Original Article

Correlation of CD4 counts with oral and systemic manifestations in HIV patients

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ABSTRACT

Aim: Aim of the study was to correlate CD4 counts with oral and systemic manifestations in HIV patients. **Materials and Methods:** Study population comprised of newly diagnosed 100 confirmed seropositive patients, before starting any antiretroviral therapy, were included. The oral lesions were diagnosed based on clinical manifestation using international criteria and CD4 count was determined within maximum 1 week of oral examination. Oral and systemic manifestations of HIV-positive patients were recorded and correlated with CD4 counts. **Results:** It was found that decrease in CD4 count is associated with a wide range of oral and systemic manifestations which can be used as prognostic marker for immune suppression in AIDS patient. **Conclusion:** Correlation of CD4 count with oral and systemic manifestation in HIV patient demonstrate the role of oral physician in identification, diagnosis, and treatment of HIV-associated lesions, providing proper guidance to the patient and allowing for an early diagnosis and treatment of the disease, which is fundamental for a successful management of the life conditions of HIV infected patients.

Keywords: Candidiasis, CD4 count, chronic genralized periodontitis, HIV, oral manifestations

Introduction

Acquired immunodeficiency syndrome (AIDS) is a disease caused by human immunodeficiency virus (HIV) infection which emerged as a pandemic in the last three decades.[1] Approximately, 36.9 million people are living globally with this infection. India itself accounts for the third largest number of HIV infected people in the world (around 2.1 million) after South Africa and Nigeria. However, UNAIDS (2018) data suggested a marked decrease in the number of new infections and AIDS related deaths by 27% and 56%, respectively, from the period of 2010--2017. The same data also estimated HIV prevalence among adults in India (15--49) to be 0.2% in which 79% of them were aware of their HIV status and 56% of them were on the anti-retroviral therapy (ART). In spite of this awareness against HIV, there were marked increase in the new infections to 88,000 from 80,000 and AIDS related deaths to 69,000 from 62,000 in the year 2017. And that's why, HIV infection is still a major health concern in India.[1] The report by UNAIDS, the United Nations programme on HIV/AIDS, said that 19 million of the 35 million people living with the virus globally do not know their HIV positive status and there will be a major AIDS pandemic threat by 2030.[1,2] HIV is a retrovirus which effects the human immune system. This virus hinders the body's defense

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mechanism by depletion of cluster of differentiation 4 (CD4) cells.[3] Human immune deficiency virus is a RNA retrovirus which attacks the immune system leading to suppression of immunity of a person infected and weakens the body defense to a level that human body becomes extremely prone to infections and cross-infections over a period of time.[4] This renders the patient susceptible to opportunistic infections and malignancies. Absolute CD4 count has been widely used as lab marker for immune suppression in HIV infection.[5,6] Specific common oral lesions and systemic manifestations have been documented to be related with immune suppression as indicated by CD4 counts that has been widely studied and reported in developed countries. However, documentation and relation of CD4 count with oral and systemic manifestation in Asian countries specifically India have been sparse.

There are considerable regional variations in the oral manifestations of HIV infection, depending both on the populations studied and on the clinical heterogeneity. The oral manifestations in Asian countries as compared to western countries and other developing nations in Africa and Latin Americas are relatively different. The constraint of resources in Asian countries hinders the possibility of providing an effective healthcare system. Though many studies have been conducted on oral manifestations in HIV, the research in Asia is currently at a pivotal juncture as the existing research is getting repetitive.[7,8] Currently, Asian studies predominantly focus on prevalence of oral manifestations and assess their association with parameters of HIV infection, sociodemographic data, and deleterious habits. Hence, a cross-sectional study was undertaken among HIV population in western India, Gujarat with objectives to (1) to calculate CD4 count of HIV-positive patients, (2) to evaluate systemic manifestations of HIV-positive patients, (3) to detect oro-maxillofacial manifestations in HIV-positive patients, (4) to compare and correlate systemic and oro-maxillofacial manifestations of HIV-positive patients with the CD4 count.

