

**ORIGINAL ARTICLE****Association of CD4 count with Oral Manifestations among the HIV infected patients of Central India**Kumar Pushpanshu<sup>1</sup>, Rachna Kaushik<sup>2\*</sup><sup>1</sup>MDS, Associate Professor & Head, Department of Dentistry, Sri Krishna Medical College & Hospital, Muzaffarpur, India,<sup>2</sup>MDS, Assistant Professor, Department of Dentistry, Sri Krishna Medical College & Hospital, Muzaffarpur, India**ABSTRACT:**

**Objective:** Human immunodeficiency virus (HIV) disease presents a plethora of oral manifestations, which provide valuable diagnostic and prognostic information. The oral presentations reflect the underlying immune status of the patient. Morphology and multiplicity of these lesions in an individual are correlated with disease progression. A CD4<sup>+</sup> lymphocyte count of less than 200/μL has been postulated as indicative of an active disease and thus can be used to monitor the progress of the disease and plan suitable therapy. The purpose of this study was to explore the oral features of a group of HIV patients and survey their CD4<sup>+</sup> counts. **Study design:** This was a cross sectional study where 120 HIV infected patients were recruited. Investigations included; interviews, physical examinations and enumeration of CD4<sup>+</sup> T cells. Based on CD4<sup>+</sup> count, participants were grouped into: a) < 200 cells/μL and b) ≥ 200 cells/μL. **Results:** A total of 10 HIV-associated oral lesions were observed in 88 (73.33 %) patients. Oral candidiasis and oral hairy leukoplakia were the commonest (26.67% each), followed by melanin hyperpigmentation (25 %). There was a significant association between the presence of oral lesions and CD4<sup>+</sup> count < 200 cells/μL (p = 0.001). **Conclusions:** The oral health status of a HIV infected patient at presentation is an extremely important parameter, as it may reveal important information regarding the immune status of the individual. This reiterates the need for thorough oral examination in HIV positive patients, and provision of optimal medical care to these patients.

**Key words:** Human immunodeficiency virus, CD4<sup>+</sup> count, oral manifestations, oral candidiasis.

**Corresponding Author:** Dr. Rachna Kaushik, MDS, Assistant Professor, Department of Dentistry, Sri Krishna Medical College & Hospital, Muzaffarpur, India

**This article may be cited as:** Pushpanshu K, Kaushik R. Association of CD4 count with oral manifestations among the HIV infected patients of Central India. J Adv Med Dent Sci Res 2016;4(6):310-314.

**INTRODUCTION**

Since the discovery of the first cases of AIDS in India among female commercial sex workers in 1986, HIV has spread to all states in the country. India has a large population and population density, low literacy levels and consequently low levels of awareness, thus HIV/AIDS is one of the most challenging public health problems ever faced by the country (1). India has the second largest number of HIV infections in the world following South Africa and accounts for nearly 10% of the global HIV/AIDS prevalence (2). Central Intelligence Agency's National Intelligence Council predicted that there will be 20- 25 million AIDS cases in India by 2010, which will be more than any other country in the world (3). With a population of over one billion, the HIV epidemics in India will have a major impact on the overall spread of HIV in Asia - Pacific and indeed worldwide. Profound immunosuppression, primarily affecting cell-mediated immunity, is the hallmark of this disease. This results chiefly from infection and a severe loss of CD4<sup>+</sup> T cells as well as impairment in the function of surviving helper T cells (4). CD4 molecule is a high affinity receptor for HIV. The clinical staging of HIV disease and the relative risk of developing opportunistic infections have relied on the CD4 cell count as the principal laboratory marker of immune status (5).

In the field of dentistry, the lack of knowledge regarding the systemic aspects of AIDS, and its subsequent oral

manifestations leads to severe limitations and deficiencies in the treatment of HIV positive patients. Oral lesions are common in patients infected by the HIV and may indicate an impairment in the patient's general health status and consequently a poor prognosis (6). Many such HIV-associated diseases occur initially, thus providing an opportunity for early diagnosis (7). Some authors state that oral manifestations are the earliest sign of HIV infection (8). HIV related oral lesions are used in several HIV disease staging and classification designations because of their prognostic significance and their diagnostic simplicity, requiring no sophisticated laboratory tests (9). Thus, in the absence of parameters indicating the degree of immunosuppression (CD4<sup>+</sup> cell counts and viral load), these oral lesions may be considered strong indicators of immunodeficiency (10-13). This study aimed to determine the prevalence and types of oral manifestations of HIV/AIDS and correlate them with CD4<sup>+</sup> cell count.

