

Prevalence of oral manifestations among HIV patients – A cross sectional study

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Abstract

Introduction Oral manifestations can occur in 80% of patients infected with HIV. It causes significant morbidity and also provide diagnostic clues to the underlying immunocompromised status.

Objective The present study was conducted to determine the prevalence of oral manifestations in HIV infected patients and to correlate those manifestations to the degree of cellular immune deficiency.

Material & Methods This was a cross sectional study conducted in Out patient department of SKIN & STD between September 2016 and March 2018. A total of 192 HIV patients between 18- 70 years of age were included in the study. Oral lesions were diagnosed clinically, according to the presumptive diagnostic criteria established by the European Community Clearinghouse on oral problems related to HIV infection in August 1990 and September 1992. Data were coded and analyzed.

Results The prevalence of oral manifestations in our study was 49.0%. More commonly seen in the age group of 40-45 years (34%) and males were more commonly affected (56%). Pseudomembranous candidiasis (28.6%) was the most common oral manifestation in our study followed by Aphthous ulcer (16.14%), linear gingival erythema (13.2%) and Oral hairy leukoplakia (10.4%). It was observed that more number of patients having oral manifestations had a CD4+ count of less than 200 cells/ mm³.

Conclusion Oral manifestations are highly predictive markers of severe immune deterioration and disease progression. Oral examinations are an essential component for early recognition of disease progression and comprehensive evaluation of HIV infected patients.

Key words

Aphthous ulcer, CD4 count, HIV/AIDS, Oral candidiasis.

Introduction

Oral manifestations are common in patients with HIV infection. They cause significant morbidity and also provide diagnostic clues to the

underlying immunocompromised status. These may be a reason for referral and investigations for HIV infection.¹ Oral manifestations can occur in 80% of patients infected with HIV.

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For individuals with unknown HIV status, oral manifestations may suggest possible HIV infection, although they are not diagnostic of infection. For persons living with HIV disease who are not yet on therapy, the presence of certain oral manifestations may signal the

progression of HIV disease. For patients on antiretroviral therapy, the presence of certain oral manifestations may signal an increase in the plasma HIV-1 RNA level. Based on standard classification and diagnostic criteria, common HIV-associated oral disorders can be broadly classified into four categories by pathophysiological process.² 1. Infections: fungal, viral, bacterial. 2. Neoplasms 3. Immune-mediated disorders 4. Others: xerostomia etc.

Oral hairy leukoplakia (OHL) and pseudomembranous candidiasis are the most common lesions seen in HIV infection and are used in all current classifications of HIV disease. The presence of either of these oral lesions indicates progression to AIDS.³ This emphasizes the importance of a thorough oral examination at every stage in the diagnosis and management of all HIV-positive patients, as well as those thought to be infected or at risk.⁴ Factors that predispose to HIV-related oral conditions include CD4+ cell count of less than 200/ μ L, plasma HIV RNA levels greater than 3000 copies/mL, xerostomia, poor oral hygiene and smoking.

The rationale of the study is to investigate oral manifestations in HIV-infected individuals as a marker of immune status for field-based settings. The fact that oral lesions can be readily detected by a trained clinician in a standardized, objective fashion without any complicated or expensive diagnostic technique has increased their utility.

Objectives

The objective of the study was to determine the prevalence of oral manifestations in HIV infected patients and to correlate those manifestations to the degree of cellular immune deficiency.

Materials and Methods

This was a cross sectional study conducted in out patient department of Skin & STD after getting approval from ethical committee of our institution. This study included all the HIV patients between 18-70 years of age who attended the out patient department during the study period of September 2016 to March 2018. Those HIV positive patients who were of less than 18 years of age and more than 70 years, patients with trismus were excluded from the study. Written informed consent was obtained from all the participants for the clinical examination.

Baseline information regarding demographic features (residence, age, sex), history of ART (Antiretroviral therapy), duration of illness was collected from all the individuals on a pre-tested structured questionnaire. The previous CD4+ counts of each patient (maximum of 6 months) were recorded from the patient's medical records. Then oral examination was carried out wearing sterile gloves and mask with artificial illumination using a sterile mouth mirror and probe. The oral manifestations found in our study were categorized according to 1993 EC Clearinghouse-WHO classification system which is as follows⁵: a) Strongly associated lesions (SA): oral candidiasis, HIV associated periodontal conditions. b) Less commonly associated lesions (LCA): Herpes Simplex, Herpes Zoster, and Ulceration not otherwise specified c) Lesion seen (LS): Aphthous ulcers and hyperpigmentation.

