VIRUSES: A CONUNDRUM IN PERIODONTAL DISEASES - A REVIEW

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Abstract

Periodontal diseases are multifactorial, and many etiological agents are suggested to play a role in their etiopathogenesis. There are several risk factors which are associated with progression of periodontal disease. Even though, specific bacteria were considered as major pathogens for the disease, but, the occurrence of periodontal disease in some patient groups is still poorly understood, and the role of other initiating agents is being investigated. The virulence of infecting agents was also suggested as a major determinant in the onset and severity of periodontitis, as in any other human disease. With this background, the importance of viruses in periodontal etiopathogenesis has emerged as a major research area in recent years. However their role as a causative agent for periodontitis still remains unclear. In this review, we discuss the role of viruses in different periodontal diseases, its possible mechanism and role in perio medicine. Possible Clinical implications and future directions are also mentioned. The aim of the present review is to provide a critical evaluation of the role of viruses in periodontal etiopathogenesis and their future clinical implications might revolutionize existing strategies to diagnose, prevent, and treat the disease.

Keywords: Virus, etiopathogenesis, Periodontal Disease, Herpes virus, Human Immunodeficiency Virus

Introduction

A complex disease is a disease in which different biological factors lead to a similar clinical manifestation. Periodontitis is a common, complex, inflammatory disease characterized by destruction of tooth-supporting soft and hard tissue of periodontium and eventually may lead to loss of teeth. Though bacterial plaque is considered to be the commonest etiological factor in development of periodontitis, periodontitis is a multifactorial where in microbial species, host immune responses and ecosystem based factors are responsible for its development.

Even though specific infectious agents are key in the development of periodontitis, it is unlikely that a single agent or even a small group of pathogens are the only cause or modulator of this complex disease. In order to answer many questions regarding the etiopathogenesis of periodontitis, it is necessary to give up bacteria as a single cause of periodontitis. There are some critical questions that remain unanswered when it is discussed in etiopathogenesis of periodontitis: why in some individuals only few teeth are affected despite the omnipresence of periodontopathic bacteria, why some teeth show alveolar bone loss up to apical area whereas the destruction is minimal in adjacent teeth and how some form of disease have bilaterally symmetrical pattern and although subjects with poor oral hygiene develops gingivitis, not every case of gingivitis progresses to attachment loss.

Periodontitis frequently affects individuals who are immunocompetent, genetically or environmentally susceptible. Since many bacterial infections occur as superinfection to viral diseases, the studies in viruses as an etiological factor for periodontitis has led to unlocking of new door on the pathway of periodontal research which otherwise till recently was focused on the bacterial etiology. Herpes viruses, especially herpes simplex virus (HSV), Epstein Barr virus (EBV) and Human cytomegalovirus (HCMV) are the most frequently researched viruses in periodontology.

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major determinant in the onset and severity of periodontitis, as in any other human disease. With this background, the importance of viruses in periodontal etiopathogenesis has emerged as a major research area in recent years. However their role as a causative agent for periodontitis still remains unclear. The aim of the present review is to provide a critical evaluation of the role of viruses in periodontal etiopathogenesis and their future clinical implications.

CLASSIFICATION OF VIRUSES:

Viruses are classified according to nucleic acid composition: Deoxyribonucleic acid (DNA) or ribonucleic acid (RNA).(Table 1)

Table 1 shows the main viral infections that may be associated with an oral manifestation. Almost all infections described in this table can develop lesions on the gingiva. Except for human immunodeficiency virus (HIV) and enteroviruses, most viruses potentially involved in periodontal disease are DNA viruses. An involvement in periodontal diseases has been suspected specifically for HIV and herpes viruses. DNA viruses : Herpes viruses (herpes simplex virus [HSV], Varicella-zoster virus [VZV], Epstein-Barr virus [EBV], Cytomegalovirus [CMV], human herpes virus 6, Pox viruses, Papillomavirus, Hepatitis B virus RNA viruses : Coxsackie virus, Orthomyxoviruses, Enterovirus, Influenza virus, Mumps, Measles, Rubella, Retroviruses, Human immunodeficiency viruses, Rhabdoviruses, Rabies, double-stranded Reoviruses, Paramyxoviruses, Parainfluenza, Rotavirus, Picornaviruses, Rhinovirus, Echovirus, Toga viruses, Polio virus, Chickengunya Virus.

