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Viruses and Their Role in Periodontal Diseases: A Review

Yashica Dhingra[1,*], Mayur Kaushik[2], Shivi Khattri[3], Soundarya Singh[4]

Abstract

Periodontal diseases are a group of inflammatory conditions that primarily affect the gums and other tissues surrounding the teeth. Traditionally, these conditions were thought to be driven largely by bacterial infections, with the bacteria triggering an immune response that leads to inflammation and tissue damage. However, recent research has revealed that viruses also play a significant role in the development and progression of periodontal diseases. Viruses, such as Human Cytomegalovirus, Herpes Simplex Virus, and Epstein-Barr Virus have been identified as key players in the etiopathogenesis of various types of periodontitis. These viruses can alter the host's immune response, making the tissues more susceptible to bacterial invasion and inflammation. Furthermore, they can directly affect the cells in the periodontium, contributing to tissue destruction and disease progression. This review article explores the involvement of different viral families in periodontal diseases, highlighting the complex interactions between viruses, bacteria, and the host's immune system. Understanding these interactions is crucial for developing more effective treatment strategies that address not only bacterial infections but also viral contributions to periodontal health.

Keywords: Periodontal diseases, inflammatory conditions, viruses, periodontium, viral-bacterial interaction.

INTRODUCTION

Periodontal diseases, include various inflammatory conditions affect the gums and other tissues supporting the teeth. Although these diseases are mainly caused by a complex interaction between bacteria and the body's immune response. Recent studies suggest that viruses might also play a role in their development and progression [1].

What are Viruses?

Viruses are intracellular pathogens that can infect and replicate within host cells, causing damage and altering the immune response. Some of the viruses that have been implicated in periodontal diseases include herpesviruses, human papillomavirus (HPV), and cytomegalovirus (CMV) [2].

The mechanisms by which viruses may contribute to the development of periodontal diseases are not fully understood, but it is thought that they may act synergistically with bacteria to promote inflammation and tissue destruction. Viruses may also alter the host immune response, making the host more susceptible to bacterial infection [3].

Classification of Viruses

Viruses are a diverse group of infectious agents that cannot replicate outside of host cells. Viruses can infect all living organisms, from bacteria and plants to animals and humans. They are typically

*Author for Correspondence
Yashica Dhingra
E-mail: yashicadhingra03@gmail.com

[1]Student, Department of Dentistry, Swami Vivekanand Subharti University, Subharti Puram, Meerut, Uttar Pradesh, India.
[2]Professor & Head, Department of Dentistry, Swami Vivekanand Subharti University, Subharti Puram, Meerut, Uttar Pradesh, India.
[3-4]Associate Professor, Department of Dentistry, Swami Vivekanand Subharti University, Subharti Puram, Meerut, Uttar Pradesh, India.

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classified based on their genetic material, methods of replication, structure, and other key characteristics. Below are some of the most used systems for virus classification [4].

- *Genetic material:* The genetic material of a virus can be either DNA or RNA. DNA viruses can be further classified into single-stranded (ss) or double-stranded (ds) DNA, while RNA viruses can be classified into positive-sense RNA (+RNA), negative-sense RNA (–RNA), or double-stranded RNA (dsRNA) viruses.
- *Replication strategy:* Viruses can replicate using either the lytic or lysogenic replication strategy. Lytic viruses reproduce quickly, leading to the destruction of the host cell and the release of new viral particles. Lysogenic viruses integrate their genetic material into the host genome and replicate with the host cell until a trigger causes them to switch to the lytic cycle.
- *Morphology:* Viruses can have a variety of morphologies, including icosahedral, helical, and complex shapes. Some viruses are enveloped, meaning they have a lipid membrane surrounding their protein capsid, while others lack this outer membrane and are classified as non-enveloped [5].
- *Host range:* Viruses can have a broad or narrow host range, meaning they can infect a wide range of hosts or only specific hosts, respectively.
- *Disease caused:* Viruses can also be classified based on the type of disease they cause. For example, some viruses cause respiratory infections, while others cause gastrointestinal or neurological diseases [6].

Overall, the classification of viruses is a complex and evolving field, as new viruses are discovered and our understanding of their biology and evolution improves.

ROLE OF VARIOUS VIRUSES IN PERIODONTAL DISEASES

HIV and Periodontal Diseases

The Human Immunodeficiency Virus (HIV) is a retrovirus that targets the immune system and can progress to acquired immunodeficiency syndrome (AIDS). Individuals infected with HIV are at a higher risk of various infections, including periodontal diseases.

Periodontal diseases are bacterial infections that impact the gums and other supporting structures of the teeth, resulting from a complex interaction between bacteria and the host's immune response. In individuals with HIV, the immune system is compromised, making them more susceptible to bacterial infections, including those that cause periodontal diseases [7].

