

# Prevalence of oromucosal lesions in HIV positive patients receiving haart-A prospective clinical study

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## ABSTRACT

**Aim:** To determine the preponderance of oral mucosal lesions and conditions in patients receiving highly active antiretroviral therapy (HAART) for Human Immunodeficiency virus (HIV). **Material and Methods:** Patient tested Seropositive for HIV and on HAART therapy were clinically examined to evaluate prevalence of oral lesions. **Results:** In the pool of 152 HIV positive patients in the study, age ranged from 7 to 71 years, 67 were males and 85 females. The duration of the HAART medication was 43 months. Oral lesion was present in 51.32% of patients related to infection. Oral lesions seen in descending order of frequency were periodontitis, mucosal hyperpigmentation, acute gingivitis, oral candidiasis, linear gingival erythema, stomatitis, and nonspecific ulcers. Totally, 48.68% of patients had no oral lesions. **Conclusion:** Majority of the HIV patients on HAART exhibited periodontitis (30.77%), mucosal hyperpigmentation (17.44%), gingivitis (10.77%), anemic stomatitis (11.28%), and other oral lesions accounted to 29.74% which may be attributed to Anti Retro Viral Therapy.

**Keywords:** HIV patients, hyper-pigmentation, oral lesions

## Introduction

Worldwide HIV infection and AIDS are of big concern since a long time. 2017 UNAIDS revealed that approximately 37 million humans globally are right now having HIV infection and new infection rate is increasing by 5000 persons per day. CD4 + T lymphocytes are the main target cells of HIV and the development of full-blown viral infection leads to depletion of these cells which in turn worsens body's immunity.<sup>[1]</sup>

Immunosuppression is the main cause for opportunistic infections, secondary neoplasms, and neurologic manifestations

seen in Acquired Immunodeficiency Syndrome (AIDS) which is an infectious disease of Human Immunodeficiency Virus (HIV).<sup>[2]</sup>

Poor immune system leads to a plethora of manifestations of HIV/AIDS especially in head and neck (H&N) region. Mostly skin as well as upper aero-digestive tract is affected by lesions due to HIV infection. Around 50% of patients who are HIV positive have various oral lesions singly or in combination. Oral lesions are one of the earliest signs and can estimate the progression of HIV into AIDS.<sup>[1]</sup>

According to epidemiological report, 2.08 million out of total 34 million HIV-infected people of the world are in India.<sup>[3]</sup> 53% of all HIV infected population in Indian subcontinent are in the states of Andhra Pradesh, Telangana, Karnataka, Maharashtra, and Tamil Nadu. HIV-associated oral lesions and conditions are one of the

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earliest clinical presentations seen in 20–80% of HIV patients<sup>[4]</sup> to predict the progression of HIV to AIDS. The systemic use of highly active antiretroviral therapy (HAART) causes significant reduction in incidence of oral lesions by 10–15%.<sup>[5]</sup> Among the various types of opportunistic infections associated with HIV, oral candidiasis, and oral hairy leukoplakia appears to be the most common. Other HIV associated oral lesions include linear gingival erythema, acute necrotizing ulcerative gingivitis (ANUG), acute necrotizing periodontitis (ANUP), Kaposi's Sarcoma, Non-Hodgkin's lymphoma.<sup>[6,7]</sup>

HAART lessens HIV RNA level in the plasma that is the viral load is decreased with CD4 count which rises steadily. With this treatment, possibility of opportunistic infections, malignancies also decline. In areas where CD4 + T cells counting is jeopardized, a secondary indicator that is oral candidiasis, can be used for evaluating the immunity status of HIV patient.<sup>[1]</sup>

We aimed to assess the prevalence of oral mucosal lesions in HIV seropositive patients visiting outpatient department of our center.