PATHOGENESIS OF DISEASES OF VIRAL ORIGIN:

Viruses usually gain entry into the host through different routes which include:
(a) Inoculation (via the skin and mucosa) as in needle stick injury, bites or accidental abrasions
(b) Inhalation (via the respiratory tract) as in aerosol or droplet
(c) Ingestion (via the gastrointestinal tract) as in the feco-oral route and
(d) the genitourinary tract as in sexual activity.

Once, the virus enters the host cell through direct local spread on epithelial and sub epithelial surfaces, lymphatic spread, vascular spread, and central nervous system and peripheral nerve spread, it can interact with the host cell in two main ways namely permissive and non-permissive mode.

• Permissive infection: Here, there is a synthesis of viral components, their assembly and release with a consequent death of the host cell
• Non permissive infection: Here, the infection can result in cell transformation often with the integration of viral DNA into the host genome. Here, there is viral replication within the cell but the cell remains alive. Examples are hepatitis B viruses, herpes viruses and retroviruses infection.

DETECTION OF VIRUSES IN THE ORAL CAVITY

The preferred methods are based on variants of real-time PCR, which not only offer a test for the viral presence, but also yield quantitative data. A main limitation of PCR-based methods is that they only detect the viruses they are designed to detect. Moreover, the cost of the methods restricts analysis to a few viral species; thus the total spectrum of potentially relevant viruses is rarely tested. Two recent strategies compensate for this limitation: microarrays and pyrosequencing. In microarrays, probes detecting different viruses (or other agents) can be applied to a slide and the sample DNA or RNA hybridized onto the slide, thus offering the possible detection of all known viruses. In pyrosequencing, the complete nucleic acids present in the sample are sequenced to look for recognizable viral sequences by searching relevant databases. Both these methods have the same, twofold limitations: one, they are less sensitive than PCR; and two, they are considerably more expensive, although the costs for pyrosequencing is becoming more cost-efficient. Thus, these techniques are not useful for routine diagnostics, but they may be valuable when investigating a possible viral cause of unknown conditions. Electron microscopy has been used to detect various virions in periodontal tissues. The presence of herpes virus in the periodontium has also been studied.

Table 01: Classification of Virus

<table>
<thead>
<tr>
<th>DNA-Viruses</th>
<th>Group</th>
<th>Pathology</th>
<th>Oral manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpes simplex virus (HSV)</td>
<td>Primary herpetic gingivostomatitis</td>
<td>Vestibular ulceration</td>
<td></td>
</tr>
<tr>
<td>Varicella-Zoster virus (VZV)</td>
<td>Varicella (chicken pox)</td>
<td>Vestibular ulceration</td>
<td></td>
</tr>
<tr>
<td>Varicella (chicken pox)</td>
<td>Herpes zoster (shingles)</td>
<td>Vestibular ulceration</td>
<td></td>
</tr>
<tr>
<td>Epstein-Barr virus (EBV)</td>
<td>Infectious mononucleosis</td>
<td>Ulcerations and palatal detectable White lesion</td>
<td></td>
</tr>
<tr>
<td>Cytomegalovirus (CMV)</td>
<td>Infectious mononucleosis</td>
<td>Retrovaccination</td>
<td></td>
</tr>
<tr>
<td>Human herpes virus 5 (HHV 5)</td>
<td>Unknown</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Human herpes virus 7 (HHV 7)</td>
<td>Unknown</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Human herpes virus 8 (HHV 8)</td>
<td>Kaposi's sarcoma</td>
<td>Epithelial nodules</td>
<td></td>
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</tbody>
</table>

