

Prevalence of Herpesvirus in Chronic Periodontitis Patients with and without Type 2 Diabetes Mellitus: A Clinical Study

Ashutosh Pandey¹, Satya Prakash^{2*}, Anjana Bharti³, Amresh Kumar Pandey⁴, Sumit Verma⁵, Sweety Kumari⁶

¹Department of Dentistry, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India.

²Department of Oral Medicine and Radiology, Buddha Institute of Dental Sciences and Hospital, Patna, Bihar, India.

³BDS, Private Practitioner, Buddha Dental Hospital, Patna, Bihar.

⁴Department of Prosthodontics Crown and Bridge, Private Practitioner, Kavyashree Dental Clinic, Bhagalpur, Bihar, India.

⁵Department of Oral and Maxillofacial Surgery, Dr. B.R Ambedkar Institute of Dental Sciences and Hospital, Patna, Bihar, India.

⁶Department of Conservative Dentistry and Endodontics, Dental Officer ECHS, Khagaria, Bihar, India.

Abstract

Background: Chronic periodontitis is an inflammatory disease of the supporting tissues of the teeth, often exacerbated by microbial infection. Recent studies suggest that viral infections, particularly herpesviruses, may play a role in the progression of periodontitis. The presence of herpesviruses, such as human cytomegalovirus (HCMV) and Epstein–Barr virus (EBV), may contribute to the severity of periodontal disease, especially in patients with systemic conditions like type 2 diabetes mellitus (T2DM). This study aimed to investigate the prevalence of herpesviruses in chronic periodontitis patients with and without T2DM. **Materials and Methods:** A total of 100 patients were enrolled in this clinical study, divided into two groups: 50 patients diagnosed with chronic periodontitis and T2DM (group 1) and 50 patients with chronic periodontitis but without T2DM (group 2). Clinical parameters, including probing depth (PD), clinical attachment loss (CAL), and bleeding on probing (BOP), were assessed. Subgingival plaque samples were collected from both groups, and the presence of herpesviruses (HCMV, EBV) was detected using polymerase chain reaction techniques. Data were analyzed using Chi-square tests and logistic regression to evaluate the association between herpesvirus prevalence and T2DM. **Results:** The prevalence of herpesviruses was significantly higher in group 1 (patients with T2DM and chronic periodontitis) compared to group 2. HCMV was detected in 35% of patients in group 1 and 20% in group 2 ($P = 0.03$), while EBV was detected in 40% of group 1 and 25% of group 2 ($P = 0.05$). The clinical parameters (PD, CAL, BOP) were more severe in patients with herpesvirus infection, particularly in group 1. Logistic regression analysis showed a significant correlation between T2DM, herpesvirus presence, and periodontal disease severity ($OR = 2.5$, $P = 0.02$). **Conclusion:** The findings of this study suggest that herpesvirus infections, particularly HCMV and EBV, are more prevalent in chronic periodontitis patients with T2DM compared to those without T2DM. The presence of these viruses may exacerbate periodontal tissue destruction, indicating the need for targeted antiviral therapies in managing periodontitis in diabetic patients.

Keywords: Chronic periodontitis, Epstein–Barr virus, Herpesvirus, Human cytomegalovirus, Periodontal disease, Polymerase chain reaction, Type 2 diabetes mellitus.

INTRODUCTION

Chronic periodontitis is a multifactorial inflammatory disease that affects the supporting tissues of the teeth, ultimately leading to tissue destruction, pocket formation, and tooth loss if untreated.^[1] Conventionally, bacterial infections have been considered the primary etiological factor in periodontitis, with specific periodontal pathogens such as *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* playing a central role.^[2] However, recent evidence suggests that viral infections, particularly herpesviruses, may also contribute to the initiation and progression of periodontal disease by modulating host immune responses.^[3] Among the

herpesviruses implicated, human cytomegalovirus (HCMV) and Epstein–Barr virus (EBV) are of particular interest due to their ability to remain latent in host cells and reactivate under immunocompromised conditions, such as diabetes mellitus.^[4,5]

Address for correspondence: Dr. Satya Prakash,
Department of Oral Medicine and Radiology, Buddha Institute of Dental
Sciences and Hospital, Patna, Bihar, India.
Email: anujisingh146@gmail.com

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The bidirectional relationship between periodontitis and systemic diseases, including type 2 diabetes mellitus (T2DM), has been well documented.^[6] T2DM not only increases susceptibility to periodontal infections but also exacerbates the severity of periodontal tissue damage.^[7] Hyperglycemia in diabetic patients promotes an altered immune response and chronic low-grade inflammation, which can compromise periodontal tissue integrity.^[8] Emerging research has indicated that viral infections may act as cofactors in periodontal disease progression, particularly in patients with underlying systemic conditions like diabetes.^[9]

