Original Article

Periodontal status in HIV-positive individuals and its possible correlation with CD4+T cell count

Abstract

Background: Infection with human immunodeficiency virus (HIV) results in loss of immunologic functions, especially those coordinated by CD4+ T-helper cells and consequent impairment of immune response. Periodontal disease has been associated with HIV infection, and HIV infection has been considered a modifier of periodontal disease. **Aim:** The aim of this study was to report the severity of periodontal disease in HIV-positive individuals and its association between clinical periodontal indices and CD4+T-cell count. **Materials and Methods:** 25 HIV-positive individuals were recruited and medical history was recorded. To evaluate periodontal disease, clinical attachment loss (CAL), oral hygiene index (OHI), and gingival bleeding index (GI) were recorded. Immune suppression was measured by peripheral blood CD4+T cells/mm^3 as analyzed by flow cytometry. **Statistical Analysis:** Association between CD4+ T levels and clinical parameters were determined using correlation coefficient test. **Results:** When all subjects were evaluated, a negative correlation was obtained between CD4+ T-cell count and clinical attachment loss (r = -0.68226). In individuals with CD4+cell counts <200 cells/ mm^3, a negative correlation was obtained between clinical attachment loss (-0.35467) and GI (-0.35202). In patients with CD4 count <200, a negative correlation was obtained between CAL (-0.30361), GI (-0.29711), and OHI (-0.14669). **Conclusion:** Immune suppression in combination with risk factors may increase progression of periodontal disease. Hence, these individuals should practice better oral hygiene and regular follow-up.

Key words:
CD4+T cell count, HIV, periodontal disease

Introduction

Infection with human immunodeficiency virus (HIV) results in loss of immune functions, especially those coordinated by CD4+ T-helper cells and consequent impairment of immune response. The course is associated with further depletion of CD4+ cells and increasingly severe disease manifestation.[1]

Periodontal manifestations in patients with HIV infection were first described in 1987.[2] HIV infection in adults is linked with the expression of various types of periodontal lesions, which include specific form of gingivitis and periodontal disease.[3] HIV-infected individuals usually present more severe periodontitis than non-HIV subjects. Areas of necrosis and ulceration may be present probably as a result of immune suppression. The association of between HIV infection and gingivitis, pocket depth, and attachment loss has been shown to be independent of other known risk factors for periodontal diseases, such as age, subgingival biofilm, and smoking.[4] Lamster *et al*,[5] theorized that persons with different behavioral risk factors, and thus lifestyles, may present with different clinical manifestation of the HIV disease.

Other reports have demonstrated that the prevalence of periodontal disease in HIV-infected patients is highly variable.[6] Some cross-sectional investigations have failed to detect any difference in prevalence and severity of

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periodontal disease in HIV/AIDS individuals compared with healthy controls. This may be due to the different clinical criteria used to define periodontitis, as well as population studied and the presence of antiretroviral therapy.[7] The HAART regimen has resulted in a significant reduction in mortality and morbidity.[8] These benefits may be extended to the oral cavity by decrease in prevalence of oral diseases, but the impact of these changes in periodontal disease is less clear.[9]

Persons in early stages of HIV infection appear to present with good periodontal health, but progressive HIV disease may increase the susceptibility to severe chronic periodontitis. It has been suggested that in immunocompromised HIV patients, preexisting periodontitis may be exacerbated and, thus, HIV infection can be considered as modifier of periodontitis. However, the question of whether the stage of HIV disease, as expressed by CD4+ cell counts, affects the course and severity of chronic periodontal disease still remains unclear.

The purpose of this study was to report the prevalence and severity of periodontal disease in HIV individuals and to investigate the association between the clinical periodontal indices and the stage of HIV disease, as expressed by CD4+ cell count.

Materials and Methods

This study was conducted in the Department of Periodontics KLE's Institute of Dental Sciences, Belgaum, Karnataka. In all, 25 HIV-positive individuals who were serologically confirmed with mean age of 37 years who were hospitalized for medical care in KLE's medical hospital and research center, Belgaum, were included in this study. All participants enrolled in this study were verbally explained regarding the examination procedure. Ethical clearance was obtained before the commencement of study. Participants were privately and confidentially interviewed to obtain information regarding general health, age, medical history and medications, social history of alcohol, and tobacco use. The subjects were clinically grouped according to the Center for Disease Control (CDC) classification for HIV infection after their medical history was reviewed. Participants were excluded from the study if they were unable to tolerate the periodontal examination. CD4+T-cell counts were obtained from their records as analyzed by flow cytometry. Patients were excluded if their CD4+ T-cell count was not updated within last 1 month.

Exclusion criteria included pregnancy, nursing, diabetes, patients on antibiotics, and with history of antiviral therapy.

Periodontal examination was done with the aid of William's graduated probe at six sites around each tooth excluding third molars. Assessment of gingivitis and oral hygiene status was done by gingival index (GI)[10] and oral hygiene index simplified,[11] respectively. For assessment of clinical attachment loss, the number of sites with attachment loss of >4 mm was recorded. The presence of any other oral lesions was recorded.

