0.0
TOTAL	**160**	**100**

Table 6. *Association between cd4 cell count and oral lesions in HIV/ AIDS patients.*

CD 4 cell counts	Oral disease Absent (%)	Oral disease Present (%)	Total
< 200	30 (57.7)	22 (42.3)	52
200 – 500	81 (75.0)	27 (25.0)	108
TOTAL	**111**	**49**	**160**

Figure 2. *The prevalence of oral lesions among HIV/AIDS patients in the study. (31%) of the respondents had oral lesions.*

of the male, M/F sex ratio of 1:3. This is similar to the study of Rao et al. [14] while studying gender differences in oral lesions among persons with HIV disease in Southern Indian where he reported that males had 1.58 times of having any oral lesion compared to females. This is similar to llyasu et al. [15] study that reported a M/F ratio of 1:2.5. The study findings contrasted with Ines and co-workers in a study Prevalence of oral lesions in HIV patients related to CD4 cell count and viral load in a Venezuelan population where he reported that 81% of the respondents were male while 18.7% were female with a male/female ratio of 4:1 [16]. In Nigeria, the National data indicated equal prevalence of HIV/AIDS amongst males and females. The National data finding was attributed to economic selection factors, as men have economic advantage over females, and a lot of males may be receiving treatment, while their potentially positive partners are not even aware of their serostatics. In a developing country like Nigeria, where women are largely not economically independent, it is not surprising that the prevalence was higher in women.

The age characteristics of HIV infected patients in this study agree with previous studies from Nigeria [2] and other parts of Africa [11,17].

With regards to age groups, respondents in age group 20-29 years were more predominant in this study constituting about 57% (n=92) of all respondents. Similar observations were made by Ines and co-workers [16] where the age range of evaluated individuals was between 20-55years, with a mean of 35years, and in agreement with previous studies from Ceballos-Salobrena et al. [18]. In Kano [12] the age group was 25-30 years and in Makurdi where the age groups 30-35 years were more predominant. The implication of these age groups with the higher prevalence of HIV/AIDS is that, youths, are the worst affected group and should thus be targeted for HIV interventions.

Most of the patients were married (67.8%). This is supported by Iliyasu et al. [15] study where 68.8% of the respondents were married. (8.1%) were divorced (9.4%) widowed and (1.9%) separated. This implies that the HIV pandemic will continue to increase at an exponential rate since the married HIV patients are most likely to infect their sexual partners/spouses. Indeed, being separated, divorced or widowed is a risk factor for HIV infection. Certainly, such patients are more likely to have multiple sexual partners.
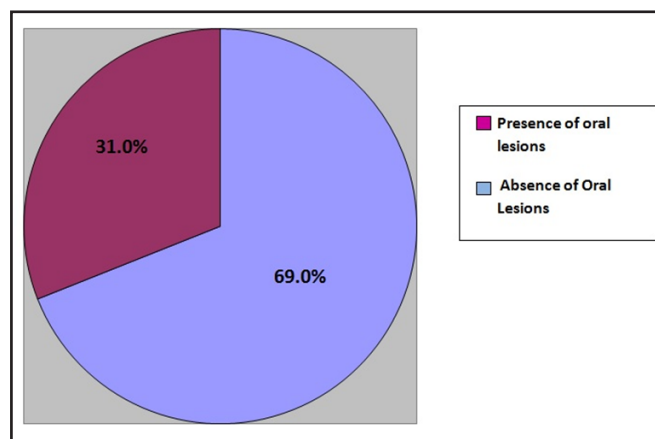
This study points to the fact that HIV is more prevalent (65%) in the lower socio-economic group. This is corroborated by a study in Ibadan that showed that (40%) of HIV/AIDS patients were traders [16]. In such settings, women are more likely to engage in sex for commercial and financial reasons.

The prevalence of oral lesions was 31% (*Figure 2*). This figure compares well with the prevalence of 35% from St. Francis Hospital, Zambia, in the study, conducted by Hodgson and co- workers [19]. On the contrary, this prevalence was lower than 92% reported in 100 Zimbabwean HIV patients [1], 85% prevalence reported by Ines and co-workers, 74.7% reported by Karuna et al. [20]. 73% reported by Kamiru et al. [21] in Maseru, Lesotho and 60.4% reported in a group of South Africa patients [22] but lower than 15.6% reported in a group of Kenyan commercial sex workers [23]. It was also higher than local studies. Eighty four percent (84%) at Ife-Ijesha zone of Nigeria [24], 68.3% in patient seen in Kano [3] Nigerian, 66.7% found in Ibadan, Nigeria by Adurogbangba et al. [25] and 53% obtained by Anteyi et al. [26], in the study of oral manifestation of HIV/AIDS in Nigerian patients.

The disparity in the prevalence of oral lesions in HIV/ AIDS reported in the various studies may be dependent on the prevalence and stage of HIV infection in the study population and could also be due to differentiate in methodology. Where the prevalence of HIV/AIDS is high and the disease is in advanced stage, the prevalence of oral lesions in HIV/ AIDS will be high and vice –versa. Other factors that may influence the prevalence rate of oral lesions in HIV/AIDS include nutritional status of the patients, sexual orientation and practices. A malnourished patient with antecedent immunosuppression is more likely to develop opportunistic infections like oral lesions than a well- nourished immunocompetent individual.