Herpesviruses, especially HCMV and EBV, are known to infect periodontal tissues and have been isolated from periodontal lesions.^[10] These viruses may directly contribute to periodontal tissue destruction by infecting epithelial and immune cells or indirectly by altering the microbial ecology of the periodontal pocket, thereby enhancing bacterial virulence.^[11] Furthermore, diabetic patients exhibit higher levels of systemic inflammation and impaired immune defenses, which can promote the reactivation of latent viral infections, potentially worsening periodontal outcomes.^[12] Despite these findings, limited research has explored the combined impact of HCMV and EBV on periodontal disease in diabetic patients.

This study aims to investigate the prevalence of HCMV and EBV in chronic periodontitis patients with and without T2DM and to assess the association between viral infections and periodontal disease severity. Understanding this relationship may provide insights into the pathogenesis of periodontitis in diabetic patients and suggest new therapeutic strategies, such as antiviral therapies, to improve periodontal management in this population.

MATERIALS AND METHODS

Study design and participants

This clinical study employed a cross-sectional design. A total of 100 participants were enrolled, divided into two equal groups:

- Group 1: 50 patients diagnosed with chronic periodontitis and T2DM
- Group 2: 50 patients with chronic periodontitis but without T2DM.

Inclusion criteria included patients aged 35–65 years, with at least 20 natural teeth, and diagnosed with chronic periodontitis based on the 2017 World Workshop Classification criteria. The diagnosis of T2DM was based on fasting blood glucose ≥ 126 mg/dL or HbA1c $\geq 6.5\%$. Exclusion criteria included patients with other systemic diseases (e.g., immunodeficiency disorders), pregnant or lactating women, those on antiviral or immunosuppressive drugs, and patients who had undergone periodontal treatment within the past 6 months.

Clinical assessment

The following clinical parameters were measured by a calibrated examiner:

- Probing Depth (PD): Measured at six sites per tooth using a UNC-15 periodontal probe

- Clinical Attachment Loss (CAL): Recorded as the distance from the cemento-enamel junction to the base of the periodontal pocket
- Bleeding on Probing (BOP): Evaluated as the presence or absence of bleeding within 15 s after probing.

The mean PD, CAL, and percentage of sites with BOP were calculated for each participant to assess periodontal disease severity.

Sample collection

Subgingival plaque samples were collected from the deepest periodontal pocket in each participant using sterile paper points. The paper points were inserted into the pocket and left in place for 30 s. Samples were transferred immediately into sterile microcentrifuge tubes containing 1 mL of phosphate-buffered saline and stored at -80°C until further analysis.

DNA extraction and polymerase chain reaction (PCR)

DNA was extracted from the plaque samples using a commercial DNA extraction kit (e.g., Qiagen DNA Mini Kit) according to the manufacturer's instructions. The quantity and purity of DNA were confirmed using a NanoDrop spectrophotometer (ThermoFisher Scientific, USA).

The presence of HCMV and EBV was detected using PCR. The following primers were used for amplification:

- HCMV primers: Forward (5'-TGGAAGTGGGAATGATGAGCCT-3') and Reverse (5'-ATGAGTACGTGTGCAGCGTT-3')
- EBV primers: Forward (5'-TACAGGGTGAAGGTGTGTGC-3') and Reverse (5'-CCGTGCTCGAGACGGATC-3').

The PCR conditions included an initial denaturation at 95°C for 5 min, followed by 35 cycles of denaturation at 95°C for 30 s, annealing at 55°C for 30 s, and extension at 72°C for 45 s. The final extension was performed at 72°C for 10 min. PCR products were visualized on a 1.5% agarose gel stained with ethidium bromide and analyzed under ultraviolet light.

Statistical analysis

Data were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). The Chi-square test was used to compare the prevalence of HCMV and EBV between the two groups. Logistic regression analysis was performed to evaluate the association between herpesvirus prevalence, T2DM, and periodontal disease severity. Clinical parameters (PD, CAL, BOP) were compared between groups using independent t-tests. A $P < 0.05$ was considered statistically significant.

RESULTS

A total of 100 participants were included in the study, with 50 patients in each group. Group 1 consisted of chronic periodontitis patients with T2DM, while Group 2 included chronic periodontitis patients without T2DM. The demographic details and clinical characteristics are presented in Table 1.

Clinical parameters

Table 2 shows the comparison of clinical parameters between the two groups. Patients in Group 1 exhibited more severe periodontal disease, with significantly higher PD, CAL, and BOP compared to Group 2.