Statistical analysis

Analysis of association between the periodontal parameters and CD4+ T cell count was performed by correlation coefficient test. The level of significance "*P*" value at 95% confidence interval was calibrated as nonsignificant: $P>0.05$, significant: $0.01 < P < 0.05$ and highly significant: $P<0.001$.

Results

In all, 25 participants had mean age of 37 years (range 28-54 years). Over 92% of them were males out of which 30% were smokers. CD4+ cell count ranged from 30.3 –to 470 cells/mm^3 with mean of 207.86 cells/mm^3. In all, 15 subjects were grouped under severe immune suppression with CD4+ cell count <200 cells/mm^3 (mean 100.4 cells/mm^3) and remaining under mild to moderate immune suppression (CD4+ count: 200–500 cells/mm^3) (mean 358) [Table 1]. The most prevalent HIV-related oral mucosal conditions were oral candidiasis (24%), nonspecific ulcer (12%), and oral hairy leukoplakia (4%) of subjects. The

Table 1: Age, sex, and CD4+T-cell count of patients

Age	Sex	CD 4 +T-cell count	Other findings
28	M	120	
27	M	54	Oral cindidiasis
26	M	450	
42	M	199	
35	M	225	
37	M	470	Ulcer
29	F	104	
31	M	83	
28	M	179	Oral cindidiasis
45	M	351	
50	M	410	
51	M	30	Oral candidiasis, oral hairy leukoplakia
29	M	359	
33	M	75	Oral cindidiasis
42	F	315	
44	M	35	
36	M	177	Ulcer
34	M	350	
30	M	400	
31	M	70	
47	M	84	
48	M	250	
54	M	165	Oral cindidiasis
50	M	140	Ulcer
29	M	101	Oral cindidiasis

prevalence of oral candidiasis was 33.3% in patients with CD4+ cell count <200 cells/mm^3 compared with 10% in patients with CD4+ cell count >200 cells/mm^3.

When all patients were evaluated, a negative correlation was obtained (r = -0.68266) between CD4 count and CAL only. Individuals with CD4 count >200 cells/mm^3 were evaluated for this group, a negative correlation was obtained between CD4 cell count and CAL (-0.35467) and GI (-0.35202). Individuals with CD4 cell count <200 cells/mm^3 were evaluated for this group and a negative correlation was obtained between CD4 cell count and CAL (-0.30361) and GI (-0.29711) and OHI (-0.14669) [Table 2].

The most prevalent HIV-related mucosal condition was oral candidiasis which was found in 24% of subjects, nonspecific ulcers in 12%, and oral hairy leukoplakia in 4% of them. The prevalence of candidiasis was 33% in patients CD4 count <200 cells/mm^3.

Discussion

Several studies have shown the association between the severity of periodontal disease and HIV infection, mainly in condition of severe immune suppression determined by decrease in CD 4+ cell count.[12]

Others, however, have indicated that the periodontal status in HIV-infected individuals is comparable to noninfected individuals[13] Many studies refer to HIV-infected individuals, without mentioning the stage of AIDS or the use of antiretroviral therapy, the use of protease inhibitors or not, as well as the use of adjunctive use of antimicrobials. Factors that influence periodontal disease such as smoking and oral hygiene are not always taken into consideration. In view of the previous studies suggesting increased severity and prevalence of periodontal disease in HIV-positive individuals, we examined the association of periodontal indices to CD4 count.

Our study reported individuals with immune suppression in both groups presented with higher gingivitis score and displayed more clinical attachment loss.

Similar to this study, Barr *et al*[14] assessed the attachment loss over 20-month period. Periodontal changes were analyzed in relation to HIV-1 serostatus, immune status, age, and plaque. GI, plaque index, and relative attachment levels recorded by the computerized Florida disk probe were performed every 4 months. RAL ≥3 mm occurred 6.16 times more frequently among subjects with T4 counts <200 compared with subjects with counts of 200 or more. They concluded that immunosuppression, especially in combination with older age, may be a risk factor for attachment loss, and HIV seropositivity, independent of T4 cell counts, may be a risk factor for gingival inflammation.

Robinson *et al*[4] reported a higher prevalence of chronic gingivitis and adult periodontitis in HIV-infected individuals. They also reported an increased risk of periodontal attachment loss and gingival recession without increase in pocket depth. Smith *et al*[15] in cross-sectional study reported that progressive HIV disease may increase susceptibility to chronic periodontitis.

Similarly, Mckaig *et al*[12] in a southeastern US HIV-positive population reported that HIV patients with extreme immune suppression (CD 4 <200 cells/μl) were less likely to have increased probing depth when compared with patients with cd4+ count >200 cells/μl.

It has been suggested that T cell could modulate bacterial-induced periodontal inflammation and alveolar bone destruction.[16] However, the exact role of T-cell subtypes and B cell in periodontitis, the role of antibacterial immunity in local bone destruction, and the mechanisms by which host immune response contribute to bone destruction and tooth loss remains unclear. In a study with immunodeficient mice which lacked B and T lymphocytes, considerably less bone loss was observed after oral infection with p gingivalis. Also, it has been proved that mice lacking CD4, but not CD8+ T cells, loose less alveolar bone in response to oral infection than do immunocompetent mice of same genetic background, indicating that CD4+T cells contribute to bone resorption.[17]

Contradictory results have also been reported by Vastardis *et al*,[18] who investigated the association between clinical periodontal indices and the stage of HIV disease, as expressed by CD4 cell counts. Immunocompromised patients showed significantly lower BI and fewer sites with PD and CAL >4 mm compared with patients with CD4 cell counts >200 cells/μl. When patients with CD4 counts <500 cells/μl were considered alone, a correlation was observed between CD4 cell counts and bleeding index.

Table 2: Correlation between CD4+ cell count and periodontal parameters all patients, in patients with CD4+ cell count >200 cell/mm^3 and in patients with <200 cell/mm^3

CD 4+T-cell count	All subjects	CD4 T cells more than 200	CD4 T cells less than 200
Clinical attachment loss	–0.68226	–0.35467	–0.30361
Gingival index	0.29088	–0.35202	–0.29711
Oral hygiene index	0.23875	0.43394	–0.14669

Yeung *et al*[19] studied prospectively over an 18-month period 30 HIV infected, but asymptomatic, patients and compared the rate of periodontal attachment loss with that of a healthy control group matched for age and plaque index. Every 6 months, there was no correlation between any clinical parameter measured and periodontal status as determined by PI or GI. However, a significant difference in the change of periodontal disease index was observed between the HIV-infected and control groups. They concluded that HIV-infected patients with preexisting periodontitis tend to experience a greater rate of attachment loss over time compared with controls.

Silvin *et al* observed[20] clear reduction in gingival parameters and improvement in gingival condition in different HIV staging groups evident after mechanical therapy. They concluded that oral hygiene including supportive periodontal therapy improves gingival condition and not dependent on immunodeficiency when an oral hygiene protocol is applied.

Together with other oral infections, HIV-associated periodontal diseases are regarded as serious complications of HIV infection and have an important diagnostic and prognostic value. They belong among the earliest clinical features of the infection and could predict progression of HIV disease to AIDS.[21]

Introduction of antiretroviral therapies and mainly the HAART in 1995 has changed the epidemiology of opportunistic infections in HIV-infected patients and has decreased the mortality and morbidity of HIV infection.[22] After the introduction of HAART, findings from relevant studies also vary and cannot be compared, partly because of the different types of therapy received by participating patients.

Among oral manifestation, oral candidiasis[23] appears to be the lesion most significantly decreased after introduction of HAART therapy. Our study reported that the prevalence of oral candidiasis was 33.3% in patients with CD4+ cell count <200 cells/mm^3 compared with 10% in patients with CD4+ cell count >200 cell/mm^3. Oral opportunistic infections, mainly oral candidiasis and oral hairy leukoplakia, have been associated with CD4+ count in both the pre-HAART and the HAART era in several studies. Based on these findings, low CD4+ counts are now considered as the main risk factor associated with the development of oral lesions and especially of oral candidiasis.[24] It should also be mentioned that for patients on antiretroviral therapy, HIV-related oral lesions in general may suggest possible treatment failure.

However, HIV-associated periodontal infections are less common than oral candidiasis and oral hairy leukoplakia and thus not included as criteria in the CDC classification. Overall, findings from the above mentioned studies suggest the value of the identification of periodontal disease, even in patients on HAART therapy, in screening the immune suppression, both in diagnosed and undiagnosed HIV infection in adults.

Conventional periodontitis progresses gradually, causing no or minimal pain or discomfort, being thus undiagnosed, until considerable tissue loss occurs. Research nowadays is focused on the accelerated rate with which chronic adult periodontitis presents in seropositive patients.[25]

Limitation

Limitation of the study is the relatively small number of patients. In order to reach more reliable conclusion, more number of patients should be included. No healthy controls were included to serve as controls, because the different cohorts of HIV+ patients were compared with one another.

Conclusion

It can be concluded that the progression of periodontal disease in the presence of HIV infection is dependent on the immunologic competency of the host and the local inflammatory response to typical and atypical subgingival microorganisms.

The multifactorial nature of periodontal disease in combination with complex evolution of HIV makes interpretation of data difficult. In these individuals, the CD4 +T-lymphocyte dependent mechanism is lost resulting in prolonged activation of neutrophils and increased risk of periodontal disease progression.

Immune suppression in combination with age may be a risk for attachment loss and gingival inflammation. Hence, these individuals should practice good oral hygiene, require frequent dental treatment, and follow-up.

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