**MATERIALS AND METHODS**

This was a cross sectional study where the patients visiting the Anti Retroviral Therapy clinic, Government Medical College and Hospital, Nagpur (India) were examined. A total of 120 HIV-infected patients in the age group 19 – 57 years participated in the study. Of these 80 (66.67%) were males and 40 (33.33%) were females. There were no specific eligibility criteria.

Exclusion criteria included: patients below 18 years of age; patients with past/ current antiretroviral therapy. This study was approved by an institutional ethical committee and written consents were taken from each subject for their willingness to participate in the study.

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. Thorough physical examination was performed in each patient with emphasis on oral manifestations. Oral examination was carried out by a qualified dental surgeon without knowing CD4+ cell count level of the patient. A standard oral examination method recommended by WHO (14) 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. (15). 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. Diagnosis of oral lesions associated with HIV infection was made by using presumptive criteria given by EC-Clearinghouse, 1993 (16). CD4<sup>+</sup> count was estimated using BD FACS Caliber system<sup>TM</sup>. The participants were divided into two groups, low count (LC) patients with CD4<sup>+</sup> count < 200/ $\mu$ L (n=60) and high count (HC) patients with CD4<sup>+</sup> count  $\geq$  200/ $\mu$ L (n=60).

Data were coded, entered in a spreadsheet application and analyzed using the SPSS version 14.0. Independent Samples t test was applied to compare the CD4<sup>+</sup> counts of patients having oral manifestations with those without them. Degree of associations was determined between the degree of immunosuppression and occurrence of oral manifestations (in general), oral candidiasis and oral hairy leukoplakia using chi square test. A P-value of < 0.05 was considered significant.

## RESULTS

Among 120 HIV patients, 80 (66.67%) were males and 40 (33.33%) were females (Table 1). Of these, most patients, 44 (36.67%), were in 29–38 years age group.

The majority of patients (74, i.e., 61.67%) were illiterate; only 12 (10%) were graduates. Of these sufferers, 85% belonged to lower socioeconomic status; only 1.67% were from high socioeconomic status. The predominant mode of transmission was heterosexual contact (85%), only 14 patients were infected through transfusion of infected blood. There was no history of vertical (mother to child) transmission and homosexuality. There were 60 patients each, in LC (< 200/ $\mu$ L) and HC ( $\geq$  200/ $\mu$ L) groups. X

**Table 1:** Socio-demographic parameters and CD4 cell counts of study participants.

Characteristics	All patients (%)	Patients with oral lesions (%)*
<b>GENDER</b>		
Male	80 (66.67)	66(82.5)
Female	40 (33.33)	22 (55)
<b>AGE (years)</b>		
19-28	34 (28.33)	24 (70.59)
29-38	44 (36.67)	32 (72.72)
39-48	28 (23.33)	22 (78.57)
49-57	14 (11.67)	10 (71.43)
<b>TOBACCO</b>		
Chewing	30 (25)	26 (86.67)
Smoking	18 (15)	16 (88.89)
Both	26 (21.67)	18 (69.23)
<b>ALCOHOL CONSUMPTION</b>	54 (45)	46 (85.18)
<b>CD4 count (cells/<math>\mu</math>L)</b>		
< 200	60 (50)	52 (86.67)
$\geq$ 200	60 (50)	36 (60)
<b>SOCIOECONOMIC STATUS</b>		
Upper class	02 (1.67)	0
Middle class	16 (13.33)	04 (25)
Lower class	102 (85)	84 (82.35)
<b>EDUCATIONAL STATUS</b>		
Illiterate	74 (61.67)	60 (81.08)
High school study	34 (28.33)	24 (70.59)
Undergraduate	10 (8.33)	04 (40)
Postgraduate	02 (1.67)	0
<b>MODE OF TRANSMISSION</b>		
Heterosexual contact	102 (85)	
Blood transfusion	14 (11.67)	
IV drug abuser(syringe)	04 (3.33)	
Mother to child	0	
Homosexual contact	0	