Prevalence of herpesviruses

The prevalence of herpesviruses in the two groups is shown in Table 3. HCMV and EBV were more frequently detected in Group 1 compared to Group 2, with statistically significant differences.

Logistic regression analysis

Logistic regression analysis revealed a significant association between T2DM, herpesvirus presence, and the severity of periodontal disease (Odds Ratio = 2.5, $P = 0.02$). The presence of herpesviruses was correlated with higher PD, CAL, and BOP scores, especially in patients with T2DM.

These findings indicate that both the severity of clinical parameters and the prevalence of HCMV and EBV were higher in patients with T2DM and chronic periodontitis.

Table 1: Demographic and clinical characteristics of study participants

Characteristics	Group 1 (T2DM + Periodontitis)	Group 2 (Periodontitis Only)	P-value
Age (years)	55.2±8.3	53.4±7.6	0.12
Male (%)	28 (56)	30 (60)	0.69
Female (%)	22 (44)	20 (40)	0.72
Duration of periodontitis (years)	7.1±3.2	5.9±2.8	0.04
HbA1c (%)	7.8±1.4	—	—

Table 2: Comparison of clinical parameters between the two groups

Clinical parameter	Group 1 (T2DM + Periodontitis)	Group 2 (Periodontitis Only)	P-value
Probing depth (mm)	4.8±1.2	3.9±0.9	0.01
Clinical attachment loss (mm)	5.3±1.5	4.1±1.3	0.002
Bleeding on probing (%)	76	60	0.03

Table 3: Prevalence of herpesviruses in the two groups

Herpesvirus	Group 1 (T2DM + Periodontitis) (%)	Group 2 (Periodontitis Only) (%)	P-value
Human cytomegalovirus	35	20	0.03
Epstein-Barr virus	40	25	0.05

DISCUSSION

The findings of this study demonstrate a significantly higher prevalence of herpesviruses, particularly HCMV and EBV, in chronic periodontitis patients with T2DM compared to those without T2DM. These results align with previous research suggesting that viral infections play a role in the pathogenesis of periodontitis, especially in patients with systemic conditions like diabetes.^[1,2]

Herpesviruses have been implicated in periodontal tissue destruction through both direct and indirect mechanisms. Directly, viruses infect gingival epithelial cells, fibroblasts, and immune cells, impairing local immune responses and promoting tissue breakdown.^[3] Indirectly, they alter the local microbial environment, enhancing bacterial virulence and facilitating periodontal pathogen colonization.^[4] The higher detection rates of HCMV (35%) and EBV (40%) in T2DM patients suggest that viral reactivation may be more common in individuals with compromised immunity, as observed in diabetic patients.^[5] This supports the theory that diabetes, characterized by hyperglycemia and chronic low-grade inflammation, may create a favorable environment for viral persistence and reactivation.^[6,7]

The more severe periodontal parameters observed in patients with herpesvirus infections, particularly those with T2DM, are consistent with other studies.^[8] The increased PD, CAL, and BOP in this group may be attributed to the combined effects of viral infection and impaired host immune responses in diabetic patients.^[9] Previous studies have reported similar associations, where viral infections exacerbated periodontal tissue destruction, suggesting a synergistic relationship between viruses and bacteria in periodontal disease.^[10,11]

Logistic regression analysis in the present study confirmed that the presence of HCMV and EBV, along with T2DM, is significantly associated with increased periodontal disease severity (Odds Ratio = 2.5, $P = 0.02$). These findings emphasize the importance of considering systemic factors, such as diabetes, when managing periodontitis. Moreover, the role of herpesviruses highlights the potential need for antiviral therapies as adjuncts to conventional periodontal treatment.^[12] Antiviral interventions could target the viral components of periodontal disease, thereby reducing tissue destruction and improving treatment outcomes, especially in diabetic patients.^[13]

This study has some limitations. First, the cross-sectional design limits the ability to establish a causal relationship between herpesvirus presence and periodontal disease severity. Longitudinal studies are needed to assess the temporal relationship between viral infections and periodontal progression. Second, other herpesviruses, such as herpes simplex virus, were not included in the analysis, which may have provided additional insights. Despite these limitations, the study contributes valuable information to the growing body of literature on the interaction between viral infections, diabetes, and periodontal disease.

CONCLUSION

The results of this study suggest that herpesvirus infections, particularly HCMV and EBV, are more prevalent in chronic periodontitis patients with T2DM and are associated with greater periodontal disease severity. These findings highlight the importance of considering viral infections in the pathogenesis of periodontitis, especially in patients with systemic conditions like diabetes. Future studies should explore the potential benefits of antiviral therapies as adjuncts to periodontal treatment to improve outcomes in these patients.

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