Studies have shown that individuals with HIV are more likely to develop periodontitis, a severe form of periodontal disease that can lead to tooth loss. HIV-positive individuals may also experience more rapid progression of periodontal disease and have a higher risk of developing oral infections, such as thrush, which can also contribute to periodontal disease.

Periodontal diseases that are commonly associated with HIV include [8]:

- *Gingivitis:* Gingivitis is a mild form of periodontal disease that causes inflammation of the gums. In individuals with HIV, gingivitis can progress more rapidly and become more severe.
- *Necrotizing ulcerative gingivitis (NUG):* Necrotizing ulcerative gingivitis (NUG) is a serious type of gingivitis that results in painful ulcers on the gums. NUG is more common in individuals with HIV due to the weakened immune system and can be a sign of advanced HIV disease.
- *Periodontitis:* Periodontitis is an advanced stage of gum disease that may result in the deterioration of bones and teeth. Periodontitis can advance quicker and be more intense in people living with HIV.
- *Linear gingival erythema (LGE):* LGE is a red band that appears on the gums and is associated with HIV infection. LGE can progress to NUG or periodontitis if left untreated.

HSV AND PERIODONTAL DISEASES

HSV is a group of DNA viruses that have two strands and are common among people. In periodontal diseases, two types of herpes viruses have been identified as potentially involved in the pathogenesis of the disease [9] and they are:

- *Herpes Simplex Virus 1 (HSV-1):* This virus is a member of the alpha herpesvirus family and is known to cause cold sores or fever blisters on the lips and mouth. Studies have suggested that HSV-1 may play a role in the development and progression of periodontitis, a common form of gum disease.
- *Cytomegalovirus (CMV):* This virus is a member of the beta herpesvirus family and is known to cause a range of clinical manifestations, including salivary gland disease, hepatitis, and retinitis. CMV has been discovered in periodontal pockets and has been linked to the development of periodontitis.

Both HSV-1 and CMV are known to establish latent infections, which can reactivate under certain conditions, leading to recurrent episodes of disease. While the exact mechanisms by which these viruses contribute to periodontitis are not fully understood, it is thought that their presence may exacerbate inflammation and impair the host immune response, leading to tissue destruction and bone loss in the affected areas.

HSV-1 has been discovered in the pockets of the gums, gum tissue, and saliva of individuals with periodontal disease. It has been shown to modulate the host immune response and may exacerbate inflammation, leading to tissue destruction and bone loss in the affected areas. Furthermore, some studies have suggested that the presence of HSV-1 in periodontal pockets may promote the growth of periodontal pathogens and increase the virulence of these bacteria, further contributing to the progression of periodontitis.

EPSTEIN BARR VIRUS

Pathogenesis

Epstein-Barr virus (EBV) is a highly prevalent human herpesvirus that is known to cause infectious mononucleosis (also known as glandular fever), as well as several types of cancers, including Burkitt's lymphoma, Hodgkin's lymphoma, and nasopharyngeal carcinoma.

The pathogenesis of EBV involves several steps. The virus first infects epithelial cells in the oropharynx, where it replicates and spreads to the B cells in the lymphoid tissue. Once inside the B cells, EBV can establish a latent infection, in which the viral genome persists in the host cell without producing infectious virions.

During the latent phase, the virus expresses a limited set of genes that allow it to evade the host immune system and maintain its persistence. The expression of some of these genes can also promote cell growth and division, which can contribute to the development of cancer. In some cases, the latent infection can be reactivated, leading to the production of infectious virions and the spread of the virus to new cells. Various factors, such as stress, immune suppression, and specific medications can initiate this reactivation process.

EBV AND PERIODONTAL DISEASES

Certain research has indicated that EBV might play a role in the advancement of periodontitis by increasing the release of pro-inflammatory cytokines and chemokines, resulting in tissue damage. Other studies have found no association between EBV and periodontal disease. It is important to note that periodontitis is a multifactorial disease, and while EBV may play a role in some cases, it is unlikely to be the sole cause of the disease. Additional factors, such as genetics, smoking, and inadequate oral care also play a role in causing periodontitis.

In general, the relationship between EBV and periodontal diseases continues to be a focus of ongoing research, and additional studies are required to completely grasp its impact. Nonetheless, practicing proper dental care and promptly addressing periodontal disease can aid in stopping the onset and advancement of the illness, regardless of the influence of EBV.

CMV AND PERIODONTAL DISEASES

Cytomegalovirus, a prevalent herpesvirus, can lead to various clinical manifestations, ranging from no symptoms to severe illness in those with weakened immune systems. The role of CMV in periodontal diseases is still under investigation, but some studies have suggested that it may contribute to the development and progression of these conditions. CMV has been detected in the periodontal tissues of patients with periodontitis, and some studies have found an association between CMV infection and increased severity of periodontal disease [10].