HIV infection is a major health concerned in India. The importance of oral lesions as clinical features have been reported worldwide. However, there are very few reports on correlation of systemic and oral manifestations of HIV seropositive individuals with CD4 count in Indian subcontinent especially the western region.

Study Population

The total of 100 HIV seropositive subjects were screened for the cross-sectional prospective study over a period of 3 years starting from January 2007--2010 with the approval of institutional research ethical committee SUVEC/ON/20/2007 (dated 20-08-2007) along with approval taken from NACO to conduct the study. Written informed consents were taken from all the participants in their regional language. The patients were selected from outpatient departments of infectious disease, Dheeraj General Hospital, Department of Oral Medicine and Radiology, K M Shah Dental College and Hospital Piperia,

Vadodara, and non-governmental organizations working for HIV-positive individuals in Vadodara for a period of over 3 years. Newly diagnosed HIV seropositive patients before starting anti-retroviral therapy (ART) were selected. Participants were excluded who already started ART and who were not ready to be part of study preclude informed consent. The personal and medical history along with the findings of oral examination and investigations were recorded in the proforma specially designed for this study. Patients according to CD4+ counts were clustered into three groups and randomly selected: 0–200 cells/mm³, 201–499 cells/mm³, and more than 500 cells/mm³. A single examiner trained in oral diagnosis examined and recorded all oromucosal lesions. Oral lesions were diagnosed according to presumptive criteria of EEC Clearinghouse Classification.[9]

Statistical analysis

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) version 17 statistical analysis software. The tests used for analysis were *t*-test for independent samples, Chi-square test, and Pearson's correlation. Probability values (*P* value) were obtained and the statistical significance of the data was determined.

Results

The study group consisted of total 100 HIV seropositive, 57 (57%) males, and 43 (43%) females. The age range for study group was from 6 years to 65 years with mean age of 34.14 ± 11.51 years. In study group, out of total 57 males, 40 (70%) were married, 12 (21%) were unmarried, 4 (7%) were divorcees, and 1 (1.75%) was widower, whereas out of total 43 females, 25 (58.13%) were married, 5 (11.6%) were unmarried, 2 (4.65%) were divorcees, and 11 (25.5%) were widows. Most common mode of HIV transmission was unprotected sexual practices (70%) followed by blood transfusion (18%), vertical transmission (9%), and intravenous drug users (3%). In study group, mean CD4 count in males was 253.51 ± 220.773, whereas it was 230.86 ± 153.327 in females. On applying independent *t*-test no correlation was found between CD4 count of males and females population ($P > 0.005$). In study group of 100 patients, 55% patients had CD4 count below 200 (Category C), 34% had CD4 count between 201 and 499 (Category B), and 11% had CD4 count above 500 (Category A) as shown in Table 1. Out of total 57 males, 21 (36.8%) had tuberculosis followed by 3 (5.2%) cases of herpes zoster, 2 (3.5%) cases of pneumonia, 1 (1.75%) case of typhoid, jaundice, and malaria each. Out of total 43 females, 13 (30.2%) had tuberculosis, 2 (4.6%) cases of pneumonia, 2 (4.6%) cases of anemia, 2 (4.6%) of typhoid. The most common systemic manifestation in HIV-positive patients was tuberculosis [Table 2]. Out of total 55 patients in the category C, 34 (61.8%) had systemic manifestations. In the category B, out of 34 patients 12 patients (35.2%) had systemic manifestations, whereas only 2 (18.1%) patients out of 11 had systemic manifestation in the category A as shown in Table 3. On applying Chi-square test for statistical analysis, *P* value was less than 0.05 which showed a significant correlation between