## Material and Methods

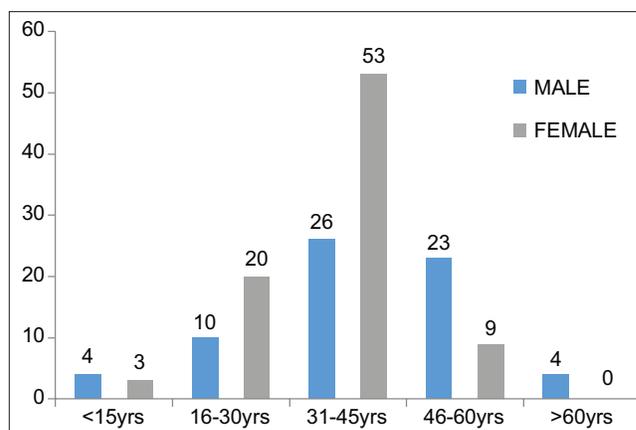
A prospective clinical study was conducted on patients who were diagnosed as HIV positive and on HAART therapy, independent of age, and sex visiting outpatient of our center.

Approval from the Institutional Ethical Committee of Koppal institute of medical sciences, Koppal was taken on 15/11/2016. After taking written informed consent from the patients about the study, they were clinically examined to evaluate presence or absence of oral lesions. The patient's information regarding demographic data, data of HIV conformity, associated systemic illness, and duration of HAART therapy (medication they might be on apart from HAART) were gathered from their record. Patients who are taking HAART (Drugs includes; abacavir, efavirenz, and ritonavir) were included. The data obtained were statistically analyzed.

## Results

The study sample comprised of 152 patients of age ranges from 7 to 71 years among which 67 were males and 85 were females. The mean age was 37.74 years [Figure 1]. The mean duration of HAART medication was 43 months. Most of the patients had previous history of treated tuberculosis and were anemic. Oral lesion was present in 51.32% of patients related to infection [Table 1]. After periodontitis (30.77%), most commonly reported lesion was mucosal hyperpigmentation (17.44%). Among common HIV specific oral lesions candidiasis was seen in 9.74% patients, followed by linear variant gingival erythema (5.13%), necrotizing gingivitis (2%), necrotizing periodontitis (1%) along with only one patient of oral hairy leukoplakia.

Oral lesions seen in descending order of frequency were periodontitis, mucosal hyper pigmentation, acute gingivitis, oral



**Figure 1:** Age and gender distribution of study sample

candidiasis, linear gingival erythema, stomatitis, and nonspecific ulcers. 48.68% of patients had no lesions.

## Discussion

One of the major epidemics of our country, HIV has drastic effects on social and economic aspects of human population. HIV is a chronic infection which has an initial asymptomatic phase followed by early symptoms due to progression of immunosuppression. However, AIDS is always the end result. The targeting of T- helper cells by the virus causes the drastic decrease in the immunity of the concerned person. Apart from systemic lesions, oral lesions start developing due to imbalance in microbiota of the oral cavity leading to various opportunistic infections. Deteriorating oral health has a bad impact on quality of life, nutrition, psychosocial behavior of a person as well as it creates problems in treatment of various systemic diseases.<sup>[8]</sup>

A combination of three or more than three anti-viral drugs constitute a treatment regimen of Highly active antiretroviral therapy (HAART). It is also named as antiretroviral therapy (ART) or combination antiretroviral therapy (cART). Foundation of HAART is administration of various drugs which decreases replication of viral particles with the use of various pathways which has an advantage that if there is a resistance to a single drug it can be tackled by other drug agents as well. Other agents can be added to the main drug co-formulations which can comfort the patient. Once the therapy starts, within 16 weeks viral suppression should be accomplished. Viral limit should remain below 50 copies/ml to ensure the success of HAART. Regular monitoring should be done every 3 to 6 months intervals, of various lesions, CD4 + T cells count, blood count, urea, and electrolytes.<sup>[9]</sup>

In the present study, 152 HIV infected patients on HAART treatment were examined of which 67 (44.1%) were male and 85 (55.9%) were female patients. The age group ranged from 31 to 45 years with a mean age of 37.74 years and this result assessed was similar to that of Bravo *et al.*<sup>[10]</sup>

**Table 1: Prevalence of oral lesions among the HIV patients on HAART**

Oral Manifestations	No of Patients	Males (%)	Females (%)	Total Percentage
Periodontitis	60	27 (31.76)	33 (30)	30.77
Hyperpigmentation	34	16 (18.82)	18 (18)	17.44
Acute Gingivitis	21	8 (9.41)	13 (13)	10.77
Anemic stomatitis	22	6 (7.05)	16 (11.81)	11.28
Candidiasis	19	11 (12.94)	8 (14.54)	9.74
Aphthous Stomatitis	5	2 (2.35)	3 (7.27)	2.56
Leukoplakia	5	3 (3.52)	2 (2.72)	2.56
Recurrent herpes viral infection	4	2 (2.35)	2 (1.81)	2.05
Nonspecific Ulcers	3	1 (1.17)	2 (1.81)	1.54
Lichenoid Reaction	2	1 (1.17)	1 (0.90)	1.03
Salivary Gland Enlargement	2	0	3 (2.72)	1.03
Oral Lichen Planus	1	0	1 (0.90)	0.51
Linear Gingival Erythema	10	5 (5.88)	5 (4.54)	5.13
Acute necrotizing gingivitis (ANUG)	4	2 (2.35)	2 (1.81)	2.05
Acute necrotizing periodontitis (ANUP)	2	1 (1.17)	1 (0.90)	1.03
Oral Hairy Leukoplakia	1	0	1 (0.90)	0.51
Total	195	85	110	100

Interleukin 17 (IL-17), also known as (IL-17A), is a major, strongly proinflammatory cytokine produced by Th17 helper cells. This cytokine has potent proinflammatory properties, which have been associated with the development of inflammatory processes, acute immunological graft rejection, and autoimmune diseases such as pre-eclampsia in pregnant females and HIV/AIDS patients.<sup>[11]</sup>

Out of 152 patients, we observed 51.32% of them had one or the other oral lesions and 48.68% had no noticeable oral lesions. About 32–46% of oral lesion among patients on HAART was stated in various studies by Schmid- Werthausen *et al.*, Garcia, Almeida *et al.*<sup>[7,12,13]</sup>. However, lower manifestation by Ferreira *et al.*<sup>[14]</sup> has also been reported in another study.

Most of the patients with oral lesions were females 56.41%. In our study most of the females were illiterate and had acquired the infection by heterosexual mode of transmission. However, Indian studies of Bodhade *et al.*<sup>[15,16]</sup> and Ranganathan *et al.*<sup>[17]</sup> noted male predominance.

HIV associated common oral lesions are oral candidiasis, oral hairy leukoplakia, Kaposi's sarcoma, linear gingival erythema (LGE), necrotizing ulcerative gingivitis (NUG), necrotizing ulcerative periodontitis (NUP), nonspecific lymphoma, and squamous cell carcinoma of head and neck region.<sup>[15,18-20]</sup>

Cross-contamination is a very prominent concern amidst dental treatment. Usually it occurs by handling contaminated material like using needles which are soiled by viral particles. Because of saliva and blood which splashes across during treatment causes cross-contamination. But the risk of this spread is approximately 0.3%. Consequently, dental surgeons are required to be vigilant while treating patient with HIV, where oral lesions often precede the systemic manifestations.<sup>[21]</sup>

Clinical signs of HIV associated periodontitis is described as pronounced periodontal inflammation and loss of attachment than in conventional periodontitis. It is assumed that periodontal inflammation is significantly associated with immunosuppression and a risk factor for LGE, NUG, and NUP.<sup>[22]</sup>

We observed gingival and periodontal related diseases in more than 40% of screened population; periodontitis (30.8%), linear gingival erythema (5.13%), ANUG (2.05%), ANUP (1.03%). The common occurrence is in accordance with other studies in Indian population.<sup>[16,20]</sup> Even after controversial existence of chronic periodontitis in HIV infected patients, exacerbation of pre-existing periodontal disease has been noted.<sup>[18,20,23]</sup> Variable data exists in different population studies, Ranganathan *et al.*<sup>[17]</sup> with prevalence rate of 37.3%, in German population by Kroidl A *et al.*<sup>[23]</sup> as 30% and higher prevalence of 52% by Brady *et al.* and 73% by Rao *et al.*<sup>[24]</sup> The variable prevalence could be due to determinants like senescence, oral habits, immunological status, and oral hygiene levels along with the criteria used for periodontal diagnosis. In our study, most patients had poor oral hygiene which is the main reason for majority of patients with gingivitis and periodontitis.