\* Row percentages

**Table 2:** Comparison of mean CD4<sup>+</sup> counts between patients with and without oral manifestations

Oral manifestations	Number of patients (n)	Mean CD4 <sup>+</sup> count (cells/ $\mu$ L)	p value
Present	88	198.705	0.000 <sup>a</sup>
Absent	32	403.063	
<b>Total</b>	<b>120</b>		

a – statistically significant

**Table 3:** Distribution of study population according to their oral lesions and CD4<sup>+</sup> counts

Oral lesions	Number of cases (n)	Percentage (%)	Mean CD4 <sup>+</sup> count (cells/ $\mu$ L)
Oral candidiasis	32	26.67	191.313
Oral hairy leukoplakia	32	26.67	176.125
Melanin hyperpigmentation	30	25	232.933
Periodontal diseases	16	13.33	171.25
Recurrent aphthous ulcers	16	13.33	248.125
Herpes zoster	6	5	280
Molluscum contagiosum	4	3	89
Dry mouth	2	1.67	530
Ulcers - NOS	2	1.67	237
Thrombocytopenic purpura	2	1.67	70

Oral manifestations were observed in 88 (73.33%) patients. Mean CD4<sup>+</sup> cell count in the patients having oral lesions was 198.705 cells/ $\mu$ L (32 - 749 cells/ $\mu$ L). 32 (26.67%) patients did not have any oral lesion, their mean CD4<sup>+</sup> cell count being 403.062 cells/ $\mu$ L (36 - 640 cells/ $\mu$ L). There was a significant difference ( $p = 0.000$ ) between the mean CD4<sup>+</sup> values of patients with and without oral manifestations (Table 2). Association between the occurrence of oral manifestations and degree of immunosuppression (CD<sup>+</sup> count <200 cells/ $\mu$ L) reached statistical significance ( $p = 0.001$ ). There were a total of 10 different types of oral lesions present (Table 3). There were 52 patients with a single oral lesion, 22 with two oral lesions and 14 with multiple (3 or more) oral lesions.

Overall, oral candidiasis (OC) and oral hairy leukoplakia (OHL) were the commonest oral lesions seen in 32 (26.67%) patients each, followed by mucosal hyperpigmentation 30 (25%). Mean CD4<sup>+</sup> counts of the patients with OC and OHL were 191.313 and 176.125 cells/ $\mu$ L, respectively. Significant association between occurrence of oral candidiasis and immunosuppression ( $p = 0.013$ ) was observed. However, occurrence of oral hairy leukoplakia was not associated with degree of immunosuppression ( $p = 0.099$ ).

## DISCUSSION

The oral manifestations in HIV patients, including many opportunistic infections, are very common. The oral health status of a HIV-infected patient at presentation is an extremely important parameter, as it may reveal important information regarding the immune status of the individual. This study mainly focused on the oral manifestations of HIV positive patients attending Anti Retroviral Therapy clinic, Government Medical College and Hospital, Nagpur, India. Results of this study showed several facts about the HIV infected population of Central India (Table 1). Most of the patients were non-

graduates and belonged to lower socioeconomic strata. This indicates low awareness and poor nutritional status, which itself can accelerate the progression of HIV.

Present study reported 73.33% prevalence of oral lesions, which is higher than the reported 64% in India and 56% in the West (7). Similar findings were reported by Marcenes, et al. (17), who observed oral lesions in 76.5% of cases. However, in a study conducted by Pinheiro, et al. (18), only 33.5% of HIV-positive patients exhibited oral lesions. This high prevalence of oral manifestation in the present study can be due to the fact that the study group comprised only of freshly diagnosed cases of HIV infection. Patients were not taking any anti retroviral (ART) drugs or any other medications. Most of these patients had poor oral hygiene, which may also be a reason for this increased number of oral lesions. Of these 88 patients with oral manifestations, 62 had oral habits (tobacco chewing/smoking, alcohol or both).

In the present study, there were a total of 10 different types of oral lesions present in 88 patients (Table 3). The most commonly occurring oral lesions were oral candidiasis (OC) and oral hairy leukoplakia (OHL) - 26.67% each, followed by melanin hyperpigmentation - 25%. Similar findings have been reported in earlier studies (11, 13, 19 - 21), where OC and OHL were the most prevalent HIV associated oral lesions. Other lesions noted were periodontal diseases, recurrent aphthous ulcers, herpes zoster, molluscum contagiosum, thrombocytopenic purpura, dry mouth and ulcers not otherwise specified. Kaposi's sarcoma was noted by its absence, possibly due to low number of cases reporting homosexual behavior in contrast to reports from Europe and the United States. Homosexual behavior has been identified as a risk factor for KS (7).

It was noted that out of 88 patients presenting with oral lesions, CD4<sup>+</sup> count of 52 patients were below 200cells/ $\mu$ L. Only 8 patients with CD4<sup>+</sup> count <

200cells/ $\mu$ L were without oral lesions. Thus, CD4<sup>+</sup> count < 200cells/ $\mu$ L was significantly associated ( $p = 0.001$ ) with the presence of oral manifestation. Other studies (9, 11, 19 – 23) reported similar association. In the present study, prevalence of oral candidiasis (but not oral hairy leukoplakia) significantly associated with CD4<sup>+</sup> count of <200 cells/ $\mu$ L ( $p = 0.013$ ), consistent with earlier reported studies (19, 20, 22, 24). Though, pseudomembranous/erythematous variety and angular cheilitis were recorded separately during clinical evaluation, they were broadly grouped under OC for analysis.

Candidiasis is known as 'a disease of the diseased'. It is the most common opportunistic infection in India (25). There is a need to identify patients who have a greater risk of developing oral candidiasis, so that interventions can be designed to reduce the frequency of this infection. This is particularly important as there is evidence that candidal infection may induce immunosuppression and this may influence the prognosis of the HIV- infected individuals (24). The number of episodes of OC is the most significant predictor for change in CD4<sup>+</sup> count (26). HIV- infected patients with OC of any subtype, are significantly more immunosuppressed and show a faster development of AIDS than HIV- infected patients without OC (27).

## CONCLUSION

The oral manifestations have high prevalence among HIV positive subjects; of these, oral candidiasis is significantly correlated with low CD4<sup>+</sup> counts. This may provide a clue to the diagnosis of HIV in patients seeking dental care, who should be motivated to report for voluntary counselling and treatment. This also reiterates the need for thorough oral examination in HIV positive patients, and provision of optimal medical care to these patients. The significant association between occurrence of oral lesions with CD4<sup>+</sup> counts < 200 cells/ $\mu$ L found in this study underscores the prognostic significance of these manifestations in HIV disease.

The issues addressed above demonstrate the dentist's role as a health professional in the identification, diagnosis and treatment of HIV-associated lesions, providing proper guidance to the patient, and allowing for an early diagnosis of the disease, which is fundamental for a successful management of the HIV-infected patients.

## REFERENCES

- 1) UNPAN (2003) National AIDS Prevention and Control Policy (India) www.unpan.org.
- 2) USAID (2003) 'HIV/AIDS Country Profile India', March.
- 3) National Intelligence Council (2002) 'The Next wave of HIV/AIDS: Nigeria, Ethiopia, Russia, India and China', September, p.3.
- 4) Abbas AK. Diseases of immunity. In:Robbins and Cotran Text book of Pathologic Basis of Diseases. Edited by Kumar V, Abbas AK, Nelson F. 7th edition, Saunders (Imprint of Elsevier), Philadelphia, Printed in India 2004. p.193-267.
- 5) Patton LL. HIV Disease. Dent Clin N Am 2003;47:467-92.
- 6) Pedreira EN, Cardoso CL, Barroso Edo C, Santos JA, Fonseca FP, Taveira LA. Epidemiological and oral

- manifestations of HIV-positive patients in a specialized service in Brazil. J Appl Oral Sci. 2008 Nov-Dec;16(6):369-75.
- 7) Shobhana A, Guha SK, Neogi DK. Mucocutaneous manifestations of HIV infection. Indian J Dermatol Venereol Leprol 2004;70:82-6
- 8) Faria PR, Vargas PA, Saldiva PH, Bohm GM, Mauad T, Almeida OP. Tongue diseases in advanced AIDS. Oral Dis. 2005;11(2):72-80.
- 9) Ramirez-Amador V, Esquivel-Pedraza L, Sierra-Madero J, Ponce-de-Leon S, Ponce-de-Leon S. Oral manifestations of HIV infection by gender and transmission category in Mexico City. J Oral Pathol Med. 1998 Mar;27(3):135-40.
- 10) Tsang P. C. S, Samaranyake, L. P. Oral manifestations of HIV infection in a group of predominantly ethnic Chinese. J Oral Pathol Med. 1999;28:122-27.
- 11) Nittayananta W, Chanowanna N, Winn T, Silpapojakul K, Rodklai A, Jaruratanasirikul S, Liewchanpatana K. Co-existence between oral lesions and opportunistic systemic diseases among HIV-infected subjects in Thailand. J Oral Pathol Med. 2002 Mar;31(3):163-8.
- 12) Reichart PA, Khongkhunthian P, Bendick C. Oral manifestations in HIV-infected individuals from Thailand and Cambodia. Med Microbiol Immunol. 2003 Aug;192(3):157-60.
- 13) Bravo IM, Correnti M, Escalona L, Perrone M, Brito A, Tovar V, Rivera H. Prevalence of oral lesions in HIV patients related to CD4 cell count and viral load in a Venezuelan population. Med Oral Patol Oral Cir Bucal. 2006 Jan 1;11(1):E33-9.
- 14) Krammer IR, Pindborg JJ, Bezroukov V, Infirri JS. Guide to epidemiology and diagnosis of oral mucosal diseases and conditions. World Health Organization. Community Dent Oral Epidemiol. 1980;8:1-16.
- 15) Greenspan JS, Barr CE, Sciubba JJ, Winkler JR. Oral manifestations of HIV infection: definitions, diagnostic criteria and principles of therapy. Oral Med Oral Pathol Oral Radiol. 1992;73:142-44.
- 16) [No authors listed]. Classification and diagnostic criteria for oral lesions in HIV infection. EC-Clearinghouse on Oral Problems Related to HIV Infection and WHO Collaborating Centre on Oral Manifestations of the Immunodeficiency Virus. J Oral Pathol Med. 1993 Aug;22(7):289-91.
- 17) Marcenes W, Pankhurst CL, Lewis DA. Oral health behaviour and the prevalence of oral manifestations of HIV infection in a group of HIV positive adults. Int Dent J. 1998;48(6):557-62.
- 18) Pinheiro A, Marcenes W, Zakrzewska JM, Robinson PG. Dental and Oral lesions in HIV infected patients: a study in Brazil. Int Dent J. 2004(3);54:131-7.
- 19) Kerdpon D, Pongsirwet S, Pangsomboon K, Iamaroon A, Kampoo K, Sretrirutchai S, Geater A, Robison V. Oral manifestations of HIV infection in relation to clinical and CD4 immunological status in northern and southern Thai patients. Oral Dis. 2004 May;10(3):138-44.
- 20) Tappuni AR, Fleming GJP. The effect of antiretroviral therapy on the prevalence of oral manifestations in HIV-infected patients: a UK study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2001;92:623-8.
- 21) Margiotta V, Campisi G, Mancuso S, Accurso V, Abbadessa V. HIV infection: oral lesions, CD4+ cell count and viral load in an Italian study population. J Oral Pathol Med. 1999 Apr;28(4):173-7.
- 22) Campo J, Del Romero J, Castilla J, García S, Rodríguez C, Bascones A. Oral candidiasis as a clinical marker related to viral load, CD4 lymphocyte count and CD4 lymphocyte

- percentage in HIV-infected patients. J Oral Pathol Med. 2002 Jan;31(1):5-10.
- 23) Campisi G, Pizzo G, Mancuso S, Margiotta V. Gender differences in human immunodeficiency virus-related oral lesions: an Italian study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2001 May;91(5):546-51.
- 24) McCarthy GM, Mackie ID, Koval J, Sandhu HS, Daley TD. Factors associated with increased frequency of HIV-related oral candidiasis. J Oral Pathol Med. 1991 Aug;20(7):332-6.
- 25) Brig Sharma YK, Col Sawhney MPS, Lt Col Bhakuni DS, Maj Gera. Orocutaneous manifestations as markers of disease progression in HIV infection in Indian setting. MJAFI. 2004; 60:239-43.
- 26) Coogan MM, Greenspan J, Challacombe SJ. Oral lesions in infection with human immunodeficiency virus. Bull World Health Organ. 2005 Sep;83(9):700-6. Epub 2005 Sep 30.
- 27) Nielsen H, Bentsen KD, Hojtvad L, Willemoes EH, Scheutz F, Schiodt M, Stoltze K, Pindborg JJ. Oral candidiasis and immune status of HIV-infected patients. J Oral Pathol Med. 1994;23:140-43.

**Source of support:** Nil

**Conflict of interest:** None declared

This work is licensed under CC BY: *Creative Commons Attribution 3.0 License*.