Statistical analysis:

Data was entered using SPSS Version 16 (SPSS, Inc., Chicago, IL, USA). Student "t" test was carried out to find the association between various factors. Level of significance was estimated with 95% confidence intervals and

Table 1 Mean CD4⁺ counts for presence/absence of oral manifestations

Oral manifestations	No.	Mean CD4 ⁺ count ± S.D.	't' value	'p' value	Inference
Present	94	158.503 ± 187.87	5.219	0.001	Significant
Absent	98	397.195 ± 256.76			

Table 2 Frequency of Oral manifestations

Sr.	Oral Manifestations	Frequency	%
1	Pseudomembranous candidiasis	55	28.6 %
2	Aphthous ulcer	31	16.14%
3	Linear gingival erythema	25	13.02 %
4	Erythematous candidiasis	20	10.41 %
5	Oral hairy leukoplakia	20	10.41 %
6	Angular cheilitis	18	9.37 %
7	Hyper Pigmentation	16	8.2 %
8	Necrotising ulcerative periodontitis	11	5.3 %
9	Hyperplastic Candidiasis	5	2.6%
10	Herpes Zoster	4	2.08 %
11	Herpes Simplex	2	1.4 %

p<0.05 was considered to be statistically significant.

Results

During the study period (September 2016-March 2018), a total of 192 HIV positive patients who presented to the ART centre in the age group of 18-70 years were included in the study. The following observations were made in our study. In our study most of the patients belonged to the age group of 32-40 years (32.3%). In our study 92 patients were males and 100 patients were females. There was a female preponderance, and the female: male ratio was 1:0.9.

The prevalence of oral manifestations in our study was 49.0% i.e. amongst the 192 patients 94 had oral manifestations. Regarding distribution of oral manifestations among various age groups, it was more commonly seen in the age group of 40-45 years (34%), when compared to the 31% in the 32-40 years age group and 22% in more than 45 year group. In our study 56% of males and 44% of females had oral manifestations. The distribution of oral

manifestations amongst gender was not statistically significant (p>0.05). Among this 94 patients, 77% had single oral lesion, 17% had two lesions and 6% had three lesions. The total number of oral manifestations observed in this study was 73. In our study 49.5% of the patients had CD4⁺ count of <200, 23.4% had CD4⁺ between 200-500 and 27.1% had CD4⁺ counts >500. The mean CD4⁺ count when any oral manifestation present was 158.503±187.867. The mean CD4⁺ count of patients in whom there were no oral manifestations was 397.195±256.757 which is significantly higher than the mean CD4⁺ count of patients with oral manifestations and it was statistically significant (p 0.001) (**Table 1**).

Pseudomembranous candidiasis (28.6%) (**Figure 1**) was the most common oral manifestation in our study followed by Aphthous ulcer (16.14%), linear gingival erythema (13.2%) (**Figure 2**), Oral hairy leukoplakia (10.4%) (**Figure 3**), Erythematous candidiasis (10.4%), Angular cheilitis (9.37%), Melanotic pigmentation (8.2%), Necrotizing ulcerative periodontitis (5.3%), Hyperplastic candidiasis (2.6%) (**Figure 4**), Herpes zoster (2.08%) and Herpes simplex (1.4%) (**Table 2**).

Amongst the 94 patients who had oral manifestations, 71 (75.5%) belonged to the strongly associated category of 1993 E C Clearinghouse on Oral Problems Related to HIV,⁵ 21 (22.3%) belonged to the less commonly associated category, 2 (2.1%) belonged to the lesion seen category. The mean CD4⁺ count of patients having strongly associated lesion was 182.256±205.441. The mean CD4⁺ count of patients having less



Figure 1 Pseudomembranous candidiasis



Figure 2 Linear gingival erythema



Figure 3 Oral hairy leukoplakia



Figure 4 Hyperplastic candidiasis

commonly associated lesion was 79.440 ± 97.097 . The mean CD4+ count of patients having oral manifestation was 118.333 ± 14.503 . Among the 71 patients having strongly associated lesion 46 (64.7%) had CD4 count of less than 200 cells/mm³, 15 (21.1%) had CD4 count of 200-500 cells/mm³ and 10 (14.0%) had CD4 count of more than 500 cells/mm³. Of 210 patients having less commonly associated lesion, 16 (76.1%) belong to the category of less than 200 CD4+ count with only 5 (23.0%) belonging to the category of 200-500 CD4+ counts. All the 5 patients having oral manifestations belonging to the category of lesions seen had a CD4+ count of less than 200 cells/mm³. It can be observed that more number of patients having oral manifestations had a CD4+ count of less than 200 cells/mm³.