the systemic manifestations and CD4 count categories. In study group of 100 subjects, 17 (20.2%) had candidiasis, 14 (16.6%) cases of chronic generalized periodontitis, 9 (10.7%) gingivitis, 7 (8.3%) apthous 6 (7.1%) premalignant lesions and conditions, 4 (4.7%) complained of recurrent apthous ulceration and angular chelitis each, 3 (3.5%) cases each of erythema multiformae and hairy leukoplakia, 2 (2.3%) herpes zoster, herpes labialis, and periodontal abscess each and remaining others had single lesions like fissured tongue, mucous patches of secondary syphilis, acute necrotizing ulcerative periodontitis, linear gingival erythema, molluscum contagiosum, and oral pemphigus as seen in Figure 1. The most common oral manifestation in males was found to be candidiasis 12 (21%) and chronic generalized periodontitis in 11 (19.2%) cases with an average CD4 count of 322.46 ± 219.14 and 191.76 ± 120.05, respectively, whereas in females the common oral manifestations was candidiasis and apthous in 5 (11.6%) cases with an average CD4 count of 191.76 ± 120.05 and 130.08 ± 77.35, respectively. Most frequently encountered variant of candidiasis was pseudo-membranous candidiasis in total 9 (52.9%) patients (5 males and 4 females), while 6 (35.2%) patients (5 males, 1 female) had erythmatous candidiasis and only 2 (11.7%) patients (2 males) had hyperplastic type of candidiasis. Thus, the most common oral manifestation was candidiasis in males and candidiasis and recurrent apthous in females [Table 4]. In study group out of 100 HIV-positive patients, 84 showed oral manifestations. In the category of CD4 count below 200 (Category C) out of 55 patients, 54 (99%) had oral manifestations. In patients having CD4 count between 200 and 499 (Category B) out of 34 patients, 30 patients (88.2%) had oral manifestations whereas no oral manifestations (0%) were seen in patients with CD4 count above 500 (Category A). On applying Chi-square test for statistical analysis, P value was less than 0.05 (0.027) which showed a significant correlation between the oral manifestations and CD4 count categories (Figure 2 and Table 5).

Discussion

Oral health is general health. Screening and diagnosis is crucial to understand the disease and obtain a certain diagnosis. Counteractive action and treatment of HIV contamination have changed impressively in the previous couple of years. Refreshed screening proposals give family doctors a significant job in evaluating patients in danger of HIV disease, distinguishing the individuals who are tainted, and suggesting treatment choices. Oral manifestations of HIV gives us probable diagnosis to
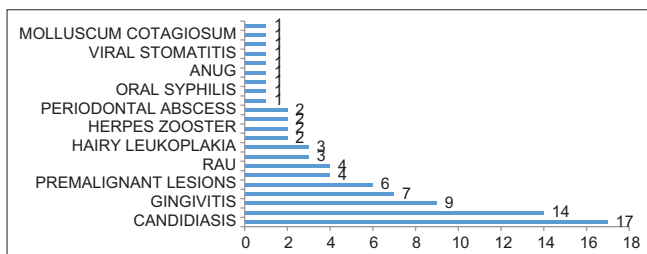
undergo definitive diagnosis for proper care. Family doctors may choose to allude a few patients to a HIV sub-specialist for helpful medications, they may keep on giving irregular or ceaseless consideration to these patients. Additionally, it is significant for family doctors to perceive intricacies of treatment and potential prescription communication. This is prime form in primary care.

HIV-associated oral lesions are frequent and often an early finding in HIV infection.[10] These lesions are not only important for morbidity but also helpful for diagnostic value in monitoring the immune status of patient. CD4 count can be easily used as prognostic marker in cases of HIV infections. The fall in CD4 count below 200/μml leads to severe immune deficiency which

Table 1: Gender-wise distribution of study group according to CD4 count categories

CATEGORIES	CD4 COUNTS	MALES	FEMALES
A	>500	7	4
B	200--499	17	17
C	<200	33	22
TOTAL	--	57	43

Table 2: Systemic manifestations in study group

Most Common Systemic Features	Study Group (*n*=100)	
	MALE (*n*=57)	FEMALE (*n*=43)
Tuberculosis	21	13
Pneumonia	2	2
Anemia	0	2
Jaundice	1	0
Typhoid	1	2
Herpes	3	0
Malaria	1	0

Table 3: Correlation of CD4 count categories with systemic manifestations

CATEGORIES	CD4-COUNT	TOTAL PATIENTS	SYTEMIC MANIFESTATIONS
A	>500	11	2
B	200--499	34	12
C	<200	55	34 (*P*<0.05)