Oral Hairy Leukoplakia and Kaposi's Sarcoma is found in severe immunosuppressed individuals and we had not found even a single patient of Kaposi's sarcoma which was similar as reported in studies of south East Asian countries.<sup>[25-27]</sup> High prevalence of its occurrence in developed countries is due to homosexual mode of transmission. However, in India, transmission of HIV infection seen is heterosexuality and its incidence are rare.<sup>[16]</sup>

Oral candidiasis is the stereotyped oral lesion associated with HIV infection<sup>[16]</sup> and its prevalence noticed among patients on antiretroviral treatment was 50% lower as compared to the prevalence rate in pre HAART era.<sup>[28,29]</sup> Oral candidiasis was present in 9.74% of patients out of which more than 50% of patients had erythematous candidiasis

comparable to findings by Sharma *et al.*<sup>[30]</sup> Presence of oral candidiasis is suggestive of severe immunosuppression. Smoking habit and antibiotic usage by HIV patients may have contributed to increase in prevalence of candidiasis.<sup>[28,29]</sup>

Oral melanotic hyperpigmentation was one of the common manifestations in our patients with prevalence of 17.4%. Hyperpigmentation possibly be linked to stimulation of melanocytes due to immunopathologic changes and use of antiretroviral medication containing zidovudine<sup>[30,31]</sup> and antifungal agents.<sup>[24]</sup> Findings was comparable to studies by Ashish S. Bhodhade<sup>[15]</sup> who reported 19%, 23% by Ranganathan *et al.*<sup>[17,18]</sup> Common occurrence of intraoral hyperpigmentation is also reported in literature.<sup>[29,30]</sup>

Fourteen Patients had xerostomia due to hyposalivation and could be due to long-term use of HAART therapy. Nittayananta *et al.*<sup>[32]</sup> had found decreased saliva in HAART groups. 3.5% xerostomia was observed by Tiawo *et al.*<sup>[33]</sup>

We found 1.54% of cases with nonspecific ulcers, other oral lesions such as anemic stomatitis (11.28%), lichenoid reaction (2%), and salivary gland enlargement (0.3%). Lesser prevalence of aphthous ulcers 2.56% is comparable to other studies of Indian population.

Immunological dysfunction due to decrease in serum CD4 T lymphocyte count is responsible for occurrence of oral lesions.<sup>[27]</sup> As HIV specifically acts on CD4 cells so, AIDS has been defined clinically if CD4 count is below 200 (<15%) by Centre for Disease Control and Prevention (CDC).<sup>[28,34]</sup>

There are some limitations in this study as this was conducted among patients on HAART. Study subjects should have been compared according to their CD4 counts among those with and without HAART. The subjects were not followed for progression of oral diseases. Further studies are required with larger sample size with long term follow-up to get a conclusive result on effectiveness of HAART in reducing oral lesions. This study is relevant for primary care physicians as it gives an insight to them how with the help of resolution of oral lesions can help to determine the success of HAART as does the CD4 + T cell count. Thus, it is imperative to identify these oral lesions as they serve as early diagnostic and treatment success sign as well.

## Conclusion

The presence of HIV-specific oral diseases may serve to detect, diagnose the progression of HIV infection, and efficacy of antiretroviral therapy. Majority of the HIV patients on HAART exhibited periodontitis in 30.77% and overall oral lesions accounted to 51.32% which may be attributed to their better immune status secondary to Anti Retro Viral Therapy.

## Summary

Mostly in female HIV positive patients receiving HAART

treatment has shown prevalence of oral lesion in descending order of frequency: periodontitis, mucosal hyper pigmentation, acute gingivitis, oral candidiasis, linear gingival erythema, stomatitis, and nonspecific ulcers.

## Key message

Prevalence of oral lesions can be used as a tool to diagnose disease progression among sero-positive patients during HAART.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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