RNA-Viruses

<table>
<thead>
<tr>
<th>Retrovirus</th>
<th>HIV</th>
<th>AIDS</th>
<th>Candidiasis</th>
<th>Recurrent herpetic gingivostomatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterovirus species</td>
<td>Coxsackievirus</td>
<td>Herpangina</td>
<td>Hand-foot-and-mouth disease</td>
<td>Ulcerous stomatitis</td>
</tr>
</tbody>
</table>

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using various methods, such as labeled DNA probes, flow cytometry and immunofluorescence staining.\textsuperscript{3,4,5} The newer technological advancements in viral diagnosis are described in (Table 2).\textsuperscript{6}

**VIRUSES IN PERIODONTAL ETIOPATHOGENESIS:**

Several mechanisms that would explain the potential role of viruses in the etiopathogenesis of periodontal diseases have been proposed such as an impaired local host response or modulation of local cytokine expression induced by viruses, increasing the levels and virulence potential of periodontal pathogens. It has been demonstrated that herpesviruses can produce virus-derived homologues of the anti-inflammatory cytokine interleukin-10 and other inhibitors of a T helper cell-1 response. In animal models, cytomegalovirus can impair neutrophil chemotaxis, phagocytosis, oxidative burst and intracellular killing capacity. Periodontitis subjects with subgingival herperviruses had reduced neutrophil chemotaxis and bactericidal activity compared to herpesvirus-free individuals. Herpesviruses can also interfere with macrophage and complement system antibacterial functions.

In addition, human cytomegalovirus interleukin-10 can suppress tumor necrosis factor-α and interleukin-1β transcription. Alternatively, viruses might induce the release of catabolic inflammatory mediators or other immunopathological mechanisms, causing indirect damage to periodontal tissues. For instance, herpervirus reactivation induces a major increase in cytotoxic T-cells and proinflammatory cytokines. In fact, several of the features of periodontal disease pathogenesis can potentially be explained by viral infections. For instance, the conversion of a gingivitis lesion to a periodontitis lesion and of a stable lesion to a progressing one could reflect cycles of activity and latency in herpes virus infection of the periodontium. Herpesvirus reactivation can be triggered by many immunosuppressing factors which have also been implicated as risk factors or risk indicators for periodontal infections. In addition, the localized nature of the periodontal lesions could be associated with the tissue tropism of herpes virus infections, while absence of viral infection or latency of the infection might help explain the presence of periodontal pathogens in periodontally healthy tissues and stable periodontal lesions.

**Cytopathic effects**

Herpes viruses can create direct cytopathic effects on fibroblasts, keratinocytes, endothelial cells, and inflammatory cells, including polymorphonuclear leukocytes, lymphocytes, monocytes, macrophages, and possibly bone cells in periodontitis lesions. As a result of herpes virus periodontal infection, aggressive periodontitis lesions contain fewer overall viable cells, more T-suppressor lymphocytes, and more B lymphocytes (EBV effect) than chronic periodontitis lesions or healthy periodontal sites.\textsuperscript{7} Viruses can invade the defense cells of periodontium, thereby influencing host response to infections. HCMV infects periodontal monocytes/macrophages and T lymphocytes, and EBV infects periodontal B lymphocytes.\textsuperscript{4} By infecting and altering the function of fibroblasts and other periodontal cells, herpes viruses might reduce healing after surgery and the regenerative potential of periodontal ligament.

**Host response**

Herpes virus infection triggers the release of proinflammatory cytokines that have the potential to impair antibacterial immune mechanisms, causing an upgrowth of periodontopathic bacteria.\textsuperscript{8} The herpes virus-associated pro-inflammatory cytokines and chemokines also stimulate bone-resorbing osteoclasts, up regulate matrix metalloproteinase, and down regulate tissue inhibitors of metalloproteinase, thereby impeding tissue turnover and repair, and increasing the risk of periodontal tissue breakdown.\textsuperscript{9} An active periodontal herpes virus infection might be partially responsible for the increased level of gingival interleukin-1β and tumor necrosis factor-α.

**Synergism with bacteria**

Periodontal herpes virus infection is typically associated with an increased occurrence of periodontopathic bacteria. Quantitative PCR studies of severe periodontitis have revealed a close relationship between EBV with CMV and

**Table 2. Recent techniques for viral diagnosis**

<table>
<thead>
<tr>
<th>Serial no.</th>
<th>Technique</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nested PCR</td>
<td>Can detect small quantities of bacterial or viral DNA</td>
<td>Cumbersome, prone to contamination, viability or quantity of organism cannot be assessed</td>
</tr>
<tr>
<td>2</td>
<td>Real time PCR or reverse transcriptase PCR</td>
<td>Reproducibility, specificity, can quantify, speed, less contamination</td>
<td>Less sensitive than nested PCR</td>
</tr>
<tr>
<td>3</td>
<td>Multiplex PCR</td>
<td>Multiple organisms can be detected simultaneously</td>
<td>Difficulty to perform non-specific amplifications</td>
</tr>
<tr>
<td>4</td>
<td>Metagenomic pyrosequencing &amp; microarray</td>
<td>Can detect complete set of viruses in the sample</td>
<td>Less sensitive and less expensive</td>
</tr>
</tbody>
</table>
pathogens P. gingivalis, Tannereilla forsythia, Prevotella intermedia, Prevotella nigrescens, and Treponema denticola. Periodontal HCMV showed a particularly close association with the occurrence of Dialister pneumosintes and P. gingivalis. Recent evidence shows that P. gingivalis induces the EBV lytic switch transactivator Z Epstein–Barr replication activator by histone modification. Viruses predispose the host to secondary infections by inducing abnormalities in the adherence, chemotaxis, phagocytic, oxidative, secretory, and bactericidal activities of polymorphonuclear leucocytes. Th1 cytokines associated with active herpes virus infections reduce Th2 cell responses and the antibody-mediated control of pathogenic bacteria. Viral proteins expressed on eukaryotic cell membranes and the basement membrane of virus damaged epithelial cells can act as bacterial receptors and generate new bacterial-binding sites. CMV can enhance the adherence of Aggregatibacter actinomycetemcomitans to primary periodontal pocket epithelial cells and to HeLa cells. EBV active infection can also generate antineutrophilic antibodies and neutropenia, and polyclonally stimulate the proliferation and differentiation of B lymphocytes.

Viral pathogenesis of aggressive periodontitis
Repeated evidence suggests that active CMV might be the primary cause for the disease in aggressive periodontitis, and can be a secondary invader after the pathological changes in the periodontium, or it can be a combination of the two. Primary CMV infection at the time of root formation of permanent incisors and first molars can be the reason for defective periodontium in aggressive cases. Viral infection can disrupt normal cell differentiation and can result in cemental hypoplasia. Profound hormonal changes at the onset of puberty might reactivate a periodontal CMV infection, resulting in the suppression of antibacterial immune defenses and the overgrowth of exogenous-like bacteria in the early phases of localized aggressive periodontitis. Localized aggressive periodontitis lesions harboring an active CMV infection tend to be more heavily infected with A. actinomycetemcomitans than sites showing a latent CMV infection. CMV-mediated damage to the periodontal tissue constituents, antiviral pro-inflammatory cytokine responses, and bacteria induced injury of the epithelium might allow gingival tissue invasion by A. actinomycetemcomitans and the breakdown of the periodontal attachment and alveolar bone.