The exact mechanism by which CMV contributes to the pathogenesis of periodontitis is still unclear, but it is thought to involve the modulation of the host immune response. CMV can infect and replicate in several cell types, including epithelial cells and leukocytes, and it has been shown to affect the function of immune cells, such as macrophages and T cells. It has been demonstrated that CMV infection can elevate the levels of pro-inflammatory cytokines and chemokines, resulting in tissue destruction and bone resorption, both key features of periodontal disease. Additionally, CMV may interfere with the function of immune cells that are important for controlling bacterial infections in the oral cavity, further contributing to the development of periodontal disease.

In general, the impact of CMV on periodontal diseases is an ongoing research topic, and more studies are necessary to comprehend its role completely. However, maintaining good oral hygiene and seeking prompt treatment for periodontal disease can help prevent the development and progression of the disease, regardless of the role of CMV.

SARS COV2 AND PERIODONTAL DISEASES

The COVID-19 pandemic is caused by the virus known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). While the primary impact of SARS-CoV-2 is on the respiratory system, there is some evidence to suggest that it may also affect other parts of the body, including the oral cavity. Research discovered that individuals with periodontal disease had nearly nine times higher risk of dying from COVID-19 compared to those without periodontal disease. Another study found that periodontal disease was associated with an increased risk of COVID-19 hospitalization [11]. The exact mechanism by which periodontal disease may increase the risk of COVID-19 complications is not yet clear. However, it is thought that the chronic inflammation associated with periodontal disease may contribute to a dysregulated immune response to SARS-CoV-2, which can lead to more severe disease.

Furthermore, the oral cavity, including the periodontal tissues, can also be infected and replicate SARS-CoV-2. In summary, while the relationship between SARS-CoV-2 and periodontal disease is still under investigation, there is evidence to suggest that periodontal disease may increase the risk of COVID-19 complications. It is essential to keep up with oral hygiene and promptly address periodontal disease for optimal health and potentially lowering the chances of experiencing complications related to COVID-19.

VIRUSES IN PREGNANCY GINGIVITIS

Pregnancy gingivitis is a common oral condition that occurs during pregnancy. It is defined by gum inflammation and bleeding, stemming from hormonal shifts in pregnancy. While bacteria are the primary cause of periodontal diseases, viruses may also play a role in the development of pregnancy gingivitis.

One virus that has been studied in the context of pregnancy gingivitis is HSV. HSV is a prevalent virus that can lead to a range of clinical presentations, such as oral herpes (cold sores). HSV has been

detected in the gingival tissues of pregnant women with gingivitis, and some studies have suggested that HSV infection may be associated with an increased risk of pregnancy gingivitis.

The exact mechanism by which HSV contributes to the development of pregnancy gingivitis is not yet clear. However, it is thought that the virus may induce an exaggerated inflammatory response in the gingival tissues, leading to increased tissue damage and bleeding.

Human cytomegalovirus (HCMV) is another virus that has been linked to the onset of pregnancy gingivitis. HCMV has been detected in the gingival tissues of pregnant women with gingivitis, and some studies have suggested that HCMV infection may be associated with an increased risk of pregnancy gingivitis.

The exact mechanism by which HCMV contributes to the development of pregnancy gingivitis is also not yet clear. However, it is thought that the virus may modulate the host immune response in a way that promotes inflammation and tissue damage.

ANTIVIRAL AGENTS

Antiviral drugs are medications used for the treatment of viral infections. They operate by focusing on stages in the viral life cycle, either by blocking viral reproduction or by stopping the virus from infecting host cells.

Some instances of antiviral medications consist of [12]:

- *Acyclovir:* Used to treat infections caused by herpes simplex virus and varicella-zoster virus.
- *Oseltamivir:* Used to treat infections caused by the influenza virus.
- *Ribavirin:* Used to treat respiratory syncytial virus, hepatitis C virus, and various other viral infections.
- *Sofosbuvir:* Used to treat hepatitis C virus infections.
- *Zanamivir:* Used to treat influenza virus infections.
- *Remdesivir:* Used to treat COVID-19.

Antiviral agents can be administered orally, intravenously, or topically, depending on the virus being treated and the severity of the infection. They can be effective in reducing the duration and severity of symptoms, as well as preventing complications and reducing the spread of infection. However, it is important to note that antiviral agents are not effective against all viruses, and they may have side effects and drug interactions. Furthermore, the development of viral strains that are resistant to drugs can reduce the ability of antiviral agents to work effectively in the long run. In general, the decision to use antiviral medications should be made by a healthcare provider depending on the viral infection being addressed.

CONCLUSION

Having a more thorough grasp of the causes of periodontitis is essential to create effective methods of detection and treatment, allowing periodontists to maintain control over the disease. Reducing the chance of contracting viral diseases can be achieved by professional periodontal treatments and good oral hygiene practices to keep the gums healthy. Quick progress in medical field

The field of virology can also contribute to understanding the development and therapy of viral mouth diseases. Antiviral methods for prevention and treatment could help stop the development and advancement of viral-induced periodontal disease.

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