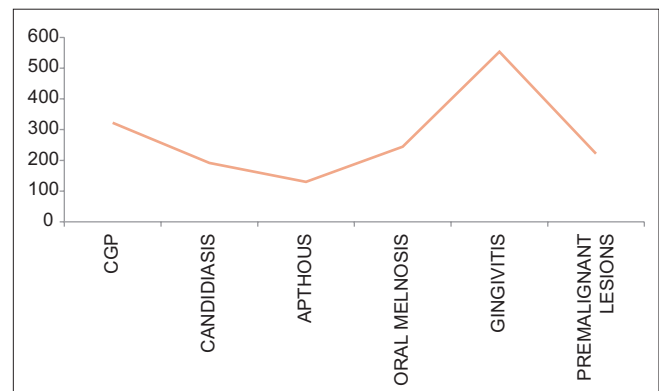**Figure 1:** Oral manifestations in HIV-positive patients

Figure 2: Correlation of oral manifestation with CD-4 count

Table 4: Most common oral manifestation in males and females of HIV patients

ORAL MANIFESTATIONS	TOTAL (*n*=84)	MALES (*n*=48)	FEMALES (*n*=36)	AVG CD4 COUNT	STD DEVIATION
Candidiasis	17	12	5	191.76	120.05
Chronic Generalized Periodontitis	14	11	3	322.466	219.14
Apthous	13	8	5	130.08	77.35
Gingivitis	9	5	4	553.4	273.96
Premalignant Lesions	6	4	2	221.857	99.8

Table 5: Correlation of CD4 count categories with oral manifestations

CATEGORIES	CD4 COUNT	TOTAL PATEINTS	ORAL MANIFESTATIONS
A	>500	11	0
B	200--499	34	30
C	<200	55	54 *P*<0.05

Table 6: Gender-wise comparison of CD4 counts with previous studies

Author	Year	CD4 count	
		Males	Females
Campisi *et al.*	2001	325.3±144	225.3±124
K. Ranganathan *et al.*	2004	295.28±270.53	453.77±376.98
Vohra *et al.*	2010	253.51±220.73	230.86±153.32

can be easily manifested in form of various oral and systemic manifestations. This has been studied by various researchers since 1994.[8,10-12] Glick *et al.* in 1994 suggested oral manifestation associated with HIV related disease as marker for immune suppression and AIDS. Greenspan *et al.* in 1997 suggested the epidemiological significance of oral manifestation in HIV disease. We calculated CD4 count of study group and their systemic and oral manifestations were recorded in a preformed proforma.

The mean average CD4 count in males was 253.51 ± 220.73 and 230.86 ± 153.32 in females, respectively. Thus there was no significant difference in the average CD4 counts of males and females as previously reported by Campisi *et al.* in 2001 and K. Rangnathan *et al.* in 2004.[13,14] The average CD4 count in males and females recorded by Campisi *et al.* and K. Rangnathan *et al.* is given in Table 6.

The distribution of study population was done according to CD4 count by EEC clearing house classification as categories A (CD4 count above 500), B (CD4 count between 201 and 499) and C (CD4 count below 200). It was found that 7 (7%) males and 4 (4%) females had CD4 count above 500 (Category A), whereas 17 (17%) males and females each had CD4 count between 200 and 499 (Category B). There were 33 (33%) males and 22 (22%) females had CD4 count below 200 (Category C).

In study group, 48 (48%) of HIV-positive individual had systemic manifestation. The systemic manifestations were seen in 2 (18.1%), 12 (35.2%), and 34 (61.8%) patients in category A, B, and C, respectively. On applying Chi-square test, the *P* value

was less than 0.05 which suggested a significant correlation between the systemic manifestations and CD4 counts categories. There were 29 males and 19 females in which the systemic manifestations were recorded. Out of 29 males, 21 (72.4%) had tuberculosis followed by 3 (10.3%) cases of herpes zoster, 2 (6.8%) cases of pneumonia, 1 (3.4%) cases of typhoid, jaundice, and malaria each. Out of 19 females, 13 (68.4%) had tuberculosis, 2 (10.5%) cases of pneumonia, anemia, and typhoid each.

Thus, the most common systemic manifestation in HIV-positive males and females was tuberculosis (70.4%) and the average CD4 count of these patients was 190.58 ± 149.01 which was congruent to previous studies conducted by K. Ranganathan *et al.* in the year 2000 and 2004.[8,14]

In the study group, 84 (84%) patients had oral manifestations. The oral manifestation were seen in 30 (88.2%) and 54 (99%) individuals in Category B and C, respectively, whereas no oral manifestations were noted in Category A. These results were highly significant with *P* value of 0.027 (<0.05), suggesting correlation of oral manifestation with CD4 count categories.

Similar high frequency of 76.5% and 85% of oral lesions in HIV-positive patients have also been reported by Marcenes *et al.* in 1998 and Bravo *et al.* in 2006, respectively, but recent study by Erick *et al.* in 2008 only, 47% of total 79 HIV-positive patients exhibited oral lesions.

In our study, 17 (20.2%) had candidiasis, 14 (16.6%) cases of chronic generalized periodontitis, 9 (10.7%) had gingivitis, 7 (8.3%) cases of apthous, 6 (7.1%) premalignant lesions and conditions, 4 (4.7%) complained of recurrent apthous ulceration and angular chelitis each, 3 (3.5%) cases each of erythema multiformae and hairy leukoplakia, 2 (2.3%) cases of herpes zoster, herpes labialis, and periodontal abscess each and remaining others had single lesions like fissured tongue, acute necrotizing ulcerative periodontitis, linear gingival erythema, molluscum contagiosum, and oral pemphigus.

Out of total 84, the oral manifestations were seen in 48 (57%) males and 36 (42.8%) females.

The common oral manifestations recorded in males were candidiasis (25%), followed by chronic generalized periodontitis (22.9%), apthous stomatitis (16.6%), gingivitis (10.4%), and premalignant lesions (8.3%).

The common oral manifestations recorded in females were candidiasis (13.8%) and apthous stomatitis (13.8%), followed by chronic generalized periodontitis (8.3%), gingivitis (11.1%), and premalignant lesions (5.5%).

Unlike the previous studies by Campisi *et al.* and K. Rangnathan *et al.*, no significant difference was found in prevalence of oral lesions in both sexes in our study.[13,14] Campisi *et al.* found the higher prevalence of oral lesions in males, whereas K. Rangnathan *et al.* found higher prevalence of oral lesions in females.

The most common oral manifestation in males and females was found to be candidiasis (19.4%) with the average CD4 count of 191 ± 120.05 and the most common variant of candidiasis encountered was pseudomembranous type. These results are consistent with findings by various other investigators[8,15-18] who examined oral lesions and conditions associated with HIV-positive patients.

It was found that decrease in CD4 count is associated with a range of oral and systemic manifestations and can be used as prognostic immune depression markers which could be helpful for management of AIDS patients. These results were congruent with previous studies.[8,9,11,14-21]

Conclusion

The main mode of HIV transmission in males is unprotected sexual practices with multiple partners including commercial sex workers by heterosexual route and most of women has acquired HIV infection from there infected spouses. There was no significant difference in the average CD4 count of males and females. Most common systemic manifestation of HIV-positive patients in both males and females was tuberculosis. Oral manifestations were recorded in almost all HIV-positive patients with CD4 count below 500. There is equal prevalence of oral lesions in both sexes. Most common oral manifestation in both males and females is candidiasis with CD4 count below 200. Limitation of the study is that there was no significant correlation between any particular oral lesion and CD4 count. There is a significant correlation between decrease in CD4 count and prevalence of oral lesions, therefore decrease in CD4 count can be used as a prognostic marker in HIV-positive patients but to exactly pin point which particular oral or systemic manifestation has to have direct correlation with disease progress and formulate a classification based on that similar studies with larger sample size and different geographical locations in India have to be conducted.

Summary

Correlation of CD4 count with oral and systemic manifestation in HIV patient demonstrate the role of oral physician in identification, diagnosis, and treatment of HIV associated lesions, providing proper guidance to the patient and allowing for an early diagnosis and treatment of the disease, which is fundamental for a successful management of the life conditions of HIV infected patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflicts of interest

There are no conflicts of interest.

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