The mean CD4+ count of patients not having oral candidiasis was significantly higher ($p < 0.05$), i.e. 305.508 as compared to the mean CD4+ count of patients having oral candidiasis i.e. 139.502. Similarly the mean CD4+ count of patients without HIV associated periodontal conditions (255.48) was higher than the mean CD4+ count of patients with HIV associated periodontal conditions (96.75) and it was statistically significant.

Amongst 192 patients, 171 patients were on antiretroviral therapy. The prevalence of oral manifestations among patients who had received antiretroviral therapy was 46.1% which is lesser than the prevalence of oral manifestations among patients who had not received antiretroviral therapy.

Discussion

Since the first report of HIV infection in 1981, the importance and frequency of the associated oral manifestations have been recognized. It is generally agreed that the recognition of some oral manifestations of HIV disease is of great significance because they may represent the first sign of the disease and they have been shown to be highly predictive markers of severe immune suppression and disease progression.⁶ This study was undertaken to correlate oral manifestations of HIV/ AIDS to the levels of circulating CD4+ T lymphocytes, so that the oral manifestations can be used as markers of immune suppression, where resources are limited.

Prevalence

The prevalence rate of oral manifestations was observed to be 49% in our study. Several

investigators have reported the prevalence of oral lesions to range from 40-70%.

Roberto Barone M D *et al.*,⁷ observed a prevalence rate of 41% among 217 patients. Ramirez-Amador V *et al.*,⁸ reported a higher prevalence of 75%, whereas Aguirre-Urizar J M⁹ observed oral lesions in 99.5% of his study population.

These substantial differences in the prevalence of HIV related oral lesions may be explained by many factors.

1. As reported by Ira B Lamster and co-workers¹⁰ life style, access to health care and the condition of the oral cavity before infection influence the development of oral lesions in persons with HIV infection.
2. Recruitment of an appropriate study population is a crucial point in any study design. Different populations, clinical settings used for evaluation of clinical stage, distribution of risk groups, race and socioeconomic status are the major confounding factors.
3. Other factors that may have an influence are the examiner's clinical experience and use of different diagnostic criteria.

Because the entry criteria in our study population did not select or exclude patients on the basis of either lesion status or CD4+ T cell count, we believe that estimates presented herein are largely unbiased. However, the conditions of the oral cavity and habits like smoking and tobacco chewing, socioeconomic status have not been considered in our study.

Age and sex ratio

Most of the patients in our study group (34%) who had oral manifestations belonged to the age group of 40-45 years. Higher prevalence of oral

lesions was observed in the older age group. This observation can be substantiated by the fact that the risk of development of AIDS increases with age with the older individuals having a higher rate of disease progression.¹¹

The prevalence of HIV related oral lesions has been reported to be significantly higher in women than in men, especially for oral candidiasis by Giuseppe Campisi and coworkers.¹² whereas Shiboki *et al.*,¹³ reported male specificity for oral hairy leukoplakia and oral candidiasis. In contrast, HIV positive women were found to have specificity for gynaecological disease and esophageal candidiasis. However in our study not much of a difference was found in the distribution of oral manifestations amongst gender.

Prevalence of common oral manifestation and its Correlation with CD4 count

Oral manifestations have been reported to appear more frequently below a CD4+ count of 200 cells/ mm³. This result is expected because the association between progression of HIV disease and CD4+ depletion is well established. Accordingly, in our study also the mean CD4+ count was less i.e. 158 when any oral lesion was present when compared to the mean CD4+ count of 397 when no oral lesions were reported. Similar observations were reported in a study population of 606 patients by Lauren L Patton, and Chapel Hill of North Carolina.¹⁴ The mean CD4 count for any lesion present was 243 as compared to 416 when lesion was absent in homosexual men and 332 as compared to 411 among intravenous drug users in a study conducted by Lamster *et al.*¹⁰

In our study, 49.5% of the oral manifestations occurred in patients with a CD4+ count of <200 cells/mm³ 23.4% of oral manifestations occurred with patients having a CD4+ count of 200-500

cells/ mm³ and 27.1% of oral manifestations were seen in patients having a CD4+ count of > 500 cells/mm.³ Anwar R. Tappuni and coworkers¹⁵ showed that subjects with a CD4+ count of < 200 cells/ mm³ and viral load > 3000 copies/ ml, irrespective of the treatment, they were more likely to experience oral manifestations of HIV than the other study subjects with CD4+ count of >200 cells/ mm³.