VIRUSES IN DIFFERENT FORMS OF PERIODONTAL DISEASE:
The virus detection depends on several factors, like the type of periodontal lesion studied, disease activity at the sampling site, influence of periodontal treatment, patient’s immune status, identification method of virus used, and ethnic/geographic factors. False positive and negative results can occur due to a variation in any of these factors. In spite of all these, different studies showed presence of different strains of viruses in periodontal disease.

Gingivitis
Rotola A et al(2008) performed gingivitis studies which reveal a median genome detection rate of 20% for EBV and 33% for CMV. Herpes virus-infected periodontally-healthy and gingivitis sites typically harbour the viruses in a non- transcriptional state. Eres G et al (2011) stated that Pregnancy might increase the risk of subgingival EBV presence by 3.647 times.

Periodontitis
Studies showing wide variation in the occurrence of HSV (13–100%), EBV (3–89%), and CMV (0.3–83%) have been reported in periodontitis lesions due to multiple factors involved. There are conflicting reports regarding the number of viruses detected in chronic and aggressive periodontitis sites. Most studies report a higher level of viruses in aggressive lesions, some describe a similar occurrence, or even a lower occurrence in aggressive cases.

Aggressive periodontitis
Michalowicz BS et al(2000) detected Cytomegalovirus and Porphyromonas gingivalis in sites with localized aggressive periodontitis in Afro-Caribbean adolescents. The cytomegalovirus transcription of the major cuspid protein was detected in deep periodontal pockets of patients with localized aggressive periodontitis of 10–14 years of age. Saygun I et al(2004) demonstrated HSV-1, EBV, and CMV in advanced sites of generalized aggressive periodontitis in 73–78% young military recruits in Turkey, the viruses were absent in the subgingival sites of healthy periodontium. Kamma JJ et al(2001) observed EBV, CMV, and EBV– CMV cohabitation was significantly associated with periodontitis active areas in early onset periodontitis in a Greek population.

Chronic periodontitis
The main herpes viruses identified in chronic periodontitis are EBV-1, HSV-1, and CMV. The latent form of CMV is seen in the majority of chronic periodontitis sites, which might account for the slow progression of the disease.
Contreas A et al (1999) detected antibodies against EBV in 32%, and against CMV in 71% of gingival crevicular fluid samples from 34 study sites. Cytomegalovirus and human herpes virus-7 can be present in periodontitis-affected sites, but are uncommon in healthy sites. Thomasoni RL et al (2012) stated that CMV can be related to an inflammatory infiltrate with a predominance of CD3 (+) T cells, whereas human herpes virus 7 can be associated with an infiltrate with predominance of T\(-\)CD4 (+) cells. All these data indicate that herpes viruses could play a role in human chronic periodontitis by the modulation of the T-cell response.  

**Periodontal abscess**

In abscess studies, Saygan I et al (2004) detected Epstein–Barr virus (72%), CMV (67%), and co-infection with the above two viruses (56%), while the herpes viruses were not detected in healthy periodontium or after treatment of the periodontal abscess. CMV has been implicated in periodontal and extraoral abscesses of HIV-infected individuals. It is suggested that reactivation of a periodontal herpes virus latent infection impairs the periodontal host defense and permits bacterial pathogens to enter the gingiva, causing periodontal abscess.  

**HIV-associated periodontitis**

HIV-induced immunosuppression facilitates herpes virus reactivation, but active herpes viruses might also activate latent HIV. The reactivation of latent periodontal herpes viruses by HIV might start a cascade of tissue destructive events, leading to periodontal breakdown. CMV is the most common herpes virus in HIV-associated periodontitis. Cobb M et al (2003) detected herpes virus-like virions electron microscopically in 56% of gingival tissue from HIV-seropositive patients with necrotizing ulcerative periodontitis. EBV-1 was identified more frequently in subgingival sites, and EBV-2 was detected in 57% of biopsies from HIV-associated periodontitis lesions. Blackbourn DJ et al (1998) detected HSV, EBV, CMV, and HSV-8 genomes in the saliva of HIV-infected individuals. Grande SR et al (2011) showed significant association of EBV-1 and co-infection (EBV-1–HCMV) with HIV-associated periodontitis. HPV was detected in the gingival crevicular fluid of HIV-positive patients under highly active anti-retroviral treatment (HAART), independently of the periodontal conditions.  

**Necrotizing ulcerative gingivitis/periodontitis**

Contreas A et al (1997) studied necrotizing gingivitis lesions in malnourished children which showed 23% HSV, 27% EBV, and 59% CMV, while periodontal sites of malnourished but periodontally-normal children revealed virtually no herpes viruses. It has been suggested that necrotizing ulcerative gingivitis in African children might be caused by the acquisition of herpes viruses in early childhood as a consequence of impaired immune defenses, malnutrition, and plenty of virulent periodontal bacteria.  

**Syndromes**

Cytomegalovirus was detected in periodontitis lesions in Guillain–Barre syndrome, Kostmann syndrome, Papillon–Lefevre syndrome, Fanconi’s anemia, and Down syndrome. Natural killer cells play a crucial role in the antiherpes viral host defense. The suppressed killer cell activity in these syndromes might have been induced by CMV as an immunoevasive strategy.  

**Peri-implantitis**

A statistically-significant correlation was found between the presence of HCMV-2 and EBV-1 genotypes and the clinical parameters of peri-implantitis. Jankovic S et al (2011) performed a pilot study and confirmed the high prevalence of HCMV and EBV in subgingival plaque, which suggests that there is correlation in pathogenic role of these viruses in peri-implantitis.  

**Other oral lesions**

Sabeti M et al (2009) used multicolor flow cytometry and identified cytomegalovirus infection in periapical lesions. Saygan I et al (2009) detect CMV and EBV in virological sample of peripheral giant cell granuloma of a 47-year-old female. Viruses might play a role in refractory periodontitis cases. Hernandez G et al (2011) reported the failure of free connective tissue grafts due to recurrent HSV-1 infection. Despite, there are plenty of evidence which support the presence of viruses in periodontal health and disease. There are also published contradictory reports. Saygun I et al (2011) revealed that there is no significant difference in salivary copy counts of EBV among a sample of patients with gingivitis, chronic periodontitis, and aggressive periodontitis compared to periodontally-healthy participants. Nibali L et al (2009) did not detect DNA of HCMV, HSV, and VZV in any of the plaque samples taken from aggressive periodontitis patients. EBV DNA was detected in four localized aggressive periodontitis (25%), two generalized aggressive periodontitis (3%) patients and four healthy individuals (10%). In another published study done by Dawson DR et al (2009) reported that EBV was not frequent and CMV was rarely present in individual subgingival sites affected by chronic periodontitis.
These variations could be due to different factors, like variations in race, sampling site selected and technique used.

VIRUSES: ROLE IN PERIODONTAL MEDICINE
Several reports suggested that periodontitis is a major risk factor for various systemic diseases, like atherosclerosis, preterm low birth weight, diabetes mellitus, osteoporosis, and rheumatoid arthritis. Several mechanisms have been suggested to explain this periodontal systemic interrelationship. Direct viral invasion into systemic circulation or the effect of viral-induced changes in host response can be responsible for the systemic impact.

• Atherosclerosis might develop as a result of infection with CMV, HSV, Chlamydia pneumoniae, Helicobacter pylori, or periodontopathic bacteria. CMV seropositivity has been linked to cardiovascular disease. CMV and HSV, especially when acting together, have the potential to promote the inflammatory and procoagulant environment that underlies the pathogenesis of atherosclerosis. CMV infection of vascular cells and cells of cardiac musculature induces cell activation, leading to the expression of adhesion proteins, major histocompatability complex molecules, and cytokine receptors, and to the release of cytokines and growth factors.9

• In some patients, CMV might be a common etiology of periodontitis and premature birth. Arvin AM et al (2004) reported that CMV can be transmitted transplacentally to the fetus, and a proportion of premature births are caused by a congenital CMV infection.35

• Casarin RC et al (2010) found a more number of EBV in the shallow pockets of patients with poor glycemic control. Glycemic control was moderate or good in EBV-free patients. Glycemic control did not influence the frequency of CMV in all pocket categories.36

• Pischon N et al (2008) reported that Periodontitis has correlated with several other diseases/conditions, including rheumatoid arthritis,37 which in turn has been interrelationship with EBV and CMV; some renal diseases (associated with CMV and several other viruses); and with premature death from neoplasms and from vascular and digestive diseases, which have a herpes viral etiology.

• Garlet GP et al (2010) reported Human T-lymphotropic virus (HTLV)-1-positive patients have higher incidence of periodontitis, which is characteristically associated with a systemic immune-mediated inflammatory disease that results in tissue damage.38 It has also been reported that HTLV-1 infection can modify the pathophysiology of osteoarthritis, which

• Katti R et al (2011) reported in Indian population that Chikungunya virus may be associated with gingivitis, as well as arthritis.39

• Oral diseases, such as carcinoma of tongue, hairy leukoplakia, oral leukoplakia, and lichen planus, can be caused by papilloma virus and EBV. Periodontal pockets can serve as a reservoir for viruses for these various oral diseases.

CLINICAL RELEVANCE AND FUTURE IMPLICATIONS
Conventional periodontal therapy, including scaling and root planing, eliminates HCMV and EBV or reduces HSV and the number of herpetic lesions. Complete elimination, at least in some selected cases, requires the administration of specific antiviral agents. Povidone–iodine and sodium hypochlorite solutions applied subgingivally demonstrate potent antiviral and antimicrobial chemotherapeutics.9 Systemic acyclovir can result in the long-term suppression of EBV, and probably also of other herpes viruses in subgingival sites.9 The antiviral activity of interferon can also be a contributing factor. The HAART might not significantly reduce the prevalence or the load of herpes viruses in saliva;40 therefore, better protocols should be established to eradicate the oral burden of viruses from saliva, plaque, and from within the gingiva in HIV patients.

CONCLUSION
According to currently accepted hypothesis on the etiopathogenesis of periodontitis, bacteria are imperative for the development of periodontitis. However bacterial-host interaction does not suffice to explain the localized distribution and the periods of exacerbations and quiescence during tissue breakdown. It is hypothetized that an active herpes virus infection can initiate periodontal tissue breakdown. It triggers a release of proinflammatory cytokines that have potential to activate osteoclasts and matrix metalloproteinases and impair antibacterial immune mechanisms causing an up-growth of periodontopathic bacteria. Herpes virus can extent direct cytopathic effects on cells such as fibroblasts, keratinocytes and endothelial cells.

Recent researches suggest that high load of EBV and CMV is statistically associated with aggressive periodontitis and HSV with chronic periodontitis. High counts of EBV and HCMV and their presence in proportion with severity of underlying disease render them unlikely to be mere bystanders in the pathogenesis of periodontitis. The ability of herpes virus to alter the immune responses may increase the severity of periodontitis.
Frequent occurrence of herpes virus in various types of severe periodontal disease makes the participation of herpes virus species in the etiology of periodontitis as a possibility. Decrease in the counts of viruses in treated sites with periodontal disease can indicate the quantification of herpes virus in periodontal sites as a prognostic importance. Also ongoing research on anti-herpes virus vaccination may offer hope for prevention of periodontitis in large group population. The detection of virus within periodontal pockets by various studies proves that virus do have a role to play in periodontitis. However there is ‘what came first, what came first, hen or egg?’ situation when it comes to considering viruses for periodontitis. The virus infection may be primary infection causing bacterial periodontitis as a superinfection or it may be the bacterial host response resulting in reactivation of latent virus then affecting the severity and progression of periodontitis.

Reference


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