HIV - infection and Periodontal disease: a Hidden Truth

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ABSTRACT:
The association of periodontal disease in HIV-infected patients had been initially considered to be the first clinical expression or indication of profound immunodeficiency and stage of HIV-disease as expressed by CD₄-cells in the peripheral blood circulation. Three entities were majorly described and are strongly associated with HIV-infection include (a) Linear gingival erythema (LGE), (b) Acute necrotizing ulcerative gingivitis (ANUG) and (c) Acute necrotizing ulcerative periodontitis (ANUP). Many studies and case reports initially had reported higher prevalence of periodontal disease and also higher severity and rapid progression of existing gingivitis or periodontitis which was clinically assessed by measuring periodontal pockets and attachment loss. The prevalence and severity of periodontal disease in HIV-seropositive or AIDS patients is due to severe immune suppression expressed by rapid depletion of CD₄-cells/T-helper cells. HIV-infected patients are more prone to get periodontal disease when the CD₄-cell count falls below 200 cells/µL or the stage of HIV-infection progresses to AIDS. In contrast, considerable variation has been observed in recent studies that there were less severity of progression and prevalence of periodontal disease in AIDS patients whose CD₄-cell is below 200 cells/µL compared to HIV-infected patients whose CD₄-cell count is above 200 cells/µL. The aim of this article is to review old and present concepts based on studies and case reports and also to encourage researchers to explore the changing face of disease progression in HIV-positive individuals.

Key words: HIV-infection, AIDS, Periodontal disease, CD₄-cell count.

INTRODUCTION
The incidence and severity of infections are higher in patients with HIV-infection and AIDS, presumably due to impaired function of immune system and also greater propensity for getting opportunistic infections and tumors. Oral lesions are common among HIV-infected patients and associated oral manifestations of HIV-infection include Pseudomembranous Candidias, Hairy leukoplakia, Recurrent herpetic infections, Papilloma virus infection and Kaposi's sarcoma.¹,²,³,⁴ Indeed it is made clear that some of the oral lesions associated with HIV-infection are often considered as first clinical expression of HIV-infection or AIDS.

Several forms of periodontal diseases have been described in HIV-infected or AIDS patients. The commonly associated Periodontal disease in HIV-infected patients include a Rapidly progressive form of periodontitis named AIDS-virus associated periodontitis or HIV-associated periodontitis (HIV-P),...
clinically resembling Acute necrotizing ulcerative gingivitis. The clinical features of HIV-P includes rapid onset and progression, interproximal necrosis, ulceration and cratering, marked edema and erythema of attached and marginal gingiva, acute pain and spontaneous bleeding. The second common form of periodontal manifestation is characterized by marginal gingivitis accompanied by petechiae-like and diffuse red lesions of the attached gingiva and oral mucosa. The free gingival margin presents a distinct linear red band with an increased tendency to bleed spontaneously and it is resistant to conventional periodontal therapy. This lesion is being termed as HIV-associated gingivitis (HIV-G).

Another severe periodontal manifestation was also been described and associated with HIV-seropositive subjects, termed as Necrotizing stomatitis; characterized by widespread and rapid destruction of the periodontium, as well as adjacent hard and soft tissues. The severity of progression of chronic periodontitis in HIV-seropositive patients showed considerable variation. A number of studies reported rapid progression and higher severity of existing chronic periodontitis in HIV-seropositive patients with severe attachment loss. It has been suggested that the preexisting periodontitis may be exacerbated in HIV-infected patients due to the severe immunosuppression and also HIV-infection is being considered as modifier of periodontal disease. The prevalence and severity of periodontal disease in HIV-positive patients is because of severe immune deterioration especially those coordinated by CD4+ cells or T-helper cells and consequent impairment of immune response. The course of the HIV-infection is associated with further depletion of CD4+ T-cells, increasing the prevalence and severity of periodontal manifestations.