The clinical spectrum of the oral lesions in order of occurrence was candidiasis (oral thrush, 53% (*Figure 3*), herpetic stomatitis 27% (*Figure 4*)), condyloma acuminata 8% (*Figure 5*), recurrent apthous ulcerations 6% (*Figure 6*), HIV gingivitis 4% (*Figure 7*) and oral hairy leukoplakia 2% (*Figure 8*). This study is similar to that by Hodgson et al. [19] where candidiasis had a prevalence of 49% and to the study of Patton and colleagues where oral candidiasis has been

Figure 3. Candidiasis(Oral thrush).

Figure 4. Herpetic stomatitis.

Figure 5. Condyloma acuminate.

Figure 6. Aphthous ulcers in one of the subjects.

Figure 7. Chronic gingivitis in one of the respondent.

Figure 8. Oral hairy leukoplakia.

consistently reported as the most prevalent HIV-associated oral lesions in all ages [27].

The overall prevalence rate of 53% for oral candidosis was higher than 12.1% from Taiwanese [28], 22% from Zimbabwean [11] and 37.8% from South Africa [17]. On the contrary, Ranganathan and colleagues in a study Oral lesions and conditions associated with HIV-infection in 300 south Indian patients found out that Gingivitis 47% and pseudomembranous candidiasis 33% were the most common oral lesions [29]. In Nigeria Eweka et al. while studying prevalence of oral lesions and the effects of HAART in adult HIV patients, attending a tertiary hospital in Lagos,

Nigeria found out that Oral candidiasis accounted for 47.7% [30]. The results are also similar to that of Adedigba and co-workers [24] where the commonest oral lesion was pseudo-membranous candidiasis (43.1%) and oral hairy leukoplakia (1.3%) was the least prevalent. Anteyi et al. [26] found that lesions due to candidiasis were present in (49%) of the patients. Adurogbangba et al. [25] concluded that pseudomembranous candidiasis (33.3%) was the commonest followed by Herpetic stomatitis (25%) and this compares favourably with the finding of this study. Mithra et al. [31] reported a prevalence of 71% with periodontitis 52% and erythematous candidiasis

45% being the most prevalent oral lesions. This study is similar to Ranganathan et al. [29] who reported only one case of Oral Leukoplakia, but contrasted with the high prevalence of Oral leukoplakia observed in the study of Ines, where Oral Leukoplakia represented 34% of the evaluated cases [16].

Oropharyngeal candidiasis 26 (53.1) was the most common oral infection, followed by viral infections 18 (36.7%). The commonest type of candidosis in our patients was pseudomembranous candidosis seen in 13 (26.5%), followed by angular cheilitis 8 (16.3%), erythematous candidosis 3 (6.1%), while hyper-plastic variety was the least 2 (4.1%). This finding is similar to various study in Africa, for example in Kenya, Zaire, South Africa and Zimbabwe [11,32-34].

Hyperplastic or chronic candidiasis presents as white non-removable plaque over the mucosal surface, hence they cannot be scaped off. Erythematous candidiasis presents as a red flat subtle lesion either on the dorsal surface of tongue and / or the hard/ soft palate. Patients complained of burning sensation in the mouth, more so while eating salty and spicy food. Pseudomembranous candidiasis appears as creamy white curd like plaque on the buccal mucosa and tongue that could be whipped away, leaving a red or bleeding surface. Angular chelitis presents as redness, ulceration and fissuring along the corners of the mouth.

In this study, the predictive value of oral lesions in HIV/AIDS sero-positive was 30.6 as calculated thus A/(A+B)×100, where A represents those with oral lesions, B represents those without oral lesions and A + B, the total sample respondents.

Most of the oral lesions occurred when the CD4 cell counts were less than 200 cells/μl. There was a strong association (p = 0.03) between CD4 cell count and occurrence of oral lesions in HIV/AIDS patients. This is similar to the finding of Bodhade and co-workers in India [35], where the present of oral lesion was correlated with CD4 count < 200 cells/ mm^3, a statistically significant associated was found between occurrence of oral lesions in HIV-positive patients and reduction in CD4 count < 200 cells/mm^3.

Conclusion

The prevalence of 31% of oral lesions in HIV/AIDS seen in this study implies that these lesions are common in people living with HIV/AIDS in our environment. Oral candidiasis is therefore strongly associated with HIV/AIDS infection.

This result also shows that subjects with very low CD4 cell counts ≤ 200 cell/mm^3 had more chances of having significant mucoccotaneous disorders than individual with CD4 cell counts of ≥ 500 cells/μl. This clearly indicates an inverse relationship between incidence of mucocutaneous disorders and CD4 cell counts.

Oral lesions can not only indicate infection with HIV, they are also among the early clinical features of the infection and can predict progression of HIV disease to AIDS. They can, therefore, be used as determinants of opportunistic infections, staging and classification systems.

The strong positive association between the occurrence of oral and peri-oral lesions and low CD4 cell counts found in is study could be regarded as an important result in the light of the need for inexpensive surrogate markers of HIV disease progression in resource-poor countries, where the measurement of CD4 cell count is expensive and in some areas not available.

It is therefore important for Primary care physicians as physicians of first contact to be familiar with oral manifestation of HIV infection so that identification and recognition of these conditions early can help to reduce morbidity and mortality associated with HIV/AIDS.

Acknowledgement

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