In our study, the most frequent lesion was oral candidiasis with a frequency of 41.6% with pseudomembranous subtype (28.6%) being the most frequent. This finding is most consistent with clinical studies conducted by Phelan *et al.*,¹⁶ Barone *et al.*⁷ and Nielsen H *et al.*¹⁷ where pseudomembranous and erythematous candidiasis were predominantly present. The mean CD4 count of 139.5 was seen in patients with oral candidiasis of our study and is similar to the mean CD4 count of 149.5 cells/mm³ reported in Glick M *et al.*'s study.¹⁸

The mean CD4+ count of patients with pseudomembranous candidiasis and erythematous candidiasis was 120.3 and 213.8% respectively. As reported by Pindborg¹⁷ from Copenhagen, the mean CD4+ count of patients with pseudomembranous and erythematous candidiasis were 220 and 320 respectively. Angular cheilitis was present in 9.37% of our study population and the mean CD4+ count of patients with angular cheilitis was 98.5. The frequency observed is similar to that seen in other series. A higher prevalence was noted by Aguirre-Urizar in a Spanish population.⁹

The prevalence of HIV associated periodontal conditions (linear gingival erythema and necrotizing ulcerative periodontitis) in our study population was 18.5 %. The prevalence of periodontitis in HIV infected patients as reported in the literature varies between 5-17%. The prevalence rate of NUP was 5.3% and the mean

CD4+ count of patients with NUP was 96.7. Michel Glick, Brian C Muzyka¹⁹ have investigated the association between NUP diagnosis and CD4 count < 200 cells/mm.³ The prevalence of NUP as reported by them was 6.3% and the mean CD4 count was 51.8 cells/mm.³ It was suggested by them that NUP should be considered to be included as a clinical marker for staging of HIV disease and AIDS.

Atypical presentation of ulcers was noted in 31 patients (16.14%). The mean CD4+ count in these patients was 103.5. The reported prevalence of these ulcers in the literature ranges from 1.1% to 12%.²⁰ A frequency of occurrence of 2.08% was noted with herpes zoster in our study. Multidermatomal involvement and a higher rate of complications have been reported in the literature. Of four patients one had extensive multidermatomal lesions with a CD4+ count of 358.

Kaposi's sarcoma and Non Hodgkin's lymphoma, HIV associated salivary gland diseases were not observed in our study population. This could be attributed to smaller sample size of our study and may be related to the higher heterosexual transmission category of HIV infection as compared to the homosexual transmission categories prevalent in other study groups.

Compared with the patients who had not received ART, patients who had received ART had fewer HIV related oral manifestations. This is in agreement with the studies conducted by Greenspan *et al.*,²¹ Velegraki *et al.*²² and Kerdpon *et al.*²³ where they have reported a decline in the HIV associated oral lesions in the HAART era. This reduction can be probably attributed to the result of an expression of the reconstituted immune system.

In our study, oral manifestations have been compared with the CD4+ counts. Most of the studies have correlated the lesion presence and immune suppression defined as a CD4+ count of <200 cells/ mm³. This reliance on the CD4+ cell count as the sole measure of immune status implies that immune function and ultimately disease progression are mediated by this factor alone. Clearly, this assumption is flawed. Many researchers have also noted the shortcomings inherent in the measurement of CD4 count including the diurnal variation and laboratory variability. Though CD4+ count is the principal laboratory marker, comparisons with other laboratory parameters like viral load, p24 antigen, β2 microglobulin etc. are recommended in future.

Conclusion

Immune dysregulation is of paramount importance factor in the development of oral manifestations in HIV patients. Our study serves once more to show that most oral lesions associated with HIV infection increase in frequency as the CD4+ counts decrease. The prevalence becomes particularly important when the count falls to below 200 cells/ mm³. Oral manifestations are highly predictive markers of severe immune deterioration and disease progression. Oral examinations are an essential component for early recognition of disease progression and comprehensive evaluation of HIV infected patients.

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