Currently, three periodontal disease entities were described which are considered to be common and also reported to be the first clinical expression of HIV-infection or an indication of severe immune deterioration as shown by CD4+ T-cell values include: (1) Linear gingival erythema (LGE), (2) Necrotizing ulcerative gingivitis (ANUG) and (3) Necrotizing ulcerative periodontitis (ANUP).

However recent studies have shown considerable lower rate of prevalence of NUG and NUP among HIV-positive individuals. In this regard a review of old and present concepts are done to know about new face of concept, regarding HIV-seropositive or AIDS patients with regards to prevalence and severity of periodontal manifestations with respect to the stage of HIV-infection as expressed by CD4+ - T-cell counts.

### 1993 REVISED CLASSIFICATION SYSTEM FOR HIV INFECTION AND EXPANDED AIDS SURVEILLANCE CASE DEFINITION FOR ADOLESCENTS AND ADULTS

<table>
<thead>
<tr>
<th>CD4+ T Cell Categories</th>
<th>A Asymptomatic, Acute (Primary) HIV or PGL</th>
<th>B Symptomatic, Not A or C Conditions</th>
<th>C AIDS-Indicator Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 500 / µL</td>
<td>A1</td>
<td>B1</td>
<td>C1</td>
</tr>
<tr>
<td>200-499 / µL</td>
<td>A2</td>
<td>B2</td>
<td>C2</td>
</tr>
<tr>
<td>&lt; 200 / µL</td>
<td>A3</td>
<td>B3</td>
<td>C3</td>
</tr>
</tbody>
</table>

### PATHOPHYSIOLOGY AND PATHOGENESIS

The hallmark of HIV-infection is profound immunodeficiency resulting primarily from a progressive quantitative and qualitative deficiency of the subset of T lymphocytes referred to as Helper T cells (CD4+ cells). This subset of T cells is defined phenotypically by the presence on its surface of the CD4 molecule which serves as the primary cellular receptor for HIV. A co-receptor must also be present together with CD4 for efficient fusion and entry of HIV-1 into its target cells. HIV uses two major co-receptors for fusion and entry; these co-receptors are also the primary receptors for certain chemoattractive cytokines termed chemokines and belong to the seven transmembrane domain G protein coupled family of receptors. CCR5 and CXCR4 are the major co-receptors used by HIV. A number of mechanisms responsible for cellular depletion and/or immune dysfunction of CD4+ T cells have been demonstrated in vitro; these include direct infection and destruction of these cells by HIV and immune clearance of infected cells, as well as indirect effects such as immune exhaustion due to aberrant cellular activation and activation-induced cell death. Patients with CD4+ T cell levels below certain thresholds are at high risk of developing a variety of opportunistic disease, particularly the infections and neoplasms.
that are AIDS-defining illnesses. Some features of AIDS, such as Kaposi’s sarcoma and neurologic abnormalities, cannot be explained completely by the immunodeficiency caused by HIV infection, since these complications may occur prior to the development of severe immunologic impairment.

**Studies establishing the relationship between Periodontal Disease and HIV-infection:**

Periodontal manifestations in HIV-positive patients were first observed in 1983 by Gottlieb.

Three periodontal entities associated with HIV-seropositive or AIDS patients are LGE, ANUG and NUP, were first described in 1987 by Winkler et al.

Smith et al. from their study of comparison of periodontal disease in HIV-seropositive subjects and controls had examined 29 HIV-seropositive subjects and 27 control subjects at base-line and at 3-months interval for attachment loss found that HIV-seropositive subjects had experienced more severe attachment loss, localized to lower incisor region and also showed significant mean % of sites exhibiting suppuration and redness compared to the controls after 3 months. A wide spread attachment loss was detected in a distinct subgroup of 9 HIV-seropositive subjects.11

Murray et al. examined subgingival plaque samples from 45 HIV-seropositive homosexual men and from 44 HIV-seronegative control subjects. Plaque samples were examined by indirect immunofluorescence with polyclonal antisera to detect *Bacteroides gingivalis, B. intermedia*, *Fusobacterium nucleatum* and *Actinobacillus actinomycetemcomitans*. The results appeared that *B. gingivalis, B. intermedia, F. nucleatum* and *A. actinomycetemcomitans* were significantly more in HIV-periodontitis sites and HIV-gingivitis sites than in HIV-seropositive healthy and control sites. These results indicated that microbiota found in HIV-periodontitis is similar to that of classical periodontitis. In contrast, the microbiota associated with HIV-gingivitis is strikingly different from that of conventional gingivitis and it is similar to that of HIV-periodontitis, indicating that HIV-gingivitis sites may be precursor to the tissue destruction observed in HIV-periodontitis12(Figure 1).

Heimdahl et al. had analyzed Visible Plaque Index (VPI), gingival bleeding index and pocket depth in relation to potential periodontal pathogenic microorganisms and peripheral number of $T_4^+$ and $T_8^+$ lymphocyte subsets in 10-HIV-infected patients without clinical signs of infection, 10-patients with AIDS-related complex (ARC) and 10-patients with AIDS and in 10-healthy controls found that there were no significant correlation between VPI and peripheral $T_4^+$ lymphocyte numbers, but GBI increased significantly and it was inversely correlated to the number of $T_4^+$ lymphocytes. The periodontal pockets > 4mm as well as mean value of pocket depths were significantly increased in ARC and AIDS patients compared to HIV-positive patients and controls and it is inversely correlated to the number of $T_4^+$ in peripheral blood13(Figure 2).

Figure 1: Box plots showing distribution of relative % of periodontal pathogens in subgingival plaque samples.
Cross F et al. had investigated subgingival plaque samples from 29 HIV-seropositive and 27 control subjects to determine periodontal pathogenic organisms collected from mesiobuccal sites of all teeth by using non-isotopic chromosomal DNA probes and colony lift method. The microbiological results in this study revealed that the only difference between the 2-groups of subjects was a statistically significant higher mean % of P. gingivalis in the HIV-seropositive compared to control patients. Furthermore, 7 HIV-seropositive patients had a tendency for higher mean levels of P. gingivalis, P. intermedia, C. ochracea and V. parvula.14

Vastardis et al. from their study of association of periodontal indices with stages of HIV-disease found that immunocompromised patients with CD4 cell count < 200 cells / uL showed significant lower Bleeding index (BI) and fewer sites with probing depth (PD) and AL > 4mm compared to patients with CD4 cell count > 200 cells / uL. An interesting finding is that HIV-positive patients with moderate or severe immunosuppression (CD4 < 500 cells / ul) showed a significant positive correlation of CD4 count to modified gingival index and bleeding index. Therefore HIV +ve patients with CD4 cell count less than < 200 cells / ul showed less severe periodontal disease compared to those with higher CD4 cell counts15(Figure 3).

Conclusion:-

The periodontal manifestations associated with HIV-infection were reported to be the first clinical expression or an indication of severe immune deterioration as it is expressed CD4+ cell count in peripheral blood circulation. In fact, the HIV-positive patients had experienced rapid progression of periodontal disease which was assessed clinically by deep periodontal pockets and severe attachment loss. During the past years many studies reported that periodontal manifestations such as LGE, ANUG and NUP are strongly associated in HIV-seropositive
patients whose CD4⁺ cell counts fall below 200 cells / uL who were considered as AIDS patients according to Revised CDC classification system for HIV-infected adolescents and adults. There appeared changes in subgingival microbiota in HIV-seropositive patients when compared to HIV-negative controls. The changes in microbiota in HIV positive patients are also correlated with severe immune suppression associated with HIV-infection.

But recent studies reported that in HIV-positive patients with extreme immunosuppression had experienced less severe periodontal disease when compared to HIV-positive patients with mild immunosuppression which is expressed by number of CD4 cells. Finally few studies determined that periodontal attachment destruction was less in HIV positive patients with CD4 cell count < 200 cells / uL compared to HIV-positive patients with CD4 cell count > 200 cells / uL.

REFERENCES:


